STUDIES RELATED TO THE THERMAL REARRANGEMENT
OF 1,2-DIVINYLCYCLOPROPANES

by

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The work in this thesis was undertaken in order to determine the kinetic factors responsible for the regioselectivity in enol ether formation in 2-vinylcyclopropyl cyclohexyl ketone systems.

Conversion of commercially available 4-carbethoxy-3-methyl-2-cyclohexen-1-one (106) into 3,3-dimethylcyclohexanecarboxylic acid chloride (105) was accomplished via a straightforward sequence of reactions. Treatment of (105) with lithium (phenylthio)(cis-2-vinylcyclopropyl)cuprate (33) afforded the ketone (101). Alternatively, reaction of (105) with a mixture of the cuprate reagent (33) and the isomeric reagent (34), followed by base-catalyzed equilibration of the resultant mixture of ketones, provided the ketone (103). Hydrogenation of cis-2-vinylcyclopropyl cyclohexyl ketone (89) with diimide provided the ketone (104).

Treatment of the ketone (101) with lithium diisopropylamide in tetrahydrofuran at -78°C, followed by trapping of the resultant mixture of enolate anions with tert-butyldimethylsilyl chloride, gave a mixture of the enol silyl ethers (120) and (121), in a ratio of 12 : 88. Thermolysis of the latter mixture (160°C, neat) afforded a mixture of the annulated materials (122) and (123) (ratio ~14 : 86), which, upon acid hydrolysis under mild conditions, gave the cycloheptenone (127) and compound (123). The latter two substances could be separated by column chromatography.

Subjection of the ketone (103) to a sequence of reactions similar to that described above (lithium diisopropylamide, tetrahydrofuran; tert-butyldimethylsilyl chloride; thermolysis, 240°C, neat; acid hydrolysis) gave the final products (127) and (123) in a ratio of 87 : 13, respectively.
Treatment of cis-2-ethylcyclopropyl cyclohexyl ketone (104) with lithium diisopropylamide in tetrahydrofuran, followed by trapping of the resultant mixture of enolate anions with tert-butyldimethylsilyl chloride afforded the two enol silyl ethers (125) and (126) in a ratio of 1:1.

The results summarized above are discussed in terms of the factors which might be affecting the regioselectivity of kinetic deprotonation of 2-vinylcyclopropyl cyclohexyl ketone systems.
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TABLE I: Enolate Formation of cis ketone (89) with Various Bases.
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The line between failure and success is so fine that we scarcely know when we pass it: so fine that we are often on the line and do not know it.

- Elbert Hubbard, *The Note Book* (1927) -
INTRODUCTION

In the last twenty years the [3,3] sigmatropic Cope rearrangement has come into increasing importance in modern organic chemistry. Of particular interest is its use in the formation of ring systems in one step that would take many synthetic steps to form by more conventional organic chemistry.

I. The Cope Rearrangement of Divinylcyclopropanes

When butadiene (1) is heated at 150-300°C, 1,5-cyclooctadiene (3) is produced. While investigating this process, Vogel postulated that a possible intermediate in the reaction was 1,2-divinylcyclobutane (2).

\[
\begin{array}{c}
\text{1} \quad \rightarrow \quad \text{2} \quad \rightarrow \quad \text{3}
\end{array}
\]

To test this hypothesis, he synthesized cis-1,2-divinylcyclobutane (2) and found that when it was heated to 120°C for 10 minutes, it rearranged to 1,5-cyclooctadiene (3).

The trans-1,2-divinylcyclobutane (4) molecule, however, did not rearrange to 1,5-cyclooctadiene (3) but instead decomposed at 240°C to give two 1,3-butadiene units.

Vogel then synthesized a series of cis-1,2-divinylcycloalkanes and
studied their rearrangements. He noted that cis-1,2-divinylcyclopropane (5) rearranged to 1,4-cycloheptadiene (6) even below room temperature.

Since he was unable to isolate the cis compound, Vogel decided to prepare the isomeric trans-1,2-divinylcyclopropane (7). When the compound was heated at 190°C for 2 hours it also rearranged cleanly to provide 1,4-cycloheptadiene (6). Vogel felt that this result could be rationalized by either of two routes (Scheme 1). One possibility (route A) involved an isomerization of (7) to cis-1,2-divinylcyclopropane (5) followed by subsequent [3,3] sigmatropic rearrangement (Cope) of the latter substance to 1,4-cycloheptadiene (6). Alternatively (route B), compound (7) could rearrange to 4-vinylcyclopentene (8) which could then undergo rearrangement to the final product (6). Vogel subsequently prepared 4-vinylcyclopentene.
Scheme 1

(8) and found that it did not isomerize to the cycloheptadiene molecule even at 300°C. Therefore, he preferred route A, Scheme 1.

The mechanism of the trans to cis isomerization is not fully understood. The isomerization is thought to involve either a one centre or a two centre epimerization of the cyclopropane ring possibly via a radical process. Berson has coined the term stereomutation to describe all processes in which stereoisomers interconvert. Using deuterated compounds, Berson found that cyclopropane and phenylcyclopropane isomerizations could best be described by a two centre inversion. Baldwin synthesized a constrained divinylcyclopropane system (9) in order to determine whether or not the epimerization was a one centre or a two centre inversion.
The compound (9), which was known to possess absolute configuration as shown, rearranged at 195°C in one hour to give compound (11) which was found to be enantiomerically pure. Baldwin then synthesized the endo compound (10) which also rearranged to give enantiomerically pure compound (11). He concluded that in this case, a one centre epimerization was occurring converting compound (9) into compound (10) and subsequently, the latter rearranging to compound (11). A two centre epimerization of compound (9) would have produced the enantiomeric product (12) which was not observed experimentally.

The main driving force for the Cope rearrangement in 1,2-divinyl-cyclopropanes is the relief of ring strain when the 1,2-divinylcyclopropane rearranges to the corresponding 1,4-cycloheptadiene. This was demonstrated
by Vogel\textsuperscript{5} when he found that \textit{cis}-1,2-divinylcyclopentane (13), when heated to 300°C, isomerized to the \textit{trans}-1,2-divinylcyclopentane (14) rather than undergoing Cope rearrangement to compound (15). Compound (15) is more highly strained as compared to (13) due to the presence of two \textit{trans} double bonds ("chair" type transition state).

\begin{center}
\begin{tikzpicture}
    \node (13) at (0,0) {\includegraphics[width=1cm]{13.png}};
    \node (14) at (1.5,0) {\includegraphics[width=1cm]{14.png}};
    \node (15) at (0.75,1) {\includegraphics[width=1.5cm]{15.png}};
    \draw[->] (13) -- (15);
    \draw[->] (15) -- (13);
    \draw[->] (14) -- (15);
    \node at (1.5,0) {$300^\circ$C};
\end{tikzpicture}
\end{center}

It has been reported\textsuperscript{6} that \textit{cis}-1,2-divinylcyclopropane (5) could not be isolated even at -40°C. However, recent work done by Brown and associates\textsuperscript{7} demonstrated that this compound could be isolated at -20°C and that its nmr spectrum could be obtained. It was found that compound (5) has a half-life of 449 seconds at 20°C.

It has been suggested that Cope rearrangement of \textit{cis}-1,2-divinylcyclopropane systems proceeds via a "boat" type transition state (Scheme 2)\textsuperscript{1}. This transition state leads to the \textit{cis},\textit{cis}-1,5-cycloheptadiene
system (6) whereas other possible transition states would result in formation of two *trans* double bonds or a *cis* and a *trans* double bond being formed.

This mechanistic proposal was supported by work carried out by Baldwin\(^8,9\) and Schneider\(^10\) who studied the Cope rearrangement of various substituted *cis*-1,2-divinylcyclopropane systems. For example, the *cis-, cis,cis*-1,2-dipropenylcyclopropane (16) did not undergo thermal Cope rearrangement\(^8,10\) at 179°C, but instead formed an equilibrium mixture with the *trans* isomer (17). It was postulated that this result was due to steric interactions between the methyl substituents on the double bonds and the hydrogen on C-3 of the cyclopropane ring in the required "boat-like" transition state. Baldwin\(^8\) also thermolyzed compound (17) at
178°C for 4 h and again obtained an equilibrium mixture of isomers (16) and (17).

However, trans,trans,trans-1,2-dipropenylcyclopropane (18) did undergo rearrangement to provide (19) when heated at 178°C for 4 h. This rearrangement probably occurs via the cis isomer (20) in the required
boat type transition state.

The thermal rearrangement of the former compound (18) was slower, when compared to the parent cis-1,2-divinylcyclopropane (5), possibly due to the steric interaction of the two methyl groups in the transition state. In general, it was found that the greater the steric interaction of various "R" groups on the double bond with the proton at C-3 on the cyclopropane ring, or with each other [for example compound (20)] the slower the Cope rearrangement. In extreme cases this rearrangement did not occur; instead only cis to trans isomerization was observed.

II Previous Work

Although the kinetics and mechanism of the Cope rearrangement of 1,2-divinylcyclopropanes have received much attention, this reaction has not been employed extensively in organic synthesis. Recently, however, a number of reports concerning the use of this rearrangement as a synthetic method have appeared and these will be discussed briefly.

Marino\textsuperscript{11} prepared the divinylcyclopropane derivative (21) and thermally rearranged it, at 140°C, to the annulation product (22) which, he postulated, results from a 1,3 hydrogen shift in the initially formed compound (23). Marino\textsuperscript{12} later extended this work to include the cyclopentenone derivatives (24) and subsequently rearranged them to give (25).

Compounds of type (24) were prepared (Scheme 3) by the conversion of 2-methyl-1,3-cyclopentanedione (26) into the sulfoxonium ylides (27). This ylide was reacted with acrolein to produce the 2-cyclopropyl aldehyde (28) which was subsequently reacted with different Wittig-type reagents to give compounds (24).
$R = \text{CO}_2\text{CH}_2\text{CH}_3, \text{SO}_2\text{C}_6\text{H}_5,$

$\text{SC}_6\text{H}_5, \text{SOC}_6\text{H}_5$
In a later publication, Marino described a modified procedure to prepare substituted divinylcyclopropanes starting from the enol ether of 2-methyl-1,3-cyclopentanedione (29) and reacting it with vinylcyclopropyl-lithium reagents (30). Work up of the reaction with aqueous ammonium chloride produced the substituted cyclopropanes (31) and (32).
Piers and Nagakura\textsuperscript{14} prepared various substituted $\beta$-(2-vinylcyclopropyl)enones by conjugate addition of lithium phenylthio (2-vinylcyclopropyl) cuprate (33) and (34) onto the appropriate $\beta$-iodo enone. For example, the compound (35) was prepared by reaction of a \textit{cis} and \textit{trans} isomer mixture of the cuprate reagent (33) and (34) with 3-iodo-2-cyclohexen-1-one (36). Upon distillation at 62-88°C, a mixture of the \textit{trans}
compound (37) and the product (35) was obtained. Further heating of this mixture at 180°C for 30 min converted the entire mixture into compound (35) in 75% yield (Scheme 4).

They also prepared spiro cycloheptadiene compounds such as (38) and (39) by the same route in reasonable yields.
Piers$^{15}$ later extended this idea by preparing the isomeric lithium phenylthio[2,2-dimethyl-\textit{cis}-\textit{(and}-\textit{trans}-)3-vinylcyclopropyl] cuprates (40) and (41) from the isomerically pure bromides (42) and (43). The cuprates were allowed to react with various β-iodo enones, as previously described, to produce the highly functionalized isomeric divinylcyclopropane derivatives (44) and (45) (\textit{cis} series); and (46) and (47) (\textit{trans} series).

These compounds were prepared to study the effects of structural variation on the course of the Cope rearrangement and to act as suitable precursors for natural product syntheses.

The \textit{cis} compound (44) rearranged to the cycloheptadiene system (48) on refluxing for 4 h in hexane (bp 69°C). Thermolysis of compound (48) or the \textit{cis} compound (44) briefly at 110°C gave the conjugated ketone (49) in >90% yield. Compound (44) was in fact found to rearrange to (48) slowly upon standing at room temperature.
The analogous compound with a methyl group in the \( \alpha \)-position (45) was more resistant to Cope rearrangement. This compound required higher temperatures (refluxing \( \Theta \)-xylene, bp 144\(^\circ\)C, 48 h) to effect the rearrangement to give the methyl derivative (50) as well as a significant amount of isomerized starting material (47) which was stable under the reaction.
This significant difference between the thermal rearrangement of compound (44) and compound (45) can be rationalized as follows: in the boatlike transition state proposed for divinylcyclopropane rearrangements, there is a steric interaction in compound (45) between the α methyl group and one of the methyls on the cyclopropane ring.

