AN ABSTRACT OF THE THESIS OF

Earl Philip Seitz, Jr. for the degree of Doctor of Philosophy
in Chemistry presented on June 3, 1977

Title: RING EXPANSION REACTIONS OF ALKOXIDES AND THEIR APPLICATION TOWARD SYNTHESIS OF LARGE RING HORMONE MODELS

Abstract approved: Redacted for privacy

Richard W. Thies

The potassium salts of a series of 1-vinylcycloalk-3-en-1-ols were found to undergo ring expanding [1, 3]-sigmatropic shifts at 25° when dissolved in hexamethylphosphoramide (HMPA) or 1, 2-dimethoxyethane (DME) with 18-crown-6. The yields and reaction rates were compared with those of the corresponding Siloxy-Cope ring expansions. These anionic cases showed about $10^{16}$ to $10^{17}$ faster reaction rates but lower yields.

The possible application of this anionic ring expansion to the synthesis of 8:9,13:14-disecosteroids was explored by testing a series of the potassium salts of 6-alkyl-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenols under the same conditions as above. Alkyl=vinyl, 1, 3-butadienyl, and 1, 3-cis-pentadienyl underwent 2-carbon ring expansions in better yields than the corresponding siloxy-Cope reactions. Alkyl=cyclopropyl or 2-vinylcyclopropyl gave ring fragmentation instead of ring expansion. An open chain example,
2-methyl-1-phenyl-but-3-en-2-ol (potassium salt) was also found to undergo a [1, 3]-sigmatropic shift as well as fragmentation. Other cases, two 1-vinylcycloalkanols and two 1-vinyl-1, 2-cycloalkanediols (potassium salts) failed to undergo ring expansions under these conditions.
Ring Expansion Reactions of Alkoxides and their Application toward Synthesis of Large Ring Hormone Models

by

Earl Philip Seitz, Jr.

A THESIS submitted to
Oregon State University

in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

Completed June 3, 1977
Commencement June 1978
APPROVED:

Redacted for privacy

Associate Professor of Chemistry
in charge of major

Redacted for privacy

Chairman of Department of Chemistry

Redacted for privacy

Dean of Graduate School

Date thesis is presented ________________ June 3, 1977 ________________

Fran McCuistion and
Typed by Opal Grossnicklaus and Earl Philip Seitz, Jr.
To

Judy, Earl, Ethel, and Dave,
Fred and Mary Ellen
ACKNOWLEDGMENTS

The author is sincerely grateful to the following people whose guidance, moral support, and expertise made this thesis a reality: Dr. Richard W. Thies, my wife, Judy, Ms. Susan Randall, Mr. Karl Swenson, Dr. Larry Hutchinson, Dr. Richard Wielesek, and the other members of the Chemistry Department who helped along the way.
# TABLE OF CONTENTS

**INTRODUCTION**

**HISTORICAL**

<table>
<thead>
<tr>
<th>Part</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>The Siloxy-Cope Reaction</td>
<td>3</td>
</tr>
<tr>
<td>II</td>
<td>Anionic Rearrangements</td>
<td>7</td>
</tr>
</tbody>
</table>

**RESULTS AND DISCUSSION**

<table>
<thead>
<tr>
<th>Part</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Anionic Rearrangements</td>
<td>18</td>
</tr>
<tr>
<td>II</td>
<td>Synthetic Methods</td>
<td>43</td>
</tr>
</tbody>
</table>

**EXPERIMENTAL**

|                  | 52   |

**BIBLIOGRAPHY**

<p>|                  | 135  |</p>
<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Rearrangements of Derivatives of cis-1-vinylcyclonon-3-en-1-ol (6b)</td>
<td>20</td>
</tr>
<tr>
<td>2  Rearrangements of Derivatives of cis and trans-1-vinylcyclodec-3-en-1-ol (18b, 14b)</td>
<td>28</td>
</tr>
<tr>
<td>3  Rearrangements of Derivatives of trans-1-vinyl-1-vinylcyclotridec-3-en-1-ol (19b)</td>
<td>29</td>
</tr>
<tr>
<td>4  Rearrangements of Derivatives of 6-vinyl-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (85b)</td>
<td>33</td>
</tr>
<tr>
<td>5  Rearrangements of Derivatives of cis and trans-6-(1, 3-butadienyl)-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (103a, b) and cis and trans-6-(1, 3-cis-pentadienyl)-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (105a, b)</td>
<td>38</td>
</tr>
<tr>
<td>6  Reaction Conditions for Attempted Rearrangement of 81a, b</td>
<td>62</td>
</tr>
<tr>
<td>7  Mass Spectral Data for Rearrangement Products of 95</td>
<td>71</td>
</tr>
<tr>
<td>8  Mass Spectral Data for Rearrangement Products of 127</td>
<td>101</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>1.</td>
<td>NMR Spectrum of 9,10,11,12-tetrahydro-6-vinyl-8(5,7H)-benzocyclo decenone (104)</td>
</tr>
<tr>
<td>2.</td>
<td>NMR Spectrum of 6-(cis-1-propenyl)-9,10,11,12-tetrahydro-8(5,7H)-benzocyclodecenone (106)</td>
</tr>
<tr>
<td>3.</td>
<td>Apparatus for Preparation of Vinyl Magnesium Bromide.</td>
</tr>
</tbody>
</table>
RING EXPANSION REACTIONS OF ALKOXIDES AND THEIR APPLICATION TOWARD SYNTHESIS OF LARGE RING HORMONE MODELS

INTRODUCTION

As part of a program aimed at the synthesis of 8:9, 13:14-disecosteroid 1, new conditions were found to effect a 2-carbon ring expansion of medium sized rings. It is hoped that compound 1, or derivatives thereof, might possess estrogenic activity and therefore provide a useful addition to the presently available list of birth control drugs.

The initial general approach to the synthesis of a model of 1 was a 4-carbon ring expansion of 107a, b followed by a 1-carbon expansion to give 4 (Scheme 1).

Scheme 1

107a, b  R = TMS
        (Si(CH₃)₃)
103a, b  R = H

\[ \Delta \rightarrow \]

2 (cis)  \[ \rightarrow \]
3 (trans) \[ \rightarrow \]
4
The thermal approach failed, but in the course of this investigation it was discovered that the potassium salt of 103a, b as well as a variety of other medium sized ring systems, would undergo 2-carbon ring expansions under the influence of hexamethylphosphoramide (HMPA) or 1,2-dimethoxyethane (DME) and 18-crown-6. The scope and possible applications of this anionic rearrangement was therefore explored, and the results are presented in the following pages.
HISTORICAL

Part I. The Siloxy-Cope Reaction

When heated, a 3-hydroxy-1,5-hexadiene system can rearrange in a number of different ways. As shown below (Scheme 2) when this molecular reorganization results in moving a sigma bond from the 1,1 position to the 3,3 position the rearrangement is termed a [3,3]-sigmatropic shift.  

\[ \text{[3,3]-sigmatropic shift} \]

In like manner, rearrangement of the bond from the 1 to the 3 position is called a [1,3]-sigmatropic shift (Schemes 3 and 4).

\[ \text{[1,3]-sigmatropic shifts} \]

\[ 1 \]In this thesis the term "sigmatropic shift" will be used to indicate sigma bond reorganization regardless of whether the mechanism is concerted or otherwise.
Another path, β-hydroxy olefin cleavage (Scheme 5), results in fragmentation.

Scheme 5

\[
\begin{array}{c}
\text{H} \\
\text{O} \\
\text{C} \\
\text{=C} \\
\text{H} \\
\end{array} \xrightarrow{\Delta} \begin{array}{c}
\text{O} \\
\text{C} \\
\text{=C} \\
\end{array}
\]

The enol formation in Schemes 2 and 3 provides an important driving force for these reactions.

If part of the 3-hydroxy-1,5-hexadiene system is linked together with a ring (5), then conceivably a [1, 3]-sigmatropic shift could result in a 2-carbon ring expansion (Scheme 6).

Scheme 6

\[
\begin{array}{c}
\text{RO} \\
\text{C} \text{H} \text{=CH} \\
\text{5}_a, \text{R=H} \\
\text{b, R=TMS} \\
\end{array} \xrightarrow{\Delta} \begin{array}{c}
\text{RO} \\
\text{C} \text{H} \text{=CH} \\
\end{array}
\]

The difficulty with this approach is that β-hydroxy olefin cleavage competes, and the ring simply fragments. In 1972 R. W. Thies (2) introduced the use of a trimethylsilyl blocking group for systems like 5 which eliminated the cleavage and allowed, in most cases, an effective 2-carbon ring expansion to occur. The initial report of this Siloxy-Cope rearrangement \(^2\) (2) and following papers (4, 5, 6) explored

---

\(^2\) In this thesis the term "Cope rearrangement" will be used for either [1, 3] or [3, 3]-sigmatropic shifts. Berson and Jones (3) have previously used the term "Cope rearrangement" in this manner.
the scope of the new modifications, and the results are presented below\(^3\) (Schemes 7 - 11).

\textbf{Scheme 7}

\begin{align*}
\text{6a} & \quad \text{OTMS} \\
\text{1) 5.25 hr, 299°} \\
\text{2) H}_2\text{O} \\
\rightarrow & \quad \text{7 (55%)} + \text{8 (38%)} \\
\text{10} & \quad \text{OTMS} \\
\end{align*}

\textbf{Scheme 8}

\begin{align*}
\text{1) 4 hr, 316°} \\
\text{2) H}_2\text{O} \\
\rightarrow & \quad \text{11 (4%)} + \text{12 (7%)} \\
\end{align*}

\textbf{Scheme 9}

\begin{align*}
\text{14a} & \quad \text{OTMS} \\
\text{1) 30 min, 310°} \\
\text{2) H}_2\text{O} \\
\rightarrow & \quad \text{15 (6%)} + \text{16 (83%)} \\
\text{17 (11%)} & \quad \text{ring contracted products (48%)} \\
\end{align*}

\(^3\)Reaction times, temperatures, and yields represent typical values only.
The Siloxy-Cope reaction has recently been applied successfully to the 2-carbon ring expansion of 22 (7) as part of the program to prepare the hormone model system 4.

It is important to note the rather high temperatures that are required to bring about the thermolytic ring expansions reviewed above. These temperatures are in sharp contrast to the conditions required for anionic rearrangements as will be seen in the following section.
Part II. Anionic Rearrangements

Perhaps one of the most well studied anionic rearrangements in organic chemistry is the transformation of allyl Grignard adducts. Reactions of 3-substituted allyl Grignard reagents can give either 25 or 26.

For most ketones the rearranged adduct, 26, prevails (8, 9), and the mechanism of this transformation has been the topic of much discussion. Until recently the most widely accepted picture of this rearrangement involved the six-membered transition state shown below (Scheme 12).

There are also views which involve rearrangement of the Grignard reagent before attack and a non-cyclic mechanism, whereby the remote end of the allyl Grignard is the site of attack, but concomitant magnesium-oxygen coordination is unnecessary (9).
If, on the other hand, the ketone 24 possesses a great deal of steric bulk, the unrearranged adduct 25 is the major product. Benkeser and Broxterman (10) showed that sterically hindered ketones initially give adduct 26 (kinetic product) but subsequently rearrange to 25 (thermodynamic product) due to steric crowding. This rearrangement (26 → 25) could be formally viewed as a [1, 3] -sigmatropic shift, but recent work by the Benkeser (11) group implies that this shift is nonconcerted in nature. A crossover experiment between 27 and 28 was conducted, and the resulting products (29, 30, 31, and 32) indicate that these magnesium salts must fragment during the course of the rearrangement.
A related [1, 3] sigmatropic rearrangement of an organolithium compound was discovered by Dalton and Chan (12). They found that the reaction of 31 with methyl lithium yields the rearranged ketone 32 in ether but unrearranged 33 in hexane.

![Diagram](image)

A later investigation with an open-chain system (Scheme 13) gave similar results (13), and a fragmentation type of mechanism was invoked to account for this unusual behavior.

![Diagram](image)

One of the earliest reported base-catalyzed sigmatropic rearrangements was the novel ring enlargement reported by Swaminathan et al. (14, 15). Under the influence of either equivalent or catalytic amounts of potassium hydroxide, the epimeric alcohols, 37, are smoothly converted to 38 (formally a [3, 3] -sigmatropic shift).
It is interesting to note that the same conversion can be effected with p-toluenesulfonic acid, although the yield is much lower, and other compounds are produced as well (16). Like the previous cases, the authors felt this base induced rearrangement was best explained by a fragmentation-recombination mechanism.

An attempt to synthesize 39 for an electron spin resonance experiment led to the unexpected [1, 3] -shift products 40 and 41 (17).

![Diagram showing conversion of 39 to 40 and 41](image)

$\text{R}_1, \text{R}_2 = \text{CH}_3 \text{orH}$

Both a biradical and concerted [1, 3] -sigmatropic mechanism were mentioned as possible explanations for this transformation.

A base catalyzed sigmatropic shift could be the possible explanation for another interesting result. Wilson et al. (18) reacted the lithium pentadienylide 42 with a variety of electrophiles (E) and adducts 43 and 44 were formed.
Furthermore, they determined that $44$ would rearrange to $43$ under the reaction conditions. Further investigation by Wilson and coworkers (18, 19) indicated that in the case where $E$ is a carbonyl compound, the conversion $44$ to $43$ might be a base-facilitated shift.

One feature of anionic rearrangements which first caught the attention of early workers in the field was the tremendous effect the anion had on the rate of rearrangement. Krow and Reilly (20) found that the conversion of $45a$ to $46a$, a $[1,3]$-sigmatropic shift, occurred readily on a gas chromatograph injector port heated to $250^\circ$. 

\[
\begin{align*}
45a, \ R=H \\
b, \ R=Li
\end{align*}
\]
They were even more surprised to find that when $45a$ is treated with methyllithium in either pentane or ether the conversion of $45b$ to $46b$ takes place in 1 minute at $30^\circ$. Careful nuclear magnetic resonance studies of the rearrangement of deuterated $45b$ indicated that the transformation went with retention of configuration at the migrating carbon. The authors concluded that the results were consistent with a concerted mechanism, but stepwise ionic or radical pathways could not be excluded.

The work of Franzus et al. (21) provides another example of this striking rate effect. With a catalytic amount of sodium hydroxide, the rearrangement of 7-norbornadienol ($47a$) to the tropyl skeleton $48$ is complete within 5 minutes at room temperature. When a potassium $t$-butoxide / $t$-butanol system is used, the rearrangement occurs about 10,000 times faster yet. These results are especially dramatic when compared to the $170^\circ$ temperatures required to effect thermal rearrangements of similar systems (22).

Rather extensive considerations (especially a deuterium labeling experiment) indicated that the rearrangement involved a $[1,3]$-sigmatropic shift as pictured below (Scheme 14).
One of the best comparisons to date of an anionic rearrangement to its thermal counterpart can be found in the work of Evans and Golob (23) (Scheme 15).
Alkoxides with different counter ions were tested in refluxing tetrahydrofuran (THF) (66°), and the following results were obtained: $51a$, $M=$lithium or magnesium bromide showed no evidence of rearrangement; $51a$, $M=$sodium rearranged with a half-life of 1.2 hours; and $51a$, $M=$potassium rearranged with a half-life of about 1.4 minutes. Further tests indicated that even faster rates (180-fold) could be obtained with the potassium alkoxide in the presence of 18-crown-6 or hexamethylphosphoramide (HMPA). When compared to the rearrangement rates of the parent alcohol, $50a$, the alkoxide rearranges from $10^{10}$ to $10^{17}$ times faster. A further important development of this work is the observation that use of either 18-crown-6/THF (0°) or HMPA (10°) results in the same rate increase. The authors feel that this implies that ion-pair dissociation is the important factor in the rate enhancement and not solvent dielectric constant.

The Evans group later discovered that anion-accelerated sigmatropic shifts could provide the basis for a clever approach to regiospecific quinone-isoprene coupline (24). Additions of Grignard $53$ to the masked quinone $54$ followed by quenching, deblocking, and purification gave vitam K$_2$(5) (55b) in 71% overall yield. The transformation was thought to occur by an initial 1,2 Grignard addition followed by a low temperature [3,3] -sigmatropic shift.
A base catalyzed Claisen rearrangement has recently provided a convenient conversion of allyl esters to their corresponding γ, δ-unsaturated acids (25, 26) (Scheme 16).
Although in many cases the reaction is best conducted using the trimethylsilyl enol ethers (56b), the fact that the transformation of the enolate occurs at 25° serves as a nice contrast to similar purely thermal rearrangements which require over 100° to give a comparable conversion (25). A similar Claisen rearrangement of zinc enolates has also been observed by Baldwin and Walker (27), though somewhat higher temperatures are required.

At the other end of the spectrum, cationic centers have also been observed to enhance rearrangement rates. When small amounts of sulfuric acid are added to solutions of cyclohexadiene 58 in methanol or acetic acid, rapid disappearance of 58 to give the [1, 3] -rearranged products 59 and 60 as well as the [1, 2] -rearrangement product 61 occurs (solvolysis products are also observed (28).
Another cation assisted sigmatropic shift was uncovered by Breslow and Hoffman (29). When cyclopentadiene dimer 62 is solvolyzed at 95°, it apparently undergoes a rapid solvolytic Cope rearrangement to give 63.

\[
62a, \quad X = \text{P-CH}_3\text{C}_6\text{H}_4\text{SO}_2 \\
b, \quad X = \text{P-NO}_2\text{C}_6\text{H}_4\text{SO}_2 \\
c, \quad X = \text{H}
\]

The Cope rearrangement of the parent alcohol 62c is rapid only above 140°. Even more dramatic is the silver assisted solvolytic cope of 64 which occurs rapidly at -15°.
RESULTS AND DISCUSSION

Part I. Anionic Rearrangements

The first set of rearrangements to be discussed is that of cis-1-vinylcyclonon-3-en-1-ol (6b). The overall transformation is shown in Scheme 17, and the products were cis-5-cycloundecenone (7), trans-5-cycloundecenone (8), and 4-vinylcyclononanone (9). Table 1 is a presentation of the results, and the definitions of the abbreviations used are given below.

Scheme 17

\[
\begin{align*}
\text{6b} & \xrightarrow{1)} \text{KH} \quad 2) \text{H}_2\text{O} \quad \rightarrow \quad \text{7} + \text{8} \\
& \quad + \quad \text{9}
\end{align*}
\]
Conditions are given in the following order: time/temperature/solvent system. The abbreviation D indicates that a duplicate run was made, and the yields were obtained by averaging the two results.

"t 1/2" represents the calculated half-life for the thermal reaction, but for the alkoxide rearrangements it only represents the approximate time where the gas chromatogram peak area of the starting material is equal to the areas of the developing products. This figure is only intended to be used as a rough guide and does not take into account the disappearance of starting material or products by other pathways.

"A. M. " represents acidic material, and the numbers in this column represent an estimate of the yield of such materials. The estimates were obtained by correcting the weight of the crude acidic fraction for HMPA or DME contamination using NMR integrations.

Numbers under the product columns represent the yields of that particular compound, and numbers in parenthesis under each yield represent the variation, \( S^4 \) of three yield determinations. Each yield determination was conducted by adding a known

\[
S = \left( \frac{\sum (x - \bar{x})^2}{N-1} \right)^{\frac{1}{2}}
\]
Table 11. Rearrangements of Derivatives of cis-1-vinylcyclonon-3-en-1-ol (6b)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conditions</th>
<th>t 1/2</th>
<th>6b</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>A. M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5.25 hr/299° (0.5 hr)</td>
<td>33 min</td>
<td>0</td>
<td>55 (72)</td>
<td>36 (15)</td>
<td>10 (12)</td>
<td>- (-)</td>
</tr>
<tr>
<td>6b</td>
<td>1.5 hr/25°/HMPA</td>
<td>40 min</td>
<td>5</td>
<td>30</td>
<td>19</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>6b</td>
<td>2.75 hr/25°/HMPA</td>
<td>2.75 hr/25°/HMPA</td>
<td>1</td>
<td>34</td>
<td>20</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>6b</td>
<td>2.75 hr/25°/HMPA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2</td>
<td>36</td>
<td>23</td>
<td>7</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>6b</td>
<td>5.5 hr/25°/HMPA</td>
<td>0</td>
<td>28</td>
<td>14</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>6b</td>
<td>17 hr/25°/DME/18-crown-6/D</td>
<td>24 hrs/25°/23 hrs/66°/THF</td>
<td>5 hr&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0</td>
<td>30</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6b</td>
<td>No Reaction</td>
<td>67&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup>See text for definition of symbols
<sup>b</sup>Run in deoxygenated HMPA (see text)
<sup>c</sup>Data from reference 2; numbers in parentheses represent data for the shorter reaction time; all numbers for thermal arrangements represent product ratios, yields of 7 and 8 were ca. 70%.
<sup>d</sup>A similar run in THF/18-crown-6 gave almost the same half-life
<sup>e</sup>Crude yield
weight of internal standard to a known weight of sample and analyzing the mixture by gas chromatography (GLC).

The identities of the products from the HMPA rearrangements were initially assigned by comparing the GLC retention times of 7, 8, and 9 to the times of previously characterized samples (2, 30). A further verification was obtained by comparison of the mass spectra of 7, 8, and 9 to the spectra of authentic samples. Finally the NMR spectrum of 7 was found to be like that of an authentic sample. The identities of the products from the DME/18-crown-6 rearrangements were assigned by GLC, thin layer chromatography (TLC), NMR and IR comparisons similar to those mentioned above.

If the activation parameters for the thermolysis of 6a (2) are employed to provide an estimate of the rate at 25°C, it can be seen that the HMPA and DME/18-crown-6 rates are approximately $10^{17}$ and $10^{16}$ times greater (respectively) than the thermolytic process. These figures are comparable to those for [3,3] shifts obtained by Evans and Golob (23).

