FRISTAD, WILLIAM EDWARD
SYNTHETIC APPLICATIONS OF SILANES. STERIC
REQUIREMENTS OF SINGLET OXYGEN AND EPOXIDE
ANISOTROPY. AN APPROACH TO
FURANOSESQUIETERPENES.

THE OHIO STATE UNIVERSITY, PH.D., 1979

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SYNTHETIC APPLICATIONS OF SILANES. STERIC REQUIREMENTS
OF SINGLET OXYGEN AND EPOXIDE ANISOTROPY. AN
APPROACH TO FURANOSQUITERPENES

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

By

William Edward Fristad, B.A.

* * * * *

The Ohio State University

1979

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Approved By

Leo A. Paquette
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To my mother, who taught me the value of learning, and to my wife, who sustains it.
ACKNOWLEDGMENTS

I am most grateful to Professor Leo Paquette for his assistance throughout this research as well as his career guidance. He has served as both a friend and a man held in esteem. As I step out to become a colleague, I hope that my students will learn as much as he taught me.

I wish to thank those who performed work in support of this dissertation. They include Professor Rolf Gleiter, Professor Gary Christoph, Mr. Mark Beno, Mr. Michael Höhm, and Mr. Cliff Schuman. The efforts of Mr. Rhys Daniels, Dr. David Dime, Dr. Y. K. Han, and Dr. Guy Kretschmer were also instrumental to the results reported here. Particularly I wish to thank Mr. Thomas Bailey for his direct assistance in performing many of the experiments described herein. Of course, the general enthusiasm and knowledge of the over 70 Paquette research group members whom I have known is greatly appreciated.

Finally, I must thank my wife, Deb, who has survived not only the rigors of her own graduate studies, but mine as well.
VITA

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PUBLICATIONS


FIELDS OF STUDY

Major Field: Organic Chemistry
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The research in this dissertation consists of three chemically unrelated topics. The presentation and discussion of each topic constitutes a separate chapter. Within each chapter are contained sections to separate the various facets of the particular research area. In this way, each section introduces, presents, and concludes a single problem. Throughout the dissertation, however, a continuous series of numbering exists for compounds, footnotes, figures, etc.
CHAPTER 1

Introduction

Synthetic organic chemistry is built upon manipulation, alteration, and elaboration of functional groups. With the monumental achievements of the synthetic chemist over the past century, it is remarkable that only a handful of functional groups have come into prominence as being highly useful. Understandably, those commonly found in naturally occurring substances were given attention initially. During the last two decades, functional groups containing selenium, boron, phosphorous, and silicon have been investigated. These functional groups have opened exciting new frontiers to the synthetic chemist who has rapidly assimilated them into his repertoire of useful reactions. The objective of this chapter is to present a new preparation of the vinylsilane functional group and to illustrate some of its unique chemistry.
SECTION 1

Preparation of Vinylsilanes

The synthetic utility of enamines (1) is derived in large part from their ready availability via the condensation of aldehydes and ketones with secondary amines,\textsuperscript{1-3} and their intrinsic mesomeric nature which negatively polarizes the β-carbon atom (cf 2) and facilitates electrophilic attack at that site.\textsuperscript{4} A functional group which reverses

\[
\text{N} - \text{C} = \text{C} \quad \leftrightarrow \quad \text{N}^+ - \text{C} - \text{C} \\
\text{1} \quad \text{2}
\]

\[
\text{Si} - \text{C} = \text{C} \quad \leftrightarrow \quad \text{Si}^+ - \text{C} - \text{C} \\
\text{3} \quad \text{4}
\]

this polarizability would therefore permit nucleophilic attack at the β-carbon and electrophilic attack at the α-carbon. Although carbon is more electronegative (2.55) than silicon (1.90) and other Group IV elements (e.g., germanium and tin), $d_{\pi}-p_{\pi}$ electron withdrawal in vinyl derivatives of these metals (such as 3) provides for polarization in the opposite sense (cf 4). Exploitation of the latent potential for
synthesis conveyed by such reversed polarization appears to have been limited by the absence of a general synthetic approach to vinylsilanes or their congeners.

A number of synthetic pathways to vinylsilanes have been developed, particularly in the past several years; however, many are subject to substantive limitations. The most common limitation is that only terminal vinylsilanes can be produced. Methods in this category include 1,2-addition reactions of $R_3SiCH_2MgX$ and subsequent dehydration, a variation of the Peterson olefination procedure in which the trialkylsilyl group is not eliminated. A closely related process is 1,2-addition of $((CH_3)_3Si)_2CHLi$ to aldehydes and non-enolizable ketones with elimination of trimethylsilanoxide. Lithium aluminum hydride reduction of $R_3SiC=CHCH_2OH$ presents another method requiring a highly specific substrate.

Other procedures which result in the construction of internal vinylsilanes are fraught with problems. Base promoted cleavage reactions and eliminations lack the desired generality for true synthetic utility. Hydrosilylation of acetylenes provides a route to vinylsilanes when a symmetrical or terminal acetylene can be used. The use of an unsymmetrical acetylene, of course, leads to a mixture of vinylsilanes; however, in certain cases such reactions can produce one isomer stereoselectively. Certain organometallics add across silylacetylenes to give substituted vinylsilanes. These reactions appear to be very sensitive to conditions and limited as to reactive substrate. Hydroboration and hydroalumination provide routes to internal
vinylsilanes, but again require a silylacetylene as starting material. Recently, two methods for the preparation of vinylsilanes of the type \( R_2Si(R)C=CH_2 \) have been developed starting from silylacetylenes\(^{16}\) and 1-trimethylsilyl-1-bromoethene.\(^{17}\) There also exists a selection of other schemes of little proven generality.\(^{18}\)

Because the predescribed methods require a variety of starting materials which often are only indirectly available, a more universal approach to vinylsilanes was clearly needed. The new strategem must also allow for the formation of internal vinylsilanes with well defined regiochemistry and double bond stereochemistry. Furthermore, the method must make use of a readily available functional group, preferably with utilization of well developed chemistry so as to allow for sound predictability of product structure. Such was the initial goal of this project.

The present approach takes advantage of the proclivity of arenesulfonfonylhydrazones for conversion to the vinyl carbanion intermediates \( \delta \) with greater than two equivalents of \( n \)-butyllithium in \( N,N,N',N' \)-tetramethylethylenediamine solution,\(^{19}\) and the ready in situ reaction of these anions with commercially available chlorotrimethylsilane.\(^{20}\) Importantly, the trimethylsilyl group becomes bonded exclusively to the original carbonyl carbon atom. Thus the vinylsilane is produced from a readily available carbonyl precursor in a regioselective fashion (vide infra). An identical procedure was developed simultaneously by Chan et al. which utilized benzenesulfonfonylhydrazones.\(^{20a}\) Their results were similar with regard to procedure and yield. At a slightly later
date Bond and coworkers published similar findings in the preparation of vinylsilanes and in particular they promoted the use of 2,4,6-triisopropylbenzenesulfonylhydrazones.  

The conversion of arenesulfonylhydrazones to vinyl carbanions is a well studied process. When the intermediate carbanion is protonated with resulting olefin formation, it is referred to as the Shapiro reaction. In the many studies of this transformation, it has been found that the direction of deprotonation of the arenesulfonylhydrazone is highly controlled. Similar findings with dimethylhydrazones and oximes have been reported. The proton on carbon which is removed is positioned syn (5) to the arenesulfonylhydrazone. This effect has been verified in a number of cases and appears to be general. The exact controlling factors, however, have not been pinpointed. For example, Jung has shown that kinetic deprotonation of dimethylhydrazones results in anti-carbanion formation with subsequent conversion to the thermodynamically more favored syn-carbanion. Oximes have been found to give the syn-dianion directly. Ensley also has observed that tetrahydropyranylated oximes give the syn-carbanions as both the kinetically and thermodynamically favored products. It would appear that the kinetic bias towards deprotonation syn to the hydrazone
functionality may be directed through chelation of the alkyl lithium base by the hydrazone nitrogen. Such an explanation has been used for many other selective deprotonations. Thus, in effect the hydrazone steers the base so as to deprotonate exclusively syn to the functionality. It must then follow that vinyl carbanion production conforms to the same regiochemical restraints, as long as the decomposition mechanism outlined below is followed (Scheme I).

\[ \text{Scheme I. Vinyl anion formation} \]

In general, steric factors largely control arenesulfonfylhydrazone stereochemistry. The bulky \(-\text{NHSO}_2\text{Ar}\) group positions itself syn to the less substituted side of the original carbonyl. In this way, the vinyl carbanion produced is always the less substituted. In addition, it has been shown that the stereochemistry of tosylhydrazones can be determined from \( ^{13} \text{C} \) NMR chemical shifts of the \( \alpha \)-methylene carbons. As shown in 12, \( \delta_{C_\alpha} < \delta_{C_\alpha'} \), as consequence of steric compression. When the \( ^{13} \text{C} \) chemical shifts of the two carbon atoms in the tosylhydrazone were compared with shifts in the derived ketones, \( C_\alpha \) was seen to differ by 12-15 ppm while \( C_\alpha' \) showed only a \( \Delta \delta \) of 3-6 ppm.
An additional restraint imposed by the mechanism is that the resultant olefin geometry must be of the $Z$-type if unfavorable interactions between the substituent on the incipient olefin and $-\text{NHSO}_2\text{Ar}$ are to be minimized.

Experimentally, we have developed the conversion of arenesulfonylhydrazones to vinylsilanes into a well honed process. Examination of numerous sets of reaction conditions has led us to a final procedure which efficiently, frequently in excess of 90%, yields vinylsilanes uncontaminated by the corresponding olefin. More specifically, the arenesulfonylhydrazone (Table 1) is added to a $-45^\circ\text{C}$ solution of excess $n$-butyllithium in tetramethylethylenediamine. Under these conditions, the dianion $\mathbf{8}$ is formed. The stability of this species was proven by trapping the dianion with chlorotrimethylsilane to yield a bistri-methylsilylated species $\mathbf{10}$. On warming to above $-30^\circ\text{C}$, dianion $\mathbf{8}$
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<sup>a</sup> Data from Table 1.
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<td><img src="image" alt="Ketone 27" /></td>
<td>BSH, 56</td>
<td>83</td>
</tr>
<tr>
<td><img src="image" alt="Ketone 28" /></td>
<td>BSH, 57</td>
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</tr>
<tr>
<td><img src="image" alt="Ketone 29" /></td>
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</tr>
<tr>
<td><img src="image" alt="Ketone 30" /></td>
<td>BSH, 59</td>
<td>95</td>
</tr>
<tr>
<td>Ketone</td>
<td>Arenesulfonylhydrazone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Yield, %</td>
</tr>
<tr>
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<tr>
<td>Ph(_2)C(_2)Ph</td>
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<td>BSH, 61</td>
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<td>Ph(_2)C(_2)Ph</td>
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<td>BSH, 62</td>
</tr>
<tr>
<td>Ph(_2)C(_2)Ph</td>
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TABLE 1 (continued)

<table>
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<th>Yield, %</th>
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<td>&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>TSH, 66</td>
<td>15</td>
</tr>
</tbody>
</table>

<sup>a</sup> BSH = benzenesulfonylhydrazone, TSH = p-toluenesulfonylhydrazone (tosylhydrazone).  <sup>b</sup> Yield not calculated.
spontaneously decomposes to the vinyl carbanion, nitrogen, and arenesulfinate anion. This process can easily be followed by observing the loss of nitrogen. The vinyl carbanion is then trapped with chlorotrimethylsilane to generate the vinylsilane (Table 2).

Stringently anhydrous conditions were necessary to avoid concomitant formation of the corresponding olefin. This necessitated the use of tetramethylethylenediamine as solvent. Ethereal solvents can be slowly deprotonated by the highly basic vinyl carbanion. The amine solvent also retards the decomposition of the arenesulfinate anion to sulfur dioxide and arene anion. This decomposition has been found to cause problems when tetrahydrofuran is used as solvent. Likewise, the hydrolytically unstable chlorotrimethylsilane must be freshly distilled from calcium hydride as even newly opened bottles contained enough hydrogen chloride to cause production of relatively large quantities of olefin.

According to the proposed mechanism, only two equivalents of base are needed to generate a vinyl carbanion. It was found experimentally, however, that at least three equivalents of base were needed to maximize the yield of vinylsilane. This is the result of partial deprotonation of the arene ring by n-butyllithium. This problem could be averted by the use of the 2,4,6-triisopropylbenzenesulfonylhydrazone as shown by Bond; however, throughout this study an excess of n-butyllithium was simply used.

As with any synthetic method, limitations were uncovered in the arenesulfonylhydrazone to vinylsilane sequence. The first and most serious is the requirement for substrate stability to alkyllithiums.
TABLE 2. Vinylsilane Data

<table>
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<th>Ketone</th>
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<th>Yield, %</th>
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<tr>
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</tr>
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<td><img src="image9" alt="Ketone 5" /></td>
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<table>
<thead>
<tr>
<th>Ketone</th>
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<th>Yield, %</th>
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<tbody>
<tr>
<td>H2C=CHCH2CH2CH3</td>
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</tr>
<tr>
<td>H2C=CHCH2CH2CH3</td>
<td>SiMe3</td>
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</tr>
<tr>
<td>C3H7C=CHC2H5</td>
<td>SiMe3</td>
<td>75</td>
</tr>
<tr>
<td>H2C=CHC12H21</td>
<td>SiMe3</td>
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<td>PhCH=CHC2H5</td>
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TABLE 2 (continued)

<table>
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</thead>
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<td>SiMe₃ 78</td>
<td>a</td>
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<tr>
<td></td>
<td>Ph      78</td>
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</tr>
<tr>
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<td>SiMe₃ 79</td>
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</tr>
<tr>
<td></td>
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<td>85</td>
</tr>
<tr>
<td>C₆H₅ 24</td>
<td>SiMe₃ 80</td>
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</tr>
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<td>C₆H₅ 32</td>
<td>SiMe₃ 82</td>
<td>a</td>
</tr>
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<td>Ketone</td>
<td>Vinylsilane</td>
<td>Yield, %</td>
</tr>
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<td>-------------</td>
<td>---------</td>
</tr>
<tr>
<td><img src="image1" alt="Ketone Structure" /> 36</td>
<td><img src="image2" alt="Vinylsilane Structure" /> Me₃Si 83</td>
<td>50&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Yield not calculated.  
<sup>b</sup> It has been previously shown that the Shapiro reaction gives exclusively the Δ<sup>2</sup> olefin; J. E. Herz, E. Gonzales, and B. Mandel, *Aust. J. Chem.*, 48, 819 (1970).
The second resides in the fact that aldehyde arenesulfonylhydrazones do not undergo the reaction. These have been shown to undergo alkyl-lithium addition across the carbon-nitrogen double bond with eventual decomposition to a secondary alkyllithium. The lack of deprotonation on carbon can be explained satisfactorily in terms of the absence of a chelation effect, the hydrazone expectedly being positioned syn to the aldehyde hydrogen.

A certain amount of caution must also be exercised when using phenyl or benzyl ketones (e.g. 20). In these cases, it was found that partial conversion to the allyl anion \( \text{85} \) resulted when the vinyl anion \( \text{84} \) was allowed to sit for extended periods of time at room temperature.

When the vinyl anion \( \text{84} \) was actually heated to 50°C for 2 hours, the rearrangement resulted in predominant allylsilane formation \( (\text{78}:{\text{87}}:{\text{88}}) \) \( (26:13:40 \text{ ratio}) \). This rearrangement and its development into a successful allylsilane preparation is discussed in Section 7, Chapter 1.
The desired vinylsilane \( \frac{84}{24} \), however, can still be produced by quenching the vinyl anion solution immediately after nitrogen evolution at room temperature or as low as -20°C.

Advantages to this sequence are the ready availability of precursors and reagents, the overall simplicity of the reaction conditions, the amenability to acid-sensitive functionality, and the fact that all steps of the reaction can be carried out below 0°C.
SECTION 2

1,2-Ketone Transposition

The carbonyl group plays a pivotal role in bringing latitude to organic synthesis. The need to relocate this functional group within a molecule occurs with such frequency that interest in efficient methods of carbonyl transposition remains high. Various procedures have been developed for effecting site exchange within saturated \(^{31-39}\) and \(^{40-43}\) \(\alpha,\beta\)-unsaturated ketones, sometimes in tandem with an alkylation step, \(^{44-47}\) and these have met with varying degrees of accepted usage. In this section is described a quite different approach to the 1,2-transposition of ketones which takes advantage of the chemical properties associated with covalently bonded silicon.

In the previous section, it was demonstrated that vinyl carbanions generated through ketone arenesulfonylhydrazones with alkyllithium reagents in tetramethylethylenediamine solution condense with chlorotrimethylsilane to deliver vinylsilanes in excellent yield. Where relevant, this transformation is regiospecific, deprotonation occurring preferentially for electronic and steric reasons at the lesser substituted \(\alpha\) position. With the introduction of such unsaturation comes the further possibility of functionalizing the carbon \(\beta\) to silicon. This phenomenon provides for the possibility of vinylsilane mediated oxygen transposition.
The process envisioned for the 1,2-ketone transposition is illustrated in Scheme II. The vinylsilane is epoxidized to give the epoxy silane (89), cleavage of which at the α-carbon-oxygen bond can be accomplished by hydride reduction. Oxidation of the resulting β-silyl alcohol 90 and hydrolytic desiliconation delivers the new ketone 91.

A summary of results is presented in Table 3.

Epoxidation of vinylsilanes was found to be a smooth process when conducted at 0°C in buffered dichloromethane solution with 1.1 equivalents of m-chloroanisylbenzoic acid. While the rate of epoxidation of vinylsilanes is slower than that of similarly substituted olefins, the reaction, conveniently monitored by thin layer chromatography, requires but 0.5-2 hours. These results conform to earlier studies of vinylsilane epoxidation. The epoxy silanes themselves are capable of further reaction when 2 equivalents of m-chloroanisylbenzoic acid are used or the buffer is not employed. In these cases, the epoxides suffered ring opening by m-chlorobenzoate ion with resultant formation of high molecular weight products which were not further investigated.
### TABLE 3. Carbonyl Transposition Data\textsuperscript{a,b}

<table>
<thead>
<tr>
<th>Substrate\textsuperscript{c}</th>
<th>Vinylsilane</th>
<th>Epoxy silane</th>
<th>β-Silanol</th>
<th>Ketone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH\textsubscript{3}</td>
<td>CH\textsubscript{3}</td>
<td>CH\textsubscript{3}</td>
<td>CH\textsubscript{3}</td>
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<td>X</td>
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<td>X</td>
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<td>X</td>
</tr>
<tr>
<td>SiMe\textsubscript{3}</td>
<td>SiMe\textsubscript{3}</td>
<td>SiMe\textsubscript{3}</td>
<td>SiMe\textsubscript{3}</td>
<td>SiMe\textsubscript{3}</td>
</tr>
<tr>
<td>73</td>
<td>92</td>
<td>98</td>
<td>104</td>
<td>84</td>
</tr>
<tr>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
</tr>
<tr>
<td>72</td>
<td>89</td>
<td>99</td>
<td>91</td>
<td>84</td>
</tr>
<tr>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
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<td>71</td>
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<td>66</td>
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<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
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<td>76</td>
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<td>101</td>
<td>107</td>
<td>63</td>
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<tr>
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<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
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<td>Me\textsubscript{3}Si</td>
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<tr>
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<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
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<td>103</td>
<td>109</td>
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<td>76</td>
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<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
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<tr>
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<td>Me\textsubscript{3}Si</td>
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<td>Me\textsubscript{3}Si</td>
<td>Me\textsubscript{3}Si</td>
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</tbody>
</table>

\textsuperscript{a,b} Chemical shifts for carbons 1-4, and 5.7 of each compound are given in parentheses.

\textsuperscript{c} X represents carbonyl.
<table>
<thead>
<tr>
<th>Substrate&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Vinylsilane</th>
<th>Epoxysilane</th>
<th>β-Silanol</th>
<th>Ketone</th>
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<tbody>
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<td><img src="image4" alt="Chemical Structure" /></td>
<td><img src="image5" alt="Chemical Structure" /></td>
</tr>
</tbody>
</table>

<sup>a</sup> All compounds were identified by IR, NMR, and accurate mass spectral measurements. Additionally, the vinylsilanes were characterized by combustion analysis. The transposed ketones were identified by comparison with authentic samples of the ketones or derivatives thereof. <sup>b</sup>The percentage yields which are provided in parentheses represent the isolated yields at each step. <sup>c</sup>For convenience purposes, these structures will be further defined as follows: a, X = O; b, X = NH₂SO₂C₆H₅. <sup>d</sup>These intermediates were not isolated under the conditions employed (see text). <sup>e</sup>See text for discussion of results. <sup>f</sup>The spiro series was carried out by Mr. R. Daniels. <sup>g</sup>G. Bodennec and M. St. Jacques, Can. J. Chem., 55, 1199 (1977). <sup>h</sup>The remainder of the product was the α-silyl alcohol.
Epoxidation of several of the vinylsilanes studied was capable of producing stereoisomers. The first such example was epoxidation of vinylsilane 72, which was presumed to exist as a pair of rapidly equilibrating conformational isomers. This resulted in the formation of two isomeric epoxides 89a and 89b (38:62). These epoxides were separated via preparative gas phase chromatography, and identified by Eu(fod)$_3$ shifting of their $^1$H NMR spectra (Table 4).

Vinylsilane 71, while probably existing in only one conformation, had no obviously less hindered face. The $^1$H NMR spectrum of the epoxidation mixture was found to exhibit two signals for protons on an epoxide ring near $\delta$ 3.0 (approx. 60/40). The major, downfield signal is considered to correspond to epoxide 95b which has its CHO- proton locked into a quasi-equatorial position. The minor isomer should then be represented by cis-epoxide structure 95a if the usual rule of chemical shifts in axial/equatorial cyclohexyl hydrogens is obeyed. The
TABLE 4. Lanthanide Induced Shifting (CDCl₃ solution, 90 MHz)

<table>
<thead>
<tr>
<th>Compd</th>
<th>Signal</th>
<th>Eu(fod)₃, mol %</th>
<th>δ</th>
<th>ΔEu, ppm</th>
<th>Slope, Δδ/Δ mol %</th>
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</thead>
<tbody>
<tr>
<td>39a</td>
<td>α-Epoxy H</td>
<td>0</td>
<td>2.80</td>
<td>21</td>
<td>0.21</td>
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<td></td>
<td></td>
<td>12.8</td>
<td>5.00</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>20.1</td>
<td>6.41</td>
<td></td>
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<td>9.09</td>
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<td>3-CH₃</td>
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<td>0.82</td>
<td>8.5</td>
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<td>2.25</td>
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<td>3.32</td>
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<tr>
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<td>19.7</td>
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<td>25.0</td>
<td>7.58</td>
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<td>42.3</td>
<td>10.58</td>
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</tr>
<tr>
<td>3-CH₃</td>
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<td>0</td>
<td>0.88</td>
<td>4.8</td>
<td>0.048</td>
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<td></td>
<td></td>
<td>25.0</td>
<td>2.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>42.3</td>
<td>2.89</td>
<td></td>
<td></td>
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</table>
general trend is that axial hydrogens resonate at higher field than otherwise equivalent equatorial hydrogens. These assignments were corroborated by hydride reduction (vide infra). The mixture of isomers 25a and 25b proved impossible to separate by gas phase chromatography, and decomposed upon attempted column chromatography on neutral alumina.

Steroidal vinylsilane 83 appeared to give a single epoxide. Since the trimethylsilyl group placed no new steric demands on the molecule, the epoxidation was assumed to proceed from the φ-face as was known in the parent 2-cholestene 50 as well as in 3-methylcholest-2-ene. 51

The key principle on which the 1,2-ketone transposition rested was the regioselective ring opening with hydride to give β-hydroxy-silanes. This pathway had been previously established by Eisch and Trainor for epoxysilane 112. In this simple system, however, the reaction lost regiospecificity with use of excess lithium aluminum hydride. More recently, Robbins and Whitham demonstrated that hydride
reduction of the conformationally flexible 1,2-epoxy-1-trimethylsilyl-
cyclohexane also gave cleavage of the α-carbon-oxygen bond. In addi-
tion, this reduction proved to be stereospecific with cis-2-trimethyl-
silylcyclohexanol being the sole product.

In the present study, reduction of the epoxysilanes was carried
out with lithium aluminum hydride in ether at room temperature (80,
22, 23) or at reflux (26). Epoxysilane 24 was successfully reduced
in refluxing tetrahydrofuran. In all the above acyclic or flexible
ring cases, the epoxysilane was cleanly opened to the β-silylalcohol.
The electronic directing effect of silicon, however, was inadequate
to overcome the normal kinetic bias for trans diaxial ring opening
in conformationally rigid systems. When ring inversion was not severe-
ly impeded as in 82, 23, 24, and 26, ring opening occurs by regiospe-
cific α attack in the usual manner. Yet, if the identical procedure
was applied to a more rigid epoxysilane such as 25 or 27, mixtures re-
sulted. Findings with 25 are included in Table 5. The steroidal
epoxysilane 27 underwent solely the expected trans diaxial opening
exhibited by its all carbon counterpart, 2α,3α-epoxy-3β-methylcholest-
2-ene,51 to give 3α-hydroxy-3β-trimethylsilylcholestan.

It is, of course, not feasible to estimate accurately the ground
and transition state conformational interaction energies which gain
importance within 25a and 25b as reduction proceeds. Nor can some de-
gree of anomalous mechanistic behavior be ruled out in such reactions.
However, the levels to which 113a and 113b were produced in the pre-
ence of lithium aluminum hydride alone were clearly not at all ac-
ceptable for synthetic purposes.
TABLE 5. Specificity of Mixed Hydride Reductions, \( \text{25a} \) and \( \text{25b} \)^a, b

<table>
<thead>
<tr>
<th>LiAlH(_4):AlCl(_3)</th>
<th>Probable effective reagent</th>
<th>113a</th>
<th>113b</th>
<th>101b</th>
<th>101a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:0</td>
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<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1:1</td>
<td>AlH(_2)Cl</td>
<td>5</td>
<td>64</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>2:1</td>
<td>AlH(_2)Cl + AlH(_2)</td>
<td>9</td>
<td>50</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>3:1</td>
<td>AlH(_2)</td>
<td>11</td>
<td>57</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

^a Reactions conducted in anhydrous ether at 0°C to room temperature. The percentage values given were obtained by vapor phase chromatography (thermal conductivity detector), are uncorrected as to relative response to detection, and are normalized to exclude small amounts of recovered epoxide. Structural assignments to these alcohols were made chiefly on the basis of their \(^1\)H NMR spectra [W. K. Musker and G. L. Larson, Tetrahedron Lett., 3481 (1968)].
As a means of enhancing the electrophilic nature of the α carbon in such epoxides, the efficacy of various "mixed hydrides" was examined. A remarkably enhanced specificity for α attack, particularly with AlH₂Cl (95% combined yield of 101a and 101b) was uncovered. Application of similar methodology to 97 likewise resulted in higher levels of C-C bond fission, thereby illustrating the versatility of this modification.

The stereochemistry of 101a and 101b was established on several grounds. The fact that 101b was the only β-silylalcohol formed from the lithium aluminum hydride reduction was proof enough that the hydroxyl group must be axial. Thus, the new β-silylalcohol product found in the aluminum hydride reductions must be the equatorial isomer 101a. This identification was also corroborated by the H NMR chemical shift of CH-OH. The equatorial alcohol 101a having the axial hydrogen exhibits a signal 0.25 ppm to higher field than the axial alcohol with the equatorial hydrogen. This was in accord with the normal NMR behavior of axial/equatorial cyclohexyl hydrogens.

During the course of this work, it was suggested that reduction studies of epoxysilanes may be confused because of prior rearrangement to the β-trimethylsilylketone. The actual results observed would
then arise from hydride reduction of carbonyl functions. To investigate this possibility a "mixed hydride" reduction was performed on using lithium aluminum deuteride. Were the products to result from carbonyl reduction, then a deuterium must be to the trimethylsilyl group. If, however, the epoxide is directly reduced, the deuteride must attack the carbon. Upon work-up, deuterium was found to be incorporated into the two β-silylalcohols produced, and . Both compounds appeared to have deuterium exclusively to silicon as integration for one hydrogen was obtained for the signal. Mass spectral data also were fully consistent with the incorporation of one deuterium atom. The β-silylalcohol upon treatment with sodium hydride in refluxing tetrahydrofuran eliminated trimethylsilanoxide to generate 1-deuterio-4-t-butylcyclohexene (115). The deuterated olefin was again evidenced by the accurate mass obtained and a integration of exactly 1.0 hydrogen in the vinyl region. Thus, the initial assumption of direct epoxide reduction was upheld.

Oxidation and desilylation of the β-silylalcohols would complete the ketone transposition. Several methods were tried which performed the oxidation and to varying degrees desilylated the ketone produced.
The most successful procedure required treatment of the β-silylalcohols with a stoichiometric quantity of chromic acid and 10 mole equivalents of sulfuric acid in a two phase system (ether/water). Under these protic conditions, the intermediate β-silylketones suffered carbon-silicon bond cleavage to produce their enol forms and hexamethyldisiloxane. Oxidation yields were routinely greater than 80% with this modification of the original Brown procedure.

β-Trimethylsilylketones are known to be very susceptible to cleavage of the carbon-silicon bond by either strong acid or base. In general, the ease of silicon-carbon bond cleavage by a nucleophile depends upon the stability of the carbanion produced as a leaving group. An example of this effect can be seen in Table 6. β-Silyl

<table>
<thead>
<tr>
<th>Compound</th>
<th>$pK_a$</th>
<th>rel. rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhC≡C-SiMe₂</td>
<td>21</td>
<td>$2 \times 10^7$</td>
</tr>
<tr>
<td>Ph₂C-SiMe₂</td>
<td>22</td>
<td>$1.9 \times 10^6$</td>
</tr>
<tr>
<td>PhCH=CH₂-SiMe₂</td>
<td>30</td>
<td>$10^5$</td>
</tr>
<tr>
<td>Ph₂C-SiMe₂</td>
<td>31.5</td>
<td>$1.8 \times 10^3$</td>
</tr>
<tr>
<td>Ph₂CH-SiMe₂</td>
<td>33</td>
<td>$1.4 \times 10^3$</td>
</tr>
<tr>
<td>PhCH₂-SiMe₂</td>
<td>35</td>
<td>1</td>
</tr>
</tbody>
</table>

TABLE 6. Relative Rate of Nucleophilic Silicon-Carbon Bond Cleavage


carbonyl compounds have also been successfully cleaved with anhydrous sources of fluoride ion to generate stabilized anions capable of
further reactions. Considering the sensitivity of β-silyl ketones to pH, a range of acidic and basic oxidation conditions was studied.

Acidic media methods included the ultimate method of choice described previously, Jones oxidation, and utilization of pyridinium chlorochromate. Jones oxidation of 101 resulted in complete removal of the trimethylsilyl group; however, only a 27% yield of 3-t-butyl-cyclohexanone (107) was achieved. Pyridinium chlorochromate, a mildly acidic oxidant, retained the trimethylsilyl group in oxidizing 90 to yield the silylketone 116 in 51% yield.

Several basic conditions were employed which, it was hoped, would specifically retain or remove the silyl group. Collins oxidation of 90 again yielded the silylketone in 67% yield; pyridine therefore was an insufficiently strong nucleophile in the anhydrous medium. Cleavage of silicon-carbon bonds with fluoride ion is well known, and it
was envisioned that the addition of fluoride ion to the Collins oxidation medium might result in direct isolation of the desilylated ketone. When a Collins oxidation was performed in conjunction with the addition of tetraethylammonium fluoride, a mixture of ketones \( \text{117} \) and \( \text{107} \) (3:1) was produced. The incomplete desilylation may have been a result of poor solubility of the tetraethylammonium salt in methylene chloride or simply the inapplicability of these conditions to desilylate this ketone quickly. Further work was not carried out.

In summary, oxidation conditions were developed which specifically produced either a \( \beta \)-silylated ketone or the desilylated 1,2-transposed ketone. The \( \beta \)-silylated ketone may additionally be utilized as a specific enolate precursor allowing the process to be used as an alkylative 1,2-ketone transposition.

Before the close of this section, it should be noted in Table 3 that the activated vinylsilanes \( \text{80} \) and \( \text{81} \) gave directly the \( \beta \)-tetralone upon treatment with buffered m-chloroperbenzoic acid under the usual conditions. The precise course of these one-step transformations has not been elucidated. No epoxide intermediates were ever observed by thin layer chromatography. Additionally, treatment of the
analogous olefin 118 under identical conditions cleanly led to the formation of epoxide 119 in high yield. Thus the presence of the trimethylsilyl group is of paramount importance.

The present approach to 1,2-carbonyl transposition complements the existing methods. It employs a different substrate, a vinylsilane, as the relay intermediate. Since the ready availability of the latter from ketones is now documented (vide supra), and since their subsequent chemical manipulation is exceptionally efficient, the scheme serves as a promising means for effecting the 1,2-migration of a carbonyl group. Furthermore, the benchtop beauty of this sequence rests on the fact that no purification steps need be performed until final isolation of the transposed ketone. The crude vinylsilane, epoxide, and alcohol are all suitable for the subsequent step, and even residual solvent is fully compatible with the following reagent.
SECTION 3
Theoretical Treatment of Epoxysilanes

With the recent heightened interest in synthetic organosilicon chemistry has come an increased awareness that epoxysilanes experience ring opening with a regioselectivity contrary to that followed by epoxides lacking carbon-metal bonds. Thus, exposure of \( \text{120} \) and its congeners to a variety of electrophilic reagents, which include Bronsted and Lewis acids, cuprates, and aluminum hydrides, generally results in efficient cleavage of the more hindered C-O bond proximate to the silicon atom. Since cationic charge \( \alpha \) to silicon \( (\text{R}_2\text{Si-C-Cl})^+ \) enjoys considerable stabilization because of \( \sigma-\pi \) hyperconjugation with the C-Si bond while cations in the \( \alpha \) position \( (\text{R}_2\text{Si-C})^+ \) are destabilized, it is all the more remarkable that epoxysilane chemoselectivity appears not to be governed by similar electronic constraints. Past attempts to rationalize this seemingly anomalous behavior have focused upon the
involvement of silicon's vacant d orbitals, the possible intervention of pentacoordinate silicon intermediates, as well as an invoking of $S_N^2$ borderline behavior. Such empiricisms have proven ambiguous and fall short in predictive capability as well.

In this section an explanation is advanced based on the electronic structure of the ground state of epoxy silanes. While information on the epoxy silane ground state need not translate directly into corresponding transition state features, such data should provide a reasonable approximation and a convenient focal point for calculations as well. Specifically, calculations can be applied to a broad selection of examples; in addition, they are capable of generating predictions of eventual cross-overs in reaction pathways, and of quantifying relative tendencies. In this study, calculations performed by Böhm and Gleiter are used to predict the direction of product-forming bond fission. In the extended Hückel calculations, standard bond lengths and parameters were adopted for the oxirane ring and a value of 1.86 Å was selected for the carbon-silicon bond length. The valence state ionization potentials employed for silicon were $H_{1s}$ (3s) -17.3 eV and $H_{1s}$ (3p) -9.2 eV. The orbital exponents were derived from Burn's rules. The relevant data which are listed in Table 7 were obtained without consideration of the 3d orbitals of silicon; inclusion of these additional orbitals did not alter the relative ordering of the reduced overlap populations. The reduced Mulliken overlap populations are related to the effective bond strength. Thus a higher overlap population implies a greater bond strength.
The results of the extended Hückel calculations carried out on model compounds 120-123 prove to be consistent; bond 2-3 is always the stronger bond. If the assumption is made that the weaker bond is broken during epoxide opening, then bond 1-2 would be expected to cleave. This is indeed the regioselectivity seen with epoxysilane opening (vide supra).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Bond 1-2</th>
<th>Bond 2-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>0.4720</td>
<td>0.5501</td>
</tr>
<tr>
<td>121a</td>
<td>0.5086</td>
<td>0.5610</td>
</tr>
<tr>
<td>122a</td>
<td>0.4520</td>
<td>0.5571</td>
</tr>
<tr>
<td>121b</td>
<td>0.4975</td>
<td>0.5662</td>
</tr>
<tr>
<td>122b</td>
<td>0.4901</td>
<td>0.5644</td>
</tr>
<tr>
<td>121c</td>
<td>0.5257</td>
<td>0.5586</td>
</tr>
<tr>
<td>122c</td>
<td>0.4978</td>
<td>0.5496</td>
</tr>
<tr>
<td>123</td>
<td>0.5461</td>
<td>0.5620</td>
</tr>
</tbody>
</table>
Deeper insight into the outcome can be gained by comparing the two interaction diagrams presented in Figure 2. The left diagram shows that the highest occupied molecular orbital (HOMO) of propylene oxide (123) can be regarded as a linear combination of an oxygen 2p orbital and a σ-orbital strongly localized on the C-C and C-H bonds. It is important to note that the wave function of the HOMO is C-O antibonding. Replacing one C-C fragment by a C-Si unit leads to a stronger antibonding interaction between the 2p lone pair and the corresponding σ-orbital (Fig. 2 right). This is due mainly to a reduction of the energy difference between the oxygen 2p orbital and the C-Si σ-orbital in comparison with the C-C σ-orbital. From photoelectron spectroscopic investigations, it can be estimated that the basis orbital energy of a C-C bond is more than 4 eV lower than that of a C-Si bond. The enhanced antibonding interaction leads to a weakening of the C-O bond α to silicon. In the case of compounds 121a-121c (122a-122c), the interaction of the oxygen 2p orbital and the carbon-silicon σ-orbital is somewhat mitigated due to the tetrahedral nature of oxiranium ions. This has been shown by Lambert and Johnson for O-alkyloxiranium ions, and there is good reason to believe that coordination of an epoxy-silane oxygen to electrophiles will similarly result in rehybridization of the oxygen from sp² toward sp³. Upon rehybridization, the 2p lone pair on oxygen is replaced by an spⁿ hybrid directed away from the carbon-silicon bond. This is indicated below for 120, 121a, and 122a.
FIGURE 2. Interaction diagrams for $^{120}$ (right) and $^{123}$ (left).
From the above, several general conclusions can be drawn. Notwithstanding that the C-Si and O-Si bonds in 120-123 are not favorably aligned for stabilization of a developing positive charge at C₃, it is clear that this geometric constraint does not account for the facilitation of nucleophilic displacement α to silicon. Rather, the enhanced ground state electrophilicity of the α carbon is considered to materialize because of the antibonding interactions discussed above.

At this point, it is informative to examine the response of epoxysilane 95 to hydrides of varying Lewis acid strength. With LiAlH₄, the normal kinetic preference for trans-diaxial opening (i.e., β cleavage) is not overtaken and 113a is produced predominantly. In contrast, α attack leading to 101a is remarkably enhanced when use is made of AlH₂Cl. From the reduced overlap populations for 120, 121b, and 122b (see Table 7), it can be seen that hydride reductions proceeding with or without strong
prior complexation of the reducing agent (e.g., BH₃, AlH₃Cl₃-n) should lead to cleavage of the α carbon-oxygen bond. This is indeed seen with lithium aluminum hydride on flexible systems. Thus, this reagent is capable of regioselective reduction. It is only when pitted against the strong kinetic effect of trans-diaxial opening that this normal regioselectivity is lost. This may be explained by an "early" transition state 81 for lithium aluminum hydride reduction which does not allow the full influence of the weaker carbon-oxygen bond to be felt. In contrast, the alane or "mixed hydride" reductions may proceed by way of a "later" transition state thereby allowing for a greater importance to the relative epoxide bond strengths. The uncharged nature of the "mixed hydride" reductant may well facilitate the "late" transition state when compared to the charged tetrahydroaluminate anion.

The calculations also identify the unsymmetrical nature of the perepoxide intermediate 121c and 122c which can be formalized more explicitly as in 124. The longer carbon-oxygen bond should reveal itself by a pronounced regioselectivity which delivers an allylic
hydroperoxide with a retained (though relocated) vinylsilane moiety 125 instead of an α-hydroperoxy silane 126. This prediction has been put to rather extensive test and is the subject of Section 4, Chapter 1.

The purpose of the calculations presented here is to allow their comparison to experimental facts and to permit the prediction of future experimental results. While these calculations do not unequivocally prove any mechanism, they do provide a relative bond strength solution to some perplexing problems in epoxysilane reactivity. However, the manner in which various reaction courses follow these guidelines can vary greatly when kinetic controls are imposed as illustrated by the reductions with complex hydrides.
SECTION 4

Photooxyg enation of Vinylsilanes

As illustrated in previous sections, the positioning of a trimethyilsilyl group on a carbon-carbon double bond or an oxiranyl ring allowed for considerable control of regiochemistry. As a continuation of our interest in silicon-oxygen compounds, the photooxyg enation of vinylsilanes was investigated. It was anticipated that the silicon substituent might direct the reaction of singlet oxygen within the unsaturated moiety.

