1971

The Influence of a Neighboring Methoxy Group on Solvolyses of Cyclooctyl Para-Toluenesulfonates.

Richard Arthur Evans
Louisiana State University and Agricultural & Mechanical College

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THE INFLUENCE OF A NEIGHBORING METHOXY GROUP ON SOLVOLYSES OF CYCLOOCTYL p-TOLUENESULFONATES.

The Louisiana State University and Agricultural and Mechanical College,
Ph.D., 1971
Chemistry, organic

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THE INFLUENCE OF A NEIGHBORING METHOXY GROUP
ON SOLVOLYSES OF CYCLOOCTYL p-TOLUENESULFONATES

A Dissertation
Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy
in
The Department of Chemistry

by
Richard Arthur Evans
B.S., Tougaloo College, 1959
M.A., Western Michigan University, 1965
August, 1971
PLEASE NOTE:

Some Pages have indistinct print. Filmed as received.

UNIVERSITY MICROFILMS
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ABSTRACT

Product distribution data for solvolyses of cis- and trans-2-methoxycyclooctyl p-toluenesulfonates (tosylates) in 80% aqueous ethanol and glacial acetic acid solvents have been obtained. The product mixtures from aqueous ethanol solvolyses contained substantial amounts of both normal and transannular products, whereas the product mixtures from acetic acid solvolyses contained almost exclusively transannular products.

The product data show a definite dependence upon the configuration of the tosylate. Solvolysis of the cis-tosylate produces cycloheptanecarboxaldehyde as the major carbonyl product, and 5-methoxycyclooctene as the major olefinic product. Solvolysis of the trans-tosylate produces cyclooctanone as the major carbonyl product and 4-methoxycyclooctene as the major olefinic product.

Solvent attack on the methyl of the methoxy group is proposed for the formation of carbonyl products, of bicyclic ether, and, in the acetic acid product mixtures, of methyl acetate.

Added lithium perchlorate did not affect product distributions in 80% ethanol solvolyses, but it drastically changed product composition in glacial acetic acid solvolyses. The effect of lithium perchlorate upon solvolysis products of cis- and trans-tosylates in acetic acid was interpreted in terms of intimate and solvent separated normal (unrearranged) and transannularly rearranged ion-pairs.
CHAPTER I

INTRODUCTION

A. General Description of Medium Ring Compounds

The paucity of research on 1,2-disubstituted medium ring compounds has been the main inspiration for the project described herein. For many years medium ring compounds were not readily available for study because fruitful synthetic procedures for obtaining them did not exist. Only in recent years have satisfactory procedures been developed for synthesis of medium ring compounds. Craig summarizes some of the more successful synthetic methods used in medium ring synthesis in a comprehensive review of the eight-membered carbocycles. \(^1\)

The purpose of the present research study was to synthesize \textit{cis}- and \textit{trans}-2-methoxycyclooctyl \(p\)-toluenesulfonates (2-methoxycyclooctyl tosylates), \(\text{lc}\) and \(\text{lt}\), and to assess the effect of the neighboring methoxy group on the carbonium ion-like reactions of these cyclooctane derivatives.

\[ \text{lc} \quad \text{lt} \quad \text{Ts} \]

The alteration of product distribution occurring upon addition of small amounts of lithium perchlorate was examined. Observations have been correlated with established phenomena wherever possible.

General interest in medium ring (8-11 carbons) compounds was stimulated by the independent and almost simultaneous reports in 1952...
SCHEME I

\[
\begin{align*}
\text{O} & \xrightarrow{	ext{HCO}_2\text{H}} \text{OH} \xrightarrow{(i) \text{HCO}_2\text{H}} \text{OH} \\
\text{25-30\%}
\end{align*}
\]

\[
\begin{align*}
\text{HO} & \xrightarrow{} \text{OH} + \text{OH} + \text{OH} + \text{trace} \\
5-19\% & + 11\% + 4\% + \text{trace}
\end{align*}
\]

\[
\begin{align*}
\text{+} & \text{+} \\
0.1\% & + 0.1\%
\end{align*}
\]
by Cope\textsuperscript{2} in this country and by Prelog\textsuperscript{3} in Switzerland of transannular (across ring) rearrangements occurring in reactions, presumably carbonium ion-like, in the eight and ten membered ring systems. Both Cope and Prelog found that 1,3- or 1,5-hydride shifts to intramolecular cationic centers are quite facile and can account for many products formed in the reactions of the compounds studied. Scheme I (page 2) illustrates the reaction of \textit{cis}-cyclooctene with peroxyformic acid.\textsuperscript{2} Scheme II illustrates the mode of product formation from the intermediate protonated \textit{cis}-cyclooctene oxide.

\textbf{SCHEME II}

\begin{center}
\begin{tikzpicture}
\end{tikzpicture}
\end{center}

\textbf{TRANSANNULAR PRODUCTS} \hspace{2cm} \textbf{NORMAL PRODUCTS}
<table>
<thead>
<tr>
<th>n</th>
<th>$\Delta H/n$</th>
<th>Total Strain $n \cdot (\Delta H_c/n - 157.4)$ kcal/mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>158.7</td>
<td>6.5</td>
</tr>
<tr>
<td>6</td>
<td>157.4</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>158.3</td>
<td>6.3</td>
</tr>
<tr>
<td>8</td>
<td>158.6</td>
<td>9.6</td>
</tr>
<tr>
<td>9</td>
<td>158.8</td>
<td>12.6</td>
</tr>
<tr>
<td>10</td>
<td>158.6</td>
<td>12.0</td>
</tr>
<tr>
<td>11</td>
<td>158.4</td>
<td>11.0</td>
</tr>
<tr>
<td>12</td>
<td>157.7</td>
<td>3.6</td>
</tr>
<tr>
<td>13</td>
<td>157.8</td>
<td>5.2</td>
</tr>
<tr>
<td>14</td>
<td>157.4</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>157.5</td>
<td>1.5</td>
</tr>
<tr>
<td>16</td>
<td>157.5</td>
<td>1.6</td>
</tr>
<tr>
<td>17</td>
<td>157.2</td>
<td>-3.4</td>
</tr>
</tbody>
</table>
Transannular products result from both solvent attack on C-5 (or C-7 if shift occurs from this position) and intramolecular attack on C-5 (or C-7) by oxygen.

The origin of the special properties of medium ring compounds is largely steric in nature. In contrast to the six-membered ring, the medium rings exhibit considerable ground state strain. Careful gas-phase combustion studies by van Kamp and Coops\(^4\) on C\(_5\)-C\(_{17}\) cycloalkanes have shown that the medium ring cycloalkanes, compared with normal alkanes and cyclohexane, possess considerable thermochemical strain, which reaches a maximum of about 12 kilocalories per mole in cyclononane and cyclodecane (Table I, page 5).