By examining Table 1, it can be seen that the ratio of 7:8 for the HMPA reaction varied only slightly from 1.57 to 2.00 with different reaction times. This is in contrast with the thermolytic reaction in which the ratio of 7:8 varied from 6.3 to 1.5 with longer reaction times; a fact which was accounted for by the ring contraction/ring expansion sequence pictured below. (Scheme 18, compounds
The fact that isomerization of the internal double bond is observed in the HMPA ring expansion of 6c does not completely discount a concerted mechanism for the process. A pathway like Scheme 18 (i.e. 6c, 66b, 67b, 68b) could easily account for the observed isomerization. As will be later seen, however, isomerization of the internal double bond is exceptional.

Another trend which can be observed in Table 1 is the solvent effect. Apparently the rate effect in the HMPA system as compared to DME/18-crown-6 is the reverse of that previously reported for [3, 3].

---

5A preliminary trial with 6c in the THF/18-crown-6 gave about the same rate as DME/18-crown-6 (See Table 1, footnote d). DME was selected as a solvent based on the suggestion by S. R. Wilson (19) that DME is not as easily degraded under basic conditions as THF.
shifts. Evans and Golob (23) have stated that the rearrangement of their alkoxide (51a, M=K) proceeded at the same rate with 3 equivalents of 18-crown-6 in THF at 0° or with HMPA at 10°. From other data they present it can be estimated that the rearrangement of (51a, M=K) in the THF with 1.1 equivalents of 18-crown-6 proceeds about 2 times faster at 10° than the comparable transformation in HMPA at 10°.

Since the DME/18-crown-6 experiments in the present work were also carried out with approximately 1.1 equivalents of 18-crown-6, a comparison can be made. The results in Table 1 indicate that the rearrangement of 6c proceeds about 7.5 times slower in DME/18-crown-6 than in HMPA.

Another useful comparison can be made by calculating the rate of reaction of 51a (M=K) at 25° from the published data (23) and comparing this figure to the rates of 6c rearrangement. If this is done, it can be seen that 6c proceeds about 50 times slower in HMPA (25°) and 375

---

6 The activation parameters E and A for the rearrangement of 51a, M=K in THF with 1.1 equivalents of 18-crown-6 are presented. The report also includes a plot of the rearrangement rate of 51a, M=K in THF at 0° as a function of added 18-crown-6 (0-3 equivalents). The estimation was made by calculating the rate with 3 equivalents 18-crown-6 at 0° (and hence the rate with HMPA at 10°) from figures in the plot. The rate with 1.1 equivalents 18-crown-6 at 10° was then calculated from the Arrhenius Equation, and the 2 rates were compared.
times slower in DME/18-crown-6 (25°) than 51a (M=K) in THF/18-crown-6 (25°). These results are in accord with the higher activation energy expected for a [1, 3] shift as compared to a [3, 3] shift. Apparently this difference in activation energy is great enough as to prevent the [1, 3] shift from occurring at all in THF (see Table 1).

When the yields of the HMPA and DME/18-crown-6 rearrangements are compared to those of the thermolytic reaction, it is obvious that the thermolytic reaction is superior for this particular rearrangement.

One troublesome side reaction of the anionic rearrangements is the production of acidic by-products. The nature of these by-products was indicated by their solubility in dilute base, their spectral properties,\(^7\) and the known propensity of cyclic ketones to undergo base-catalyzed autoxidation in HMPA (31). A typical autoxidation of a cyclic ketone to a diacid is shown in Scheme 19. The identities of the diacids

\[ \begin{align*}
\text{Scheme 19} \\
\text{(CH}_2\text{)}_n \text{CO} + \frac{7}{4} \text{O}_2 & \rightarrow \text{(CH}_2\text{)}_n \text{COO}^- + \frac{1}{2} \text{H}_2\text{O} \\
\end{align*} \]

\(^7\)Generally the by-products showed broad NMR signals (ca. 5 10) which shifted upon warming (-COOH) and signals in the vinyl, and saturated regions which might be expected from diacids resulting from cleavage of ketones 7, 8, and 9. Additionally the by-products showed the strong 3600-2200 cm\(^{-1}\) and 1710 cm\(^{-1}\) bands characteristic of carboxylic acids.
produced from side reactions of 7, 8, and 9 was not pursued due to the relatively low overall yield of the material (5-16%), and due to the presumed complexity of the mixture. On one occasion the HMPA was degassed by the freeze-thaw method (32), but the yield of acidic material was only cut from 7% to 3% (Table 1).

When the crude reaction mixture was analyzed by GLC (column H, 255º, 72mL/minute) a long retention time mixture (74) was seen. The mass spectrum (70 eV) of the mixture showed a peak at m/e 332 and the IR spectrum showed bands at 3600-3200 cm⁻¹ and 1700 cm⁻¹, data which could indicate the formation of dimers. A possible mode of formation of a typical dimer is outlined in Scheme 20.

8 If each product ketone 7, 8, and 9 cleaved at both sides of the carbonyl group, at least six diacids would be produced.

9 See experimental section for column type.
As with the acidic by-products the expected complexity of the mixture suggested the further analysis would be fruitless. Additionally, any attempts to reduce the dimerization by dilution would greatly diminish any synthetic utility of the reaction.  

The next set of rearrangements to be discussed is that of cis and trans-1-vinylcyclododec-3-en-1-ol (18b, 14b). The overall process is shown in Scheme 21, and the products are cis-cyclododec-5-en-1-one (15), trans-cyclododec-5-en-1-one (16), and 4-vinylcyclodecanone (17).

\[ \begin{align*}
\text{Scheme 21} \\
\end{align*} \]

\[ \begin{align*}
14b \\
\xrightarrow{1) \text{KH} \, 2) \text{H}_2\text{O}} \\
\text{15} + \text{16} + \text{17}
\end{align*} \]

10 The weight/volume ratio used was about 0.1g/25mL HMPA or about 0.4%.
Table 2 is a presentation of the results, and the abbreviations are the same used as in Table 1.

The identities of the products from the HMPA and DME rearrangements were assigned by comparing the NMR and mass spectra and GLC retention times of 15, 16, and 17 to the same data from authentic samples (5, 33).

The most obvious difference between the anionic ring expansions of the nine and the ten membered cases is the difference in retention of internal bond stereochemistry. For the ten membered cases this stereochemistry is completely retained. Loss of the stereochemistry via a pathway like Scheme 18 would require a ring contraction of the ten membered ring to an eight membered ring which would be an energetically unfavorable process (5).

By using the activation parameters available for the pyrolysis of 14a and 18a (5) to estimate rates at 25°, it can be seen that the anionic rearrangement of 14b in both HMPA and DME/18-crown-6 proceeds about $10^{16}$ times faster than the pyrolytic reaction and that the anionic rearrangement of 18b proceeds about $10^{15}$ times as fast as its thermal counterpart. These figures are comparable to the results of the nine membered case. The difference in rate between 14b and 18b can probably be attributed to ring strain energy differences as in the thermal cases (5). The relatively high ring strain in 14b was probably
<table>
<thead>
<tr>
<th>Compound</th>
<th>Conditions</th>
<th>t 1/2</th>
<th>Starting material</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>A.M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>14a</td>
<td>30 min/310° b/</td>
<td>4.7 min</td>
<td>1</td>
<td>6</td>
<td>83</td>
<td>11</td>
<td>--</td>
</tr>
<tr>
<td>14b</td>
<td>3 hr/25°/HMPA/D</td>
<td>46 min</td>
<td>2</td>
<td>0</td>
<td>57</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>14b</td>
<td>14 hr/25°/DME/</td>
<td>3.2 hrs</td>
<td>3</td>
<td>0</td>
<td>39</td>
<td>7</td>
<td>--</td>
</tr>
<tr>
<td>14b</td>
<td>18-crown-6/D</td>
<td>3.2 hrs</td>
<td>(-)</td>
<td>(-)</td>
<td>(6)</td>
<td>(3)</td>
<td>--</td>
</tr>
<tr>
<td>14b</td>
<td>183 hr/66°/THF</td>
<td>--</td>
<td>--</td>
<td>0</td>
<td>29</td>
<td>2</td>
<td>--</td>
</tr>
<tr>
<td>18a</td>
<td>2.2 hr/310° b/</td>
<td>20 min</td>
<td>--</td>
<td>81</td>
<td>15</td>
<td>6</td>
<td>--</td>
</tr>
<tr>
<td>18b</td>
<td>27.5 hr/HMPA</td>
<td>15.7 hrs</td>
<td>11</td>
<td>31</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

a/ Same symbol definitions as Table 1

b/ Data from reference 5; half-life calculated from the data; numbers represent product ratios, material balance ≥80%.
responsible for the detection of some rearrangement of this compound after several days of refluxing in THF.

The rearrangement of 19b in HMPA required heating to 60°. The overall reaction and products, trans-cyclopentadec-5-en-1-one (20) and 4-vinylcyclootridecanone (21) are shown in Scheme 22. Table 3 presents the yield and reaction times for this conversion.

**Scheme 22**

![Scheme 22](image)

**Table 3 a/ Rearrangements of Derivatives of trans-1-vinylcyclootridec-3-en-1-ol (19b)**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conditions</th>
<th>19b</th>
<th>20</th>
<th>21</th>
<th>A. M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>19a</td>
<td>2.5 hr/299° b/</td>
<td>-</td>
<td>46 b/</td>
<td>39 b/</td>
<td>-</td>
</tr>
<tr>
<td>19b</td>
<td>4.5 hr/60°/HMPA/D</td>
<td>0</td>
<td>9</td>
<td>61</td>
<td>8</td>
</tr>
</tbody>
</table>

a/ Same symbol definitions as Table 1

b/ Reaction time and yields estimated from data given in reference 6
If the activation parameters for the thermolysis of 19a (6) are used to provide an estimate of the rate at 60°, the [3, 3] shift process should be about 238 times faster than the [1, 3] process. The observed selectivity for the HMPA rearrangement of 19b is not that great, but the trend is in the right direction.

As can be seen from Scheme 23, 3, 4 - unsaturation seems to be necessary for the anionic rearrangement to occur. This same type of behavior was noted in an attempt to effect a siloxy-Cope ring expansion of 77a (5).

Scheme 23

Scheme 24

77 a, R= OTMS
b, R=H

78
Based on an unpublished report (19) that the rearrangement of 79 to 80 would take place, rearrangements of 81a, b and 83a, b were attempted. As can be seen from Schemes 25 and 26, the desired ring expansions were not achieved.
As can be seen from Scheme 27 and Table 4, the rearrangements of both 85a and 85c lead to a variety of interesting products. The thermolysis of 85a leads to 86, but at longer reaction times a new product 90 appears. Due to the small quantities involved, the exact nature of 90 was not determinable.

In contrast to earlier results, the HMPA rearrangement of 85c gave better yields than the thermolytic reaction. Additionally no evidence of a ring opened compound like 91 was seen by NMR spectroscopy\textsuperscript{11}. Later it will be seen that ring opening becomes the dominant process in many rearrangements.

\textsuperscript{11}In most cases the NMR spectrum of a ring opened compound shows a sharp singlet (-CH\textsubscript{3}) at ca. 2.3.
Table 4\(^2\). Rearrangements of Derivatives of 6-vinyl-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (85b)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conditions</th>
<th>85b</th>
<th>86</th>
<th>88</th>
<th>89</th>
<th>90</th>
<th>A. M.</th>
</tr>
</thead>
<tbody>
<tr>
<td>85a</td>
<td>350°/9.75 hr</td>
<td>13</td>
<td>31</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>(1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85a</td>
<td>350°/11 hr</td>
<td>16</td>
<td>47</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>(2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85a</td>
<td>350°/24 hr</td>
<td>&lt;1</td>
<td>1</td>
<td>--</td>
<td>--</td>
<td>12b</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>(-)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85a</td>
<td>350°/24 hr</td>
<td>4</td>
<td>9</td>
<td>--</td>
<td>--</td>
<td>14b</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>(1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85c</td>
<td>25°/5.5 hr/HMPA/(\text{C/c})</td>
<td>3</td>
<td>56</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>(-)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85c</td>
<td>25°/17 hr/DME/18-crown-y/D</td>
<td>15</td>
<td>27</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>(1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>85c</td>
<td>66°/26.3 hr/THF</td>
<td>--</td>
<td>--</td>
<td>55d</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>85c</td>
<td>162°/21 hr/diglyme</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>8d</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

\(a/\) Same symbol definitions as Table 1

\(b/\) Response factor not used

\(c/\) Based on 4 runs

\(d/\) Crude yield
From consideration of the spectral data it was possible to reduce the list of compounds which conform to the spectral data to 86 and 92. NMR shift reagent studies of either 86 or 93 and Eu (fod) failed to clarify the situation due to severe broadening of the shifted peaks. The final assignment of structure 86 was made on the basis of analogy to the earlier results of both anionic and thermolytic ring expansions of non-benzoid medium sized rings.

The rearrangement of 85b in DME/18-crown-6 gave considerable amounts of acidic material, and it was possible to isolate a diacid (thought to be 87) from the crude acidic fraction. The other obvious possibility for the structure of 87 is 94. Compound 87 is suggested as the correct structure because of the symmetrical appearance of the NMR spectrum.
The rearrangement of 85c in refluxing THF (66°) gave the elimination product 88 which could possibly be an intermediate to the cyclized product, 89. Compound 89 was isolated in low yield from refluxing (162°) a solution of 85c in bis-(2-methoxyethyl) ether (diglyme). No explanation can be offered at present which accounts for the tendency of 85c to take a different reaction path in the solvents of lower ionizing power.

The rearrangement of 2-methyl-1-phenyl-but-3-en-2-ol (95) in HMPA is a good example of competition between the cleavage and [1, 3] shift processes. The overall transformation, yields and reaction products are shown in Scheme 28.

Scheme 28

\[
\text{95} \xrightarrow{1) \text{KH/HMPA, 4 hr}} \text{96} \quad \text{21% (S=2)} + \quad \text{97} \quad \text{9% (CH3)}
\]

The product identification was made by comparison of NMR and mass spectra to spectra of authentic samples\(^{12}\). Gas chromatographic

\(^{12}\) See experimental section.
analysis of 96 on both OV101 and AN600 columns showed only one peak. Analysis by GLC/mass spectroscopy and thin layer chromatography (TLC), however, indicated the presence of a small impurity under the major peak. By consideration of the appearance of the NMR spectrum, it was concluded that the impurity was not present in a significant amount, and it was disregarded for the yield calculation. The fact that toluene was isolated from this reaction is consistent with a fragmentation-recombination mechanism for this particular transformation.

To answer the question of whether or not a phenyl group would undergo an anionic [1, 3] -shift, the potassium salt of 1, 1-diphenyl-2-propen-1-ol (98) was allowed to stand for 96 hours at room temperature and heated at 98°C for 22 hours. The lack of any [1, 3] -shift product indicates that the phenyl group exhibits little migratory aptitude under these conditions.

\[
\begin{align*}
\text{98} & \xrightarrow{1)} \text{KH} \\
 & \xrightarrow{\text{HMPA}} \xrightarrow{2)} \text{H}_2\text{O} \\
\text{99} & \text{29}
\end{align*}
\]
An attempt to induce 100 to undergo a 3-carbon ring expansion was thwarted by a ring cleavage process. As shown in Scheme 29, both the ring opened product 101 and an oxidized product 102 was formed.

The crude yields of this reaction varied considerably; in one trial ca. 34% of 102 was formed with a trace of 101, and in another trial ca. 42% 101 and a trace of 102 were formed.

It was hoped that dienols 103a, b and 105 a, b would undergo 4-carbon ring expansions. Instead they are each thought to have undergone [1, 3] -shifts to the middle of the diene as pictured in Scheme 30. The reaction times and yields for both rearrangements are presented in Table 5.
Table 5. Rearrangements of Derivatives of cis and trans-6-(1,3-buta dienyl)-7,8,9,10-tetrahydro-6(5H) benzocyclooctenol (103a,b) and cis and trans-6-(1,3-cis-pentadienyl)-7,8,9,10-tetrahydro-6(5H) benzocyclooctenol (105a,b)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conditions</th>
<th>104 or 106</th>
</tr>
</thead>
<tbody>
<tr>
<td>103a,b</td>
<td>3.92 hr/25°/HMPA</td>
<td>20 (1)</td>
</tr>
<tr>
<td>105a,b</td>
<td>4.5 hr/25°/HMPA</td>
<td>26b/</td>
</tr>
</tbody>
</table>

a Same symbol definitions as Table 1
b Chromatographed yield
The suggestion of structure 104 for the HMPA rearrangement product of 103a and b was based mainly on NMR data. The assignments of the various NMR signals to their respective protons is shown in Figure 1. Further information about the structure was gained through decoupling experiments. The two sets of overlapping doublet of doublets (C and D) were markedly altered upon irradiation at B, indicating that B, C, and D are coupled. The fact that B is the most complex of the three signals indicates that it is the proton adjacent to the ring. Assignment of proton D and proton C follows from the $J_{BC}$ coupling of 16 Hz and the $J_{BD}$ coupling of 11 Hz. Irradiation at E, F causes a visible change in the B multiplet, indicating that one of the protons E, F is adjacent to the vinyl group. Unfortunately a Eu(fod)$_3$ shift study was unable to clearly establish that E, F was adjacent to H.

The suggestion of structure 106 for the HMPA rearrangement product of 105a and b again was based mainly on NMR data. The assignments of the various NMR signals to their respective protons is shown in Figure 2. Some information about the structure was gained through Eu(fod)$_3$ shift reagent studies, but as before decoupling provided the bulk of the information. Irradiation at D caused a marked change at B, C indicating coupling to at least one proton in that group. After Eu(fod)$_3$ addition, the protons in the B, C region separated into 2 multiplets of 1 proton each. The multiplet which showed the
Figure 1. NMR Spectrum of 9, 10, 11, 12-tetrahydro-6-vinyl-8(5, 7H)-benzocyclo decenone (104).
Figure 2. NMR Spectrum of 6-(cis-1-propenyl)-9, 10, 11, 12-tetrahydro-8(5, 7H)-benzocyclodecenone (106).
slower shift rate (i.e. the one farther upfield) was found to be coupled to the allylic methyl group I. Thus the fragment I, C, B, D was established. Attempts to show that D was coupled to the protons at G (which should theoretically show the fastest shift rate) with both Eu(fod)_3 and Pr(fod)_3 did not produce a clear result.

The results of the HMPA rearrangements of 103a,b and 105a,b are in contrast with attempts to thermolytically rearrange the corresponding trimethylsiloxy derivatives (107a,b and 108a,b respectively). Several attempts at pyrolytic rearrangement of these derivatives failed to produce significant results. An attempt\(^1\) to induce ketone 106 to undergo a second [1, 3] shift produced two new ketones, compound 109 (MW=242) and compound 110 (MW=244), but structure assignments could not be made.

The final attempt at a multi-carbon ring expansion was hoped to give a ring system like 4 directly. Unfortunately, like the cyclopropyl derivative 100, 111a,b gave the ring opened product 112 (Scheme 31).

**Scheme 31**

\[\text{111a,b} \xrightarrow{\text{1) KH, HMPA, 17 hrs}} \text{112}\]

\(^1\)Pyrolysis for 6.25 hr at 350°
If the results presented in this section are considered as a whole, two extremes can be seen. On one hand, the ring expansions of the vinyl- and dienylcycloalkenols give results which are consistent with either a concerted or fragmentation-reclosure type of mechanism. On the other hand, the fragmented products observed with the rearrangements of the open-chain case 95, cyclopropylbenzocyclooctenol 100, and the 2-vinylcyclopropylbenzocyclooctenol 111 a, b support a non-concerted type of mechanism. Clearly more evidence is needed to determine the nature of the mechanism. In spite of the unsettled mechanistic question, the present work provides a useful contribution to an understanding of the overall scope of anionic rearrangements.

Part II. Synthetic Methods

Application of the recent method of Evans, Carrol, and Truesdale (34) for the preparation of β-amino alcohols followed by a classic Tiffeneau type ring expansion afforded a ready source of cyclononanone. Exhaustive vinylation of the resultant ketone afforded 117 in 30% overall yield. The overall conversion is outlined in Scheme 32.
Preparation of the mixture of cis and trans 1-vinyl-1,2-cyclohexanediols 81a,b was a simple matter of vinylating the commercially available (Aldrich) 2-hydroxycyclohexanone. The synthesis of the diols 83a,b, however was a more difficult matter.

The overall synthetic plan is shown in Scheme 33.

The preparation of 119 from 118 was carried out by the well-known method of House, Czuba, Gall and Olmstead (35). Oxidation of the
resulting trimethylsilyl enol ether with m-chloroperbenzoic acid (36) gave 120. Deblocking the silylated suberoin 120 with aqueous acetic acid followed by treatment with excess vinyl magnesium bromide gave the desired mixture of 1, 2-vinylcyclooctanediols, in 9% overall yield.

The preparation of the benzocyclooctene systems was preceded by a considerable amount of effort in making the precursors to 7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenone (122) itself. Since the synthesis of 122 or its 3-methoxy derivative involves the ring expansion of benzosuberone (123a) (discussed later), the starting point of the overall synthetic plan was the preparation of benzosuberone (or 3-methoxybenzosuberone) by cyclization reactions. Scheme 34 gives an outline of the plan.