As a way of introduction, the reaction of singlet oxygen with olefins generally proceeds via the "ene" process to yield an allylic hydroperoxide (127 to 128). A subsequent reduction step produces the allylic alcohol. The mechanism of this "ene" process is currently under intensive experimental and theoretical investigation. The three mechanistic paths currently being considered are shown in Figure 3. While the actual mechanism followed is not of direct relevance to
this study, the peroxide intermediate 130 is of special interest because of the calculations discussed previously.

Photooxydogenation of olefins is a reaction very sensitive to electronic and steric effects, often producing a single product despite the availability of several pathways. Steric requirements for the ene reaction lead to attack from the less hindered face (singlet oxygen is a very small electrophile, see Chapter 2). Additionally, the molecular framework must allow the allylic hydrogen abstracted to become coplanar with the π orbital of the olefin. Electronic effects can direct the regioselectivity of the reaction or completely retard it.

It is presently recognized that the relative reactivities of sterically similar π systems toward singlet oxygen are controlled to a large extent by their ionization potential. Unsaturated systems of
very high ionization potential are found to be unreactive to singlet oxygen. Because silicon (1.9) is more electropositive than carbon (2.55), the trimethylsilyl group should donate electrons to the vinyl moiety by an inductive mechanism. However, silicon also has empty low-lying d-orbitals which can result in electron withdrawal by resonance with the π system. This interaction would deplete the π bond of electron density, lower the HOMO energy, and curtail reactivity.

Photoelectron spectroscopic data reveal that vinylsilanes actually have π-HOMO energies rather comparable to those of structurally related all-carbon compounds. As an example, \( \text{CH}_2=\text{CHSi(CH}_3)_3 \) \((-9.8 \text{ eV})\) has only a very slightly higher (more negative) ionization potential than \( \text{CH}_2=\text{CHC(CH}_3)_3 \) \((-9.6 \text{ eV})\). Thus these two effects, along with possible \( d_{\pi}-p_{\pi} \) hyperconjugative backbonding, stabilize the HOMO to an extent which are almost mutually compensatory.

Another mode of singlet oxygen reaction is dioxetane \((\text{132})\) formation which occurs chiefly with very electron-rich olefins. While dioxetane formation is not expected with vinylsilanes, reactions of the ene type should not be electronically impeded if ionization potentials do serve as useful guides to reactivity.

\[
\begin{align*}
\text{\begin{tikzpicture}[baseline=-0.5ex]
\draw (0,0) -- (0.5,0);
\draw (0.5,0) -- (1,0);
\end{tikzpicture}} & \xrightarrow{\ \text{102}\ } \begin{tikzpicture}[baseline=-0.5ex]
\draw (0,0) -- (0.5,0);
\draw (0.5,0) -- (0,0.5);
\draw (0,0.5) -- (1,0);
\end{tikzpicture}
\end{align*}
\]

The synthetic procedure utilized in this work was the customary dye sensitization technique. In this procedure, ground state triplet
oxygen is excited to the singlet ($^1\text{g}$) state by energy transfer from the excited dye, in this case rose bengal. The initially produced allylic hydroperoxide was immediately reduced with sodium borohydride (methanol solution) to the allylic alcohol (Scheme IV). No attempt was made to analyze products at the hydroperoxide stage. A list of results

![Scheme IV](image)

**Scheme IV.** Ketone to 1,2-transposed allylic alcohol

is contained in Table 8.

The most important feature to notice is production of a single silylated allylic alcohol in each case. While two possible products could be expected to result from oxygenation α or β to the trimethylsilyl substituent, only the β-silylated allylic alcohol was formed. In these products, the vinylsilane moiety has apparently been migrated. In order to follow this pathway, the substrate must contain the partial structure $\text{13}\text{c}$ having a conformation which aligns the hydrogen to be abstracted into coplanar arrangement with the $\pi$ system. All compounds which contain this subunit were found reactive; those not
TABLE 8. 1,2-Oxidative Transposition of Vinylsilanes\textsuperscript{a}

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Vinylsilane</th>
<th>Isolated Yield, $%$</th>
<th>$\alpha$-Silylated allylic alcohol</th>
<th>Reaction time, hr.</th>
<th>Conversion, $%$</th>
<th>Isolated Yield, $%$</th>
<th>Allylic alcohol Yield, $%$</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>(\text{CH}_3) (\text{CH}=\text{CH}\text{SiMe}_3)</td>
<td>91</td>
<td></td>
<td>12</td>
<td>12</td>
<td>25</td>
<td>51</td>
</tr>
<tr>
<td>12</td>
<td>(\text{CH}_3) (\text{CH}=\text{CH}\text{SiMe}_3)</td>
<td>87</td>
<td></td>
<td>26</td>
<td>100</td>
<td>56</td>
<td>97</td>
</tr>
<tr>
<td>14</td>
<td>(\text{CH}_3) (\text{CH}=\text{CH}\text{SiMe}_3) (cis/trans=1:3)</td>
<td>97</td>
<td></td>
<td>30</td>
<td>50</td>
<td>59</td>
<td>96</td>
</tr>
<tr>
<td>18</td>
<td>(\text{CH}_3) (\text{CH}=\text{CH}\text{SiMe}_3)</td>
<td>96</td>
<td></td>
<td>4</td>
<td>86</td>
<td>25</td>
<td>98</td>
</tr>
<tr>
<td>22</td>
<td>(\text{SiMe}_3\text{CH}=\text{CHCH}_2\text{SiMe}_3)</td>
<td>95</td>
<td></td>
<td>48</td>
<td>59</td>
<td>38</td>
<td>96</td>
</tr>
</tbody>
</table>

\textsuperscript{a}See footnotes for details.
**TABLE 8 (continued)**

<table>
<thead>
<tr>
<th>Ketone</th>
<th>Vinylsilane</th>
<th>Isolated (\text{Yield, %})</th>
<th>(\alpha)-Silylated-alcoholic (\text{Yield, %})</th>
<th>Reaction (\text{time, hr.})</th>
<th>Conversion, (\text{Isolated \text{Yield, %}})</th>
<th>Allylic-alcoholic (\text{Yield, %})</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>76</td>
<td>89</td>
<td>12</td>
<td>62</td>
<td>76</td>
<td>56</td>
</tr>
<tr>
<td>143</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>144</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>145</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>151</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>152</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)All compounds were characterized by IR, NMR, and accurate mass spectral measurements.  \(^b\)These yields have been normalized to account for recovered starting material.  \(^c\)Partial dehydration occurs upon purification to give 30\% benzocycloheptatriene.
containing this subunit were found to be unreactive or exceedingly sluggish in their response.

For conformational reasons, vinylsilanes such as \(71\) have quasi-axially locked hydrogens cis and trans to the t-butyl group. Upon oxygenation, the axial alcohol \(139a\) was the favored product involving axial abstraction through the "regioallowed" pathway. The stereochemistries of the two allylic alcohols were considered established on the basis of the following information. The product obtained upon column chromatography appeared to be homogeneous by NMR analysis of the t-butyl and trimethylsilyl regions. When the sample was treated with a lanthanide shift reagent (Eu-Resolve) the original two signals separated into four, both pairs having a ratio of 1:3. The t-butyl group of the major isomer exhibited the greater \(\Delta\delta\) in the presence of the Eu-Resolve and was assigned the anti-isomer \(139a\). The trimethylsilyl signal with
the greater $\Delta \delta$ belongs to the minor isomer and reasonably this should correspond to allylic alcohol $139b$. As additional $^1H$ NMR evidence, the olefinic signal of the mixture showed two merging multiplets, the higher field multiplet belonging to the minor allylic alcohol $139b$. The major alcohol $139a$ which contained an equatorial hydrogen $\alpha$ to the hydroxyl group was assigned to the lower field multiplet. The relative field position of these two signals thus matched the expected behavior of axial/equatorial cyclohexyl hydrogens. The structure of $139a$ was finally shown by conversion to $147$ with fluoride ion (Figure 4). The major compound of the desilylated mixture agrees

\[ \text{Me}_2\text{Si} \quad + \quad \text{Bu}_4\text{NF}^- \quad \rightarrow \quad \text{OH} \]

$139a$  \hspace{1cm} $139b$

$\delta H_a \begin{cases} 5.78 \\ 5.83 \\ 5.78 \end{cases}$

$\delta H_b \begin{cases} 4.11 \\ 4.16 \\ 4.13 \end{cases}$

FIGURE 4. $^1H$ NMR comparison of 5-t-butylocyclohex-2-enols
spectrally with the known anti allylic alcohol. The 3:1 ratio of allylic alcohols produced in vinylsilane 71 is identical to the ratio of axial/equatorial allylic alcohols produced upon photooxygenation of the corresponding olefin.

Examples 72 and 77 more precisely defined the requirement of axial hydrogen abstraction. Vinylsilane 72 underwent slow photooxy-

\[
\text{72}
\]

\[
\text{73}
\]

genation during 12 hours (only 12\% conversion). The phenyl substituted vinylsilane 77 was completely inert to photooxygenation during the same elapsed time. This lack of reactivity can be explained by inspection of molecular models and the allylic strain theory. The bulky phenyl and trimethylsilyl groups are prevented from both residing in equator-

\[
\text{77a}
\]

\[
\text{77b}
\]
torial positions. Conformation 77a with the phenyl substituent axially oriented is presumed to be dominant. In conformation 77a, the hydrogen to be abstracted is equatorial, thereby negating reaction through the normal ene pathway. Importantly, an axial hydrogen is always positioned on the opposite side of the double bond; however, this "regioversed" hydrogen abstraction pathway was never followed.
2-Trimethylsilyl-3-methylcyclohexene is, of course, subject to a similar conformational equilibrium. The smaller size of the methyl substituent should now allow population of the conformation analogous to 77a and reaction to proceed slowly.

The powerful control which the trimethylsilyl group exerts on the regiochemistry of the ene reaction is nicely pointed out by the two similar vinylsilanes 78 and 153. Under conditions which trans-

\[
\begin{align*}
78 & \quad 153 & \quad 154 \\
\end{align*}
\]

formed 153 to 154 (40% conversion), vinylsilane 78 was recovered in high yield with no trace of any photooxygenation product. Again, no "regioversed" reactivity was seen.

As a further test, the vinylsilane 76 was chosen. It was well known that benzyllic hydrogens are abstracted in preference to unactivated hydrogens in other systems. In the case of 76 the benzyllic abstraction would lead to the "regioversed" product 145 while

\[
\begin{align*}
76 & \quad 144 & \quad 145 \\
\end{align*}
\]

SCHEME V. Photooxygenation paths of 76
"regioallowed" abstraction of an unactivated hydrogen would give $^{144}$. When the reaction was carried out, $^{144}$ predominated by a ratio of 3:1. The lower pathway of Scheme V shows the reactive intermediates in the production of $^{145}$. This process was verified by changing the reducing agent to aqueous sodium sulfite. Now the α,β-unsaturated ketone $^{155}$ was isolated in place of the allylic alcohol $^{145}$. As a control experiment, olefin $^{156}$ was photooxygenated, and, as expected, it cleanly led to $^{145}$ as the only observable product. These last few examples

\[\text{156}\quad\text{145}\]

clearly demonstrate the impressive regiocontrol associated with the photooxygenation of vinylsilanes.

Further it has been found that photooxygenation of more flexible vinylsilanes affords mixtures of cis- and trans-β-silylated allylic alcohols (Table 8) which can be efficiently separated by gas phase or column chromatography. The structures of the cis and trans isomers were easily delineated on the basis of chemical shifts of the olefin protons. In the cis isomers, the hydroxyl group shields the spatially proximal olefinic proton, and shifts it to higher field. Such effects did not operate in the trans series. For isomers $^{140}$ and $^{141}$ produced from 1-trimethylsilyl-3-heptene, the magnitude of $\Delta$ was 0.45. For $^{142}$ and $^{143}$ obtained from 1-trimethylsilylcyclooctadecene, the difference was 0.56. Analogously, the allylic proton $\alpha$ to the hydroxyl group
appeared at higher field in the cis olefin of each series.

Only one type of vinylsilane has been found which did not undergo a "regioallowed" photooxygenation when sterically permitted. This was the terminal vinylsilane $\text{74}$. Apparently a monosubstituted vinylsilane is too electron deficient to react at an appreciable rate.

The predescribed photooxygenation process has allowed for the conversion of a saturated ketone to a 1,2-transposed allylic alcohol. The final step (Scheme IV), cleavage of the silicon-vinyl carbon bond, was accomplished by taking advantage of the affinity of fluoride ion for silicon and the accelerating effect of a $\beta$-hydroxyl group. $^{92}$ Chan has found that the silicon-vinyl carbon bond was difficult or impossible to cleave under ordinary circumstances; however, when a $\beta$-hydroxy group was present desilylation with fluoride ion became more facile. The acceleration was explained by hydrogen bonding of the fluoride ion to the hydroxyl group, thus positioning the fluoride ion for attack on silicon. The most effective conditions uncovered involved heating with tetra-$n$-butylammonium fluoride (10 equivalents) in dry acetonitrile. Requisite reaction times varied from 1-36 hours, with the more flexible, open systems reacting faster. Of particular note here was the preservation of geometry about the $\pi$ linkage during silicon-carbon bond fission (Table 8). $^{93}$
The versatility of this transposition method is illustrated by the examples provided in Table 8. In practical terms, its utilitarian nature does not stop here since the allylic alcohols so produced can in principle be converted by existing methodology into a wide range of functionalized molecules, some of which are illustrated in Figure 5.

The β-silylated allylic alcohols appeared to be interesting compounds in their own right and so some further chemistry was investigated. β-Trimethylsilanol is known to undergo syn-elimination under basic conditions. Chan had pointed out that a silicon atom bonded to a sp²-hybridized center could not be eliminated in this manner. In fact under their conditions no reaction occurred. When the

![Scheme VI: Desilylation with sodium hydride](image)

**Scheme VI.** Desilylation with sodium hydride
FIGURE 5. Some elaboration products of a transposed allylic alcohol.

References to the reagents used are given in footnote 94.
β-silylated allylic alcohol 143 was treated with sodium hydride in refluxing tetrahydrofuran followed by an aqueous work-up, the desilylated allylic alcohol 151 was produced. Likewise 142 could be converted to 150 and 139 to 147. However, this last example could only be pushed to 60% completion. The mechanism of this process has not been determined, but the intermediacy of the trimethylsilylether 157 is implicated by thin layer chromatography of the reaction mixture. After hydrolytic work-up, a high r.f. spot is lost and replaced by a new

\[ \begin{array}{c}
143 \xrightarrow{\text{NaH}} 151 \\
\text{H}_2\text{O}
\end{array} \]

r.f. < 0.1  \quad r.f. = 0.75  \quad r.f. < 0.1

spot corresponding to the allylic alcohol 151. The logical structure for the spot represented at r.f. = 0.75 would be the non-polar silyl-ether 157.

The oxidation of allylic alcohols with activated manganese dioxide is a very useful process because of the mild conditions and easy work-up. Consequently this oxidation method was investigated with the photooxygenation products. Table 9 contains a summary of the results. While oxidation produced solely the α,β-unsaturated ketones, the process was exceptionally slow and did not go to completion. The manganese dioxide used in these experiments had been prepared by the method of Attenburrow, however, manganese dioxide on charcoal prepared by the method of Carpino was no more successful.
TABLE 9. MnO₂ Oxidations

<table>
<thead>
<tr>
<th>Allylic Alcohol</th>
<th>Reaction Time (days)</th>
<th>Product</th>
<th>Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me₃SiOH</td>
<td>4.5</td>
<td>Me₃SiO</td>
<td>86</td>
</tr>
<tr>
<td>139</td>
<td>12</td>
<td>158</td>
<td>90</td>
</tr>
<tr>
<td>Me₃SiOH</td>
<td>17</td>
<td>Me₃SiO</td>
<td>20</td>
</tr>
<tr>
<td>138</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me₃SiOH</td>
<td>2</td>
<td>Me₃SiO</td>
<td>trace</td>
</tr>
<tr>
<td>140</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The inefficiency of this oxidation may be traced back to the slightly electron deficient double bond of a vinylsilane. To effect this oxidation in high yield, a stronger oxidant appears to be necessary.

Lastly, two elimination reactions were performed. When the β-silylated allylic alcohol \( \text{143} \) was treated with one equivalent of \( p \)-toluenesulfonic acid, dehydration was accompanied by desilylation to give cyclododeca-1,3-diene \( \text{172} \) in quantitative yield. Büchi and Wüest have also reported that \( p \)-toluenesulfinic acid can be used to convert vinylsilanes to olefins. While the conversion to a diene may not be useful, stopping the elimination at \( \text{171} \) would still give an unsymmetrically substituted diene system. This indeed could be effected by treating \( \text{143} \) with trifluoroacetic anhydride in pyridine. The silyldiene \( \text{171} \) could be obtained in 80% yield based on recovered starting material.

The further manipulation of the photooxygenation products, β-silylated allylic alcohols, has not been exhaustive, but should suffice to indicate the variety of transformations which are possible. The importance of the photooxygenation reaction of vinylsilanes is
that the reaction is generally regiospecific, and that the controlling factor, the trimethylsilyl group, can be easily attached and removed to leave behind a nonsilylated product.
The efficient conversion of a ketone to a fused cyclopentenone of type 173 holds considerable promise as a powerful annulation tool. Not only does a new five-membered ring result, but the endocyclic carbon-carbon double bond provides for subsequent control of ring fusion stereochemistry, stereoselective attachment of appendages and/or functional groups, and ring expansion through cleavage (when the starting material is cyclic). Although various methods have been employed to gain access to 173 (R1 = R2 = H and R1 = H, R2 = CH₃), the lack of a general procedure appears to have impeded the growth of this important area of synthetic methodology.

In this section is described a general route to compounds of the type 173 (R1 = R2 = CH₃ and R1 = H, R2 = CH₃), with the method being less useful for preparation of 173 (R1 = R2 = H). It involves conversion of the ketone to a vinylsilane, Friedel-Crafts acylation and cyclization of the dienone.
Annulation processes mediated through a carbonyl may suffer from lack of regiospecificity when the remaining bond of the annulated ring is formed. Often the position of annulation is dependent upon dehydration of the alcohol resulting from nucleophilic attack on the carbonyl. In some cases, prior activation of an α position by a carbomethoxy group, enamine, or silyl-enol ether is necessary to insure regiospecificity. The method described here utilizes the almost universal regiospecificity of vinylsilane formation to insure proper orientation of the annulated cyclopentenone. The trimethylsilyl group powerfully activates and directs the Friedel-Crafts acylation of the double bond resulting in the acylium ion becoming bonded directly to the silicon-bearing carbon with subsequent loss of the trimethylsilyl group. The particular stabilization of carbonium ions β to silicon allows this high degree of directionality.

Pentadienyl cations are well known to undergo conrotatory electrocyclic ring closure. These cations have been generated from a
number of species including the following: conjugated eneyne alcohols, 111 acetylenic diols, 100b,c,101,104a 112 \( \alpha,\beta \)-unsaturated esters, 104b \( \alpha' \)-trimethylsiloxyl-\( \alpha,\beta \)-unsaturated ketones, 104a hydroxydichloro olefins, 113 and, most importantly, dienones. All of the above cases require protic acid conditions to generate the pentadienyl cation.

No study of dienone cyclizations under catalysis from Lewis acids has been uncovered. The approach described here represents the first successful cyclization under Lewis acid conditions.

The overall concept is illustrated for the specific case of 2-methylcyclopentanone and \( \beta,\beta \)-dimethylacryloyl chloride in Scheme VII.

SCHEME VII. Cyclopentenone annulation of ketones

Reaction of 174 with 1 equiv each of acid chloride and aluminum chloride in anhydrous dichloromethane at -78°C for 5 min effected conversion to 175 which was isolated but not purified. Treatment of 175
with 3 equiv of stannic chloride in refluxing dichloromethane (3 days) followed by preparative layer chromatography produced a mixture of \(\text{176}\) and \(\text{177}\) in isolated yields of 33 and 19%, respectively. Alternatively, prior exposure of these unpurified enones to rhodium(III) chloride tri-hydrate in hot ethanol gave rise exclusively to \(\text{177}\) (5%). A complete summary of results is contained in Table 10.

During the development of suitable reaction conditions, several key factors were identified. These include the order of mixing reagents, the particular Lewis acid, temperature, and work-up. Lack of proper control of these factors was observed to give low yields and numerous side products.

The order of mixing proved crucial to obtaining high yields. Addition of the Lewis acid directly to a solution containing only vinylsilane resulted in partial conversion to olefin. This, of course, eliminates any control of the acylation regiochemistry. In addition, it has been found that olefins do not acylate under the mild conditions applicable to vinylsilanes. Addition of the Lewis acid to a solution of acid chloride followed by the vinylsilane proved to be a more efficacious procedure.

Reaction at the lowest convenient temperature resulted in the fewest side-reactions. At \(-78^\circ\text{C}\), acylation with \(\beta,\beta\)-dimethylacryloyl chloride was complete within 5 minutes; however, little or no ensuing cyclization occurred. At higher temperatures (0\(^\circ\text{C}\), cyclization did materialize, but large amounts of silylenol ether formation and 1,4-addition of chloride ion was also seen (vide infra).
<table>
<thead>
<tr>
<th>Vinylsilane</th>
<th>Reaction Conditions</th>
<th>Initial Cyclization Products</th>
<th>Yield</th>
<th>Rh(III) Catalysis Product</th>
<th>Overall Yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. β,β-Dimethylacryloyl Chloride</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image1" alt="Vinylsilane_A" /></td>
<td>(1) AlCl₃, CH₂Cl₂</td>
<td><img src="image2" alt="Cyclization.Products_A_1" /></td>
<td></td>
<td><img src="image3" alt="Rh(III).Catalysis.Product_A_1" /></td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>-78°C, 15 min.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image4" alt="Vinylsilane_A" /></td>
<td>(2) SnCl₄, CH₂Cl₂</td>
<td><img src="image5" alt="Cyclization.Products_A_2" /></td>
<td></td>
<td><img src="image6" alt="Rh(III).Catalysis.Product_A_2" /></td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>reflux 8-12 hrs.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image7" alt="Vinylsilane_A" /></td>
<td>as above</td>
<td><img src="image8" alt="Cyclization.Products_A_3" /></td>
<td></td>
<td><img src="image9" alt="Rh(III).Catalysis.Product_A_3" /></td>
<td></td>
</tr>
<tr>
<td><img src="image10" alt="Vinylsilane_A" /></td>
<td>as above</td>
<td><img src="image11" alt="Cyclization.Products_A_4" /></td>
<td></td>
<td><img src="image12" alt="Rh(III).Catalysis.Product_A_4" /></td>
<td>57</td>
</tr>
<tr>
<td><img src="image13" alt="Vinylsilane_A" /></td>
<td>(1) as above</td>
<td><img src="image14" alt="Cyclization.Products_A_5" /></td>
<td></td>
<td><img src="image15" alt="Rh(III).Catalysis.Product_A_5" /></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2) BF₃·Et₂O, C₆H₆, reflux</td>
<td><img src="image16" alt="Cyclization.Products_A_6" /></td>
<td></td>
<td><img src="image17" alt="Rh(III).Catalysis.Product_A_6" /></td>
<td>43</td>
</tr>
<tr>
<td><img src="image18" alt="Vinylsilane_A" /></td>
<td>1-3 days</td>
<td><img src="image19" alt="Cyclization.Products_A_7" /></td>
<td></td>
<td><img src="image20" alt="Rh(III).Catalysis.Product_A_7" /></td>
<td></td>
</tr>
<tr>
<td><img src="image21" alt="Vinylsilane_A" /></td>
<td>as above</td>
<td><img src="image22" alt="Cyclization.Products_A_8" /></td>
<td></td>
<td><img src="image23" alt="Rh(III).Catalysis.Product_A_8" /></td>
<td>62</td>
</tr>
<tr>
<td><img src="image24" alt="Vinylsilane_A" /></td>
<td>as above</td>
<td><img src="image25" alt="Cyclization.Products_A_9" /></td>
<td></td>
<td><img src="image26" alt="Rh(III).Catalysis.Product_A_9" /></td>
<td></td>
</tr>
<tr>
<td><img src="image27" alt="Vinylsilane_A" /></td>
<td>as above</td>
<td><img src="image28" alt="Cyclization.Products_A_10" /></td>
<td></td>
<td><img src="image29" alt="Rh(III).Catalysis.Product_A_10" /></td>
<td>60</td>
</tr>
<tr>
<td>Vinylsilane</td>
<td>Reaction Conditions</td>
<td>Initial Cyclization Products</td>
<td>Yield %</td>
<td>Rh(III) Catalysis Product</td>
<td>Overall Yield %</td>
</tr>
<tr>
<td>------------</td>
<td>---------------------</td>
<td>-----------------------------</td>
<td>---------</td>
<td>-------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>B. Crotonyl Chloride</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| \[
\begin{align*}
\text{SiMe}_3 \\
\text{SiMe}_3
\end{align*}
\] |
| as above |
| \[
\begin{align*}
\text{C}_{21}
\end{align*}
\] |
| 58 |
| (1) \(\text{AlCl}_3 \cdot \text{CH}_2\text{Cl}_2\) |
| R.T., 1 hr. |
| (2) \(\text{BF}_3 \cdot \text{Et}_2\text{O}, \text{C}_6\text{H}_6, \text{reflux}\) |
| C. Acryloyl Chloride |
| \[
\begin{align*}
\text{SiMe}_3 \\
\text{SiMe}_3
\end{align*}
\] |
| \[
\begin{align*}
\text{AlCl}_3 \cdot \text{CH}_2\text{Cl}_2
\end{align*}
\] |
| R.T., 2 hr. |
| \[
\begin{align*}
\text{C}_{21}
\end{align*}
\] |
| 27 |
| \[
\begin{align*}
\text{C}_{21} \quad (1.25:1)
\end{align*}
\] |
| (1) \(\text{AlCl}_3 \cdot \text{NaOAc}\) |
| \(\text{CH}_2\text{Cl}_2, -45^\circ\) |
| 15 min. |
| (2) \(\text{CF}_3\text{COOH}, \text{R.T., 3 hr.}\) |
Lewis acid selection became the bane of the sequence. The proper Lewis acid could provide encouraging results in one system, yet prove pernicious in another. Titanium tetrachloride gave mixtures of up to six products from simple acylation efforts. Silylenol ether formation and 1,4-addition of chlorotrimethylsilane became dominant pathways (see 196 and 197). Boron trifluoride etherate, on the other hand, neither promoted acylation of the vinylsilane, nor even formed a colored complex. Stannic chloride resulted in facile acylation of the vinylsilane, yet it also gave partial 1,4-addition of chlorotrimethylsilane (Scheme VIII). The tendency of these Lewis acids to catalyze 1,4-addition may be the result of crowded coordination spheres which prohibit them from tightly binding to all of the chloride ligands. The small ionic radius of titanium(IV), 0.68 Å, makes it a more serious offender than tin(IV), 0.71 Å. To minimize the 1,4-addition problem, aluminum...
chloride was investigated (Scheme IX). Tetrachloroaluminate appears to remain more tightly coordinated as it gives little or no 1,4-addition, and yet aluminum chloride promotes instantaneous acylation of vinylsilanes. This is not to say aluminum chloride does not permit silylenol ether formation; however, such an intermediate could be easily reconverted to the desired dienone by a hydrolytic work-up.

\[
\begin{align*}
\text{SiMe}_3 & + \text{Cl} & \text{AlCl}_3 & \rightarrow \text{H}_2\text{O} / \text{HCl} \\
125 & & 127
\end{align*}
\]

SCHEME IX. Acylation with aluminum chloride

For this reason, a two-step procedure had to be developed, as the intermediate silylenol ethers resisted cyclization and did not interconvert with the dienone under the requisite anhydrous conditions.

The optimum conditions for annulation with β,β-dimethylacryloyl chloride required acylation using aluminum chloride followed by stirring with dilute hydrochloric acid to generate free dienone. This acid treatment, incapable of reversing the 1,4-addition of chlorotrimethylsilane, produced the β-chloroenone from the 1,4-addition
The dienone could be cyclized in a second step by treatment with a several fold excess of a Lewis acid. Stannic chloride proved to be the most useful for cyclization; however, in some cases boron trifluoride etherate was used advantageously. If desired, the dienone could also be cyclized under protic conditions. Care must be exercised in that rearrangements are possible during the cyclization procedure or after formation of the cyclopentenone. As an example, dehydration of 199 is reported to give mixtures of cyclopentenones in aqueous acid. Indeed, when cyclization of 200 was carried out with aluminum chloride, only products of rearrangement were observed (201 and 202). Cyclization with stannic chloride on the
other hand produced no undesired rearranged cyclopentenones (Table 10).

The cyclized products were often obtained as a mixture of double bond isomers. Although the endocyclic/exocyclic ratios expectedly varied from system to system, this phenomenon has presented no complications because subsequent exposure to rhodium(III) chloride in ethanol promoted isomerization to a single product in most instances. Alternatively, treatment with dilute acid produces the most stable isomer.

From the results summarized in Table 10, it can be seen that the annulation sequence gives respectable yields with \( \beta,\beta \)-dimethylacryloyl chloride and crotonoyl chloride, while acryloyl chloride lacks particular utility. These results come from a combination of factors. The major factor is ease and cleanliness of acylation. In this regard relative ease of acylation decreases with lessening of the degree of methyl substitution on the acid halide. Whereas condensation with \( \beta,\beta \)-dimethylacryloyl chloride was complete within several minutes at \(-78^\circ C\), crotonoyl chloride required one hour at room temperature to achieve complete acylation. Reactions with acryloyl chloride were less predictable due to simultaneous destruction of products. Thus the ease of acylation increases on the order of acylum ion stability.

As an example of this cyclopentenone annulation process, the natural product \( \beta \)-cuparenone (203) appeared to be a reasonable target. It has been synthesized previously, and it has also been shown that the enone 204 can be converted to \( \beta \)-cuparenone (203). Thus, production of 204 constitutes a formal synthesis of \( \beta \)-cuparenone (203).
Annulation of the vinylsilane 205 with β,β-dimethylacryloyl chloride should afford the desired enone 204, and so the synthesis appeared to be simply that of vinylsilane 205.

The vinylsilane 205 was easily prepared by bromination of p-methylcinnamic acid to 207, bromodecarboxylation to the bromostyrene 208, and low temperature metal-halogen exchange followed by a

Scheme X. Preparation of vinylsilane 205
chiorotrimethylsilane quench. During the metal-halogen exchange, a small amount of p-methylphenylacetylene (209) was formed by base-promoted elimination of hydrogen bromide. The acetylene was subsequently deprotonated and converted to p-methylphenyltrimethylsilylacetylene (210). The acetylenic product was separated chromatographically from the vinylsilane.

Treatment of 205 with β,β-dimethylacryloyl chloride and aluminum chloride in methylene chloride at -78°C followed by the work-up described previously afforded dienone 211 quantitatively. Designation 211 of the E olefin geometry is derived from the observed coupling constant of 16 Hz for the two styrene vinyl protons as well as desiliconation from the less hindered rotamer.

The dienone proved resistant to cyclization under a variety of conditions. The usual heating with stannic chloride was fruitless; dienone 211 was recovered in high yield. Boron trifluoride etherate
in refluxing benzene produced a separable mixture of decomposition products, starting dienone (31%), and the desired α,β-unsaturated ketone (10%). Despite many efforts, this set of conditions turned out to be the only effective one. Harsher Lewis acid conditions led solely to decomposition. Trifluoroacetic acid resulted in either no reaction at room temperature or total decomposition at 70°C. Refluxing dienone \(\text{211}\) with ethanolic hydrochloric acid, a procedure developed by Shoppee for other phenyl substituted dienone systems, \(\text{113f}\) cleanly formed \(\text{p-methylbenzylidene acetone (213)}\) in 65% yield (Scheme XI). Because subjection of the protonated dienone

\[
\begin{align*}
\text{211} & \quad \text{HCl} \quad \text{EtOH} \\
\text{212} & \quad \text{Nu}^- \\
\text{213} & \quad \text{Nu}
\end{align*}
\]

SCHEME XI. \(\text{p-Methylbenzylidene acetone formation}\)

\(\text{212}\) to nucleophiles appeared to give carbon-carbon bond cleavage, the less nucleophilic system glyme/concentrated sulfuric acid (10 ml/20
drops) was tried. Again only the same carbon-carbon bond cleavage resulted. To further reduce the nucleophilicity of the counterion, the medium was changed to fluorosulfonic acid in deuteriochloroform and the reaction was conducted at either room temperature or 70°C. These studies were performed in NMR tubes and enabled the protonated diene 212 to be seen spectrally. Notable points were the general downfield shift of all signals and removal of the allylic coupling in the vinyl methyl signals. They were left as closely spaced singlets.

Likewise, solution of the diene in concentrated sulfuric acid gave a downfield shifted NMR spectrum. In neither case was cyclization to the α,β-unsaturated ketone seen. From the studies performed, it appears that the protonated or Lewis acid complexed diene is too stable with the addition of aromatic conjugation to overcome the necessary activation energy to cyclize irreversibly to the complexed cyclopentenone.
SECTION 6
Alkylative Cyclization

The successful development of the annulation scheme described in the previous section inspired a conceptually related but differently executed procedure. In the last scheme a cyclopentenone annulation was achieved by introducing the darkened bonds in \( \text{173} \). Another approach which reverses the control of bonds being formed is illustrated by \( \text{214} \). This approach is potentially similar to cuprate addition, followed by trapping of the resultant enolate, and reintroduction of the double bond (Scheme XII). This sequence has the disadvantage

\[
\begin{align*}
\text{Scheme XII. Preparation of } &\text{214 via cuprates}
\end{align*}
\]
that multiple steps and relatively costly and unstable cyclopentenones are involved. The new approach envisioned for the generation of involves regiocontrolled 1,2-addition across a silylacetylene and subsequent trapping of the organometallic with an electrophile (Scheme XIII). An oxidative cyclization would be facilitated by desilica-

![Chemical structure](image)

\( B = \text{acid labile blocking group} \)

**SCHEME XIII.** Alkylative cyclization

Reaction scheme XIII consists of essentially two reactions. The 1,2-addition of an organometallic species across an acetylene has been documented for a variety of metallic species including cuprate, Grignard, \(^{12a,122}\) aluminum, \(^{15,123}\) zirconium, \(^{124}\) boron, \(^{14,125}\) and nickel or titanium aluminates. \(^{12b,13,126}\) In the boron and zirconium cases \( R = H \) (see Scheme XIII). In the aluminum chemistry studied, aluminum hydrides and alkenylaluminums have been shown to add in a 1,2-fasion. \(^{123b}\) The nickel and titanium catalyzed processes are also
restricted to the transfer of alkyl groups from a trialkylaluminum. Grignard additions to acetylenes must have strategically located hydroxyl groups to assist the process and so are of limited utility. The cuprate and alkenylaluminum additions appear to be the most generally useful.

The second reaction of the sequence is an oxidative cyclization to the cyclopentenone. Oxidative cyclizations are known in a variety of other systems; however, the present case is special. The cyclization is "5-endo-trig" according to Baldwin's rules \(^\text{127}\) which makes it an unfavored bond formation (Figure 6).

![Figure 6. Favored/unfavored cyclizations](image)

Examples of "5-exo-trig" and "6-endo-trig" closures are well documented. Importantly, "5-endo-trig" processes have been found not to operate under conditions sufficient for "5-exo-trig" closure (Figure 7). The crucial factor in the present cyclization attempt is whether the extra stabilization offered by the silicon as well
FIGURE 7. Examples of cyclization
as its increased tendency to react with positively charged intermediates is sufficient to overcome the poor orbital interaction which underlies the "5-endo-trig" cyclization. In this section are described experimental observations relevant to this question.

The substrate selected for alkylative cyclization was 5-pentynol (217) which was readily obtained in two steps from tetrahydrofurfuryl (215). Treatment of 215 with thionyl chloride in pyridine yielded 216 which was dehydrochlorinated and ring opened by sodium amide in liquid ammonia. The 5-pentynol can be obtained in 100 g lots with little expenditure of reagents. For cyclization trials, the acetylenic alcohol was bistrimethylsilylated, monotrimethylsilylated, and
hydrotriethyisilylated to give $218$, $219$, and $220$, respectively.
Silylalcohol $220$ was used as the model compound for cyclization studies. Conditions examined include pyridinium chlorochromate, pyri-
dinium chlorochromate with a trace of trifluoroacetic acid, pyridinium chlorochromate with added boron trifluoride etherate, pyridinium chloro-
chromate with added aluminum chloride, pyridinium fluorochromate, and
chronic acid. All the above conditions afforded only the aldehyde or
acid (chronic acid) with no trace of cyclopentenone.

An attempt at radical induced closure also met with failure.
Treatment of the aldehyde $221$ with benzoyl peroxide in carbon tetra-
chloride appeared to give only the acid chloride; no signals due to
cyclopentenone were observed in the $^1$H NMR spectrum of the crude re-
action mixture.$^{132}

The remaining possibility of treatment of the acid chloride $222$
with a Lewis acid similar to the work described in Section 5 was not
attempted. Based on the apparent decomposition of less hindered di-
eneones and/or cyclopentenones under the Lewis acid conditions, it was
felt that the sensitive, unsubstituted 2-cyclopentenone system would
not survive the treatment.

Concurrent with these cyclization attempts, several avenues of
1,2-addition to the silylacetylene were studied. Earlier work had
established that hydroalumination of silylacetylenes regiospecifically \(^{123}\) generated an alkenylaluminum \(\alpha\) to the silicon substituent.

\[
\text{DIBAL} \quad \begin{array}{c}
R-C≡C-SiMe_3 \\
\xrightarrow{} \\
R \quad \text{H} \quad \text{SiMe}_3 \\
\text{Al(Bu)}_{\text{l}}^\text{i} \quad \text{EX} \\
R \quad \text{H} \quad \text{SiMe}_3
\end{array}
\]

Zweifel and Miller had also shown that alkenylaluminum compounds could, under more vigorous conditions, undergo a second 1,2-addition of an acetylene to generate a new vinylalane, trapable with an electro-

\[
\text{DIBAL} \quad \begin{array}{c}
R-C≡CH \\
\xrightarrow{} \\
R \quad \text{H} \quad \text{H} \\
\text{Al(Bu)}_{\text{l}}^\text{i} \quad \Delta \\
R \quad \text{H} \quad \text{H} \quad \text{H} \\
\text{Al(Bu)}_{\text{l}}^\text{i} \quad \text{EX} \\
\text{E}
\end{array}
\]

phile. \(^{123b}\) Based on the previous information, hydroalumination of the protected alcohol \(^{223}\) was attempted with the intention of subsequently

\[
\text{DIBAL} \quad \begin{array}{c}
\text{H-C≡C-C-Et} \\
\xrightarrow{} \\
\text{Me} \quad \text{H} \quad \text{CMeEt} \\
\text{OSiMe}_2\text{Bu}^\text{t} \quad \text{Me}_3\text{SiO(CH}_2)_2\text{C≡C-SiMe}_3
\end{array}
\]
adding the vinylalane to the bistrimethylsilylated pentynol 218. Under the usual hydroalumination conditions, no reaction occurred. The forcing conditions of refluxing tetrahydrofuran also failed to result in any hydroalumination, as indicated by the lack of olefinic products upon aqueous work-up and the high return of acetylene 223. After termination of further work along these lines, the similar results of Weiss et al. were published.153 They had found that hydroalumination of propargylic alcohols of the type 225 were peculiarly

\[
\text{HC} = \text{C-CHR} \\
\text{OH}
\]

sensitive to the blocking group used. After trying six different protecting groups including t-butyldimethylsilyl, only the triphenylmethyl group allowed correct hydroalumination, and in this case the yield was low. Thus, the hydroalumination of functionalized acetylenes is a very capricious reaction.

Attention was next turned to cuprate addition on the protected pentynol 218. Under three differing cuprate conditions, including

\[
\text{Me}_3\text{SiO-(CH}_2)_3\text{C}=\text{SiMe}_3 \xrightarrow{\text{Bu}_2\text{CuLi}} 218
\]

\[
\text{EtCu(Me}_2\text{S-MgBr})\text{Br} \xrightarrow{\text{BuLi/CuC}=\text{C-Pr}} 218
\]

\[
218
\]

...
those conditions currently favored, no 1,2-addition could be seen. The complete failure of these methods was unexpected and can only be attributed to complications resulting from the protected alcohol as with the hydroalumination. These discouraging findings taken in conjunction with the failure to achieve oxidative cyclization, led to the abandonment of this scheme.
Preparation and Reactions of 1-Aryl Allylsilanes

Allylsilanes and their anions have recently emerged as important synthetic reagents. There exist at the present time several procedures for preparing allylsilanes including the hydro-silylation of dienes, condensation of allylic Grignard reagents and related organometallics with chlorotrimethylsilane, Diels-Alder addition of 1-trimethylsilylbutadiene, reaction of β-trimethylsilylethyltriphenylphosphonium ylide with carbonyl compounds, and others. In this section is described a complementary new technique by which unsubstituted and 2-aryl ketones may be transformed expeditiously to 1-aryl substituted allylsilanes, and selected reactions of such compounds.