Heats of hydrogenation of the C\(_6\)-C\(_{10}\) cycloalkenes (Table II) also reflect ground state strain in medium ring cycloalkanes.\(^5,6\)

**TABLE II**

<table>
<thead>
<tr>
<th>Cycloalkene</th>
<th>(-\Delta H, (\text{25}^\circ \text{C}) \text{ kcal/mole})</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cis</td>
</tr>
<tr>
<td>Cyclohexene</td>
<td>27.10</td>
</tr>
<tr>
<td>Cycloheptene</td>
<td>25.85</td>
</tr>
<tr>
<td>Cyclooctene</td>
<td>22.98</td>
</tr>
<tr>
<td>Cyclononene</td>
<td>23.62</td>
</tr>
<tr>
<td>Cyclodecene</td>
<td>20.67</td>
</tr>
</tbody>
</table>

The types of strain characteristic of medium rings are due to (1) deviation of the valence angle of the ring atoms from the optimal value (angle or Bayer strain), (2) eclipsing interaction of atoms in the 1,2 or vicinal positions (Pitzer strain) and (3) steric interference between non-adjacent atoms which results in "transannular" strain.\(^7\)
X-ray studies by Dunitz and co-workers on derivatives of the C₉, C₁₀ and C₁₂ cycloalkanes provided information about the conformations of the compounds studied in the solid state. Since the positions of hydrogens are not directly determined by X-ray measurements, there was no direct physical evidence for transannular strain. However, calculations based on the positions of the carbon atoms (as determined by X-ray studies) indicate that certain hydrogens in the 1,3,1,4, and 1,5 positions must be very close to each other.

X-ray crystallographic studies on derivatives of cyclooctane have indicated that the ring adopts a stretched crown conformation.²

![Crown](image1)

![Stretched Crown](image2)

One of the major features of such a structure is the presence of several conformationally different positions.²⁰ Seemingly there are three different axial-like positions and three different equatorial-like positions, making conformational analysis of the cyclooctane system much more complicated than that of the extensively studied cyclohexane system. Extension of the Winstead-Holness treatment¹¹ (i.e., "locking" the conformation with a bulky substituent) of the cyclohexane ring system to the cyclooctane system has been considered inapplicable on the grounds that introduction of a substituent into the ring will affect the conformational equilibria among the different axial and equatorial positions in different ways.¹² Therefore, the correlation
of product distribution with conformational differences is not always as clear-cut for medium rings as for cyclohexyl derivatives. Along with earlier studies by others, the present study has, however, demonstrated that conformational differences in a medium ring system may be responsible for marked differences in product formation. In the present study the stretched crown conformation will be considered to be closest to the species responsible for the observed products.

The reaction of cis-cyclooctene oxide with formic acid is considered to proceed through a cationic intermediate to the rearranged products. Rearrangements associated with medium ring systems involving anionic, radical, and carbene intermediates have been documented, although more examples of cationic rearrangements have been reported. ¹³

B. Selected Experiments Related to the Present Study

1. Formolysis of cis-cyclooctene oxide¹⁴

Cope and co-workers in studying the formolysis of cis-cyclooctene oxide utilized deuterium labelling to reveal the extent of 1,3- and 1,5-hydride shifts in the formation of certain transannular products (Scheme I, page 2). Using a simple degradation scheme, they showed that 39% of the cis-1,4-cyclooctanediol was formed by a 1,3-hydride shift and 61% by a 1,5-hydride shift. They further showed that only 6% of the 3-cyclooctene-1-ol is formed by a 1,3-hydride shift and 94% by a 1,5-hydride shift. Since there are significantly different amounts of 1,3- and 1,5-shifts in formation of the 1,4-diol and the unsaturated alcohol, they concluded that the latter could not
have been formed by dehydration of the diol.

![Chemical Structure]

Of particular interest are the relative amounts of elimination products (73% 3-cyclooctene-1-ol and 27% 4-cyclooctene-1-ol) formed in this reaction. The fact that 3-cyclooctene-1-ol is the major product resulting from the transannular ion suggests that there is some conformational preference which results in this selectivity. It is also interesting to note that the only olefinic product reported from the solvolysis of trans-cyclooctene oxide is 4-cyclooctene-1-ol, isolated in 12% yield.

2. Acetolysis of cis- and trans-1,2-Cyclooctylene Ditosylates

This study was undertaken to demonstrate the effect of neighboring p-toluene sulfonate (tosylate) on the extent of transannular hydride shift. The distribution of olefinic products obtained is outlined below:

![Chemical Structures]

Here some selectivity was indicated for the solvolysis of the trans-ditosylate and statistical elimination seemingly occurred for the
cis-ditosylate. The authors conclude that planar (or other equilibrium conformation) carbonium ions cannot be involved here, otherwise the observed difference in product distribution would not occur.

3. Acid-Catalyzed Rearrangements of cis- and trans-Cyclooctene Glycols

One of the interesting features of the dilute sulfuric acid decomposition of the cis- and trans-1,2-cyclooctanediols is the formation of 3-cycloocten-1-ol solely from trans-diol and an approximately 1:1 mixture of 3-cycloocten-1-ol and 4-cycloocten-1-ol from cis-diol, indicating some degree of selectivity in olefin formation. Included among the other products formed were cyclooctanone (5-9%) and the 1,4 and 1,5 bicyclic ethers (40% from trans-diol, largely 1,4 isomer; 20% from cis-diol).

4. Solvolyses of Medium-Ring 2-Halocycloalkanols

The solvolyses of the trans-chloro- and bromohydrins closely paralleled the present work in terms of the types of product obtained. Here again, selectivity in olefin formation is noted. The ratio of 3-cycloocten-1-ol to 4-cycloocten-1-ol was 5.6/1 for silver nitrate assisted acetolysis of trans-2-bromocyclooctanol. This study implies that free carbonium ions are not responsible for the products obtained, since a comparison of cis- and trans-bromohydrin solvolyses showed quite different product distributions.
5. Solvolyses of Cyclooctyl and trans-2-Hydroxycyclooctyl Bromides and p-Toluenesulfonates

This study provided activation parameters for solvolyses of unsubstituted and 2-substituted cyclooctyl tosylates. The authors concluded that the 2-hydroxy substituent gives rise to an unfavorable enthalpy change (i.e., a destabilizing effect upon the initially-formed cation) as one traverses solvent polarity from more ionizing to less ionizing solvents. Since the olefinic and bicyclic ether components were not separated from each other in this investigation (being mainly a kinetic study), conclusions cannot be made regarding any apparent selectivity in product formation. Although the product distribution in the case of the trans-hydroxy bromide is quite similar to that of the trans-hydroxy tosylate, the change from bromide to tosylate as leaving group affects the composition of the product mixtures by increasing the proportion of cyclooctanone, a non-transannular product, at the expense of the bicyclic ethers, products of transannular hydride shift. The authors conclude that this observation is significant for establishing an inverse relationship between the extent of transannular reaction and the ease of charge development in the transition state (compare the extensive formation of transannular products in the acid catalyzed rearrangements of cyclooctene glycols with the slight amount formed by nitrous acid deaminations of the corresponding amino alcohols).