Scheme 34

\[ \text{Scheme 34} \]

\[
\begin{align*}
\text{AlCl}_3 & \quad \rightarrow \quad \text{Zn (Hg)} \\
\text{(124a, } R=H \text{; 124b, } R=\text{OCH}_3) & \quad \rightarrow \quad \text{(125a, } R=H \text{; 125b, } R=\text{OCH}_3) \\
\end{align*}
\]

\[ \text{123a, } R=H; 123b, \text{ } R=\text{OCH}_3 \]

\[ \text{124a, } R=H; 124b, \text{ } R=\text{OCH}_3 \]

\[ \text{125a, } R=H; 125b, \text{ } R=\text{OCH}_3 \]

\[ \text{14 The 3-methoxy derivative was desired for the synthesis of 1.} \]
The preparation of 1,25a and b by Friedel-Crafts acylation and Clemmensen-Martin reduction was carried out without difficulty in 62% and 86% overall yields respectively. Cyclization of 1,25a with polyphosphoric acid gave only a modest yield (40%) of 1,23a instead of the reported (37) 83%. Three different methods: polyphosphoric acid (37), phosphorus pentoxide (38), and the acid chloride of 1,25b with aluminum chloride (39) were unsuccessfully employed to cyclize 1,25b. This difficulty has been observed previously with 1,25b (40) and similar systems (39, 41, 42).

The problems encountered in preparing 1,23a and 1,23b were circumvented by purchasing 1,23a and synthesizing 1,23b by another route. In view of the cost of some of the reagents in Scheme 34 (especially zinc amalgam), the purchase of 1,23a is quite sensible.

The overall conversion of 1,23a to 1,22 is outlined in Scheme 35.

---

1,23b was synthesized by M. Meshgini by using the method of Smith and Berry (43) to produce 1,23, R=OH and then methylating with dimethyl sulfate.
The method used for the conversion is a slight modification (see experimental section) of the method of Evans, Carrol, and Truesdale (34) which the author found to give the most reproducible results. The procedure was found to give an 80% yield of 122 with 82% purity. This purity was sufficient for most of the synthetic work carried out with the product.

Another method for synthesizing 122 has been devised by Huisgen et al. (44). Although the overall yield from 128 (72%) is good, though 128 is not as easily obtained as 123a.

![Chemical Diagram]

Scheme 36

Some difficulty was noted in recrystallizing the semicarbazone derivative of 122. To obtain a relationship between 122 and a known

16 Other workers in our laboratories have found the use of the potassium cyanide/18-crown-6 complex as a catalyst (34) gives more reproducible results.
compound, 122 was reduced with lithium aluminum hydride, and the resulting alcohol possessed spectral features and refractive index consistent with the known alcohol 132 (44).

![132](OH)

Most of the precursors for rearrangement were prepared by addition of organolithium or magnesium compounds to the parent ketone. These reactions were conducted by common methods and their synthesis does not require special mention.

The preparation of 103a, b and 105a, b gave some rather atypical results and is discussed below. Attempts to reduce 133 and 134 with hydrogen and the Lindlar catalyst were completely unsuccessful. This is not surprising in view of the experiences of previous authors (45, 46, 47). Reduction of the enynes was successfully carried out by the use of lithium aluminum hydride in refluxing ether (47). The conversion is pictured in Scheme 37. The unusual facet of this reduction

Scheme 37

![Scheme 37](LiAlH₄ ether)

133, R=H
134, R=CH₃
103a, R=H
103b, R=H
105a, R=CH₃
105b, R=CH₃

is that isomeric dienes are produced, because in the majority of cases
of reductions of this type only the trans product is observed (46, 48), though other workers have observed production of both cis and trans isomers (49). The major isomer from the reduction of both 133 and 134 was assumed to be the trans isomer due to the literature precedents mentioned above.

The last work to be discussed in this section involves some preliminary work based on a [3, 3] ring expansion approach to the hormone model system 4. The synthetic plan was to synthesize divinyl alcohol 138 and rearrange it via a [3, 3] sigmatropic shift to 139 (Scheme 39). This type of ring expansion has been explored by Conia et al. (50). The readily available 123a was chosen as a model ketone and the first attempt to produce divinyl alcohol 144 is shown in Scheme 40.
A rather poor yield (12%) of 141 was obtained, but enough material was available to attempt conversion to 142. Since treatment of 141 with m-chloroperbenzoic acid yielded an inseparable mixture, an alternate approach (Scheme 41) was adopted. It was hoped that 149 might be produced by Scheme 41 and subsequently reduced to 143. Ethynylation of 123a followed by elimination produced 12% of 146. Epoxidation of 146 with m-chloroperbenzoic acid yielded a material (148) which did not appear to be 147.

![Scheme 41](image)

The last approach to 149 (Scheme 42) also failed, though the intermediate steps proceeded in good yield.
Although the target disecosteroid has not yet been prepared, many of the synthetic procedures represent useful applications of recently developed methodology. To summarize, many ideas for synthesis of the disecosteroid \( 1 \) via anionic rearrangements were explored, some useful examples of the trimethylsilyl cyanide-based ring expansion were produced, an example of the preparation of an \( \alpha \)-hydroxy ketone via the trimethylsilyl enol ether was investigated, and many reactions of the relatively unstudied benzocyclooctyl system were carried out. The work as a whole should provide a useful contribution to the program of disecosteroid synthesis as well as to an understanding of anionic rearrangements.
EXPERIMENTAL

General Laboratory Procedures and Conditions

All temperatures are uncorrected. Nuclear magnetic resonance (NMR) spectra were obtained on Varian EM-360 (60MHz) and Varian HA-100 (100 Mhz) spectrometers. Unless otherwise specified, tetramethylsilane was used as an internal reference, and the following abbreviations were used: \( s \) = singlet, \( d \) = doublet, \( t \) = triplet, \( q \) = quartet. Infrared (IR) spectra were obtained on Beckman IR-8 and Perkin-Elmer 621 and 727B infrared spectrophotometers, and polystyrene was used as a standard. Ultraviolet (UV) spectra were obtained on a Cary 15 spectrophotometer. Low resolution mass spectra were obtained from an Atlas CH7 instrument using a 70 eV excitation potential. High resolution mass spectra were obtained from a CEC 110B instrument.

Gas-liquid chromatography (GLC) analyses were carried out on a Varian 920 thermal conductivity detector, 0.25 in. columns) and Varian 1200 (flame ionization detector, 0.125 in. or less columns). The columns used will be referred to by the letter designation as defined below:

Column A 9' X 0.25" 3% AN600 on Chromosorb G, 60-80
Column B 50' X 0.03" OV101 P. L. O. T. (51)
Column C 16' X 0.25" 2.5% OV101 on Chromosorb G, 60-80
Column D  20' X 0.125" 4.9% OV101 on Chromosorb G, 80-100
Column E  5' X 0.25" 1.6% stabilized DEGS on Chromosorb G, 80-100
Column F  75' X 0.01" DEGS capillary
Column G  4.8' X 0.25" 6.5% OV101 on Chromosorb G, 80-100
Column H  5' X 0.25" 1.5% OV101 on Chromosorb G, 80-100
Column I  5' X 0.25" 5% OV101 on Chromosorb G, 60-80
Column J  8.5' X 0.25" 3% AN600 on Chromosorb G, 60-80
Column K  6' X 0.125" 7.4% OV101 on Chromosorb W, 80-100
Column L  7' X 0.25" 4% OV101 on Chromosorb G, 60-80
Column M  50' X 0.03" DEGS P.L.O.T. (51)
Column N  5.25' X 0.25" 7.4% stabilized DEGS on Chromosorb G, 80-100
Column O  2' X 0.125" 5% OV101 on Chromosorb W, 80-100
Column P  6' X 0.375" 4.9% OV101 on Chromosorb G, 80-100
Column Q  2.75' X 0.125" 7% OV101 on Chromosorb W

GLC data is given as follows: column X, column temperature, flow rate (the flow rate for columns used on the Varian 1200 is given in seconds for a methane injection to elute from the column).

Thin layer chromatography (TLC) was conducted on pre-coated TLC sheets (EM Reagents).

Tetrahydrofuran (THF), 1,2-dimethoxy-ethane (DME), and bis-(2-methoxyethyl) ether (diglyme) were distilled from the sodium
benzophenone dianion under nitrogen. Hexamethylphosphoramide (HMPA) was dried by heating the solvent under nitrogen at 200° over 13X molecular sieves (predried under nitrogen at 350° for 4 hours) overnight (52). Other solvents were dried by standard published procedures (53, 54). All reactions involving air or moisture sensitive materials were conducted under a nitrogen atmosphere.

**General Procedure for Rearrangements in hexamethylphosphoramide (HMPA)**

A 50 mL, conical flask was charged with 0.75 g (4.7 moles) of 25% potassium hydride in oil (Ventron) and placed in a nitrogen atmosphere. The oil was rinsed from the potassium hydride with five 7.5 mL portions of hexane by adding hexane, stirring briefly (magnetic stirrer), and allowing the hydride to settle. The hexane-oil layer was then carefully removed with a pipette. Twenty-three mL of HMPA was then added, followed by a solution of 1.5 mmoles of alcohol in 2 mL of HMPA. The mixture was then stirred for 10 minutes and then allowed to stand for the required amount of time. The reaction was then quenched by addition of a few mL of water, acidified with 10% sulfuric acid, and diluted with 125 mL of water.

17 Acidification seems to prevent emulsion formation which occurs when work up is attempted with the initially basic aqueous layer.

18 As little as 3 volumes of water per volume of HMPA was used in some other experiments when that ratio was more convenient for the size of continuous extractor being used.
The aqueous layer was then either continuously extracted with 200 mL of ether or manually extracted with five 25 mL portions of ether. The ether layer was then extracted with five 30 mL portions of 5% sodium hydroxide and washed with two 30 mL portions of saturated ammonium chloride and 30 mL of brine. Finally, the ether layer was dried over magnesium sulfate, filtered, and the ether was removed by rotary evaporation. The basic extract from above was acidified with 6 N hydrochloric acid, cooled, and extracted with five 30 mL portions of ether. The ether extract was then washed with three 30 mL portions of water and 30 mL of brine, dried over magnesium sulfate, filtered, and the ether removed at reduced pressure.

**General Procedure for Rearrangements in 1,2-dimethoxyethane (DME) with 18-crown-6**

A factory bottle containing 18-crown-6 (Aldrich) was warmed to just above the melting point (ca. 40-50°), and about 1 g of the crown ether was transferred to a dry, tared 5 mL volumetric flask. The flask was then evacuated to 1 mm and warmed at 80° for 2 hours. The flask was then weighed, and enough DME was added to make 5 mL of solution.

A 25 mL conical flask was then charged with 0.5 g (3.1 mmoles) of 22.1% potassium hydride in oil (Ventron) and placed under a nitrogen atmosphere. The oil was rinsed from the potassium hydride
with five 5 mL portions of hexane in the same manner as in the experiments with HMPA. Thirteen mL of DME was then added, followed by a solution of 0.75 mmoles of alcohol in 2 mL of DME and enough crown ether solution to contain 0.80 mmoles of 18-crown-6. The mixture was then stirred for 10 minutes and allowed to stand for the required amount of time. The reaction was then quenched by addition of 1 mL of water and transferred to a separatory funnel with 25 mL of ether. The organic layer was then extracted with five 5 mL portions of saturated sodium bicarbonate, dried over magnesium sulfate, filtered, and the ether was removed by rotary evaporation. The basic extract was then cautiously acidified with 6 N hydrochloric acid and extracted with five 5 mL portions of ether. The ether layer was then dried and concentrated as above.

Rearrangement of the potassium salt of cis-1-vinylcyclonon-3-en-1-ol (6b) in HMPA

Rearrangements of the potassium salt of cis-1-vinylcyclonon-3-en-1-ol (2) in HMPA were conducted by the standard procedure, and the progress of the reaction was followed by GLC (column A, 170°, 41 mL/minute). The half-life and the yields of the reaction are presented in Table 1. The yields were determined by GLC (column B, 120° 177 seconds) using the starting alcohol 6b as an internal standard and assuming the response factors to be equal. On one occasion a
HMPA/KH mixture was prepared as usual and the solvent was degassed by freezing it in a liquid nitrogen bath, evacuating the flask to ca. 0.2 mm, sealing the flask (stopcock), and then allowing the flask to warm to room temperature (32). This cycle was repeated five times; and after the last cycle, prepure nitrogen was bubbled through a solution of the sodium benzophenone dianion and then admitted to the flask. The reaction was then carried as usual, and the results are included in Table 1.

Rearrangement of the potassium salt of cis-1-vinylcyclonon-3-en-1-ol (6b) in DME with 18-crown-6

Rearrangements of the potassium salt of cis-1-vinyl-cyclonon-3-en-1-ol (2) in DME with 18-crown-6 were carried out by the usual method, and the progress of the reaction was followed by GLC (column C, 170°, 56 mL/minute). The half-life and the yields of the reaction are presented in Table 1. The yields were determined by GLC (column D, 140° 100 seconds) using the same standard and method as for the HMPA rearrangement.
Attempted Rearrangement of the potassium salt of cis-1-vinylcyclonon-3-en-1-ol (6b) in tetrahydrofuran (THF)

A solution of the potassium salt of 0.226 g (1 mmole) of cis-1-vinylcyclonon-3-en-1-ol (2) in 25 mL of THF was prepared in a manner like that used for the HMPA experiments. The reaction mixture was then allowed to stand at 25° for 24 hours and was refluxed (66°) for another 23 hours. The progress of the reaction was followed by GLC (column B, 115°, 180 seconds), and no product development was noted. The reaction mixture was then quenched with water, and much of the solvent was removed by rotary evaporation. The reaction mixture was then taken up in 45 mL of ether, and the ether layer was washed with five 10 mL portions of water, dried over magnesium sulfate, filtered, and the solvent removed in vacuo giving 0.186 g of a light yellow oil. The NMR and IR spectra and GLC retention time of the product all confirmed that the oil was starting material. A 0.092 g portion of the oil was vacuum transferred (110° at 0.35 mm) producing 0.070 g (67%, adjusted for volume of GLC samples taken) of the starting alcohol.

Rearrangement of the potassium salt of trans-1-vinylcyclodec-3-en-1-ol (14b) in HMPA

Rearrangements of the potassium salt of trans-1-vinylcyclodec-3-en-1-ol (5, 33) in HMPA were conducted by the standard procedure,
and the progress of the reaction was followed by GLC (column E, 150°, 44 mL/minute). The half-life and the yields of the reaction are presented in Table 2. The yields were determined by GLC (column B, 115°, 184 seconds) using the starting alcohol 14b as the internal standard and assuming the response factors to be equal.

Rearrangement of the potassium salt of trans-1-vinylcyclodec-3-en-1-ol (14b) in DME with 18-crown-6

Rearrangements of the potassium salt of trans-1-vinylcyclodec-3-en-1-ol (5, 33) in DME with 18-crown-6 were conducted by the standard method, and the progress of the reaction was followed by GLC (column C, 190°, 71 mL/minute). The half-life and the yields of the reaction are presented in Table 2. The yields were determined by GLC (column B, 127°, 180 seconds) using the same standard as for the HMPA rearrangement.

Rearrangement of the potassium salt of trans-1-vinylcyclodec-3-en-1-ol (14b) in THF

A solution of the potassium salt of 0.205 g (1 mmole) of trans-1-vinylcyclodec-3-en-1-ol (5, 33) in 25 mL of THF was prepared as usual and refluxed for 183 hours. The reaction mixture was then worked up in the same way as the THF reaction for the nine membered analogue 6b, and the yield was determined using the same standard
and GLC column employed in the analogous HMPA experiments. The course of the reaction was followed by GLC (column B, 115°, 180 seconds), and the half-life and the yield are presented in Table 2.

Rearrangement of the potassium salt of cis-1-vinylcyclodec-3-en-1-ol (18b) in HMPA

Rearrangements of the potassium salt of cis-1-vinylcyclodec-3-en-1-ol (5, 33) in HMPA were done by the normal procedure, and the progress of the reaction was followed by GLC (column A, 157°, 56 mL/minute). The half-life and the yields of the reaction are presented in Table 2. The yields are determined by GLC (column B, 115°, 184 seconds) using the starting alcohol 18b as an internal standard and assuming the response factors to be equal.

Rearrangement of the potassium salt of trans-1-vinylcyclotridec-3-en-1-ol (19b) in HMPA

Solutions of the potassium salt of trans-1-vinylcyclotridec-3-en-1-ol (6) in HMPA were prepared by the standard procedure, and heated in a 60° bath for 4.5 hours. The reactions were then worked up as usual (manual extraction) and the yields were determined by GLC (column B, 125°, 151 seconds) using the starting alcohol 19b as the standard and assuming the response factors to be equal.
Attempted Rearrangement of the potassium salt of 1-vinylcyclononanol (75) in HMPA

A solution of the potassium salt of 0.223 g (1.3 mmole) of 1-vinylcyclononanol in 25 mL of HMPA was allowed to stand at room temperature for 24 hours. No indication of product formation could be detected by GLC (column B, 112°, 118 seconds) as time progressed. The standard work up (manual extraction) produced 0.200 g of material with the same NMR and IR features as the starting material. The material was vacuum transferred (110-115° at 0.3 mm) giving 0.120 g (54%) recovery of 1-vinylcyclononanol.

Attempted Rearrangement of the potassium salt of 1-vinylcyclodecanol (77b) in HMPA

1-vinylcyclodecanol (5) was subjected to the usual conditions for rearrangements in HMPA for 4.17 hours at 25°. The progress of the reaction was followed by GLC (column F, 105°, 1.8 mL/minute) and the formation of a new product at ca. 60% of the retention time of the starting material was observed. The standard work up (manual extraction) produced an oil containing 31% of the starting alcohol 77b and 23% of the new product. The yields were determined by GLC\(^\text{19}\) (column B, 140°, 132 seconds) using cycloundecanone (Aldrich) as an internal standard and assuming the response factors to be equal. The retention time of the new product was shorter than that of cycloundecanone. If cyclododecanone had been formed, it would

\(^\text{19}\) The yield study was conducted by Dr. R. W. Thies.
be expected to have a longer retention time than cycloundecanone.

**Attempted Rearrangement of the dipotassium salts of 1-vinyl-1, 2-cyclohexanediols 81a, b in HMPA**

A solution of the dipotassium salts of 0.20 g (1.4 mmoles) of the 1-vinyl-1, 2-cyclohexanediols in 25 mL of HMPA was prepared as previously described, and the progress of the reaction was followed by GLC (column A, 130°, 60 mL/minute). Table 6 summarizes the conditions used and the observations made for this experiment. The starting material consisted of peak a (retention time = 3.8 minutes) and peak b (retention = 4.7 minutes). The sample taken at 24.00 hr. was worked up in the usual manner and gave 0.006 g of neutral material and 0.006 g of acidic material. Work up of the final reaction mixture (55.91 hr.) yielded 0.009 g of neutral material and 0.010 g of the acidic fraction. The NMR spectra of all four of the fractions resembled that of a hydrocarbon grease (55).

**Table 6. Reaction Conditions for Attempted Rearrangement of 81a, b**

<table>
<thead>
<tr>
<th>Time after start of reaction</th>
<th>Temperature</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.08 hr</td>
<td>25°</td>
<td>a:b = 64:36</td>
</tr>
<tr>
<td>23.75 hr</td>
<td>25°</td>
<td>a:b = 87:13</td>
</tr>
<tr>
<td>24.00 hr</td>
<td>25°</td>
<td>10 mL sample taken</td>
</tr>
<tr>
<td>53.75 hr</td>
<td>25°</td>
<td></td>
</tr>
<tr>
<td>54.00 hr</td>
<td>120°</td>
<td>reaction quenched</td>
</tr>
<tr>
<td>55.91 hr</td>
<td>120°</td>
<td></td>
</tr>
</tbody>
</table>
A sample of peak b was prepared by collection from the same column used above and submitted to the rearrangement conditions. GLC analysis by the same column used above showed that b did not rearrange to a under the conditions employed.

Attempted Rearrangement of the dipotassium salt of 1-vinyl-1,2-cyclooctanediols 83a, b in HMPA

A solution of the dipotassium salt of 0.13 g of the crude mixture of 1-vinyl-1,2-cyclooctanediols in 10 mLs of HMPA was prepared as discussed earlier, and the course of the reaction was followed by GLC (column G, 170°, 64 mL/minute). The reaction mixture was allowed to stand at 25° for 20.8 hours, heated at 70° for 23.75 hours, heated at 120-130° for 24.0 hours, and refluxed for 1.5 hours. GLC samples were taken at appropriate times and no new product development was observed throughout the reaction period. The usual work up (manual extraction) produced 0.031 g of a neutral gum and 0.20 g of acidic material. The NMR spectrum of the gum had some of the features (vinyl pattern) of the starting material, but no other useful spectral data could be obtained.

Rearrangement of the potassium salt of 6-vinyl-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (85b) in HMPA

Rearrangements of the potassium salt of 6-vinyl-7,8,9,10-tetrahydor-6(5H)-benzocyclooctenol in HMPA were conducted by the
standard procedure, and the yields of the reaction are presented in Table 4. The yield studies were done by GLC (column G, 210°, 49 mL/minute and column H, 175°, 54 mL/minute) using benzosuberone as an internal standard. The product, 5, 6, 9, 10, 11, 12-hexahydro-8(7H)-benzocyclodecenone (86), was found to have a response factor of 1.26 (S=0.1) relative to the internal standard.

The product ketone 86 was purified by GLC (column A, 225°, 67 mL/minute or column I, 210°, 60 mL/minute) to provide the analytical samples. NMR (CCl₄) 6 7.0-7.25 (m, 4H), 2.5-2.8 (m, 4H), 1.5-2.4 (broad m, 10H); IR (neat) 3055, 3014, 2995, 2930, 2860, 1700, 1600, 1490, 1470, 1445, 1420, 1410, 1370, 1330, 1260, 1240, 1215, 1200, 1160, 1150, 1120, 1105, 1045, 1000, 960, 950, 840, 800, 785, 760, 730, 700 (cm⁻¹); mass spectrum m/e (rel %) 202 (89.8), 129 (100); m/e 202.138 (calcd for C₁₄H₁₈O, 202.136).