The *trans* compound (46) was rearranged at a higher temperature (0-dichlorobenzene, sealed tube, 220°C) than the *cis* compound (44) to give the rearranged product (49) in 59% yield.

The corresponding *trans* compound with an α methyl group (47) was thermolyzed under similar conditions, as described above, to produce the annulated product (50). However, it also produced a predominance of trienone (51), presumably because of a homo-[1,5]-sigmatropic hydrogen shift.
Wender\textsuperscript{16} prepared various divinylcyclopropane derivatives by a method similar to Marino\textsuperscript{13}. For example, the 3-alkoxyenone (52) was allowed to react with a solution of 1-lithio-2-vinylcyclopropane (30) (R=R'=H, cis and trans) and the resulting reaction mixture was poured into aqueous hydrochloric acid to give the divinylcyclopropane (53). Compound (53) was thermolyzed at 170-180°C for 2 h (sealed tube) to give the cycloheptadiene (54) in 73% yield.

Wender\textsuperscript{16} modified this sequence to prepare the natural product karahanaenone (55) (Scheme 5). The 2-vinylcyclopropyl ketone (56) was prepared via reaction of a mixture of cis- and trans- 1-lithio-2-methyl-
2-vinylcyclopropane (57) with isobutyraldehyde followed by oxidation of the resultant product.

The ketone (56) was treated with a solution of lithium diisopropylamide in tetrahydrofuran and the resulting enolates were trapped with trimethylsilyl chloride to give the enol silyl ethers (58) (cis and trans). The enol silyl ethers (58) were thermolyzed at 165-175°C and the resultant product (59) was desilylated (n-butyllithium) to provide karahanaenone (55) in 54% overall yield based on isobutyraldehyde.

In a later publication, Wender used these Cope rearrangements to prepare the natural products (±)-damsinic acid (60) and (±)-confertin (61).
Both compounds were derived from a common precursor. The 3-alkoxyenone (62) was allowed to react with the 1-lithio-1-methyl-2-vinylcyclopropane mixture (30; R=Me, R'=H) to make isomers (31) and (32).

Wender observed mainly ring opened product (63) when he tried to
rearrange the mixture of divinylcyclopropanes (31) and (32) \((\geq 140^\circ \text{C})\); 
presumably because of a homo-[1,5]-sigmatropic hydrogen shift as observed 
by Piers\(^{15}\). The expected product (64) was the minor component (<20%).

Thermolysis at a lower temperature (98°C) gave about the same amount 
of (64), a trace of compound (63) and mainly the trans isomer (32).

The stereoselective preparation of the cis-isomer (31) would have 
circumvented this problem, but Wender found that photoisomerization of the 
mixture (31) and (32) was most convenient. This was accompanied by
simultaneous thermolysis (at 98°C) of the mixture to give the desired product (64) as the major product in a 80-90% yield with only a trace of (63). The ketal (65) was used as the general precursor for the natural products (60) and (61).
Piers and Ruediger synthesized (±)-β-himachalene (66) via a Cope rearrangement. The trans-1-bromo-1-methyl-2-isobutenyl cyclopropane (67) was prepared and converted to its lithium phenylthiocuprate (68). The cuprate solution was allowed to react with the β-iodo enone (36) to give the divinylcyclopropane (69) which was thermolyzed (m-xylene, bp 138°C, 3 h) to give the cycloheptadiene system (70).
The cycloheptadiene system (70) was methylated and the resultant product (71) was hydrogenated \([\text{H}_2, (\phi_3\text{P})_3\text{RhCl}, \text{C}_6\text{H}_6]\) to give the cycloheptene system (72). This was transformed into the enol phosphate (73) which was reduced with lithium to give \((\pm)-\beta\text{-himachalene (66).} \)
Recently Wender has used divinylcyclopropane Cope rearrangements to prepare more complicated multiple ring systems. A model system for his study was the tricyclic methoxyketone (74). Natural products with structures related to compound (74) are known and it was Wender's hope that they could be prepared via a thermal Cope rearrangement. The postulated precursor to compound (74) would be compound (75) which could rearrange to (74) upon heating.

Compound (75) was novel because of the oxygen functionality (as the methyl enol ether) that was \( \alpha \) to the ketone. The effect of the oxygen functionality on the Cope rearrangement was unknown.

As previously discussed, systems with an alkyl group \( \alpha \) to the \( \alpha,\beta \)-unsaturated ketone are known to have a steric effect on the course of the rearrangement, but no system with an oxygen functionality had been tried.

Wender prepared the 1-bromo-2-vinylcyclopropane (76) in six steps from the \( \alpha \)-bromoenone (77). Compound (76) was treated with tert-butyllithium, to effect lithium halogen exchange, and a solution of the resulting lithium derivative was allowed to react with 2,3-dimethoxy-2-vinylcyclopropane (78) to produce, after work up, the 1,2 adduct (79).
Treatment of compound (79) with a 0.01 N aqueous sulfuric acid solution in acetone at room temperature for seven minutes gave the rearranged product (74) directly presumably via the divinylcyclopropane (75) – although compound (75) was not detected.

Wender also synthesized the α-methoxyenone (80) and found that it rearranged with a half-life of 9.3 h at room temperature. As a comparison,
the α-methylenone \((31; \text{R}=\text{R'}=\text{H})\) had a half-life of 316 h at room temperature and substituting the cyclopropane ring in \((31)\) with a methyl group \((31; \text{R}=\text{Me}, \text{R'}=\text{H})\) lowered the half-life to 54 h at room temperature.

Although these were cursory studies, Wender\(^{19}\) states that these results seem to suggest that replacing the α-methyl group with an oxygen functionality and increasing the alkyl substitution on the cyclopropane ring both contribute to the reduction of the half life of compound \((75)\).

\[
\text{80} \quad \text{31 } \text{R} = \text{R'} = \text{H} \]

\[
\text{31 } \text{R} = \text{Me}, \text{R'} = \text{H} 
\]

\[
\text{75} 
\]

Piers and Reissig\(^{20}\) further extended the methodology of Wender\(^{16}\) to more complicated systems. A solution of cis-1-bromo-2-vinylcyclopropane \((81)\) in ether was allowed to react with tert-butyllithium\(^*\). Successive

\* The configurational stability of lithiovinylcyclopropanes generated from the analogous bromo compounds is well known\(^{21,22}\).
addition of tetrahydrofuran and phenylthiocopper produced a solution of the cuprate reagent (33).

The cuprate reagent solution (33) was allowed to react with cyclopentanecarboxylic acid chloride (82) and the reaction mixture was worked up to give the 2-vinylcyclopropyl ketone (83) in high yield.

A solution of the ketone (83) was allowed to react with lithium diisopropylamide, under kinetic conditions, and the resulting enolate was trapped with trimethylsilyl chloride to give the enol silyl ether (84).
The enol silyl ether (84) was thermolyzed and the rearranged enol silyl ether (85) was hydrolyzed with aqueous 1 N hydrochloric acid in methanol to give the spiro cycloheptenone (86) in 70% overall yield from (82).

The above procedure was also used to prepare the cyclobutane derivative (87) and the n-butane derivative (88) in good yields.
When the cis-cyclohexane derivative (89) was prepared and subsequently kinetically deprotonated and the enolate trapped with trimethylsilyl chloride, a mixture of enol silyl ethers (90) and (91) resulted. These were obtained in a ratio of approximately 1 : 1 if lithium diisopropylamide was the base used. (See Scheme 6).

Thermolysis of the mixture of enol silyl ethers (90) and (91) at 150°C for 30 min leads to the products (92) and (93). Hydrolysis of the mixture selectively hydrolyzed the enol silyl ether (92) to the ketone (94) and left the silyl ether (93) untouched. Compound (93) results from a vinylmethylene cyclopropane rearrangement.

Generation of the enolates of the cis ketone (89) with various bases, under kinetic conditions, followed by trapping with trimethylsilyl chloride or tert-butyldimethylsilyl chloride, produced different relative amounts of the enol silyl ethers (90) and (91). These results are summarized in Table I.

As previously stated, lithium diisopropylamide (LDA) generated an approximately 1 : 1 mixture of enolates. A more sterically hindered base, lithium 2,2,6,6-tetramethylpiperidide (LiTMP) removed the less sterically hindered proton in preference to the more hindered one and so the observed ratio of enol silyl ethers (90) and (91) changed to 3 : 7 respectively.

A less sterically hindered base such as lithium diethylamide gave an observed ratio of enol silyl ethers (90) and (91) of 7 : 3 respectively.

* For a further discussion of this type of thermal rearrangement, see reference 23 and references cited therein.
Scheme 6
Table I. Enolate Formation of \textit{cis} Ketone (89) with Various Bases.

\begin{align*}
\text{Base} & \quad \text{Relative Ratio of Enol Silyl Ethers (90) and (91)} \\
\text{N-Li (LDA), THF, -78°C} & \quad 1 : 1 \\
\text{N-Li (LiTMP), THF, -78°C} & \quad 3 : 7 \\
\text{Et}_2\text{N-Li, THF, -78°C} & \quad 7 : 3
\end{align*}

R = Me; Me\text{\textsubscript{2}}, \text{t-Bu}
Treatment of the cis cycloheptyl ketone (95) with lithium diisopropylamide and subsequent trapping of the enolates, as described above, gave the enol silyl ethers (96) and (97) in a ratio of approximately 4 : 1 respectively.

\[
\begin{align*}
R &= \text{Me; Me}_2, \text{t-Bu} \\
95 &\rightarrow 96 + 97
\end{align*}
\]

The cis neo-pentyl substituted compound (98) gave an approximately 1 : 1 mixture of enolates when treated with lithium diisopropylamide under kinetic conditions.

\[
\begin{align*}
98 &\rightarrow 99
\end{align*}
\]

The cyclohexylcyclopropyl ketone (99) when reacted under the same conditions, as described above, gave 100% enolate formation towards the cyclohexane ring. In this case, it was postulated that the absence of a cis vinyl group on the cyclopropane ring caused the cyclopropane proton adjacent to the ketone to become less acidic.
In all of the trans vinyl cases studied, the deprotonation with lithium diisopropylamide followed by trapping of the resulting enolate with trimethylsilyl chloride or tert-butyldimethylsilyl chloride gave only the enol silyl ether resulting from deprotonation of the respective "R" group in (100)

\[
\text{R= } \text{ cis-cyclohexyl, } \text{CH}_2 \text{, n-C}_5\text{H}_11
\]

These observations further support a possible electronic effect of a cis vinyl group on the outcome of the deprotonation. However, there may also be steric effects, in the trans cases (100), due to interaction between the vinyl group and the proton cis to it on the cyclopropane ring.

III. The Problem

The previously mentioned work, in our laboratory, left questions unanswered as to the factors affecting enolate formation. Of particular interest was the observed steric factor in the case of the cis-cyclohexyl
ketone (89). As discussed above, the ratio of enolates changed when a more sterically hindered or less sterically hindered base as compared to lithium diisopropylamide was used to deprotonate the ketone. In the case of lithium diisopropylamide, a 1 : 1 ratio of enolates (90) and (91) resulted.

![Chemical Diagram](image)

It was felt that the approach of the base to the cyclohexane ring proton adjacent to the ketone (arrow) was sterically hindered by the circled protons above, in a 1,3 diaxial sense.

To test this steric effect, one of the circled protons from above was replaced with a methyl group which would presumably make the ring proton adjacent to the ketone more sterically congested. Treatment with lithium diisopropylamide should result in a different ratio of enolates. The dimethyl ketone (101) was synthesized and treated with lithium diisopropylamide followed by trapping of the enolates under identical conditions as the cis-cyclohexyl ketone (89).

In each of the trans ketone cases studied (100) enolate formation was only towards the respective "R" group (102). It was postulated, that one of the controlling factors in this deprotonation was a steric interaction between the vinyl group and the proton cis to it (H<sub>B</sub>), for
example, the trans cyclohexyl ketone (100, R = ).

The analogous 3,3-dimethyl derivative (103) with a trans geometry was prepared to see if increasing the steric hindrance, to base attack, at $H_A$ would change the ratio of enolates that resulted.
Also of interest, in this study, was the possible electronic effect that a vinyl group had on the proton trans to it [circled proton in compound (89) below]. The vinyl group may be increasing the acidity of this proton since in the cis cyclohexyl ketone (89), a mixture of enolates results but in the cyclohexyl cyclopropyl ketone (99) enolate formation is only observed towards the cyclohexane ring.

The model compound for this study was the cis-2-ethylcyclopropyl cyclohexyl ketone (104). This compound was kinetically deprotonated and the resulting enolates were trapped under identical conditions as compound (89).

This thesis describes the preparation of the compounds (101), (103) and (104), their enol silyl ether formation, and subsequent thermal
rearrangement of the ethers derived from compounds (101) and (103) to try to understand the previously mentioned ideas.
Discussion

The Preparation of the Target Compounds.