In some of the investigations already described reference was made to the carbonium ion character of the reactive species leading to product formation. In certain cases conclusions were drawn about the occurrence of free carbonium ions. Within the scope of
carbonium ion theory as it exists today, one should further question the nature of the species responsible for the formation of products in reactions of medium-ring compounds.

One of the most revolutionary contributions to carbonium ion theory has been Winstein's elucidation of the effect of certain added salts (lithium perchlorate, especially) upon the rates of certain reactions involving cationic species. For some compounds, addition of small amounts of lithium perchlorate produces an initial steep rate acceleration followed by a normal linear acceleration. This effect has been termed the "special salt effect" and was initially observed for only a few systems such as 1-methyl-2-(4-methoxyphenyl)propyl p-toluenesulfonate and 2-(2,4-dimethoxyphenyl)ethyl p-bromobenzencesulfonate, which give relatively stable carbonium ions upon solvolysis. The special salt effect is attributed to a direct reaction of an intermediate ion-pair with a lithium perchlorate ion-pair to give a carbocation-perchlorate ion-pair. The carbocation-perchlorate ion-pair exhibits little tendency to form covalent perchlorate and instead reacts with solvent to yield products (Scheme III). Therefore, that portion of carbocation-sulfonate ion-pair that would ordinarily have returned to reactant goes instead to product, and a higher observed rate results. Only when the carbonium ion reacts competitively with the solvent-separated leaving group and with solvent does the special salt effect occur. It has been found that a change to a more nucleophilic solvent or to solvents of higher ionizing power can completely eliminate the effect. Usually, special salt effects are found only in solvents of low ionizing power and low nucleophilicity.
SCHEME III

B-X \rightleftharpoons (R^+X^-) \rightleftharpoons R^+ | X^- \rightleftharpoons R^+ + X^-  

intimate ion pair  solvent separated ion pair  solvated (free) ions

\text{products} \quad \text{products} \quad \text{products}

\text{products} \quad \text{products}

\text{LiClO}_4 \text{ scavengers here}

R^+ | \text{ClO}_4^- \rightleftharpoons R^+ + \text{ClO}_4^-
CHAPTER II
RESULTS AND DISCUSSION

A. Synthesis of cis- and trans-2-Methoxycyclooctyl Tosylates

The synthesis of trans-2-methoxy-1-cyclooctanol was achieved by following a patented procedure illustrated by the following equations.21

\[
\begin{align*}
\text{cis-2-methoxy-1-cyclooctanol} & \stackrel{\text{BF}_3\text{Et}_2\text{O}}{\longrightarrow} \text{trans-2-methoxy-1-cyclooctanol} \\
\text{trans-2-methoxy-1-cyclooctanol} & \stackrel{\text{HCl}}{\longrightarrow} \text{cis-2-methoxy-1-cyclooctanol}
\end{align*}
\]

The high yield of 1,2-isomer was quite surprising in view of the marked tendency of medium ring compounds to undergo rearrangements in acidic polar solvents. In an earlier study on the solvolysis of cis-cyclooctene oxide, Cope reported a direct correlation between increasing solvent acidity and proportion of transannular rearrangement products.22 The correlation, however, was for carboxylic acids and may not be valid for more nucleophilic Lewis acid solutions such as the methanolic boron trifluoride-etherate solution employed above.

Many attempts of varying success were employed to synthesize cis-2-methoxycyclooctanol (see Experimental Section). The best route was found to be the reaction of methyl iodide with the half sodium salt of cis-1,2-cyclooctanediol.
This procedure produced a single methoxy alcohol and only one by-product, cis-1,2-dimethoxycyclooctane, which was easily separated from the desired product by chromatography on silica gel.

The cis- and trans-tosylates were prepared according to a standard method\textsuperscript{23} from pyridine solutions of p-toluenesulfonyl chloride and the alcohol.

trans-2-Methoxycyclooctyl p-toluenesulfonate, a solid compound, proved to be stable for many months when stored in a stoppered vial in a freezer at \(-20^\circ\) C. The cis isomer seemed to show some sign of decomposition after only two weeks storage under the same conditions. Therefore,
only small samples of the cis-tosylate were made, and these samples were used immediately.

B. Solvolyses of the cis- and trans-2-Methoxycyclooctyl Tosylates

1. Solvolyses in 80% Aqueous Ethanol

These solvolyses were carried out at 60°C for six hours with added calcium carbonate to neutralize p-toluenesulfonic acid formed in the reaction. Reactions carried out without added calcium carbonate, however, gave product mixtures identical on the basis of gas liquid partition chromatographic (glpc), infrared (ir) and nuclear magnetic resonance (nmr) data to those obtained from reactions with the added salt. Calcium carbonate was added to the initial reaction mixture to assess its effect on the formation of cyclooctanone in the reaction. The products obtained from the solvolyses of the cis- and trans-tosylates are shown in Chart I. Table III gives the product distribution in mole percents for both cis- and trans-isomers. The products (2-9) are arranged in Chart I according to increasing retention times on a 10' X 1/8" aluminum column packed with 10% Carbowax 20M on 80/100 mesh Chromosorb. Products 2, 3, and 4 were not resolved on this column but were separated on a 10' X 1/8" XF-1150 (silicone nitrile) column.

Each experiment was run as a 0.1 M solution of tosylate in 80% (v/v) ethanol. Lithium perchlorate (0.1 M) was added to some solutions of the trans-tosylate to assess the effect of this added salt upon the product composition; the distribution was unaffected by lithium perchlorate (Table III).
CHART I

PRODUCTS FORMED IN THE SOLVOLYSIS OF cis- AND trans-2-METHOXCYCLOOCTYL p-TOLUENESULFONATES (1t AND 1c) IN 80% AQUEOUS ETHANOL

1t

1c

2

3

4

6

7

8t

8c

9t

9c

16
<table>
<thead>
<tr>
<th>Reactant</th>
<th>Added Salt</th>
<th>Product Distribution, mol %&lt;sup&gt;a,b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>lt</td>
<td>None</td>
<td>39 -- 6 0.8 12 39 -- 1.6 ---</td>
</tr>
<tr>
<td>lt</td>
<td>0.1 M LiClO₄</td>
<td>39 -- 6 0.9 11 39 -- 1.8 ---</td>
</tr>
<tr>
<td>lc</td>
<td>None</td>
<td>-- 54.3 - 11.3 3 0.7 24 1.0 3.1</td>
</tr>
</tbody>
</table>

<sup>a</sup> Cyclodecane was used as internal standard for quantitative determinations.