Rearrangement of the potassium salt of 6-vinyl-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (85b) in DME with 18-crown-6 was carried out as previously described, and the yields are presented in Table 4. The yield studies were carried out by the same procedure used for the analogous HMPA rearrangement. This particular set of conditions gave considerable amounts of an acidic fraction (Table 4) which was isolated as usual.
and recrystallized twice from benzene giving a white solid (87) (mp 118.0-118.5°). NMR (CDCl₃) δ 10.7-10.9 (broad s, 2H, shifts upon warming to 60°), 7.15 (s, 4H), 2.6-2.85 (m, 4H), 2.35-2.6 (m, 4H), 1.75-2.15 (broad m, 4H); IR (CHCl₃) 3500-2400, 3010, 1710 (cm⁻¹); mass spectrum m/e (rel %) 250 (4.5), 131 (100); m/e 250.121 (calcd for C₁₄H₁₈O₄; 250.121).

Attempted Rearrangement of the potassium salt of 6-vinyl-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (85b) in THF

A solution of the potassium salt of 0.10 g (ca. 0.4 mmoles) of 81% 6-vinyl-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol in 15 mL of THF was refluxed for 26.33 hours. The reaction mixture was then taken up in 25 mL of ether, and the organic layer was washed with 10 mL of water, dried over magnesium sulfate, filtered, and the solvent removed by rotary evaporation. This procedure afforded 0.21 g of material. A 0.148 g sample of this material was then vacuum transferred to give 0.077 g of a clear oil. The oil was analyzed and purified by GLC (column N, 210°, 64 ml/minute). The analysis indicated that the oil consisted of ca. 50% 88, 1% starting alcohol, 85b, and a variety of other compounds none of which made up greater than 10% of the total area. This analysis indicates a crude yield of ca. 55% for the conversion of alcohol 85b to compound 88.

In another experiment the potassium salt 85b was refluxed in
THF, and the reaction was followed by GLC (column I, 225°, 55 mL/minute). Samples were taken at 45 minutes, 1.75 hours, 2.75 hours, and 18.25 hours, and no appearance of ketone 86 was observed. The following spectral data is for the GLC (column N) purified material:

NMR (CDCl₃) δ 7.0-7.2 (m, 4H), 6.54 (s, 1H), 6.45 (d of d, J=11, 18 Hz, 1H), 5.23 (d, J=18 Hz, 1H), 5.04 (d, J=11 Hz, 1H), 2.55-2.72 (m, 2H), 2.05-2.22 (m, 2H), 1.35-1.90 (m, 4H); IR (neat) 2950, 2920, 2850, 1470, 1380 (cm⁻¹); UV λ (C₂H₅OH) nm (ε) 216 (1.7 X 10⁴), 261 (1.9 X 10⁴); mass spectrum m/e (rel %) 184 (39.1), 128 (100); m/e 184.126 (calcd for C₁₄H₁₆O: 184.125).

Rearrangement of the potassium salt of 7,8,9,10-tetrahydro-6-vinyl-6(5H)-benzocyclooctenol (85b) in bis-(2-methoxyethyl) ether (diglyme)

A mixture of 0.60 g (3.7 mmoles) of 25% potassium hydride in oil and 0.50 g (2.5 mmoles) of 7,8,9,10-tetrahydro-6-vinyl-6(5H)-benzocyclooctenol was refluxed in 60 mL of dry diglyme, and the progress of the reaction was followed by TLC. After 21 hours, the reaction mixture was cooled and taken up in 100 mL of hexane. The aqueous and organic layers were separated, and the organic layer was washed with four 100 mL portions of water, dried over

The observed product 88 has the same retention time as the starting alcohol 85 on an OV-101 column, but ketone 86 could have been seen if it had been formed.
magnesium sulfate, filtered, and the solvent was removed by rotary evaporation. This procedure yielded 0.32 g of an oil which was then chromatographed on a 1.7 cm × 25 cm neutral alumina (Brockman grade III) (56) column. The fractions containing the desired material were collected, dried over magnesium sulfate, and the solvent removed at reduced pressure giving 0.035 g (8%) of product 89. The product was tested with bromine in carbon tetrachloride and observed to discharge the color of bromine. NMR (CCl₄) δ 6.9-7.3 (m, 4H), 2.65-3.0 (m, 4H), 2.2-2.65 (m, 4H), 1.7-2.65 (m, 4H); IR (neat) 3080, 3040, 3025, 2925, 1630, 1600, 1485, 1440, 1420, 1320, 1280, 1120, 1045, 900, 750, 730 (cm⁻¹); UV λ (C₂H₅OH) nm (ε) 265 (1.4 × 10⁴); mass spectrum m/e (rel %) 184 (89.5), 141 (100).

Pyrolysis of 7, 8, 9, 10-tetrahydro-6-trimethylsiloxy-6-vinyl-5H-benzocyclooctene (85a)

Pyrex glass ampoules were first washed with acetone, distilled water, and then 28% ammonia in water. The ampoules were then dried overnight in a 110° oven, cooled, and then charged with samples of 7, 8, 9, 10-tetrahydro-6-trimethylsiloxy-6-vinyl-5H-benzocyclooctene. Finally the ampoules were evacuated at 0.2 mm for 0.5 hour, weighed, evacuated for another 0.5 hour, and then sealed with a torch. After heating, the ampoules were opened, and the contents were hydrolyzed with pyridine hydrochloride/water as previously
described (2, 57). The hydrolysis products were taken up in 5 mL of ether, and the ether layer was washed with three 5 mL portions of 10% sulfuric acid and 5 mL of saturated sodium bicarbonate. The results of these experiments are presented in Table 4. The yield studies were done by GLC (column H, 170°, 44-63 mL/minute) using the same standard and response factor employed in the HMPA work with the unsilylated alcohol 85b.

Preparation of 5, 6, 9, 10, 11, 12-hexahydro-8(7H)-benzocyclodecenol (93)

A solution of 0.12 g (0.59 mmoles) of 5, 6, 9, 10, 11, 12-hexahydro-8(7H)-benzocyclodecenone and 0.5 mL of ether was added dropwise to a mixture of 0.2 g (5 mmoles) of lithium aluminum hydride and 0.5 mL of ether. The syringe used to add the ketone was then rinsed into the reaction vessel with an additional 0.2 mL of ether, and the mixture was stirred at room temperature for 55 minutes. The reaction was then quenched by cautious addition of 0.2 mL of water, 0.2 mL of 15% sodium hydroxide, and 0.6 mL of water (58). The white, granular precipitate which formed was then filtered off and washed thoroughly with ether. The filtrate and washings were then dried over magnesium sulfate, refiltered, and the ether was removed by rotary evaporation. This procedure yielded 0.10 g of crude 5, 6, 9, 10, 11, 12-hexahydro-8(7H)-benzocyclodecenol.
(clear oil) which was of sufficient purity to use in an NMR shift reagent study. NMR \((\text{CCl}_4)\) \(\delta\) 7.03 (s, 4H), 3.6-4.0 (m, 1H), 3.35-3.6 (broad s, 1H), 2.5-3.0 (m, 4H), 0.8-2.1 (m, 10H) (60 MHz);
IR \((\text{CHCl}_3)\) 3600-3200, 3050, 3000, 2920, 2850, 1485, 1470, 1450, 1440, 1350, 1230, 1170, 1100, 1060, 1040, 1025, 980, 950, 920, 910 (cm\(^{-1}\)); mass spectrum m/e (rel %) 204 (32.7), 90 (100).

**Rearrangement of the potassium salt of 2-methyl-1-phenyl-but-3-en-2-ol (95) in HMPA**

A solution of the potassium salt of 0.50 g (2.8 mmoles) of 89% 2-methyl-1-phenyl-but-3-en-2-ol in 25 mL of HMPA was prepared as before and allowed to stand at room temperature for four hours. The reaction mixture was then quenched by addition of a few drops of water and then transferred to a separatory funnel with 75 mL of water. The aqueous layer was then worked up by the usual method (manual extraction) up to the point of solvent removal. The ether layer was then dried over magnesium sulfate, filtered, and the ether was distilled off through a 17 cm, vacuum-jacketed Vigreux column. The residue was then distilled in vacuo \((25^\circ \text{ at 0.5 mm})\) into a -78\(^\circ\) trap. The 0.62 g of distillate thus obtained was then analyzed by GLC (column C, 100\(^\circ\), 75 mL/minute) using published response factors (59). The mixture was found to contain 28% diethyl ether, 64% hexane, and 7% of a substance with the same retention time as
toluene. An NMR spectrum of the distillate confirmed the presence of toluene by comparison to a published spectrum (60). This analysis demonstrated that toluene was produced in 9% overall yield. The material remaining in the pot was also analyzed by GLC (column O, 135°, 23 seconds) and found to contain 9% of a material which is presumably 2-phenyl-2-propanone, 7% of starting alcohol 95, and 84% of a new product. Further analysis (same GLC conditions) using alcohol 95 as an internal standard (and assuming the response factors to be equal) indicated that the overall yield of the new product was 21% (S=2). A sample of the new product was purified by GLC (column G, 180°, 55 mL/minute) and was observed to have only one peak upon reinjection onto column G and upon GLC analysis on column A (160°, 67 mL/minute). Furthermore, the purified sample showed one spot when analyzed by TLC (silica gel; solvent, chloroform) when visualized by ceric sulfate/sulfuric acid, but a small overlapping spot was visible when the sample was visualized by UV light. The mixture before purification was analyzed by GLC-mass spectrometry (column O, 135°, 23 seconds), and the total ion current and peak intensities at m/e 91, 104, and 162 were monitored. By this technique, it appeared as if there were two compounds under the main

2-phenyl-2-propanone is a 3% impurity in the starting material.
product peak. The mass spectra of the leading and trailing edges of the peak are presented in Table 7. The mass spectrum of the trailing edge is very similar to the published spectrum of 5-phenyl-2-pentanone (61). The following spectral data refers to the GLC purified sample above: NMR (CDCl₃) δ 6.95-7.35 (m, 5H), 2.55 (5, J=7 Hz, 2H), 2.31 (s, J=7 Hz, 2H), 1.98 (s, 3H), 1.82 (quintet, J=7 Hz, 2H); IR (neat) 3090, 3060, 3030, 3000, 2940, 2860, 1710, 1670, 1600, 1500, 1460, 1370, 1360, 1250, 1220, 1180, 1160, 1080, 1030, 750, 700 (cm⁻¹).

Table 7. Mass Spectral Data for Rearrangement Products of 95

<table>
<thead>
<tr>
<th>m/e</th>
<th>leading</th>
<th>91</th>
<th>trailing</th>
</tr>
</thead>
<tbody>
<tr>
<td>162</td>
<td>58.8</td>
<td>92.5</td>
<td>14.4</td>
</tr>
<tr>
<td>105</td>
<td>45.5</td>
<td>100.0</td>
<td>12.6</td>
</tr>
<tr>
<td>104</td>
<td>91</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>91</td>
<td>98.3</td>
<td>33.1</td>
<td>25.3</td>
</tr>
</tbody>
</table>

Attempted Rearrangement of the potassium of 1,1-diphenyl-2-propen-1-ol (98) in HMPA

A solution of the potassium salt of 0.30 g (1.3 mmoles) of 92% 1,1-diphenyl-2-propen-1-ol in 25 mL of HMPA was prepared as previously described, and the progress of the reaction was followed

²² Irradiation at the center of the quintet causes both triplets to collapse to singlets.

²³ The intensity of the 1670 band is greatly reduced when compared to the spectrum of the crude sample.
by GLC (column A, 205°, 57 mL/minute). The reaction mixture was allowed to stand at 25° for 96 hours and heated at 98° for 22 hours, and no change was observed by GLC. Work up of the reaction mixture by the usual method (manual extraction) gave 0.20 g of neutral material and 0.04 g of crude acidic material. A 0.119 g portion of the neutral material was vacuum transferred (130° at 0.35 mm) to give 0.112 g (63%, adjusted) of a clear oil which had the same NMR and IR spectra as the starting material.

Rearrangement of the potassium salt of 6-
cyclopropyl-7,8,9,10-tetrahydro-6(5H) -
benzocyclooctenol (100) in HMPA

A solution of the potassium salt of 0.029 g (0.1 mmoles) of 6-cyclopropyl-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol in 1.2 mL of HMPA was allowed to stand at room temperature for 45.58 hours. Quenching the reaction mixture with water followed by the normal work up (manual extraction) afforded 0.010 g of neutral material. The material was analyzed by GLC (column J, 205°, 63 mL/minute) and found to contain 18% starting material, 5% unknown substances, and 77% (<34% overall yield) of 1-cyclopropyl-5-(o-toly1)-2,3-pentanedione (102). The mixture was purified by GLC (column J, same conditions as above) to provide the analytical samples. NMR (CCl₄) 7.01 (s, 4H), 2.5-2.9 (m, 4H), 2.28 (s, 3H), 1.6-2.2 (m, 2H), 1.2-1.4 (m, 1H), 0.8-1.2 (m, 4H); IR (CCl₄) 3080,
73020, 2940, 2860, 1700, 1500, 1460, 1390, 1040, 950 (cm\(^{-1}\)); mass spectrum m/e (rel %) 230 (23.5), 161 (100), 105 (69.9), 69 (64.1); m/e 230, 130 (calcd for \(\text{C}_{15}\text{H}_{18}\text{O}_{2}\): 230.131).

In another experiment a solution of the potassium salt of 0.114 g of a mixture containing 58% of the cyclopropyl alcohol \(100\) (also contained 33% of 7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenone and 9% of unknown material) in 5 mL of freshly dried HMPA was allowed to stand at 25° for 46 hours. The reaction mixture was quenched with water and worked up by the normal procedure (manual extraction) giving 0.089 g of neutral material and 0.019 g of acidic material. Seventy mg of the neutral material was then vacuum transferred (120° at 0.35 mm) producing 64 mg of a light yellow oil. The oil was purified and analyzed by GLC (column J, 210°, 63 mL/minute), and the analysis showed that the oil contained 3% unknown material, 32% 7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenone, 6% starting alcohol \(100\) and 59% 1-cyclopropyl-5-(o-tolyl)-2-pentanone (101). This implies a 42%\(^{24}\) overall yield of ketone \(101\) (72% if corrected for % starting material in mixture). NMR (\(\text{CCl}_4\), \(\text{CH}_2\text{Cl}_2\) reference)\(^{25}\) 6 7.15 (s, 4H), 2.55-3.01 (m, 4H), 2.38 (s, 3H), 1.45-2.09 (m, 5H),

\(^{24}\)Uncorrected for small % dione \(102\) in mixture.

\(^{25}\)Another sample with tetramethylysilane as reference was checked and found to have no signals in the area where dichloromethane (\(\text{CH}_2\text{Cl}_2\)) absorbs.
Rearrangement of the potassium salts of cis and trans-6-(1,3-butadienyl)-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (103a, b) in HMPA

The general method of Chanley and Sobotka (47) was used to produce a mixture of butadienyl alcohols 103a, b. A solution of 0.404 g (1.4 mmoles) of 77% 6-(3-buten-1-ynyl)-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (133) and 1.6 mL of ether was added to a suspension (25°) of 0.12 g (3 mmoles) of lithium aluminum hydride and 4 mL of ether. Two 0.8 mL portions of ether were used to rinse the butenynyl alcohol container into the reaction vessel, and the mixture was refluxed for 4 hours. The excess lithium aluminum hydride was quenched by cautious addition of 0.12 mL of water, 0.12 mL of 15% sodium hydroxide, and 0.36 mL of water (58), and the white precipitate which formed was filtered off and washed thoroughly with ether. The filtrate and washings were dried over magnesium sulfate, re-filtered, and the solvent was removed at reduced pressure. The

26 Corrected for dione 102 fragments.
0.382 g of material which remained showed a strong band 3600-3100 cm\(^{-1}\) (OH) in the IR, and the NMR spectrum indicated that no starting butenynol 133 remained.

A solution of 0.326 g of the crude butadienol mixture from above and 5 mL of HMPA was added to 20 mL of HMPA containing excess potassium hydride, and the whole was allowed to stand for 3.92 hours. The usual work up (continuous extraction) afforded 0.265 g of neutral material.\(^{27}\) The material was analyzed by GLC (column K, 175°, 68 seconds), using butenynol 133 as an internal standard and assuming the response factors to be equal. The results of the analysis are presented in Table 5. Material from a similar preparation was purified on a 2 ft. X 0.375 in. stainless steel column containing 33 g of Woelm neutral alumina (activity II) (56). The column was eluted with hexane and then a linear gradient (62) of ether/hexane. Fractions containing material with Rf = 0.38 (TLC on silica gel; solvent, chloroform) were collected and repurified by GLC (column G, 240°, 63 mL/minute) to provide the analytical samples of 9,10,11,12-tetrahydro-6-vinyl-8(5,7H)-benzocyclo-decanone (104). NMR (CCl\(_4\)) \(\delta\) 6.95-7.25 (m, 4H), 5.9-6.4 (broad m, 1H), 5.01 (d of d, J=2, 11 Hz, 1H), 4.99 (d of d, J=2, 16 Hz, 1H), 2.85-3.2 (broad m, 2H), 2.45-2.85 (broad m, 3H), 1.9-2.45 (broad m, 27Acidic material not isolated for this rearrangement.)
6H), 1.55-1.9 (m, 2H); IR (neat) 3060, 3010, 3000, 2930, 2860, 1700, 1640, 1490, 1470, 1450, 1425, 1410, 1370, 1120, 1000, 990, 920, 800, 780, 760, 740, 710 (cm⁻¹); mass spectrum m/e (rel %) 228 (47.9), 174 (33.4), 118 (100); m/e 228.151 (calcd for C₁₆H₂₀O: 228.151).

Pyrolysis of cis and trans-6-(1,3-butadienyl)-6-trimethylsiloxy-7,8,9,10-tetrahydro-5H-benzocyclooctene (107a,b)

Pyrex glass ampoules were cleaned with distilled water, acetone, distilled, and 28% ammonia water, and then dried overnight in a 110° oven. The ampoules were then cooled and charged with appropriate amounts (2) of a mixture containing about 70% of the trimethylsiloxy dienes 107a,b and other materials which had a much shorter retention time than the dienes and made up 30% of the total area (indicated by GLC analysis, column C, 235°, 40 mL/minute). The ampoules were then heated, cooled, opened, and analyzed by GLC (same as above). Runs were made at 310° for 15 minutes and for 1 hour; at 270° for 1 hour; and at 200° for 1.17 hours. In all cases the peaks representing the dienes 107a,b diminished with respect to the impurity peaks, and no new product peaks appeared.
Rearrangement of the potassium salts of cis and trans-6-(1, 3-cis-pentadienyl)-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (105a, b) in HMPA

The general method of Chanley and Sobotka (47) was used to produce a mixture of pentadienyl alcohols 105a, b. A solution of 1.53 g (5 mmoles) of 79% 6-(cis-3-penten-1-ynyl)-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (134) and 6 mL of ether was added (over 10 minutes) to a suspension (25°) of 0.43 g (11 mmoles) of lithium aluminum hydride in 15 mL of ether. Two 3 mL portions of ether were then used to rinse any residual enynol into the reaction vessel, and the mixture was then refluxed for 4 hours. The mixture was then cooled, and the excess lithium aluminum hydride was quenched by cautious addition of 0.43 mL of water, 0.43 mL of 15% sodium hydroxide, and 1.29 mL of water (58). The ether/aluminum salt mixture was then dried with magnesium sulfate, filtered, and the solvent was removed at reduced pressure. This procedure afforded 1.58 g of a light yellow oil which was used in the rearrangement without further purification. The NMR spectrum of the oil indicated that no enynol 134 remained and the IR spectrum showed a strong band 3650-3150 cm⁻¹ (OH). GLC analysis of the crude mixture of dienols (column H, 205°, 70 mL/minute) indicated that it contained ca. 9% short retention time materials, 10% of material with the same retention time as the starting enynol, and 81% new products (presumably the dienols).
A solution of 0.77 g of the crude material from above and 5 mL of HMPA was added to 45 mL of HMPA containing excess potassium hydride, and the whole was allowed to stand for 4.5 hours at room temperature. The usual work up (continuous extraction) afforded 0.66 g of neutral material and 0.022 g (ca. 3%) of acidic material. A 0.218 g portion of the neutral material was purified on a 2 ft. X 0.375 in. stainless steel column containing 33 g of Woelm neutral alumina (activity II)(10). The column was eluted with hexane and then a linear gradient (11) of hexane and 50/50 ether/hexane. Fractions containing material with $R_f = 0.5$ (TLC on silica gel; solvent, chloroform) were collected, dried, and the solvent removed in vacuo to give 0.086 g of material. Fifty mg of this material was vacuum transferred (130° at 0.35 mm) to give 47 mg (26% adjusted overall yield, 33% if corrected for actual enynol 134 in starting material) of 6-(cis-1-propenyl)-9,10,11,12-tetrahydro-8(5,7H)-benzocyclo-decenone (106). NMR (CDCl₃) δ 7.03-7.3 (m, 4H), 5.3-5.8 (m, 2H), 3.12-3.5 (broad s, 1H), 2.8-3.12 (m, 1H), 2.45-2.8 (m, 3H), 2.2-2.45 (m, 3H), 1.87-2.2 (m, 3H), 1.5-1.87 (m, 5H, contains doublet at 1.72, $J=5$ Hz); IR (neat) 3050, 3010, 2930, 2860, 1700, 1490, 1470, 1450, 1420, 1400, 1360, 1330, 1270, 1230, 1190, 1110, 990, 920, 790, 770, 750, 730, 710 (cm⁻¹); mass spectrum m/e (rel %) 242 (23.2)

28 Adjusted for HMPA content by NMR and based on the starting material containing 81% dienols 105a,b.
174 (32.3), 118 (100); m/e 242.167 (calcd for C_{17}H_{22}O: 242.167).