The methodology is typified by our initial observation that treatment of N,N,N',N'-tetramethylethylenediamine solutions of propiophenone benzenesulfonylhydrazone with excess n-butyllithium in hexane at -45°C, followed by heating at 60°C for 3 hr and addition of chlorotrimethylsilane, produced the allylsilane (58% isolated yield) instead of the vinylsilane. When conditions were ameliorated somewhat (50°C, 2 hr), (40%), (36%) and (13%) were obtained. At a somewhat later date, Knorr and Lattke reported their independent discovery of a similar vinyl anion to allyl anion.
SCHEME XV. Allylsilane formation

Further study on their part revealed the reaction to be governed by a strongly negative entropy of activation, to exhibit 0.5th order in 227 and to likely proceed by an intermolecular transmetalation mechanism involving small amounts of β,β-dimethylstyrene.

Recent theoretical considerations suggest that allyl anions need not necessarily be thermodynamically favored relative to vinyl anions in every instance. The stability of both species appears to be critically dependent upon the geometry of the system, the optimal vinyl anion and allyl anion internal angles being 110° and 132.5°.
respectively.\textsuperscript{147} Stated differently, an allylic hydrogen increases in acidity as the C-C-C angle is increased on the vinyl anion, thereby in principle engendering more facile isomerization. Of course, this acidity is also dependent on the C-C-H torsional angle; the closer the C-H bond comes to eclipsing the \(
\phi\) orbital, the greater the rate of proton migration. This would represent the least motion pathway in intramolecular processes. On this basis, the ensuing order of acidity of cyclic olefins has been derived:\textsuperscript{142}

\[
\begin{array}{c|c|c|c}
\text{rel rate} & 1 & 3.1 & 15.9 & 3.3 \\
\end{array}
\]

Calculations on the preferred stereochemistry of crotyl anions have also been performed by Schleyer, \textit{et al.}, who concluded that cis form \textsuperscript{229} is favored over trans form \textsuperscript{230} by 1.5 kcal/mol.\textsuperscript{143} This analysis warrants comparison with gas-phase ion cyclotron measurements which have shown \textsuperscript{230} to be 0.2 kcal/mol lower in free energy than \textsuperscript{229} and solution studies which have revealed a 2.2 kcal/mol free energy preference for the cis geometry.\textsuperscript{144}

Two important points emerge: (a) all vinyl anions need not be prone to isomerize readily to allylic anions; (b) solvation factors cannot be neglected. As concerns the present work, the vinyl \(\rightarrow\) allyl
anion rearrangement was found to proceed at convenient rates only when the allyl anion is additionally conjugated to an aryl substituent. It appears therefore that a rather high energy barrier must be crossed in most, if not all ordinary circumstances. Presumably, the role played by the neighboring aromatic ring is one of lowering the customarily demanding energetics through inductive and resonance contributions.

These considerations are reflected in the behavior of vinyl anion derived from phenylacetone benzenesulfonylhydrazone (59) which rearranged completely within 2 hr at 50°C to furnish ultimately in 60%

![Chemical Reaction](image)

yield. The availability of a benzylic proton in 231 (as compared to a methyl proton in 88) is clearly responsible for the heightened rate of isomerization to 88.

The behavior of 2-phenylcyclohexanone benzenesulfonylhydrazone (42) at these temperatures is essentially comparable, affording 232 in 73%

![Chemical Reaction](image)

yield despite the smaller internal angle which must prevail in the allylic anion.
The need for 2-phenyl ketones led to adaptation of the methodology developed by Sacks and Fuchs for the α-arylation of carbonyl compounds. As an example, cyclooctanone was brominated and converted to tosylhydrazone in conventional fashion. Treatment with phenyl-

copper furnished which in turn smoothly gave (70%) accompanied by lesser amounts of 3-phenylcyclooctene.

Despite such successes, the method is not free of complications. For example, comparable handling of and (60°C, 2 hr) provided exclusively the related olefins. Therefore, in spite of the incipient stabilization of the derived allylic anions, the vinyl anions instead undergo kinetically-controlled protonation by solvent (or other species present). Additionally, we have not found it possible to effect proton migration within the cyclic vinyl anion systems. Although these
limitations do detract from the generality of the synthetic operation,

\[
\begin{align*}
\text{240} & \quad \text{241} & \quad \text{242}
\end{align*}
\]

the methodology does have utilitarian value. Further, its scope may be expanded as knowledge of the controlling factors underlying vinyl-allyl anionic rearrangements is developed.

Although carboxations which are benzylic or \( \beta \) to a C-Si bond are recognized to be inherently stabilized, there appear to be only limited instances where benzylic resonance delocalization has been pitted directly on intramolecular terms against the hyperconjugative ability of silicon. Since phenyl substituted allylsilanes of the present type do allow for examination of this mechanistically informative question (see 243 and 244), several electrophilic reactions were studied by this

\[
\begin{align*}
\text{243} & \quad \text{244}
\end{align*}
\]

author in conjunction with Dr. Y. K. Han in the more conformationally rigid systems where stereoelectronic factors also gain significance.

Simmons-Smith cyclopropanation of 232 gave in 86% yield a stereochemically homogeneous bicyclo[4.1.0]heptane assigned structure 245 on the basis of steric considerations and the appearance of the cyclopropylcarbinyl proton adjacent to silicon as a singlet (\( \delta = 2 \text{ Hz} \)) at \( \delta 0.73 \). Through use of the Karplus equation \( ^{149} \) as modified by Abraham
and Gatti for vicinal couplings to cyclopropane rings ($J_{\text{vic}} = 10 \cos^2 \theta$), it can be shown that the experimentally determined signal width agrees with that calculated for $H_{2\text{exo}}$ in the cis-boat conformation $^{151,152}$. When stirred in acetic acid containing a catalytic quantity of sulfuric acid at $50^\circ C$ for 2 days, $^{245}$ was cleanly converted with

![Chemical Structures]

loss of the trimethylsilyl group to 3-methyl-3-phenylcyclohexene. Thus, the arylcyclopropane, while somewhat unresponsive to ring opening ($^{245}$ is unreactive toward mercuric acetate in aqueous tetrahydrofuran $^{153}$), reacts entirely under the control of the silicon substituent. This behavior, which contrasts with that followed by 1-aryl bicyclo[4.1.0]-heptanes $^{153,154}$ where cleavage operates exclusively in the direction of the benzylic carbon, is attributed to attainment of proper stereoelectronic overlap with the carbon-silicon bond in $^{245}$.

Although epoxidation reactions of allylsilanes are reported to give poorly characterized mixtures of cleavage products in many instances, $^{48a,b,1341,135,155,156}^{232}$ reacted with 40% peracetic acid (pretreated with sodium acetate) to provide $^{247}$ and $^{248}$ in the approximate ratio of 1:1. Since separation of these isomers could not be achieved chromatographically for lability reasons, the unpurified mixture was treated directly with dilute aqueous sulfuric acid at room temperature. There resulted a mixture of $^{249}$ (48%) and $^{250}$ (28%). Allylic alcohol
249 results from acid-promoted 1,3-hydroxyl migration within the initially formed 251, an assumption substantiated by independent submission of authentic 251 to the reaction conditions and an earlier literature report. 157 Jones oxidation of 249 furnished the known 3-phenylcyclohexenone (252). 158 The genesis of 250, a previously described substance, 159 is less easily traced. A possible, though unsubstantiated pathway involves regiospecific opening of 248 toward the phenyl substituent to give 253 which undergoes 1,3-hydroxyl migration to generate 254. Protonolysis of this allylsilane would give 255, the less conjugated precursor of 250.

Thus, the anti epoxide 247 appears to be subject to electronic controls similar to cyclopropane 245. The possible attainment of axial coplanarity within the carbon-oxygen and carbon-silicon molecular fragment of 247 insures ring opening under silicon control to form the
axial alcohol 251 initially. Protonolysis of the syn epoxide 248 is not subject to such exclusive control. Because it lacks stereoelectronically allowed stabilization through the silicon substituent, 248 presumably opens with benzylic stabilization.

\[
\begin{align*}
\text{Me}_3\text{Si} & \quad \text{H}_3\text{O}^+ \\
\text{H} & \quad \text{H}^+ \\
\text{OH} & \quad \sim \text{H}^+ \\
\text{Ph} & \quad \text{Me}_3\text{Si} \\
\text{Ph} & \quad \text{Ph} \\
252 & \quad 253 & \quad 254 & \quad 255 & \quad 250
\end{align*}
\]

Friedel-Crafts acetylation of 232 afforded a reaction mixture consisting of 256-258 in the relative ratio 39:38:23. The three components were obtained pure by preparative layer chromatography and isolated in yields of 32%, 32%, and 19%, respectively. Ketone 258, which was identified by spectral and combustion analysis, is clearly the result of phenyl control during acylation. On the other hand, ketones 256 and 257 are believed to arise from acetylation of the phenylcyclohexenes 259 and 260 which were independently shown to be produced upon exposure.
of $2^{32}$ to Lewis acids such as AlCl$_3$ and TiCl$_4$. While not directly controlling the Friedel-Crafts acylation, the silicon substituent nevertheless dictates the reaction course for the majority of the material.

In a pair of reactions which probably have a sizable free radical component, $2^{32}$ was treated with N-bromosuccinimide in carbon tetrachloride and bromine in cyclohexane. In both instances, a mixture of the biphenyls $261$ and $262$ resulted, although in differing proportions.

![diagram](image)

Lastly, reaction of $2^{32}$ as well as $2^{63}$ with singlet oxygen under dye-sensitized irradiation conditions similar to those described before led to the formation of $2^{68}$ and $2^{49}$ respectively, as the major products after sodium borohydride reduction (Table 11). Elucidation of the electronic controlling factors in this reaction is simplified by the availability of the photooxygenation data for $2^{64}$-$2^{67}$. Since $2^{64}$ and $2^{65}$ are converted to the hydroxyvinylsilanes $2^{70}$ and $2^{71}$, the reaction manifold preferred by the allylsilane moiety is made clear. Photooxygenation of the styrene systems $2^{66}$ and $2^{67}$ have been shown by Jefford and Rimbault to result in retention though transposition of the styrene groups to yield $2^{50}$ and $2^{72}$. Comparison of these data indicate that in the 1-phenyl allylsilanes studied the reaction course is controlled by the phenyl group.
TABLE 11. Photooxyg enation of Allylsilanes

<table>
<thead>
<tr>
<th>Allylsilane</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph(\text{SiMe}_3)</td>
<td>(\text{Ph}^{\text{OH}}\text{SiMe}_3 + \text{Ph}^{\text{OH}})</td>
</tr>
<tr>
<td>265</td>
<td>268 + 262</td>
</tr>
<tr>
<td>Ph(\text{SiMe}_3)</td>
<td>HO(\text{SiMe}_3)</td>
</tr>
<tr>
<td>264</td>
<td>270</td>
</tr>
<tr>
<td>Ph(\text{SiMe}_3)</td>
<td>HO(\text{SiMe}_3)</td>
</tr>
<tr>
<td>266</td>
<td>271</td>
</tr>
<tr>
<td>Ph(\text{SiMe}_3)</td>
<td>(\text{Ph}^{\text{OH}}) + (\text{Ph}^{\text{OH}})</td>
</tr>
<tr>
<td>267</td>
<td>272</td>
</tr>
</tbody>
</table>
In summary, the variety of reaction mechanisms which can operate with different electrophilic reagents and the wide range of prevailing stereoelectronic factors make sweeping generalizations of the preferred reaction mode of cyclic 1-aryl allylsilanes unwarranted.
CHAPTER 2

Introduction

In the development of organic chemistry, the concepts of molecular shape through discrete bonds, and the tetrahedral nature of carbon bonding allowed chemists to visualize the three-dimensional character of molecules. This picture was later refined through improved understanding of free and hindered rotation, ring inversion, pyramidal inversion, and very importantly conformation. This last aspect is still the object of intense research, as much chemistry of a particular system is intimately tied to its conformation. The ability to accurately determine conformations and importantly how to bring about conformational changes within systems provides the chemist with powerful new tools with which to design syntheses.

In this chapter the stereochemical outcome of the addition of singlet oxygen, Br\(^+\), and peracid to four structurally varied 3-norcarenes is investigated to obtain direct insight into prevailing product-determining steric effects in these systems. The various end-products were interconverted chemically to elucidate relative configuration. The stereochemical assignments were established by reference to two 7,7-dibromo epoxides, the structures of which were elucidated by three-dimensional X-ray methods.
These results are then compared with several snoutanes having a fused cyclohexene ring and therefore a 3-norcarene part structure which had entered into "ene" reaction with singlet oxygen and N-methyltriazolinedione with highly stereoselective or completely stereospecific approach to the anti surface (relative to the cyclopropane ring) of the double bond. When epoxidation and bromohydrin formation of these snoutanes was examined, the preferred direction of electrophilic attack was shown to be syn. The causative factors underlying this striking reversal in the stereochemistry of electrophilic additions to the snoutanes are discussed.

Lastly, the preferred conformations of the 3-norcarene epoxides are assessed by $^1$H NMR spectroscopy through analysis of vicinal coupling constants. This information allows the question of epoxide ring anisotropy effects to be addressed.
SECTION 1

Stereochemistry of Electrophilic Additions to 3-Norcarenes

Recently, several papers from this laboratory described the impressively stereocontrolled photooxygenation reactions of 3-norcarenes and norcaradienes which were interpreted in terms of effective quenching by proximate hydrazide functionality.\textsuperscript{161-163} The electronic relaxation of $^1\Delta_g$ singlet oxygen was thought to arise when the ionization potentials of $^1\text{O}_2$, the hydrazide moiety, and the olefinic center, as well as the frontier orbital relationship between them, were properly ordered. Structural assignments to the individual products were made on the basis of their respective $^1\text{H}$ NMR spectra, supportive Eu(fod)$_2$ pseudocontact shifting in selected cases, and chemical interconversions where suitable.

In view of the important implications of these conclusions, it was desirable to further substantiate these observations and test the scope of the phenomenon by more extensive experimentation. Unfortunately, it has not been found possible to duplicate certain fundamental experimental data reported earlier;\textsuperscript{164} also, Kretschmer has shown that various hydrazides are not truly effective in their ability to quench the reactivity of singlet oxygen.\textsuperscript{165,166} Subsequently, it was concluded that some of the original stereochemical assignments were likely in error, despite the large number of experiments addressed previously to this question. Additional work of a totally unequivocal nature was
obviously required and recourse has now been made to complementary three-dimensional X-ray crystallographic analysis. The present section addresses the general question of electrophilic additions (including $^1{O_2}$) to variously substituted 3-norcarene systems.

**3-Norcarene.** Early $^1$H NMR studies of the alicyclic methylene proton region of 273, readily available from the Simmons-Smith cyclopropanation of 1,4-dihydrobenzene, were interpreted as consistent with either a cis-boat (273a) or planar (273b) form for the parent system. Notwithstanding, the trans-boat form (273c) has been widely used to describe the three-dimensional character of 3-norcarene derivatives.

An inspection of molecular models reveals that certain (but not all) eclipsing interactions which prevail in 273a and 273c are avoided when the central ring is planar as in 273b. In this context, Abraham's recent spectral examination of 3-carene (the 3,7,7-trimethyl derivative) is informative. The data show $H_{\text{anti}}$ and $H_{\text{syn}}$ to have vicinal coupling constants of ca 0 and 7.5 Hz, respectively, and a large $J_{\text{gem}}$ value (20.0 Hz); these findings cannot be accounted for in terms of a rapidly interconverting mixture of 3,7,7-Me$_3$-273a and 3,7,7-Me$_3$-273c, but are compatible with the planar conformation 3,7,7-Me$_3$-273b. These deductions contradict those arrived at earlier by Acharya who concluded that 3,7,7-Me$_3$-273c was favored.

\[ \text{273a} \quad \text{273b} \quad \text{273c} \]
The actual conformational situation is almost certainly one in which the energy separating the three forms is low (barring excessive steric constraints), such that rapid mutual interconversion operates during any intended chemical transformation. Consequently, predictions concerning the stereoselectivity of attack at the double bond must necessarily be clouded with uncertainty in most instances. The large degree of confusion which has surrounded the simple epoxidation of (+)-3-carene speaks clearly to this point.169a,b,172-173

When a continuously oxygenated dilute solution of 273 and rose bengal in dichloromethane-methanol (9:1) was irradiated with a Sylvania DYV light source and the resulting allylic hydroperoxide was directly reduced with sodium borohydride, an isomerically pure alcohol was isolated whose spectral properties showed it to be either 274 or 275. Since the stereochemical outcome of this highly stereoselective process could not be ascertained unequivocally from the \textsuperscript{1}H NMR data, two additional sets of convergent experiments were initiated (Scheme XVI). In the first, 273 was oxidized with \textit{m}-chloroperbenzoic acid in dichloromethane buffered with solid sodium bicarbonate at 25°C and two epoxides, easily separated by vapor phase chromatography, were determined to be present in a 62:38 ratio. As can be seen in Figure 8, the cyclopropyl methylene protons of the major component (top) appear as two widely separated multiplets centered at δ -0.4 and +0.7 (the latter signal overlaps with those due to H\textsubscript{1} and H\textsubscript{6}), while the same pair in the minor isomer (bottom) resonate closer together at 0.26 and 0.62 (with major H\textsubscript{1},H\textsubscript{6} overlap).
SCHEME XVI. Electrophilic additions to 3-norcarene

FIGURE 8. $^1$H NMR spectra of 3-norcarene oxides $^{276}$ (top) and $^{277}$ (bottom) (60 MHz, CDCl$_3$, CH$_2$Cl$_2$ as internal standard).
On the strength of earlier work by Tori and coworkers\textsuperscript{176} who have shown that the bridge protons in \textit{exo}-norbornene oxide, \textit{exo}-norbornadiene oxide, \textit{exo}-benzonorbornadiene oxide, and \textit{endo} are widely spaced while those in endo isomer \textit{281} nearly overlap, we originally considered the major component to be the syn isomer \textit{277}. To gain further evidence for these assignments, recourse was made to Eu(fod)\textsubscript{3} pseudocontact shifting. With the epoxide oxygen as the only Lewis basic functionality, the simplified version of the McConnell-Robertson equation\textsuperscript{177,178}

\[
\delta = \frac{K(3\cos^2 \beta - 1)}{r^3}
\]

was deemed applicable, given the anticipated presence of an axially symmetric dipolar magnetic field. For our models, the europium atom was placed 2 Å from the oxygen in the plane of the oxirane ring and bisecting the \$\text{CCO}\$.\textsuperscript{179} Tables 12 and 13 summarize the shift sequences calculated for three conformations each of \textit{276} and \textit{277}. The relevant distances and angles were obtained with Dreiding models. Strikingly, we see that the extended boat conformations of \textit{276} and \textit{277} as well as the planar forms of both isomers lead to almost identical predictions, the exception being the relative ordering of H\textsubscript{1}. In contrast, the two
TABLE 12. Calculated Paramagnetic Shifts for 276

<table>
<thead>
<tr>
<th>Structure</th>
<th>Proton</th>
<th>R, Å</th>
<th>R^3</th>
<th>θ, deg</th>
<th>3cos^2θ-1</th>
<th>R^3 x 10^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>H_3</td>
<td>3.9</td>
<td>59.3</td>
<td>14</td>
<td>1.82</td>
<td>3.07</td>
<td></td>
</tr>
<tr>
<td>H_{2syn}</td>
<td>5.2</td>
<td>141</td>
<td>18</td>
<td>1.71</td>
<td>1.22</td>
<td></td>
</tr>
<tr>
<td>H_{2anti}</td>
<td>4.6</td>
<td>97.3</td>
<td>21</td>
<td>1.62</td>
<td>1.65</td>
<td></td>
</tr>
<tr>
<td>H_1</td>
<td>3.7</td>
<td>50.6</td>
<td>62</td>
<td>-0.34</td>
<td>-0.67</td>
<td></td>
</tr>
<tr>
<td>H_{7endo}</td>
<td>5.9</td>
<td>205</td>
<td>32</td>
<td>1.16</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td>H_{7exo}</td>
<td>5.7</td>
<td>185</td>
<td>54</td>
<td>0.04</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

Predicted sequencing: H_3, H_{2anti}, H_{2syn}, H_{7endo}, H_{7exo}, H_1.

<table>
<thead>
<tr>
<th>Predicted sequencing: H_3, H_{2anti}, H_{2syn}, H_1, H_{7exo}, H_{7endo}.</th>
</tr>
</thead>
<tbody>
<tr>
<td>H_3</td>
</tr>
<tr>
<td>H_{2syn}</td>
</tr>
<tr>
<td>H_{2anti}</td>
</tr>
<tr>
<td>H_1</td>
</tr>
<tr>
<td>H_{7endo}</td>
</tr>
<tr>
<td>H_{7exo}</td>
</tr>
</tbody>
</table>

Predicted sequencing: H_3, H_{2anti}, H_{2syn}, H_{7endo}, H_{7exo}, H_1.
TABLE 13. Calculated Paramagnetic Shifts for 277

<table>
<thead>
<tr>
<th>Structure</th>
<th>Proton</th>
<th>R, Å</th>
<th>R³</th>
<th>θ, deg</th>
<th>3cos²θ-1/R³ x 10²</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₃</td>
<td>3.9</td>
<td>59.3</td>
<td>15</td>
<td>1.80</td>
<td>3.04</td>
</tr>
<tr>
<td>H₂syn</td>
<td>3.5</td>
<td>42.9</td>
<td>33</td>
<td>1.11</td>
<td>2.59</td>
</tr>
<tr>
<td>H₂anti</td>
<td>4.6</td>
<td>97.3</td>
<td>16</td>
<td>1.77</td>
<td>1.82</td>
</tr>
<tr>
<td>H₁</td>
<td>6.0</td>
<td>216</td>
<td>22</td>
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<td>0.73</td>
</tr>
<tr>
<td>H₇endo</td>
<td>4.8</td>
<td>111</td>
<td>47</td>
<td>0.40</td>
<td>0.36</td>
</tr>
<tr>
<td>H₇exo</td>
<td>6.5</td>
<td>274</td>
<td>40</td>
<td>0.76</td>
<td>0.28</td>
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Predicted sequencing: H₃, H₂syn, H₂anti, H₁, H₇endo, H₇exo

<table>
<thead>
<tr>
<th>Structure</th>
<th>Proton</th>
<th>R, Å</th>
<th>R³</th>
<th>θ, deg</th>
<th>3cos²θ-1/R³ x 10²</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₃</td>
<td>3.9</td>
<td>59.3</td>
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<td>1.80</td>
<td>3.04</td>
</tr>
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<td>1.71</td>
<td>2.01</td>
</tr>
<tr>
<td>H₂anti</td>
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<td>140</td>
<td>17</td>
<td>1.74</td>
<td>1.24</td>
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<tr>
<td>H₁</td>
<td>4.8</td>
<td>111</td>
<td>48</td>
<td>0.34</td>
<td>0.31</td>
</tr>
<tr>
<td>H₇endo</td>
<td>1.9</td>
<td>6.86</td>
<td>31</td>
<td>1.20</td>
<td>17.5</td>
</tr>
<tr>
<td>H₇exo</td>
<td>3.0</td>
<td>27</td>
<td>72</td>
<td>-0.71</td>
<td>-2.64</td>
</tr>
</tbody>
</table>

Predicted sequencing: H₇endo, H₃, H₂syn, H₂anti, H₁, H₇exo

<table>
<thead>
<tr>
<th>Structure</th>
<th>Proton</th>
<th>R, Å</th>
<th>R³</th>
<th>θ, deg</th>
<th>3cos²θ-1/R³ x 10²</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₃</td>
<td>3.9</td>
<td>59.3</td>
<td>15</td>
<td>1.80</td>
<td>3.04</td>
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<tr>
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<td>3.9</td>
<td>59.3</td>
<td>31</td>
<td>1.20</td>
<td>2.02</td>
</tr>
<tr>
<td>H₂anti</td>
<td>5.1</td>
<td>132</td>
<td>16</td>
<td>1.77</td>
<td>1.34</td>
</tr>
<tr>
<td>H₁</td>
<td>5.9</td>
<td>205</td>
<td>38</td>
<td>0.86</td>
<td>0.42</td>
</tr>
<tr>
<td>H₇endo</td>
<td>3.4</td>
<td>39.3</td>
<td>56</td>
<td>0.062</td>
<td>0.16</td>
</tr>
<tr>
<td>H₇exo</td>
<td>5.2</td>
<td>141</td>
<td>58</td>
<td>-0.16</td>
<td>-0.11</td>
</tr>
</tbody>
</table>

Predicted sequencing: H₃, H₂syn, H₂anti, H₁, H₇endo, H₇exo
cis boat conformations differ appreciably, the predicted position of \( H_{7\text{endo}} \) being diametrically opposite in the two series.

At the experimental level, the intrinsic LIS parameters of the major epoxide (\( H_3 > H_{2\text{anti}} > H_{2\text{syn}} > H_1 > H_{7\text{endo}} > H_{7\text{exo}} \)) were seen to differ significantly from those of the minor isomer (\( H_3 > H_{7\text{endo}} > H_{2\text{syn}} > H_{2\text{anti}} > H_1 > H_{7\text{exo}} \)). Although alterations in substrate conformation are known to occur upon coordination to lanthanide ions and such effects must be given their due consideration, these data are best accommodated if the prior working assumption of epoxide stereochemistry is reversed.

As a means of resolving this dilemma, 7,7-dibromonorcarene (282) was subjected to epoxidation (Scheme XVII). The lone epoxide which was produced was established to be the anti isomer 283 by X-ray crystallographic analysis performed by Schuman, Beno, and Christoph (see Figure 9 and Appendix A). Tri-n-butylin hydride reduction of 283 which could be cleanly accomplished under a variety of conditions, resulted in high yield conversion to the major norcarene epoxide which, as a result, must necessarily be formulated as the anti isomer. syn-7,7-Dibromonorcarene oxide (285) was produced exclusively from 282 by the action of N-bromosuccinimide in aqueous glyme, followed by cyclization of bromohydrin 284 with sodium hydride in refluxing tetrahydrofuran. Comparable treatment of 273 afforded 278 and 279 in a 13:87 ratio. It can therefore be concluded of the previous spectroscopic tests that lanthanide induced shift techniques were reliable while those chemical shift criteria customarily applied to the \(^1\)H NMR analysis
FIGURE 9. Final X-ray structures of 293 (a) and 283 (b) showing the transoid configuration of the cyclopropane and epoxide rings across the approximately planar six-membered ring. The atomic numbering is that used in Table 19 and Table 20 in Appendix A; one half of the molecule is related to the other by a mirror plane containing C(1) and O.
SCHEME XVII. Electrophilic addition to 7,7-dibromonorcarene

of epoxides were not. The apparent lack of conventionality in the latter area will be discussed in Section 3.

Ring opening of 276 with lithium diethylamide proceeded smoothly to give 274, the product of 3-norcarene photooxygenation. Epoxide 277 was similarly converted to 275 providing the opportunity to demonstrate that the syn allylic alcohol was not a contaminant in the photooxygennation product (the isomers are distinctive on VPC).

The pair of bromine atoms in 282 appear to generate sufficient steric hindrance on the syn face of the molecule to direct electrophilic attack exclusively anti. In the absence of the halogens, anti attack remains kinetically favored but at a reduced level. Epoxidation of 282 is the least stereoselective reaction (62% anti), followed by bromonium ion formation (87% anti). Allylic hydroperoxidation with $^1$O$_2$ is fully stereoselective.

1,6-Dimethyl-3-norcarene. The second line of inquiry dealt with 288, prepared conveniently by regioselective dibromocarbene addition to
the Birch reduction product (286) of \( \beta \)-xylene and dehalogenation of \( \textbf{287} \) with sodium in liquid ammonia. The methyl groups in \( \textbf{288} \) introduce nonbonded steric interactions (see Newman projections in Figure 10)

which could lower the energy of cis-boat conformer \( \textbf{288a} \) relative to those of \( \textbf{288b} \) and \( \textbf{288c} \). Were this factor uniquely influential, 1,6-dimethyl substitution might lessen the energy requirements for anti attack. However, the X-ray crystallographic findings described later point to the likelihood that the transition state structures for the reactions being utilized might well be planar in the central ring, i.e., most closely related to \( \textbf{273b} \) and \( \textbf{288b} \). If so, then the pendant methyl groups could have an untoward effect on the energetics of the anti pathway.

\[\text{FIGURE 10. Newman projections for 1,6-dimethylnorcarene}\]
The singlet oxygenation of 288 produced the allylic alcohol 289 with 10% stereoselectivity (Scheme XVIII). Proof of the indicated stereochemistry was achieved as before by epoxidation of the hydro-

[Diagrams of molecular structures are shown with arrows indicating chemical reactions and intermediates.]

SCHEME XVIII. Electrophilic additions to 1,6-dimethylnorcarenes

carbon, separation of the isomers, and base-promoted opening. Under our standardized conditions, the relative amounts of 291 and 292 proved to be 74:26. Individual treatment of the pure isomers gave 289 and 290, respectively. Application of the NBS-aqueous glyme epoxide inversion scheme to 288 gave 295 and 296 in the ratio 17:83. Therefore, the presence of methyl groups at positions 1 and 6 does little to alter
the stereochemical course of electrophilic additions to the $\pi$ bond (relative to 273).

As Figure 11 illustrates, anti epoxide 291 shows a sharp singlet absorption of area 2 at $\delta$ 0.07 for its cyclopropyl methylene protons, whereas syn epoxide 292 exhibits the same two protons at widely different chemical shifts ($\delta$ -0.20 and +0.97). Because these patterns are the reverse of those previously seen with the 3-norcarene oxides (Figure 8), concern was raised for the accuracy of our assignments and the behavior of dibromide 287 was investigated.

FIGURE 11. $^1$H NMR spectra of 1,6-dimethylnorcarene oxides 291 (bottom) and 292 (top) (60 MHz, CDCl$_3$, CH$_2$Cl$_2$ as internal standard)

The epoxidation of 287 gave rise only to 293, the stereochemistry of which was again confirmed by the X-ray analysis of Schuman, Beno,
and Christoph (see Figure 9 and Appendix A). The isomeric epoxide 294 was obtained cleanly via bromohydrin 293. Tri-n-butyltin hydride reduction of 293 furnished 291.

Again, we see that the 1H NMR spectra of the epoxides demand further interpretation. No such difficulties appear to complicate the spectra of the epimeric 2-norcarene alcohols. This may be because a single pseudo-boat conformation is adopted by these molecules in order to maximize overlap of the 1,7-sigma bond with the p orbital at C2. Thus, the olefinic hydrogens of anti alcohols 274 and 289 are characterized by distinctive chemical shifts and multiplicities. For example, both components of the olefinic region are basically doublets; however, the one at lower field is more extensively spin coupled with neighboring protons than that found at ca δ 5.3. The Δδ of the absorptions is 0.3-0.4 ppm. In contrast, the syn alcohols show greater multiplicity in their more upfield olefinic proton signal.

[4.3.1]Propell-3-ene. To determine if annulation effects would be influential in modifying stereoselectivity, [4.3.1]propell-3-ene (299) was utilized as the basis of comparison. Whereas the direct epoxidation of 299 produced 303 and 305 in a 69:31 ratio and the indirect pathway via 307 and 308 generated a 7:93 mixture of the same tetracyclic epoxides, dibromide 300 was converted exclusively to 304 and to 306 (via 302) (Scheme XIX). With the assumption that the bromine atoms exert their usual overwhelming steric effect, the structural assignments to the dibromo epoxides was considered established. These were converted to 303 and 305 by tin hydride reduction and the latter were transformed into the isomerically pure allylic alcohols
301 and 302. To complete the sequence, 299 was photooxygenated; this reaction gave only 301.

\[ \text{O}_2 \xrightarrow{\text{LiNEt}_2} 301 \]

\[ \text{NBS, H}_2\text{O, glyme} \xrightarrow{\text{NaH, THF}} 303, R = H \quad 304, R = Br \]

\[ \text{RCO}_3\text{H} \xrightarrow{\text{LiNEt}_2} 307, R = H \quad 308, R = Br \]

SCHEME XIX. Electrophilic addition to [4,3,1]propell-3-ene

The stereochemical consequences of epoxidation, bromohydrin formation, and allylic hydroperoxidation reveal 273, 288, and 299 to be consistently more disposed to attack from the direction anti to the cyclopropane ring under conditions of kinetic control. There is seen throughout the series a gradual progression in the level of anti stereoselectivity which is lowest when epoxidation is involved and a maximum in the singlet oxygen examples. Such effects do not speak directly to the mechanism of the \(^1\text{O}_2\) reactions, although they likely do have a direct bearing on the fact that singlet oxygen is the only reagent of the
three which must abstract an allylic hydrogen to deliver product. The base of the cyclopropane ring must be approached more closely and the well known sensitivity of singlet oxygen to prevailing steric factors is made apparent.

The $^1$H NMR spectra of 303 and 305 (Figure 12) continue to exhibit highly pertinent features. Thus, the environment of $H^\text{exo}$ in the anti epoxide is such that increased shielding occurs relative to the syn isomer. Contrariwise, $H^\text{endo}$ in 305 is significantly down-field shifted. The spectra of allylic alcohols 301 and 302 follow the trend discussed earlier (see Experimental).

![Figure 12](image)

**FIGURE 12.** $^1$H NMR spectra of [4.3.1]propell-3-ene oxides 303 (top) and 305 (bottom) (60 MHz, CDCl$_3$, CH$_2$Cl$_2$ as internal standard)

**7,7-Dimethyl-3-norcarene.** In an effort to link the above findings more closely to earlier work with (+)-3-carene, the 7,7-dimethyl
derivative 310 was prepared through reaction of 282 with lithium dimethyl cuprate. When subjected to epoxidation, 310 was converted to anti epoxide 311, the 100% stereoselectivity paralleling that observed earlier with dibromide 282. A sample of 312 was prepared via the bromohydrin. These configurational assignments are based upon 1H NMR spectra (Figure 13) which conform to those obtained for the 3-carene oxides. In the case of 311, two widely spaced methyl singlets are immediately apparent; the NMR results for 312 show two nearly overlapping methyl signals.

Not unexpectedly, singlet oxygenation of 310 produced only 312. The pair of allylic alcohols became independently available by treatment of 311 and 312 with phenylselenide anion and oxidative elimination of the β-seleno alcohols with hydrogen peroxide. 2-Norcarenes which carry a syn methyl group at C7 are believed to relieve intramolecular crowding by adopting a pseudo-chair conformation rather than the customarily favored pseudo-boat shape. This leads to marked alterations in the chemical shifts of the olefinic protons such that merging of the two signals into a multiplet of rather narrow width at
FIGURE 13. $^1$H NMR spectra of 7,7-dimethylnorcarene oxides 311 (top) and 312 (bottom) (60 MHz, CDCl₃, CH₂Cl₂ as internal standard).

An intermediate field position obtains. The spectra of 313 and 314 do not deviate from this norm.
SECTION 2
Stereoreversed Electrophilic Additions to 3-Norcarenes

The preceding investigation has shown that electrophilic additions to a series of 3-nor­carene derivatives proceed with a decided stereochemical preference for initial attack anti to the cyclopropane ring. The allylic hydroperoxidations with singlet oxygen proved to be stereospecific, whereas epoxidation and bromohydrin formation were 62-95% stereoselective depending upon the substrate. The simple mechanistic picture to emerge is that the conformationally flexible hydrocarbons experience predominant or exclusive capture of the electrophilic reagent on that molecular surface opposite to the cyclo­propane ring for the usual steric reasons. Since the stereoselectivity was uniformly in one direction, it was not possible to recognize any characteristics of those electrophilic reagents examined which may be regarded as distinctive. This section compares a companion study investigated by Dr. G. Kretschmer to our earlier work in which 3-nor­carene derivarives chosen with the intent of incorporating only a small additional structural perturbation are shown to undergo striking stereochemically reversed electrophilic behavior in a number of in­stances. Because the product-determining transition states are now imbalanced, certain interesting features which distinguish the steric demands of singlet oxygen and other "enophiles" from the more usual electrophilic species are made apparent.
The substrates for this study are $315-318$, commonly referred to as snoutanes, in which the 3-norcarene unit is built into the right hand side. As with simpler norcarenes, the double bond in $315-318$

\[ R_1 = R_4 = OCH_3, \]
\[ R_2 = R_3 = H \]
\[ R_1 = R_2 = R_3 = R_4 = H \]

is amenable to syn and anti attack (the cyclopropane ring comprises the point of reference). The added structural perturbation is located on the anti surface of the π bond and is positioned somewhat remotely from the reaction center. The rigid geometry in the snoutane component of the molecules $315, 316$, and $317$ serves to predispose the ethano bridge in $317$ and the aromatic ring in $315$ and $316$ to a relatively invariant position in space. The principal alteration is electronic. Thus, the benzo ring in $315$ is quite electron rich while that in $316$ is much less so. The bridge in $317$ has no π electrons. The urazole bridged snoutane $318$ is free to undergo pyramidal inversion at nitrogen and is predisposed with lone electron pairs. On this basis, the IP's of these molecules can be expected to vary widely.

The conformational properties of $315-318$ in the vicinity of the 3-norcarene part structure were not amenable to spectral analysis. Not
only were the signals due to the allylic protons complex, but they
overlapped uniformly with several cyclopropyl hydrogen absorptions at
60 and 100 MHz.

The electrophilic reactions examined by Kretschmer with \textsuperscript{315-318} were identical to those of the previous study with two additions.
Compounds \textsuperscript{315} and \textsuperscript{318} were exposed to N-methyltriazolinedione (MTAD) which, like \textsuperscript{1}O\textsubscript{2}, readily enters into "ene" reactions and should therefore provide an additional point of reference. The stereochemistry of all products from electrophilic addition was determined by spectral characteristics held in common with the earlier 3-norcarene products. \textsuperscript{166}

A summary of results from the study described in Section 1, Chapter 2 is included in Table 14 for comparison purposes, while results from compounds \textsuperscript{315-318} are included in Table 15.

With this evidence in hand, we see that \textsuperscript{1}O\textsubscript{2} and MTAD show a strong predilection to attack the 3-norcarene part structure of the snoutanes from the anti direction. The sole example where complete stereospecificity is not witnessed is the singlet oxygenation of \textsuperscript{315}. These stereochemical observations entirely parallel the characteristics previously determined for simpler 3-norcarenes. The reversed stereoselectivity presently found for peracid oxidation and NBS bromination stands in contrast with the previous findings. This absence of stereochemical commonality in the product ratios is believed to have its origins in certain structural features unique to the snoutanes.