The syntheses of compounds (101), (103) and (104) will be discussed in this section.

cis-2-Vinylcyclopropyl ketones have been prepared in our laboratory via a cuprate type reaction on the appropriate acid chloride. The starting material for compounds (101) and (103) was therefore the acid chloride (105). This compound was prepared in the following manner.

Hagemann's ester, 4-carbethoxy-3-methyl-2-cyclohexen-1-one (106), which is commercially available, was hydrolyzed in refluxing methanol and aqueous 2 N sodium hydroxide for 24 h. The resulting solution was worked up by the addition of acid to give 3-methyl-2-cyclohexen-1-one (107) in 71% yield after distillation. The compound (107) had the characteristic infrared bands at 1660 and 1630 cm$^{-1}$ due to the $\alpha,\beta$-unsaturated ketone functionality.
The ketone (107) was converted into 3,3-dimethylcyclohexanone (108) with a copper catalyzed Grignard\textsuperscript{26,27} reaction using cupric acetate as the catalyst. A solution of methylmagnesium iodide in anhydrous ether was added to a solution of the ketone (107) and the catalyst in anhydrous tetrahydrofuran. The resulting ketone (108), after work up, could be further purified by high pressure liquid chromatography (HPLC) on silica gel. The infrared spectrum of the product (108) showed an absorbance at 1710 cm\(^{-1}\) characteristic of a cyclohexanone carbonyl group and the \(^1\text{H}\) nmr spectrum did not show any signal due to an olefinic proton. High resolution mass spectrometry indicated the correct molecular mass. Approximately 3% of the 1,2 addition product resulting from the reaction was separated by HPLC.
At this point in the synthesis, it was necessary to convert the dimethyl ketone (108) into 3,3-dimethylcyclohexanecarboxylic acid. Many papers have been published on one carbon homologations, but it was found that a convenient method was to prepare the enol ether (109) and later hydrolyze this material to the aldehyde (110).

The enol ether (109) was synthesized via a Wittig reaction utilizing the commercially available (methoxymethyl)triphenylphosphonium chloride (111).

\[
\begin{align*}
\text{K} & \to \text{OCH}_3 \\
108 & \to 109 & \to 110 \\
(C_6H_5)_3PCH_2OCH_3Cl & \\
111
\end{align*}
\]

The anion of the phosphonium salt (111) was initially generated by treatment of this substance with n-butyllithium in ether or tetrahydrofuran, since this had been previously reported using a phenyllithium solution. Possibly due to the easy enolizability of the ketone (108), only starting material was recovered in this case.

Corey reported that the Wittig reaction proceeds much faster and more efficiently using the methylsulfinyl carbanion (112) in dimethyl sulfoxide. He generated the anion \textit{in situ} using sodium hydride and then immediately used it. We found that we obtained better results if a
standardized (titrated) solution of this base was used. The anion solution (112) could be stored for months in the freezer.

The methylsulfinyl carbanion (112) solution in dimethyl sulfoxide was added to a solution of the phosphonium salt (111) in dimethyl sulfoxide until the reddish colour of the anion persisted. A solution of the ketone (108) in dimethyl sulfoxide was then added and the resulting mixture was stirred for 2 h at room temperature. A mixture of the enol ethers (109) with an E : Z ratio of approximately 1 : 1 (glc analysis) resulted, in a yield of 90%. The methyl groups of the two isomeric enol ethers had different chemical shifts in the $^1$H nmr spectrum ($\delta$ 3.56, 3.53) as did the protons on the double bond ($\delta$ 5.73, 5.88).

The enol ethers (109) were hydrolyzed to the aldehyde (110) using a solution of 70% aqueous perchlroric acid in ether. The $^1$H nmr spectrum of the aldehyde showed a peak at $\delta$ 9.75, attributable to the aldehyde proton, as a doublet with a coupling constant of 2 Hz. The infrared spectrum had an absorbance at 2700 cm$^{-1}$ due to the aldehydic C-H stretch and a carbonyl absorbance at 1725 cm$^{-1}$.

If the enol ether mixture (109) was purified by HPLC on silica gel, and then hydrolyzed, as above, a solid with melting point 124-126°C
resulted. This solid was identified as the trimer (113) of the aldehyde. The infrared spectrum showed no carbonyl or aldehydic proton stretch. The \(^1\)H nmr spectrum had a peak at \(\delta 4.43\) as a doublet \((J = 5 \text{ Hz})\) due to the proton between the two oxygens in structure (113). The high resolution mass spectrum had a fragmentation pattern consistent with that expected for the trimer (113).

The aldehyde (110) was oxidized by the method of Jones\(^{31}\) (\(\text{CrO}_3/\text{H}_2\text{SO}_4/\text{H}_2\text{O}/\text{acetone}\)) to form the carboxylic acid (114). The purified carboxylic acid, as an oil, exhibited, in the infrared spectrum, a broad band at \(3200-2500 \text{ cm}^{-1}\) due to the hydroxyl group on the acid and an absorbance at \(1700 \text{ cm}^{-1}\) due to the carbonyl functionality. The \(^1\)H nmr spectrum had a multiplet at \(\delta 2.34-2.72\) due to the ring proton adjacent to the carboxylic acid and a broad peak at \(\delta 10.5\) due to the proton on the carboxylic acid.
The carboxylic acid chloride (105) was prepared by refluxing a solution of the carboxylic acid (114) in two equivalents of thionyl chloride, as per Vogel. The carboxylic acid chloride (105) was thus obtained in high yield. The signal in the $^1$H nmr spectrum assigned to the proton adjacent to the carbonyl in (105), appeared as a multiplet at $\delta$ 2.70-3.10. The infrared spectrum showed a carbonyl stretch at 1790 cm$^{-1}$.

It was now necessary to prepare the 1,1-dibromo-2-vinylcyclopropane (115). This was synthesized by a carbenoid reaction on 1,3-butadiene. The butadiene was condensed into a flask and bromoform, methylene chloride, and the phase transfer catalyst benzyltriethylammonium chloride (TEBA), were added. Ethyl alcohol was also added and a 50% aqueous sodium hydroxide solution was added dropwise. The reaction mixture was stirred for 8 h at approximately -5°C (refluxing butadiene) and subsequently the mixture was worked up.

The crude dibromo compound (115) was reduced with a suspension of zinc in glacial acetic acid and ether. A glc analysis of the product showed that it was an approximately 82 : 18 mixture of the cis and trans isomers of 1-bromo-2-vinylcyclopropane (81) and (116) respectively. These compounds could be distinguished by $^1$H nmr spectroscopy. The pure cis isomer (81) was obtained by a careful fractional distillation (140 torr) of the mixture through a Vigreux column.
Initially, a mixture of cis and trans ketones (101) and (103) were prepared. A solution of the cis and trans bromide mixture (81) and (116) (approximately 1 : 1) in anhydrous ether was allowed to react with tert-butyllithium at -78°C for 2 h. This effected lithium bromine exchange. Phenylthiocopper and anhydrous tetrahydrofuran were added and a clear brown solution resulted. The lithium phenylthiocuprates (33) and (34) are stable at -20°C.

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

81

\[
\begin{align*}
\text{LiCuSC}_6\text{H}_5 & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\end{align*}
\]

33

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

116

\[
\begin{align*}
\text{LiCuSC}_6\text{H}_5 & \quad \text{H} \\
\text{H} & \quad \text{H} \\
\end{align*}
\]

34

The mixture of cuprate reagents (33) and (34) was allowed to react with the previously prepared carboxylic acid chloride (105) to form the 2-vinylcyclopropyl ketone mixture (101) and (103). The ketone mixture (101) and (103) was analyzed by glc which indicated that they were present in a ratio of approximately 1 : 1. The mixture appeared as one spot when observed by thin layer chromatography.
The infrared spectrum of the mixture of (101) and (103) showed a weak absorbance at 3060 cm\(^{-1}\), characteristic of the C-H stretch of a cyclopropane ring, an absorbance at 1685 cm\(^{-1}\) due to the carbonyl group, and an absorbance at 1630 cm\(^{-1}\) due to the double bond stretch of the vinyl group. The \(^1\)H nmr spectrum indicated a complex multiplet at \(\delta\) 4.88-5.85 due to the protons on the double bond. A high resolution mass spectrum measurement showed the correct molecular mass.

The cis-2-vinylcyclopropyl ketone (101) was prepared in a manner analogous to that described above. A solution of cis-1-bromo-2-vinylcyclopropane (81) (from fractional distillation, 95% pure) in anhydrous ether was treated with a tert-butyllithium solution at -78°C and the resulting mixture was stirred for 2 h. Anhydrous tetrahydrofuran and solid phenylthiocopper were added as before. A solution of the acid chloride (105) in anhydrous tetrahydrofuran was added to the mixture. Usual work up of the reaction mixture, by addition of ether, and filtering the resultant suspension through a short column of Florisil,
gave the *cis* ketone (101). Distillation of the product gave an 87% yield of a colourless oil which appeared as a single component when analyzed by glc.

The infrared spectrum showed an absorbance at 1690 cm\(^{-1}\) due to the carbonyl group and an absorbance at 1630 cm\(^{-1}\) due to the C=C stretch of the vinyl group. The \(^1\)H nmr spectrum of this material was more clearly defined as compared to that of the mixture. The proton H\(_1\) (see diagram) appears as a doublet of doublets with one coupling constant of 10 Hz, due to the *cis* H\(_1\), H\(_3\) coupling, and a geminal coupling H\(_1\), H\(_2\) of 2.5 Hz. These coupling constants are in the normal range for this sort of double bond proton. Proton H\(_2\) resonated at \(\delta\) 5.17 as a doublet of doublets with a *trans* coupling (H\(_2\), H\(_3\)) of 17 Hz. Proton H\(_3\) gave rise to a doublet of doublet of doublets centred at \(\delta\) 5.66 with, besides the above mentioned couplings, a coupling of 8 Hz between itself and proton H\(_4\).

The *trans*-2-vinylcyclopropyl ketone (103) was prepared by treatment of a solution of the mixed ketones (101) and (103) (1:1 from above) in anhydrous tetrahydrofuran with a solution of potassium tert-butoxide in tert-butyl alcohol. The resulting mixture was stirred for 3 h at room temperature. The reaction solution was worked up with 1 N hydrochloric acid and the resultant oil was analyzed by glc. This analysis revealed
a trans : cis ratio of approximately 93 : 7 respectively. Longer reaction times (~18 h) resulted in approximately the same trans : cis ratio.

![Chemical structure](image)

The $^1$H nmr spectrum of this ketone (103), showed a doublet of doublets due to $H_1$ at $\delta$ 4.98 with a $H_1$, $H_3$ coupling of 9 Hz and a $H_1$, $H_2$ coupling of approximately 3 Hz. Proton $H_2$ also gave rise to a doublet of doublets with coupling of 17 Hz for $H_2$, $H_3$, the same geminal coupling as mentioned above (3 Hz), and a chemical shift of $\delta$ 5.14. The proton $H_3$, in this case, resonated as a complex multiplet at $\delta$ 5.28-5.70.

The cis-2-ethylcyclopropyl ketone (104) was also synthesized. It

![Chemical structures](image)

was felt that this ketone could be prepared by hydrogenation of the corresponding cis-2-vinylcyclopropyl ketone (89).

The cis-2-vinylcyclopropyl ketone (89) was synthesized by means of a cuprate reaction, as described above, using the cis-1-bromo-2-vinyl-
cyclopropane (81) and cyclohexanecarboxylic acid chloride, in 78% yield. This ketone (89) was purified by chromatography on a silica gel column 
($R_f = 0.55$). The column was eluted with a mixture of petroleum ether and ether in a ratio of 7 : 1 respectively.

The infrared spectrum of the purified material exhibited absorbances at 1690 cm$^{-1}$ due to the carbonyl group and at 1635 cm$^{-1}$ due to the olefinic double bond. The $^1$H nmr spectrum had a doublet of doublets centred on $\delta$ 4.94 attributable to proton $H_1$, with coupling constants of 10.5 Hz for $H_1$, $H_3$ (see diagram) and 2.3 Hz for $H_1, H_2$. The proton $H_2$ resonated at $\delta$ 5.13

![Diagram](image)

as a doublet of doublets and is coupled to proton $H_3$ with a coupling constant of 17 Hz as well as being coupled to proton $H_1$, as described above. The signal due to proton $H_3$ appeared as a doublet of doublet of doublets centred at $\delta$ 5.62 with, besides the above mentioned couplings, a coupling of 9 Hz between itself and proton $H_4$.