<sup>b</sup> All solvolyses were carried out for six hours; each solution was 0.1 M in tosylate.
One of the interesting features revealed in Table III is the
distribution of the major carbonyl products obtained from the stereo-
isosomers 1t and 1c. The cis-tosylate produced cycloheptanecarbox-
aldehyde (6) as the main carbonyl product, and the trans-tosylate
produced cyclooctanone (7). Another observation of interest is the
selectivity in formation of olefinic products. The trans-tosylate
gave exclusively 4-methoxy-1-cyclooctene (2), whereas the cis-tosylate
gave solely 5-methoxy-1-cyclooctene (2). These results and other as-
pects of these experiments will be discussed further in the Dis-
cussion Section.

2. Solvolyses in Glacial Acetic Acid

Solvolyses of these cis- and trans-tosylates were conducted
at 60° in glacial acetic acid containing small amounts of acetic an-
ydride to insure dryness. Each solution was 0.1 M in tosylate and
in added salt, if any. Experiments were carried out to determine the
effect of varying the lithium perchlorate concentration and of addition
of sodium acetate. Chart II on the following page shows the products
of the acetolyses of cis- and trans-tosylates. Tables IV and V give
product distribution data for the acetolyses of the isomeric tosylates.

Except for two components, the product mixtures were very
well separated on a 10' X 1/8" Carbowax 20M column at 170°. The re-
tention times of the components from the trans-tosylate acetolysis
were: 2 and 4, 3.6 min.; 7, 6.8 min.; 10, 9.5 min.; 11t, 19.2 min.;
12t, 26.2 min.
CHART II

PRODUCTS FORMED IN THE SOLVOLYSIS OF cis- AND trans-2-METHOXYCYCLOOCTYL p-TOLUENESULFONATES IN GLACIAL ACETIC ACID

\[ \text{OCH}_3 \]

\[ \text{CHO} \]

\[ \text{OAc} \]

\[ \text{OCH}_3 \]

\[ \text{OAc} \]

\[ \text{OAc} \]
TABLE IV

PRODUCT DISTRIBUTION DATA FROM SOLVOLYSIS OF cis-2-METHOXYCYCLOOCTYL p-TOLUENESULFONATE IN GLACIAL ACETIC ACID AT 60° C

<table>
<thead>
<tr>
<th>Added Salt</th>
<th>Product Distribution, mol %</th>
<th>3</th>
<th>10</th>
<th>12c</th>
<th>12c</th>
</tr>
</thead>
<tbody>
<tr>
<td>I None</td>
<td></td>
<td>46.8</td>
<td>2.2</td>
<td>1.9</td>
<td>35</td>
</tr>
<tr>
<td>II 0.1 M LiClO₄</td>
<td></td>
<td>17.1</td>
<td>23.0</td>
<td>1.4</td>
<td>13.6</td>
</tr>
</tbody>
</table>

a. Cyclodecan was used as internal standard for quantitative determinations; all solvolyses were carried out for six hours; each solution was 0.1 M in tosylate.
b. Transannular products.
c. Non-transannular products.
TABLE V

PRODUCT DISTRIBUTION DATA FROM SOLVOLYSIS OF trans-2-METHOXYCycLOOCYCYL P-TOLUENESULFONATE IN GLACIAL ACETIC ACID AT 60° C\textsuperscript{a}

<table>
<thead>
<tr>
<th>Added Salt</th>
<th>Product Distribution, mol %</th>
<th>2</th>
<th>4</th>
<th>10</th>
<th>12t</th>
<th>5</th>
<th>8</th>
<th>11t</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>None</td>
<td>25.5</td>
<td>12.5</td>
<td>5</td>
<td>39</td>
<td>-</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>II</td>
<td>None</td>
<td>23.2</td>
<td>11.2</td>
<td>6</td>
<td>40</td>
<td>-</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>III\textsuperscript{d}</td>
<td>0.1 M LiClO\textsubscript{4}</td>
<td>7</td>
<td>43</td>
<td>27</td>
<td>7</td>
<td>3</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>IV\textsuperscript{d}</td>
<td>0.1 M LiClO\textsubscript{4}</td>
<td>7.3</td>
<td>40.7</td>
<td>28</td>
<td>8</td>
<td>3</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>V</td>
<td>0.2 M LiClO\textsubscript{4}</td>
<td>7.7</td>
<td>44.3</td>
<td>28</td>
<td>6</td>
<td>3</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>VI</td>
<td>0.4 M LiClO\textsubscript{4}</td>
<td>7.6</td>
<td>43.4</td>
<td>30</td>
<td>9</td>
<td>3</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

\textsuperscript{a} All solvolyses were carried out for six hours and were 0.1 M in tosylate. Cyclohexane was used as internal standard for quantitative determinations.

\textsuperscript{b} Transannular products.

\textsuperscript{c} Non-transannular products.

\textsuperscript{d} Five grams of tosylate was used here; two grams was used in all other cases.
The two-component nature of the first peak was not immediately apparent, but was detected by preparative gas chromatography on a 9' X 3/8" Carbowax column followed by nmr analyses of the collected fractions (nmr spectrum No. 14). The first component peak proved to be a 2/1 mixture of 4-methoxy-1-cyclooctene and 9-oxabicyclo[4.2.1]nonane (1,4-bicyclic ether). This distribution was subsequently confirmed by use of a 10' X 1/8" XF-1150 (silicone nitrile) column on which the components were well separated at 170°.

The isomeric methoxycyclooctenes, 2 and 3, were differentiated by means of their nmr spectra. The doublet of doublets pattern (see Appendix, nmr spectra Nos. 10 and 12) arising from one (or both) of the allylic hydrogens situated between the double bond and the oxygen-substituted carbon is particularly characteristic and useful. This characteristic is not exhibited by either the allylic (nmr spectrum No. 13) or the 5-substituted cyclooctene (nmr spectrum No. 9).

Also included in the appendix are decoupling studies on compounds 2 and 10. The position of the double bond in the two compounds is suggested by the interpretation of these studies. Comparison of the 60 MHz spectra of the isomeric acetoxyoctolctenes, (10 and 3-acetoxyoctolctene, nmr spectra 9 and 10) and the isomeric methoxyoctolctenes (2 and 3, nmr spectra 12 and 13) vividly illustrates the similarities and differences in vinyl hydrogen patterns in these compounds.
CHAPTER III
DISCUSSION OF RESULTS
A. Solvolyses in 80% Aqueous Ethanol

The results of the solvolyses in 80% aqueous ethanol (and in acetic acid) of the cis- and trans-2-methoxycyclooctyl tosylates (Tables III, IV, and V) may be discussed from the standpoints of (1) solvent effects, (2) effect of neighboring group, and (3) conformational effects. A carbonium ion type mechanism was assumed to be involved in the solvolyses of both cis- and trans-tosylates.