The mechanistic significance of the present results may best be grasped by reference to the four transition state representations \textsuperscript{319-322}
TABLE 14. Stereochemistry of Electrophilic Addition to the Norcarenes

<table>
<thead>
<tr>
<th>Norcarene</th>
<th>Singlet Oxygen</th>
<th>NBS, H₂O glyme</th>
<th>MCPBA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>syn  anti</td>
<td>syn anti</td>
<td>syn anti</td>
</tr>
<tr>
<td><img src="image1" alt="Norcarene" /></td>
<td>0 100</td>
<td>13 87</td>
<td>38 62</td>
</tr>
<tr>
<td><img src="image2" alt="Norcarene" /></td>
<td>0 100</td>
<td>17 83</td>
<td>26 74</td>
</tr>
<tr>
<td><img src="image3" alt="Norcarene" /></td>
<td>0 100</td>
<td>7 93</td>
<td>31 69</td>
</tr>
<tr>
<td><img src="image4" alt="Norcarene" /></td>
<td>0 100</td>
<td>0 100</td>
<td>0 100</td>
</tr>
</tbody>
</table>
TABLE 15. Stereochemistry of Electrophilic Additions to the Various Snoutanesa

<table>
<thead>
<tr>
<th>Snoutane Bridge Substitution</th>
<th>Singlet Oxygen syn anti</th>
<th>NBS, H2O glyme syn anti</th>
<th>MCPBA syn anti</th>
<th>MTAD syn anti</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCH3</td>
<td>21 79b</td>
<td>62 38</td>
<td>100c 0</td>
<td>0 0 100</td>
</tr>
<tr>
<td>CH3</td>
<td>0 100</td>
<td>67 33</td>
<td>100 0</td>
<td>-- --</td>
</tr>
<tr>
<td>CH3</td>
<td>0 100</td>
<td>-- --</td>
<td>66 34</td>
<td>-- --</td>
</tr>
<tr>
<td>R</td>
<td>0 100</td>
<td>82 18</td>
<td>92 8</td>
<td>0 100</td>
</tr>
</tbody>
</table>

a Relative percentage values are given for all products after physical separation of the isomers had been achieved. bA small amount of an overoxygenation product was also isolated. cBoth possible epoxides shown to be partially decomposed under the conditions of purification.
shown in Figure 14. For illustrative convenience, (unsymmetrical)

![Chemical Structures](image1)

FIGURE 14. Electrophilic transition state representations for snoutanes perepoxide structures have been employed in the singlet oxygen formulations. Rationalization of the experimental results requires that different kinetic preferences be shown in attacking the syn and anti faces of the 3-norcarene double bond in the snoutanes, which phenomenon does not prevail in simpler analogs where anti bonding proceeds exclusively. Access of $^{1}O_2$ and MTAD to that surface of the π bond shared by the cyclopropane ring has remained hindered, whereas NBS and m-chloroperbenzoic acid actually prefer syn attack by a significant margin. An attractive
working hypothesis views the "tying back" of the norcaranyl cyclopropane through bonding to the second three-membered ring as a non-perturbing factor in the maintenance of the planar cyclohexene conformation generally preferred by 3-norcarenes. With the added assumption that the transition states in question are reactant-like, one would expect from consideration of molecular models that the steric environment for syn attack by NBS and \( m \)-chloroperbenzoic acid is less congested than that associated with anti attack. Given the transition state descriptions generally accepted for this pair of reactions, the bulk of the reagent is seen not to manifest itself in the close proximity of the double bond, but at a somewhat more remote distance. Consequently, in the syn transition state exemplified by \( 3\text{a}2 \text{a} \), the proximal cyclopropyl hydrogen offers appreciably less steric impedance to attack than the substituted ethano bridge in the anti transition state \( 3\text{a}2 \text{b} \). In the latter instance, geometric and proximity factors combine to cause the buildup of serious steric interference as illustrated. Such considerations conform to our knowledge of typical one-step cyclic additions where steric factors present in the reactant are frequently determinative of stereochemistry. The exo/endo ratio of 200:1 observed for the epoxidation of norbornene is exemplary. The "ene" reagents typified by \( ^1\text{O}_2 \) and MTAD depend upon the availability of at least one allylic C-H bond which is properly aligned stereoelectronically with the \( p\alpha \) orbitals of the double bond. Such a necessary condition requires that the atom comprising the negative terminus of the "ene" dipole approach the allylic hydrogen to effect
its ultimate migration. This precondition for effective reaction necessitates a particular orientation of the "enophile" as shown for singlet oxygen in 321 and 322. In the syn bonding process, the reagent must enter into the immediate vicinity of the cyclopropane ring (see 321). This event presents steric constraints of much greater magnitude than those prevailing during anti attack as a direct result of the greater remoteness of the ethano bridge in 322.

At this point, it becomes important to recognize not only the high sensitivity of singlet oxygen to steric factors, but also the various ways in which such effects can develop within differently constructed cyclic olefins. In cases where the allylic hydrogen is positioned on a pendant methyl group as in 323, the trailing perepoxide oxygen must actually be oriented away from the region of major steric interference (cf 324). Nonetheless, the composition of the allylic alcohol product mixture 325 is 98.5% exo and only 1.5% endo. Since

\[
\begin{array}{c}
\text{323} \\
\text{CH}_3
\end{array} \rightarrow \begin{array}{c}
\text{324} \\
\text{CH}_2
\end{array} \rightarrow \begin{array}{c}
\text{325} \\
\text{CH}_2
\end{array}
\]

this ratio is less than that observed upon epoxidation of norbornene, the cyclic "ene" transition state has been characterized as "loose."188 The entire range of available data including the present results are not consistent with such a mechanistic picture. Care must be taken to draw comparisons between like processes. Not surprisingly then, the snoutanes undergo "ene" reactions only from the far less congested
anti direction, since the allyl hydrogen abstraction process must proceed \textit{internally} within the existing six-membered ring (see 321 and 322).

Syn approach to 315-318 is apt to be minimally perturbed by the extensively varied electronic features which have been purposefully positioned on the snoutane bridge. Any stereoelectronic control of syn transition states of the type observed recently by Mukai\textsuperscript{189} and Paquette\textsuperscript{190} and their coworkers should therefore be negligible. Of the examples where anti attack is favored, the reaction of 1,4-dimethoxybenzene derivative 315 with singlet oxygen is the only one which is not fully stereoselective. This result may be a consequence of the fact that the trailing negatively charged oxygen is required to be projected into the vicinity of the electron-rich aromatic ring. Under these circumstances, untoward electronic forces may arise to a degree sufficient to cause syn attack to become competitive.

Finally, the present observations attest to the fact that the urazole ring is not capable of quenching $^1O_2$, despite its often favorable ionization potential (8.0 eV for 318) relative to cyclohexene (> 9 eV) and other olefinic \pi bonds, and the appropriate antisymmetric nature of its highest occupied orbital (\textit{n}). This factor distinguishes urazoles from amines which are known to quench $^1O_2$ physically\textsuperscript{191} at rate constants which increase as the individual ionization potentials decrease,\textsuperscript{192} as well as other good electron donors such as sulfides,\textsuperscript{193} phenols,\textsuperscript{192g} and azides.\textsuperscript{194} The carbonyl groups adjacent to the urazole nitrogens have been shown to exert a powerful electron-withdrawing effect.\textsuperscript{165,195} Presumably as a consequence of such deactivation, this ability to quench singlet oxygen is lost.
SECTION 3
Long Range Epoxide Ring Anisotropy

The magnetic anisotropy effects of cyclopropane rings has been a subject of immediate concern to a number of investigators for almost two decades. Initially, the high shifts of protons directly bonded to three-membered carbon rings were attributed to a ring current effect,\textsuperscript{196} a concept also utilized at that time to rationalize long-range shielding phenomena.\textsuperscript{197} This theory was never firmly established and more recent work has resulted in development of more semi-quantitative treatments.\textsuperscript{198} The two hypotheses which have emerged are referred to as the group anisotropy and bond anisotropy models (Figure 15). In the latter instance, the contour of the

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{cyclopropane_models.png}
\caption{Cyclopropane anisotropy models}
\end{figure}
magnetic field arises from the combined fields of the three cyclopropane C-C bonds, and a proton which finds itself on a line which makes an angle greater than 55° to the center of the nearest cyclopropane bond should experience anisotropic shielding. According to the group anisotropy model, a proton positioned at an angle less than 55° with the plane of the cyclopropane ring at its center should be deshielded. Therefore, the models can be distinguished only when a proton falls into that rather limited region of space where the screening predictions differ in sign. Hahn and Howard have acquired experimental data which agree completely with group anisotropy theory and have concluded that this concept is the superior one in its present application.\textsuperscript{199}

NMR studies on epoxides have been more limited and have not lent themselves as conveniently to a model. At first, it was believed that epoxide rings exerted magnetic anisotropic effects comparable to those of their cyclopropane congeners. However, later work\textsuperscript{176} showed this assumption to be incorrect. Tori and his coworkers concluded that a proton situated above the plane of the ring is more shielded, whereas a proton located near the plane or in the neighborhood of the heteroatom is less shielded. However, their data base was quite limited. More recent investigations now suggest that shielding above and below the plane of an epoxide ring can be expected except when the proton is close to the oxygen atom, in which case deshielding results.\textsuperscript{200,201} At least two supportive\textsuperscript{13} C NMR studies have become available.\textsuperscript{202}
For the present purposes, it is also important to recognize that H<sub>7endo</sub> in simple 7-substituted norcaranes such as 315<sub>a</sub> and 315<sub>b</sub> resonate at higher field than their H<sub>7exo</sub> counterparts in 316<sub>a</sub> and 316<sub>b</sub>, respectively. For example, H<sub>7</sub> appears as a multiplet at δ 0.6-0.3 in

![Diagram](image)

315<sub>a</sub>, R = CH<sub>3</sub>  
316<sub>a</sub>, R = CH<sub>3</sub>

and at δ 0.7-0.9 in 316<sub>b</sub>. The methyl groups, on the other hand, are nearly indistinguishable (δ 0.96 and 0.94, respectively). Apparently, H<sub>7endo</sub> is subjected to various local diamagnetic anisotropy effects generated by the C-C bonds of the cyclohexane ring.

On this basis, the NMR results for 276 which reveal H<sub>7endo</sub> to resonate above TMS can be considered consistent only with an enhanced diamagnetic contribution from the carbon atoms of the epoxide ring. The protons bonded to the identical C<sub>2</sub>C<sub>5</sub> methylene groups of this molecule should in principle permit, by analysis of their vicinal spin-spin interactions, a direct assessment of the dominant conformation. To this end, use has been made of the Karplus equation as modified by Abraham and Gatti for vicinal couplings to cyclopropane rings (J = 10 cos<sup>2</sup>θ). Vicinal coupling to epoxide protons were calculated with an equation modified by Casadevall et al. from earlier work of Forest and Tori (J = 4 cos<sup>2</sup>θ). The results for 276 are summarized in Table 16. The experimentally determined couplings are J<sub>endo</sub> ≈ 3-4 Hz and J<sub>exo</sub> ≈ 8 Hz. Comparison of the observed coupling constants
TABLE 16. Calculated Coupling Constants for 276

<table>
<thead>
<tr>
<th></th>
<th>H_2endo</th>
<th>H_2exo</th>
<th>H_2endo</th>
<th>H_2exo</th>
<th>H_2endo</th>
<th>H_2exo</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\phi^a)</td>
<td>130°</td>
<td>15°</td>
<td>55°</td>
<td>70°</td>
<td>90°</td>
<td>30°</td>
</tr>
<tr>
<td>(J_{1,2}^b)</td>
<td>4.1</td>
<td>2.4</td>
<td>3.3</td>
<td>1.2</td>
<td>0</td>
<td>7.5</td>
</tr>
<tr>
<td>(\phi^c)</td>
<td>77°</td>
<td>45°</td>
<td>7°</td>
<td>125°</td>
<td>30°</td>
<td>90°</td>
</tr>
<tr>
<td>(J_{2,3})</td>
<td>0.2</td>
<td>2.0</td>
<td>3.2</td>
<td>1.3</td>
<td>3.0</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^a\) Dihedral angle of the cyclopropyl proton with the methylene proton.
\(^b\) Dihedral angle of the epoxide proton with the methylene proton.
\(^c\) The larger coupling constant is underlined when coupling to cyclopropyl and epoxy protons is possible.

with the calculated values in Table 16 show a nice match with the values corresponding to the planar conformation. The calculated values for the cis-boat conformation, showing nearly equal \(J^e\)'s, clearly do not agree. The values calculated for the trans-boat conformation more closely fit; however, they give too large a \(J^e\) value.

The assignment of \(H_2endo\) and \(H_2exo\) to the methylene signals must be made carefully. For 276 and 277, they have been determined through LIS \(\Delta\delta\) measurements. In syn-epoxide 277, \(H_2endo\) has a greater \(\Delta\delta\) than \(H_2exo\); conversely with anti-epoxide 276, \(\Delta\deltaH_2exo > \Delta\deltaH_2endo\). These results place the methylene proton syn to the epoxide ring at lower field relative to the anti proton. Thus when the syn-anti
epoxide pair 276 and 277 is compared, cross-over in methylene signal assignments is observed.

Next, the calculated coupling constants for 277 are listed in Table 17. The agreement between the experimental results ($J_{2\text{endo}} \approx$ $J_{2\text{exo}} \approx 1-2$ Hz and $J_{2\text{exo}} \approx 5-7$ Hz) and the planar conformation are again easily seen. Neither possible boat conformation closely approximates the results.

To illustrate the possibly confusing relative position, syn-epoxide 312 is analyzed next (see values of Table 17). This epoxide sterically must adopt the trans-boat conformation. The observed coupling constants

TABLE 17. Calculated Coupling Constants for 277

<table>
<thead>
<tr>
<th></th>
<th>$H_{2\text{endo}}$</th>
<th>$H_{2\text{exo}}$</th>
<th>$H_{2\text{endo}}$</th>
<th>$H_{2\text{exo}}$</th>
<th>$H_{2\text{endo}}$</th>
<th>$H_{2\text{exo}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\phi^a$</td>
<td>140°</td>
<td>20°</td>
<td>57°</td>
<td>62°</td>
<td>90°</td>
<td>30°</td>
</tr>
<tr>
<td>$J_{1,2}$</td>
<td>5.0°</td>
<td>5.5</td>
<td>2.9</td>
<td>2.2</td>
<td>0</td>
<td>7.5</td>
</tr>
<tr>
<td>$\phi^b$</td>
<td>130°</td>
<td>15°</td>
<td>48°</td>
<td>66°</td>
<td>85°</td>
<td>30°</td>
</tr>
<tr>
<td>$J_{2,3}$</td>
<td>1.7</td>
<td>3.8</td>
<td>1.8</td>
<td>0.6</td>
<td>0</td>
<td>2.7</td>
</tr>
</tbody>
</table>

$^a$ Dihedral angle of the cyclopropyl proton with the methylene proton.
$^b$ Dihedral angle of the epoxide proton with the methylene proton.
$^c$ The larger coupling constant is underlined when coupling to cyclopropyl and epoxy protons is possible.
are \( J \approx 12 \) Hz and \( J \approx 4 \) Hz, which do indeed fit the calculated values for the trans-boat conformation. It is important to note (see Figure 13) that \( \text{H}_2\text{endo} \) is now at higher field than \( \text{H}_2\text{exo} \). Thus the relative ordering has changed from that found for the unsubstituted 3-norcarene oxide. Apparently the steric shielding effect of the 7-endo-methyl group is sufficient to overcome the previously dominant effect in the 3-norcarene oxides.

The anti-7,7-dimethylnorcarene oxide \( 311 \) has experimentally observed values of \( J_{2,\text{endo}} \approx 3 \) Hz, \( J_{2,\text{exo}} \approx 8-9 \) Hz, and \( J_{2,3} \approx 2-3 \) Hz. When compared to the values of Table 16, they most closely match those for the planar conformation. The trans-boat conformation, while agreeing reasonably closely with the measured \( \text{H}_2\text{exo} \) signal, is definitely eliminated by the observed \( \text{H}_2\text{endo} \) signal which is too narrow to fit the calculated \( J \approx 4 \) Hz. Here also the \( \text{H}_2\text{endo} \) signal is at higher field than the \( \text{H}_2\text{exo} \).

The calculated coupling constants for \( 291 \) are presented in Table 18.

**TABLE 18. Calculated Coupling Constants for 291**

<table>
<thead>
<tr>
<th></th>
<th>( \text{H}_2\text{endo} )</th>
<th>( \text{H}_2\text{exo} )</th>
<th>( \text{H}_2\text{endo} )</th>
<th>( \text{H}_2\text{exo} )</th>
<th>( \text{H}_2\text{endo} )</th>
<th>( \text{H}_2\text{exo} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \phi )</td>
<td>77°</td>
<td>45°</td>
<td>70°</td>
<td>125°</td>
<td>30°</td>
<td>90°</td>
</tr>
<tr>
<td>( J_{2,3} )</td>
<td>0.2</td>
<td>2.0</td>
<td>3.9</td>
<td>1.3</td>
<td>3.0</td>
<td>0</td>
</tr>
</tbody>
</table>
The observed coupling constants ($J \approx 1\text{-}2 \text{ Hz}$ and $J \approx 4 \text{ Hz}$) reasonably fit either the cis-boat or planar conformation. From the accuracy of the data, it is difficult to predict either conformation, and the molecule very likely exists as an equilibrium mixture of the two conformations. The stability of the cis-boat conformation may arise from a tendency to minimize eclipsing interactions, specifically with the pendant methyl groups (see Newman projections, Figure 10). Steric shielding of $H_{2\text{exo}}$ by the 1,6-dimethyl substituents causes this proton to resonate at higher field than $H_{2\text{endo}}$ (see Figure 11).

Similar calculations on the syn-epoxide 292 (Table 19) indicate again the likely conformation to be an equilibrium mixture of planar and cis-boat conformations (observed: $J_{2\text{endo}} \approx 2 \text{ Hz}$, $J_{2\text{exo}} \approx 2.5 \text{ Hz}$).

The close similarity of the methylene multiplicities of 292 (Figure 10) and 305 (Figure 12) ($J_{2\text{endo}} \approx 1\text{-}2 \text{ Hz}$, $J_{2\text{exo}} \approx 2\text{-}3 \text{ Hz}$) provides convincing evidence that these epoxides share the same conformational equilibrium. The fact that the chemical shifts of the two methylene

**TABLE 19. Calculated Coupling Constants for 292**

<table>
<thead>
<tr>
<th></th>
<th>$H_{2\text{endo}}$</th>
<th>$H_{2\text{exo}}$</th>
<th>$H_{2\text{endo}}$</th>
<th>$H_{2\text{exo}}$</th>
<th>$H_{2\text{endo}}$</th>
<th>$H_{2\text{exo}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\delta$</td>
<td>130° 15°</td>
<td>48° 66°</td>
<td>85° 30°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$J_{2,3}$</td>
<td>1.7 3.8</td>
<td>1.8 0.6</td>
<td>0 2.7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
protons in the anti-epoxide are virtually equal makes a firm conformational prediction impossible. Because the syn-epoxides 292 and 305 appear to be conformationally equivalent, it would seem reasonable that the anti-epoxide be controlled by similar conformational factors also. Thus, an equilibrium of cis-boat and planar conformations is predicted.

To summarize, the above analysis provides supportive evidence for the conclusion that the three epoxides 276, 277, and 311 appear in a predominantly planar conformation with the syn-epoxide 312 required to be in a trans-boat conformation. The remaining four epoxides appear to be more conformationally flexible, undergoing a cis-boat to planar conformational inversion.

There now remains the key question of why the chemical shifts of the syn and anti substituents positioned at C7 vary to the extent that they do within each of the three structural subgroups. To provide additional comparison and because electron diffraction measurements suggest that a fused three-membered ring frequently has the same effect on the conformation of a six-membered ring as an internal double bond, the data for the 3-norcarene precursors are utilized as points of reference. In the parent hydrocarbon system 273, the combined anisotropic effects of the C-C and C=C bonds cause $H_{7\text{endo}}$ and $H_{7\text{exo}}$ to overlap with $H_1$ and $H_6$ as a broad multiplet of area 4 at 6 0.8-0.2. From a knowledge of the properties of 315 and 316, the endo proton can be safely assumed to resonate on the high field side of the multiplet and the exo proton on the low. In [4,3,1]propell-3-ene (299), the $\Delta_{\text{gem}}$ of the C7 hydrogens is reduced to zero, undoubtedly because of the enhanced shielding of
H$_{7\text{exo}}$ by the trimethylene bridge. On the other hand, the $\Delta \delta_{\text{gem}}$ value for 288 is large (0.76 ppm), chiefly because of the marked upfield shift of H$_{7\text{endo}}$ (Table 20). This phenomenon denotes adoption by 288 of enhanced levels of the cis-boat conformation, as anticipated earlier on conformational grounds.

The long range shieldings caused by the anti epoxide rings in 291, 303, and 311 do not parallel those in the 3-norcarenes in an immediately obvious way and point out the extreme level of caution which must be exercised in extrapolating such data, even when very closely related molecules are involved. Thus, the $\Delta \delta_{\text{gem}}$ for 291 is now zero, while those for 276 and 303 are quite large. Additionally, the methyl groups in 311 appear little affected (relative to 310) by introduction of the anti epoxide ring. In contrast, the syn epoxides are more systematically related (Table 20).

Nonetheless, reliable correlation of this seemingly diverse collection of shift data is possible provided that proper attention is given to conformational similarities and differences. For example, our experimental results show epoxides 276 and 277 to exist in planar conformations comparable to that presumably adopted by 273. Given these three-dimensional similarities, the anti epoxide ring in 276 is seen to generate relative to 273 an upfield shift for H$_{7\text{endo}}$ of 0.6 ppm and a downfield shift for H$_{7\text{exo}}$ of 0.25 ppm (Table 18). The situation is reversed in 277, H$_{7\text{endo}}$ being deshielded (0.4 ppm) and H$_{7\text{exo}}$ shielded (0.5 ppm) as compared to 273. Such an analysis clearly demonstrates that progression from 276 to 277, or vice-versa, results in a crossing of the two sets of resonance lines. The data for 299, 303, and 305
<table>
<thead>
<tr>
<th>Compd</th>
<th>7endo</th>
<th>7exo</th>
<th>Compd</th>
<th>7endo Δδ</th>
<th>7exo Δδ</th>
<th>Compd</th>
<th>7endo Δδ</th>
<th>7exo Δδ</th>
</tr>
</thead>
<tbody>
<tr>
<td>273</td>
<td>0.2 - 0.8&lt;sup&gt;b&lt;/sup&gt; (multiplet)</td>
<td></td>
<td>276</td>
<td>-0.4 (+0.6) 0.55 (-0.25)</td>
<td></td>
<td>274</td>
<td>0.62 (-0.4) 0.26 (+0.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>278</td>
<td>-0.07 0.69</td>
<td></td>
<td>279</td>
<td>0.07 (-0.14) 0.07 (+0.6)</td>
<td>280</td>
</tr>
<tr>
<td></td>
<td>(0.25)&lt;sup&gt;c&lt;/sup&gt; (0.35)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td>(+0.2)&lt;sup&gt;d&lt;/sup&gt; (-0.3)&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td>(-0.7)&lt;sup&gt;d&lt;/sup&gt; (+0.6)&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>299</td>
<td>0.35 (singlet)</td>
<td></td>
<td>303</td>
<td>-0.17 (+0.5) 0.06 (-0.25)</td>
<td></td>
<td>304</td>
<td>0.71 (-0.4) 0.18 (+0.2)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Proton chemical shifts.

<sup>b</sup> Multiplet.

<sup>c</sup> Values in parentheses are estimated.

<sup>d</sup> Values in parentheses are relative to the corresponding proton in the parent molecule.
<table>
<thead>
<tr>
<th>Compd</th>
<th>Tendo</th>
<th>7exo</th>
<th>Compd</th>
<th>Tendo</th>
<th>Δδ&lt;sup&gt;a&lt;/sup&gt;</th>
<th>7exo</th>
<th>Δδ&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Compd</th>
<th>Tendo</th>
<th>Δδ&lt;sup&gt;a&lt;/sup&gt;</th>
<th>7exo</th>
<th>Δδ&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Diagram 1" /></td>
<td>0.80</td>
<td>1.04</td>
<td><img src="image2" alt="Diagram 2" /></td>
<td>0.76</td>
<td>(+0.04) 1.04</td>
<td></td>
<td></td>
<td><img src="image3" alt="Diagram 3" /></td>
<td>2.95</td>
<td>(-0.15) 0.90</td>
<td>(+0.14)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>The Δδ values are given relative to the chemical shifts observed for the 3-norcarene. <sup>b</sup>These protons overlap with H<sub>1</sub> and H<sub>6</sub> in this region. <sup>c</sup>Chemical shifts calculated for the planar six-membered ring conformation of 288 based chiefly upon data for 273 and 274. <sup>d</sup>These values relate to planar 288. <sup>e</sup>Assignments substantiated by nuclear Overhouser experiments.
show a remarkably similar trend. The properties of the 310-312 triad are again in the same direction, although the magnitudes of the shift changes are lessened in this series because of increased distances.

At first glance, the group 288, 291, and 292 is seen to generate anomalous correlations. This is because a correction must be applied to the data for 288, since this 3-norcarene uniquely adopts a cis-boat conformation which leads to more intense anisotropic perturbations in the region around C7. However, with values of $H_{\text{endo}}$ and $H_{\text{exo}}$ shifts adapted to the hypothetical planar form, the $\Delta\delta$'s are seen to correlate closely with those in the other examples (Table 20).

At this point, it should be mentioned that the simple anisotropy model illustrated in Figure 16 is not sufficiently detailed to account entirely for the observations. Moreover, it is likely that the screening effects emanating from the rearside of an epoxide ring are dependent not only on distance (the result of shielding contours) but also on group anisotropy contributions (a $\cos^2$ angular dependence) as summarized in the previously cited McConnell equation. Such added considerations concisely explain, for example, the significantly

![FIGURE 16. Simple anisotropy model for epoxides](image-url)
enhanced shielding of $H_{7\text{exo}}$ in 277, 292, and 305 relative to their 3-norcarene counterparts as well as that encountered in the exo-7-methyl group of 312 (as compared to 310).

The epoxides prepared in this study serve to illustrate some of the problems which can arise even for closely related structures. Although the bond anisotropy treatment can sometimes be helpful in predicting $\Delta\delta$, it takes account neither of the electron cloud volume around the three-membered ring nor the effect of the oxygen $p$ orbitals. On occasion, slight changes in geometry can generate key alterations in shielding patterns, the magnitudes of which may not be recognized in the absence of proper conformational analysis and analog intercorrelation. The development of an accurate and convenient method by which shielding effects of an epoxide ring might be estimated must therefore take these many factors into account. In the interim, the working concepts detailed herein should find application, but only with utmost reasonable precaution.
CHAPTER 3

Furanosesquiterpene Synthesis

In the sesquiterpenoid family, a number of analogs exist containing a furan ring annulated to a carbocyclic system or bonded to an isoprenoid chain. While usually possessing skeletons common in the sesquiterpene field, furan congeners have received comparatively little synthetic attention. This lack of interest may stem from the instability and air-oxidizability of many furan compounds. In this light, the synthetic approach to furanosesquiterpenes has often involved construction of the furan ring into a pre-designed skeleton. Furan ring formation thus becomes the last step in the synthetic process. In this chapter is described a potentially new synthetic approach which introduces the furan ring intact at an early stage, and quickly builds up the remaining carbon framework.

The first furanosesquiterpene (317) was discovered in the fruit bodies of Collybia maculata by Goris in 1911. Collybolide (317), however, was not structurally elucidated until over a half century
later by Bui, et al. in 1974. The problem of structural determination plagued the early work in this field. Up to 1960, the formulas of only 8 furanosesquiterpenoids had been established, and these included only those containing the farnesane skeleton. With the rapid advances in separation methods and physico-chemical determination in the last 20 years, the number of naturally-occurring furanosesquiterpenoids and their catabolites has risen to more than 250, possessing a variety of skeletons.

Taxonomically, furanosesquiterpenes are very widespread in the plant kingdom, although principally concentrated in the Compositae family. The animal kingdom is less represented; however, it has recently provided several interesting new classes, particularly isolated from sponges.

The known furan-containing sesquiterpenoids may be classified into 13 types based on their carbon skeleton. These are illustrated in Figure 17. In general they are found to exist in the same structural types as normal sesquiterpenes. A common degradation yields furans in which the β-methyl group has been lost.

The synthetic approach developed herein is potentially capable of producing furanosesquiterpenes in which the furan ring is bonded at contiguous α- and β-positions to the remaining carbon framework.
FIGURE 17. Structural types of furanosesquiterpenes
Thus, of the nine types with this construction, the method is designed to allow access to six. The general process is described in Scheme XX.

\[ \text{Scheme XX. General route to furanosesquiterpenes} \]

The furan is introduced via condensation of a simple carbonyl derivative with a vinyl carbanion. Such chemistry is reminiscent of that described in Chapter 1, Section 1. The key transformation is the simultaneous introduction of the remaining carbon with rearrangement of an initial allylic alcohol 319 to the homoallylic alcohol 320. [2,3]Sigmatropic shifts involving ether anions have been well documented. The particular process which utilizes tin-lithium exchange was developed by Still. The subsequent cyclization could be preceded by oxidation or manipulation of the double bond to achieve the desired functionality.

To date this furanoannulation scheme has been mainly directed to the synthesis of spiniferin I (325) (vide infra). Additional preliminary studies have been applied toward furodysin (322) as well.
In this work, construction of the key intermediate 323 has been achieved. This molecule is rather unstable, and its immediate precursor 324 is even more so. Purified samples turn black within hours upon exposure to the laboratory atmosphere. Presently crystalline derivatives of 323 are being sought to impede decomposition. Elaboration of furodysin awaits further experimentation.

Spiniferin I (325) was chosen as the first target molecule. It should allow a good test of the furanoannulation scheme above as well as being a very interesting molecule in itself. First isolated from the Mediterranean sponge *Pleraplysilla spinifera* in 1975 by G. Cimino and coworkers, spiniferin I was found along with spiniferin II (326) and longifolin (327). Initially, the structures 328 or 329 were
assigned to spiniferin I based on $^1$H NMR, mass spectral, and UV data. In addition, it was known that catalytic hydrogenation gave a dihydro derivative whose $^1$H NMR spectrum lost two olefinic signals and whose UV spectrum had lost an element of conjugation leaving a double bond conjugated to the furan.

Upon further $^{13}$C NMR studies the revised structure 325 was assigned by Cimino. This structure was backed up by spectral analysis of a tetrahydroxydihydro derivative prepared by osmylation of the dihydro derivative. Correspondingly, ozonolysis of the dihydro derivative gave diketone 330. The related structure 331 was ruled out on bigeneric grounds as well as an LIS study of the dihydroxy derivative 332. The
assignment of 325 to spiniferin I nicely explains the $^1$H NMR chemical

shifts of the two methano bridge protons. One, held over the unsaturation, is strongly influenced by the ring current and appears at $\delta$ 0.75. Its geminal partner, on the other hand, resonates at 3.62.

The particular interest in 325 stems from the unique structure ascribed to this furanosesquiterpene. It is the only natural product for which a 1,6-methano bridged cyclodecane carbon framework is proposed. The closest structural counterparts are the 1,6-methano[10]annulenes (333) prepared by Vogel and coworkers. While spiniferin I

\[ \text{333} \]

does not have the homoaromatic character which 333 was designed to investigate, it does have a network of extended conjugation as shown by Cimino, et al. This conjugation, plus the inherent oxidizability of the furan nucleus, makes total synthesis of spiniferin I a reasonable challenge.

An antithetic view of a spiniferin synthesis is illustrated in Figure 18. Once the requisite carbon atoms have been assembled, the functional group manipulation necessary to approach the target consists
FIGURE 18. Antithetic view of spiniferin I

only in introduction of the three double bonds. The most reasonable approach introduces the double bond furthest removed from the furan last.

This scheme also should allow for spectral comparison with the known dihydro derivative. Molecular models as well as the UV spectrum indicates good conjugation through this diene unit, and traditional allylic functionalization and elimination should allow for introduction of this double bond from diene 334. The diene should be accessible through a 1,4-elimination mediated by the furan ring, if not the cyclopropyl group, of a reduced derivative of ketone 335. The
cyclopropyl group must be introduced at some stage, either via a car-
bonyl compound (i.e. \textsuperscript{335}) or an alcohol. Cyclization to the furan
should present no problem as the furan ring is activated and addi-
tionally prefers to acylate at an \(\alpha\) position. Homoallylic alcohol \textsuperscript{337}
is the expected product from \([2,3]\) sigmatropic rearrangement of allylic
alcohol \textsuperscript{338}. This allylic alcohol should be easily prepared by con-
densation of the vinyl carbanion generated from the benzenesulfonyl-
hydrazone of \(2,2\)-dimethylcyclohexanone (\textsuperscript{33}) and 3-furaldehyde (\textsuperscript{339}).
Thus in this approach, the bulk of the molecule is built up in one
condensation. One subsequent set of reactions generates a difunctional
compound \textsuperscript{337} which with the introduction of only a cyclopropyl carbon
should be convertible to spiniferin I.

The synthesis began with preparation of the condensation partners.
\(2,2\)-Dimethylcyclohexanone is easily prepared and purified by the method
of Dev. \textsuperscript{216} 3-Furaldehyde, not distillable from corncobs like \(2-
furaldehyde, can be prepared by oxidation of 3-furfuryl alcohol (\textsuperscript{341})

\[
\begin{align*}
\text{HOOC} & \xrightarrow{\text{LiAlH}_4, 100\%} \text{HOH}_2\text{C} \\
\text{\textsuperscript{340}} & \xrightarrow{\text{PCC, 54\%}} \text{OHC} \\
\text{\textsuperscript{341}} & \xrightarrow{} \text{\textsuperscript{339}}
\end{align*}
\]

with pyridinium chlorochromate (PCC) buffered with sodium acetate.
This procedure, while not giving the aldehyde in good yield, was the
best uncovered. 3-Furaldehyde is a light-, air-, and acid-sensitive
compound, and so it was utilized quickly after production (within one
day). Until then it was stored in the dark under nitrogen at -10°C. This instability may be the cause of the low yield in the oxidation. Pyridinium dichromate, a reagent recently introduced by Corey and Schmidt, is claimed to be a less acidic agent than PCC.\cite{217} Use of this oxidant, however, afforded a mixture of 3-furaldehyde and pyridine which was inseparable by extraction and azeotroped upon attempted distillation. A modified Rosenmund reduction of the acid chloride \cite{218} failed to produce any desired alcohol. The same low yield had been encountered earlier by Sondheimer and Cresp in the preparation of a similar 3-furaldehyde, and in their case PCC also gave the best yield (40\%).\cite{219}

With the 2,2-dimethylcyclohexanone benzenesulfonylhydrazone (62) and 3-furaldehyde in hand, the condensation was ready to be carried out. Conditions analogous to those described previously (Chapter 1, Section 1) were found to suffice very well. The vinyl carbanion \cite{343}
was cooled to \(-45°C\) and 3-furaldehyde was added. The bright red color immediately turned to a light tan with formation of a heavy precipitate. Upon work-up, the desired allylic alcohol was obtained along with the \(n\)-butyllithium addition product \(\text{34}_1\). These could easily be separated by high pressure liquid chromatography, and gave the allylic alcohol \(\text{33}_8\) in 58% purified yield. Attempted condensation of the vinyl carbanion with 3-fuoryl chloride (\(\text{34}_2\)) even with inverse addition led mostly to intractible material. The major chromatographable product was the dimer of the acid chloride.

\[
\begin{align*}
\text{C}_2\text{H}_4\text{Li}^+ & + \text{C}_6\text{H}_5\text{C} = \text{O}^\text{O} \rightarrow \text{C}_6\text{H}_5\text{C} = \text{O}^\text{O} \quad + \text{polymer}
\end{align*}
\]

The \([2,3]\)sigmatropic rearrangement of \(\text{33}_8\) to \(\text{33}_7\) requires that the rearrangement be mediated through the isolated double bond, not the furan ring. It has been shown by Cazes and Julia that a similar process can occur with involvement of the furan ring. They had utilized the \([2,3]\)sigmatropic shift to synthesize Elsholtzia ketone (\(\text{34}_5\)). We felt that in the presence of an isolated double bond the rearrangement would prefer not to destroy the aromaticity of the furan ring, even temporarily.
Toward this objective, tri-$n$-butylstannylmethyl iodide (346) was synthesized as described by Still$^{212}$ and Seyferth.$^{220}$ This is a relatively stable reagent which does slowly (over several months) lose some activity. It was found that potassium hydride quickly deprotonated the allylic alcohol 338, and addition of 346 gave the stannyl-ether within one hour at room temperature. The stannylether 347 could be isolated in 96% yield or directly treated with $n$-butyllithium at -78°C to effect lithium-tin exchange. This lithium species spontaneously underwent $[2,3]$ sigmatropic rearrangement to generate the homoallylic alcohol 337 in 77% yield. Because of the high yield in the ether formation, it was found to be most convenient to perform the two steps directly as a one-pot procedure. Isolation of the homoallylic alcohol 337 could be achieved by a filtration chromatography. Elution first with hexane removed tetra-$n$-butyltin followed by ether/hexane which afforded the product. The homoallylic alcohol 337 was identified by the usual spectral means as well as combustion analysis. The
stereochemistry about the double bond was proven by eventual cyclization \textit{(vide infra)}. The double bond stereochemistry could also be predicted by inspection of the Newman projections in Figure 19. Rearrange-

![Chemical Structure](image)

FIGURE 19. Transition states for \([2,3]\) sigmatropic rearrangements

ment is presumed to involve a coplanar \(\pi\)-carbon-oxygen system as shown. The rotomer which minimizes interaction with the \(\text{gem}\)-dimethyl group places the furan ring toward the initial double bond. The new double bond generated forces the furan to be oriented on the same side as the hydroxymethyl substituent as shown in 337.

With the success of these two reactions, the synthesis appeared to be in good stead. The desired transformations had led to incorporation of all but one of the necessary carbon atoms and introduced the correct geometry about the double bond. The next phase involved oxidation and conjugation of the double bond with the carbonyl (see 336 in Figure 18). This proved to be a formidable task. Initially the oxidation was attempted with Jones reagent in the anticipation that acid would lead to carbonyl conjugation of the double bond and formation of carboxylic acid 342. The acidic conditions, causing much decomposition of the material, however did not afford any carboxylic acid products. Amidst the numerous products obtained, only benzofuran
350 was identified. This resulted from electrophilic cyclization of the protonated or chromate complexed aldehyde, followed by elimination of water. It appeared reasonable that the acidic conditions were responsible for this cyclization process. To avoid cyclization, pyridinium dichromate (PDC) in dimethylformamide was used as the oxidation medium. This has been shown to oxidize alcohols and aldehydes to acids under essentially neutral conditions. Corey had found that easily cyclizable geraniol could be oxidized without competing cyclization which was seen with more acidic reagents. Once again, however, PDC oxidation resulted in formation of the benzofuran 350. In this case it was the sole product and isolated in 49% yield. It was now apparent that even neutral conditions were sufficient to lead to cyclization. One last aprotic oxidation was tried. In this case Collins reagent led to the same cyclized benzofuran in 78% isolated yield. Thus, the problem appeared to arise from furan attack on the electron deficient aldehyde carbon during attempted oxidation instead of an external oxygen nucleophile.
To increase the possibility of external oxygen attack, aqueous base seemed the best medium. This greatly restricts the oxidants available; however, silver(II) oxide (351) and nickel "peroxide" remained. The nickel reagent, prepared from nickelous sulfate and commercial bleach,\(^{221}\) proved incapable of oxidizing the alcohols. Silver(II) oxide\(^{222}\) on the other hand appeared to effect the transformation to unsaturated lactone 352 (5%). This presumably occurred through the intermediate carboxylic acid salt which cyclized under nucleophilic response to the silver complexed olefin. This oxidative lactonization reaction proved to be impossible to reproduce. Nonetheless, the material from the first reaction was used in an attempted cyclopropanation. Cyclopropanation of α,β-unsaturated ketones has been accomplished using dimethylsulfoxonium methyldide.\(^{223}\) This reaction, when applied to the α,β-unsaturated lactone, resulted in total destruction of the material.

While this negative result is difficult to interpret, it appeared that 1,4-addition of a nucleophilic ylide or other reagent to a system containing the partial structure 353 would be difficult. Considering
the vector approach angle, the neopentyl carbon β to the carbonyl becomes very hindered. This problem would be alleviated by reversing the unsaturated ketone (i.e. 334). Anticipating 1,4-addition to this type of molecule, oxygenation of the double bond in homoallylic alcohol 337 was investigated.

One approach to this problem was to convert this olefin 337 into the allylic alcohol 355. This conceivably would be produced by a singlet oxygen "ene" reaction. Furans are known to react with singlet oxygen in methanolic solution to yield lactone products resulting from the Diels-Alder addition to the furan 225 (cf 356). Thus, the reaction was undertaken with trepidation. Indeed, 337 was found to react very rapidly (within 30 minutes). After mild reductive work-up (sodium bisulfite), the furan ring was lost by 1H NMR evidence, and no products were positively identified. Conjugated carbonyl moieties did appear to be present by infrared analysis of several chromatographed products.
The same overall transformation may be anticipated from epoxidation and ring opening. To this end, 337 was subjected to m-chloroperbenzoic acid in buffered methylene chloride solution at 0°C for one hour. All starting material was shown to be consumed by thin layer chromatography; however, upon chromatography the expected epoxide 357 (38% yield) comprised only half of the product mixture. Additionally, there appeared to be products of internal ring opening. When 337 was treated with peroxynitrobenzimidic acid, a neutral epoxidizing agent, no reaction was observed. From these results, it was obvious that successful electrophilic attack at the double bond would have to be conducted on a protected form of the alcohol.

In order to investigate this chemistry, the original [2,3]sigma-tropic shift reaction was modified. The homoallylic alcohol, generated as the potassium or lithium salt, was silylated in situ with t-butyl-dimethylsilyl chloride. In this manner, the protected alcohol 358...
was produced directly from 358 in 60-70% yield. Upon treatment with m-chloroanbenzoic acid, a mixture of epoxide 359 (60%) and an unknown product (~30%) were isolated by chromatography. The epoxide, when treated with lithium diisopropylamide in ether/hexamethylphosphoric triamide at 0°C, was totally destroyed. Repetition of the reaction conditions at -20°C for only 20 minutes still led to partial decomposition of starting material 359 with no identifiable products observed. These two results caused us to abandon epoxidation and ring opening pathways to compounds of the type 354 or 355.