It was expected that the desired product (104) could be prepared from ketone (89) via a catalytic hydrogenation. Heathcock$^{37}$ reported that the catalytic hydrogenation of various substituted vinyl cyclopropane derivatives (117) proceeded most efficiently if he used Wilkinson's$^{38}$ catalyst, tris(triphenylphosphine)rhodium chloride (118).
The cis-2-vinylcyclopropyl cyclohexyl ketone (89) was hydrogenated with 5 mole % of Wilkinson's catalyst in benzene at atmospheric pressure and room temperature. However, none of the expected product (104) was obtained and only a small amount of starting material (89) was recovered with no other identifiable products. Other hydrogenation catalysts were also used (10% Pt/C; 5% Rh/alumina), in benzene or isopropyl alcohol, as solvents, with varying results. These catalysts gave poor yields of the hydrogenated product (104).
To circumvent this problem, it was felt that a diimide reduction might work in this case. Following the method of Fieser, a solution of the cis ketone (89) in ethyl alcohol and 95% hydrazine hydrate was put in a round bottomed flask at 0°C. A drop of an approximately 1% aqueous cupric sulfate pentahydrate solution was added followed by a 30% hydrogen peroxide solution and the mixture was allowed to warm to room temperature and stirred for 5 h. The cis-2-ethylcyclopropyl cyclohexyl ketone (104) was obtained in 69% yield. A glc analysis of this oil showed only one component and no starting material.

The infrared spectrum had an absorbance at 1685 cm$^{-1}$ due to the carbonyl group and the $^1$H nmr spectrum had a triplet centred at $\delta$ 0.85 due to the methyl group of the ethyl substituent. The proton on the cyclopropane ring adjacent to the ketone ($H_1$) appeared as a multiplet at $\delta$ 2.02-2.12 while the proton on the other side of the ketone ($H_2$) resonated as a multiplet at $\delta$ 2.42-2.55.

To prove that no cis to trans isomerization of the substituted vinylcyclopropyl ketone (89) had taken place during the diimide reduction the analogous trans compound (100, $R = \bigcirc$) was prepared and reduced under conditions identical with those described above. This ketone was synthesized by treatment of a solution of the cis ketone (89) in tetra-
hydrofuran with a solution of potassium tert-butoxide in tert-butyl alcohol as previously described. A glc analysis of the product (100) indicated one peak with a retention time similar to that of the cis ketone (89).

The $^1$H nmr spectrum showed a multiplet at $\delta$ 2.55-2.68 due to the cyclohexane ring proton adjacent to the carbonyl group. Proton $H_1$ appeared as a doublet of doublets centred on $\delta$ 4.96 with geminal coupling of 2.4 Hz and $H_1$, $H_3$ coupling of 7.8 Hz. Proton $H_2$ resonated at $\delta$ 5.12 as a doublet of doublets with, besides the previously mentioned geminal
coupling, a coupling between H₂ and H₃ of 15 Hz. Proton H₃ appeared as a complex multiplet between δ 5.28 and δ 5.70.

The trans vinyl ketone (100) was reduced under similar diimide reduction conditions, as previously described, to give the trans-2-ethyl-cyclopropyl cyclohexyl ketone (119) in 65% yield. The product, upon glc analysis, had a retention time similar to that of the cis ketone (104).

The ¹H nmr spectrum differed from that of ketone (104). A multiplet at δ 0.67-0.74 was due to one of the cyclopropane protons. The methyl of the ethyl substituent appeared as a triplet centred at δ 0.96. The cyclohexane proton adjacent to the carbonyl group resonated as a multiplet at δ 2.42-2.55.

II  Enol Ether Formation and Rearrangement

The enol ether formation of compounds (101), (103) and (104) and thermal rearrangement of those resulting from (101) and (103) will be discussed in this section.

A solution of the cis ketone (101) in anhydrous tetrahydrofuran was added dropwise to a solution of lithium diisopropylamide (LDA) in anhydrous tetrahydrofuran at -78°C. The resulting mixture of enolates
was trapped at \(-78^\circ\text{C}\) by the addition of a solution of freshly sublimed tert-butyldimethylsilyl chloride in anhydrous tetrahydrofuran followed by dry hexamethylphosphoramide (HMPA). The mixture was subsequently stirred for 15 min at \(-78^\circ\text{C}\) and 3 h at room temperature. Following work-up, a glc analysis of the resulting oil (87% yield) revealed that it consisted of a mixture of enol silyl ethers (120) and (121) in a ratio of approximately 12 : 88 respectively.

\[
\begin{align*}
\text{101} & \quad \text{120} & \quad \text{121}
\end{align*}
\]

The infrared spectrum of this mixture had an absorbance at 1760 cm\(^{-1}\) which was attributed to the double bond stretch of the bond \textit{exo} to the cyclopropane ring in compound (121). The \(^1\text{H} \text{nmr} \) spectrum had a peak at \(\delta\ 0.16\) as a singlet due to the methyl group protons on the enol silyl ethers.

This 12 : 88 mixture of (120) and (121) was thermolyzed neat at \(160^\circ\text{C}\) for 45 min in a previously equilibrated Kugelrohr distillation apparatus, under an argon atmosphere, to give the rearranged products (122) and (123) in a 88% yield after distillation. Compound (123) results from a vinylmethylenecyclopropane rearrangement as previously discussed\(^{23}\). A glc analysis of the mixture (122) and (123) revealed that the compounds were present in a ratio of approximately 14 : 86 respectively. The two compounds (122) and (123) could not be separated via column chromatography on silica gel or Florisil.
The infrared spectrum of the mixture of (122) and (123) showed an absorbance at 1630 cm$^{-1}$ due to an olefinic double bond stretch. The $^1H$ nmr spectrum had the following peaks attributed to the major product (123). A singlet at $\delta$ -0.04 was due to the methyl group hydrogen of the silyl ether. A broad singlet at $\delta$ 4.88 was assigned to proton $H_1$ which is long range coupled with $H_3$. This broadening is due to trans vinylic coupling which is reported to be in the range of 0.5-2.5 Hz. A sharp singlet at $\delta$ 5.02 was assigned to the proton $H_2$ (geminal coupling must be $\leq 1$ Hz). Proton $H_3$ appeared as a multiplet at $\delta$ 6.04-6.20, deshielded by the exo double bond and proton $H_4$ appeared as a multiplet at $\delta$ 5.86-6.01.

The trans ketone (103) (trans : cis, 93 : 7) was also treated with
lithium diisopropylamide, under kinetic conditions and the resulting mixture of enolates was trapped with tert-butylidimethylsilyl chloride in the presence of hexamethylphosphoramide, as previously described. A glc analysis of the distilled oil (84% yield) revealed that the mixture was composed of compounds (124) and (121) in a ratio of approximately 87:13 respectively.

The infrared spectrum had an absorbance at 1660 cm\(^{-1}\) due to the double bond \textit{exo} to the cyclohexane ring. The \(^1\text{H}\) nmr spectrum had a pair of singlets at \(\delta\) 0.10 and \(\delta\) 0.13 due to the methyl group hydrogens on the enol silyl ethers.

The enol silyl ether mixture (124) and (121), from above, was thermolyzed at 230°C for 1 h in a previously equilibrated Kugelrohr distillation apparatus (argon). The mixture was distilled (72% yield) and the resulting oil was analyzed by glc which showed that it consisted of a mixture of compounds (122) and (123) in a ratio of approximately 82:18 respectively.

An infrared spectrum of the mixture was similar to that resulting from the \textit{cis} compound (101). The \(^1\text{H}\) nmr spectrum had the following peaks attributable to the major product (122). The enol silyl ether methyl
groups appeared as a pair of singlets at $\delta$ 0.17 and 0.19. Proton $H_1$

appeared as a triplet centred at $\delta$ 4.72 and protons $H_2$ and $H_3$ gave rise to a multiplet at $\delta$ 5.60–5.86.

The enol silyl ethers of the cis-2-ethylcyclopropyl ketone (104) were prepared, as described above, by treatment of the ketone with lithium diisopropylamide and trapping the resulting enolates with tert-butylidimethylsilyl chloride in the presence of hexamethylphosphoramide. Work up of the mixture and distillation of the resulting oil gave a 74% yield of the enol ethers (125) and (126). A glc analysis of this oil had one major peak (~97%). However, the infrared spectrum, of this material, showed an absorbance at 1765 cm$^{-1}$ due to a double bond $\text{exo}$ to the cyclopropyl ring and an absorbance at 1670 cm$^{-1}$ due to an olefinic
bond exo to the cyclohexane ring. This indicated that both isomers were present. The ratio of the two enol silyl ethers (125) and (126) was determined by careful integration of the methyl signals of the silyl ethers on a high resolution nmr spectrometer. Integration showed the mixture of (125) and (126) was in a ratio of approximately 1 : 1.

III. Hydrolysis of the Thermolysis Mixtures

The thermolysis mixtures, from the cis and trans ketones (101) and (103) respectively, were not separated at this stage but instead each mixture was allowed to react with a solution of 1 N hydrochloric acid in tetrahydrofuran. This effectively hydrolyzed the enol silyl ether functionality in compound (122). The resulting mixtures were then
chromatographed and the pure compounds were characterized.

The thermolysis mixture (122) and (123) from the cis ketone (101), in a ratio of approximately 14 : 86 respectively, was hydrolyzed in a solution of 1.5 mL of tetrahydrofuran and 0.75 mL of 1 N hydrochloric acid. The resulting mixture was analyzed via glc and was found to be a mixture of compounds (127) and (123) in a ratio of approximately 10 : 90 respectively. This mixture was subjected to column chromatography on silica gel. The column was eluted with a petroleum ether : ether mixture (approximately 7 : 1 respectively) to give the silyl ether (123) (Rf = 0.64).

\[ 122 + 123 \rightarrow 123 + 127 \]

The infrared spectrum of the purified silyl ether (123) had an absorbance at 1630 cm\(^{-1}\) due to the olefinic double bond stretch and also a peak at 1250 cm\(^{-1}\) characteristic of the methyl-silicon stretch.\(^{36}\) The \(^1\)H nmr spectrum had a singlet at \(\delta = -0.07\) due to the silyl methyl groups.
Proton $H_1$ appeared as a broad singlet at δ 4.88 due to a small trans vinylic coupling with proton $H_3$, as previously discussed. Proton $H_2$ resonated as a sharp singlet at δ 5.02. Protons $H_3$ and $H_4$ each appeared as multiplets at δ 6.04-6.20 and δ 5.86-6.00 respectively. A high resolution mass spectrometric measurement gave the correct molecular mass for the compound (123).

The thermolysis mixture (122) and (123) from the trans ketone (103), in a ratio of approximately 82 : 18 respectively, was hydrolyzed in a solution of 2 mL of tetrahydrofuran and 1 mL of 1 N hydrochloric acid. The resulting mixture of compounds (127) and (123) was analyzed by glc and the two compounds were found to be present in a ratio of approximately 87 : 13 respectively. This oil was subjected to column chromatography on silica. The column was eluted with a petroleum ether : ether mixture (approximately 7 : 1 respectively) to give the purified ketone (127) ($R_f = 0.36$).

The infrared spectrum of the purified ketone (127), as an oil, had a sharp absorbance at 1690 cm$^{-1}$ due to the carbonyl functionality. The $^1H$ nmr spectrum had a pair of singlets at δ 0.76 and 0.91 due to the two methyl groups. The two olefinic protons appeared as complex multiplets.
at $\delta$ 5.72-5.84 and $\delta$ 5.86-5.97. A high resolution mass spectrometric measurement gave the correct molecular mass for the compound (127).

IV Further Work

To reaffirm the previously observed result$^{24}$ that cyclohexyl cyclopropyl ketone (99) deprotonated only towards the cyclohexane ring, it was prepared and its enol silyl ether formed.

![Diagram]

The ketone was synthesized via a cuprate reaction of the lithium (phenylthio)cyclopropylcuprate with cyclohexanecarboxylic acid chloride. The enol silyl ether (128) was prepared by treating the ketone (99) with lithium diisopropylamide and trapping the resulting enolate with a tert-butyltrimethylsilyl chloride solution as described previously. A glc analysis of the isolated product showed that it consisted of one component.

The infrared spectrum had an absorbance at 1660 cm$^{-1}$ characteristic of a double bond exo to the cyclohexane ring. The $^1$H nmr spectrum had a singlet at $\delta$ 0.13 due to the methyl groups on the enol silyl ether. The four protons $\alpha$ to the double bond on the cyclohexane ring appeared as a pair of multiplets at $\delta$ 2.11-2.18 and $\delta$ 2.21-2.80.
Conclusions

As shown earlier, generation of the enolates of the cis-2-vinyl-cyclopropyl ketone (89) with lithium diisopropylamide, followed by trapping of these enolates gave an approximately 1:1 mixture of enol silyl ethers (90) and (91). The use of a more sterically or less sterically hindered base (see Table I), to form the enolates, and the trapping of these, gave different ratios of enol silyl ethers, suggesting that a steric effect may be affecting the deprotonation although this may not be the only effect. The more congested 3,3-dimethyl derivative (101), when treated with lithium diisopropylamide and trapping of the enolates, was expected to show more enolate formation towards the cyclopropane ring if there was a steric effect. Indeed, formation of the enolates with lithium diisopropylamide followed by the trapping of these under conditions identical with those used in the cyclohexyl case (89), gave a ratio of the enol silyl ethers (120) and (121) of 12:88 respectively. This confirmed
that there is some steric hindrance to base attack in this system.