Scheme IV shows possible routes for formation of products. For convenience, the classical representation of ions formed from cis- and trans-tosylates is depicted. Route (a) represents the "normal" solvolysis which gives 1,2-disubstituted product. Routes (b) and (c) are rearrangements involving 1,2-migration of hydride and alkyl group, respectively. Route (d) is a transannular hydride migration (both 1,3- and 1,5-migration of hydride give the 4-methoxy cation) which can lead, by proton loss, to olefin or, by combination with solvent, to a 1,4-disubstituted compound. Transannular hydride shift puts the positive charge in a more remote position away from the destabilizing effects of the methoxy oxygen. The alternative 1,2-hydride migration (from C-2) gives a resonance stabilized oxonium ion, which is probably the intermediate involved in the formation of cyclooctanone. Route (e) represents formation of a bridged transannular methoxonium ion and is seemingly more important in acetic acid solvolyses than in 80% ethanol solvolyses.
SCHEME IV
The salient features of the solvolysis of the cis- and trans-tosylates in 80% aqueous ethanol are (1) formation of cyclooctanone as the major carbonyl product from trans-tosylate and cycloheptanecarboxaldehyde as the major carbonyl product from the cis-tosylate; (2) formation of exclusively trans-1,2-disubstituted products from trans-tosylate and largely cis-1,2-disubstituted products from cis-tosylate; (3) formation of mainly non-transannularly disubstituted products, and (4) absence of product distribution changes upon addition of lithium perchlorate. Features (1) and (2) may be classed as conformational effects, and (3) and (4) as solvent effects. Another feature, (5) the selectivity of olefin formation, (4-methoxy-1-cyclooctene from trans-tosylate and 5-methoxy-1-cyclooctene from cis-tosylate) is not as easily rationalized by use of present carbonium ion theory.

An example which parallels feature (1) has been observed in the cyclohexane ring system for deamination of cis- and trans-4-tert-butyl-2-aminocyclohexanols.25 The conclusions were that an equatorial hydrogen adjacent to the cationic center prevents ring contraction and results in 1,2-hydride shift, whereas an axial hydrogen has no effect on ring contraction. (Figure 1)

FIGURE 1
A similar situation may be implied to explain the formation of the carbonyl products in the medium-ring stereoisomers. (Figure 2).

**FIGURE 2**

A. 

B. 

C. 

D. 

\( \text{Ts}^+ \text{OCH}_3 \) 

\( \text{CIS} \) 

\( \text{trans} \) 

\( \text{D} \)
Figure 2 depicts the "p" orbital resulting from the departure of the p-toluenesulfonate leaving group as being directed towards the alkyl migrating group in the cis-tosylate, (cation A) facilitating ring contraction in this case. The resonance stabilized oxonium-ion, (B), undergoes solvent attack to give cycloheptanecarboxaldehyde and the methylated solvent derivative. (For acetic acid solvolyses, methyl acetate was observed in the reaction mixtures. Similar examples of methoxy-methyl involvement in solvolysis reactions have been reported.26) The departure of p-toluenesulfonate from the trans-isomer leaves a "p" orbital oriented orthogonally towards the alkyl migrating group and parallel to the adjacent methine hydrogen (cation C). Migration of this hydrogen occurs, giving the resonance stabilized oxonium-ion, (D), which undergoes attack by solvent to give cyclooctanone. The Newman projection formulas below illustrate more clearly the conformational differences between the cis- and trans-isomers. Although there are probably other conformations of almost equal energies which could lead to the observed products, the conformations below must be considered significant contributions to product formation.

FIGURE 3
Scrutinization of cation (A), Figure 3, suggests the possibility of both alkyl and hydrogen migration. Alkyl migration which gives rise to cycloheptanecarboxaldehyde seems more probable since this takes place in a rearward displacement mode (anti) and facilitates departure of the p-toluenesulfonate anion. Hydride migration, which gives rise to cyclooctanone, must occur after p-toluenesulfonate leaves but can occur readily because the adjacent "p" orbital is almost parallel to the migrating hydrogen. In cation (C), Figure 3, the "p" orbital is oriented almost parallel to the adjacent methine hydrogen but almost completely orthogonal to the carbon-carbon bond of the potentially migrating alkyl group. Therefore, 1,2-hydride shift leading to ketone formation is more facile than alkyl migration in this case. The ratios of carbonyl products obtained from the stereoisomeric tosylates lend support to the above conclusions:

\[
\begin{align*}
\text{from } \text{trans-tosylate} & \quad \text{via cation C} \\
\frac{\text{(ketone)}}{\text{(aldehyde)}} & = \frac{11}{1} \\
\frac{\text{(ketone)}}{\text{(aldehyde)}} & = \frac{1}{1} \\
\text{from } \text{cis-tosylate} & \quad \text{via cation A} \\
\frac{\text{(aldehyde)}}{\text{(ketone)}} & = \frac{k}{1}
\end{align*}
\]
In a study of the deamination of cis- and trans-2-aminocyclooctanols, Traynham and Yang reported cyclooctanone to be the major carbonyl product from cis-2-aminocyclooctanol and cycloheptanecarboxaldehyde as the major carbonyl product from trans-2-aminocyclooctanol. These results are exactly opposite to those reported for the stereoisomeric tosylates in the present study. However, it is well known that deamination reactions usually lead to more energetic intermediates than solvolysis reactions, and it may be that the conformational requirements for the two types of reactions (solvolysis and deamination) are quite different.

The formation of exclusively trans-1,2-disubstituted products from trans-tosylate is attributed to the neighboring group effect of the adjacent methoxy substituent. The neighboring methoxy group protects the rear-side of the carbon from which tosylate leaves, so that solvent attack occurs exclusively to give trans-isomer.

Studies on the silver-ion assisted acetolysis of trans-2-methoxy-1-cyclohexyl bromide have shown that the major product is trans-2-methoxy-1-cyclohexyl acetate. To rationalize this stereochemical result, participation by neighboring methoxy was deemed necessary. This rationale also required that both the methoxy and leaving group adopt the diaxial conformation rather than the more stable di-equatorial conformation. The importance of this factor, however, was considered difficult to estimate.
The formation of cis-1,2-disubstituted products from cis-tosylate was thought to be the result of solvent attack on an ion-pair intermediate leading to retention of configuration (Figure 4).

There is probably very little neighboring group participation involved here because of the cis orientation of the methoxy and tosylate groups. (Neighboring group participation usually requires trans-diaxial orientation in acyclic and cyclohexane systems.) Solvent attack on ion-pairs has been implicated in reactions involving both $S_{N}^1$ and $S_{N}^2$ type reactions.  