Another process which effectively performs the singlet oxygen "ene" reaction was investigated next. Treatment of the homoallylic alcohol 358 with selenenic acid generated in situ from diphenyldiselenide and 30% hydrogen peroxide appeared to give the hydroxyselenide by thin layer chromatography. Oxidation to the selenoxide by t-butylhydroperoxide and in situ elimination did not produce the expected allylic alcohol 360. Contrary to the findings of Sharpless and Reich, elimination took place toward the hydroxyl group producing the enol form of ketone 361 in 25% yield. This may result from preferential removal of the more acidic proton adjacent to the furan ring. Alternatively, the syn-elimination mechanism invoked for selenoxide
eliminations may not be allowed in the desired direction because of

the intermediacy of hydroxyselenide 362. Compound 362 could only elimi-

nate to give the observed ketone 361.

The hydroxyselenation procedure of Nicolaou,\textsuperscript{229} N-phenylselenyl-

phthalimide in aqueous methylene chloride, produced no useful results

with several products formed all in low yield. An alternative electrophilic functionalization, N-bromosuccinimide in aqueous glyme,

likewise gave an unusable mixture of compounds.

To summarize the present efforts towards spiniferin I, the

preparation of intermediate 337, or its protected form 358, was

accomplished directly; however, appropriate functionalization of

this compound proved to be difficult. Clean introduction of elec-
Trophiles in a regiospecific manner could not be accomplished under the variety of conditions investigated. Through oxidation attempts, it became obvious that cyclization onto the furan nucleus was a very favorable process. This propensity to cyclize severely limited the synthetic avenues of approach to spiniferin I.

Premature cyclization, while thwarting the synthetic program to spiniferin I, could be judiciously designed into syntheses of certain furanosesquiterpenes. Thus, modified eremopholane structures (e.g. cacalol, 363 and maturinone, 364) should be readily approached by the

\[
\begin{align*}
&\text{OH} \\
&\text{363} \\
&\text{O} \\
&\text{364}
\end{align*}
\]

predescribed methodology. Cacalol has been synthesized several times based on a general scheme of furan annulation to a hydroxytetrahydro-naphthalene.\textsuperscript{230-232} Maturinone was structurally revised and synthesized as the minor product from a Diels-Alder approach by Kakisawa and Inouye.\textsuperscript{233} The general scheme illustrated previously should allow construction of these tricyclic systems in a stereocontrolled fashion.
EXPERIMENTAL

Melting points were determined in open capillaries with a Thomas-Hoover apparatus and are uncorrected. Proton magnetic resonance spectra were recorded with Varian A-60A, Varian EM-360, Varian T-60, and Bruker HX-90 spectrometers. Apparent splittings are given in all cases. Infrared spectra were recorded on a Perkin-Elmer Model 467 instrument. Mass spectra were determined on an AEI-MS9 spectrometer at an ionization potential of 70 eV. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

All operations requiring dry conditions were performed in flame-dried glassware under an atmosphere of nitrogen or argon. Organic solutions were dried over anhydrous magnesium sulfate unless otherwise stated. Evaporation of solvent was performed on a Büchi rotary evaporator applying heat when appropriate. In experiments requiring dry solvents, dioxane, ether, tetrahydrofuran and glyme were distilled from sodium-benzophenone. Hexamethyldiphosphoramide, dimethylsulfoxide, dimethylformamide, benzene, and diisopropylamine were distilled from calcium hydride and stored over molecular sieves. Dichloromethane, acetonitrile, and hexane were distilled from potassium carbonate and stored over molecular sieves. Triethylamine, pyridine, and 2,6-lutidine were distilled from potassium hydroxide as well as stored over potassium hydroxide pellets. Methanol was distilled from magnesium
methyleate and stored over molecular sieves. N,N,N',N'-Tetramethyl-ethylenediamine was distilled from calcium hydride. Chlorotrimethylsilane was distilled from calcium hydride immediately before use under nitrogen and transferred with a syringe.

**General Arenesulfonfylhydrazone Procedure**

The ketone (1 equiv.) was dissolved in absolute ethanol along with the benzene or p-toluenesulfonyl hydrazide (1 equiv.) and a catalytic amount of p-toluenesulfonic acid. The mixture was heated to reflux under nitrogen for 0.4-5 hours and cooled. The crystals obtained were filtered and recrystallized from ether/hexane. If crystals did not precipitate from the reaction, the ethanol reaction was concentrated and the oily residue was taken up in ether and precipitated by the addition of hexane.

**Physical Data on Arenesulfonfylhydrazones**

**Cyclopentanone Benzenesulfonfylhydrazone (37)**

81%, m.p. 151-156°, \(^1\)H NMR (δ, CDCl\(_3\)) 8.0-7.8 (m, 2H), 7.6-7.4 (m, 3H), 2.5-2.1 (m, 4H), and 2.0-1.7 (m, 4H).

**Cyclohexanone Benzenesulfonfylhydrazone (38)**

92%, m.p. 145-150°, \(^1\)H NMR (δ, CDCl\(_3\)) 8.0-7.8 (m, 2H), 7.5-7.3 (m, 3H), 2.4-2.0 (m, 4H), and 1.7-1.5 (m, 6H).

**Cycloheptanone Benzenesulfonfylhydrazone (39)**

93%, m.p. 146-147°, \(^1\)H NMR (δ, CDCl\(_3\)) 8.0-7.8 (m, 2H), 7.5-7.3 (m, 3H), 2.5-2.2 (m, 4H), and 1.9-1.4 (m, 8H).
4-t-Butylcyclohexanone Tosylhydrazone (40)  
80%, m.p. 148-150° (dec.), $^1$H NMR (δ, CDCl₃) 7.75 (d, $\delta = 8$ Hz, 2H), 7.22 (d, $\delta = 8$ Hz, 2H), 2.42 (s, 3H), 2.2-1.0 (m, 9H), and 0.90 (s, 9H).

2-Methylcyclohexanone Benzenesulfonylhydrazone (41)  
69%, $^1$H NMR (δ, CDCl₃) 8.0-7.8 (m, 2H), 7.6-7.3 (m, 3H), 2.5-1.4 (br m, 9H), and 1.0 (d, $\delta = 6$ Hz, 3H).

2-Phenylcyclohexanone Benzenesulfonylhydrazone (42)  
74%, m.p. 119-121°, $^1$H NMR (δ, CDCl₃) 7.8-7.0 (br m, 5H), 3.5 (t, $\delta = 6$ Hz, 1H), and 2.5-1.8 (br m, 8H).

d,l-Menthone Benzenesulfonylhydrazone (43)  
m.p. 131-135° (dec.), $^1$H NMR (δ, CDCl₃) 8.0-7.8 (m, 2H), 7.6-7.3 (m, 4H), 2.7-2.4 (m, 1H), 2.0-1.3 (m, 7H), 0.98 (d, $\delta = 5$ Hz, 3H), 0.50 (d, $\delta = 6$ Hz, 3H), and 0.50 (d, $\delta = 6$ Hz, 3H).

4-Heptanone Benzenesulfonylhydrazone (44)  
91%, m.p. 102-104°, $^1$H NMR (δ, CDCl₃) 8.0-7.8 (m, 2H), 7.6-7.4 (m, 3H), 2.4-1.9 (m, 4H), 1.8-1.2 (m, 4H), and 0.83 (q, $\delta = 7$ Hz, 6H).

4-Heptanone Tosylhydrazone (45)  
87%, m.p. 79.5-80.5°, $^1$H NMR (δ, CDCl₃) 7.8 (ABq, $\delta = 8$ Hz, 2H), 7.2 (ABq, $\delta = 8$ Hz, 2H), 2.40 (s, 3H), 2.1 (br t, $\delta = 6$ Hz, 4H), 1.55 (br sext, $\delta = 6$ Hz, 4H), and 0.80 (br q, $\delta = 6$ Hz, 6H).

2-Heptanone Tosylhydrazone (46)  
75%, m.p. 82-83°, $^1$H NMR (δ, CDCl₃) 7.57 (d, $\delta = 8$ Hz, 2H), 7.20 (d,
\[ J = 8 \text{ Hz}, 3H \], 2.40 (s, 3H), 2.2-2.0 (m, 2H), 1.76 (s, 3H), 1.6-0.8 (m, 2H).

**Propiophenone Benzenesulfonylhydrazone (47)**

94%, m.p. 137-139\(^\circ\), \(^1\)H NMR (\(\delta\), CDCl\(_3\)) 8.1-7.9 (m, 2H), 7.5-7.2 (m, 8H), 2.66 (q, \(J = 7 \text{ Hz}, 2H\)), and 1.17 (t, \(J = 7 \text{ Hz}, 3H\)).

**Propiophenone Tosylhydrazone (48)**

70%, m.p. 124.5-126.5\(^\circ\), \(^1\)H NMR (\(\delta\), CDCl\(_3\)) 7.83 (m, 2H), 7.47 (m, 2H), 7.34 (m, 3H), 7.19 (m, 2H), 2.43 (q, \(J = 8 \text{ Hz}, 2H\)), 2.40 (s, 3H), and 1.00 (t, \(J = 8 \text{ Hz}, 3H\)).

**4,5-Benzocyclohept-4-enone Benzenesulfonylhydrazone (49)**

83\%, m.p. 159\(^\circ\) (dec.), \(^1\)H NMR (\(\delta\), CDCl\(_3\)) 7.8 (m, 3H), 7-05 (s, 4H), and 3.0-2.4 (br m, 8H).

**Cyclododecanone Tosylhydrazone (51)**

83\%, m.p. 157\(^\circ\), \(^1\)H NMR (\(\delta\), CDCl\(_3\)) 7.8 (ABq, \(J = 8 \text{ Hz}, 2H\)), 7.2 (ABq, \(J = 8 \text{ Hz}, 2H\)), 2.4 (s, 3H), 2.2 (t, \(J = 5 \text{ Hz}, 4H\)), and 2.0-1.0 (br m, 2OH).

**Cyclododecanone Benzenesulfonylhydrazone (50)**

97\%, m.p. 163-168\(^\circ\), \(^1\)H NMR (\(\delta\), CDCl\(_3\)) 8.0-7.8 (m, 2H), 7.6-7.4 (m, 3H), 2.2 (br t, \(J = 6 \text{ Hz}, 4H\)), and 2.0-1.8 (br m, 2OH).

**α-Tetralone Benzenesulfonylhydrazone (52)**

76\%, m.p. 191-192\(^\circ\) (dec.), \(^1\)H NMR (\(\delta\), CDCl\(_3\)) 8.2-7.8 (m, 4H), 7.6-7.4 (m, 3H), 7.2-7.0 (m, 3H), 2.9-2.3 (m, 4H), and 2.2-1.8 (m, 2H).
4-Methoxy-α-tetralone Benzenesulfonylhydrazone (53)
67%, m.p. 198-200° (dec.), 1H NMR (δ, CDCl₃) 8.0-7.8 (m, 3H), 7.5-7.3 (m, 3H), 6.70 (m, 1H), 6.58 (m, 1H), 4.70 (s, 3H), 2.8-2.4 (m, 4H), and 2.0-1.7 (m, 2H).

2-Acetynaphthalene Benzenesulfonylhydrazone (54)
74%, m.p. 163-165°, 1H NMR (δ, CDCl₃) 8.2-7.4 (m, 12H) and 2.15 (s, 3H).

Isobutyrophenone Benzenesulfonylhydrazone (55)
86%, m.p. 84-87°, 1H NMR (δ, CDCl₃) 8.0-7.8 (m, 2H), 7.6-7.3 (m, 6H), 7.1-6.9 (m, 2H), 2.8 (sept, J = 7 Hz, 1H), and 1.04 (d, J = 7 Hz, 6H).

Phenylcyclobutylketone Benzenesulfonylhydrazone (56)
83%, m.p. 125-127°, 1H NMR (δ, CDCl₃) 8.0-7.7 (m, 2H), 7.5-7.2 (m, 6H), 7.1-6.9 (m, 2H), 3.1 (t, J = 8 Hz, 1H), and 2.2-1.7 (m, 6H).

2-Norbornenylphenylketone Benzenesulfonylhydrazone (57)
47%, m.p. 93-95°.

Phenylcyclohexylketone Benzenesulfonylhydrazone (58)
80%, m.p. 108-112°, 1H NMR (δ, CDCl₃) 8.0-7.7 (m, 2H), 7.6-7.2 (br m, 6H), 7.0-6.8 (m, 2H), 2.5-2.2 (m, 1H), and 1.9-1.2 (br m, 10H).

Phenylacetone Benzenesulfonylhydrazone (59)
95%, m.p. 111-112°, 1H NMR (δ, CDCl₃) 8.0-7.8 (m, 2H), 7.5-7.3 (m, 3H), 7.2-6.8 (m, 5H), 3.44 (s, 2H), and 1.67 (s, 3H).

1,3-Diphenylacetone Benzenesulfonylhydrazone (60)
95%, too insoluble for 1H NMR spectrum.
1,1-Diphenylacetone Benzenesulfonfylhydrazone (61)
93%, m.p. 178-179°, too insoluble for \( ^1H \) NMR spectrum.

2,2-Dimethylcyclohexanone Benzenesulfonfylhydrazone (62)
\[
\text{NNH}_2\text{SO}_2\text{Ph} \quad 85\%, \text{m.p. 164° (dec.), } ^1H \text{ NMR (6, CDCl}_3) 8.0-7.8 (m, 2H), 7.6-7.2 (m, 4H), 2.4-2.1 (m, 2H), 1.8-1.4 (m, 6H), \text{and} 1.07 (s, 6H).
\]

3-Methylcyclohex-2-enone Benzenesulfonfylhydrazone (63)
\[
\text{NNH}_2\text{SO}_2\text{Ph} \quad 49\%, \text{m.p. 128° (dec.), } ^1H \text{ NMR (6, CDCl}_3) 8.0-7.3 (m, 2H), 7.7-7.3 (m, 4H), 6.08 \text{ and} 5.40 (m, 1H), 2.4-1.7 (m, 6H), \text{and} 1.83 (\text{br s, 3H}).
\]

2,2-Dimethyl-6-benzylcyclohexanone Benzenesulfonfylhydrazone (64)
\[
\text{NNH}_2\text{SO}_2\text{Ph} \quad \text{Prepared as previously described. Although the material did not crystallize, it proved to be chromatographically pure.}
\]

Cholestanone Benzenesulfonfylhydrazone (65)
\[
\text{NNH}_2\text{SO}_2\text{Ph} \quad \text{The cholestanone (5.0 g, 12.9 mmole) and benzenesulfonfylhydrazone (2.58 g, 15 mmole) were dissolved in warm absolute ethanol (230 ml) and concentrated hydrochloric acid (2.5 ml) was added to make a 0.4% hydrochloric acid/ethanol solution. The solution was refluxed under an argon atmosphere for 30 minutes and cooled; most of the ethanol was evaporated. The concentrated residue was diluted with benzene and heated on a steam cone to azeotropically}
\]

remove the water along with the remaining ethanol. The benzenesulfonylhydrazone was recrystallized from benzene/hexane to yield powdery white crystals, m.p. 213° (decomp).

Cholestanone Tosylhydrazone (66)

Cholestanone (1.1 g, 2.59 mmoles), tosylhydrazide (0.52 g, 2.8 mmoles), and concentrated hydrochloric acid (0.5 ml) were dissolved in absolute ethanol (50 ml). The solution was heated to reflux under a nitrogen atmosphere for 30 minutes. The cooled solution was concentrated to produce a solid which was recrystallized twice from ether/hexane to yield off-white crystals, m.p. 173-175° (decomp), lit. m.p. 175° \(^{23,4}\) (0.22 g, 0.396 mmole, 1%).

General Vinylsilane Procedure

A dry, three-necked flask equipped with a stirring bar, nitrogen inlet, rubber septum and an Erlenmeyer containing the arenesulfonylhydrazone (approximately 5 g) connected by a short piece of Gooch tubing was charged with dry \(N, N, N', N'\)-tetramethylethlenediamine (70 ml). The solvent was cooled to \(-45^\circ\)C and \(n\)-butyllithium in hexane (4 equivalents) was added via syringe. To this cold solution was slowly added in portions the arenesulfonylhydrazone. A dark red color developed immediately. Upon complete addition (10-20 minutes), the solution was stirred cold for another 30-60 minutes before it was allowed to warm to room temperature for 1-2 hours. During this time nitrogen was
evolved. When nitrogen evolution ceased the red solution was cooled to 0° and quenched with chlorotrimethylsilane (4 equivalents). The solution generally lightened to a yellow color then slowly turned black. After stirring the mixture at 0° for 30 minutes it was allowed to warm to room temperature and stirred for several hours. The mixture was poured onto water (200 ml) and pentane (100 ml). The organic layer was separated, extracted with water (2 x 200 ml), a saturated solution of copper(II) sulfate (2 x 200 ml), and brine (1 x 100 ml). The dried solution was concentrated, applied to neutral alumina, and eluted with pentane through a short (5 cm) plug of neutral alumina to remove all colored material. The eluant was concentrated and used as obtained or distilled. Varying amounts of octane as an impurity from the n-butyllithium were present in the crude vinylsilane samples.

Physical Data on Vinylsilanes

1-Trimethylsilylcyclopentene (68) 286

\[
\text{SiMe}_3
\]

50%, b.p. 106-108°, \textsuperscript{1}H NMR (δ, CDCl\textsubscript{3}) 6.00 (m, 1H), 2.7-2.2 (m, 4H), 2.2-1.6 (m, 2H), and 0.21 (s, 9H).

Anal. Calcd for C\textsubscript{7}H\textsubscript{16}Si: C, 68.46; H, 11.52.

Found: C, 68.34; H, 11.60.

1-Trimethylsilylcyclohexene (69) 287

\[
\text{SiMe}_3
\]

87%, b.p. 70-78°/33 torr, \textsuperscript{1}H NMR (δ, C\textsubscript{6}D\textsubscript{6}) 6.12 (m, 1H), 2.12 (m, 4H), 1.72 (m, 4H), and 0.22 (s, 9H).
Anal. Calcd for C₉H₁₈Si:  C, 70.04; H, 11.75.
  Found:  C, 70.15; H, 11.84.

1-Trimethylsilylcycloheptene (70)

\[
\begin{array}{c}
\text{SiMe}_3 \\
\text{C}_7 \text{H}_{14} \\
\end{array}
\]

94%, b.p. 90-95°/20 torr, \( ^1H \text{ NMR (δ, CDCl}_3) \)
6.23 (m, 1H), 2.5-2.1 (m, 4H), 2.1-1.3 (m, 6H), and 0.18 (s, 9H).

Anal. Calcd for C₁₀H₂₀Si:  C, 71.34; H, 11.98.
  Found:  C, 71.35; H, 11.91.

1-Trimethylsilyl-4-t-butylcyclohexene (71)

\[
\begin{array}{c}
\text{SiMe}_3 \\
\text{C}_7 \text{H}_{14} \\
\end{array}
\]

97%, b.p. 55-59°/0.3 torr, \( ^1H \text{ NMR (δ, CDCl}_3) \)
6.14 (m, 1H), 2.4-1.06 (m, 7H), 0.99 (s, 9H),
and 0.24 (s, 9).

Anal. Calcd for C₁₃H₂₆Si:  C, 74.20; H, 12.46.
  Found:  C, 74.18; H, 12.43.

2-Trimethylsilyl-3-methylcyclohexene (72)

\[
\begin{array}{c}
\text{SiMe}_3 \\
\text{C}_7 \text{H}_{14} \\
\end{array}
\]

91%, b.p. 85-105°/28 torr, \( ^1H \text{ NMR (δ, CDCl}_3) \)
5.98 (m, 1H), 2.6-1.6 (br m, 7H), 1.05 (d, \( J = 7 \text{ Hz, 3H} \)), and 0.14 (s, 9H).

Anal. Calcd for C₁₀H₂₀Si:  C, 71.38; H, 11.98.
  Found:  C, 71.42; H, 11.86.

Z-4-Trimethylsilylhept-3-ene (73)

\[
\begin{array}{c}
\text{SiMe}_3 \\
\text{C}_7 \text{H}_{14} \\
\end{array}
\]

97%, b.p. 45-32 torr, \( ^1H \text{ NMR (δ, CDCl}_3) \) 5.76
(t, \( J = 7 \text{ Hz, 1H} \)), 2.4-1.9 (m, 4H), 1.74-1.24
(m, 2H), 1.2-0.7 (m, 6H), and 0.15 (s, 9H).
Anal. Calcd for C_{16}H_{22}Si: C, 70.49; H, 13.02.
Found: C, 70.64; H, 13.03.

2-Trimethylsilylhept-1-ene (74)

\[
\text{SiMe}_3
\]

84%, b.p. 79-83°C/27 torr, \textsuperscript{1}H NMR (δ, CDCl\textsubscript{3})
5.57 (m, 2H), 2.2-0.9 (m, 11H), and 0.13 (s, 9H).

Z-1-Trimethylsilylcyclododecene (75)

\[
\text{SiMe}_3
\]

95%, b.p. 115-120°C/3 torr, \textsuperscript{1}H NMR (δ, CDCl\textsubscript{3})
5.80 (br t, \( J = 8 \) Hz, 1H), 2.5-2.0 (m, 4H),
1.6-1.3 (m, 16H), and 0.10 (s, 9H); m/e calcd
238.2117, obs 238.2121.

Anal. Calcd for C_{15}H_{30}Si: C, 75.54; H, 12.68.
Found: C, 75.50; H, 12.56.

1-Trimethylsilyl-4,5-benzocyclohepta-1,4-diene (76)

\[
\text{SiMe}_3
\]

88%, \textsuperscript{1}H NMR (δ, CDCl\textsubscript{3}) 7.4-7.1 (m, 4H), 6.05
(br t, \( J = 6 \) Hz, 1H), 3.8-3.5 (m, 2H), 3.3-3.0
(m, 2H), 2.7-2.4 (m, 2H), and 0.10 (s, 9H);
m/e calcd 216.1334, obs 216.1338.

Anal. Calcd for C_{14}H_{20}Si: C, 77.70; H, 9.32.
Found: C, 77.95; H, 9.33.

2-Trimethylsilyl-3-phenylcyclohexene (77)

\[
\text{Me}_2\text{Si}
\]

48%, \textsuperscript{1}H NMR (δ, CDCl\textsubscript{3}) 7.2 (s, 5H), 6.16 (br t,
\( J = 3 \) Hz, 1H), 3.5 (m, 1H), 2.3-2.0 (m, 2H), 2.0-
1.5 (m, 4H), and 0.10 (s, 9H); m/e calcd 230.1491,
obs 230.1497.
Z-1-Trimethylsilyl-1-phenylpropene (78)

\[
\text{SiMe}_3
\]

**\[^1\]H NMR (δ, CDCl\textsubscript{3})**: 7.3-6.8 (m, 5H), 6.16 (q, J = 7 Hz, 1H), 1.90 (d, J = 7 Hz, 3H), and 0.12 (s, 9H).

**Anal. Calcd for C\textsubscript{15}H\textsubscript{22}Si**: C, 78.18; H, 9.63.

**Found**: C, 78.20; H, 9.69.

1-Isopropyl-2-trimethylsilyl-4-methylcyclohex-2-ene (79)

\[
\text{SiMe}_3
\]

85%, b. p. 95-111°/7 torr, \[^1\]H NMR (δ, CDCl\textsubscript{3}) 5.93 (m, 1H), 2.2-1.4 (br m, 7H), 0.97 (d, J = 7 Hz, 6H), 0.73 (d, J = 7 Hz, 3H), and 0.03 (s, 9H).

**Anal. Calcd for C\textsubscript{12}H\textsubscript{18}Si**: C, 75.72; H, 9.53.

**Found**: C, 75.71; H, 9.62.

1-Trimethylsilyl-6-methoxy-3,4-dihydronaphthalene (80)

\[
\text{SiMe}_3 \quad \text{MeO}
\]

67%, b. p. 95°/100 torr, \[^1\]H NMR (δ, CDCl\textsubscript{3}) 7.15 (m, 1H), 6.8-6.6 (m, 2H), 6.34 (t, J = 4 Hz, 1H), 3.83 (s, 3H), 3.0-2.6 (m, 2H), 2.5-2.1 (m, 2H), and 0.35 (s, 9H).

1-Trimethylsilyl-3,4-dihydronaphthalene (81)

\[
\text{SiMe}_3
\]

67%, b. p. 65-80°/0.1 torr, \[^1\]H NMR (δ, CDCl\textsubscript{3}) 7.3-7.1 (m, 4H), 6.50 (t, J = 4 Hz, 1H), 3.0-2.7 (m, 2H), 2.6-2.2 (m, 2H), and 0.40 (s, 9H).
1,1-Dimethyl-2-trimethylsilylcyclohex-2-ene (82)

\[
\text{Me}_3\text{Si} \quad \begin{array}{c}
\text{C}_8\text{H}_{12}
\end{array}
\]

b.p. 70-75°/4 torr, \(^1\text{H NMR} (6, \text{CDCl}_3) 6.87 \text{ (t, } J = 3 \text{ Hz, } 1\text{H}), 2.1-1.1 \text{ (m, } 6\text{H}), 0.92 \text{ (s, } 6\text{H}), \text{ and } 0.00 \text{ (s, } 9\text{H}); \text{ m/e calcd 182.1491, obs 182.1495.}

3-Trimethylsilylcholestan-2-ene (83)

The vinylsilane was prepared in the usual manner in 50% yield, however, it was contaminated with a small amount of 2-cholestene which could not be completely removed by either high pressure liquid chromatography or recrystallization. A sample recrystallized from hexane and again from methanol had m.p. 158-165°; \(^1\text{H NMR} (6, \text{CDCl}_3) 6.0-5.5 \text{ (m, } 1\text{H}), 2.1-0.7 \text{ (series of m, } 46\text{H}), \text{ and } 0.1 \text{ (s, } 9\text{H); m/e calcd 442.3995, obs 442.4004.}

\(Z\)-4-Trimethylsilylhept-3-ene Oxide (92)

\[
\text{Me}_3\text{Si} \quad \begin{array}{c}
\text{C}_7\text{H}_{15}\text{O}
\end{array}
\]

\(Z\)-4-Trimethylsilylhept-3-ene (4.02 g, 23.7 mmoles) was dissolved in dry methylene chloride (150 ml) buffered with sodium bicarbonate (4 g). The slurry was cooled to 0° and \(m\)-chloroperoxybenzoic acid (85%, 5.28 g, 26 mmoles) was added slowly. After 90 minutes, the solvent was evaporated and replaced with ether. The solution was extracted with water (1 x 60 ml), a saturated solution of sodium sulfite (2 x 60 ml), a saturated solution of sodium bicarbonate (2 x
60 ml), and brine, before drying. The solvent was evaporated to yield the epoxide as a colorless oil (4.29 g, 23.1 mmoles, 98%); $^1$H NMR (6, CDCl$_3$) 2.7 (t, $J = 5$ Hz, 1H), 1.9-0.8 (m, 12H), and 0.10 (s, 9H); $\nu_{\text{film}}$ 2965, 2880, 1465, 1252, 840, and 752 cm$^{-1}$; m/e calcd 186.1440, obs 186.1444.

1-Trimethylsilyl-syn,anti-2-methyl-7-oxa-cis-bicyclo[4.1.0]heptane (89a and 89b)

2-Trimethylsilyl-3-methylcyclohexene, (72), (1.16 g, 6.91 mmoles) was dissolved in dry methylene chloride (50 ml) buffered with sodium bicarbonate (1 g). To the ice-cooled stirred solution was slowly added m-chloroperbenzoic acid (85%, 1.44 g, 7.1 mmoles). After the addition was complete, the slurry was allowed to warm to room temperature and stirred for 12 hours. The milky solution was extracted with a saturated solution of sodium sulfite (2 x 50 ml), a saturated solution of sodium bicarbonate (2 x 50 ml), and brine prior to drying. The solvent was removed to yield a colorless oil consisting of 36% 1-trimethylsilyl-syn-2-methyl-7-oxa-cis-bicyclo[4.1.0]-heptane, (89a); $^1$H NMR (6, CDCl$_3$) 3.0 (ABXm, 1H), 2.3-1.7 (m, 5H), 1.6-1.0 (m, 5H), 1.05 (d, $J = 7$ Hz, 3H), and 0.10 (s, 9H); and 62% 1-trimethylsilyl-anti-2-methyl-7-oxa-cis-bicyclo[4.1.0]heptane, (89b); $^1$H NMR (6, CDCl$_3$) 2.9 (ABXm, 1H), 2.3-1.7 (m, 3H), 1.6-1.0 (m, 4H), 1.05 (d, $J = 7$ Hz, 3H), and 0.10 (s, 9H); m/e calcd 184.1283, obs
184.1287 (1.13 g, 6.14 mmoles, 89%). The two isomers were separated by vpc on a 4 ft 10% SF-96 column at 140°.

1-Trimethylsilyl-syn,anti-2-isopropyl-syn,anti-5-methyl-7-oxa-cis-bicyclo[4.1.0]heptane (94)

Following the procedure described previously, the epoxysilane was produced in 77% yield as a clear oil; $^1$H NMR (δ, CDCl$_3$) 2.9 (br s, 1H), 2.3-1.2 (m, 7H), 1.1-0.8 (m, 9H), and 0.10 (s, 9H); m/e calcd 226.1753, obs 226.1758.

1-Trimethylsilyl-syn,anti-4-t-butyl-7-oxa-cis-bicyclo[4.1.0]heptane (95a and 95b)

Following the procedure developed previously, the epoxides were obtained in 87% yield as a white solid, m.p. 49-52°; $^1$H NMR (δ, CDCl$_3$) 3.2-2.9 (ABXm, 1H), 2.4-1.0 (m, 7H), 0.9 (s, 9H), and 0.1 (s, 9H). The two isomeric epoxides were inseparable by thin layer or vapor phase chromatography under a variety of conditions; however, reduction studies indicated the isomeric ratio to be 60% anti/40% syn.

4,5-Benzol-1-trimethylsilyl-8-oxa-cis-bicyclo[7.1.0]oct-4-ene (96)

Following the epoxidation procedure described previously, the epoxysilane was produced quantitatively as a clear oil; $^1$H NMR (δ, CDCl$_3$) 7.15 (s, 4H), 3.4-3.2 (m, 2H), 3.0-1.6
(m, 5H), and 0.05 (s, 9H); ν\text{film}^\text{max} 3015, 2980, 1670, 1495, 1455, 1250, 1150, 1100, 840, and 750 cm\(^{-1}\); m/e calcd 232.1283, obs 232.1289.

\textbf{2β-Trimethylsilyl-2α,3α-epoxycholestane (97)}

The epoxidation was performed as usual, with the epoxysilane obtained in 90% yield, m.p. 183-188\(^\circ\) (recrystallized from acetone/ether); \(^1\)H NMR (δ, CDCl\(_3\))

\[2.9 \text{ (d, } J = 6 \text{ Hz, 1H), 2.1-1.6 (m, 43H), and 0.1 (s, 9H)}; \text{ m/e calcd 458.3944, obs 458.3952.}\]

\textbf{syn, anti-3-Methyl-syn-2-trimethylsilylcyclohexanol (90)}

A solution of 1-trimethylsilyl-syn,anti-2-methyl-7-oxa-cis-bicyclo[4.1.0]heptane, (89), (1.45 g, 7.9 mmole) in dry ether (10 ml) was slowly added to a slurry of lithium aluminum hydride (0.34 g, 9.0 mmole) in dry ether (40 ml) while cooled to 0\(^\circ\) under argon. The reaction mixture was stirred at 0\(^\circ\) for 15 minutes, then allowed to warm to room temperature with continued stirring for 5 hours. The mixture was cooled to 0\(^\circ\), and quenched with a saturated solution of sodium sulfate. When the solids turned completely white, the mixture was suction filtered, the solids were washed with ether (2 x 20 ml), and the filtrate was dried. The solvent was evaporated and the residue was distilled to give the silylalcohol as a clear oil (b.p. 70\(^\circ\)/0.5 torr) (1.22 g, 6.57 mmole, 83%); \(^1\)H NMR (δ, CDCl\(_3\)) 4.10 (br s, 1H), 2.1-0.9 (m, 8H), 0.95 (d, \(J = 6\) Hz, 3H), and 0.16 (s, 9H); ν\text{film}^\text{max} 3480, 2940, 2880, 1460, 1250, 1030, 940, 830, 745, and 685 cm\(^{-1}\).
4-Trimethylsilyl-3-heptanol (98)

Following the reduction procedure developed previously, the corresponding epoxide (98) gave the alcohol in 52% distilled yield (b.p. 58°C/0.5 Torr); 1H NMR (δ, CDCl₃) 4.6 (s, 1H), 3.8-3.4 (m, 1H), 2.0-0.8 (m, 12H), and 0.10 (s, 5H); νmax 3400, 2950, 2870, 1450, 1250, 1100, 1060, 960, 840, and 750 cm⁻¹.

1-Isopropyl-2-trimethylsilyl-4-methylcyclohexan-3-ol (100)

A three-necked flask equipped with a condenser, nitrogen inlet, and an addition funnel was charged with dry tetrahydrofuran (40 ml) and lithium aluminum hydride (0.15 g, 4.0 mmoles). To the stirred slurry was added a solution of the epoxysilane, (94), (0.85 g, 3.8 mmoles) in dry tetrahydrofuran (10 ml). The mixture was refluxed for 40 hours, cooled to 0°C, and quenched with a saturated solution of sodium sulfate. The white solids were filtered and triturated with boiling ether (2 x 50 ml). The combined filtrates were dried and evaporated to yield the silylalcohol, (100), (0.51 g, 2.3 mmoles, 61%); 1H NMR (δ, CDCl₃) 3.72 (m, 1H), 2.1-1.1 (m, 8H), 1.1-0.7 (m, 9H), and 0.10 (s, 9H); M⁺ was not seen; base peak at m/e 138 corresponds to loss of trimethylsilylanol.

Lithium Aluminum Hydride Reduction of 1-Trimethylsilyl-syn,anti-4-t-butyl-7-oxa-cis-bicyclo[4.1.0]heptane (95a and 95b)

Following the conditions given previously, the reaction mixture
was subjected to careful gas phase chromatography (5 ft Carbowax 20M, 165°C). Three compounds were identified as follows: (a) retention time 4.5 minutes, starting epoxide, (25), (33%); (b) retention time 7.5 minutes, 1-trimethyl-syn-4-t-butyldicyclohexanol, (113), (51%); 1H NMR (δ, CDCl3) 1.9-0.8 (m, 10H), 0.85 (s, 9H), and 0.03 (s, 9H); (c) retention time 11.5 minutes, syn-1-trimethylsilyl-anti-4-t-butyldicyclohexan-2-ol (101b), (16%); 1H NMR (δ, CDCl3) 4.2-4.1 (m, 1H), 2.0-0.8 (m, 8H), 0.80 (s, 9H), and 0.00 (s, 9H).

1,2-Benzyn-5-trimethylsilylcylohepten-4-ol (102)

A three-necked flask equipped with a condenser, nitrogen inlet, and addition funnel was charged with dry ether (80 ml) and lithium aluminum hydride (0.17 g, 4.4 mmole). To the stirred slurry was added the epoxysilane, (26), (1.01 g, 4.36 mmole) in dry ether (20 ml). The mixture was refluxed for 27 hours before cooling to 0°C and quenching with a saturated solution of sodium sulfate. The white mixture was filtered with the salts being leached twice with boiling ether. The combined filtrates were dried and evaporated to yield the silylalcohol (102) in quantitative yield; 1H NMR (δ, CDCl3) 7.15 (s, 4H), 4.4-4.2 (m, 1H), 3.2-2.7 (m, 4H), 2.1-1.1 (m, 4H), and 0.06 (s, 9H); νfilm 3440, 2960, 1500, 1455, 1250, 1030, 840, and 750 cm⁻¹; no M⁺ was seen; m/z 144 (80%
of base peak) corresponds to loss of trimethylsilanol, while m/e 129 (base peak) corresponds to loss of benzocyclobutene.

\[
\begin{align*}
\text{SiMe}_3^- & \quad \rightarrow \quad \text{SiMe}_3^- \\
+ \text{H} & \quad + \quad \text{H}_2\text{C} = \text{C} = \text{SiMe}_3 \quad \text{m/e } 129
\end{align*}
\]

Lithium Aluminum Hydride/Aluminum Chloride Reduction of 1-Trimethylsilyl-syn,anti-4-t-butyl-7-oxa-cis-bicyclo[4.1.0]heptane (25a and 25b)

A three-necked flask equipped with an overhead stirrer, addition funnel, and nitrogen inlet was charged with dry ether, lithium aluminum hydride, and the slurry cooled to 0° before adding anhydrous aluminum chloride. The ratio of lithium aluminum hydride/aluminum chloride was varied. The mixture was stirred in the cold (0°) for 5 minutes, at room temperature for 15 minutes, then recooled to 0°. A solution of the epoxysilane, (25), in dry ether was added dropwise. Once the addition was complete, the solution was stirred at 0° for an additional 30 minutes before being allowed to warm to room temperature for an additional 1-3 hours. The excess reducing agent was destroyed, after cooling to 0°, by the addition of a saturated solution of sodium sulfate until the solids turned white. The solids were filtered, extracted twice with boiling ether, and the combined filtrates dried and evaporated. Separation of the products
yielded (1 ft SE-30, 155°) as follows: (a) retention time 4 minutes, starting epoxysilane, (112); (b) 6.75 minutes, 1-trimethylsilyl-syn-4-t-butylcyclohexanol, (112); (c) 9.5 minutes, syn-1-trimethylsilyl-anti-4-t-butylcyclohexan-2-ol, (101b); and (d) 13.5 minutes, syn-1-trimethylsilyl-syn-4-t-butylcyclohexan-2-ol, (101a); 1H NMR (δ, CDCl₃) 4.1-3.7 (m, 1H), 2.1-0.4 (m, 9H), 0.80 (s, 9H), and 0.03 (s, 9H).

The reduction was performed as previously described except for the reflux time which was extended to 48 hours. The crude alcohol mixture was obtained in quantitative yield in approximately a 1/4 ratio (2α-ol/3α-ol); 1H NMR (δ, CDCl₃) 3.8-3.6 (m, 0.20H), 2.1-0.6 (m, 44H), 0.12 and 0.03 (s, 9H); m/e calcd 460.4100, obs 460.4109. No attempt was made to separate the silylalcohols; the mixture was directly oxidized.

The reduction was performed as previously described using lithium aluminum deuteride in place of the protio analog. The crude
oil obtained was separated into its constituents by gas phase chromatography (6 ft 5% Carbowax 20M, 135°) as follows: (a) retention time 14.15 minutes (6%,4%) l-trimethylsilyl-syn-anti-2-deuterio-syn,anti-4-t-butylcyclohexanol, (113D); \(^1\)H NMR (δ, CDCl\(_3\)) 1.9-0.9 (m, 9H), 0.74 (s, 9H), 0.00 and 0.10 (s, 9H); m/e calcd 229.1972, obs 229.1978; (b) retention time 17 minutes (69%) syn-l-trimethylsilyl-1-deuterio-anti-4-t-butylcyclohexan-2-ol, (114b); \(^1\)H NMR (δ, CDCl\(_3\)) 4.2-4.0 (m, 1H), 1.5-0.9 (m, 8H), 0.71 (s, 9H), and -0.10 (s, 9H); m/e calcd 229.1972, obs 229.1978 (weak), m/e calcd 139.1471, obs 139.1474 (loss of trimethylsilyl); (c) retention time 26 minutes (21%) syn-l-trimethylsilyl-anti-1-deuterio-syn-4-t-butylcyclohexan-2-ol, (114a); \(^1\)H NMR (δ, CDCl\(_3\)) 4.0-3.6 (m, 1H), 1.9-0.8 (m, 8H), 0.64 (s, 9H), and -0.10 (s, 9H); m/e calcd 139.1471, obs 139.1474 (loss of trimethylsilyl, no parent ion seen).

**1-Deuterio-4-t-butylcyclohexene (115)**

The \(\beta\)-silylalcohol, (114b), (18.3 mg, 0.080 mmole) was dissolved in a slurry of dry tetrahydrofuran (5 ml) and sodium hydride (50% in oil, 8 mg, 0.17 mmole) which has been washed free of oil with pentane. The solution was refluxed for 15 hours, decomposed with 2 drops of water, and dried. The sole product isolated by gas phase chromatography (1 ft SE-30, 90°) with a retention time of 3 minutes was the deuterated olefin (2.7 mg, 0.02 mmole, 25%); \(^1\)H NMR (δ, CDCl\(_3\)) 5.7-5.5 (br s, 1H), 2.1-1.0 (m, 7H), and 0.74 (s, 9H); m/e 139.1471, obs 139.1474.
Brown Oxidation of \textit{syn,anti-5-t-Butyl-syn-2-trimethylsilylcyclohexanol (101)}^{58b}

The crude silylalcohol (101) (1.96 g, 8.6 mmoles) was dissolved in ether (3 ml) and to this ice-cold stirred solution was added dropwise a solution of sodium dichromate (0.86 g, 2.87 mmoles) in water (2 ml) and concentrated sulfuric acid (2.37 g, 23.0 mmoles). Upon complete addition, the two-phase mixture was stirred vigorously at room temperature for two hours and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether (2 \times 3 ml). The combined organic layers were extracted with a saturated solution of sodium bicarbonate (2 \times 3 ml) and brine prior to drying. Upon evaporation of the solvent, the remaining oil was pure 3-t-butylcyclohexanone (1.25 g, 7.27 mmoles, 83\%\textsuperscript{293}).