Pyrolysis of cis and trans-6-(1,3(cis)-pentadienyl)  
7,8,9,10-tetrahydro-6-trimethylsiloxy-5H-
benzocyclooctene (108a,b)

Pyrex glass ampoules were cleaned by one of the 3 following solvent series: (1) methanolic potassium hydroxide, acetone, distilled water, 28% ammonia, (2) distilled water, acetone, distilled water, 28% ammonia, (3) concentrated nitric acid, distilled water, 28% ammonia, distilled water. (the solvent series used did not significantly change the results). The ampoules were then dried overnight in a 110° oven, cooled, and charged with an appropriate amount (2.5) of sample. The ampoules were then evacuated at ca. 0.2 mm for 0.5 hour, weighed, evacuated for another 0.5 hour, and sealed. After heating, the ampoules were opened, and the contents were either hydrolyzed as previously described (2,5) or analyzed directly.

A sample of the major isomer 108b was collected from the mixture of trimethylsiloxy dienes 108a,b (column L, 234°, 50 mL/minute). Pyrolysis of this material for 4.5 hours at 340-350°, followed by hydrolysis produced a dark tar which was found to contain more than 15 different products when analyzed by GLC (column C, 235°, 49 mL/minute). Four of these products 153, 154, 155, and 156 (ratio 7:58:24:12 respectively) were purified by (column C,
same conditions as above) and some spectral data was obtained.

Compound 153: mass spectrum m/e (rel %) 174(78), 118(100), spectrum similar to that of 7,8,9,10-tetrahydro-6(5H)-benzocyclooctenone

Compound 154: NMR (CCl₄) δ 6.9-7.4 (m), 1.9-2.35 (m, contains s at 2.1), 1.1-1.9 (m); IR (CCl₄) no carbonyl or hydroxyl bands; mass spectrum m/e (rel %) 242 (<1), 240 (1.5), 226 (14), 224 (32), 223 (50), 222 (100). Compound 155: NMR²⁹ (CCl₄) δ 6.95-7.15 (s), 2.55-2.75 (m), 2.22 (s), 1.2-2.0 (m); mass spectrum m/e (rel %) 242 (<1), 240 (<1), 224 (70), 119 (60), 106 (90), 105 (100). Compound 156: mass spectrum m/e (rel %) 242 (19.1), 240 (20.8), 226 (100).

Numerous other experiments of pyrolyzing mixtures of 108a and 108b also failed to produce significant results.

Pyrolysis of 6-(1-cis-propenyl)-9,10,11,12-tetrahydro-8(5,7H)-benzocyclodecenone (106)

A 3 cm X 28 cm glass ampoule was washed with acetone, distilled water, and 28% ammonia water, and then dried overnight in a 110° oven. The ampoule was then charged with 0.36 g of crude 6-(1-cis-propenyl)-9,10,11,12-tetrahydro-8(5,7H)-benzocyclodecenone and evacuated at 0.2 mm before sealing. The ampoule was then heated for 6.25 hours at 350°, cooled and opened. The

²⁹Integrals unreliable due to sample weakness or presence of impurities.
crude reaction product was then purified by GLC (column I, 265°, 67 mL/minute). The products of interest eluted in the order 157, 158, 159 and were present in the ratio 55:16:29 respectively. Compound 158 had about the same retention time and about the same mass spectrum as the starting ketone 106. Compound 157 showed a single spot, Rf = 0.53, (same as starting ketone 158) when analyzed by TLC (silica gel; solvent, chloroform). Compound 157: NMR $^3\text{0}$ (CDCl$_3$) δ 6.9-7.3 (m), 5.2-5.65 (m), 3.7-4.1 (m), 2.5-3.1 (broad m), 1.9-2.4 (m containing singlets at 2.15 and 2.08), 1.5-1.9 (broad m), 0.85-1.15 (m, possible overlapping triplets, J=7 Hz); IR (neat) 3070, 3020, 2960, 2940, 2860, 1710, 1500, 1460, 1360, 1170, 980, 760 (cm$^{-1}$); mass spectrum m/e (rel %) 242 (25.4), 224 (10.7), 213 (11.7), 199 (100); m/e 242, 165 (calcd for C$_{17}$H$_{22}$O: 242.167). Compound 159: NMR $^3\text{1}$ (CDCl$_3$) δ 6.9-7.3 (m), 5.2-5.7 (m), 0.8-3.1 (broad m); IR (neat) 3070, 3020, 2960, 2940, 2880, 1710, 1500, 1460, 980, 750 (cm$^{-1}$); mass spectrum m/e rel (%) 244 (21.8), 243 (14.9), 242 (86.0), 229 (12), 129 (100); m/e 242, 166 (calcd for C$_{17}$H$_{22}$O$_3$: 242.167).

$^3\text{0}$Sample too weak to give reliable integrations.

$^3\text{1}$Sample too weak to give reliable integrations.

$^3\text{2}$It was originally though that m/e 242 was the molecular ion, but logical mass loss and peak intensity analysis indicated later that 244 is the probable molecular ion. It is very likely that the remaining 2 mass units are 2H and that the true formula is C$_{17}$H$_{24}$O.
Rearrangement of the potassium salts of 7, 8, 9, 10-tetrahydro-6(2-vinylcyclopropyl)-6(5H)-benzocyclooctenols 111a, b in HMPA

Rearrangements of the potassium salts of the 7, 8, 9, 10-tetrahydro-6(2-vinylcyclopropyl)-6(5H)-benzocyclooctenols in HMPA was carried out by the standard procedure, and the yield of the reaction was determined by GLC (column K, 165°, 46 seconds). The yield study was carried out using 6-(cis-3-penten-1-ynyl)-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol as an internal standard and assuming the response factors to be equal. The results of the yield study are presented in Scheme 31. The product, 5-(o-toly)-1-(2-vinylcyclopropyl)-1-pentanone 33 (112) was purified by GLC (column A, 190°, 70 mL/minute). NMR (CDCl₃) δ 7.01 (s, 4H), 5.11-5.56 (m, 2H), 4.85-5.01 (m, 1H), 2.43-2.67 (m, 4H), 2.25 (s, 3H), 1.25-1.91 (m, 7H), 0.75-0.91 (m, 1H); IR (CCl₄) 3080, 3020, 2940, 2870, 1700, 1640, 1500, 1460, 1390, 1100, 990 910 (cm⁻¹); mass spectrum m/e (rel %) 242 (1.6), 105 (100); m/e 242.166 (calcd for C₁₇H₂₂O: 242.167).

General Method for Preparation of Solutions of vinyl magnesium bromide in tetrahydrofuran (THF)

Vinyl magnesium bromide was prepared essentially the same way as previously reported (2). The apparatus used for the

33 cis or trans configuration not established.
preparation is pictured in Figure 3. The 250 mL flask was charged with 4.00 g (0.17 g-atoms) of magnesium. Ten mL of dry THF was then added to the 25 mL addition funnel, and 100 mL of THF was added to the 125 mL funnel. Enough vinyl bromide was then distilled in from port B (port A was connected to a nitrogen line) to give 18 mL of solution (ca. 0.12 moles of vinyl bromide). Port A was then stoppered, and port B was connected to the nitrogen line. About 6 mL of vinyl bromide/THF solution was then drained into the reaction vessel along with 20 mL of THF. The flask was then warmed gently, and a vigorous reaction ensued. The reaction was then moderated by judicious addition of THF and vinyl bromide/THF solution. The mixture was then stirred for an hour after the addition was complete, and the desired amount of vinyl magnesium solution was transferred from the flask for use (estimated concentration, 1 M).

General Procedures for Silylation of Alcohols

**Method A.** The procedure used was approximately the same as previously reported (2). Two to three mmoles of alcohol was added to a mixture of 2 mL of dimethylsulfoxide and 1 mL of Tri-Sil (Pierce Chemical Co.), and the whole was stirred overnight. The mixture was then taken up in 25 mL of hexane and washed with five 10 mL portions of water, two 12 mL portions of 10% sulfuric acid, and two 12 mL portions of saturated sodium bicarbonate. The hexane
Figure 3. Apparatus for Preparation of Vinyl Magnesium Bromide.
layer was then dried over magnesium sulfate, filtered, and the solvent was removed by rotary evaporation.

**Method B.** A premixed form of the silylation formula of Sweeley, Bentley, Makita and Wells (63) was made from 100 mL of dry pyridine, 20 mL of hexamethyldilazane (HMDS), and 10 mL of chlorotrimethylsilane. One to two mmoles of alcohol was then added to 5 mL of the silylating solution, and the mixture was stirred overnight. The mixture was then taken up in 20 mL of hexane and washed with three 15 mL portions of water, two 15 mL portions of 10% sulfuric acid, and 15 mL of saturated sodium bicarbonate. The remainder of the work up was as described in Method A.

**Preparation of trimethylsilyl cyanide**

**Method A.** Procedure A of Evans, Carrol, and Truesdale (34) was followed. The reaction of 28.9 g (0.22 moles) of silver cyanide and 80 mL (0.66 moles) of chlorotrimethylsilane gave 13.0 g (60%) of trimethylsilyl cyanide, bp 116.5° (760 mm) (lit (12) bp 114-118°, 760 mm).

**Method B.** Procedure B of Evans, Carrol, and Truesdale (34) afforded 69.3 g (35%) of trimethylsilyl cyanide, bp 115° (760 mm), from 16 g (2.0 moles) of lithium hydride, ca. 150 mL (3.8 moles) of liquid hydrogen cyanide (Fumico, Amarillo, Texas), and 250 mL (2.0 moles) of chlorotrimethylsilane.
Preparation of 1-vinylcyclononanol (117)

A procedure similar to that of Evans, Carrol, and Truesdale (34) was followed. A mixture of 1.08 g (8.6 mmol) of cyclooctanone (Aldrich), 1.1 mL (9.4 mmol) of trimethylsilyl cyanide, and ca. 50 mg of zinc iodide (City Chemical Co.) was warmed briefly with a heat gun and then stirred at room temperature for 7.5 hours. Then 3 mL (25.7 mmol) of additional trimethylsilyl cyanide was added, and the mixture was warmed in a 65-70° bath for another 5.5 hours. The remaining trimethylsilyl cyanide was then distilled off at reduced pressure, and the crude trimethylsilyl cyanohydrin was carried on to the next step without further purification. IR (neat) 2930, 2860, 2280, 1480, 1450, 1260, 1140, 1100, 1040, 950, 940, 850, 760 cm⁻¹.

A solution of the trimethylsilyl cyanohydrin and 3 mLs of ether was then added dropwise over 10 minutes to a stirred suspension (25°) of 0.47 g (12.3 mmol) of lithium aluminum hydride in 4 mL of ether. Stirring was continued for 1.25 hours, and then the mixture was cooled in an ice bath. The reaction mixture was then quenched by cautious addition of 0.47 mL of water, 0.47 mL of 15% sodium hydroxide, and 1.4 mL of water (58). The granular precipitate which formed was then filtered and washed thoroughly with ether. The filtrate was then dried over magnesium sulfate, refiltered, and the ether removed at reduced pressure. The 1.23 g of oil thus
obtained was then taken up in 20 mL of 10% sulfuric acid and extracted with 40 mL of ether. The acidic layer was made basic (pH ca. 10) with 15% sodium hydroxide, cooled, and then extracted with nine 10 mL portions of chloroform. The chloroform extract was then dried over magnesium sulfate, filtered, and the solvent removed in vacuo. This procedure gave 0.92 g of crude 1-aminomethyl-1-cyclooctanol 115 (clear oil containing some white crystals). IR (neat) 3600-3200, 3000, 2910, 2850, 1480, 1450, 1230 (cm\(^{-1}\)).

A solution of 0.85 g (ca. 5.4 mmoles) of the crude \(\beta\)-amino alcohol 115 and 50 mL of 5% acetic acid was cooled in an ice bath, and 22 mL (27.5 mmoles) of 1.25 M sodium nitrite was added. The mixture was then stirred for 0.5 hour at ice temperature, 0.5 hour at room temperature, and 0.5 hour on a steam bath. The reaction mixture was then cooled and made basic with 15% sodium hydroxide. The aqueous layer was then extracted with seven 10 mL portions of ether, and the ether extracts were dried over magnesium sulfate, filtered, and the ether removed by rotary evaporation. This procedure gave 0.81 g of a clear oil. A small portion of the oil was purified by GLC (column I, 160°, 70 mL/minute) for spectral analysis. NMR (\(\text{CCl}_4\)) \(\delta\) 2.3-2.5 (m, 4H), 1.3-2.0 (m, 12H); IR (neat) 2930, 2880, 1700, 1480, 1450, 1350, 1330, 1230, 1160, 1140, 1120, 1040, 1000, 950, 790 (cm\(^{-1}\)) (matches published spectrum of cyclononanone (64)); mass spectrum m/e (rel %) 140 (16.2), 98 (100).
A solution of 0.80 g (ca. 5.7 mmoles) of crude cyclononanone and 10 mL of THF was then treated with 7 mL (ca. 6 mmoles) of vinyl magnesium bromide in THF solution (prepared as described earlier). The mixture was then stirred for 1.5 hours, and then 10 mL of saturated ammonium chloride was cautiously added. The reaction mixture was then taken up in 40 ml of ether, and the aqueous and organic layers were separated. The ether layer was then washed with three 15 mL portions of water, 15 mL of saturated sodium bicarbonate, and 15 mL of saturated sodium bicarbonate, and 15 mL of saturated sodium chloride. Drying the ether layer over magnesium sulfate, filtering, and removing the solvent at reduced pressure gave 0.66 g of material. GLC analysis (column A, 130°, 60 mL/minute) of this material showed that the reaction was only about 75% complete. Therefore a solution of 0.63 g of the material in 10 mL of THF was treated again with ca. 3 equivalents of the vinyl magnesium bromide/THF solution from before, with addition of 0.3 mL of methanol between each equivalent of Grignard reagent. The whole process required 1.17 hours, and after the last equivalent was added, the reaction was quenched with saturated ammonium chloride as before. The reaction mixture was then taken up in 100 mL of ether, and the aqueous layer was separated. The organic layer was then washed with five 20 mL portions of water and 20 mL of brine, dried over magnesium sulfate, filtered, and the solvent was removed by
rotary evaporation. This procedure yielded 0.65 g of material. A 0.62 g portion of the material was then vacuum transferred giving 0.39 g of a clear oil. The oil was analyzed by GLC (column A, 130°, 60 mL/minute) and found to contain 83% 1-vinylcyclonanol (117), 4% cyclononane, and 13% unknown materials. This implies a 30% yield of 117 from cyclooctanone. NMR (CCl₄) δ 5.92 (d of d, J=11, 18 Hz, 1H), 5.14 (d of d, J=2, 18 Hz, 1H), 4.92 (d of d, J=2, 11 Hz, 1H), 1.2-1.9 (broad m, 17H); IR (neat) 3600-3200, 3090, 2920, 1640, 995, 910 (cm⁻¹); m/e 168.151 (calcd for C₁₁H₂₀O: 168.151).

Preparation of 1-vinyl-1,2-cyclohexanediols 81a,b

A procedure like that of Barnier and Conia (65) for the synthesis of the 1-vinyl-1,2-cyclobutanediols was used. A vinyl magnesium bromide in THF solution (ca. 1 M) was prepared as described earlier. Thirty-seven mL (ca. 37 mmoles) of this solution was then added over 1.5 hours to a stirred (25°) solution of 1.00 g (8.8 mmoles) of 2-hydroxycyclohexanone (Aldrich) and 7 mL of THF. Stirring was continued overnight and the excess Grignard reagent was quenched by cautious addition of 10 mL of saturated ammonium chloride. The reaction mixture was then transferred to a separatory funnel with 50 mL of ether, and the aqueous layer was drained off. The organic layer was then washed with five 10 mL portions of water, 10 mL of saturated sodium bicarbonate, and 10 mL of brine. After drying the
layer over magnesium sulfate, filtering, and removing the solvent at reduced pressure, 0.52 g of a light yellow oil remained. A 0.30 g portion of the material was vacuum transferred (90-95° at 0.4 mm) affording 0.24 g (33% adjusted yield) of a mixture of 1-vinyl-1,2-cyclohexanediols (clear semi-solid). IR (neat) 3600-3100, 3090, 2930, 2850, 1640, 1000, 990, 920, 870, 810 (cm⁻¹); Anal. Calcd for C₈H₁₄O: C, 67.55; H, 9.93. Found: C, 67.63; H, 9.56. When analyzed (and purified) by GLC (column J, 130°, 50 mL/minute), the semi-solid showed no starting material peak, a peak at 4.6 minutes retention time (64%), and a peak at 5.8 minutes retention time (36%).

Compound 81a (4.6 minutes): NMR (CCl₄) δ 5.95 (d of d, J=11, 18 Hz, 1H), 5.40 (d of d, J=2, 18 Hz, 1H), 5.20 (d of d, J=2, 11 Hz, 1H), 3.35-3.7 (m, 1H), 2.4-2.6 (broad s, 1H), 2.2-2.4 (broad s, 1H), 1.2-2.0 (broad m, 8H); mass spectrum m/e (rel %) 124 (6.1), 98 (20.1), 96 (22.5), 95 (31.5), 85 (70.4), 83 (73.2), 70 (100), 67 (28.5).

Compound 81b (5.8 minutes): NMR (CCl₄) δ 6.24 (d of d, J=11, 18 Hz, 1H), 5.42 (d of d, J=2, 18 Hz, 1H), 5.26 (d of d, J=2, 11 Hz, 1H), 3.4-3.65 (m, 1H), 3-3.4 (broad s, 2H), 1.2-2.0 (broad m, 8H); mass spectrum m/e (rel %) 124 (5.7), 98 (18.4), 96 (22.0), 95 (26.1), 85 (69.4), 83 (63.3), 70 (100), 67 (29.0).

Obtained by inspection of the spectrum of the mixture.
The procedure for making cyclooctanone trimethylsilyl enol ether (119) was the same as the general procedure B of House, Czuba, Gall, and Olmstead (35). A 100 mL flask was charged with 22 mL (40 mmoles) of 1.82 M methyllithium in ether. The ether was evaporated at reduced pressure, and then 30 mL of dry DME plus a few crystals of triphenylmethane were added. The deep red solution was then cooled in an ice-salt bath and 5.5 mL (39 mmoles) of diisopropyl amine was added via syringe over 5 minutes, and the color faded to a faint pink. Then a solution of 5.00 g (39 mmoles) of cyclooctanone in 10 mL of DME was added over 10 minutes to the ice-cold solution of lithium diisopropyl amide. A quenching solution was then prepared by mixing 20 mL of DME, 2 mL of triethylamine, and 8 mL of chlorotrimethylsilane. The solution was centrifuged, and the solution was transferred to a dropping funnel with a pipette. The quenching solution was then added to the lithium enolate over 5 minutes while the reaction vessel was kept at 0°. The reaction mixture was then allowed to warm to room temperature and stirred for 15 minutes. The contents of the reaction vessel were then transferred to a separatory funnel with 150 mL of cold pentane, and the organic layer was washed with three 100 mL portions of cold saturated sodium bicarbonate, dried over magnesium sulfate, filtered,
and the solvent removed at reduced pressure. This procedure gave 7.84 g of a clear, light oil. IR (neat) 3050, 2920, 2850, 1160, 1470, 1450, 1370, 1260, 1170, 1120, 1090, 1020, 960, 860, 760, 680 (cm⁻¹).

The procedure used for making 2-trimethylsiloxycyclooctanone (120) was the same as the general procedure formulated by Hassner, Ruess, and Pinnick (36). A solution of 7.8 g (ca. 36 mmoles) of the crude trimethylsilylenol ether 119 from above and 50 mL of methylene chloride was stirred at room temperature and treated with 8.84 g (44 mmoles) of m-chloroperbenzoic acid (Aldrich 85%). The peracid was added over 30 minutes in small solid portions. The reaction mixture was then stirred for 1.25 hours at room temperature. Thirty mL of 10% sodium sulfite were then added, and the mixture was stirred for another 15 minutes. The reaction mixture was then transferred to a separatory funnel with 50 mL of methylene chloride, and the organic and aqueous layers were separated. The organic layer was then washed with five 20 mL portions of saturated sodium bicarbonate and 20 mL of 10% sodium sulfite and dried over magnesium sulfate. The solution was then tested for peroxides with starch-potassium iodide paper and acidified potassium iodide. There was no significant color noted, so the organic layer was filtered, and the solvent was removed in vacuo at room temperature. This procedure gave 6.9 g of a clear oil. A 2.4 g portion of the oil was then distilled on an 18 cm
Vigreux column, and 0.91 g of material boiling at 78° (0.2 mm) was collected. The NMR spectrum showed a singlet at δ -0.26, and the IR spectrum showed a medium band 3600-3200 and a strong band 1705 (cm\(^{-1}\)). GLC analysis (column G, 170°, 71 mL/minute) showed two major peaks at 2.5 and 4.2 minutes retention time in a ratio of 36:64 respectively.

Application of the method of Friedman and Kaufman (57) to hydrolyze the 2-trimethylsiloxy group resulted in only a 16% recovery of material so an alternate procedure was adopted. A 0.84 g portion of the mixture from above was stirred for 20 minutes in a room temperature solution of 4 mL of water and 4 mL of glacial acetic acid. The mixture was then made basic with 15% sodium hydroxide and extracted with five 6 mL portions of ether. The ether layer was then dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure affording 0.40 g of a white solid crude suberoin (121) mp 123-128 (lit. (66) 37-38.5°). The material was analyzed by GLC (column G, same conditions as above), and showed one major peak (89%) at 2.5 minutes retention time. IR (CH\(_2\)Cl\(_2\)) 3490 cm\(^{-1}\) (2.9 μ) and 1700 cm\(^{-1}\) (5.9 μ, lit. (67) 2.92 and 5.90 μ). A small portion of the crude suberoin from above was purified by GLC.

35 The discrepancy between this mp and that reported by Cope et al. (66) could be due to the presence of suberoin dimer. Bloomquist and Liu (67) reported that their suberoin (mp 53-57°) probably contained suberoin dimer.
(column G, 170°, 71 mL/minute) for mass spectral analysis. Mass spectrum (40°) m/e (rel %) 142 (9.7), 124 (14.9), 57 (100); 100°) 157 (21), 138 (53), 55 (100); m/e 142.100 (calcd for C₈H₁₄O₂: 142.099).