The *trans*-2-vinylcyclopropyl ketone (100), when allowed to react with lithium diisopropylamide followed by trapping of the resulting enolate, gave exclusive enolization towards the cyclohexane ring [compound (102)]. In fact, in all *trans* compounds studied, enolization occurred only towards the respective "R" group (see previous discussion). We were interested in seeing how the more congested *trans*-3,3-dimethyl derivative (103) would react under similar enol ether forming conditions. When the derivative (103) was allowed to react with lithium diisopropylamide followed by trapping of the enolates, it gave a mixture of enol ethers (124) and (121) in a ratio of approximately 87 : 13 respectively. This again confirmed a steric effect.
As discussed above, the cis-2-vinylcyclopropyl ketone (89) gave a 1:1 mixture of enol silyl ethers when treated with lithium diisopropylamide followed by trapping of the resulting enolates. The cyclohexyl cyclopropyl ketone (99) when reacted, under identical conditions as above, gave enolate formation only towards the cyclohexane ring. These observations suggested that the vinyl substituent may have some sort of electronic effect on the cyclopropane proton [circled in (89)] beside the ketone. The replacement of the vinyl substituent in compound (89) with an ethyl group should reduce any electronic effect of the cyclopropane proton adjacent to the ketone. Thus, the cis-2-ethylcyclopropyl ketone (104) was expected to give, upon deprotonation and trapping of the resulting enolates, mainly enol silyl ether formation towards the
cyclohexane ring. Formation and trapping of the enolate generated from the ketone (104) gave an approximately 1:1 mixture of enol silyl ethers. This result seems to disprove an electronic effect of a vinyl substituent, although more work will have to be done in this area to further understand the above mentioned result.
Experimental

General Information

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Distillation temperatures are also uncorrected and those indicated as air-bath temperatures refer to short path (Kugelrohr) distillations. Infrared (ir) spectra were recorded on a Perkin-Elmer model 710 B infrared spectrophotometer and were calibrated using the 1601 cm\(^{-1}\) band of polystyrene film. The proton nuclear magnetic resonance (\(^1\)H nmr) spectra were taken in deuterochloroform solution and were recorded using Varian Associates HA-100, XL-100 spectrometers or a Bruker WP-80 spectrometer. The 270 MHz spectra were recorded on a unit comprised of an Oxford Instruments 63.4 KG superconducting magnet and a Nicolet 16K computer attached to a Bruker TT-23 console. Signal positions are given in parts per million (\(\delta\)) from tetramethylsilane (TMS) as internal standard. In the case of compounds containing tert-butyl-dimethylsilyl groups, the resonance positions were determined via deuterium lock (CDCl\(_3\)) on the nmr spectrometer. The multiplicity, number of protons, coupling constants (where possible) and assignments are indicated in parentheses. Low resolution mass spectra were recorded with a Varian/MAT CH\(_4\)B mass spectrometer. High resolution mass spectra were recorded with a Kratos/AEI MS 50 or MS 902 mass spectrometer.

Analytical gas liquid chromatography (glc) was performed on a Hewlett-Packard HP 5832A gas chromatograph. The following columns were used: (A) 6 ft x 0.125 in., 3% OV-17 on Chromosorb W (HP) (80-100 mesh); (B) 6 ft x 0.125 in., 5% OV-210 on Chromosorb W (HP) (80-100 mesh); (C) 6 ft x 0.125 in., 3% Carbowax 20M on Chromosorb W (HP) (80-100 mesh).
Column chromatography was done on either silica gel (E. Merck 70-230 mesh) or Florisil (J.T. Baker Chemical Co., 100-200 mesh). Analytical thin-layer chromatography (t.l.c.) was carried out on commercial, pre-coated Silica Gel plates with fluorescent indicator (Eastman Kodak, Sheet Type 13181) and visualized by iodine vapour staining. Preparative high pressure liquid chromatography (HPLC) was done on a Waters Prep LC/System 500 instrument with Prep Pak-500 silica cartridge containing chromatographic grade silica.

All reactions involving moisture and air sensitive reagents were carried out under an atmosphere of argon using carefully flame dried glassware.

Solvents and Reagents

Solutions of \textit{n}-butyllithium, methyllithium, and \textit{tert}-butyllithium were obtained from Aldrich Chemical Company Inc. and were standardized using Gilman's procedure.\textsuperscript{41} The \textit{tert}-butyldimethylsilyl chloride (Aldrich Chemical Co. Inc.) was sublimed at 20 torr and used immediately.

Petroleum ether refers to the reagent grade mixture that has a boiling range of 30-60°C. Ether refers to reagent grade diethyl ether.

Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone ketyl under nitrogen.\textsuperscript{42}

Diisopropylamine was distilled from calcium hydride and stored over freshly activated 3Å molecular sieves.

Dimethyl sulphoxide was distilled from calcium hydride at reduced pressure (20 torr).
Hexamethylphosphoramide (HMPA) was distilled from barium oxide under reduced pressure (vacuum pump) and stored over freshly activated 3 Å and 13X molecular sieves.

The 4-carbethoxy-3-methyl-2-cyclohexen-1-one (Hagemann's ester), (methoxymethyl) triphenylphosphonium chloride, and potassium tert-butoxide were obtained from Aldrich Chemical Company Inc.

All extraction solvents were reagent grade and were used as received.

The sodium methylsulfinyl methide (dmsyl sodium) solution was prepared by addition of sodium hydride (6 g, 50% wt/wt in mineral oil) to a dry flask, with reflux condenser under an atmosphere of argon. The sodium hydride was rinsed with petroleum ether (3 x 25 mL), to remove the mineral oil, dry dimethyl sulphoxide (50 mL) was added, and the mixture heated at 65°C for 3 h. The resulting grey, cloudy solution was standardized by quenching 1 mL with water and titrating the resultant basic solution with standardized 0.1 normal hydrochloric acid (1% phenolphthalein solution as indicator). The titrated solution could be stored in a round bottom flask with a septum cap in the freezer and added via syringe to the reaction mixture.

The 1,3-butadiene (gas) was purchased from the Matheson Division of G.D. Searle and Co. of Canada Ltd.
Preparation of 3-Methyl-2-Cyclohexen-1-one (107)

To a flame-dried 250 mL flask equipped with a magnetic stir bar, a reflux condenser, and an argon inlet tube was added 26.1 g (freshly distilled, 0.14 mol) of 4-carbethoxy-3-methyl-2-cyclohexen-1-one (Hagemann's ester), reagent grade methyl alcohol (40 mL) and 2 N aqueous sodium hydroxide (30 mL). The resulting mixture was refluxed for 24 h. The reaction was worked up by the addition of 1 N hydrochloric acid, until the solution was slightly acidic, and the mixture was extracted with ether (2 x 200 mL). The combined extract was washed with brine and dried over anhydrous magnesium sulfate. Removal of the ether followed by distillation of the resultant oil (air-bath temperature 90-95°C, 20 torr) gave 11.19 g (71%) of the ketone (107) as a colourless oil. A glc analysis of this material (column A) exhibited one peak. IR (film): 2940, 2860, 1660, 1630, 1430, 1380, 1350, 1325, 1250, 1195, 890 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \(\delta\): 1.85-2.22 (m, 2H), 1.92 (s, 3H, Me), 2.17-2.54 (m, 4H), \(\text{CH}_2\text{C}^-\), \(\equiv\left(\text{CH}_2\text{H}_2\right)\), 5.81-5.90 (m, 1H, \(\equiv\left(\text{H}\right)\)). Exact mass calcd. for \(\text{C}_7\text{H}_{10}\text{O}\): 110.0732; found: 110.0733.
Preparation of 3,3-Dimethylcyclohexanone (108)\textsuperscript{26,27}

\begin{center}
\begin{tikzpicture}
  \node[above] at (0,0) {\textbf{108}};
\end{tikzpicture}
\end{center}

To a 250 mL flame-dried flask, equipped with a dry ice condenser, a septum cap, an argon inlet tube and a magnetic stir bar, were added magnesium turnings (2.87 g, 0.118 mol) and 25 mL of anhydrous ether. Methyl iodide (6.79 mL, 0.109 mol) was added carefully. Anhydrous ether (60 mL) was added and the resulting solution was allowed to reflux for 30 min and then cooled to 0°C.

To a second 250 mL, flame-dried flask, equipped with a pressure equalizing dropping funnel (100 mL) containing a septum cap, an argon inlet tube and a magnetic stir bar, was added 3-methyl-2-cyclohexen-1-one (107) (10 g, 0.091 mol), cupric acetate (1.65 g, 9.1 mmol), and 43 mL of anhydrous tetrahydrofuran. The freshly prepared solution of Grignard reagent was transferred via cannula to the dropping funnel of the second flask. This solution was added dropwise to the cooled (0°C), vigorously stirred mixture in the second flask over 1 h. The resulting mixture was allowed to warm to room temperature and stirring was continued for an additional 2 h. The reaction mixture was poured into a slurry of 100 mL of crushed ice and dilute hydrochloric acid and the resultant mixture was extracted with 2 x 200 mL of ether. The combined extracts were washed with brine, dried over anhydrous magnesium sulfate and the solvent
was evaporated to give 10.45 g (91%) of the crude ketone (108) as an oil. A glc analysis of this material (column A) showed that it contained approximately 3% of the 1,2 addition product and approximately 97% of the desired 3,3-dimethylcyclohexanone (108). The mixture was conveniently purified by column chromatography on silica gel or by HPLC. In each case, a 3:2 mixture of petroleum ether and ether was used as the eluting solvent. Pure 3,3-dimethylcyclohexanone (108) exhibited IR (film): 2960, 2870, 1710, 1460, 1420, 1370, 1315, 1295, 1265, 1230 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.99 (s, 6H, methyls), 1.45-2.08 (m, 4H), 2.10-2.43 (m, 4H, -C-CH₂). Exact mass calcd. for C₁₀H₁₄O: 126.1044; found: 126.1040.

Preparation of the Enol Ether (109)

![Chemical Structure](image)

To a dry, 50 mL flask equipped with a dropping funnel, a septum cap, an argon inlet tube and a magnetic stir bar was added (methoxymethyl) triphenylphosphonium chloride (3.47 g, 10.12 mmol) and 20 mL of dry dimethyl sulphoxide. Sodium methylsulfinyl methide (dmsyl sodium) solution (2.65 M) was added dropwise to the mixture until a red colour persisted. Further dmsyl sodium solution was then added (3.82 mL, 10.12 mmol) and the resulting red solution was stirred for 15 min at room temperature. A solution of the ketone (108) (850 mg, 6.75 mmol) in 5 mL
of dry dimethyl sulphoxide was added over a period of 10 min and the resulting solution was stirred for an additional 2 h. The reaction mixture was poured into 50 mL of water and the mixture thus obtained was extracted with ether (2 x 50 mL). The combined extracts were washed with brine, dried over anhydrous magnesium sulfate, and the solvent was removed to give an oil. The oil was dissolved in hexanes and the resulting solution was passed through a short column of Florisil. The column was eluted with further volumes of hexanes. Removal of the solvent from the combined eluate gave 940 mg (90%) of an oil which was suitable for the next reaction. The material could be purified further by means of HPLC using petroleum ether and ether (7 : 1) as the eluting solvent mixture. A glc analysis (column B) of the purified material showed it to be an approximately 1 : 1 mixture of E and Z isomers IR (film): 2910, 2890, 2855, 2830, 1680, 1460, 1440, 1380, 1360, 1230, 1205, 1145, 1120, 990, 975 cm$^{-1}$; $^1$H nmr (CDCl$_3$) $\delta$: 0.86, 0.90 (s, s, 6H, methyls), 1.20-2.22 (complex m, 8H), 3.56, 3.53 (s, s, 3H, $-OCH_3$), 5.72, 5.88 (brs, brs, 1H, vinyl proton). Exact mass calcd. for $C_{10}H_{18}O$: 154.1358; found: 154.1362.