Brown Oxidation of 4-Trimethylsilyl-3-heptanol (104)

Following the modified Brown procedure described previously,\textsuperscript{240} a 64\% distilled (b.p. 45\(^0\), 30 torr) yield of 3-heptanone\textsuperscript{294} was obtained; \(^1\text{H NMR} (\delta, \text{CDCl}_3) 2.4\) (overlapping m, 4H), and 2.0-1.0 (m, 10H).

Brown Oxidation of 2-Trimethylsilyl-3-methylcyclohexanol (21)

Following the modified procedure of Brown described previously,\textsuperscript{240} an 84\% yield of 3-methylcyclohexanone\textsuperscript{295} was achieved; \(^1\text{H NMR} (\delta, \text{CDCl}_3) 2.4-1.0\) (m, 9H) and 1.0 (d, \(J = 5\text{ Hz, 3H})\); \(\nu_{\text{max}}^{\text{film}}\) 2940, 1725, 1260, 1230, 1061, and 845 cm\(^{-1}\).
Carvomenthone (106)

Following the modified Brown oxidation procedure described previously, the ketone was produced from (100) in 90% yield; \(^1H\) NMR (\(\delta\), CDCl\(_3\)) 2.5-2.1 (m, 3H), 1.9-1.2 (m, 6H), 1.1 (d, \(J = 7\) Hz, 3H), and 0.9 (d, \(J = 6\) Hz, 6H); m/e calcd 154.1358, obs 154.1362.

1,2-Benzocyclohepten-4-one (108)

Following the modified Brown oxidation procedure, the ketone was obtained as a viscous oil in 67% yield; 2,4-dinitrophenylhydrazone, m.p. 169.5-170° (lit. m.p. 169-170°); \(^1H\) NMR (\(\delta\), CDCl\(_3\)), 7.16 (s, 4H), 3.7 (s, 2H), 3.1-2.8 (pseudo t, 2H), 2.7-2.4 (pseudo t, 2H), and 2.2-1.6 (m, 2H); m/e calcd 160.0888, obs 160.0891.

Cholestan-2-one (111) and Cholestan-3-one (36)

The Brown oxidation was carried out as previously described, and the crude product was recrystallized from methanol/ether, m.p. 90-125°. The material could be partially separated by high pressure liquid chromatography with cholestan-2-one eluting (hexane/ether, 10/1) first in 9% yield, m.p. 122-126°, followed by a mixture of the two cholestanones, m.p. 94-100°, and lastly cholestan-3-one, m.p. 126-128°, in 41% yield. The fractions
containing cholestan-3-one were verified by mixed m.p. with an authentic sample; no depression was seen in the mixed m.p. The NMR spectra of the two cholestanones were also slightly different, with the last fraction again comparing identically with the cholestan-3-one spectrum; $^1$H NMR (δ, CDCl$_3$) 2.5-2.0 (m, 4H), and 2.1-0.6 (m, 42H). The cholestan-2-one spectrum has minor differences; $^1$H NMR (δ, CDCl$_3$) 2.15 (m, 4H) and 2.1-0.6 (m, 42H); m/e calcd 386.3548, obs 386.3554.

Jones Oxidation of syn,anti-5-t-Butyl-syn-2-trimethylsilylcyclohexanol (101)

The crude trimethylsilylalcohol (10₁) (10 mmoles) dissolved in acetone (6 ml) was placed in an Erlenmeyer flask immersed in a cold water bath. Jones reagent (prepared from chromium trioxide, 6.7 g; water, 12.5 ml; conc. sulfuric acid, 5.8 ml) was added dropwise until an orange-brown color persisted, then ten drops more were added. The slurry was stirred vigorously for an additional 15 minutes before quenching the oxidant by dropwise addition of isopropyl alcohol. Water was added, followed by solid sodium bicarbonate until the solution was neutralized. This mixture was diluted with water and extracted with ether (3 x 10 ml). The organic layers were dried and evaporated, leaving a residue which was fully desilylated affording 3-t-butylcyclohexanone (0.42 g, 2.74 mmoles, 27%); $^{293}$ $^1$H NMR (δ, CDCl$_3$) 2.6-1.1 (m, 9H), and 0.95 (s, 9H); $^{ν_{\text{film}}} \text{max}$ 2960, 2840, 1720, 1470, 1370, 1240, and 1230 cm$^{-1}$. 
Pyridinium Chlorochromate Oxidation of 2-Trimehylsilyl-3-methylcyclohexanol (90)

Pyridinium chlorochromate (2.15 g, 10 mmoles) was slurried in dry methylene chloride (50 ml), and the crude silylalcohol (90) (6.5 mmoles) was added. The slurry turned black very rapidly, and the progress of reaction was monitored by thin layer chromatography (silica gel eluted with pentane/methylene chloride (5/1)). The reaction continued for two hours, whereupon it was diluted with 4 volumes of ether and the liquid filtered through a short column of Florisil to remove inorganic material. The chromium salts were washed with additional ether, and the combined filtrates were evaporated and distilled (b.p. 40-50°, 0.3 torr) to yield 2-trimethylsilyl-3-methylcyclohexanone (0.62 g, 3.37 mmoles, 51%).

Collins Oxidation of 2-Trimehylsilyl-3-methylcyclohexanol (90)

A solution of pyridine (1.58 g, 20 mmoles) in dry methylene chloride (60 ml) was cooled to 0°, and oven-dried chromium trioxide (1.00 g, 10 mmoles) was added. The mixture was stirred cold for 1 minute, then was warmed to room temperature until homogeneous. After total dissolution, celite (4 g) was added followed by the silylalcohol (90) (0.91 g, 4.89 mmoles). The reaction mixture was stirred for 15 minutes before adding several drops of concentrated sulfuric acid to salt out the pyridine. The mixture was quickly suction filtered through a pad of silica gel/magnesium sulfate (1/1). The
filtrate was evaporated and distilled to yield a clear oil, 2-
trimethylsilyl-3-methylcyclohexanone (116) (b.p. 55-60°, 0.5 Torr)
(0.60 g, 3.26 mmoles, 67%); 1H NMR (δ, CDCl₃) 2.4-1.0 (m, 9H), 1.1
(d, J = 5 Hz, 3H), and 0.10 (s, 9H); ν_{max}^{film} 2960, 1715, 1700, 1255,
and 840 cm⁻¹.

Collins/Fluoride Ion Promoted Oxidation of syn,anti-5-t-Butyl-syn-
2-trimethylsilylcyclohexanol (101)

A solution of dry pyridine (3.2 g, 40 mmoles)
in dry methylene chloride (130 ml) was cooled
to 0°, and oven-dried chromium trioxide (2.00 g,
20.00 mmoles) was added. The mixture was stirred
in the cold for 1 minute before being warmed to room temperature. After
total dissolution (15 minutes), celite (6 g) and tetraethylammonium
fluoride (1.49 g, 10 mmoles) was added followed by the crude silylalcohol
(101) (7 mmoles). The slurry was recooled to 0° and stirred cold for
30 minutes before the pyridine was salted out with potassium bisulfate
and two drops of sulfuric acid. The mixture was suction filtered
through a pad of silica gel/magnesium sulfate (1/1), and the filtrate
was evaporated to yield a mixture of 25% 3-t-butylcyclohexanone (107)
and 75% 2-trimethylsilyl-5-t-butylcyclohexanone (117).

β-Tetralone (109)

1-Trimethylsilyl-3,4-dihydronephthalene (90)
(0.38 g, 1.9 mmoles) dissolved in dry methylene
chloride (25 ml) with sodium bicarbonate added
as a buffer was cooled to 0°. To this slurry
was added m-chloroperbenzoic acid (95%, 0.49 g, 2.4 mmoles). The reaction mixture was stirred in the cold (0°) for two hours under argon to prevent air oxidation of the product to β-naphthol. The solvent was evaporated and replaced with ether. The solution was washed with water (1 x 20 ml), a saturated solution of sodium sulfite (2 x 20 ml), a saturated solution of sodium bicarbonate (2 x 20 ml), and brine prior to drying. After evaporation of solvent, the residue was purely β-tetralone, the H NMR of which was identical to that of an authentic sample (0.21 g, 1.6 mmoles, 85%); H NMR (δ, CDCl₃) 7.1 (s, 4H), 3.55 (s, 2H), 5.1-2.8 (ABX pseudo t, 2H), and 2.6-2.5 (ABX pseudo t, 2H).

4-Methoxy-β-tetralone (81)

The oxidation was performed as described previously, yielding the ketone as a semi-solid in 96% yield. The NMR spectrum is identical to that of β-tetralone in the aliphatic region; H NMR (δ, CDCl₃) 7.2-6.6 (m, 3H), 3.8 (s, 3H), 3.5 (s, 2H), 3.1-2.8 (ABXY pseudo t, 2H), and 2.6-2.3 (ABXY pseudo t, 2H).

General Photooxygenation Procedure

The vinylsilane was dissolved in methanol (5 g/200 ml) along with rose bengal (1 mg/1 ml) as a sensitizer. The solution was irradiated through an air and water cooled Pyrex well with a Sylvania DXV bulb while bubbling oxygen continuously through a frit at the bottom of the well. The dye was replenished if necessary (because of bleaching) by adding a small amount of a concentrated solution about every 15 hours.
The reacted solution was poured into an Erlenmeyer flask and sodium borohydride (1 mole equiv) was slowly added. After stirring for at least one hour, the mixture was concentrated and dissolved in ether. The organic layer was extracted twice with water to remove most of the rose bengal. The last trace of dye was removed by adsorption onto basic alumina and passage through a 2 cm plug of basic alumina. The clear eluate was dried and evaporated to give a mixture of starting vinylsilane and the product which could be easily separated by chromatography (silica gel eluted with 50% ether/hexane).

Spectral Data for Photooxygenation Products

3-Methyl-2-trimethylsilyl cyclohex-2-en-1-ol (132)

\[
\begin{align*}
\text{SiMe}_3 & \quad \text{OH} \\
1^H \text{NMR} (\delta, \text{CDCl}_3) & \quad 4.5-4.1 (m, 1H), 2.2-1.0 (m, 10H), \text{and } 0.1 (s, 9H); \text{ m.p. } 44-47.5^\circ.
\end{align*}
\]

2-Trimethylsilyl cyclohex-2-enol (138)

\[
\begin{align*}
\text{Me}_3\text{Si} & \quad \text{OH} \\
1^H \text{NMR} (\delta, \text{CDCl}_3) & \quad 6.10 (\text{brt}, J = 3 \text{ Hz}, 1H), 4.24 (\text{br s}, 1H), 2.2-1.6 (\text{br m}, 7H), \text{and } 0.17 (s, 9H).
\end{align*}
\]

**Anal.** Calcd for C\textsubscript{9}H\textsubscript{18}OSi: C, 63.47; H, 10.65.

Found: C, 63.39; H, 10.64.

2-Trimethylsilyl-5-t-butylicyclohex-2-en-1-ol (139)

\[
\begin{align*}
\text{Me}_3\text{Si} & \quad \text{OH} \\
1^H \text{NMR} (\delta, \text{CDCl}_3) & \quad 6.2-5.8 (m, 1H), 4.45-4.2 (m, 1H), 2.1-1.7 (m, 2H), 1.6-1.1 (m, 4H), 0.87 (s, 9H), \text{and } 0.03 (s, 9H); \text{ m/z calcd } 226.1753, \text{ obs } 226.1758; \text{ syn/anti ratio } 1/3.
\end{align*}
\]
Anal. Calcd for C_{13}H_{28}OSi: C, 68.96; H, 11.57.
Found: C, 68.96; H, 11.44.

E-4-Trimethylsilylhept-4-en-3-ol (140)

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9H); mixture of E,Z-isomers $v_{\text{max}}^{\text{film}}$ 3370, 2940, 1605, 1465, 1250, 1010, 840, and 760 cm$^{-1}$.

Photooxygenation of 4,5-Benzocyclohepta-1,4-diene (76)

Following the general procedure the two products obtained are as follows:

5,6-Benzo-2-trimethylsilylcyclohepta-2,5-dien-1-ol, 144; $^1$H NMR (δ, CDCl$_3$) 7.2-6.7 (m, 4H), 5.95 (br d, J = 6 Hz, 1H), 3.4-3.0 (m, 2H), 2.9-2.6 (m, 1H), 2.6-2.2 (m, 2H), and 0.05 (s, 9H); m/e calcd 232.1283, obs 232.1289.

4,5-Benzocyclohepta-2,4-dienol, 145; $^1$H NMR (δ, CDCl$_3$) 7.2-7.1 (br s, 4H), 6.40 (dd, J = 12 and 1 Hz), 5.90 (dd, J = 12 and 1 Hz, 1H), 4.6-4.2 (m, 1H), and 3.2-1.8 (br m, 5H).

1-Phenyl-2-trimethylsilylprop-2-enol (154)

$^1$H NMR (δ, CDCl$_3$) 7.26 (s, 5H), 5.90 (dd, J = 2.4 and 1.6 Hz, 1H), 5.51 (dd, J = 2.4 and 1.4 Hz, 1H), 5.15 (br t, J = 1.5 Hz, 1H), 1.96 (s, 1H), and 0.08 (s, 9H).

Anal. Calcd for C$_{12}$H$_{18}$O Si: C, 69.84; H, 8.79.

Found: C, 69.77; H, 8.80.

General Tetra-n-butylammonium Fluoride Desilylation Procedure: 5-t-Butylcyclohex-2-enol (147)

The silylalcohol, 147, (100 mg, 0.442 mmole) was dissolved in dry acetonitrile (2 ml), and a solution of tetra-n-butylammonium fluoride
in acetonitrile (2 M, 2.2 ml, 4.4 mmoles) was added. The mixture was heated to reflux for 36 hours, cooled, diluted with ether (10 ml), washed with water (2 x 10 ml) and brine, and dried. The evaporated residue was chromatographed (silica gel, elution with 50% ether/hexane) to yield the desilylated product as a clear liquid (65 mg, 0.422 mmole, 96%); $^1$H NMR ($\delta$, CDCl$_3$) 5.85-5.5 (m, 1H), 4.3-3.8 (m, 1H), 2.2-1.0 (br m, 6H), and 0.80 (s, 9H).

Spectral Data and Reaction Time for Desilylated Products

3-Methylcyclohex-2-enol (134)

$^1$H NMR ($\delta$, CDCl$_3$) 5.7-5.3 (m, 1H), 4.3-4.0 (m, 1H), 2.1-1.4 (m, 7H), and 1.7 (br s, 3H).
Refluxed 1.5 hours.

Cyclohex-2-enol (146)

$^1$H NMR ($\delta$, CDCl$_3$) 5.7 (br s, 2H), 4.2-3.9 (m, 1H), and 2.1-1.1 (m, 7H).
Refluxed 1 hour.

E-Hept-4-enol (148)

$^1$H NMR ($\delta$, CDCl$_3$) 5.8-5.1 (m, 2H), 3.84 (br q, $J = 6$ Hz, 1H), and 2.2-0.6 (br m, 11H).
Refluxed 1 hour.

Z-Hept-4-enol (149)

$^1$H NMR ($\delta$, CDCl$_3$) 5.6-5.0 (m, 2H), 4.24 (br q, $J = 7$ Hz, 1H), and 2.4-0.6 (br m, 11H).
Refluxed 1 hour.
E-Cyclododec-2-enol (151)

\[ \text{1H NMR (δ, CDCl}_3\text{) 5.6-5.1 (m, 2H), 4.3-3.8 (m, 1H), and 2.5-0.6 (m, 19H); m/e calcd 182.1671, obs 182.1674.} \]

Refluxed 21 hours.

Z-Cyclododec-2-enol (150)

\[ \text{1H NMR (δ, CDCl}_3\text{) 5.6-5.1 (m, 2H), 4.9-4.4 (m, 1H), and 2.6-0.6 (m, 19H).} \]

Refluxed 1 hour.

5,6-Benzocyclohepta-1,5-dien-3-ol (152)

\[ \text{1H NMR (δ, CDCl}_3\text{) 7.15 (s, 4H), 6.47 (dt, J = 11 and 2 Hz, 1H), 5.78 (dt, J = 11 and 5 Hz, 1H), 4.4-4.0 (m, 1H), 3.4-2.3 (m, 4H), and 2.0 (s, 1H).} \]

Refluxed 1.5 hours.

Z-Cyclododec-2-enol (150)

A solution of wet tetraethylammonium fluoride (several fold excess) in dry acetonitrile (15 ml) was heated so that any water could be azeotroped out of the reaction vessel. The volume removed by distillation was replaced with dry acetonitrile, and the silylalcohol 142 (50 mg, 0.20 mmole) was added. The solution was heated to reflux and the reaction progress was monitored by thin layer chromatography (silica gel, elution with 50% ether/hexane) for 75 minutes. The solution was cooled and evaporated. The residue, taken
up in ether, was extracted with water (2 x 10 ml) and brine, and dried. The evaporated residue was pure product (27 mg, 0.15 g, 76%) which was identical to that produced and purified previously.

**Z-Cyclododec-2-enol (150)**

\[ \text{OH} \]

Sodium hydride (50%, 30 mg, 0.4 mmole) in oil was placed in a dry flask, washed free of oil with pentane (3 x 5 ml), and covered with dry tetrahydrofuran (5 ml). To this slurry was added the silylalcohol, 142 (50 mg, 0.20 mmole), and the mixture was refluxed for 21 hours. The crude reaction mixture was carefully diluted with wet ether, washed with water, dried, and evaporated. The residue was purified by chromatography (neutral alumina, elution with ether, r.f. 0.9) to yield the allylic alcohol as a clear liquid (16 mg, 0.088 mmole, 45%); \(^1\)H NMR was found to be identical to that previously obtained.

**E-Cyclododec-2-enol (151)**

\[ \text{OH} \]

Prepared as described previously in 95% yield; \(^1\)H NMR was identical to that previously obtained.

**Z,(E,Z)-2-Trimethylsilylcyclododeca-1,3-diene (171)**

A solution of dry pyridine (2 ml) and trifluoroacetic anhydride (52 mg, 28.4 \(\mu\)l, 0.20 mmole) was cooled to 0°. To this cold solution was added the silylalcohol, 142 (50 mg,
0.20 mmole) before warming the solution to room temperature for 13 hours. By thin layer chromatographic analysis (silica gel eluted with 10% ether/hexane), starting material remained; therefore the reaction mixture was heated to 70° for 5 minutes. The solution was cooled, diluted with pentane, washed with water (3 x 5 ml), and dried. The residue upon evaporation of solvent was chromatographed (silica gel, elution with 10% ether/hexane) to yield the product, 171, r.f. 0.8 (26 mg, 0.11 mmole, 56%); 1H NMR (δ, CDCl₃) 6.4-5.7 (m, 3H), 3.0-0.8 (m, 16H), and 0.01 (s, 9H); m/e 236 (too small to determine accurate mass), m/e 221 (loss of a methyl group), m/e 162 (loss of trimethylsilane). A second band (r.f. 0.1) proved to be recovered starting material (15 mg, 0.06 mmole, 30%).

1,3-Cycloododecadiene (172)  

2-Trimeethylsilylycyclododec-2-enol (50 mg, 0.20 mmole), p-toluene sulfonic acid (38 mg, 0.20 mmole) and dry benzene (2 ml) were refluxed for 1 hour, cooled, and diluted with ether. The solution was extracted with saturated sodium bicarbonate solution (2 x 5 ml) and brine before drying. The crude oil, obtained in quantitative yield, had an infrared spectrum identical to an authentic sample. 1H NMR (δ, CDCl₃) 6.6-5.1 (m, 4H), 2.3-1.7 (m, 4H), and 1.7-0.7 (m, 12H); ν<sub>film</sub> <sub>max</sub> 3010, 2940, 2870, 1470, 1450, 983, and 951 cm⁻¹; m/e calcd 164.1565, obs 164.1568.
General Procedure of Annulation with $\beta,\beta$-Dimethylacryloyl Chloride

In a dry two-necked flask equipped with a nitrogen inlet and rubber septum were placed dry methylene chloride (8 ml) and anhydrous aluminum chloride (1.0 mmole). The slurry was cooled to -78° and $\beta,\beta$-dimethylacryloyl chloride (1.0 mmole) was added via syringe followed by the vinylsilane (1.0 mmole). The solution turned slightly yellow during 30 minutes before being poured into 3 M hydrochloric acid (10 ml). After being stirred vigorously for 15 minutes, ether was added and the layers were separated. The organic phase was extracted with water (10 ml), a saturated solution of sodium bicarbonate (10 ml), and brine (10 ml). The solution was dried and evaporated and the residue was dissolved in dry methylene chloride (10 ml), and transferred to a roundbottom flask. To this solution was added stannic chloride (3.0 mmoles), and the solution was heated to reflux. The progress of reaction was monitored by thin layer chromatography, and allowed to proceed until the starting dienone was completely consumed. The purple-red solution was poured onto 1.5 M hydrochloric acid and diluted with ether. The organic layer was extracted with water (10 ml), a saturated solution of sodium bicarbonate (10 ml), and brine (10 ml), before drying. The concentrated residue was chromatographed (silica gel, elution with 50% ether/hexane) to yield the cyclized product.
Physical Data of Products

3,3-Dimethyl-3a,4,5-trihydro(2H)pentalen-1-one (176)

b.p. 44-46°/0.3 torr; $^1$H NMR (δ, CDCl$_3$) 6.40 (m, 1H), 3.3-2.5 (m, 2H), 2.34 (br d, 2H), 2.1-1.5 (m, 2H), 1.13 (s, 3H), and 0.82 (s, 3H); $v_{\text{film max}}$ 3000, 1715, 1640, and 1220 cm$^{-1}$; m/e calc 150.1045, obs 150.1048.

3,3-Dimethyl-4,5,6-trihydro(2H)pentalen-1-one (177)

b.p. 44-46°/0.3 torr; $^1$H NMR (δ, CDCl$_3$) 2.53 (s, 2H), 2.32 (br s, 6H), and 1.20 (s, 6H); $v_{\text{film max}}$ 2940, 1700, 1640, 1370, 1275, and 1050 cm$^{-1}$; m/e calc 150.1045, obs 150.1048.

3,3-Dimethyl-3a,4,5,6-tetrahydro(2H)inden-1-one (178)

2,4-Dinitrophenylhydrazone, m.p. 182-183°; $^1$H NMR (δ, CDCl$_3$) 6.68 (br d, $\delta$ = 3 Hz, 1H), 2.4-1.3 (m, 6H), 2.10 (s, 2H), 1.17 (s, 3H), and 0.78 (s, 3H); $v_{\text{film max}}$ 2940, 2860, 1720, 1655, and 1220 cm$^{-1}$; m/e calc 164.1201, obs 164.1205.

3,3-Dimethyl-4,5,6,7-tetrahydro(2H)inden-1-one (179)

2,4-Dinitrophenylhydrazone, m.p. 242-243°; $^1$H NMR (δ, CDCl$_3$) 2.22 (s, 2H), 2.2-1.9 (m, 4H), 1.8-1.4 (m, 4H), and 1.14 (s, 6H); $v_{\text{film max}}$ 2900, 1690, 1645, 1410, 1380, and 1245 cm$^{-1}$; m/e calc 164.1201, obs 164.1205.
3,3-Dimethyl-3a,4,5,6,7-pentahydro(2H)azulen-1-one (180)

b.p. 65-68°/0.1 torr; $^1$H NMR (δ, CDCl$_3$) 6.9 (m, 1H), 2.6-1.4 (m, 9H), 2.22 (s, 2H), 1.25 (s, 3H), and 0.90 (s, 3H); $v_{\text{film}}$ max 2930, 2860, 1720, 1645, and 1240 cm$^{-1}$; m/e calcd 178.1353, obs 173.1362.

Analyzed. Calcd for C$_{12}$H$_{18}$O: C, 80.55; H, 10.53.
Found: C, 80.77; H, 10.44.

3,3-Dimethyl-4,5,6,7,8-pentahydro(2H)azulen-1-one (181)

b.p. 65-68°/0.1 torr; $^1$H NMR (δ, CDCl$_3$) 2.6-1.4 (m, 8H), 2.3 (s, 2H), and 1.23 (s, 6H); $v_{\text{film}}$ max 2920, 2850, 1695, 1640, 1440, and 1285 cm$^{-1}$.

Analyzed. Calcd for C$_{12}$H$_{18}$O: C, 80.85; H, 10.53.
Found: C, 80.64; H, 10.22.

15,15-Dimethylbicyclo[10.3.0]pentadec-11-en-13-one (182)

$^1$H NMR (δ, CDCl$_3$) 6.53 (dd, J = 10 and 4 Hz, 1H), 2.7-1.0 (m, 21H), 1.05 (s, 3H), and 0.80 (s, 3H).

15,15-Dimethylbicyclo[10.3.0]pentadec-12-en-13-one (183)

$^1$H NMR (δ, CDCl$_3$) 2.5-2.0 (m, 4H), 2.23 (s, 2H), 2.0-1.3 (m, 14H), and 1.24 (s, 6H); $v_{\text{film}}$ max 2980, 1700, 1625, 1470, 1440, and 1355 cm$^{-1}$.

Analyzed. Calcd for C$_{17}$H$_{28}$O: C, 82.18; H, 11.38.
Found: C, 82.05; H, 11.36.
2-Propylidene-3-ethyl-4,4-dimethylcyclopentanone (184)

\[
\text{^1H NMR (6, CDCl}_3\text{) 6.5 (dt, J = 7 and 2 Hz, 1H), 2.5-0.8 (m, 13H), 1.20 (s, 3H), and 1.00 (s, 3H); m/e calcd 180.1514, obs 180.1519.}
\]

2-Propyl-3-ethyl-4,4-dimethylcyclopentenone (185)

\[
\text{^1H NMR (6, CDCl}_3\text{) 2.6-1.9 (m, 6H), 1.6-1.2 (m, 2H), 1.2-0.8 (m, 6H), and 1.10 (s, 6H); m/e calcd 180.1514, obs 180.1519.}
\]

\text{Anal. Calcd for C}_{12}H_{20}O: C, 79.95; H, 11.17.}

\text{Found: C, 79.73; H, 11.19.}

3,3,7-Trimethyl-3a,4,5,6-tetrahydro(2H)inden-1-one (186)

\[
\text{^1H NMR (6, CDCl}_3\text{) 2.05 (s, 3H), 2.3-0.9 (br m, 9H), 1.10 (s, 3H), and 0.75 (s, 3H); v^{\text{film max}} 2930, 1710, 1640, 1450, and 1220 cm}^{-1}.\]

\text{Anal. Calcd for C}_{12}H_{18}O: C, 80.82; H, 10.21.}

\text{Found: C, 80.66; H, 10.19.}

3,3,7-Trimethyl-4,5,6,7-tetrahydro(2H)inden-1-one (187)

\[
\text{^1H NMR (6, CDCl}_3\text{) 2.16 (s, 2H), 2.5-1.2 (m, 7H), 1.10 (s, 6H), 1.08 (d, J = 8 Hz, 3H); v^{\text{film max}} 2960, 1695, 1640, 1460, and 1245 cm}^{-1}; \text{ m/e calcd 173.1358, obs 178.1362.}
\]

\text{Anal. Calcd for C}_{12}H_{18}O: C, 80.82; H, 10.21.}

\text{Found: C, 80.41; H, 10.43.}
3,3a,4,5,6-Pentahydro(2H)inden-1-one (190) and 3,4,5,6,7-Pentahydro-(2H)inden-1-one (191)

Aluminum chloride (402 mg, 3.0 mmoles) was slurried in dry methylene chloride (10 ml) and cooled to -20°. To the cooled slurry was added acryloyl chloride (90 mg, 81 µl, 1.0 mmole) followed by 1-trimethylsilylcyclohexene (170 mg, 206 µl, 1.0 mmole). The stirred mixture was warmed to room temperature and after 2 hours, was poured onto 2 M hydrochloric acid where it was vigorously stirred for 30 minutes. The organic layer which was diluted with ether and separated was extracted with a saturated solution of sodium bicarbonate (10 ml), dried, and evaporated. The residue was chromatographed (silica gel, elution with 50% ether/hexane) to yield the external enone 190\textsuperscript{85} (20 mg, 0.15 mmole, 1%); \textsuperscript{1}H NMR (6, CDCl\textsubscript{3}) 6.45 (m, 1H) and 2.5-1.0 (m, 11H); \nu\textsubscript{max} 2900, 1715, 1650, and 1220 cm\textsuperscript{-1}; \textsuperscript{24\textit{G}} and the internal enone 191\textsuperscript{85} (17 mg, 0.12 mmole, 12%); \textsuperscript{1}H NMR (6, CDCl\textsubscript{3}) 2.5-1.9 (m, 8H) and 1.8-1.5 (m, 4H); \nu\textsubscript{max} 2910, 1690, 1645, and 1390 cm\textsuperscript{-1}. \textsuperscript{24\textit{G}}

2-Propylidene-3-ethylcyclopentanone (192) and 2-Propyl-3-ethylcyclopent-2-enone (193)

Aluminum chloride (161 mg, 1.2 mmoles) was slurried in dry methylene chloride (5 ml) and cooled to -20°. Acryloyl chloride (108 mg, 98 µl, 1.2 mmoles) and 4-trimethylsilylhept-3-ene (202 mg, 339 µl, 1.19 mmoles) were then
added and stirred cold for 15 minutes. The solution was stirred with 3 M hydrochloric acid, diluted with ether and separated. The organic phase was washed with water, a saturated solution of sodium bicarbonate, and brine prior to drying and solvent removal. The residue was dissolved in trifluoroacetic acid (2 ml) and stirred at room temperature under nitrogen for 3 hours. The solution was slowly added to a saturated solution of sodium bicarbonate and the organic material was extracted into methylene chloride. The organic layer was dried and evaporated. The residue was chromatographed (silica gel, elution with 50% ether/hexane) to give the external enone \(192\) (27 mg, 0.17 mmole, 15%); \(^1\text{H NMR (6, CDCl}_3)\) 6.5 (dt, \(J = 8\) and 2 Hz, 1H) and 3.0-0.8 (m, 15H); \(\nu_{\text{max}}^\text{film}\) 2960, 1720, 1645, and 1460 cm\(^{-1}\); and the internal enone \(192\) (8 mg, 0.05 mmole, 4%); \(^1\text{H (6, CDCl}_3)\) 2.6-1.8 (m, 6H) and 1.9-0.8 (m, 10H); \(\nu_{\text{max}}^\text{film}\) 2960, 1700, 1640, and 1460 cm\(^{-1}\); m/e calcd 152.1201, obs 152.1205.

Another preparation of these two compounds was to slurry aluminum chloride (201 mg, 1.5 mmoles), anhydrous sodium acetate (123 mg, 1.5 mmoles) and dry methylene chloride (5 ml). To this slurry, cooled to \(-45^\circ\), was added acryloyl chloride (108 mg, 98 \(\mu\)l, 1.2 mmoles) followed by 4-trimethylsilylhept-3-ene (202 mg, 229 \(\mu\)l, 1.19 mmoles, 87% vinylsilane with the remainder being octane). The mixture was stirred cold for 15 minutes, poured into 3 M hydrochloric acid, diluted with ether, and separated. The organic phase was extracted with a saturated solution of sodium bicarbonate, dried, and evaporated. The residue was treated at room temperature exactly as above, then heated to reflux for 12
hours. The work-up was performed as above also. Upon chromatography, the external enone \( 192 \) (30 mg, 0.20 mmole, 19%) and the internal enone \( 193 \) (7 mg, 0.05 mmole, 5%) were obtained.

\[ \text{3,4,5,6,7,8-Hexahydro(2H)azulen-1-one (194)} \]

Prepared as previously described, but omitting the final reflux period. The single enone obtained was the internal enone \( 194 \) in 10% yield; \( \text{\textsuperscript{1}H NMR (6, CDCl}_3\)} 2.5-2.1 (m, 6H) and 2.1-1.4 (m, 8H).

Isomerization of 3,3-Dimethyl-3a,4,5-trihydropentalen(2H)-1-one (176) to 3,3-Dimethyl-4,5,6-trihydropentalen(2H)-1-one (177)

The mixture of internal and external enones \( 176 \) and \( 177 \) (50 mg, 0.33 mmole) was dissolved in ethanol/water (10/1, 1.1 ml) and deoxygenated by bubbling nitrogen through the solution for 5 minutes. Rhodium(III) chloride trihydrate (5 mg, 0.02 mmole) was added and the solution was refluxed under nitrogen for 16 hours. The black solution was cooled, diluted with ether, washed with water, and dried. The concentrated residue was chromatographed (silica gel, elution with 50% ether/hexane) to give only the internal enone (50 mg, 0.33, 100%).

Isomerization of 3,3,7-Trimethyl-3a,4,5,6-tetrahydroindan(2H)-1-one (186) and 3,3,7-Trimethyl-4,5,6,7-tetrahydroindan(2H)-1-one (187)

Following the above procedure, an equilibrium mixture of internal, \( 187 \), and external, \( 186 \), enones was obtained after
refluxing for 25 hours. Upon chromatography the isolated enones were obtained in 11% and 71% yield, respectively.

2,3-Dibromo-3-(4-methylphenyl)propionic Acid (207)<sup>251</sup>

\[
\begin{align*}
\text{Br} & \\
\text{COOH} & \\
\text{Br}
\end{align*}
\]

Bromine (10.0 g, 3.23 ml, 62.5 mmoles) was added dropwise to a solution of p-methylcinnamic acid (10.0 g, 61.7 mmoles) in chloroform (100 ml) held under a nitrogen atmosphere. After several drops had been added, solid azobisisobutyronitrile (0.1 g) was added to initiate the reaction along with irradiation from a 150 W flood lamp. The reaction proceeded slowly with continual irradiation over 20 minutes. During the addition, the product crystallized out of solution. The reaction mixture was stirred for an additional 10 minutes before filtering the solid. The filtrate was concentrated allowing a second crop to be filtered. The snow white crystals (16.85 g, 52.3 mmoles, 85%) were vacuum dried.

2-1-Bromo-2-(4-methylphenyl)ethene (208)<sup>252</sup>

In dry acetone (500 ml) was dissolved 2,3-dibromo-3-(4-methylphenyl)propionic acid (16.85 g, 52.3 mmoles) and sodium bicarbonate (15.1 g, 180 mmoles). The flask was covered with aluminum foil and heated to reflux in a darkened hood for 8 hours before evaporation of the acetone. The residue was taken up in ether (300 ml), washed with water (2 x 200 ml) and brine (100 ml), and dried. The ether was evaporated to leave a residue from which the light-sensitive product could be distilled (65°/0.5 torr) as a clear liquid (9.95 g,
50.5 mmoles, 96%); $^1$H NMR (δ, CCl$_4$) 7.50 (ABq, $\delta = 8$ Hz, 2H), 7.07 (ABq, $\delta = 8$ Hz, 2H), 6.95 (ABq, $\delta = 8$ Hz, 1H), 6.27 (ABq, $\delta = 8$ Hz, 1H), and 2.30 (s, 3H); m/e calcd 195.9889, obs 195.9892 (calcd for 1 Br$^7$). A small forerun of acetone dimer was also collected.

Z-1-Trimethylsilyl-2-(4-methylphenyl)ethene (205)$^{253}$

To a mixture of dry tetrahydrofuran/ether/pentane (4/1/1, 120 ml) was added Z-1-bromo-2-(4-methylphenyl)ethene (9.95 g, 50.5 mmoles). The resulting solution was cooled to -120° (liquid nitrogen/n-propyl alcohol bath), whereupon a solution of t-butyllithium in pentane (2 M, 50 ml, 100 mmoles) was added via syringe. The mixture was mechanically stirred for 2 hours before being quenched with chlorotrimethylsilane (10.85 g, 12.0 ml, 100 mmoles). The mixture was allowed to warm slowly to room temperature over 16 hours. The clear mixture was poured into dilute sodium bicarbonate solution and the organic phase was separated, extracted with saturated sodium bicarbonate solution and brine, and dried. The evaporated residue was distilled (b.p. 42-45°/0.07 torr) to give a clear liquid consisting of 70% vinylsilane 205 (2.8 g, 15 mmoles, 30%); $^1$H NMR (δ, CDCl$_3$) 7.10 (ABq, $\delta = 15$ Hz, 1H), 6.95 (br s, 4H), 5.60 (ABq, $\delta = 15$ Hz, 1H), 2.20 (s, 3H), and 0.0 (s, 9H); and 30% p-tolyltrimethylsilylacetylene (1.2 g, 6.4 mmoles, 13%); $^1$H NMR (δ, CDCl$_3$) 7.0 (ABq, $\delta = 8$ Hz, 4H), 2.20 (s, 3H), and 0.05 (s, 9H); $\gamma_{\text{film}}$ max 2950, 2140, 1250, and 850 cm$^{-1}$. 
E-1-(4-Methylphenyl)-3-oxo-5-methyl-1,4-hexadiene (211)

A slurry of aluminum chloride (322 mg, 2.4 mmoles) in dry methylene chloride (20 ml) was cooled to -78°, and β,β-dimethylacryloyl chloride (285 mg, 253 µl, 2.4 mmoles) was added via syringe. To this cold slurry was added the vinylsilane 205 (450 mg, 2.37 mmoles). The solution became yellow and stirred for 30 minutes before pouring it into 3 M hydrochloric acid. This two phase system was stirred vigorously for 15 minutes and diluted with ether before the layers were separated. The organic phase was extracted with water (10 ml), a saturated solution of sodium bicarbonate (10 ml), and brine (10 ml) prior to drying. The evaporated residue was pure dienone 211 in quantitative yield which could be recrystallized, with some loss of material due to extreme solubility, from hexane to give lemon yellow crystals, m.p. 73.5-75°; 1H NMR (δ, CDCl₃) 7.5 (ABq, J = 16 Hz, 1H), 7.4 (ABq, J = 7 Hz, 2H), 7.1 (ABq, J = 7 Hz, 2H), 6.7 (ABq, J = 16 Hz, 1H), 6.3 (septet, J = 0.5 Hz, 1H), 2.35 (s, 3H), 2.20 (d, J = 0.5 Hz, 3H), and 1.96 (d, J = 0.5 Hz, 3H).

3-(4-Methylphenyl)-4,4-dimethylcyclopent-2-enone (204)

The dienone 211 (100 mg, 0.50 mmoles) was dissolved in dry benzene (4 ml) and boron trifluoride etherate (284 mg, 250 µl, 2.0 mmoles) was added. The yellow solution was heated to reflux for 72 hours. The complex formed a red solution upon heating. The cooled solution was poured into a saturated solution of sodium
bicarbonate and extracted with ether (2 x 10 ml). The organic solution was dried, evaporated and chromatographed on silica gel (elution with 50% ether/hexane). Isolated were bands corresponding to decomposition product, r.f. = 0.7, 37 mg; starting dienone 211, r.f. = 0.4, 31 mg (31%); and desired enone 204 (10 mg, 0.05 mmole, 10%) at r.f. = 0.2; $^1$H NMR (δ, CDCl$_3$) 7.4 (A$_2$B$_2$q, J = 8 Hz, 4H), 6.2 (s, 1H), 2.52 (s, 2H), 2.44 (s, 3H), and 1.50 (s, 6H). The spectrum was identical to that published for the α,β-unsaturated ketone 204.

2-Chloromethyltetrahydrofuran (216)$^{254}$

In a two liter, three-necked Morton flask, equipped with a mechanical stirrer, addition funnel, nitrogen inlet, and thermometer was placed freshly distilled tetrahydrofurfuryl alcohol 215 (408 g, 4.0 moles) and pyridine (348 g, 355 ml, 4.4 moles). The solution was cooled in an ice bath and thionyl chloride (500 g, 304 ml, 4.2 moles) was added at a rate of 3-5 drops/second. This kept the internal temperature at 30-42°. The solution immediately turned brown with a white solid forming after about one third of the thionyl chloride had been added. The mixture became thicker, and the last one third of the thionyl chloride could be added at a faster rate. After being stirred at room temperature for an additional 3 hours, the black reaction mixture was poured onto ether contained in a large beaker. The solids were repeatedly slurried and filtered. The combined filtrates were concentrated and the residue was distilled (b.p. 52-60°/20 torr) to yield a clear liquid (313.5 g, 2.85 moles, 71%).
In a dry three liter, three-necked flask equipped with a dry ice condenser, mechanical stirrer, and nitrogen inlet was condensed ammonia (1l) which had been passed through a potassium hydroxide drying tower while cooling the flask to -78°. To the cold ammonia was added a small piece of sodium to generate a blue color. The blue color was dispersed by adding hydrated ferric nitrate (1 g) to give a clear solution with a grey-brown precipitate. The remainder of the sodium pieces (80.5 g, 3.5 moles) were slowly added to the mixture with continued stirring until final traces of blue color were gone. At this point, 2-chloromethyltetrahydrofuran 216 (120.5 g, 1.0 mole) was slowly added to the refluxing mixture over 40 minutes. The mixture refluxed for an additional hour before cooling to -73°, and quenching with solid ammonium chloride. The ammonia was allowed to evaporate overnight. The remaining solids were slurried with ether, filtered, and this process repeated (5 x 500 ml). The combined filtrates were dried and slowly concentrated. The residue was distilled through a 10 cm Vigreux column (b.p. 70-76°/27 torr) to yield a clear liquid (73.0 g, 0.87 mole, 87%); 1H NMR (5, CDCl3) 3.43 (t, J = 6 Hz, 2H), 2.9 (br s, 1H), 2.4-2.1 (m, 2H), 1.92 (t, J = 3 Hz, 1H), and 1.7 (br p, J = 8 Hz, 2H).