A solution of 0.38 g of the crude suberoin from above in 7 mL of THF was treated with 37 mL (ca. 37 mmoles) of vinyl magnesium bromide in THF solution (prepared as described earlier). The reaction mixture was stirred at room temperature overnight, and then quenched by cautious addition of 20 mL of saturated ammonium chloride. The reaction mixture was then taken up in 50 mL of ether, and the aqueous and organic layers were separated. The organic layer was then dried over magnesium sulfate, filtered, and the solvent was removed by rotary evaporation affording 0.40 g of a dark oil. A 0.24 g sample of the oil was then vacuum transferred to give 0.14 g (9% adjusted overall yield from cyclooctanone) of a clear oil. The oil was analyzed by GLC (column G, 180°, 70 mL/minute) and found to contain 81% of the desired 1-vinyl-1,2-cyclooctandiols 83a,b. The material was purified by GLC (column G, 180°, 70 mL/minute) to provide the analytical samples. NMR (CCl₄) δ 5.98 (d of d, J=11, 18 Hz, 1H), 5.34 (d of d, J=2, 18 Hz, 1H), 5.14 (d of d, J=2, 11 Hz, 1H), 5.14 (d of d, J=2, 11 Hz, 1H), 3.75 (d, J=9 Hz, 1H), 2.8-3.3 (broad s, 2H, shifts upon warming to 60°), 1.2-1.9 (broad m,
IR (neat) 3700-3100, 3080, 2930, 2850, 1460, 1440, 1040, 1020, 980, 910, 740 (cm\(^{-1}\)); m/e 170.130 (calcd for C\(_{10}\)H\(_{18}\)O\(_2\): 170.131; Anal. Calcd for C\(_{10}\)H\(_{18}\)O\(_2\); C, 70.53; H, 10.66. Found: C, 70.50; H, 10.45.

Preparation of γ-anisoylbutyric acid (124b)

The same procedure as Barltrop, Johnson, and Meakins (68) used to prepare γ-(3,4-dimethoxybenzoyl)-butyric acid was employed for the synthesis of γ-anisoylbutyric acid. The reaction of 70 g (0.61 moles) of glutaric anhydride (Aldrich), 700 g (6.5 moles) of anisole, and 182 g (1.4 moles) of aluminum chloride gave 122 g (90% crude yield) of γ-anisoylbutyric acid (mp 125-133°). Recrystallization from water gave a white solid, mp 135.0-136.8° (lit (69) 137°). NMR (CDCl\(_3\)) 7.9-8.1 (m, 2H), 6.9-7.1 (m, 2H), 3.87 (s, 3H), 3.02 (5, J=7 Hz, 2H), 2.50 (m, 2H), 2.07 (m, 2H). 37

Preparation of 5-(p-methoxyphenyl)-pentanoic acid (125b)

The Clemmensen-Martin (70) method was used to produce 58 g (95% crude yield) of a white solid (mp 108.5-110.0°) from 65 g of

36 Another vinyl signal, δ 6.02 (d of d, J=11, 18 Hz), is visible and makes up about 40% of the intensity of the main signal. It presumably arises from the minor diastereomer.

37 No COOH signal observed under these conditions.
γ-anisoylbutyric acid. The product was recrystallized from water/acetone to give 5-(p-methoxyphenyl)-pentanoic acid, mp 110.5-111.5° (lit. 113-114.5). NMR (CDCl₃) 10.8-11.4 (broad s, exchanges with D₂O, 1H), 7.0-7.2 (m, 2H), 6.76-6.96 (m, 2H), 3.76 (s, 3H), 2.48-2.75 (m, 2H), 2.25-2.48 (m, 2H), 1.55-1.85 (m, 4H).

Attempted Cyclization of 5-(p-methoxyphenyl)-pentanoic acid with polyphosphoric acid

Attempted cyclization of 6.5 g of 5-(p-methoxyphenyl)-pentanoic acid by the method of Gilmore and Horton (37) produced 2.8 g of an amber tar which was not volatile at 200° and 0.5 mm.

Attempted Cyclization of 5-(p-methoxyphenyl)-pentanoic acid with phosphorus pentoxide in benzene

Application of the method that Caunt, Crow, Haworth, and Vodoz (38) used to cyclize 5-(3,4-dimethoxyphenyl)-pentanoic acid gave 4.2 g of material from 5.0 g of acid 125b. The product tarred severely when a vacuum transfer (95° at 0.5 mm) was attempted.

Attempted Cyclization of 5-(p-methoxyphenyl)-pentanoic acid chloride (160) with aluminum chloride in methylene chloride

The acid chloride 160 was generated by the method of Johnson and Shelberg (41) from 5.0 g (0.024 moles) of acid 125b and 8.3 g (0.04 moles) of phosphorus pentachloride. The crude acid chloride
was then subjected to the cyclization conditions of House and Hudson (39), and an intractable amber gum was produced.

**Preparation of γ-benzoyl-butyric acid (124a)**

Application of the method of Somerville and Allen (71) gave 181 g (63%) of a white solid (mp 124.5-125.0°, lit. (71) 125-126°) from 176 g (1.5 moles) of glutaric anhydride (Aldrich), 463 g (3.5 moles) of aluminum chloride, and 515 mL of dry benzene. NMR (CDCl₃) 7.9-8.1 (m, 2H), 7.35-7.7 (m, 3H), 3.08 (t, J=7 Hz, 2H), 2.50 (t, J=7 Hz, 2H), 2.08 (t, J=7 Hz, 2H).

**Preparation of δ-phenylvaleric acid (125a)**

The Clemmensen-Martin (70) method was used to produce 82.2 g (99% crude yield) of δ-phenylvaleric acid (mp 48-50°, lit., 51-54°) from 89.2 g of γ-benzoylbutyric acid. NMR (CCl₄) δ 10.65-10.85 (broad s, 1H), 7.0-7.3 (m, 5H), 2.45-2.7 (broad m, 2H), 2.2-2.4 (broad m, 2H), 1.5-1.9 (broad m, 4H).

**Preparation of benzosuberone (123a)**

Cyclization of 25.0 g of δ-phenylvaleric acid by the method of Gilmore and Horton (37) followed by distillation (97° at 3 mm) gave

---

\[38\text{No -COOH signal observed under these conditions.}\]
8.9 g (40%) of a clear liquid. The IR spectrum of the liquid (neat) matched that of an authentic sample (ROC/RIC).

Preparation of 5-aminomethyl-6,7,8,9-tetrahydro-5-benzocycloheptenol (127)

A procedure similar to that of Evans, Carroll, and Truesdale (34) was used. A 100 mL, one-necked flask (equipped with magnetic stirrer and nitrogen atmosphere) was charged with 2.0 g (0.05 moles) of lithium aluminum hydride and 50 mL of dry ether. This mixture was stirred for 30 minutes and then allowed to settle. Another 100 mL flask (similarly equipped) was charged with 5.02 g (0.031 moles) of benzosuberone (Aldrich, freshly vacuum transferred), and the flask was cooled in an ice bath. Meanwhile a 4 in. test tube was loaded with ca. 1 g (3 mmoles) of zinc iodide (City Chemical Co.) and quickly evacuated to 0.2 mm. The zinc iodide was then sublimed twice with gentle flame heating, cooled, and placed under a nitrogen atmosphere. The test tube was then equipped with a stirring bar, 5 mL (ca. 0.043 moles) of trimethylsilyl cyanide was added via syringe, and the mixture was stirred for 5 minutes. The trimethylsilyl cyanide/zinc iodide slurry was then added to the ice cold benzosuberone over ca. 1 minute, and this mixture was stirred for 15

39 The vials were preweighed, dried, and then loaded in a dry bag under nitrogen.
minutes. The reaction vessel was then equipped with a dropping funnel which was loaded with the clear part of the lithium aluminum hydride/ether mixture (prepared in the first part of the procedure). This solution was added (over 15 minutes) to the ice cold trimethylsilyl cyano-hydrin just formed. The rest of the grey lithium aluminum hydride/ether suspension was then added dropwise with a large bore pipette. The mixture was then stirred vigorously 15 minutes at ice temperature and 30 minutes at room temperature, and re-cooled in the ice bath. The reaction mixture was then quenched by cautious addition of 2 mLs of water, 2 mLs of 15% sodium hydroxide, and 6 mL of water (58). The mixture was then stirred until the solids became white and granular (ca. 1 hour) and filtered. The solids were then washed thoroughly with twelve 25 mL portions of ether, and the combined ether layer was extracted with six 50 mL portions of 8.6% sulfuric acid. The acidic extract was then made basic (pH ca. 10) with ca. 125 mL of 15% sodium hydroxide with frequent cooling in a cold water bath. The basic layer was then extracted with six 50 mL portions of chloroform, and the chloroform extract was dried over magnesium sulfate, filtered, and most of the solvent removed by rotary evaporation. The material was then placed under a 0.2 mm vacuum overnight, and 5.07 g (84%) of a white solid (mp 74.0-76.3°) was obtained. This material was recrystallized from redistilled petroleum ether to yield crystals of mp 73.0-73.8°. The material
was recrystallized again from petroleum ether to give a white solid mp 94.3-94.5°. Samples of the material from different preparations gave the higher melting range when recrystallized from petroleum ether. Spectral data and analysis is for material with the higher melting range. NMR (CDCl₃) δ 7.6-7.8 (m, 1H), 7.0-7.35 (m, 3H), 2.7-3.36 (m, 4H), 1.5-2.5 (broad m, 9H, reduces to 6H when treated with D₂O); IR (KBr pellet) 3350, 3300, 3100, 2910, 2850, 1600, 1480, 1450, 1360, 1330, 1280, 1230, 1200, 1170, 1120, 1090, 1040, 1000, 990, 950, 860, 760, 740 (cm⁻¹); mass spectrum m/e (rel %) 191 (1.7), 161 (100); Anal. Calcd for C₁₂H₁₇NO: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.49; H, 8.95; N, 7.41.

Preparation of 7,8,9,10-tetrahydro-6(5H)-benzocyclooctenone (122)

A 4.77 g (0.025 moles) portion of unrecrystallized 5-amino-methyl-6, 7, 8, 9-tetrahydro-5-benzocycloheptenol (127) was taken up in 50 mL of 10% acetic acid, and the mixture was cooled in an ice bath. Then 32 mL (0.04 moles) of 1.25 M sodium nitrite was added, and the mixture was stirred for 30 minutes at ice temperature and overnight at room temperature. The reaction mixture was then rechilled in an ice bath and made basic (pH ca. 10) with 15% sodium hydroxide. The basic mixture was then extracted with five 20 mL portions of ether, and the ether extract was washed with two 10 mL
portions of saturated ammonium chloride, dried over magnesiu
sulfate, filtered, and the solvent was removed by rotary evaporation. The residue was then vacuum transferred (120° at 1 mm) producing 3.49 g (80%) of a clear liquid. The liquid was analyzed by GLC (column M, 155°, 138 seconds) and by GLC-mass spectrometry (column M, 165°, 100 seconds) and the results are presented in Table 8. The semicarbazone was prepared and precipitated twice from benzene to give a white solid, mp 163-166.5° (lit. (44) 177.5-178°). The material was purified by GLC (column I, 215°, 57 mL/minute) to provide the analytical samples. NMR (CCl₄) δ 7.05-7.2 (m, 4H), 3.68 (s, 2H), 2.73-2.9 (m, 2H), 2.17-2.33 (m, 2H), 1.55-2.0 (broad m, 4H); IR (neat) 3060, 3020, 2940, 2860, 1700, 1600, 1580, 1500, 1450, 1350, 1330, 1280, 1260, 1240, 1190, 1170, 1120, 1050, 1000, 960, 880, 760, 720, 710 (cm⁻¹); mass spectrum m/e (rel %) 174 (68.3), 118 (100); Anal. Calcd for C₁₂H₁₄O: C, 82.72; H, 8.10. Found: C, 82.45; H, 8.13.

Table 8. Mass Spectral Data for Rearrangement Products of 127

<table>
<thead>
<tr>
<th>Retention time</th>
<th>Relative area</th>
<th>Molecular ion (m/e)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.9 min</td>
<td>3%</td>
<td>160</td>
<td>spectrum similar to that of 123a</td>
</tr>
<tr>
<td>9.3 min</td>
<td>6%</td>
<td>174</td>
<td>spectrum and retention time similar to that of 128</td>
</tr>
<tr>
<td>10.3 min</td>
<td>82%</td>
<td>174</td>
<td>major product 122</td>
</tr>
<tr>
<td>11.1 min</td>
<td>9%</td>
<td>190</td>
<td></td>
</tr>
</tbody>
</table>

304 Crystals would not form
Preparation of 7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (132)

A solution of 0.218 g (1.3 mmoles) of 7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenone (122) in 1.25 mL of ether was added dropwise to a room temperature mixture of 0.28 g (7 mmoles) of lithium aluminum hydride and 5 mL of ether. The reaction mixture was then stirred for 1 hour at room temperature. The mixture was then cooled in an ice bath, and the excess lithium aluminum hydride was quenched by cautious addition of 0.3 mL of water, 0.3 mL of 15% sodium hydroxide, and 1.0 mL of water (58). The white precipitate which formed was filtered off, and the filtrate was dried over magnesium sulfate. The ether solution was then refiltered, and the ether was removed by rotary evaporation affording 0.210 g of material. A 0.178 g portion of this material was then vacuum transferred (110° at 0.35 mm) to give 0.162 g of a clear oil. The oil was purified and analyzed by GLC (column N, 225°, 75 mL/minute) and found to contain 41% starting ketone 122, 1% unknown material, and 58% of the desired alcohol 132 (implies a 50% overall yield). The purified material showed $n_D^{22}$ 1.557 (lit. $n_D^{22}$: 1.5572 (74), 1.5573 (44)). NMR (CCl$_4$) $\delta$ 7.05 (s, 4H), 3.7-3.95 (m, 1H), 2.6-3.0 (m, 5H, contains s at 2.65 which shifts upon warming to 60°), 1.0-1.9 (m, 6H); IR (neat) 3600-3100, 3050, 3005, 2920, 2850, 1485, 1465, 1445, 1345, 1110, 1060, 1025, 965, 745, 710 (cm$^{-1}$); m/e 176.119 (calcd for C$_{12}$H$_{16}$O: 176.120).
Preparation of 7,8,9,10-tetrahydro-6-vinyl-6(5H)-benzocyclooctenol (85b)

A vinyl magnesium bromide in THF solution was prepared as described earlier from 7 mL (ca. 0.1 moles) of vinyl bromide, 1.4 g (0.06 g-atoms) of magnesium, and 20 mL of THF. To this was added dropwise a solution of 3.00 g (0.014 moles) of 82% 7,8,9,10-tetrahydro-6(5H)-benzocyclooctenone (122) and 10 mL of THF. The mixture was heated at ca. 40° for 1.5 hours, and then quenched by cautious addition of 15 mL of water. The organic layer was then washed with three 50 mL portions of 10% sulfuric acid, and these washings were extracted with five 40 mL portions of ether. The combined organic layers were then washed with two 125 mL portions of saturated sodium bicarbonate, dried with magnesium sulfate, filtered, and the solvent was removed by rotary evaporation. This material was vacuum transferred (130-140° at ca. 0.1 mm) which produced 3.22 g of a clear, viscous oil. GLC analysis of the oil (column I, 225°, 66 mL/minute) showed that the oil consisted of the following: 10% material with the same retention time as the 9% impurity in the starting material, 8% material with the same retention time as the starting ketone 122, and 81% of the desired alcohol 85b. This analysis implies a 75% (uncorrected) yield. Analytical samples were purified by GLC (column I, 235°, 57 mL/minute). NMR (CCl4) δ 7.06 (s, 4H), 6.03 (d of d, J=11, 18 Hz, 1H), 5.26 (d of d, J=2, 18 Hz,
1H), 5.05 (d of d, J=2, 11 Hz, 1H), 2.6-3.0 (broad m, 4H), 1.2-1.9 (broad m, 7H); IR (neat) 3400 (broad), 3070, 3030, 2940, 2860, 1645, 1500, 1475, 1455, 1420, 1170, 1140, 1120, 1050, 1000, 930, 760, 715 (cm⁻¹); mass spectrum m/e (rel %) 202 (8.3), 184 (100), 55 (100); Anal. Calcd for C₁₄H₁₈O: c, 83.12; H, 8.97. Found: c, 82.93; H, 8.75.

A second procedure involved addition of eight 5 mL portions of vinyl magnesium bromide in THF solution (prepared as before, each portion contained ca. 5 mmoles of vinyl magnesium bromide) to a refluxing solution of 1.27 g (ca. 6.0 mmoles) of 82% 7,8,9,10-tetrahydro-6(5H)-benzocyclooctenone (122) in 6 mL of THF. One tenth to 0.2 mL of methanol were added between each portion of Grignard reagent to quench any enolate of 122 formed. The whole process was followed by GLC (column G, 235°, 50 mL/minute), and after 4.75 hours, the reaction vessel was cooled, and 25 mL of saturated ammonium chloride was cautiously added. The reaction mixture was then transferred to a separatory funnel with 40 mL of ether, and the aqueous and organic layers were separated. The organic layer was then dried over magnesium sulfate, filtered, and the solvent removed by rotary evaporation, producing 1.63 g of a slightly colored, viscous oil. A 1.44 g portion of this material was then vacuum transferred (128° at 1 mm) to give 1.06 g of a clear oil. GLC analysis (column G, 200°, 59 mL/minute) showed that the oil contained 84% (S=1) of
alcohol \textit{85b} indicating the overall yield to be 61\%. Alcohol \textit{85b} was found to have a response factor of 1.24 (S=0.02) relative to benzosuberone, the internal standard used for the yield study. The material produced by this method had the same spectral features as the 7, 8, 9, 10-tetrahydro-6-vinyl-6(5H)-benzocyclo\textcircled{o}ctenol produced by the previous method.

\textbf{Preparation of 7, 8, 9, 10-tetrahydro-6-trimethylsiloxy-6-vinyl-5H-benzocyclo\textcircled{o}ctene (85a)}

A 0.53 g portion of a crude mixture containing ca. 60\% \textit{85b} was silylated by method B (described earlier) giving 0.65 g of a clear oil. This oil was vacuum transferred (120\° at 0.2 mm) giving 0.55 g of a clear oil. GLC analysis (column G, 220\°, 60 mL/minute) showed the peak area of silylated alcohol \textit{85a} to 91\% (S=1) of the total area of the chromatogram. This implies that the overall yield is ca. 70\%. The analytical samples were purified by GLC (column I, 210\°, 60 mL/minute). NMR (CCl\textsubscript{4}, p-dioxane reference) δ 7.05 (s, 4H), 6.04 (d of d, J=11, 17 Hz, 1H), 5.12 (d of d, J=2, 17 Hz, 1H), 5.10 (d of d, J=2, 11 Hz, 1H), 2.56-2.88 (broad m, 4H), 1.26-1.86 (broad m, 6H), 0.04 (s, 9H); IR (neat) 3070, 3030, 2950, 2870, 1640, 1500, 1480, 1460, 1420, 1360, 1310, 1260, 1230, 1190, 1170, 1140, 1120, 1090, 1070, 1050, 1000, 960, 920, 910, 840, 760, 730 (cm\textsuperscript{-1}); mass spectrum m/e 274 (2.7), 149 (100); m/e 274.174 (calcd for C\textsubscript{17}H\textsubscript{26}OSi: 274.175.
Preparation of 2-methyl-1-phenyl-but-3-en-2-ol (95)

A solution of 2.50 g (18.7 mmol) of phenyl-2-propanone (161) (Matheson, Coleman, and Bell) and enough THF to make 7.5 mL total volume was added over 15 minutes to 25 mL (ca. 25 mmol) of vinyl magnesium bromide in THF (page 82) at room temperature. The mixture was then stirred for 1.42 hours, and the excess Grignard reagent was quenched by cautious addition of 10 mL of saturated ammonium chloride. The aqueous and organic layers were then separated, and the aqueous layer was extracted with five 10 mL portions of ether. The combined organic layers were then dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure affording 2.90 g of a light yellow oil. A 1.49 g portion of the oil was then distilled (85-90° at 0.4 mm) to give 1.38 g of a clear oil. The oil was analyzed by GLC (column O, 135°, 23 seconds) and found to contain 3.4% starting ketone (by retention time) and 96.6% 2-methyl-1-phenyl-but-3-en-2-ol (86% overall yield). NMR (CCl₄): δ 7.14 (s, 5H), 5.90 (d of d, J=11, 18 Hz, 1H), 5.08 (d of d, J=2, 18 Hz, 1H), 4.94 (d of d, J=2, 11 Hz, 1H), 2.72 (s, 2H), 2.18 (broad s, shifts on warming to 60°, 1H), 1.18 (s, 3H); IR (neat) 3700-3150, 3090, 3060, 3030, 2980, 1640, 1610, 1590, 1500, 1460, 1420, 1380, 1290, 1240, 1160, 1100, 1060, 1040, 1020, 1000, 920, 880, 770, 720, 700 (cm⁻¹); mass
Preparation of 1,1-diphenyl-2-propen-1-ol (98)

A procedure like that of Nouri-Bimorghi (75) was used. A solution of 3.46 g (19 mmoles) of benzophenone and enough THF to make 7.5 mL total volume was added over 4 minutes to 25 mL (ca. 25 mmoles) of vinyl magnesium bromide in THF (page 82) (at 25°). The mixture was then stirred for 1.33 hours at room temperature, and the excess Grignard reagent was quenched by cautious addition of 15 mL of saturated ammonium chloride at 0°. The aqueous and organic layers were then separated, and the aqueous layer was extracted with five 10 mL portions of ether. The organic layer and ether extracts were then combined and dried over magnesium sulfate, filtered, and the solvent removed at reduced pressure yielding 3.84 g of a light amber oil. The oil was analyzed by GLC (column A, 205°, 55 mL/minute) and found to contain a single product. A 2.80 g portion of the oil was vacuum transferred (130-135° at 0.4 mm) to give 2.71 g (92% overall adjusted yield) of a clear oil. NMR (CCl₄) δ 7.0-7.5 (m, 10H), 6.32 (d of d, J=11, 17 Hz, 1H), 5.15 (m, J=2, 17 Hz, 1H), 5.13 (m, J=2, 11 Hz, 1H), 2.65 (s, shifts on warming to 60°,

41 The mass spectrum of a larger quantity of this material shows a very clear m/e 162 molecular ion as it first vaporizes from the direct inlet probe.
1H), IR (neat) 3600-3200, 3080, 3040, 3020, 1600, 1490, 1440, 1320, 1170, 1070, 990, 960, 910, 890, 770, 755, 690 (cm\(^{-1}\)); mass spectrum m/e (rel %) 210 (16.5), 105 (100).