Preparation of 3,3-Dimethylcyclohexanecarboxaldehyde (110)
To a cold (0°C), stirred solution of 70% aqueous perchloric acid (8.25 mL) in ether (25 mL), under an atmosphere of argon, was added a solution (ether, 5 mL) of the enol ethers (109) (0.52 g, 3.38 mmol). The resulting solution was allowed to warm to room temperature and was stirred for 2 h. The mixture was carefully poured into saturated aqueous sodium bicarbonate (~60 mL) and the resultant mixture was extracted with ether (2 x 50 mL). The combined extracts were washed with water and dried over anhydrous magnesium sulfate. Removal of the solvent gave an oil which was filtered through a short column of Florisil (further elution with petroleum ether). Removal of the solvent from the combined eluate gave 370 mg (94%), of the desired aldehyde (110) as an oil. A glc analysis of this material (column A) showed that it contained no starting material (109) and was 94% pure. The aldehyde (110) could be used for the following reaction without further purification. IR (film) 2910, 2930, 2850, 2700, 1725, 1460, 1380, 1260 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.91, 0.94, (s, s, 6H, methyls), 1.02-2.60 (complex m, 9H), 9.75 (d, J = 2 Hz, 1H, -CHO).

If HPLC purified enol ethers (109) were used in the reaction, a crystalline product (mp 124-126°C), identified as the trimer (113), was obtained. This material exhibited the following spectra: IR (CHCl₃): 3000, 2940, 2915, 2850, 2840, 1460, 1450, 1380, 1365, 1345, 1190, 1140, 1130, 1110, 1070, 1040 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.91, 0.94 (s, s, 18H, methyls), 1.0-2.48 (complex m, 27H), 4.43 (d, J = 5 Hz, 3H, -CHO). Exact mass calcd for C₂⁷H₄⁷O₃ (M⁺-1): 419.3525; found: 419.3510; calcd. for C₉H₁₆O (monomer): 140.1201; found: 140.1201.
Preparation of 3,3-Dimethylcyclohexanecarboxylic Acid (114)

To a cold (0°C), vigorously stirred solution of the crude aldehyde (110) (0.37 g, 2.64 mmol) in reagent acetone (16 mL), was added over a period of 5 min, a freshly prepared solution of Jones' reagent\(^\text{31}\) (0.60 mL, 8 N, 4.8 mmol). The mixture was allowed to warm to room temperature and stirring was continued for an additional 1 h. The solution was diluted with anhydrous ether (~30 mL) and filtered through a short column of Florisil. The column was eluted further with anhydrous ether.
The combined eluates were dried over anhydrous magnesium sulfate and the solvent was evaporated to give 0.27 g (65%) of an oil. This material was further purified by dissolving it in ether and successively extracting the resulting solution with 1 N aqueous sodium hydroxide. The base extracts were acidified and then re-extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate, the solvent was evaporated and the resulting oil was distilled (air-bath temperature 150-160°C, 20 torr) to give 107 mg of the acid (114) as a colourless oil. A glc analysis (column A) indicated that this material consisted of one component. IR (film): 3200-2500 (OH), 2940, 2850, 1700, 1460 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.92, 0.96 (s, s, 6H, methyls), 1.04-2.14 (complex m, 8H), 2.34-2.72 (m, 1H, CH-COOH), 10.5 (br s, 1H, -COOH). Exact mass calcd. for C₉H₁₆O₂: 156.1151; found: 156.1157.

Preparation of 3,3-Dimethylcyclohexanecarboxylic Acid Chloride (105).

![COC1](image)

105.

The purified carboxylic acid (114) (1.0 g, 6.41 mmol) was weighed into a 10 mL, flame-dried flask equipped with a magnetic stir bar and a reflux condenser with a drying tube attached. The flask was partially immersed in a warm water bath (~40°C) and thionyl chloride (0.94 mL, 12.82 mmol) was added dropwise. The solution was stirred for 5 min. The
water bath was replaced by a heating mantle and the mixture was refluxed for an additional 2 h. The solution was allowed to cool and the excess thionyl chloride was removed under reduced pressure (water aspirator, 20 torr, 30 min). The residual oil was distilled (air-bath temperature 110-120°C, 20 torr) to give 1.09 g (98%) of the acid chloride (105) as a colourless oil. A glc analysis of this material (column A) indicated that it consisted of one component. IR (film): 2940, 2850, 1790, 1460, 1390, 1370, 1340, 1280, 1180, 1000, 970, 925, 900, 820, 750, 725, 705 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \(\delta: 0.95, 0.99\) (s, s, 6H, methyls), 1.06-2.24 (complex m, 8H), 2.70-3.10 (m, 1H, \(\text{C-COCl}\)). Exact mass calcd. for \(\text{C}_9\text{H}_{15}\text{O}^{37}\)Cl: 176.0782; found: 176.0766; for \(\text{C}_9\text{H}_{15}^{35}\)Cl: 174.0811; found: 174.0800.

Preparation of 1,1,-Dibromo-2-vinylcyclopropane (115)\(^{33}\)

Butadiene (193 mL, 2.2 mol) was condensed into a cold (-78°C), 1 L flask equipped with a dry ice condenser, a 50 mL addition funnel, a gas inlet tube and a drying tube. Bromoform (19.3 mL, 0.22 mol), methylene chloride (20 mL), benzyltriethylammonium chloride (TEBA, 0.5 g, 2.2 mmol) and ethanol (100%, 1.74 mL) were added and the cooling bath was removed. A 50% aqueous sodium hydroxide solution (35.2 g, 0.44 mol) was added dropwise to the mixture (vigorous stirring) over a period of 15 min and
stirring was continued for 8 h at \(-5^\circ\text{C}\) (refluxing butadiene). The dry ice condenser was removed and the butadiene was allowed to evaporate overnight. The remaining mixture was filtered through a wide column of Florisil. The column was eluted with methylene chloride (150 mL). The combined eluate was washed with water (until neutral), brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give 43 g of an oil which, on the basis of glc analysis (column A), consisted mainly (~88%) of the desired product, 1,1-dibromo-2-vinylcyclopropane (115). This material was not purified further, but was used directly for the next reaction. IR (film): 3060, 3000, 1630, 1435, 1425, 1220, 1190, 1145, 1105, 1050, 1010, 985, 920, 720 cm\(^{-1}\).

Preparation of a Mixture of the cis and trans-1-Bromo-2-vinylcyclopropanes (81) and (116).

\[
\begin{align*}
\text{81} & \quad \text{Br} \\
\text{H} & \quad \text{H} \\
\text{81} & \quad \text{Br} \\
\text{H} & \quad \text{H} \\
\end{align*}
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To a cold (0°C) dry flask, under an argon atmosphere, was added a solution of the crude dibromide (115) (43 g) in a mixture of anhydrous ether (438 mL) and glacial acetic acid (219 mL). Zinc dust (124 g) was added in portions over a period of 15 min and the resultant mixture was stirred for 30 min at 0°C and at room temperature for 2 h. The reaction mixture was filtered through a short column of Florisil. The column was
eluted with ether. The combined eluate was washed with water until neutral and further washed with a saturated aqueous sodium bicarbonate solution (2 x 75 mL), water, and dried over anhydrous magnesium sulfate. The solvent was removed by careful distillation (atmospheric pressure) to give 12.24 g of an oil (38% over 2 steps). A glc analysis (column A) of this material showed that it consisted of a mixture of cis and trans isomers (81) and (116) in a ratio of approximately 82 : 18 respectively. The mixture was separated via careful fractional distillation through a Vigreux column (45 min) at 125 torr. The following fractions were collected; fraction 1: bp 64-70°C, 1.03 g; fraction 2: bp 72-74°C, 1.97 g; and fraction 3: bp 74°C, 3.61 g. A glc analysis (column A) of these fractions indicated cis and trans isomer (81) and (116) ratios of approximately 47 : 53; 67 : 33 and 95 : 5 respectively. The residue, on the basis of a glc analysis (column A) contained neither of the isomers. The purified cis-1-bromo-2-vinylcyclopropane (81) (95%) exhibited IR (film): 3060, 2990, 2960, 1630, 1430, 1260, 1040, 980, 800 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.80-1.02 (m, 1H, -C—C ), 1.12-1.86 (m, 2H, -CHCH=CH₂, -C—C ), 3.18 (m, HC= ), 5.10-5.88 (m, 3H, olefinic protons).
To a 25 mL, flame-dried flask, equipped with a septum cap, an argon inlet tube, a magnetic stir bar, and a stopper was added a solution of the mixture of the 2-vinylcyclopropyl bromides (81) and (116) (cis: trans ~47:53, fraction 1 from above distillation; 253 mg, 1.72 mmol) in anhydrous ether (8 mL). The solution was cooled (-78°C) and a solution of tert-butyllithium (1.26 M in pentane, 2.46 mL, 3.10 mmol) was added dropwise and stirring was continued for 2 h at this temperature. At this point, anhydrous tetrahydrofuran (8 mL) and solid phenylthiocopper (297 mg, 1.72 mmol) were added and the reaction mixture was allowed to warm to -20°C and stirring was continued at this temperature for 30 min. The resulting clear brown solution was cooled to -78°C and a solution of the acid chloride (105) (200 mg, 1.15 mmol) in 1 mL of anhydrous tetrahydrofuran was added. Stirring was continued at -78°C for 15 min and the solution was allowed to warm to -20°C with continued stirring for 1 h. The solution was subsequently warmed to room temperature and stirred for 2 additional hours. The reaction was quenched by the addition of spectro-photometric grade methanol (~1 mL). The resultant mixture was diluted with ether and then filtered through a short column of Florisil. The column was eluted with ether. The combined eluate was evaporated and the residual oil was distilled (air-bath temperature 90-110°C, 0.4 torr) giving 174 mg (73%) of the product as a colourless oil. A glc analysis (column A) of this material indicated that it was an approximately 1:1 mixture of cis and trans isomers (101) and (103). IR (film): 3060, 2990, 2940, 2910, 2850, 1685, 1630, 1460, 1380, 1080, 900 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.92 (s, 6H, methyls), 1.0-2.84 (complex m, 13H), 4.88-5.85 (m, 3H, -CH=CH₂). Exact mass calcd. for C₁₄H₂₂O: 206.1670; found: 206.1672.
Preparation of the cis-2-Vinylcyclopropyl Ketone (101).

The procedure followed was identical with that described above except that the cuprate reagent was prepared from the cis-1-bromo-2-vinylcyclopropane (81) (1.13 g, 7.72 mmol, fraction 3 from above distillation). A tert-butyllithium solution (1.26 M in pentane, 11.03 mL, 13.90 mmol) was added dropwise, as previously described, to a solution of the bromide (81) in 35 mL of anhydrous ether. Anhydrous tetrahydrofuran (35 mL) and solid phenylthiocopper (1.33 g, 7.72 mmol) were added as before. The acid chloride (105) (0.895 g, 5.51 mmol) was added in 2 mL of anhydrous tetrahydrofuran. The mixture was worked up as described above to give 1.12 g (>100%) of an oil which was distilled (air-bath temperature 90-95°C, 0.25 torr) to give 922 mg (87%) of the cis ketone (101) as a colourless oil. A glc analysis (column A) of the distilled material indicated the presence of only one component. IR (film): 3060, 2990, 2910, 2850, 1690, 1630, 1460, 1280, 1260, 1080, 900 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.94 (s, 6H, Me), 1.0-2.82 (complex, m, 13H), 4.98 (dd, J = 10 Hz, J' = 2.5 Hz, 1H, HC = C\(\hat{\text{H}}\)), 5.17 (dd, J = 17 Hz, J' = 2.5 Hz, 1H, \(\hat{\text{H}}\)), 5.66 (ddd, J = 17 Hz, J' = 10 Hz, J'' = 8 Hz, 1H, \(\hat{\text{H}}, \text{HC} = \text{CH}_2\)). Exact mass calcd. for C₁₄H₂₂O: 206.1670; found: 206.1669.
Preparation of the trans-2-Vinylcyclopropyl Ketone (103)

To a stirred solution of dry tert-butyl alcohol (3 mL) and 71 mg (0.63 mmol) of potassium tert-butoxide (Aldrich) was added dropwise a solution of a mixture of the isomers (101) and (103) (87 mg, 0.42 mmol, above preparation) in 3 mL of anhydrous tetrahydrofuran. The resulting yellow solution was stirred for 3 h at room temperature. Hydrochloric acid (1 N, 2 mL) was added and the resultant mixture was extracted with 2 x 20 mL hexanes. The combined extracts were washed with brine, dried over anhydrous magnesium sulfate and the solvent was evaporated to give 80.5 mg (93%) of the ketone (103) as an oil. A glc analysis (column C) of this material showed that it consisted of a mixture of the trans and cis ketones (101) and (103), in a ratio of approximately 93 : 7 respectively. This ratio did not change with the length of the reaction time. The isomers (101) and (103) could not be separated by distillation or by column chromatography. IR (film): 3060, 2990, 2910, 2850, 1690, 1630, 1460, 1380, 1360, 1120, 1080, 1030, 980, 900 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.94 (s, 6H, methyls), 1.02-2.14 (complex m, 12H), 2.48-2.86 (m, 1H, ), 4.98 (dd, J = 9 Hz, J' = 3 Hz, 1H, HC=CH ), 5.14 (dd, J = 17 Hz, J' = 3 Hz, 1H, HC=CH ), 5.28-5.70 (m, 1H, H=CH₂).
Conversion of the \textit{cis}-2-Vinylcyclopropyl Ketone (101) into the Enol Silyl Ethers (120) and (121) and Thermal Rearrangement of the latter into (122) and (123).