The relative amounts of 1,2-disubstitution and transannular hydride shift in 80% aqueous ethanol is attributed to a solvent effect. Solvent nucleophilicity, i.e., the ability of solvent to compete kinetically with hydride attack (from transannular hydride shift) on the initially formed cation, is considered to be the major factor promoting 1,2-disubstitution. In 80% aqueous ethanol, 1,2-disubstitution was 29% for the cis-tosylate and 41% for the trans-tosylate. These figures
represent sharp contrasts to comparable percentages of corresponding products for solvolyses in the less nucleophilic solvent, acetic acid, (Tables IV and V) in which transannular hydride shifts are $> 80\%$. Cope and co-workers have shown that in acetic acid containing sodium acetate, the solvolysis of cis-cyclooctene oxide gives mainly 1,2-disubstituted product.$^{31}$ The intermediate represented below was considered by Cope to react via two competing steps:

\[
\begin{array}{ccc}
\text{normal products} & \text{transannular products} \\
\text{products} & \text{products}
\end{array}
\]

one, (a), giving normal products, the other, (b), giving transannular products. The nucleophilic contribution of migrating hydrogen was considered to be more important in less nucleophilic media (e.g., acetic acid without added sodium acetate) in which transannular reactions predominate.

Added lithium perchlorate had no effect upon product distribution in 80% aqueous ethanol solvolyses. Only when the carbonium ion is sufficiently stable that reaction with the solvent-separated leaving group competes favorably with solvent does the special salt effect phenomenon arise. Therefore, the observed insensitivity of the present reaction to added lithium perchlorate is attributed to rapid reaction of the initially formed ion with solvent.
B. Solvolyses in Acetic Acid

Most of the features observed in 80% ethanol solvolyses were again noted in the acetolyses of cis- and trans-2-methoxy-1-cyclooctyl p-toluenesulfonates. The salient features of the acetic acid solvolyses are (1) formation of cyclooctanone as the major carbonyl product from trans-tosylate and cycloheptanecarboxaldehyde as the major carbonyl product from cis-tosylate; (2) formation of a much greater percentage of transannular products from both cis- and trans-tosylates as compared with 80% ethanol solvolyses; (3) the effect of lithium perchlorate upon acetolyses of both cis- and trans-tosylates.

Feature (1) has already been discussed in detail in the previous section. The same general considerations may be applied to solvolyses in acetic acid.

The destabilizing effect of the methoxy substituent is much more apparent in acetic acid than in 80% aqueous ethanol. Tables IV and V show that transannular products make up 80% of the products from trans-tosylate solvolysis with and without lithium perchlorate and 80% from cis-tosylate solvolysis without lithium perchlorate. The poorer nucleophile acetic acid does not successfully attack the initial cation generated from either cis- or trans-tosylate but allows it to undergo a greater degree of transannular hydride shift than does the more nucleophilic ethanol-water medium.

The effect of lithium perchlorate was quite surprising. The following table (Table VI) again summarizes the acetic acid solvolyses of cis- and trans-tosylates with and without added lithium perchlorate.
<table>
<thead>
<tr>
<th>Chemical Structure</th>
<th>1t</th>
<th>1c</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure" /></td>
<td>$\frac{25}{7}$</td>
<td>-</td>
</tr>
<tr>
<td><img src="image2" alt="Chemical Structure" /></td>
<td>-</td>
<td>$\frac{47}{17}$</td>
</tr>
<tr>
<td><img src="image3" alt="Chemical Structure" /></td>
<td>$\frac{12}{43}$</td>
<td>-</td>
</tr>
<tr>
<td><img src="image4" alt="Chemical Structure" /></td>
<td>$\frac{0}{3}$</td>
<td>-</td>
</tr>
<tr>
<td><img src="image5" alt="Chemical Structure" /></td>
<td>$\frac{15}{11}$</td>
<td>$\frac{3}{3}$</td>
</tr>
<tr>
<td><img src="image6" alt="Chemical Structure" /></td>
<td>$\frac{5}{27}$</td>
<td>$\frac{2}{23}$</td>
</tr>
<tr>
<td><img src="image7" alt="Chemical Structure" /></td>
<td>$\frac{3}{2}$</td>
<td>$\frac{5}{4}$</td>
</tr>
<tr>
<td><img src="image8" alt="Chemical Structure" /></td>
<td>$\frac{39}{7}$</td>
<td>$\frac{35}{14}$</td>
</tr>
</tbody>
</table>
The lithium perchlorate solvolysis of the trans-tosylate was investigated first. The major changes noted were in the relative amounts of 4-methoxy-1-cyclooctene (2), 9-oxabicyclo[4.2.1]nonane (4), 4-acetoxy-1-cyclooctene (10), and 4-methoxy-1-cyclooctyl acetate (12t). The 1,4-bicyclic ether (4) and the homoallylic acetate (10) became major products of acetolyses with lithium perchlorate, increasing from 12 and 5% without added salt to 43 and 27%, respectively, with added lithium perchlorate. The overall percentage of transannular products was not significantly altered by added salt.

The change in product distribution is interpreted in terms of intimate and solvent separated transannular ion pairs (Scheme IV).

SCHEME IV
The compounds (2) and (12c) are considered to be formed exclusively from the transannular intimate ion pair, A, which exists in equilibrium with the solvent separated transannular ion pair, B. Lithium perchlorate scavenges this ion, preventing return to the intimate ion pair, thereby diminishing the reaction products of the latter and enhancing the formation of (4) and (10).

The solvolysis of the cis-tosylate exhibits similar sensitivity towards added lithium perchlorate. The solvolysis without added salt produced 5-methoxy-1-cyclooctene (3), 46.8%, and 4-methoxy-1-cyclooctyl acetate (12c), 35%, as major products. Cycloheptane-carboxaldehyde (6), 3.0%, and 4-acetoxy-1-cyclooctene (10), 2.2%, constituted the minor products. Addition of lithium perchlorate increased the percentages of (6) and (10) at the expense of products (3) and (12c).

An interpretation of this phenomenon is illustrated in Scheme V on the following page. Both the initially formed and the transannular ions may exist as intimate and solvent-separated ion-pairs in acetic acid. Addition of lithium perchlorate scavenges both initially-formed and transannular solvent-separated ion pairs. Scavenging the solvent-separated initial ion enhances the formation of cycloheptane-carboxaldehyde, a rearrangement product of the 2-methoxycyclooctyl cation. Although the exact route to 4-methoxy-1-cyclooctene has not been completely elucidated, it must, vide infra, arise from a transannular solvent-separated species. Scavenging this species decreases the extent of return to intimate transannular ion-pairs, diminishing the amount of 5-methoxy-1-cyclooctene (an intimate ion-pair product), and increasing the amount of 4-acetoxy-1-cyclooctene.
SCHEME V

\[
\begin{align*}
&\text{[Octylate \( O\text{CH}_3 \)]} \\
\xrightarrow{\quad \text{reaction} \quad} \\
&\text{[Octylate \( X^- \)]} \\
&\text{[Octylate \( O\text{CH}_3 \)]} \\
\xrightarrow{\quad \text{reaction} \quad} \\
&\text{Octylacetate \( O\text{Ac} \)}
\end{align*}
\]
Although cis-cyclooctene oxide does not solvolyze in acetic acid at 60°, the accumulation of p-toluenesulfonic acid during solvolysis could effect the protonation and subsequent ring opening of the epoxide and thereby generate the observed products. To investigate this possibility, cis-cyclooctene oxide was solvolyzed with equimolar amounts of p-toluenesulfonic acid monohydrate and acetic anhydride in dry acetic acid. The product distributions which are to be compared with those from cis- and trans-2-methoxycyclooctyl tosylate solvolyses are summarized in Table VII.