Preparation of 6-cyclopropyl-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (100)

The method used to generate cyclopropyl magnesium bromide was similar to that used by Fontaine, Andre, Joliet, and Maitte (76). A mixture of 0.60 g (5 mmoles) of cyclopropyl bromide (Aldrich), 5 mL of THF, and 0.11 g (4.5 g-atoms) of magnesium was treated with a few crystals iodine. A vigorous reaction ensued, and the mixture was stirred for 30 minutes. A solution of 0.533 (2.5 mmoles) of 82% 7,8,9,10-tetrahydro-6(5H)-benzocyclooctenone (122) and 3.5 mL of THF was then added over 10 minutes, and the mixture was stirred for another 1.33 hours. The excess Grignard reagent was quenched by addition of 5 mL of saturated ammonium chloride, and the reaction mixture was transferred to a separatory funnel with 30 mL of ether. The aqueous layer was then drained off, and the organic layer was washed with 10 mL of saturated sodium bicarbonate, dried over magnesium sulfate, filtered, and the solvent removed by rotary evaporation. This procedure afforded 0.613 g of a light, amber oil. A 0.241 g portion of the amber oil was vacuum transferred (90-100° at 0.4 mm) to give 0.180 g of a clear oil. The oil was analyzed by
GLC (column G, 215°, 48 mL/minute) and found to contain 58% 100, 33% 122, and 9% of an unknown substance. This corresponds to a 50% overall yield. The 6-cyclopropyl-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol was obtained in pure form by preparative GLC (column G, 225°, 65 mL/minute). NMR (CCl₄, CH₂Cl₂ reference) δ 7.15 (s, 4H), 2.7-3.0 (m, 4H), 1.3-1.95 (m, 6H), 0.85-1.2 (m and broad s, 2H, s shifts upon warming to 60°), 0.25-0.7 (m, 4H); IR (neat) 3700-3200, 3080, 3070, 3000, 2910, 2850, 1600, 1490, 1470, 1450, 1390, 1360, 1330, 1310, 1300, 1250, 1220, 1200, 1170, 1140, 1100, 1040, 1020, 1000, 990, 940, 920, 890, 880, 860, 820, 750, 730, 700 (cm⁻¹); mass spectrum m/e (rel %) 216 (50.9), 198 (11.3), 84 (100); m/e 216.151 (calcd for C₁₅H₂₀O: 216.151).

Preparation of 6-(3-buten-1-ynyl)-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenol (133)

The procedure for making the lithium salt of 1-buten-3-yne was similar to that used by Tarrant, Savoy and Iglehart (77) for the production of propynyllithium. A 50 mL, 3-necked flask (equipped with dropping funnel, condensor, magnetic stirrer, and nitrogen atmosphere) was charged with 25 mL of ether and 8 mL (21 mmoles) of 2.6 M methylolithium in ether. The mixture was cooled in an ice bath, and 3.5 mL (ca. 24 mmoles) of 1-buten-3-yne (162) (Chemical Samples Co., 50% in xylene) was added with a cold syringe. The
ice bath was removed after a few minutes, and the reaction mixture was stirred overnight at room temperature. The ether was then evaporated with a nitrogen stream, and then 25 mL of THF was added. The mixture was then warmed in a 50° bath, and a solution of 2.03 g (9.6 mmoles) of 82%, 7, 8, 9, 10-tetrahydro-6(5H)-benzocyclooctenone (1.22) in enough THF to make 10 mL of solution was added over a 5 minute period. The mixture was then stirred for 9.25 hours, and then cooled in an ice bath. The reaction was then quenched by cautious addition of 10 mL of water. The aqueous and organic layers were then separated, and the organic layer was washed with 30 mL of brine. The aqueous layer was then extracted with three 10 mL portions of ether, and these extracts were combined with the organic layer from above. The combined organic layer was then dried over magnesium sulfate, the solvent was removed by rotary evaporation, and the material was vacuum transferred (130-150° at 0.2 mm) to give 2.31 g of a viscous oil. GLC analysis (column C, 254°, 45 mL/minute) showed that the oil contained 77% (68% overall uncorrected yield) of the desired alcohol 1.33. Purification by GLC (column G, 235°, 60 mL/minute) gave the analytical samples. NMR (CCl₄) δ 7.0-7.3 (m, 4H), 5.81 (d of d, J=10, 17 Hz, 1H), 5.53 (d of d, J=4, 17 Hz, 1H), 5.41 (d of d, J=4, 10 Hz, 1H), 3.03 (s, 2H), 2.65-2.9 (broad m, 2H), 1.2-2 (broad m, 7H); IR (neat) 3600-3150, 3100, 3060, 3010, 2930, 2850, 1610, 1490, 1470, 1450, 1410, 1360, 1340, 1300, 1260,
UV \lambda (C_{2}H_{5}OH) nm(e) 214 (1.5 \times 10^{4}), 223 (1.3 \times 10^{4}), 224 (1.0 \times 10^{4});

mass spectrum m/e (rel %) 226 (17.7), 79 (100); m/e 226.135 (calcd for C_{16}H_{18}O: 226.136.

Preparation of cis and trans-6-(1,3-butadienyl)-7,8,9,10-tetrahydro-6(5H)-trimethylsiloxo-benzocyclooctene (107a, b)

The method used to reduce butenynol 133 to the dienols 103a, b was like that described earlier for the corresponding HMPA rearrangement. From 0.60 g (2 mmoles) of 77% 6-(3-buten-1-ynyl)-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (133) was obtained 0.58 g of a crude mixture of dieneols. The material was then silylated by method A (described earlier) affording 0.63 g of crude silyl derivative. A 0.187 g portion of the crude material was then vacuum transferred (115° at 0.45 mm) to give 0.170 g of a clear oil. The oil was purified and analyzed by GLC (column P, 255, 60 mL/minute). The analysis indicated that the material contained 70% of the trimethylsiloxyl dienes 107a, b (18% shorter retention time 107a and 52% longer retention time 107b). This analysis indicates a 66% overall yield of the dienes 107a, b. Compound 107a (shorter retention time): NMR (CCl_{4}) \delta 7.06 (s, 4H), 4.95-6.4 (m), 42 2.65-2.85

\footnote{Sample too weak to give proper integration or peak intensity.}
Compound 107b (longer retention time): NMR (CCl₄) δ 7.01 (s, H), 5.31-6.51 (m, 3H), 5.15 (d of d, J=2, 15 Hz, 1H), 5.01 (d of d, J=2, 8 Hz, 1H), 2.55-3.05 (broad m, 4H), 1.3-1.87 (broad m, 6H); IR (CCl₄) 3055, 3015, 2920, 2845, 1255, 1245, 1175, 1000, 970, 900, 840, 735 (cm⁻¹); UVλ (C₂H₅OH) nm(ε) 218 (2.5 X 10⁴), 227 (2.5 X 10⁴); mass spectrum m/e (rel %) 300 (20.8), 285 (5.8), 247 (18.6), 73 (100); m/e 300.190 (calcd for C₁₉H₂₈OSi: 300.191).

Preparation of 6-(cis-3-penten-1-yne)-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (134)

The procedure for forming the lithium salt of cis-3-penten-1-yne was similar to that used by Tarrant, Savoy, and Iglehart (77) for the production of propynyllithium. A 100 mL, 3-necked flask (equipped with condenser, magnetic stirrer, addition funnel, and nitrogen atmosphere) was charged with 28 mL (0.067 moles) of 2.4 M methyl-lithium in ether. The methyllithium solution was then chilled in an ice bath, and a solution of 4.6 g (0.070 moles) of cis-3-penten-1-yne (bp 44.5°, lit. (78) 44.6°) in 15 mL of ether was added over a 10 minute period. The mixture was then stirred overnight at room

43The author wishes to thank Dr. E. N. Marvell for his gift of the sample of cis-penten-1-yne.
temperature. The ether was then evaporated by a stream of nitrogen, 50 mL of THF was added, and the mixture was heated to reflux. A solution of 10.0 g (0.047 moles) of 82% 7,8,9,10-tetrahydro-6(5H)-benzocycloëctenone (122) plus enough THF to make 20 mL total volume was then added over ca. 2 hours. The reaction mixture was then cooled, and 10 mL of saturated ammonium chloride was added. The aqueous and organic layers were then separated, and the organic layer was washed with three 50 mL portions of water, 25 mL of saturated ammonium chloride, 25 mL of 10% sulfuric acid, and 25 mL of saturated sodium bicarbonate. The aqueous layer was then extracted with three 50 mL portions of ether. The ether extracts were combined with the organic layer from above, and the whole was dried over magnesium sulfate, filtered, and the solvent was removed by rotary evaporation. This procedure produced 14.3 g of a viscous oil which was then vacuum transferred (ca. 100° at 0.1 mm) giving 10.6 g of a clear oil.

A 10.5 g portion of the oil from above was then refluxed for 1.5 hours in a mixture of 120 mL of absolute ethanol, 12.6 mL of glacial acetic acid, and 7.0 g of Girard's Reagent T (Aldrich). The mixture was then poured into an ice-cold solution of 41 g of sodium bicarbonate in 700 mL of water. The aqueous layer was then quickly extracted with 350 mL of ether. The ether extract was dried over magnesium sulfate, filtered, and the solvent removed at reduced pressure. This
procedure gave 7.43 g of an oil containing 79% of the desired penteny-nol 134 (analyzed by GLC, column H, 205°, 70 mL/minute). This implies an overall yield of 43%.

A 0.719 g sample of the material from above (79% pentenynol) was chromatographed on a 2 ft. x 0.375 in. column containing 32 g of Woelm neutral alumina (activity III) (56). The column was eluted with a linear gradient (62) of hexane/ether, and the fractions containing the desired material, Rf = 0.27 (TLC on silica gel; solvent, chloroform) were collected, dried over magnesium sulfate, and the solvent in vacuo giving 0.526 g of oil. GLC analysis of the material (column G, 255°, 57 mL/minute) indicated that it then contained 73% of the desired alcohol 134.

A 0.477 g portion of the material containing 73% 134 was then silylated by method B (described earlier) affording 0.588 g of a mobile oil. A 0.518 g portion of this oil was then purified by GLC (column P, 260°, 83 mL/minute). A 1 cm x 10 cm sand collector was used to collect the 0.386 g (75% collection efficiency) of 6-(cis-3-penten-1-yny1)-7,8,9,10-tetrahydro-6(5H)-trimethylsiloxy-benzocyclooctene (164) obtained by this procedure. NMR (CCl₄, TMS reference) δ 6.95-7.3 (m, 4H), 5.9 (d of q, J=7, 10 Hz, 1H), 5.47 (d of q, J=2, 10 Hz, 1H), 3.05 (s, 2H), 2.65-2.9 (broad m, 2H), 1.3-2.0 (broad m, 9H, at 1.82 d of d, J=2, 7 Hz), (CCl₄, CH₂Cl₂ reference) δ 0.19 (s, 9H); IR (neat) 3060, 3030, 2940, 2850, 1495, 1470, 1450, 1400,
1360, 1320, 1300, 1250, 1230, 1190, 1160, 1150, 1110, 1070, 1030, 990, 950, 920, 900, 890, 840, 755, 720, 680 (cm\(^{-1}\)); mass spectrum m/e 312 (15.7), 297 (34.7), 73(100); m/e 312.190 (calcd for C\(_{20}\)H\(_{28}\)OSi: 312.191).

A 0.382 g sample of the silyl derivative was then hydrolyzed as previously described (2) affording 0.316 g of a clear oil. A 0.316 g portion of this oil was then vacuum transferred (165-175° at 0.5 mm) to give 0.274 g (21% overall yield from 122) of analytically pure 6-(cis-3-penten-1-ynyl)-7, 8, 9, 10-tetrahydro-6(5H)-benzocyclo-octenol (134). NMR (CC\(_4\)) \(\delta\) 7.0-7.25 (m, 4H), 5.89 (d of q, J=7, 11 Hz, 1H), 5.45 (d of q, J=2, 11 Hz, 1H), 3.05 (s, 2H), 2.7-2.9 (broad m, 2H), 1.45-2.0 (broad m, 10H; 1.82, d of d, J=2, 7 Hz); IR (neat) 3650-3150, 3060, 3030, 2940, 2850, 1500, 1470, 1450, 1400, 1365, 1340, 1300, 1260, 1220, 1160, 1140, 1110, 1090, 1070, 1050, 1020, 980, 950, 930, 910, 780, 755, 720, 710 (cm\(^{-1}\)); UV\(_\lambda\) (C\(_2\)H\(_5\)OH) nm(\(\varepsilon\)) 215 (1.7 X 10\(^4\)); mass spectrum m/e (rel %) 222 (14), 117 (100); m/e 240.152 (calcd for C\(_{17}\)H\(_{20}\)O: 240.151; Anal. Calcd for C\(_{17}\)H\(_{20}\)O: C, 84.94; H, 8.39. Found: C, 84.82; H, 8.65.

In another preparation, starting with 1.81 g of 82% 122, the reaction product (2.25 g) was purified on a 2 cm X 30 cm neutral alumina column (activity III) (56). The column was eluted with a linear gradient (62) of ether/hexane, and the fractions containing the
desired material were collected, dried over magnesium sulfate, filtered, and the solvent was removed by rotary evaporation. The material was then vacuum transferred giving 0.59 g (24%) of pentenynol 134. GLC analysis (column Q, 185°) of the material showed only one peak, and the spectral features were identical to those of the material prepared above.

Preparation of cis and trans-6-(1,3-cis-pentadienyl)-7,8,9,10-tetrahydro-6(5H)-trimethylsiloxo-
benzocyclooctene (108a,b)

The method used to reduce pentenynol 134 to the dienols 105a,b was like that described earlier for the corresponding HMPA rearrangement. From 0.290 g (0.95 mmole) of 79% 6-(cis-3-pentenyl)-7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (134) was obtained 0.286 g of a crude mixture of dienols 105a,b. The material was then silylated by method B (described earlier) affording 0.358 g of the crude silyl derivative. The material was then vacuum transferred (115° at 0.35 mm) yielding 0.320 g of a clear oil. The oil was purified and analyzed by GLC (purification: column P, 260°, 94 mL/minute; analysis: column C, 235°, 55 mL/minute), and the analysis showed 76% of the material to be the trimethylsiloxo dienes 108a,b; compound 108b: shorter retention time, 51%; compound 108a: longer retention time, 25%. This analysis indicates a 64% overall yield of the trimethylsiloxo dienes 108a,b. Compound 108b: NMR
(CCl₄) δ 7.0-7.1 (s, 4H), 5.3-6.6 (m, 4H), 2.65-3.0 (broad m, 4H), 1.3-1.9 (broad m, 9H, contains d of d at 1.75, J=2, 7 Hz) ((CH₃)₃Si - peak not looked for); (CCl₄) 3060, 3020, 2940, 2860, 1495, 1470, 1455, 1410, 1375, 1360, 1255, 1080, 980, 975, 845, 740 (cm⁻¹);

UVλ (C₂H₅OH) nm (ε) 235 (1.9X 10⁴); mass spectrum m/e (rel %) 314 (47), 299 (30), 73 (100); m/e 314.207 (calcd for C₂₀H₃₀O₅Si: 314.207). Compound 108a: NMR (CCl₄) δ 6.91-7.15 (s, 4H), 5.3-6.91 (m, 4H), 2.99 (s, 2H), 2.6-2.9 (broad m, 2H), 1.1-1.9 (broad m, 9H, contains d of d at 1.78, J=2, 7 Hz) ((CH₃)₃Si - peak not looked for); IR (CCl₄) 3060, 3020, 2930, 2850, 1265, 1255, 1070, 1000, 915, 845, 740 (cm⁻¹); UVλ (C₂H₅OH) nm(ε) 239 (2.2X10⁴) mass spectrum m/e (rel %) 315 (100), 299 (48), 196 (100).

Attempted Semi-hydrogenation of 6-(3-buten-1-ynyl)-
7,8,9,10-tetrahydro-6(5H)-benzocyclooctenol (133)
and 6-(cis-3-penten-1-ynyl)-
7,8,9,10-tetrahydro-6(5H)-benzocyclooctene (134) with Lindlar's catalyst

The catalyst was prepared by the method of Lindlar and Dubuis
and tested satisfactorily with phenylacetylene (164) (79).

A 5 mL, side-arm flask (equipped with septum, magnetic
stirrer, and attached to a low pressure hydrogenation apparatus) (40)
was charged with 0.002 g of catalyst and 0.2 mL of acetone. (45) To the

Logical mass loss analysis (i.e. peak 299 = M-15) indicate
that the true M⁺ is m/e 314.

Phenylacetylene was semi-hydrogenated satisfactorily under
these conditions.
stirred mixture was added a solution of 0.085 g (0.3 mmoles) of 77% butenynol and 0.8 mL of acetone. No hydrogen uptake was noted for 45 minutes so 5 mg of additional catalyst was added. The hydrogenation was then allowed to run for 20 additional minutes, during which time ca. 60% (4.5 mL) of the required volume of hydrogen was taken up. The catalyst was filtered off, and the solvent was removed by rotary evaporation. An NMR spectrum of the product did not show any significant changes in the vinyl region when compared to the spectrum of the starting material.

In another attempt, 0.037 g of 77% butenynol was purified by TLC (silica gel; developed 5 times with 5% ether/95% pentane), the band at Rf = 0.26 was collected, and the solvent removed affording 0.021 g of butenynol. After an unsuccessful attempt at semi-hydrogenation (i.e. no hydrogen uptake, 2.3 mL of hydrogen required) using a quinoline poison (79) the butenynol was recovered by vacuum transfer. The distilled material (0.0065 g, 0.03 mmoles) was stirred with 0.5 mg of catalyst, 0.005 mL of distilled quinoline, and 0.13 mL of hexane. No hydrogen uptake was observed (0.7 mL, required amount) in 7.5 hours. The above experiments with the purified butenynol were conducted on a micro-hydrogenation apparatus (constructed by the author) which was satisfactorily tested by semi-hydrogenating a mixture of 0.05 mL (0.46 mmoles) of phenylacetylene (required 10.5 mL to semi-hydrogenate), 2.4 mg of catalyst, and
0.13 mL of hexane. The volume change indicator of the device was sufficiently sensitive to detect volume changes of the magnitude required for the above hydrogenation attempts.

Another attempt using 0.198 g (0.7 mmoles, 17 mL of hydrogen required) of 79% pentenynol134, 1.5 mg of catalyst, 0.015 mL of quinoline, and 0.4 mL of cyclohexane showed no uptake of hydrogen for 1 hour.46

**Attempted Semi-hydrogenation of phenylacetylene with P-2 nickel boride**

The procedure of Brown and Brown (81) was used to make the catalyst. A 100 mL flask was charged with 1.24 g (5 mmoles) of nickel acetate and 40 mL of 95% ethanol. The flask was flushed with hydrogen, and 5 mL 95 mmoles) of 1 M sodium borohydride in ethanol was added. A black suspension (P-2 nickel boride) immediately formed. A 0.93 g portion (9.1 mmoles, required 222 mL for semi-hydrogenation) of phenylacetylene was then introduced into the flask via syringe. The hydrogenation was followed by plotting hydrogen uptake vs. time, and no cut-off point was noted until 448 mL of hydrogen had been absorbed over a period of 3.8 hours. An NMR

---

46Phenylacetylene was semi-hydrogenated successfully under these conditions in 2.17 hours. In 1 hour the phenylacetylene had taken up one half of the required amount of hydrogen.
spectrum of the product showed a quartet, $J=8 \text{ Hz at } \delta 3.6$ and a
triplet, $J=8 \text{ Hz at } \delta 1.1$ which indicated that over-hydrogenation had
taken place.

**Preparation of tri-n-butyltin hydride**

The procedure of van der Kerk, Noltes, and Luijten (82)
afforded 14.35 g (83%) of tri-n-butyltin hydride (bp 66-69° at 0.6-
0.7 mm, lit. (82), 81° at 0.9 mm) from 19.25 (0.059 moles) of
tri-n-butyltin chloride (Ventron) and 3 g (0.079 moles) of lithium
aluminum hydride in 125 mL of dry ether. The compound reacted
violently with carbon tetrachloride and showed a strong IR band at
1810 (cm$^{-1}$).