To a cold (0°C), flame-dried flask equipped with a gas inlet tube, a magnetic stir bar, and a septum cap, was added a solution of diisopropylamine (50\muL, 0.39 mmol) in 1 mL of anhydrous tetrahydrofuran. A solution of \textit{n}-butyllithium (1.71 M in hexane, 0.18 mL, 0.32 mmol) was added dropwise and the resultant mixture was stirred for 15 min at 0°C. The solution was cooled to -78°C and a solution of the \textit{cis} ketone (101) (50 mg, 0.24 mmol) in 0.5 mL of anhydrous tetrahydrofuran was added slowly via syringe and stirring was continued for 50 min. A solution of freshly sublimed \textit{tert}-butyldimethylsilyl chloride (80 mg before sublimation, 0.53
mmol) in anhydrous tetrahydrofuran (1 mL) was added dropwise. Dry hexamethylphosphoramide (HMPA, 84 µL, 0.48 mmol) was added and the resulting mixture was stirred for an additional 15 min at -78°C, allowed to warm to room temperature, and stirring was continued for 3 h. The solution was poured into a saturated aqueous sodium bicarbonate solution (10 mL) and the resultant mixture was extracted with 2 x 20 mL hexanes. The combined extracts were washed with brine (4 x 20 mL), dried over anhydrous magnesium sulfate and the solvent was evaporated. Distillation (air-bath temperature 95°C, 0.25 torr) of the residual oil gave 67 mg (87%) of a mixture of enol ethers (120) and (121) as an oil. A glc analysis (column A) of this material showed it consisted of the enol ethers (120) and (121) in a ratio of approximately 12 : 88 respectively. IR (film): 3060, 2930, 2900, 2840, 1760 (exo double bond to cyclopropane ring), 1630 (vinyl), 1470, 1460, 1360, 1250 (O^-Si), 1235, 840, 780 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.16 (s, 6H, Me^Si), 0.89 (s, 15H, Me₂-C, tert-butyl-Si), 1.02-2.50 (complex m, 12H), 4.80-5.63 (m, 3H, HOC=CH₂).

The enol silyl ether mixture (120) and (121) from above (67 mg, 0.21 mmol) was placed in a dry round bottomed flask to which was attached a Kugelrohr receiver. The system was flushed thoroughly with argon and then the flask containing the enol silyl ethers was heated at 160°C for 45 min in a previously equilibrated Kugelrohr distillation apparatus. Distillation (air-bath temperature 95°C, 0.25 torr) of the oil gave 59 mg (88%) of a mixture of the rearranged products (122) and (123) as an oil. A glc analysis (column A) of the distilled material showed it to be composed of (122) and (123) in a ratio of approximately 14 : 86, respectively. This material was used without further purification because attempted separation of the products by column chromatography on silica
gel or on Florisil resulted in decomposition. IR (film): 3060, 3040, 2930, 2900, 2870, 2840, 1630, 1470, 1460, 1255, 1200, 1090, 840, 780 cm$^{-1}$; $^1$H nmr [CDCl$_3$, major product (123)] $\delta$: -0.04 (s, Me$_2$Si), 0.75-1.03 (series of s, Me$_2$C, tert-butyl-Si), 1.13-2.85 (complex m), 4.88 (brs, 1H, $\sim)$, 5.02 (s, 1H, $\sim)$, 5.86-6.01 (m, 1H, $\sim$H), 6.04-6.20 (m, 1H, $\sim$H).

Conversion of the trans-2-Vinylcyclopropyl Ketone (103) into the Enol Silyl Ethers (124) and (121) and Thermal Rearrangement of the latter into (122) and (123).

The procedure used was identical with that described above. The lithium diisopropylamide solution was prepared using 90 µl of diisopropylamine (0.64 mmol) in 1.5 mL of anhydrous tetrahydrofuran and a solution of $n$-butyllithium (1.71 M in hexane, 0.31 mL, 0.53 mmol) was added at 0°C.
After the appropriate amount of time a solution of the trans-2-vinyl-cyclopropyl ketone (103) (84 mg, 0.41 mmol, trans : cis; 93 : 7) in anhydrous tetrahydrofuran (0.5 mL) was added. Stirring was continued for 50 min at -78°C and a solution of freshly sublimed tert-butyldimethylsilyl chloride (136 mg before sublimation, 0.9 mmol) in 1 mL anhydrous tetrahydrofuran and hexamethylphosphoramide (HMPA, 0.14 mL, 0.82 mmol) were added. There was obtained, after the usual work up and distillation (air-bath temperature 90°C, 0.2 torr) of the crude product, 110 mg (84%) of a mixture of the enol ethers (124) and (121) as an oil. A glc analysis (column A) of the latter showed that it consisted of the two enol silyl ethers (124) and (121) in a ratio of approximately 87 : 13 respectively. IR (film): 3060, 2930, 2900, 2840, 1660, 1630, 1470, 1460, 1360, 1250, 1180, 1100, 840, 780 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \(\delta\): 0.10, 0.13 (s, s, 6H, Me\(_2\)Si-), 0.78-1.00 (series of s, 15H, Me\(_2\)C, tert-butyl-Si), 1.08-2.23 (complex m, 12H), 4.80-5.63 (m, 3H, HO-CH\(_2\)). Exact mass calcd for C\(_{20}\)H\(_{36}\)OSi: 320.2535; found: 320.2540.

The enol silyl ether mixture (124) and (121) from above (97 mg, 0.30 mmol) was placed in a dry round bottomed flask to which was attached a Kugelrohr receiver. The system was flushed thoroughly with argon and heated at 230°C for 1 h as described above. Distillation (air-bath temperature 110°C, 0.35 torr) of the thermolysis products gave 70 mg (72%) of the mixture of (122) and (123) as an oil. A glc analysis (column A) of the distilled material showed it to be composed of (122) and (123) in a ratio of approximately 82 : 18 respectively. IR (film): 3010, 2930, 2900, 2870, 2840, 1630, 1470, 1460, 1255, 1150, 880, 840, 760 cm\(^{-1}\); \(^1\)H nmr [CDCl\(_3\), major product (122)] \(\delta\): 0.17, 0.19 (s, s, Me\(_2\)Si), 0.75-1.00 (series of s, Me\(_2\)C, tert-butyl-Si), 1.01-2.75 (complex m),
4.72 (t, 1H, ) , 5.60-5.86 (m, 2H, ).

Hydrolysis of the 14 : 86 Mixture of Thermolysis Products (122) and (123)
and the Characterization of (123).

To a dry flask equipped with an argon gas inlet tube and a magnetic
stirring bar was added a solution of 1 N hydrochloric acid (0.75 mL) in
1.5 mL of tetrahydrofuran. A solution of the thermolysis products (122)
and (123) in a ratio of approximately 14 : 86 respectively (59 mg, 0.18
mmol) in tetrahydrofuran (0.5 mL) was added and the resulting mixture
stirred for 3 h at room temperature. The solution was treated with 20 mL
of a saturated aqueous sodium bicarbonate solution. The resulting
mixture was extracted with hexanes (2 x 20 mL) and the combined extracts
were washed with brine and dried over anhydrous magnesium sulfate. The
solvent was evaporated and the residual oil was distilled (air-bath
temperature 95-105°C, 0.25 torr) to give 46.8 mg of an oil. A glc
analysis (column A) of this oil showed it consisted of (127) and (123)
in the ratio of approximately 10 : 90 respectively. IR (film): 3040,
2930, 2900, 2835, 1690, 1635, 1470, 1460, 1250, 1200, 1180, 970, 840,
780 cm⁻¹; ¹H nmr (CDCl₃) δ : -0.07 (s, 6H, Me₂Si), 0.75-1.00 (series of s,
15H, Me₂C, tert-butyl-Si), 1.13-2.63 (complex m), 4.88 (brs, 1H, )

122

123

127
The above mixture of (127) and (123) (30 mg) in a ratio of approximately 10:90 respectively was loaded on a silica gel column (130 mm height × 7 mm inside diameter, 3 g). The mixture was eluted with a petroleum ether and ether solution in the ratio of approximately 7:1 respectively. After 4 mL of eluate was collected, 0.5 mL fractions were collected. Fractions 3-7 contained the silyl ether (123) (20.9 mg, R_f = 0.64) as a colourless oil. Fractions 8-20 contained nothing. A glc analysis (column A) showed that fractions 3-7 contained 94% silyl ether (123) and no cycloheptenone (127). IR (film): 3060, 3040, 2930, 2900, 2870, 2840, 1630, 1470, 1460, 1250, 1200, 1080, 840, 780 cm⁻¹; ¹H nmr (CDCl₃) δ: -0.07 (s, 6H, Me₂Si), 0.75-1.00 (s with m underneath, 17H, Me₂C, tert-butyl-Si, 2 other protons), 1.06-2.63 (complex m, 9H), 4.88 (brs, 1H, 5.02 (s, 1H, ), 5.86-6.00 (m, ), 5.02 (s, 1H, ), 5.86-6.00 (m, 1H, , 6.04-6.20 (m, 1H, )). Exact mass calcd. for C₂₀H₃₆OSi: 320.2535; found: 320.2514.
Hydrolysis of the 82 : 18 Mixture of Thermolysis Products (122) and (123) and Characterization of (127).

![Chemical Structures](image)

The procedure used was identical with that described above. A solution of the thermolysis mixture (122) and (123) (70 mg, 0.22 mmol, 82 : 18 respectively) in tetrahydrofuran (0.5 mL) was added to a solution of 1 N hydrochloric acid (1 mL) in tetrahydrofuran (2 mL). Usual work up and distillation of the residual oil (air-bath temperature 95-105°C, 0.25 torr) gave 33 mg of an oil. A glc analysis (column A) of this material showed that the mixture consisted of (127) and (123) in a ratio of approximately 87 : 13 respectively. IR (film): 3010, 2940, 2920, 2880, 2850, 1690, 1635, 1460, 1440, 1380, 1360, 1250, 1100, 1080, 840, 770 cm⁻¹; ¹H nmr (CDCl₃) δ: -0.03 (s, 6H, Me₂Si), 0.73-0.98 (series of s, 15H, Me₃C, tert-butyl-Si), 1.08-3.03 (complex m), 4.88 (brs, 1H, ), 5.02 (s, 1H, ), 5.70-6.03 (m, 2H, ).

The above mixture of (127) and (123) (47.6 mg) in a ratio of approximately 87 : 13 respectively was loaded on a silica gel column (130 mm height x 7 mm inside diameter, 5 g). The column was eluted with a petroleum ether and ether solution in a ratio of approximately 7 : 1 respectively. After
8 mL of eluate was collected, 1.0 mL fractions were collected. Fractions 2-6 contained the cyclopentadiene system \((123)\) \((R_f = 0.64)\) and fractions 19-23 contained the cycloheptenone system \((127)\) \((18.9 \text{ mg, } R_f = 0.36)\) as a colourless oil. There were no mixed fractions. A glc analysis (column A) of this oil showed that it was 98% pure. IR (film): 3000, 2930, 2900, 2880, 2850, 2825, 1690, 1460, 1440, 1390, 1370, 1340, 1300, 1180 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \(\delta: 0.76 \text{ (s, 3H, Me), 0.91 (s, 3H, Me), 1.00-2.87 (complex m, 14H), 5.72-5.84 (m, 1H, olefinic proton), 5.86-5.97 (m, 1H, olefinic proton). \) Exact mass calcd for \(C_{14}H_{22}O\): 206.1670; found: 206.1683.