**TABLE VII**

**SOLVOLYSIS OF Cis-CYCLOOCTENE OXIDE IN ACETIC ACID**

**WITH ADDED p-TOLUENESULFONIC ACID AT 60°**

<table>
<thead>
<tr>
<th>Compound</th>
<th>glpc Area % Without LiClO₄</th>
<th>glpc Area % with LiClO₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>9-oxabicyclo[4.2.1]nonane</td>
<td>5.5</td>
<td>12.5</td>
</tr>
<tr>
<td>cis-cyclooctene oxide</td>
<td>0.0</td>
<td>2.7</td>
</tr>
<tr>
<td>cyclooctanone</td>
<td>11.0</td>
<td>7.0</td>
</tr>
<tr>
<td>4-acetoxy-cyclooctene</td>
<td>27.6</td>
<td>40.0</td>
</tr>
<tr>
<td>1,2-diacetoxy-cyclooctane</td>
<td>27.7</td>
<td>6.1</td>
</tr>
<tr>
<td>unidentified</td>
<td>10.0</td>
<td>7.9</td>
</tr>
<tr>
<td>unidentified</td>
<td>18.2</td>
<td>23.0</td>
</tr>
</tbody>
</table>
The first four components are also obtained from the solvolyses of the trans-tosylate, but the last three components were not detected in the solvolysis of either cis- or trans-tosylates. The two unidentified components are very probably isomeric transannular diacetates whose glpc retention times were longer than any components obtained from tosylate solvolyses. Special efforts to detect trans-1,2-diacetoxydicyclocioctane or components corresponding to the two unidentified compounds in the solvolysis mixtures of cis- or trans-tosylates were unsuccessful. From these observations, it seemed that cis-cyclooctene oxide was not an intermediate which, through secondary reactions, led to the observed products.
A. Attempted Preparation of cis-2-Methoxy-1-Cyclooctanol: A Novel Rearrangement

One of the numerous reactions tried in the attempted synthesis of 2-methoxy-1-cyclooctanol was a Williamson synthesis using sodium metal, cis-1,2-cyclooctanediol, and methyl iodide. The expected reactions are illustrated below.

1. Experimental Procedure

To a solution of cis-1,2-cyclooctanediol (4.0 g, 0.028 mole) in 60 ml of toluene was added 0.64 g (0.028 mole) of freshly cut sodium metal, and the mixture was heated to 100°. The sodium dissolved in about 3 hrs, after which the mixture was allowed to stand for an additional 2 hrs. Freshly-distilled methyl iodide (4.0 g, 0.028 mole) was added dropwise from a pipett. After 2-3 hrs, a considerable amount of precipitate (NaI) had formed. The reaction mixture was worked up by adding water and extracting with pentane. The pentane extract was dried (Na₂SO₄) and concentrated via rotary vacuum evaporation. The crude mixture was first analyzed on a 10' X 1/8" gas chromatographic Carbowax
20M column (10% on Firebrick) at 170° C. This analysis indicated three components (other than toluene) with retention times of 10 minutes (A), 14.7 minutes (B), and 15.4 minutes (C), the latter two components overlapping each other. An authentic sample of trans-2-methoxy-1-cyclooctanol chromatographed under the same conditions had a retention time of 14.5 minutes, which corresponded to component (B). The glpc area percentages were 57% (component A) and 43% (components B and C).

This mixture was partially separated into two fractions on a 9' X 3/8" Carbowas 20M preparative gas chromatographic column; fraction one contained component A, and fraction two contained components B and C. Elemental analyses and nmr spectral data obtained for both fractions are summarized below.

Component A, nmr (CDCl₃) δ 3.32 (s, 3, CH₃-O-), 3.10 (s, 2, -O-CH₂), 2.21 (s, 1, -OH), 1.52 (m, 12, -CH₂ envelope).


Components B and C, composite data, nmr (CDCl₃) δ 3.80 (m, 1, RO-C-H), 3.30 (s, 3, CH₃-O-), 3.15 (m, 1, RO-C-H), 3.40 (s, 1, -OH), 1.52 (m, 12, -CH₂ envelope).


2. Discussion of Results

The very similar elemental analyses strongly suggested that all compounds were isomers. The simplicity of the nmr spectrum of
components B and C suggested that these two were possibly geometrical isomers. Component A was considered to have one of two structures:

![Chemical Structures]

while B and C were considered to be the cis- and trans-2-methoxy-1-cyclooctanols. Compound A represents a novel ring contraction reaction, one which has not, to the author's knowledge, been previously reported.

Further insight into this rearrangement was obtained from the successful synthesis of cis-2-methoxy-1-cyclooctanol using cis-1,2-cyclooctanediol and sodium hydride.

![Chemical Reactions]

This reaction, designed to produce the same intermediate mono-anion as that of the sodium metal reaction, (1) did not result in any detectable rearrangement product, (2) did not produce any trans-methoxy alcohol, (3) may have produced the dianion of the starting diol as implied by the formation of cis-1,2-dimethoxycyclooctane produced in an approximately 1:1 ratio along with cis-2-methoxy-1-cyclooctanol. (This last item is discussed further in a later paragraph.)
The observations outlined above led to the following conclusions: (1) since the sodium hydride reaction is known to proceed ionically, the mechanism for the ring contraction in the sodium reaction is probably not ionic, but radical in nature; (2) the dianion is probably produced in both reactions, but suffers a different fate in the presence of sodium; (3) any mechanism proposed for ring contraction must also involve an epimerization step to explain the production of both cis- and trans-methoxy alcohols. A possible mechanism is illustrated on the following page. This mechanism has not been further investigated, but at least three consequences of such a mechanism may be enumerated. (1) The mechanism indicates that both cis- and trans-diols should give the same rearrangement products, possibly in different proportions. (2) The rearrangement should be initiated by small amounts of sodium on the dianionic species: i.e., once the dianion is formed, minute quantities of sodium should effect rearrangement. (3) Radical inhibitors, stable to decomposition by sodium should inhibit rearrangement.