**Preparation of 1,1-dibromo-2-vinylcyclopropane (165)**

A combination of the procedures of Skattebøl (83) and of Skell
and Garner (84) was employed to produce the dibromovinylcyclo-
propane. A slurry of 50 g (0.45 moles) of potassium t-butoxide
(Ventron) in 250 mL of dry t-butanol was added over about 5 hours
to a chilled (0°) solution of 20 mL (0.23 moles) of bromoform
(Mallinckrodt) and ca. 12 mL (0.14 moles) of butadiene$^{47}$ (Matheson)

$^{47}$The procedure (84) calls for equimolar amounts of bromo-
form and butadiene, but our container of butadiene became exhausted
before sufficient gas had been added to the reaction mixture.
in 100 mL of t-butanol. The mixture was then stirred overnight at room temperature, and then 250 mL of water was added. The aqueous layer was then extracted with five 100 mL portions of pentane, and the pentane layer was washed with five 100 mL portions of water and 100 mL of saturated ammonium chloride. The layer was then dried over magnesium sulfate, filtered, and the solvent was distilled off through a 30 cm Vigreux column. The residue was then distilled through a 14 cm, vacuum jacketed Vigreux column, and the fraction boiling at 76-80°, 50 mm (lit. 76-82° at 50 mm) was collected affording 22.52 g (adjusted yields: 61% based on butadiene, 37% based on bromoform). NMR (CCl₄) δ 5.2-5.8 (m, 3H), 1.87-2.46 (m, 2H), 1.45-1.7 (m, 1H); IR (neat) 3090, 3020, 2290, 2960, 2925, 2870, 1640, 1440, 1420, 1220, 1190, 1150, 1100, 1050, 1010, 980, 920, 720 (cm⁻¹).

Preparation of 1-bromo-2-vinylcyclopropane (166a,b)

The method of Seyferth, Yamazaki, and Alleston (85), produced 1.73 g (65%) of a mixture of 1-bromo-2-vinyl-cyclopropanes from 3.21 g (14 mmoles) of 1,1-dibromo-2-vinylcyclopropane and 4.15 g (14 mmoles) of tri-n-butyltin-hydride. Another preparation gave 3.88 g (82%) 1-bromo-2-vinylcyclopropanes from 7.29 g (32 mmoles) of 1,1-dibromo-2-vinylcyclopropane and 9.42 g (32 mmoles) of tri-n-butyltin hydride. The material was isolated by distillation of the
crude product at room temperature (0.2 mm) into a -78° trap. An earlier attempt to distill the material at 62-74° (90 mm) (85) resulted in extensive decomposition of the product. The NMR and IR spectra agreed with the spectra described by Landgrebe and Becker (86), and the NMR spectrum indicates that the trans:cis ratio is ca. 40:60.

Preparation of 7,8,9,10-tetrahydro-6-(2-vinyl-cyclopropyl)-6(5H)-benzocyclooctenols 111a, b

Use of the general procedure of Wender and Filosa (87) produced 0.60 g of the vinylcyclopropanols 111a, b from 2.5 (5.8 mmoles) of 2.3 M t-butyllithium in pentane (Ventron), 0.80 g (5.4 mmoles) of the mixture of 1-bromo-2-vinyl-cyclopropanes, and 0.48 g (2.3 mmoles) of 82% 7,8,9,10-tetrahydro-6(5H)-benzocyclooctenone (122). The oil was vacuum transferred (135° at 0.4 mm) to give 0.55 g of product. GLC analysis (column J, 225°, 53 mL/minute) showed that the product contained 14% 122, 7% unknown material, and 77% of the vinylcyclopropanols (shorter retention time peak, ca. 28%; longer retention time peak, ca. 72%). This implies a 63% overall yield of 111a, b. Purification by GLC (column P, 250°, 70 mL/minute) gave the analytical samples. Compound 111a (shorter retention time):

NMR (CCl₄) δ 7.05 (s, 4H), 4.66-5.56 (m, 3H), 2.66-2.94 (m, 4H), 1.2-1.86 (broad m, 7H), 0.7-1.1 (m, 4H); IR (CCl₄) 3620-3400, 3070, 3050, 3010, 2990, 2920, 2840, 1630, 1490, 1465, 1450, 980, 890
(cm⁻¹); mass spectrum m/e (rel %) 242(2), 188 (100); m/e 242.165 (calcd for C₁₇H₂₂O: 242.167). Compound 11lb (longer retention time): NMR (CCl₄) δ 7.06 (s, 4H), 5.76-6.32 (m, resembles septet, 1H), 5.0-5.3 (m, 1H), 4.76-4.97 (m, 1H), 2.84-2.96 (m, 2H), 2.64-2.84 (m, 2H), 1.24-1.86 (broad m, 7H), 0.7-1.24 (m, 4H); IR (CCl₄) 3620-3400, 3070, 3050, 3010, 2990, 2920, 2840, 1625, 1490, 1465, 1450, 995, 890 (cm⁻¹); mass spectrum m/e (rel %) 242 (5), 188 (100); m/e 242.166 (calcd for C₁₇H₂₂O: 242.167).

Preparation of 8, 9-dihydro-5-vinyl-7H-benzocycloheptene (141)

A vinyl magnesium bromide in THF solution was prepared as described earlier from 2.0 g (0.08 g-atom) of magnesium, 4 mL (ca. 57 mmoles) of vinyl bromide, and 69 mL of THF. The solution was estimated to be ca. 0.8 M in Grignard reagent. The entire solution of Grignard reagent was then added in ca. 1 equivalent portions to a heated (40°) solution of 2.00 g (12.5 mmoles) of benzosuberone in 15 mls of THF. After each portion, 0.5 to 1.0 mL of methanol was added to quench any enolate anion of benzosuberone which formed. The whole process required 7 hours and was followed by GLC (column L, 175°, 48 mls/minute). The reaction mixture was then cooled in an ice bath, and the excess Grignard reagent was quenched with cautious addition of 10 mL of saturated ammonium chloride. Ten mL
of 10% sulfuric acid was then added, and the mixture was warmed at 50° for 1.25 hours. The reaction mixture was then taken up in 75 mL of ether and, the organic and aqueous layers were separated. The organic layer was then washed with two 30 ml portions of water, two 30 mL portions of saturated sodium bicarbonate, and 15 mL of brine. The organic layer was then dried over magnesium sulfate, filtered, and the solvent removed by rotary evaporation. This procedure yielded 2.11 g of an oil which when analyzed by GLC (column L, 175°, 45 mL/minute) showed 3 peaks which eluted in the following order: A(59%), B (37%), C(5%). NMR (CCl₄) δ 6.19 (d of d, J=11, 18 Hz, 1H), 5.05 (d of d, J=2, 11 Hz, 1H), 4.98 (d of d, J=2, 18 Hz, 1H) (60 MHz); IR (neat) 3600-3200 (cm⁻¹) (strong).

The material from above was then refluxed for 1.83 hours in a mixture of 1.13 g of Girard's Reagent T (Aldrich), 18 mL of absolute ethanol, and 2 mL of glacial acetic acid. The mixture was then chilled and extracted with an ice cold solution of 113 mL of water, 1.4 g of sodium hydroxide, 0.25 g of sodium bicarbonate, and ca. 6 g sodium chloride (7). The organic layer was then washed with three 25 mL portions of saturated sodium chloride, dried over magnesium sulfate, filtered, and the solvent was removed by rotary evaporation. This procedure gave 1.30 g of material which GLC analysis (column L, 175°, 45 mL/minute) showed to be free of (123a), but contained 38% of a new, long retention time impurity as well as 62% of the material
A seen in the first analysis. The NMR spectrum indicated that the vinyl region had changed and the IR spectrum showed loss of the hydroxyl band (3600-3200 cm\(^{-1}\)).

The product was then chromatographed on a 4 cm X 60 cm column of silica gel using toluene as an eluent. The fractions containing material with Rf = 0.75 (tlc on silica gel; solvent, toluene) were collected, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. The chromatography yielded 0.28 g (ca. 12% adjusted) of material (141) which showed only one peak when analyzed by GLC (column C, 205°, 63 mL/minute). NMR (CCl\(_4\)) \(\delta\) 6.9-7.4 (m, 4H), 6.49 (d of d, J=11, 18 Hz, 1H), 5.5-6.22 (m, 1H), 5.12 (d of d, J=2, 18 Hz, 1H), 5.00 (d of d, J=2, 11 Hz, 1H), 1.5-3.0 (m, 6H) (60 MHz); IR (neat) 3090, 3050, 3010, 2920, 2850, 1630, 1600, 1590, 1490, 1450, 1420, 1380, 1300, 1260, 1160, 1130, 1100, 1040, 1000, 960, 910, 860, 840, 780, 760 (cm\(^{-1}\)). Purification of the material by GLC (column G, 205°, 50 mL/minute) produced the samples for UV and mass spectral analysis. UV\(\lambda\) (C\(_2\)H\(_5\)OH) nm(\(\varepsilon\)) 224 (2.6 x 10\(^4\)), 231 (2.6 x 10\(^4\)), 240 (1.9 x 10\(^4\)); m/e 170.111 (calcd for C\(_{13}\)H\(_{14}\): 170.111).\(^48\)

---

48 Minor peaks at m/e 184.088 (C\(_{13}\)H\(_{12}\)O) and 186.105 (C\(_{13}\)H\(_{14}\)O) were also found.
Attempted preparation of 8, 9-dihydro-5, 6-epoxy-5-vinyl-7H-benzocycloheptene (142)

A solution of 0.27 g (1.3 mmoles) of m-chloroperbenzoic acid (Aldrich, 85%) and 10 mL of methylene chloride was added over 15 minutes to a chilled (ca. 10°) solution of 0.24 g (1.3 mmoles) of 8, 9-dihydro-5-vinyl-7H-benzocycloheptene (141) in 10 mL of methylene chloride. The solution was then stirred at ca. 10° for 2.5 hours, then 15 mL of 10% sodium sulfite was added, and the mixture was stirred for another 10 minutes at room temperature. The organic and aqueous layers were then separated, and the organic layer was washed with 15 mL of 10% sodium sulfite, three 15 mL portions of saturated sodium bicarbonate, and 15 mL of brine. The organic layer was then dried over magnesium sulfate, and the solvent was removed by rotary evaporation. This procedure gave 0.21 g of an oil whose NMR spectrum differed from that of the starting material: 

\[ (\text{CCl}_4) \delta 5.68 (d \text{ of } d, J=11, 18 \text{ Hz}, 1H), 5.12 (d \text{ of } d, J=2, 11 \text{ Hz}, 1H), 4.82 (d \text{ of } d, J=2, 18 \text{ Hz}, 1H). \]

Analysis of the oil by TLC (silica gel; solvent, toluene) showed two large spots (Rf = 0.33 and 0.34), one medium spot (Rf = 0.72, same as for starting material), and four smaller spots (Rf = 0.0, 0.04, 0.11, and 0.52). An attempt to purify the material on a silica gel preparative plate (E and M), using toluene as the eluent, was unsuccessful. Attempts to purify the material by GLC (column G, 195°, 75 mL/minute) were also unsuccessful.
Preparation of 8, 9-dihydro-5-ethynyl-7H-benzocycloheptene (146)

About 28 mmoles of lithium acetylide was generated by the same method used by Tarrant, Savoy, and Iglehart to prepare propynyl lithium (77). The lithium acetylide was then taken up in 100 mL of THF and the mixture was cooled in an ice bath. A solution of 3.03 g (18.9 mmoles) of benzosuberone in 50 mLs of THF was then added over 1 hour. The mixture was then stirred for another 2.42 hours at 0°, and then 15 mL of water was cautiously added. The organic and aqueous layers were then separated, and the aqueous layer was extracted with three 8 mL portions of ether. The ether extracts were combined with the organic layer, and the combined layer was dried over magnesium sulfate, filtered, and the solvent removed at reduced pressure. This procedure gave 3.18 g of material which was analyzed by GLC (column C, 210°, 64 mL/minute) and found to contain 52% 123a and 48% of a material thought to be 140.

The NMR spectrum (CCl₄, 60 MHz) showed a singlet at δ 2.50 and the IR spectrum (neat) showed bands at 3600-3200 and 3300 cm⁻¹.

A mixture of 2.9 g of the material from above, 50 mL of THF, 5 mL of concentrated sulfuric acid, and 5 mL of water was refluxed for 1 hour. The mixture was then allowed to cool for 0.5 hour, and then 100 mL of saturated sodium bicarbonate was cautiously added. The reaction mixture was then transferred to a separatory funnel with
the aid of 100 mL of ether, and the aqueous and organic layers were separated. The aqueous layer was then extracted with three 20 mL portions of ether, and the ether extracts were combined with the organic layer. The combined layer was then washed with two 40 mL portions of saturated sodium bicarbonate and 40 mL of brine, dried over magnesium sulfate, filtered, and the solvent was removed by rotary evaporation. GLC analysis (column A, 190°, 59 mL/minute) showed that the 2.59 g of material isolated by this procedure contained 31% of a substance with a shorter retention time than benzosuberone and 69% benzosuberone. The IR spectrum showed loss of the 3600-3200 (cm⁻¹) band.

A 2.38 g portion of the material from above was subjected to a Girard's Reagent T purification (see pg. 124) giving 0.56 g of material which contained 83% of enyne 146. A second Girard's purification of 0.28 g of material gave 0.19 g (12% overall adjusted yield) of the enyne 146. NMR (CCl₄) δ 6.9-7.7 (m, 4H), 6.5-6.8 (m, 1H), 2.82 (s, 1H), 2.3-2.7 (m, 2H), 1.7-2.3 (m, 4H) (60 MHz); IR (neat) 3290, 3070, 3025, 2940, 2860, 2100, 1490, 1460, 1360, 1340, 1320, 1260, 1240, 1120, 1080, 1040, 980, 950, 870, 850, 780, 760 (cm⁻¹); UV (C₂H₅OH) nm(ε) 216 (1.4 X 10⁴), 223 (1.2 X 10⁴), 255 (8.8 X 10³); mass spectrum m/e (rel %) 168 (87.2), 153 (100).
Attempted Preparation of 8, 9-dihydro-5, 6-epoxy-5-ethynyl-7H-benzocycloheptene (147)

A solution of 0.30 g (1.5 mmole) of m-chloroperbenzoic acid (Aldrich, 85%) and 10 mL of methylene chloride was added over 10 minutes to a solution of 0.185 g of 8, 9-dihydro-5-ethynyl-7H-benzocycloheptene (146) in 10 mL of methylene chloride at room temperature. The mixture was then stirred for 20 hours, then 10 mL of 10% sodium sulfite was added and the mixture was stirred for another hour. The aqueous and organic layers were then separated, and the organic layer was washed with 10 mL of 10% sodium sulfite, three 10 mL portions of saturated sodium bicarbonate, and 15 mL of brine. The organic layer was then tested with acidified potassium iodide, and no darkening was observed. The organic layer was then dried over magnesium sulfate, filtered, and the solvent removed at reduced pressure. This procedure yielded 0.178 g (88% crude yield) of material which was found to contain ca. 75% of a new material when analyzed by GLC (column A, 210°, 45 mL/minute). TLC analysis (silica gel; solvent, chloroform) showed only one spot with Rf >0.

A 33 mg portion of the material was vacuum transferred to give 19 mg of a clear oil. NMR (CCl₄), 7.4-7.6 (m, 1H), 7.35-7.64 (m, 3H), 3.0-4.3 (m, 2H), 2.5-2.8 (m, 1H), 2.26 (s, 1H), 1.2-2.24 (m, 4H); IR (neat) 3600-3150, 3285, 3060, 3020, 2850, 2760, 1720, 1485, 1440, 950, 750 (cm⁻¹).
Preparation of benzosuberol (150)

A procedure similar to that of Christol, Dehloste, and Mousseron (88) was followed. A mixture of 0.9 g (24 mmoles) of lithium aluminum hydride and 40 mL of ether was chilled to 10-12° in a circulating cold water bath. A solution of 2.52 g (15.8 mmoles) of benzosuberone (ROC/RIC) and 17 mL of ether was then added dropwise over 2 hours. The reaction mixture was then stirred for another 2 hours in the cold bath, and then chilled in an ice bath. The excess lithium hydride was then quenched by cautious addition of 0.9 mL of water, 0.9 mL of 15% sodium hydroxide, and 2.7 mL of water (58). The white, granular precipitate which formed was filtered off, washed thoroughly with ether, and the filtrate and wash ether were dried over magnesium sulfate. The ether solution was then filtered, and the solvent was removed at reduced pressure. This procedure yielded 2.48 g (97%) of 150, a white solid, mp 101.4-101.8° (lit. (88), 100-101). NMR (CDCl₃) δ 7.0-7.6 (m, 4H), 4.85-5.05 (m, 1H), 2.55-3.15 (m, 2H), 1.25-2.25 (m, 7H, singlet at 1.96 disappears upon treatment with D₂O); IR (CHCl₃) 3600-3200, 3060, 2920, 2850, 1490, 1450, 1100, 1050, 1040, 980, 940, 890 (cm⁻¹); mass spectrum m/e (rel %) 162 (17.2), 144 (100).
Preparation of 6, 7-dihydro-5H-benzocycloheptene (151)

Approximately the same procedure as Christol, Delhoste, and Mousseron (88) was used. A 2.27 g sample (14 mmoles) of benzosuberol and 2.95 g of powdered potassium bisulfate were thoroughly mixed and placed under a nitrogen atmosphere. The reaction vessel was then plunged into a 180° oil bath for 10 minutes, removed, and allowed to cool for five minutes. Twenty mL of water were then added, and the reaction mixture was transferred to a separatory funnel with 30 mL of ether. The aqueous layer was then separated and extracted with four 20 mL portions of ether. The combined ether layers were then washed with 15 mL of saturated sodium bicarbonate, dried over magnesium sulfate, filtered, and the solvent was removed at reduced pressure. This procedure gave 1.85 g (92% crude yield) of a faintly colored oil. The appearance of the NMR spectrum and gas chromatography trace\textsuperscript{49} indicated that the purity of this material was satisfactory for the next synthetic step, and it was not purified further. NMR (CCl\textsubscript{4}) δ 6.9-7.2 (m, 4H), 6.33 (d of t, J=2, 12 Hz, 1H), 5.77 (d of t, J=5, 12 Hz, 1H), 2.7-2.9 (m, 2H), 2.21-2.47 (m, 2H), 1.75-2.07 (m, 2H); IR (neat) 3050, 3000, 2900, 2870, 2850, 1490, 1450, 1420, 1360, 1290, 1260, 1180, 1160, 1100, 1040, 970, 940, 860, 840, 820, 780, 740, 700, 680 (cm\textsuperscript{-1}).

\textsuperscript{49}The material showed one peak when analyzed by GLC (column I, 205°, 49 mL/minute).
Preparation of 5,6-epoxy-5,6,8,9-tetrahydro-
7H-benzocycloheptene (152)

A procedure similar to that of Crabb and Schofield (89) was employed. A solution of 1.72 g (11.9 mmoles) of crude (see previous experiment) 6,7-dihydro-5H-benzocycloheptene (151) and 100 mL of methylene chloride was chilled in a 12° circulating water bath. A solution of 2.66 g (13.1 mmoles) of m-chloroperbenzoic acid (Aldrich, 85%) in 100 mL of methylene chloride was then added dropwise over 1.25 hours. The reaction mixture was then allowed to warm to room temperature and stirred an additional hour. Ten mL of 10% sodium bisulfite was then added, and the mixture was stirred vigorously for 45 minutes. The organic layer was then tested with starch-potassium iodide paper, and no darkening was observed. The reaction mixture was then transferred to a separatory funnel and shaken with 50 mL of 10% sodium bisulfite. The aqueous layer was then separated, and the organic layer was washed with five 50 mL portions of saturated sodium bicarbonate and 100 mL of brine. The organic layer was then dried over magnesium sulfate, filtered, and the solvent was removed in vacuo. This procedure gave 1.85 g (79% adjusted) of an oil. Analysis of the oil by GLC (column I, 210°, 49 mL/minute) indicated that the oil contained 86% (152), 5% (151), and 9% unknown material. The purity of the material was satisfactory for the trial alkylation (next procedure) and was not purified further. NMR (CCl$_3$) δ 6.86-7.5
(m, 4H), 3.78 (d, J=4 Hz, 1H), 3.1-3.3 (m, 1H), 2.65-2.75 (m, 2H), 1.4-2.2 (m, 4H); IR (neat) 3000, 2920, 2850, 1490, 1450, 1420, 1390, 1360, 1290, 1260, 1210, 1200, 1170, 1060, 1020, 980, 940, 920, 900, 860, 850, 840, 800, 780, 740, 720, 640 (cm\(^{-1}\)).

At[tempted ethynylation of 5,6-epoxy-5,6,8,9-tetrahydro-7H-benzocycloheptene (152)]

The method used to generate lithium acetylide is similar to that used by Tarrant, Savoy, and Iglehart (77) to prepare propynyllithium. A 25 mL, 3-necked flask (equipped with magnetic stirrer, drying tube, and gas addition tube with clearing rod) (90) was charged with 10 mL of ether and 2 mL (1.8 mmoles) of 0.92 M methyllithium in ether. Acetylene gas was then passed through a drying train (consisting of a brine safety valve, water scrubber, concentrated sulfuric acid scrubber, and soda-lime trap) (91) and then into the reaction vessel. The gas was allowed to flow for about 2 hours at a rate of ca. 10 bubbles/10 seconds. The ether was then evaporated with a nitrogen stream, and the lithium acetylide was taken up in a warm solution of 1 mL of THF and 1 mL of HMPA and transferred to a 10 mL flask. A solution of 0.20 g (ca. 1 mmole) of crude 5,6-epoxy-5,6,7,8-tetrahydro-7H-benzocycloheptene (152) and 1 mL of THF was then added, and the mixture was stirred at room temperature for 1 hour and then heated at 60° for 3 hours. The reaction mixture was then
cooled and quenched with 5 mL of wet ether and 5 mL of water. The mixture was then taken up in 15 mL of ether, and the ether layer was washed with six 5 mL-portions of water and 15 mL of brine. The organic layer was then dried over magnesium sulfate, filtered, and the solvent removed at reduced pressure. This procedure yielded 0.15 g (ca. 75%) of material which had the same NMR and IR spectra as the starting material.
BIBLIOGRAPHY


19. S. R. Wilson, private communication.


52. T. J. Wallace and A. Schriesheim, Tetrahedron, 21, 2271 (1965).