**Preparation of the cis-2-Vinylcyclopropyl Ketone (89).**

![Chemical structure of cis-2-Vinylcyclopropyl Ketone (89)](image)

To a 250 mL, flame-dried flask, equipped with a septum cap, an argon inlet tube, a magnetic stir bar and a stopper was added a solution of the cis-2-vinylcyclopropyl bromide \((1.24 \text{ g, 8.43 mmol})\) \((81)\) in 50 mL of anhydrous ether. The mixture was cooled to \(-78^\circ\text{C}\) and a solution of tert-butyllithium \((1.1 \text{ M in pentane, 13.8 mL, 15.17 mmol})\) was added dropwise and stirring was continued for 2 h at this temperature. At this point, anhydrous tetrahydrofuran \((50 \text{ mL})\) and phenylthiocopper \(^{35}\) \((1.45 \text{ g, 8.43 mmol})\) were added and the reaction mixture was allowed to warm to \(-20^\circ\text{C}\) and stirring was continued at this temperature for 30 min. The
mixture was cooled to -78°C and cyclohexanecarboxylic acid chloride (0.75 mL, 5.61 mmol) was added dropwise. Stirring was continued at -78°C for 15 min and the solution was warmed to -20°C with continued stirring for 1 h. The solution was subsequently allowed to warm to room temperature and stirred for an additional 2 h. The reaction was quenched by the addition of spectrophotometric grade methanol (~1 mL). The resultant mixture was diluted with ether and then filtered through a short column of Florisil. The column was eluted with ether. The combined eluate was evaporated and the residual oil was distilled (air-bath temperature 65-75°C, 0.21 torr) giving 779 mg (78%) of the ketone (89) as a colourless oil. A glc analysis (column A) of this material showed that it consisted mainly of one component in 96% purity. The ketone (89) (779 mg) was loaded on a silica gel column (78 g) and the column was eluted with a mixture of petroleum ether and ether in a ratio of 7 : 1 respectively. A column volume of 150 mL was eluted and 15 mL fractions were collected. Fractions 8-9 were a mixture of cis and trans ketones (glc analysis, column A) of approximately 93 : 7 respectively (243 mg). A glc analysis of fractions 10-12 showed the fractions consisted of only one component identified as the cis ketone (89) (449 mg, Rf = 0.55). The purified material exhibited the following spectral data; IR (film): 3060, 3000, 2910, 2840, 1690, 1635, 1455, 1390, 1295, 1240, 1150, 1075, 1010, 910, 845 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.96-2.60 (complex m, 15H), 4.94 (dd, J = 10.5 Hz, J' = 2.3 Hz, 1H, HC=C<), 5.13 (dd, J = 17 Hz, J' = 2.3 Hz, 1H, HC = -C<), 5.62 (ddd, J = 17 Hz, J' = 10.5 Hz, J'' = 9 Hz, 1H, HC = CH₂). Exact mass calcd. for C₁₂H₁₈O: 178.1358; found: 178.1358.
To a cold (0°C) dry flask equipped with a drying tube and a magnetic stirring bar, was added a solution of the cis-2-vinylcyclopropyl ketone (89) (200 mg, 1.12 mmol) in 4 mL of ethyl alcohol (100%). A hydrazine hydrate solution (95%, 0.38 mL, 7.87 mmol) and an approximately 1% aqueous cupric sulfate pentahydrate solution (~2 drops) were added to the cooled (0°C) mixture. This was followed by dropwise addition of an aqueous hydrogen peroxide solution (30%, 0.21 mL, 2.02 mmol) over 5 min. The resulting mixture was stirred for an additional 5 min at 0°C and subsequently allowed to warm to room temperature. The mixture was stirred for 5 h at room temperature. The reaction mixture was poured into 10 mL of water and the resulting mixture was extracted with ether (2 x 30 mL). The combined ethereal layers were further extracted with a dilute aqueous ferric sulfate solution (4 x 10 mL), water, and brine. The combined ether extracts were dried over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was distilled (air-bath temperature 85°C, 0.3 torr) to give 140 mg (69%) of the product (104) as an oil. A glc analysis (column A) showed this oil consisted of only one component. IR (film): 3060, 2980, 2940, 2900, 2840, 1685, 1450, 1400, 1150, 1090, 1075, 1000, 850 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.85 (t, 3H, Me), 0.90-0.98 (m, 1H,
1.00-1.08 (m, 1H), 1.10-1.50 (complex m, 7H), 1.60-1.98 (complex m, 6H), 2.02-2.12 (m, 1H), 2.42-2.55 (m, 1H), Exact mass calcd. for C_{12}H_{20}O: 180.1514; found: 180.1511.

Conversion of the cis-2-Ethylcyclopropyl Ketone (104) into the Enol Silyl Ethers (125) and (126).

To a cold (0°C) flame-dried flask equipped with an argon inlet tube a septum cap and a magnetic stir bar, was added a solution of diisopropylamine (70 μL, 0.5 mmol) in 1 mL of anhydrous tetrahydrofuran. A solution of methyllithium (1.18 M in ether, 0.31 mL, 0.36 mmol) was added dropwise to the mixture and stirring was continued for 15 min at 0°C. The mixture was cooled to -78°C and a solution of the cis-2-ethylcyclopropyl ketone (104) (50 mg, 0.28 mmol) in 0.5 mL of anhydrous tetrahydrofuran was added and stirring was continued for 50 min. A solution of tert-butyldimethylsilyl chloride (92 mg before sublimation, 0.6 mmol) in 1 mL of anhydrous tetrahydrofuran and hexamethylphosphoramide (97 μL, 0.56 mmol) were added at -78°C. The mixture was stirred for 15 min.
at this temperature and allowed to warm to room temperature with continued stirring for 3 h. Usual work up as above gave an oil that was distilled (air-bath temperature 80°C, 0.2 torr) to give 60.7 mg (74%) of the mixture (125) and (126) as an oil. A glc analysis (column A) indicated only one peak in 97% purity. The ratio of the two enol silyl ethers (125) and (126) was determined by careful integration of the Me_2Si peaks on a high resolution nuclear magnetic resonance spectrometer. Integration showed the mixture (125) and (126) consisted of the two isomers in a ratio of approximately 51:49. IR (film): 3080, 2930, 2900, 2830, 1765, 1670, 1490, 1480, 1460, 1270, 1190, 1090, 870, 860, 800 cm^{-1}; \textsuperscript{1}H nmr (CDCl\textsubscript{3}) \delta: 0.11, 0.14 (s, s, 6H, Me_2Si), 0.87-1.03 (s with overlapping t, 12H, \textsubscript{CH}_3-\textsubscript{CH}_2-\textsubscript{CH}_2-, tert-butyl-Si), 1.18-1.90 (complex m, 12H), 2.02-2.27 (m, 4H). \textbf{Exact mass calcd.} for C\textsubscript{18}H\textsubscript{34}O Si: 294.2378; found: 294.2380.

\textbf{Preparation of the \textit{trans}-2-Vinylcyclopropyl Ketone (100).}

![Chemical Structure](image)

To a stirred solution of dry \textit{tert}-butyl alcohol (2 mL) and 95 mg (0.84 mmol) of potassium \textit{tert}-butoxide (Aldrich), was added dropwise a solution of the \textit{cis}-ketone (89) (95 mg, 0.56 mmol) in 2 mL anhydrous tetrahydrofuran. The resulting yellow solution was stirred for 3 h at room temperature. Usual work up as described above gave an oil which
was distilled (air-bath temperature 80°C, 0.4 torr) to give 66.8 mg (70%) of the ketone (100) as a colourless oil. A glc analysis (column A) indicated only one component with a retention time identical with that of the cis-ketone (89). The nmr spectrum of the product (100) showed that it differed from the cis-ketone (89). IR (film): 3070, 2990, 2910, 2840, 1685, 1635, 1450, 1390, 1150, 1100, 1070, 1010, 910, 840 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.83-2.15 (complex m, 14H), 2.25-2.68 (m, 1H, \( \int \) \( \int \) \( \int \)), 4.96 (dd, J = 7.8 Hz, \( J' = 2.4 \) Hz, 1H, \( \text{HC} = \text{C} \)), 5.12 (dd, \( J = 15 \) Hz, \( J' = 2.4 \) Hz, 1H, \( \text{HC} = \text{CH} \)), 5.28-5.70 (m, 1H, \( \text{HO} = \text{CH}_2 \)).

Preparation of the trans-2-Ethylcyclopropyl Ketone (119).

To a cold (0°C) dry flask equipped with a magnetic stirring bar, and a drying tube was added a solution of the trans-2-vinylcyclopropylketone (100) (61 mg, 0.34 mmol) in 1.5 mL of ethyl alcohol (100%). A hydrazine hydrate solution (95%, 0.12 mL, 2.4 mmol) and an approximately 1% aqueous cupric sulfate pentahydrate solution (≈2 drops) were added to the mixture. This was followed by dropwise addition of an aqueous hydrogen peroxide solution (30%, 63 μL, 0.62 mmol) over 5 min at 0°C. The solution was allowed to warm to room temperature and stirring was
continued for 5 h. Usual work up as described above gave an oil that was distilled (air-bath temperature 65-75°C, 0.35 torr) to give 40 mg (65%) of the trans ketone (119) as a colourless oil. A glc analysis (column A) indicated only one component. IR (film): 3060, 2995, 2910, 2840, 1690, 1455, 1405, 1350, 1150, 1100, 1010, 900 cm\(^{-1}\); \(^1\)H nmr (CDCl\(_3\)) \(\delta\): 0.67-0.74 (m, 1H, \(\text{H}\)), 0.96 (t, 3H, methyl), 1.14-1.45 (complex m, 8H), 1.60-1.98 (complex m, 7H), 2.42-2.55 (m, 1H, \(\text{H}\))

Exact mass calcd. for \(\text{C}_{12}\text{H}_{20}\mathrm{O}\): 180.1514; found: 180.1513.

**Preparation of Cyclohexyl Cyclopropyl Ketone (99)**

To a cold (-78°C) flame-dried 25 mL flask equipped with a septum cap, an argon inlet tube and a stopper, was added a solution of cyclopropyl bromide (0.60 g, 4.96 mmol) in anhydrous tetrahydrofuran (8 mL). A solution of tert-butylithium (2.1 M in pentane, 4.25 mL, 8.93 mmol) was added dropwise and the mixture was stirred for 2 h at -78°C.

Anhydrous tetrahydrofuran (8 mL) and phenylthiocopper \(^{35}\) (856 mg, 4.96 mmol) were added, the mixture was warmed to -20°C, and stirring was continued for 30 min. The solution was recooled to -78°C and cyclohexanecarboxylic acid chloride (0.44 mL, 3.31 mmol) was added. The reaction mixture was
stirred for an additional 15 min at -78°C and then was allowed to warm to -20°C with continued stirring for 1 h. The solution was subsequently warmed to room temperature and stirred for an additional 2 h. Usual work up as described above and distillation of the resulting oil (air-bath temperature 65°C, 0.45 torr) gave 499 mg (100%) of the ketone (99) as an oil. A glc analysis (column A) showed the oil consisted of one component. IR (film): 3080, 3000, 2910, 2840, 1685, 1450, 1390, 1150, 1090, 1070, 1000, 920 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.78-0.87 (m, 2H, cyclopropane), 0.93-1.01 (m, 2H, cyclopropane), 1.12-1.46 (complex m, 5H), 1.56-2.03 (complex m, 6H), 2.42-2.55 (m, 1H, ). Exact mass calcd. for C₁₀H₁₆O: 152.1201; found: 152.1200.

Preparation of the Enol Silyl Ether (128) of the Cyclohexylcyclopropyl Ketone (99).

\[ \text{99} \rightarrow \text{128} \]

To a cold (0°C) flame-dried flask equipped with a septum cap, a magnetic stir bar and an argon inlet tube, was added a solution of diisopropylamine (0.17 mL, 1.18 mmol) in 1 mL anhydrous tetrahydrofuran. A solution of methyllithium (2.17 M in ether, 0.38 mL, 0.86 mmol) was added and the mixture stirred for 15 min at 0°C. The mixture was cooled to
-78°C and a solution of the ketone (99) (100 mg, 0.66 mmol) in 0.5 mL anhydrous tetrahydrofuran was added. The solution was stirred for 50 min at this temperature and a solution of tert-butyldimethylsilyl chloride (218 mg before sublimation, 1.45 mmol) in 1 mL of anhydrous tetrahydrofuran was added. Hexamethylphosphoramide (0.23 mL, 1.32 mmol) was added dropwise and the solution was stirred for 15 min at -78°C and then allowed to warm to room temperature with continued stirring for 3 h. Usual work up of the mixture as described above gave 181 mg (100%) of a colourless oil. A glc analysis (column A) showed this oil to be 96% pure enol silyl ether (128) as a single component. IR (film): 3060, 2940, 2910, 2840, 1660, 1470, 1465, 1450, 1360, 1260, 1240, 1210, 1175, 1140, 1120, 1080, 1010, 960, 860, 840, 780 cm⁻¹; ¹H nmr (CDCl₃) δ: 0.13 (s, 6H, Me₂-Si), 0.51-0.57 (m, 2H, cyclopropane), 0.62-0.69 (m, 2H, cyclopropane), 0.96 (s, 9H, tert-butyl), 1.35-1.54 (m, 7H), 2.11-2.18 (m, 2H, ), 2.21-2.80 (m, 2H, ). Exact mass calcd. for C₁₆H₃₀OSi: 266.2065; found: 266.2065.
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