1-Trimethylsilyl-5-trimethylsiloxy-1-pentyne (218)

n-Butyllithium in hexane (1.6 M, 82 ml, 130 mmoles) was slowly added to a -78° solution of 1-pentyn-5-ol, 217 (5.0 g, 59.6 mmoles) in dry
ether (200 ml). The mixture was stirred in the cold for 15 minutes, then warmed to room temperature for 2 hours. The white slurry was treated with chlorotrimethylsilane (14.1 g, 16.5 ml, 130 mmole) and heated to reflux for 20 hours. The cooled slurry was filtered, concentrated and distilled (b.p. 88-104\(^\circ\)/41 torr) to yield the product (5.2 g, 40.3 mmole, 68%) as a clear liquid; \(^1\text{H NMR}\) (\(\delta, \text{CDCl}_3\)) 3.64 (t, \(\delta = 12\text{ Hz}, 2\text{H}\)), 2.26 (t, \(\delta = 12\text{ Hz}, 2\text{H}\)), 1.66 (quint, \(\delta = 12\text{ Hz}, 2\text{H}\)), 0.10 (s, 9H), and 0.05 (s, 9H); m/e 228.1366, obs 223.1370.

**E-1-Triethylsilyl-1-penten-5-ol (220)**

To a stirred mixture of 1-pentyn-5-ol (8.4 g, 0.10 mole), triethylsilane (11.6 g, 0.10 mole) and isopropyl alcohol (60 ml) was added a catalytic amount of aqueous chloroplatinic acid (0.1 M, 0.5 ml, 0.05 mmole) under a nitrogen atmosphere. An exothermic reaction took place with gas evolution. When the initial reaction had subsided, the solution was heated to reflux for 4 hours, cooled, and evaporated. The crude residue was distilled (b.p. 94-114\(^\circ\)/0.06 torr) to give a clear oil (11.55 g, 0.058 mole, 58%); \(^1\text{H NMR}\) (\(\delta, \text{CDCl}_3\)) 6.00 (dt, \(\delta = 18\text{ and } 5\text{ Hz}, 1\text{H}\)), 5.55 (d, \(\delta = 18\text{ Hz}, 1\text{H}\)), 3.60 (t, \(\delta = 6\text{ Hz}, 2\text{H}\)), 2.3-1.9 (m, 2H), 1.8-1.3 (m, 3H), and 1.1-0.3 (m, 15H).

**E-5-Triethylsilyl-4-pentenal (221)**

Pyridinium chlorochromate (630 mg, 3.0 mmole) was slurried in dry methylene chloride (10 ml) and the silylalcohol 220 (100 mg, 0.50 mmole) was added slowly. The resulting black mixture was stirred at room
temperature for several hours, diluted with ether (40 ml), and filtered through a short plug of Florisil to give the aldehyde; \[^1\text{H NMR (}\delta, \text{ CDCl}_3\text{)}\] 9.7 (s, 1H), 6.0 (dt, \(\delta = 18\) and 5 Hz, 1H), 5.55 (d, \(\delta = 18\) Hz, 1H), 2.5 (m, 4H), and 1.4-0.4 (m, 15H); \(\nu_{\text{film}}^\text{max}\) 2950, 1730, 1615, 1410, 1230, 1000, and 715 cm\(^{-1}\); \(m/e\) calcld 169.1049, obs 169.1054 (calcld for \(M^+\text{-Et}^+\), no \(M^+\) peak present).

\(\text{3-t-Butyldimethylsiloxy-3-methyl-1-pentyne (223)}\)\(^{256}\) A mixture of 3-hydroxy-3-methyl-1-pentyne \(\text{CMeEt}^+\bos\text{SiMe}_2\text{Bu}^+\) (4.51 g, 50 mmoles), imidazole (8.50 g, 125 mmoles), t-butyldimethylsilyl chloride (4.03 g, 60 mmoles), and dry dimethylformamide (10 ml) was warmed to 35° for 10 hours under nitrogen, then stirred at room temperature for an additional 12 hours. The thick, two-phased mixture was poured into water (100 ml) and extracted with ether. The organic layer was washed with water (25 ml) and brine (25 ml). The first aqueous layer was re-extracted with ether (25 ml), and the combined organic layers were dried and evaporated. The residue was distilled to yield a clear oil (7.66 g, 36 mmoles, 72%) of pure silyl ether and a lower boiling fraction containing impure silyl ether; \[^1\text{H NMR (}\delta, \text{ CDCl}_3\text{)}\] 2.35 (s, 1H), 1.64 (q, \(\delta = 12\) Hz, 2H), 1.40 (s, 3H), 0.97 (t, \(\delta = 12\) Hz, 3H), 0.35 (s, 9H), and 0.15 (s, 6H); \(m/e\) calcld 197.1362, obs 197.1566 (for loss of Me\(^+\), \(M^+\) is very faint, base peak is \(M^+\text{-Bu}^+\)).

\(\text{1-Pentynylcopper (226)}\)\(^{257,258}\) In a two liter Erlenmeyer flask fitted with a rubber stopper through which a nitrogen tube was extended nearly to the eventual surface of the
contents was dissolved copper(II) sulfate pentahydrate (25.0 g, 0.10 mole) in concentrated ammonium hydroxide (100 ml) with nitrogen blowing over the surface for 5 minutes while cooled in an ice bath. Water (400 ml) was added and nitrogen was blown over the solution for an additional 5 minutes. To this dark blue solution was slowly added over 12 minutes hydroxylamine hydrochloride (13.9 g, 0.20 mole), while keeping the solution under nitrogen. The solution was stirred for 1 hour during which time it turned light blue. A solution of 1-pentyne (6.8 g, 0.10 mole) in absolute ethanol (500 ml) was added with swirling, and the flask was stirred for 5 minutes. The mixture was diluted with water (400 ml) whereupon the copious chartreuse precipitate was suction filtered through two 350 ml coarse fritted funnels. The solids were combined and washed with water (5 x 100 ml), ethanol (2 x 100 ml), and ether (2 x 100 ml), then dried under high vacuum for 12 hours. A bright yellow solid (9.10 g, 0.07 mole, 70%) was obtained.

E-1-Phenyl-3-trimethylsilylpropene (88)

\[
\begin{align*}
\text{SiMe}_3 & \\
\text{Ph} & \\
\end{align*}
\]

To a cooled solution (-45°) of n-butyllithium (1.6 M, 9.4 ml, 15 mmoles) in dry tetramethylethlenediamine (20 ml) was slowly added in portions solid propiophenone benzenesulfonylhydrazone (1.00 g, 3.47 mmoles) held in an Erlenmeyer flask which was connected to the reaction vessel by Gooch tubing. The solid quickly dissolved with generation of a red solution which was stirred at -45° for 30 minutes before warming to room temperature for two hours. The solution was heated to 60° for 3 hours followed by cooling to 0°.
Chlorotrimethylsilane (2.17 g, 2.40 ml, 20 mmoles) was added at 0°, and the black mixture was stirred at room temperature for an additional 4 hours. At this point, the solution was diluted with ether and poured onto water. The organic layer was extracted with water (2 x 30 ml), saturated copper sulfate solution (2 x 30 ml), and brine prior to drying. The evaporated residue was adsorbed onto neutral alumina and eluted down a 4 cm column of neutral alumina with pentane. The clear eluate was concentrated and the residue was distilled (b.p. 95°/2.2 torr) to give the allylsilane, 88 \textsuperscript{302} (0.38 g, 2.0 mmoles, 58%); \textsuperscript{1}H NMR (δ, CDCl\textsubscript{3}) 7.4-7.1 (m, 5H), 6.4-6.15 (ABX\textsubscript{m}, 2H), 1.68 (dd, J = 5 and 2 Hz, 2H), and 0.10 (s, 9H).

1-Phenyl-3-trimethylsilylcyclohexene (232)

\[
\begin{array}{c}
\text{Ph} \\
\text{SiMe}_3
\end{array}
\]

In a three-necked flask equipped with a septum, condenser, nitrogen inlet, and an Erlenmeyer flask containing 2-phenylcyclohexanonebenzene-sulfonylhydrazone (9.60 g, 29.3 mmoles) and connected by a piece of Gooch tubing was placed tetramethylethylenediamine (100 ml). The solvent was cooled to -45°, and n-butyllithium in hexane (1.6 M, 90 ml, 144 mmoles) was added via syringe. The hydrazone was slowly added to the stirred solution in portions by shaking. The deep red color of the dianion formed immediately. The solution was stirred in the cold for 1 hour after the addition was complete before warming to room temperature for 1 hour. The Gooch tubing connector was replaced with a glass stopper, and the solution was heated to 55-60° for 2 hours. After cooling the black solution to 0°, chlorotrimethylsilane (14 ml) was
added with the resulting solution stirred at room temperature for 15 hours. The mixture was diluted with pentane (200 ml), quenched by water, and separated into layers. The aqueous layer was extracted with pentane (2 x 200 ml) and the combined organic extracts were successively washed with water (2 x 200 ml), saturated cupric sulfate (2 x 200 ml), and brine. The solution was dried, evaporated, and distilled on a Kugelrohr apparatus (b.p. 80-90°/0.05 torr) to give the allylsilane \( \text{C}_2 \) (4.88 g, 21.2 mmoles, 72%) as a colorless oil which was 95% pure by gas phase chromatography (2 ft 5% SE-30, 150°); \(^1\)H NMR (δ, CDCl\(_3\)) 7.43 (br s, 5H), 6.27 (s, 1H), 3.23-0.97 (m, 7H), and 0.37 (s, 9H); \(v_{\text{film}}^{\text{max}}\) 3040, 3020, 2930, 1670, 1630, 1600, 1493, 1250, 830, and 745 cm\(^{-1}\); \(^{13}\)C NMR (ppm, CDCl\(_3\)) 143.5, 135.0, 128.2, 126.2, 126.0, 125.0, 27.5, 27.3, 23.4, 23.2, and 2.9; UV (2,2,4-trimethylpentane) 2509 Å (13800); m/e calcd 230.1491, obs 230.1500.


2-Bromocyclooctanone Tosylhydrazone (233)\(^{259}\)

![2-Bromocyclooctanone Tosylhydrazone](image)

A mixture of 2-bromocyclooctanone (4.1 g, 20.0 mmoles), tosylhydrazide (3.72 g, 20.0 mmoles), and a catalytic amount of p-toluenesulfonic acid in anhydrous ether (50 ml) was stirred under a nitrogen atmosphere for 4 hours. The white crystals which formed were filtered, and the filtrate was concentrated to give a second crop. The combined crystals were re-crystallized from methylene chloride/hexane to yield the hydrazone.
as white crystals (4.9 g, 13 mmol, 66%), m.p. 118-119°; ¹H NMR (δ, CDCl₃) 8.18 (br s, 1H), 7.73 (ABq, J = 8 Hz, 2H), 7.22 (ABq, J = 8 Hz, 2H), 4.65 (t, J = 8 Hz, 1H), 2.42 (s, 3H), 2.60-1.90 (br m, 4H), and 1.43 (br m, 8H); νₑₓₑₑₘₐₓ 3240, 2940, 1600, 1350, and 1170 cm⁻¹.

3-Bromo-4-heptanone Tosylhydrazone Precursor to (236)²⁵⁹

Prepared as above in 70% yield giving white crystals, m.p. 10-106°; ¹H NMR (δ, CDCl₃) 7.71 (ABq, J = 8 Hz, 2H), 7.22 (ABq, J = 8 Hz, 2H), 4.32 (t, J = 7 Hz, 1H), 2.43 (s, 3H), 2.43-1.16 (m, 6H), and 0.88 (m, 6H).

3-Bromo-4-heptanone Benzenesulfonylhydrazone Precursor to (236)²⁵⁹

Prepared as described above, and recrystallized from methylene chloride/hexane to give white crystals, m.p. 116-117°, in 74% yield; ¹H NMR (δ, CDCl₃) 8.23 (br s, 1H), 7.90 (m, 2H), 7.53 (m, 3H), 4.33 (t, J = 8 Hz, 1H), 2.07 (m, 4H), 1.50 (m, 2H), and 0.85 (m, 6H); νₑₓₑₑₘₐₓ 3220, 3070, 1640, 1590, 1480, 1395, and 1340 cm⁻¹.

2-Bromocyclododecanone Benzenesulfonylhydrazone Precursor to (236)²⁵⁹

2-Bromocyclododecanone (3.25 g, 12.4 mmol) and benzenesulfonylhydrazide (2.15 g, 12.5 mmol) were reacted in dry tetrahydrofuran as before. No product was obtained when the reaction was performed in ether. Recrystallization gave the product (2.95 g, 7.16 mmol, 57%) as white crystals;
\[^{1}\text{H NMR (d, CDCl}_3\) 8.00 (br s, 1H), 7.83 (m, 2H), 7.50 (m, 3H), 4.60 (ABq, J = 12 and 4 Hz, 1H), 2.38 (m, 2H), and 2.20-0.6 (br m, 18H).}\]

3-Phenyl-4-heptanone Tosylhydrazone (236)\[^{146,259}\]

A solution of phenylocopper was prepared by adding phenyllithium in ether/benzene (1 M, 3 ml, 3.0 mmole) to cuprous iodide (0.63 g, 3.3 mmole) in dry ether (5 ml) at 0° with stirring. After 10 minutes, most of the cuprous iodide had dissolved to form a black solution. Dry tetrahydrofuran (5 ml) was added at 0°, and the mixture further cooled to -60°. A solution of 3-bromo-4-heptanone tosylhydrazone (0.35 g, 0.97 mmole) in dry tetrahydrofuran (5 ml) was added dropwise to the phenylocopper solution, and the resulting mixture continued to be stirred in the cold for 15 minutes. The reaction was arrested by addition of acetic acid while cold. The mixture was allowed to warm to room temperature and hydrolyzed with a saturated ammonium chloride/ammonium hydroxide (3/5, 65 ml) solution. The layers were separated, and the aqueous layer was extracted with ether (2 x 20 ml). The organic phase was dried and evaporated. The solid obtained was slurried in hexane and filtered to remove biphenyl. Recrystallization from methylene chloride/hexane gave the product 236 (3.23 g, 0.90 mmole, 95%) as white crystals, m.p. 119-120°; \[^{1}\text{H NMR (d, CDCl}_3\) 7.73 (ABq, J = 8 Hz, 2H), 7.56 (br s, 1H), 7.20 (ABq, J = 8 Hz, 2H), 6.98 (m, 5H), 3.15 (t, J = 8 Hz, 1H), 2.43 (s, 3H), 1.82 (m, 5H), 1.27 (m, 2H), and 0.76 (m, 6H); \[^{\text{v}}_{\text{max}}\text{ cm}^{-1}\) 3220, 1495, 1390, 1350, 1175, and 680 cm\(^{-1}\).\]
2-Phenylcyclooctanone Tosylhydrazone (234)\textsuperscript{259}

Prepared as above giving white crystals in 85% yield; \( ^1H \) NMR (\( \delta, \text{CDCl}_3 \)) 7.70 (ABq, \( J = 8 \text{ Hz} \), 2H), 7.70 (br s, 1H), 7.17 (ABq, \( J = 8 \text{ Hz} \), 2H), 6.96 (m, 5H), 3.57 (m, 1H), 2.43 (s, 3H), and 2.27-0.77 (m, 12H); \( \nu_{\text{max}}^{\text{film}} \) 3220, 2940, 1640, 1600, 1500, 1380, 1340, and 1165 cm\(^{-1}\).

3-Phenyl-4-heptanone Benzenesulfonylhydrazone (236)\textsuperscript{259}

Prepared as above giving white crystals, m.p. 117-118°, in 78% yield; \( ^1H \) NMR (\( \delta, \text{CDCl}_3 \)) 7.90 (m, 2H), 7.70 (br s, 1H), 7.53 (m, 3H), 7.03 (m, 5H), 3.18 (t, \( J = 8 \text{ Hz} \), 1H), 1.83 (m, 4H), 1.23 (m, 2H), and 0.70 (m, 6H); \( \nu_{\text{max}}^{\text{film}} \) 3225, 2980, 1630, 1605, 1495, 1475, 1385, 1250, and 1180 cm\(^{-1}\); m/e calcd 344.155, obs 344.156.

2-Phenylcyclododecanone Benzenesulfonylhydrazone (238)\textsuperscript{259}

Prepared as above giving crystals in 95% yield; \( ^1H \) NMR (\( \delta, \text{CDCl}_3 \)) 7.92 (m, 3H), 7.53 (m, 3H), 7.12 (s, 5H), 3.62 (br d, 1H), 2.35 (m, 2H), and 2.05-06 (br m, 18H).

1-Phenyl-3-trimethylsilylcyclooctene (235)\textsuperscript{259}

Following the procedure developed previously,\textsuperscript{261} the vinylanion was heated to 57° for 25 hours. After suitable quenching, work-up, and Kugelrohr distillation (b.p. 95-120°/0.05 torr) the oily product was found to consist of a
mixture of 71% allylsilane and 29% olefin, 3-phenylcyclooctene, determined by gas phase chromatography (2 ft 5% SE-30, 150°). The yield of the desired compounds was 65%. Allylsilane, \( \text{H NMR} \) (δ, CDCl\(_3\)) 7.30 (s, 5H), 5.77 (d, \( J = 9 \text{ Hz} \), 1H), 2.62 (m, 2H), 2.33 (m, 1H), 2.10-1.20 (m, 8H), and 0.08 (s, 9H); \( \nu_{\text{film}} \) 3090, 2840, 1600, 1495, 1250, and 840 cm\(^{-1}\); \( \text{13C NMR} \) (ppm, CDCl\(_3\)) 144.2, 140.6, 129.2, 126.2, 125.8, 30.5, 30.0 (2C), 28.0, 27.1, 26.9, and 3.1

**Anal.** Calcd for C\(_{17}\)H\(_{26}\)Si: C, 79.00; H, 10.14.


3-Phenylcyclooctene; \( \text{H NMR} \) (δ, CDCl\(_3\)) 7.20 (s, 5H), 5.67 (s, 1H), 5.57 (s, 1H), 3.73 (m, 1H), 2.28 (m, 2H), and 1.70 (br s, 8H); \( \nu_{\text{film}} \) 3080, 2940, 2865, 1605, 1495, 1455, 745, and 700 cm\(^{-1}\).

**1-Phenyl-exo-5-trimethylsilyl-cis-bicyclo[4.1.0]heptane (245)**

A mixture of powdered zinc (1.5 g, 23.7 mmole) and cuprous chloride (0.25 g, 2.5 mmole) in dry ether was refluxed for 1 hour with vigorous stirring. After cooling of the mixture to room temperature, 1-phenyl-3-trimethylsilylcyclohexene, \( 232 \) (0.85 g, 3.7 mmole) and a small crystal of iodine were added. To this mixture methylene iodide (3.99 g, 1.2 ml, 14.9 mmole) was slowly added via syringe. The resulting mixture was refluxed for 6 hours before an additional quantity of methylene iodide (2.0 g, 0.6 ml, 7.5 mmole) was added and reflux was continued for an additional 18 hours. The reaction mixture was slowly poured into a saturated solution of ammonium chloride, and the aqueous layer was extracted with ether (2 x
The organic phase was dried and evaporated to yield a mixture of unreacted starting allylsilane (11%) and cyclopropanated silane, 245 (89%) (0.80 g total, 1.6 mmole, 86%); $^1$H NMR (δ, CDCl$_3$) 7.23 (s, 5H), 2.47-0.8 (m, 9H), 0.73 (s, 1H), and 0.17 (s, 9H); ν$^{\text{film}}$ max 2940, 2860, 1495, 1450, 1250, 865, 760, and 650 cm$^{-1}$; $^{13}$C NMR (ppm, CDCl$_3$) 149.8, 128.2, 125.7, 31.8, 25.7, 24.4, 24.1, 22.7, 20.0, 19.5, and 3.4

Anal. Calcd for C$_{16}$H$_{24}$Si: C, 78.61; H, 9.90.

Found: C, 78.06; H, 9.93.

**Reaction of 1-Phenyl-exo-5-trimethylsilyl-cis-bicyclo[4.1.0]heptane (245) with Acetic Acid/Sulfuric Acid**

The bicyclic silane 245 (0.123 g, 0.5 mmoles) was stirred in glacial acetic acid (0.65 ml) containing a catalytic amount of sulfuric acid (0.035 g/10 ml acetic acid) at 50° for two days. The mixture was diluted with pentane and water. The two layers were separated and the pentane phase was extracted with a saturated solution of sodium bicarbonate, dried, and evaporated. The residue was chromatographed (silica gel, elution with 40% ether/hexane) to give 3-methyl-3-phenylcyclohexene, 246, (0.074 g, 0.42 mmoles, 86%); $^1$H NMR (δ, CDCl$_3$) 7.28 (m, 5H), 5.77 (s, 2H), 1.45 (s, 3H), and 2.50-0.8 (m, 6H); m/e calcd 172.1252, obs 172.1258.

**1-Phenyl-endo-exo-5-trimethylsilyl-7-oxa-cis-bicyclo[4.1.0]heptane (247 and 248)**

In a flask equipped with an addition funnel and drying tube was placed 1-phenyl-3-trimethylsilylcyclohexene, 232, (0.43 g, 1.9 mmoles) and dry...
ether (5 ml). To this solution was slowly added 40% peracetic acid (0.5 ml) which had been treated with sodium acetate to remove any traces of sulfuric acid which destroyed the epoxide. After 7 hours, the mixture was diluted with water (10 ml) and extracted with methylene chloride (3 x 20 ml). The combined organic layers were extracted with 10% sodium carbonate solution and water before drying. Upon evaporation of solvent, the crude product (0.41 g, 1.42 mmoles, 79%, 83% pure by gas phase chromatography, 2 ft 10% SE-30, 135°) was obtained; $^1$H NMR (δ, CDCl₃) 7.32 (s, 5H), 3.12 and 3.02 (d, J = 3.5 Hz, 1H), 2.60-0.9 (m, 7H), 0.18 and 0.12 (s, 9H); $\nu_{\text{max}}$ 2950, 1490, 1450, 1250, 840, 760, and 695 cm⁻¹; m/e calcd 246.1439, obs 246.1444.

Reaction of 1-Phenyl-endo,exo-5-trimethylsilyl-7-oxa-cis-bicyclo[4.1.0]-heptane (247 and 248) with Sulfuric Acid

A suspension of epoxide 247-248 (0.19 g, 10.78 mmoles) in water (17 ml) and 2 N sulfuric acid (2 ml) was stirred at room temperature for two days. The resulting mixture was extracted with ether and the combined organic extracts were washed with water, dried, and concentrated. The crude oil was chromatographed (silica gel, elution with 40% ether/hexane) to yield 249, 49%; $^1$H NMR (δ, CDCl₃) 7.30 (m, 5H), 6.13 (m, 1H), 4.25 (br m, 1H), 2.43 (m, 2H), and 1.90 (m, 5H); $\nu_{\text{max}}$ 3340 cm⁻¹; and 250, 28%; $^1$H NMR (δ, CDCl₃) 7.33 (br s, 5H), 6.13 (m, 1H), 4.37 (br m, 1H), 2.43 (m, 2H), 2.23 (br s, 1H), and 1.83 (m, 4H); $\nu_{\text{max}}$ 3340, 1640, 1600, 1495, 750, and 690 cm⁻¹. Compound 249 was identified by comparison of spectra with an authentic sample prepared by the addition of phenyl-lithium to 2-cyclohexenone followed by acidic work-up. Oxidation with Jones reagent also led to 3-phenylcyclohex-2-enone.
Reaction of 1-Phenyl-3-trimethylsilylcyclohexene (232) with Acetyl Chloride

In a three-necked flask equipped with a septum and nitrogen inlet was placed dry methylene chloride (6 ml), anhydrous aluminum chloride (0.50 g, 3.7 mmoles), and acetyl chloride (0.31 g, 0.28 ml, 4.0 mmoles) while cooling to -25°. Most of the aluminum chloride dissolved within 30 minutes, at which time 1-phenyl-3-trimethylsilylcyclohexene, 232, (0.90 g, 3.9 mmoles) was added dropwise via syringe. The reaction mixture became brown immediately, and after stirring for 2 hours, it was poured into ice water and extracted with ether (2 x 20 ml). The combined organic phases were washed with water, dried, and evaporated to give the crude product (0.79 g). Gas phase chromatography (2 ft 5% SE-30, 150°) indicated the presence of 256, 3%; ¹H NMR (δ, CDCl₃) 7.13 (s, 5H), 5.68 (m, 2H), 3.68 (m, 1H), 2.66 (ABq, J = 10 and 3 Hz, 1H), 2.43-1.63 (m, 4H), and 1.83 (s, 3H); νmax 3040, 2940, 1718, 1605, 1585, 1495, 1468, 1365, 1160, and 760 cm⁻¹; ¹³C NMR (ppm, CDCl₃) 211.4, 144.4, 130.1, 128.1, 126.6, 55.7, 43.9, 30.0, 25.0, and 24.6; UV (2,2,4-trimethylpentane) 2475 (ε 225), 2531 (260), 2588 (175), 2644 (200), and 2641 Å (150).

Anal. Calcd for C₁₄H₂₀O₂: C, 83.96; H, 8.05.

Found: C, 83.94; H, 8.09.

256, 2%; ¹H NMR (δ, CDCl₃) 7.20 (s, 5H), 6.13 (t, J = 4 Hz, 1H), 3.60 (m, 1H), 2.23 (m, 2H), 2.07-1.50 and 1.90 (m, 5H), 1.35 (t, J = 6
1H), and 0.15 (s, 5H); \( \nu_{\text{film max}} ^{\text{max}} \) 2960, 1710, 1600, 1495, 1355, 1250, 855, 835, and 755 cm\(^{-1}\); UV (2,2,4-trimethylpentane) 2438 Å (9800).

**Anal.** Calcd for C\(_{17}\)H\(_{24}\)O\(_2\)Si: C, 74.94; H, 8.88.

Found: C, 75.30; H, 8.80.

and 257, 35%; \( ^{1}H\) NMR (\( \delta \), CCL\(_4\)) 7.17 (s, 5H), 6.13 (t, \( J = 4 \) Hz, 1H), 3.62 (m, 1H), 2.27 (m, 2H), 2.03-1.47 (m, 4H), and 1.83 (s, 3H); \( \nu_{\text{film max}} ^{\text{film max}} \) 1710 cm\(^{-1}\); m/e calcd 200.1201, obs 200.1206. For spectral purposes the compounds were isolated by chromatography (silica gel, elution with 10% ether/hexane) resulting in isolated yields of 256, 32%; 257, 38%; 258, 15%.

**Reaction of 1-Phenyl-3-trimethylsilylcyclohexene (232) with N-Bromo-succinimide\(^{259}\)**

A mixture of 1-phenyl-3-trimethylsilylcyclohexene, 232 (0.41 g, 1.8 mmoles) and N-bromosuccinimide (0.35 g, 2.0 mmole) in carbon tetrachloride (5 ml) was irradiated with a 150 W sun lamp with simultaneous heating for 1 hour. After cooling the reaction mixture, the succinimide was filtered, and the concentrated filtrate was found to consist of biphenyl, 261, 28%, and 3-trimethylsilylbiphenyl, 262, 72%; \( ^{1}H\) NMR (\( \delta \), CCL\(_3\)) 7.20 (m, 9H), and 0.43 (s, 9H).

**Reaction of 1-Phenyl-3-trimethylsilylcyclohexene (232) with Bromine\(^{259}\)**

A solution of bromine (0.58 g, 3.6 mmoles) in cyclohexane (4 ml) was added dropwise to a solution of 1-phenyl-3-trimethylsilylcyclohexene, 232 (0.45 g, 1.95 mmoles) in cyclohexane (5 ml) at room temperature,
with the red color disappearing immediately. The concentrated reaction mixture was shown by gas phase chromatography (2 ft 5% SE-30, 130 °) to be 58% biphenyl and 42% 3-trimethylsilylbiphenyl.

2-Phenyl-syn-3-hydroxy-4-trimethylsilylcyclohexene (268)

The general photooxygenation procedure was employed with an irradiation time of 4.5 hours. The following products were obtained upon chromatography (silica gel, elution with 50% ether/hexane): r. f. = 0.9, traces of starting allylsilane 232; r. f. = 0.8, 268 (86 mg, 0.35 mmole, 40%); \(^1\)H NMR (δ, CDCl\(_3\)) 7.6-7.2 (m, 5H), 6.08 (br t, J = 5 Hz, 1H), 4.70 (br d, J = 4 Hz, 1H), 2.4-1.2 (m, 6H), and 0.10 (s, 9H); r. f. = 0.3, 242 (19 mg, 0.11, 17%).

2-Phenyl-3-hydroxy-4-trimethylsilylcyclooctene (269)

When the above procedure was followed with an irradiation time of 20 hours, the product was obtained in 70% chromatographed yield with no unreacted starting material; \(^1\)H NMR (δ, CDCl\(_3\)) 7.30 (s, 5H), 5.75 (t, J = 8 Hz, 1H), 5.00 (dd, J = 12 and 6 Hz, 1H), 2.5-1.0 (m, 10H), and 0.10 (s, 9H). Upon addition of deuterium oxide, the dd at 5.00 collapsed to a d, J = 10 Hz.

1-Trimethylsilyl-3-hydroxycyclooctene (271)

When the above procedure was followed with an irradiation time of 10 hours, the product was isolated by chromatography in 40% yield (based
on recovered starting material); \(^1\)H NMR (δ, CDCl\(_3\)) 5.63 (d, \(J = 6\) Hz, 1H), 4.50 (br m, 1H), 2.4-1.0 (m, 11H), and -0.02 (s, 9H); along with 3-hydroxycyclooctene in 20\% yield (based on recovered starting material).

**1-Trimethylsilyl-3-hydroxycyclohexene (270)**

![Me₃Si](image)

When the above procedure was followed with an irradiation time of 6 hours, the product was isolated by gas phase chromatography (3 ft 5\% SE-30, 95°) or column chromatography (silica gel, elution with 50\% ether/hexane) to give the product in 55\% yield (based on recovered starting material); \(^1\)H NMR (δ, CDCl\(_3\)) 5.95 (br d, \(J = 3\) Hz, 1H), 4.1 (br m, 1H), 2.1-1.4 (m, 7H), and 0.10 (s, 9H).

**8,8-Dibromo-4-oxa-anti,cis,cis-tricyclo[7.1.0\(^3,5\).0]octane (285)**

To a methylene chloride (25 ml) solution of 7,7-dibromonorcar-3-ene (2.40 g, 0.953 mmole) buffered with solid sodium bicarbonate (2.5 g) which had been cooled to 0° was added m-chloroperbenzoic acid (85\%, 2.64 g, 1.30 mmoles). The reaction mixture was stirred cold for 30 minutes followed by warming to room temperature. After 3.5 hours, the reaction was judged complete by thin layer chromatography (silica gel elution with 10\% ether/hexane). The slurry was concentrated, diluted with ether, and the solution was extracted with water (1 x 20 ml), a saturated solution of sodium bisulfite (2 x 20 ml), a saturated solution of sodium bicarbonate (1 x 20 ml), and
brine prior to drying. The solid residue upon evaporation was re-
crystallized from hexane to give white crystals (2.49 g, 0.93 mmole,
97%) which were sublimable (40-50°/0.1 torr) and had m.p. 50-51°;
¹H NMR (δ, CDCl₃) 3.00 (d, J = 1 Hz, 2H), 2.44 (ABq, J = 16 and 8 Hz,
2H), 1.87 (ABq, J = 16 and 1 Hz, 2H), and 1.70 (m, 2H).

Found: C, 51.38; H, 3.00.

4-Oxa-anti-cis-cis-tricyclo[7.1.03,5.0]octane (276)

The dibromo-anti-epoxide 283 (1.00 g, 0.373 mmole) was dissolving in dry hexane (5 ml),
and tri-n-butylin hydride (2.32 mg, 0.80 mmole) added under nitrogen. The clear solution
was refluxed for 28 hours, concentrated, and the products molecularly
distilled from the higher boiling tin compounds (b.p. 90-100°/23-35
torr). The distillate was purified by preparative gas phase chroma-
tography (12 ft 20% Carbowax 20M, 140°, 60 ml/min) giving one peak
with a retention time of 14 minutes; ¹H NMR (δ, CDCl₃) 2.92 (d, J =
1 Hz, 2H), 2.24 (br ABq, J = 16 Hz, 2H), 1.80 (ABq, J = 16 Hz, 2H),
0.65 (br s, 5H), and -0.48 (m, 1H).

8,8-Dibromo-4-oxa-syn-cis-cis-tricyclo[7.1.03,5.0]octane (285)

To a solution of the dibromonorcarrene 282
(300 mg, 1.19 mmoles) in glyme/water (9/1, 30 ml) was slowly added solid N-bromosuccini-
mide (250 mg, 1.4 mmoles). After the addition
was complete, the reaction mixture was stirred for 15 hours before quenching with several drops of a saturated sodium bisulfite solution. The solvent was evaporated, and the residue taken up in ether. The organic solution was extracted with a saturated solution of sodium bisulfite and brine prior to drying. The solution was evaporated to dryness and added to a slurry of sodium hydride (several fold excess), which had been washed free of oil, in dry tetrahydrofuran (20 ml). This slurry was refluxed for 15 hours and evaporated, and the residue was taken up in wet ether. This organic solution was extracted with brine and dried. Upon evaporation the solid obtained consisted of a single epoxide which could be sublimed (40-50°/0.1 torr) and gas chromatographed (1 ft SE-30) on a preparative scale. This epoxide was unstable, turning from white to brown during several weeks making elemental analysis impossible; $^1$H NMR ($\delta$, CDCl$_3$) 3.0 (br d, $J = 4$ Hz, 2H), 2.8-2.1 (br ABq, $J = 16$ Hz, 2H), 1.8-1.7 (ABq, $J = 16$ Hz, 2H), and 1.9-1.7 (m, 2H).

2,3-Dimethyl-1,4-dihydrobenzene (286)

In a 1 l 3-necked flask equipped with a dry ice bath, dry ice condenser, addition funnel and mechanical stirrer was condensed ammonia (300 ml). To the ammonia (-78°) was added sodium (20.6 g, 0.89 g-at) and o-xylene (20 g, 22.7 ml, 0.19 mole). The cold, blue solution continued stirring while a mixture of o-xylene (20 g, 22.7 ml, 0.19 mole) and methanol (40 ml) was added dropwise. Upon complete addition, the solution stirred for another 0.75 hour before methanol (40 ml) was
added which turned the reaction mixture white. The mixture was slowly warmed to room temperature overnight, and the ammonia allowed to evaporate. Water was slowly added to dissolve the salts, and the organic layer separated. The organic phase was washed with water (4 x 50 ml) and dried. The liquid was distilled (b.p. 60-63°/48 torr) to yield the clear dihydro o-xylene (21.7 g, 0.21 mole, 55%); ¹H NMR (δ, CDCl₃) 5.52 (s, 2H), 2.50 (s, 4H), and 1.60 (s, 6H).

1,6-Dimethyl-7,7-dibromobicyclo[6.1.0]oct-3-ene (287)

![Diagram](image)

A 3-necked flask equipped with a mechanical stirrer, nitrogen inlet, and addition funnel was charged with potassium t-butoxide (44.2 g, 0.394 mole) and dry pentane (350 ml). The slurry was cooled to -45°, and dihydro o-xylene (21.5 g, 0.20 mole) added. A solution of bromoform (50 g, 17.3 ml, 0.20 mole) in pentane (125 ml) was slowly added over 2.3 hours. After complete addition the mixture was warmed to room temperature and continued stirring for 4 hours. The mixture was poured onto water and separated. The organic layer was washed with water and dried. Upon concentration of the solvent a small amount of tetrabromo-adduct crystallized (m.p. 147-148°). This was filtered from the solution, and the remaining solvent evaporated. The crude product was sublimed (80°/45 torr) to yield white crystals (23.0 g, 0.082 mole, 42%) m.p. 105-106°; ¹H NMR (δ, CDCl₃) 5.48 (t, J = 1 Hz, 2H), 2.30 (s, 4H), and 1.31 (s, 6H).

Anal. Calcd for C₉H₁₂Br₂: C, 38.60; H, 4.32.

Found: C, 38.60; H, 4.24.
1,7-Dimethyl-8,8-dibromo-4-oxa-anti,cis,cis-tricyclo[7.1.03,5.0]-octane (293)

Prepared as previously described\(^\text{266}\) yielding white crystals which were sublimed (50°/0.05 torr), m.p. 90-94°; \(^1\text{H NMR (\(\delta\), CDCl}_3)\) 3.4-3.0 (m, 2H), 2.6-1.6 (m, 4H), and 1.23 (s, 6H).

1,7-Dimethyl-8,8-dibromo-4-oxa-syn,cis,cis-tricyclo[7.1.03,5.0]-octane (294)

Prepared as described previously,\(^\text{267}\) and sublimed (40-50°/0.07 torr) to give white crystals, m.p. 89.5-90.5°; \(^1\text{H NMR (\(\delta\), CDCl}_3)\) 3.1-3.0 (m, 2H), 2.2-2.05 (m, 4H), and 1.20 (s, 6H).

1,7-Dimethyl-4-oxa-syn and anti,cis,cis-\(\text{Tricyclo[7.1.03,5.0]}\)octane (291, 292)

Prepared as previously described,\(^\text{266}\) with the two isomers separated by preparative gas phase chromatography (5 ft di-n-butyltetrachlorophthalate, 130°, 60 ml/min) with a retention time of 38 minutes for the syn-isomer (60%); \(^1\text{H NMR (\(\delta\), CDCl}_3)\) 3.1-2.4 (m, 2H), 2.1 (br ABq, \(J = 16\) and 4 Hz, 2H), 1.8 (ABq, \(J = 16\) Hz, 2H), 1.07 (s, 6H), and 0.07 (s, 2H); and a retention time of 42 minutes for the anti-isomer (40%); \(^1\text{H NMR (\(\delta\), CDCl}_3)\) 3.04 (m, 2H), 2.24 (br ABq, \(J = 16\) Hz, 2H), 1.87 (br ABq, \(J = 16\) Hz, 2H), 0.97 (br s, 7H), and -0.20 (d, \(J = 4\) Hz, 1H).
11,11-Dibromo-4-oxa-syn,cis,cis,cis-tetracyclo[7.3.1.03,5.0]undecane

Prepared as described previously. The solid obtained was sublimed (60°/0.07 torr) to give a single isomeric epoxide as white crystals, m.p. 105-106°; $^1$H NMR (δ, CDCl$_3$) 3.3-3.0 (br d, $J$ = 6 Hz, 2H), and 2.7-1.2 (m, 10H).

11,11-Dibromo-4-oxa-anti,cis,cis,cis-tetracyclo[7.3.1.03,5.0]undecane

Prepared as previously described. The solid obtained was sublimed (60°/0.07 torr) to yield white crystals, m.p. 104-105°. If the crystals were allowed to slowly form from ether they had a m.p. 120-122°; $^1$H NMR (δ, CDCl$_3$) 3.25 (m, 2H), and 2.7-1.5 (br m, 10H).

4-Oxa-syn,cis,cis,cis-tetracyclo[7.3.1.03,5.0]undecane

Prepared as previously described. The material was isolated by preparative gas phase chromatography (2 ft SE-30, 120°) with retention time of 9 minutes (97%); $^1$H NMR (δ, CDCl$_3$) 3.02 (m, 2H), 2.06 (br s, 4H), 1.9-1.2 (m, 6H), 0.56 (d, $J$ = 4 Hz, 1H), and -0.20 (d, $J$ = 4 Hz, 1H); along with a minor amount of the syn-isomer, retention time of 6 minutes (3%).
4-Oxa-anti,cis,cis,cis-tetracyclo[7.3.1.0^3,5.0]undecane (305)

Prepared as previously described. The material was isolated by preparative gas phase chromatography (2 ft SE-30, 120°) with a retention time of 6 minutes; \(^1\)H NMR (6, CDCl\(_3\))

3.07 (m, 2H), 2.54 (br ABq, \(J = 15\) Hz, 2H), 1.96 (br ABq, \(J = 15\) Hz, 2H), 1.7-1.2 (m, 6H), 0.79 (ABq, \(J = 4\) Hz, 1H), and 0.17 (ABq, \(J = 4\) Hz, 1H).

7,7-Dimethyl-cis-bicyclo[6.1.0]hept-3-ene (310)

A solution of methyllithium (2.0 M, 15 ml, 30 mmoles) in dry ether (50 ml) was cooled to 0°, and solid cuprous iodide (2.86 g, 15 mmoles) was slowly added. This slurry was stirred until all the solid had dissolved, and the pale yellow solution was treated with the dibromonorcarene 282 (2.20 g, 12.8 mmoles). The reaction mixture was stirred for several minutes, sealed with parafilm, and stored in a freezer at -11° for 110 hours. Methyl iodide (5 ml) was added to methylate any organocuprates, and the entire slurry was poured onto cold ammonium hydroxide/ammonium chloride solution. Air was bubbled through the solution to oxidize all insoluble copper(I) to soluble copper(II). The mixture was extracted with ether (2 x 20 ml) and the organic layers were washed with a saturated solution of ammonium chloride and brine, dried, and evaporated. The residue was distilled to give a clear liquid (0.443 g, 3.36 mmoles, 28%); \(^1\)H NMR (6, CDCl\(_3\)) 5.53 (m, 2H), 2.6-1.7 (br m, 4H), 1.02 (s, 3H), 0.79 (s, 3H), and 0.62 (dd, \(J = 10\) and 4 Hz, 2H).
8,8-Dimethyl-4-oxa-syn,cis,cis-tricyclo[7.1.0\(^3\),5.0]octane (312)

The compound was prepared as described previously, and a single isomeric epoxide was obtained which was isolated by preparative gas phase chromatography with a retention time of 4.5 minutes (3 ft SE-30, 138°C); \(^1\)H NMR (δ, CDCl\(_3\)) 3.02 (br d, J = 4 Hz, 2H), 2.6-2.0 (br ABq, J = 16 Hz, 2H), 1.8 (ABq, J = 16 Hz, 2H), 0.93 (s, 3H), 0.88 (s, 3H), and 0.50 (br d, J = 7 Hz, 2H).

2,2-Dimethylcyclohexanone (33)\(^{216}\)

To a solution of potassium t-butoxide (56 g, 0.50 mole) in dry t-butanol (350 ml) was slowly added 2-methylcyclohexanone (56 g, 0.50 mole). The light yellow solution was stirred for 30 minutes at room temperature before cooling to 0°C. Methyl iodide (97.8 g, 33.8 ml, 0.54 mole) was added, and the solution was stirred in the cold for 2.5 hours before heating to reflux for 2 hours. Most of the t-butanol was distilled off and water (300 ml) was added slowly. The solution was diluted with benzene, the layers were separated, and the organic layer was washed with a saturated solution of sodium bisulfite (3 x 150 ml) and water (1 x 150 ml), and dried (sodium sulfate). The benzene was evaporated leaving a light yellow liquid.

Sodium methoxide was prepared by slowly adding small pieces of sodium (23 g, 1.0 g-at) to a dry methanol/tetrahydrofuran (2/1) mixture (200 ml), and when all the sodium had reacted the solvent was
evaporated. Last traces of methanol were removed azeotropically by adding benzene and evaporating. To the white solid was added dry benzene (450 ml), and the slurry was cooled in an ice bath while a solution of the crude dimethylcyclohexanone in ethyl formate (55 g, 60 ml, 0.53 mole) was slowly added over a 2-hour period. The reaction mixture stood for 44 hours before a small amount of water was slowly added while cooled again in an ice bath. Then the mixture was poured onto ice water. The organic layer was separated, and extracted with 5% sodium hydroxide solution (2 x 100 ml). The basic extracts were combined with the original aqueous layer, and extracted once with ether.

The basic layer was next made acidic with ice-cold concentrated hydrochloric acid, and the oily mixture was extracted with ether (2 x 300 ml). This organic solution was concentrated, poured onto 5% sodium hydroxide solution (1600 ml), and slowly distilled. A total distillate of 500 ml was collected over 4 hours. The product was isolated by separation of the two layers and extraction of the aqueous layer with ether (2 x 100 ml). The combined organic layers were extracted with brine, dried, and evaporated. The residue was distilled (bp 65—87°/50 torr) to give a clear liquid (33.6 g, 0.267 mole, 54%).

3-Furaldehyde (339) 243

\[
\begin{array}{c}
\text{CHO} \\
\hline
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\]

Pyridinium chlorochromate (105 g, 0.5 mole) which had been powdered with a mortar and pestle was slurried in dry methylene chloride (800 ml) along with anhydrous sodium acetate (10.3 g, 0.125 mole) by mechanical stirring under a drying tube. A
methylene chloride (100 ml) solution of 3-hydroxymethylfuran (24.5 g, C. 25 mole) was added slowly to the oxidant with simultaneous cooling in an ice bath. After being stirred at room temperature for 3 hours, the mixture was diluted with ether (2500 ml), and filtered through a column of Florisil. The filtrate was evaporated slowly, and the residue was distilled (b.p. 54-58°/24 torr) to yield the clear liquid aldehyde (13.0 g, 0.155, 54%); \textsuperscript{1}H NMR (6, CDCl\textsubscript{3}) 9.50 (s, 1H), 8.64 (d, \( \delta = 1 \) Hz, 1H), 7.45 (m, 1H), 6.73 (d, \( \delta = 2 \) Hz, 1H). \textsuperscript{3}C\textsubscript{4}  3-Furaldehyde was a light sensitive compound prone to polymerize. It was best stored under nitrogen in a freezer protected from the light. Even under these conditions, it became colored after several weeks.

3-Hydroxymethylfuran (\textsuperscript{31}C, \textsuperscript{26}F)

Lithium aluminum hydride (11.4 g, 0.30 mole) was slurried in dry ether (300 ml) in a three-necked three liter flask equipped with a condenser, addition funnel, and mechanical stirrer.

The 3-furoic acid (25.0 g, 0.223 mole) was dissolved in dry ether (200 ml) and slowly added while keeping the mixture at reflux. Upon complete addition, the mixture was refluxed for an additional 5 hours before being cooled to 0° and treated with Glauber's salt (hydrated sodium sulfate) followed by a saturated solution of sodium sulfate. When the salts turned white, the mass was filtered, and the filter cake was washed with ether (2 x 100 ml). The combined ether solutions were evaporated giving pure alcohol (21.45 g, 0.219 mole, 98%); \textsuperscript{1}H NMR (6, CDCl\textsubscript{3}) 7.3 (d, \( \delta = 2 \) Hz, 2H), 6.33 (t, \( \delta = 2 \) Hz, 1H), 4.42 (s, 2H) and 2.80 (s, 1H).
3-Furoyl Chloride \((3\text{H})^2\)

3-Furoic acid (25.0 g, 0.223 mole) was heated to reflux in neat thionyl chloride (80.5 g, 49 ml, 0.60 mole) for 1.5 hours. The solution was concentrated by distillation, and the residue was distilled \((72^0/46 \text{ torr})\) to yield a low melting white crystalline solid. The acid chloride, very hygroscopic and a powerful lachrymator, was stored sealed in a freezer to facilitate handling as a solid; \(\text{H}^1\) NMR \((6, \text{CDCl}_3)\) 5.20 (tr s, 1H), 7.40 (t, \(J = 2 \text{ Hz}, 1\text{H}\)), and 6.75 (t, \(J = 2 \text{ Hz}, 1\text{H}\)).

1,1-Dimethyl-2-(3-hydroxymethylfuran)cyclohex-2-ene \((3\text{H})\)

A three-necked flask fitted with a septum, nitrogen inlet, and Erlenmeyer flask containing 2,2-dimethylcyclohexanone benzenesulfonylhydrazone \((5.60 \text{ g}, 20.0 \text{ mmoles})\), connected by a short piece of Gooch tubing was charged with dry \(\text{K},\text{K}',\text{N},\text{N}'\)-tetramethylethlenediamine \((60 \text{ ml})\) and \(n\)-butyllithium in hexane \((1.5 \text{ K}, 33 \text{ ml}, 60 \text{ mmoles})\). The solution was cooled to \(-45^0\), and the solid benzenesulfonylhydrazone was added in portions. After complete addition (15 minutes), the red solution was stirred at \(-45^0\) for 15 minutes before being warmed to room temperature for 1 hour. When nitrogen evolution ceased, the solution was recooled to \(-45^0\) and 3-furaldehyde \((4.80, 5.55 \text{ ml}, 50 \text{ mmoles})\) was added via syringe. The mixture lightened and was slowly warmed to room temperature over several hours. The beige solution was slowly poured into water and diluted with ether. The
organic layer was consecutively extracted with water (2 x 100 ml), saturated sodium bisulfite solution (100 ml), saturated copper sulfate solution (100 ml), and brine prior to drying. The concentrated residue was quickly chromatographed on silica gel to remove low r.f. impurities, and the product was separated from n-butyl-3-furylcarbinol by high pressure liquid chromatography (2.40 g, 11.7 mmoles, 58%); 

$^1$H NMR (6, CDCl$_3$) 7.33 (br s, 2H), 6.27 (t, $J$ = 2 Hz, 1H), 5.85 (t, $J$ = 4 Hz, 1H), 5.23 (br s, 1H), 2.2-1.5 (m, 3H), 1.7-1.3 (m, 4H), 1.16 (s, 3H), and 0.95 (s, 3H); accurate mass was obtained on gas phase chromatographed material which had thermally eliminated water, $M^+$ caled 198.1201, obs 198.1205.

**Tri-n-butylstannyliodomethane (540)**

Cupric acetate (0.15 g, 0.62 mmole) was dissolved in hot acetic acid (15 ml) by heating on a steam bath. To the hot solution was added 30-mesh zinc (5.51 g, 0.15 mole) and the mixture was swirled with heating for 2 minutes. The acetic acid was decanted off and replaced by fresh acetic acid (15 ml). This was heated with swirling for another 2 minutes and decanted off. The cooled couple was washed with dry ether (3 x 30 ml) and then dried under a stream of nitrogen.

The couple was placed in a dry three-necked round bottom flask constructed with a stopcock in the bottom which was plugged with glass wool (see the accompanying diagram). The flask was equipped with a stirring bar, addition funnel, nitrogen inlet, reflux condenser, and
stirred with a mechanically powered magnet held at an angle. During the reaction the flask was tilted to stir on its side. The couple was covered with dry tetrahydrofuran (25 ml) and several drops of a methylene iodide (40.2 g, 12.1 ml, 0.15 mole) in dry tetrahydrofuran (25 ml) solution were added.

Quickly the reaction was initiated with generation of a light purple solution and more dry tetrahydrofuran (50 ml) added. The methylene iodide solution was slowly added over 1 hour while keeping the reaction temperature at approximately 4°C. When the addition was complete, the mixture was occasionally warmed with a heat gun to maintain the temperature for another hour. During the time methylene iodide was exposed, the hood was darkened. The flask was uprighted and the solution was filtered directly into a dry three-necked flask with mild suction. While the solution of iodomethylzinc iodide stirred at room temperature, tri-n-butyltin chloride (22.5 g, 26 ml, 0.10 mole) was slowly added via an addition funnel under nitrogen. This solution was stirred for 20 hours before being poured onto pentane (250 ml) and washed with water (2 x 200 ml) and brine, and dried. The evaporated residue was distilled (b.p. 112-114°C/0.2 torr) to yield a clear liquid (40.4 g, 0.0917 mole, 92%); 1H NMR (δ, CDCl3) 1.90 (s, 2H) and 2.0-0.7 (m, 27H).

1,1-Dimethyl-2-(0-methylene-3-tri-n-butylin-3-furylhydroxymethyl)-cyclohex-2-ene (347)

\[
\begin{align*}
\text{OCH}_2\text{SnBu}_3
\end{align*}
\]

Potassium hydride (24%) in oil (60 mg, 1.5 mmol) was washed free of oil with hexane (3 x 2 ml), and slurried in dry
tetrahydrofuran (5 ml) under nitrogen. The allylfuryl alcohol 338 (206 mg, 1.0 mmole) was added with immediate hydrogen evolution. Gas evolution subsided within 5 minutes; however, the solution was stirred for 1 hour before addition of the tri-n-butylstannyliodomethane (441 mg, 1.0 mmole). This solution was stirred at room temperature for 1 hour before reaction was quenched with several drops of methanol. The mixture was poured into ether/water and separated. The organic layer was washed with water and brine before drying. The evaporated residue was chromatographed (silica gel, elution with hexane) to yield a small amount of starting alcohol and the product (392 mg, 0.755 mmole, 56%) based on recovered starting material; $^1$H NMR (δ, CDCl$_3$) 7.2 (m, 2H), 6.2 (m, 1H), 5.65 (t, J = 1 Hz, 1H), 4.5 (s, 1H), 3.7-3.2 (m, 2H), 3.6 (s, 2H), and 2.2-0.7 (m, 3H).

1,1-Dimethyl-2-(3-furylidene)-5-hydroxymethylcyclohexane (337)

The tri-n-butylstannyl ether 347 (392 mg, 0.755 mmole) was dissolved in dry tetrahydrofuran (10 ml) and cooled to -78°.

To the cold solution was added n-butyllithium in hexane (1.6 M, 0.62 ml, 1.0 mmole) via syringes, and the brown solution was stirred in the cold for 30 minutes. The reaction mixture was quenched with several drops of a saturated ammonium chloride solution and poured into dilute ammonium chloride solution. Ether (10 ml) was added and the organic phase was separated, extracted with brine, dried, and evaporated. The resulting residue was chromatographed (silica gel, elution with 5% ether/hexane) to give the oily alcohol 337 (128 mg, 0.585 mmole, 77%); $^1$H NMR (δ, CDCl$_3$) 7.50 (m, 1H), 7.34
The alcohol 338 (610 mg, 2.96 mmole) was added to hexane (3 x 2 ml) washed potassium hydride - oil dispersion (2.4 eq) (285 mg, 7.0 mmole) in dry tetrahydrofuran (15 ml) at room temperature with stirring. After 1 hour, tri-n-butyldiastannyliodomethane (1.3 eq, 3.1 mmole) was added, and the resulting solution was stirred for 1 hour at room temperature before being cooled to -78°. n-Butyllithium in hexane (1.6 M, 3.1 ml, 5.0 mmole) was added and the brown solution was stirred in the cold for 30 minutes before being quenched with methanol. The mixture was poured into a saturated solution of ammonium chloride, diluted with ether and separated. The organic layer was washed with water and brine, and dried. The resultant solution was evaporated and chromatographed to yield the rearranged alcohol 337 (502 mg, 2.26 mmole, 77%).

5,5-Dimethyl-6,7,8-trihydronaphtho[1,2-b]furan (350)

The primary alcohol 337 (125 mg, 0.585 mmole) was dissolved in dry dimethylformamide (3 ml) and pyridinium dichromate (752 mg, 2.6 mmole) was slowly added while being cooled in an ice bath under a drying tube. The mixture was stirred at room temperature for 10 hours before being diluted with water (20 ml) and
extracted with ether (4 x 5 ml). The combined ether layers were washed with brine, dried, and evaporated to give a crude product which upon chromatography (silica gel, elution with 50% ether/hexane) gave the naphthofuran 350 (57 mg, 0.255 mmole, 49%); \( ^1H\) NMR (\( \delta \), CDCl\(_3\)) 7.52 (s, 1H), 7.47 (d, \( J = 2.5 \) Hz, 1H), 7.05 (br s, 1H), 6.55 (dd, \( J = 2.5 \) and 1 Hz, 1H), 2.88 (br t, \( J = 6 \) Hz, 2H), 2.6-1.8 (m, 4H), and 1.30 (s, 6H); \( \nu_{\text{max}} \) 2920, 1460, 1260, 1020, 795, and 730 cm\(^{-1}\); \( M^+ = 200\), \( M^+ - 15 \) = base peak (loss of Me\(^+\)).

**Anal.** Calcd for C\(_{14}\)H\(_{16}\)O: C, 53.5; H, 6.2.

Found: C, 53.9; H, 6.2.

Silver(II) Oxide (351)

Sodium hydroxide (72.0 g, 1.8 mmoles) was dissolved in a small amount of distilled water, then diluted to 1000 ml and heated to 85°. Potassium peroxysulfate (75 g, 0.25 mole) as an aqueous slurry was added to the hot solution. This was immediately followed by addition of an aqueous silver nitrate (5.1 g, 0.30 mole) solution in a minimum amount of water. The vigorously stirred black slurry was then heated to 90° for 15 minutes. The black silver(II) oxide was filtered with suction on a large Büchner funnel, washed with a very dilute sodium hydroxide solution, and vacuum dried (37.7 g, 0.30 mole, 100%).

2,2-Dimethyl-7-oxo-5-oxa-5-(3-furyl)bicyclo[4.3.0]nona-1(6)-ene (352)

The primary alcohol 357 (102 mg, 0.464 mmole) was dissolved in water/tetrahydrofuran (1/3, 6 ml) and silver(II) oxide (570 mg, 4.6 mmoles) was added. The
slurry was stirred at room temperature for 41 hours before being filtered through a Celite pad. The filter cake was extracted with ether and the combined organic layers were extracted with brine, dried, and evaporated. The crude material was chromatographed (silica gel, elution with 50% ether/hexane) to yield the unsaturated lactone (60 mg, 0.256 mmole, 5%); $^1$H NMR (δ, CDCl$_3$) 6.20 (m, 1H), 6.10 (m, 1H), 5.85 (m, 1H), 4.1 (br d, $J = 15$ Hz, 1H), 3.70 (d, $J = 2$ Hz, 1H), 3.42 (dd, $J = 13$ and 6 Hz, 1H), 2.0-1.4 (m, 4H), 1.20 (s, 3H), and 1.16 (s, 3H); $\nu_{\text{film}}$ 2920, 1760, 1640, 1560, 1595, 1150, 945, 900, and 722 cm$^{-1}$. 3-Methylocyclohex-2-enone ($\delta_2^7$)

1,3-Cyclohexandione (112.1 g, 1.0 mole) was dissolved in absolute ethanol (1200 ml) and added to benzene (5000 ml) in a one-necked flask equipped with a Claisen head, thermometer, drainable Dean-Stark trap, and condenser. A catalytic amount of p-toluenesulfonic acid (1 g) was added and the solution was heated to reflux. During 16 hours of reflux, a total of 2000 ml of azeotrope (t.p. 67-69$^\circ$) was collected. The remaining solution was cooled, poured into a separatory funnel and extracted with 10% sodium hydroxide which had been saturated with sodium chloride (4 x 200 ml). The organic solution was then washed with water (4 x 100 ml) until neutral and finally with brine. The dried (potassium carbonate) solution was concentrated and distilled (b.p. 83-84$^\circ$/0.8 torr) to give a clear liquid (114.5 g, 0.777, 78%), 3-ethoxycyclohex-2-enone.
To an ice-bath cooled solution of methylolithium in ether (1.8 M, 1.0 mole) in dry ether (100 ml) was slowly added 3-ethoxycyclohex-2-enone (107.4 g, 0.727 mole). The solution was stirred at 0° for 1 hour and warmed to room temperature for 30 minutes. A saturated solution of ammonium chloride was added dropwise to the 0° cooled solution to decompose excess methylolithium. This was followed by 2 N hydrochloric acid. This mixture was stirred vigorously for 20 minutes before the layers were separated and the organic layer was washed with saturated sodium bicarbonate solution and brine and dried. The concentrated residue was distilled (b.p. 86-93°/20 torr) to give a clear liquid (60.7, 0.55, 76%); $^1$H NMR (δ, CDCl$_3$) 5.5 (q, J = 1 Hz, 1H), 2.5-1.8 (m, 6H), and 1.96 (s, 3H).
APPENDIX A

Three-Dimensional X-Ray Crystal Structure Studies

The crystal structure studies described herein were kindly performed by C. A. Schuman, M. A. Beno, and G. G. Christoph.

The data crystal of $\text{Br}_2$, a colorless rectangular prism of approximate dimensions $0.32 \times 0.56 \times 0.60 \text{ mm}^3$, was mounted on an automated four circle diffractometer with an axis (later assigned as $c$) approximately colinear with the $c$-axis. Triclinic cell constants ($a = 7.562(3)$, $b = 10.438(5)$, $c = 6.738(2)$, $\alpha = 86.15(3)$, $\beta = 76.76(3)$, and $\gamma = 75.10(4)$ at $21^\circ\text{C}$) were determined by least squares fit of the optimized setting angles of ten reflections in the range $13^\circ < 2\theta < 20^\circ$ ($\lambda \text{MoK} \alpha = 0.71069 \text{ Å}$). The crystal density was not measured due to the reactivity or ready solubility in the available standards, but the calculated density of $1.76 \text{ g cm}^{-3}$ is in good agreement with that found for brominated hydrocarbons. Using graphite monochromatized radiation, the data were collected at $21^\circ\text{C}$ by the $\omega-2\theta$ scan technique, yielding after correction for crystal decay, Lorentz and polarization effects and absorption, and averaging of multiply measured reflections a final set of 1773 unique data, approximately one-third of which was less than $3\sigma$ above background. The space group was determined to be $P\bar{1}$ ($C_2$, No. 2) based upon the intensity statistics and this assignment was later confirmed by the successful refinement.
of the structure. The structure was solved by the heavy atom Patterson method and refined by conventional Fourier and full matrix least squares techniques. Hydrogen atom contributions were included in the calculations, their positions about the methyl groups being determined from difference Fourier maps, but their parameters were not refined. The conventional R-factor at the current stage of refinement is 10.7% and the goodness of fit, 3.5. Substantial improvement is not expected because of the low quality of the data (the disagreement R-index for the multiply measured reflections was 7.4% and the Bragg peaks were very broad), thus the values of the derived bond parameters given here (Table 21) are essentially final. The values of the refined parameters appear in Table 23 following this discussion.

A colorless crystalline fragment of 293 was mounted in a capillary tube and aligned on a four-circle automated diffractometer in a cold (-58°C) N₂ gas stream to retard crystal decomposition. The orthorhombic cell constants \(a = 10.918(2)\), \(b = 8.539(2)\) and \(c = 8.896(2)\) were obtained by least squares refinement of the setting angles of 32 carefully centered reflections having \(15° < 2\theta < 29°\). Using graphite monochromatized MoKα radiation and the \(w-2\theta\) scanning method, 1411 reflection intensities were measured, of which 666 were greater than \(3\sigma\) above background. Correction for \(I_P\), absorption and crystal decay were performed in the same manner as for 283. Averaging of multiply measured reflections (chiefly check reflections) resulted in a final data set of 1285 unique reflections. Inspection of the intensities unambiguously determined the space group as Pnm\(r\) (\(C_{16}^{2h}\), No. 62; absences: \(kh0, h = 2n+1; 0kl, k+l = 2n+1\)) and the intensity statistics verified the centric
nature of the distribution expected for Pnma. Assuming a comparable density to $^{233}U$ led to assignment of $Z = 4$, a calculated density of 2.146 g cm$^{-3}$, and the requirement that the molecule possesses a crystallographically imposed mirror plane.

The phase problem was solved by the heavy atom Patterson method and refined by Fourier and least squares analysis. All the non-hydrogen atoms were given anisotropic thermal parameters and all but the coordinates and isotropic temperature factors of the hydrogen atoms were refined in the least squares. The final R-factor and goodness of fit for all 1265 reflections were 10.0% and 1.50. The final difference Fourier map possessed several peaks of ca $1.5 \text{e}^{-\text{A}^3}$ in the vicinity of the bromine atoms. The high R-factor and residual difference Fourier features are ascribed to the inadequacies of the absorption corrections and to the large number of very weak reflections (The R-factor for the most significant (I > 3σ(I) data is about 7.8%). The bond distances and angles calculated from the refined parameters are given in Table 21. The structures of the two compounds are illustrated in Figure 5. The conformation of the multiply fused ring system is surprisingly unperturbed by the presence of the methyl groups in $^{293}$T. The six-membered rings in the two compounds are essentially planar, although each possesses a very small boat-form pucker. The C(3) and C(3)' methylene carbon atoms in $^{293}$T are about 0.07 Å above the plane of the remaining four carbon atoms. In $^{293}T$, the corresponding value is 0.08 Å. This translates into dihedral angles of 6.4° for $^{293}T$ and 7.6° for $^{293}T$ for the two four-atom planes C(3)-C(4)-C(4)'-C(3)' and C(3)-C(4)-C(4)'-C(3)'.
rings in the pair of compounds are much closer to orthogonality to
the mean plane of the six-membered ring than the 120° that would be
expected from consideration of the geometries of cyclopropane rings
fused to medium-sized carbocycles.273

Despite the relatively low accuracy (by current standards) of
the results in Table 21, the consistency of the result for 253 and 253
recommends a greater reliability than the esd's suggest. Consequently,
the much longer than normal C(2)-C(2)' distances are viewed as real,
and quite in keeping with available predictions274 of π-acceptor and
π-donor substituents effects on the opposite cyclopropane C-C bond.
Similar effects were noted by Leuker and Hers275 in the case of 1,1-
ditromo-2,2-diphenylcyclopropane, but the interpretation was made
more difficult by the presence of the phenyl substituents. The re-
main ing bonds in the structure are all normal in comparison with
standard values.276
TABLE 21. Bond Distances (Å) and Angles (degrees) for 283 and 292

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<tr>
<th>Bond</th>
<th>293</th>
<th>283</th>
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<tr>
<td>C(1)-Br(1)</td>
<td>1.920(5)</td>
<td>1.894(9)</td>
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<tr>
<td>C(1)-Br(2)</td>
<td>1.913(5)</td>
<td>1.527(10)</td>
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<tr>
<td>C(1)-C(2)</td>
<td>1.515(17)</td>
<td>1.453(11)</td>
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<tr>
<td>C(2)-C(3)</td>
<td>1.517(17)</td>
<td>1.505(10)</td>
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<tr>
<td>C(3)-C(4)</td>
<td>1.452(18)</td>
<td>1.502(10)</td>
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<td>C(2)-C(2)'</td>
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<td>1.554(14)</td>
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<td>C(4)-C(4)'</td>
<td>1.450(17)</td>
<td>1.458(14)</td>
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<tr>
<td>C(4)-O</td>
<td>1.414(16)</td>
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<td>C(2)-C(5)</td>
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<td>C(3)-C(2)-C(5)</td>
<td>112.8(12)</td>
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The reported values have been averaged for chemically equivalent bonds. The standard deviations in the parameters have been calculated using variances in the coordinates derived from the diagonal elements of the inverted matrix from the final least squares cycle. The numbering scheme relates to that given in Figure 9 only.
TABLE 22. Least Squares Refined Parameters for $2^{1/2}$ at $K = 0.107$ for 1773 Reflections

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<th>Atom</th>
<th>X</th>
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<th>Z</th>
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<th>U22</th>
<th>U33</th>
<th>U12</th>
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<td>119628(21)</td>
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<td>22507(17)</td>
<td>119707(22)</td>
<td>390(10)</td>
<td>740(13)</td>
<td>347(10)</td>
<td>-318(10)</td>
<td>179(7)</td>
<td>-29(9)</td>
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<td>O</td>
<td>61724(138)</td>
<td>29057(114)</td>
<td>51419(142)</td>
<td>491(66)</td>
<td>1049(93)</td>
<td>296(57)</td>
<td>-407(65)</td>
<td>118(49)</td>
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</tr>
<tr>
<td>Cl</td>
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<td>24835(131)</td>
<td>102556(204)</td>
<td>262(72)</td>
<td>300(78)</td>
<td>448(81)</td>
<td>-83(62)</td>
<td>118(62)</td>
<td>24(64)</td>
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<tr>
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<td>32631(128)</td>
<td>82652(185)</td>
<td>238(71)</td>
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<td>77584(199)</td>
<td>318(81)</td>
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<td>590(109)</td>
<td>599(114)</td>
<td>524(99)</td>
<td>-326(93)</td>
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<td>C5</td>
<td>64197(170)</td>
<td>21938(162)</td>
<td>69773(216)</td>
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<td>788(128)</td>
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<td>C6</td>
<td>52926(194)</td>
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<td>466(95)</td>
<td>376(84)</td>
<td>-215(79)</td>
<td>138(69)</td>
<td>-90(71)</td>
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<td>C7</td>
<td>31681(170)</td>
<td>17495(142)</td>
<td>82649(131)</td>
<td>228(71)</td>
<td>558(100)</td>
<td>231(69)</td>
<td>-163(69)</td>
<td>86(57)</td>
<td>-82(64)</td>
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<td>C7M</td>
<td>21253(196)</td>
<td>8876(135)</td>
<td>75424(207)</td>
<td>552(101)</td>
<td>402(89)</td>
<td>440(87)</td>
<td>-302(81)</td>
<td>-49(75)</td>
<td>-34(70)</td>
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TABLE 22 (continued)

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<th>Z</th>
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<td>4335(0)</td>
<td>7552(0)</td>
<td>4.00(0.0)</td>
</tr>
<tr>
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<td>1660(0)</td>
<td>7532(0)</td>
<td>4.00(0.0)</td>
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<td>H3A</td>
<td>3442(0)</td>
<td>4695(0)</td>
<td>8941(0)</td>
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<td>H3B</td>
<td>3167(0)</td>
<td>4805(0)</td>
<td>6718(0)</td>
<td>4.00(0.0)</td>
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<td>H6A</td>
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<td>748(0)</td>
<td>8833(0)</td>
<td>4.00(0.0)</td>
</tr>
<tr>
<td>H6B</td>
<td>5565(0)</td>
<td>594(0)</td>
<td>6599(0)</td>
<td>4.00(0.0)</td>
</tr>
<tr>
<td>H1</td>
<td>360(0)</td>
<td>4733(0)</td>
<td>7105(0)</td>
<td>4.00(0.0)</td>
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<tr>
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<td>350(0)</td>
<td>3268(0)</td>
<td>6541(0)</td>
<td>4.00(0.0)</td>
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<tr>
<td>H3</td>
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<td>8738(0)</td>
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<td>7552(0)</td>
<td>4.00(0.0)</td>
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<tr>
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<td>1660(0)</td>
<td>7532(0)</td>
<td>4.00(0.0)</td>
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<tr>
<td>H6</td>
<td>1829(0)</td>
<td>239(0)</td>
<td>8671(0)</td>
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</tbody>
</table>

UIJ has been multiplied by $10^{3\\beta}$. The conversion of RIJ to UIJ for I, NE, J, includes multiplication by $\frac{1}{2}$. The form of the anisotropic temperature factor is: $\exp 2\pi^2(h^2a^2u_{11}+\ldots+2klh^k e^ku_{23})$ Coordinates have been multiplied by $10^{3\\beta}$. The esd's in the least significant digits are given in parentheses.
TABLE 23  Least Squares Refined Parameters for 23 at R = 0.10 for 1285 Reflections

<table>
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<tr>
<th>Atom</th>
<th>X</th>
<th>Y</th>
<th>Z</th>
<th>U11</th>
<th>U22</th>
<th>U33</th>
<th>U12</th>
<th>U13</th>
<th>U23</th>
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<tr>
<td>BR1</td>
<td>58683(12)</td>
<td>25000(0)</td>
<td>64145(13)</td>
<td>707(9)</td>
<td>32(6)</td>
<td>26(6)</td>
<td>0(0)</td>
<td>155(6)</td>
<td>0(0)</td>
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<tr>
<td>BR2</td>
<td>81258(11)</td>
<td>25000(0)</td>
<td>42168(13)</td>
<td>42(7)</td>
<td>36(6)</td>
<td>43(7)</td>
<td>0(0)</td>
<td>16(6)</td>
<td>0(0)</td>
</tr>
<tr>
<td>C1</td>
<td>65652(92)</td>
<td>25000(0)</td>
<td>43742(102)</td>
<td>37(5)</td>
<td>25(5)</td>
<td>22(4)</td>
<td>0(0)</td>
<td>-1(4)</td>
<td>0(0)</td>
</tr>
<tr>
<td>O</td>
<td>58560(81)</td>
<td>25000(0)</td>
<td>-136(83)</td>
<td>666(55)</td>
<td>5.0(55)</td>
<td>298(44)</td>
<td>0(0)</td>
<td>-98(42)</td>
<td>0(0)</td>
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<tr>
<td>C2</td>
<td>56426(66)</td>
<td>15901(81)</td>
<td>32480(74)</td>
<td>47(4)</td>
<td>24(3)</td>
<td>35(4)</td>
<td>17(3)</td>
<td>59(3)</td>
<td>22(3)</td>
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<tr>
<td>C4</td>
<td>62496(71)</td>
<td>6882(90)</td>
<td>20001(78)</td>
<td>520(51)</td>
<td>3h(4)</td>
<td>36h(10)</td>
<td>-83(39)</td>
<td>64(37)</td>
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<td>C6</td>
<td>67088(71)</td>
<td>16466(84)</td>
<td>7007(79)</td>
<td>6h8(4)</td>
<td>3.5(1)</td>
<td>353(4)</td>
<td>86(39)</td>
<td>-3(37)</td>
<td>-22(35)</td>
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</table>

<table>
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<th>Z</th>
<th>P</th>
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</thead>
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<tr>
<td>H1h</td>
<td>5681(0)</td>
<td>-6h(0)</td>
<td>1606(0)</td>
<td>h.00(0,0)</td>
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<tr>
<td>21h</td>
<td>6925(0)</td>
<td>111(0)</td>
<td>2429(0)</td>
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</tr>
<tr>
<td>H2</td>
<td>5015(0)</td>
<td>789(0)</td>
<td>3292(0)</td>
<td>h.00(0,0)</td>
</tr>
<tr>
<td>H6</td>
<td>7354(0)</td>
<td>838(0)</td>
<td>53h(0)</td>
<td>h.00(0,0)</td>
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</tbody>
</table>

UIJ has been multiplied by 10**4. The conversion of BIJ to UIJ for I,HE, J includes multiplication by 1/2. The form of the anisotropic temperature factor is: exp 2π^2(l^2a^2u_{11} + ... + 2klb^c^u_{23}) Coordinates have been multiplied by 10**5. The esds in the least significant digits are given in parentheses.
REFERENCES

1. C. Mannich and H. Davidson, Ber., 66, 2106 (1936).

2. a. M. E. Herr and F. W. Heyl, J. Amer. Chem. Soc., 75, 3627 (1953);
   b. F. W. Heyl and M. E. Herr, ibid., 75, 1918 (1953).

   c. G. Stork, A. Frizzolara, H. Landesman, J. Szmuszkovicz, and

   Marcel Dekker, New York 1969.

5. a. C. Eatorm and R. W. Bott, "Organometallic Compounds of the
   2, Chap. 4.

   and relevant references cited therein.


   96, 3634 (1974). Silane additions to acetylenes are also well
   recognized reactions.

9. See for example:
   (1973).
10. See for example:


12. Grignards:

13. Nickel-Aluminum complex:


20. For a similar procedure, see:


24. Regiospecificity is seemingly dependent also upon tosylhydrazones stereochemistry, at least in certain cases:


56. The author thanks Prof. P. D. Magnus for suggesting this possibility.

57. For examples of epoxysilane rearrangement to \(\alpha\)-trimethylsilyl ketones see:


60. For early reports concerning desilylation of \(\beta\)-silyl ketones in acidic media, see:

61. For reports concerning Si-C cleavage by base, see:


73. All calculations were performed by R. Gleiter and M. C. Böhm at the Institut für Organische Chemie der Technischen Hochschule, Darmstadt, West Germany.


82. For a general review, see:

   g. N. M. Hasty and D. R. Kearns, ibid., 95, 5380 (1973).


89. Synthetic material was identical to an authentic sample.

90. Gas phase chromatographic separations should be restricted to the lower molecular weight systems where excessive temperatures are not required. At more elevated temperatures, conversion to allenes has been observed.


115. Structural assignment to 177 follows from its lithium/liquid ammonia reduction to 4,4,8-trimethylbicyclo[3.3.0]octan-2-one, which ketone was independently synthesized by lithium dimethylcuprate addition to 4,8-dimethylbicyclo[3.3.0]oct-3-en-2-one.116


117. Heinrich Schostarez, private communication.


132. The acid and the acid chloride could also be produced by pyridinium dichromate oxidation in dimethylformamide and treatment with oxalyl chloride in methylene chloride.


134. Recent examples include:
h. A. Hosomi, A. Shirahata, and H. Sakurai, ibid., 3043 (1975).


137. The following listing provides only leading references and is not meant to be comprehensive:


152. See related calculations in Chapter 2.
156. A significant exception appears to be the 3-silacyclopentene:


164. See footnote 10 of reference 10 and the results for compound 5 described in that communication.


169. As selected examples are cited:


174. Photooxygernations of $^{27}$, $^{23}$, $^{29}$, and $^{31}$ were performed by Dr. D. Liotta and Mr. C. Lau.

175. A spectral method of identification was required allowing comparison with later compounds. Thus hydrogenation to the known 3- or 4-methylcyclohexanol was deemed insufficient for our purposes.


180. Comparable LIS studies on this isomer pair have been carried out by Prof. Casadevall (Paris) with analogous results (private communication with L. A. Paquette, January 15, 1975 and later published.


The X-ray crystal structures of 264 and 293 bear this out at least in the solid state.


Epoxidation:


b. N. Hasty, P. M. Merkel, P. Radlick, and D. R. Kearns, ibid., 45 (1972).


201.  

202.  

203.  

204.  

205.  

206.  
V. A. Naumov, *Top. Stereochem.*, 1, 100 (1971).

207.  
A. Goris and M. Mascre, *Compt. rend.*, 153, 1082 (1911).

208.  

209.  

210.  

211.  
[2,3]Sigmatropic shifts from ethers of cyanohydrins:

212.  

213.  

214.  
225. a. C. S. Foote and M. Thomas, unpublished results.

236. Preparation for 89a and 89b, p. 171.

237. Preparation for 90, p. 173.

238. See text, p. 23-30, for ratios of reactants used and the products obtained.

239. Preparation for 100, p. 174.

240. Preparation for 101, p. 175.


242. Both cholestanones have reported m.p. 125°.


244. Preparation for 104, p. 135.

245. The easiest way uncovered with which to work with relatively dry tetra-n-butylammonium fluoride was to make a stock solution. This was stored over molecular sieves in acetonitrile under a three-way stopcock.


247. Preparation for 150, p. 196.

248. Compound 151, p. 196.

249. Both "H NMR spectra are identical to those of authentic samples.


259. This procedure was performed by Dr. Y. K. Han.


261. Preparation for 232, p. 207.


265. General procedure described on p. 124.

266. Preparation for 233, p. 213.


268. Preparation for 275, p. 219.


272. The absorption correction was effected by an empirical technique based upon psi-scan data: M. A. Beno and G. G. Christoph, to be published.

273. In fact, at 104-105° they are the smallest ever observed; see compilation in G. G. Christoph and M. A. Beno, J. Amer. Chem. Soc., 100, 3156 (1978).


277. Lit. m.p. 145-145°.

278. Lit. m.p. 146-148°.


280. No data reported in earlier preparation.

281. Lit. m.p. 102-103°.

282. No data reported in earlier preparation.


284. Lit. m.p. 157-158°.

285. Lit. m.p. 135-137°.


287. Lit. b.p. 51-83°/35 torr; 1H NMR is identical to that reported.

288. Lit. b.p. 50-55°/5 torr; 1H NMR is identical to that reported.

289. Lit. b.p. 86-37°/47 torr; 1H NMR is identical to that reported.

290. 1H NMR is identical to that previously reported; E.-T. Grobel and D. Seebach, Chem. Ber., 110, 867 (1977).

291. 1H NMR is identical to 81 in the aliphatic region.

292. Lit. b.p. 51-81°/0.9 torr; 1H NMR is identical to that reported.

293. The product was spectrally identical to that reported; "The Saddler Standard Spectra," Saddler Research Laboratories, Philadelphia, 1972, no. 5740.

295. The product was spectrally identical to that reported; J. D. Connolly and R. McCrindle, Chem. and Ind., 37 (1965).

296. See discussion and references in text, p. 51.

297. The product was spectrally identical to that reported; G. Magnusson and S. Thorén, J. Org. Chem., 38, 1350 (1973).

298. The product was spectrally identical to that reported; C. J. Pouchert and J. R. Campbell, "The Aldrich Library of NMR Spectra," Vol. 1, Aldrich Chemical Co., Inc., Milwaukee, 1974, p. 113A.

299. The product was spectrally identical to that reported earlier.

300. Lit. m.p. 242.5-243°C.

301. The product was spectrally identical to that reported previously; M. Jones, H. T. Taylor, and E. Rudd, J. Chem. Soc., 1324 (1961).

302. Lit. b.p. 260°C/1 torr; R. M. G. Roberts and F. El Kaissi, J. Organomet. Chem., 12, 79 (1968); the product was spectrally identical to that reported earlier.


304. Lit. b.p. 420°C/20 torr; the product was spectrally identical to that reported earlier; S. Gronowitz, G. Sorlin, E. Gestril, and R. A. Hoffman, Arkiv Kemi, 12, 455, 515 (1962).