Epimerization should occur from the radical species formed in equation (2).
PROPOSED MECHANISM FOR THE RING CONTRACTION OF

\textit{cis}-1,2-CYCLOOCTANEDIOL IN THE PRESENCE OF SODIUM METAL

1. \[
\text{OH}^- + \text{OH}^- \rightleftharpoons \text{O}^- + \text{OH}^- + \text{OH}^- 
\]

2. \[
\text{OH}^- + \text{Na} \longrightarrow \text{OH}^- + \text{Na}^+ + \frac{1}{2}\text{H}_2 
\]

3. \[
\text{OH}^- 
\]

4. \[
\text{OH}^- + \text{OH}^- \rightarrow \text{HO}^- + \text{OH}^- + \text{OH}^- 
\]

5. \[
\text{OH}^- + \text{CH}_3\text{I} \longrightarrow \text{H}^- + \text{OCH}_3^- 
\]

6. \[
\text{H}_2\text{O} \quad \text{(workup)} 
\]

\[
\text{OH}^- + \text{OH}^- + \text{OH}^- 
\]

\[
\text{OH}^- + \text{OH}^- + \text{OH}^- 
\]

\[
\text{OH}^- + \text{OH}^- + \text{OH}^- 
\]
An attempt was made to determine the point at which ring contraction occurred by quenching the reaction of the diol and sodium with water before addition of methyl iodide. The components formed were not thoroughly characterized; therefore, definite conclusions were not possible. An alternative mechanism for formation of 1,2-dimethoxycyclooctane which has not been ruled out is outlined below:

\[
\begin{align*}
\text{OCH}_3 & \quad \text{OH} \\
\text{OH} & \rightarrow \\
\text{OCH}_3 & \quad \text{OH}
\end{align*}
\]

This mechanism does not require formation of a dianionic species, and, without evidence to the contrary, cannot be disregarded. This mechanism has one weak point. It does not become important until after methyl iodide has been added to the reaction mixture. It does not seem likely that the monoanion of cis-1,2-cyclooctanediol would be much more effective in abstracting a proton from the methoxy alcohol than from another monoanionic species.

The details of this reaction have yet to be worked out, and it is hoped that subsequent investigators will completely elucidate this rearrangement.
The 60 MHz nmr spectra were obtained utilizing tetramethylsilane as internal standard with a Varian Associates Model A-60-A spectrometer. The 100 MHz spectra were run by Mr. Gregory White and Mr. William Wegner with a Varian Associates Model HA-100 spectrometer. Infrared spectra were determined with a Perkin-Elmer Infracord, Model 137 spectrophotometer. Melting points were taken with open capillary tubes in a Thomas-Hoover melting point apparatus and are uncorrected. Microanalyses were performed by Mr. Ralph Seab at Louisiana State University. Analytical gas chromatography was performed with a Hewlett-Packard Model 700 flame ionization chromatograph by use of a 10' x 1/8" aluminum tube packed with 10% Carbowax 20M on Chromosorb W, 80/100 mesh, or a 9' x 1/8" aluminum tube packed with 10% XF-1150 (Silicone Nitrile) on Chromosorb W, 80/100 mesh. An Aerograph Autoprep Model A-700 instrument, equipped with a 10' x 3/8" aluminum tube packed with 10% Carbowax 20M on Chromosorb W, 60/80 mesh, was used for preparative gas chromatography. Commercially available cyclooctanone obtained from Aldrich Chemical Company was used without further purification for glpc and nmr comparisons. Cyclodecane obtained from Columbian Carbon was distilled before use as an internal standard. The author gratefully acknowledges the gift of an authentic sample of cycloheptanecarboxaldehyde from Mr. Ronald Lilienthal.
A. Synthesis of cis- and trans-2-Methoxycyclooctyl p-Toluenesulfonates

1. cis-Cyclooctene Oxide\(^{34}\)

Commercially available cis-cyclooctene (55.0 g, 0.50 mole) was dissolved in 500 ml of absolute methanol along with 52.5 g (0.5 mole) of benzonitrile. To this solution was added, with cooling, 52.3 g (0.50 mole) of 30% hydrogen peroxide. Additional peroxide was added if, after 24 hrs, all olefin and benzonitrile had not been consumed. The methanol was evaporated under vacuum, and the residue of solid benzamide was filtered. The filtrate was diluted with 100 ml of chloroform, washed with three portions of warm (60\(^{\circ}\)) water, and dried (MgSO\(_4\)). After filtration of the drying agent and any remaining benzamide, the solution was concentrated and distilled to yield 48.5 g (77%) of cis-cyclooctene oxide, bp 106-108\(^{\circ}\) (50-51 mm) [lit. bp, 90-95\(^{\circ}\) (37 mm)].

2. trans-2-Methoxycyclooctanol\(^{35}\)

cis-Cyclooctene oxide (25.2 g, 0.20 mole) was dissolved in 150 ml of absolute methanol and added to a solution of 30 g of 98% boron trifluoride etherate in 100 ml of methanol. Cooling was not necessary for this addition since little temperature change was observed. The epoxide addition was complete in 30 minutes. The solution was stirred for 2 hrs and allowed to stand for 24 hrs. The mixture was cooled in an ice bath and was neutralized with 21.0 g (0.20 mole) of diethanolamine [bis(2-hydroxyethyl)amine] dissolved in 20 ml of methanol. The methanol was removed by rotary evaporation and the resultant two-layered mixture was poured into 300 ml of water
and extracted with three 75 ml portions of ether. The ether extract was washed twice with water, dried over sodium sulfate, concentrated and distilled to give 28 g (88%) of trans-2-methoxycyclooctanol, bp 53° (0.4 mm); nmr (CCl₄) δ 3.50 (m, 1, H-C-OR), 3.31 (s, 3, -OCH₃), 3.05 (m, 1, H-C-OR), 1.60 (m, 12, -CH₂ envelope).

3. trans-2-Methoxycyclooctyl p-Toluenesulfonate

trans-2-Methoxycyclooctanol (5.0 g, 0.031 mole) was dissolved in 50 ml of dry pyridine. To this clear, colorless solution was added, all at once, 10.0 g (0.50 mole) of recrystallized p-toluenesulfonyl chloride. The yellowish mixture was shaken at 5-minute intervals for about 30 minutes, allowed to set at room temperature for one hour, and stored in a freezer overnight. The solution containing crystals of pyridine hydrochloride was then poured into 300 g of ice water. The viscous oil which separated was agitated with a stirring rod for about 5 to 10 minutes, after which crystallization of the tosylate occurred. After the crystals were crushed with a stirring rod, they were filtered, thoroughly washed with cold water and with cold (-20° C) petroleum ether (30-60°), and dried in a vacuum desiccator. These crystals were pure white and sufficiently pure for use in solvolysis reactions. There was obtained 7 g (72%) of trans-2-methoxycyclooctyl p-toluenesulfonate, mp 51-52°; nmr (CDCl₃) δ 7.50 (m, 4, aromatic ring protons), 4.55 (m, 1, H-COSO₂⁻), 3.22 (m, 1, H-COCH₃), 3.00 (s, 3, OCH₃), 2.43 (s, 3, C₆H₄CH₃), 1.69 (m, 12, CH₂ envelope). Anal. Calcd. for C₁₆H₂₄O₄S: C, 61.52; H, 7.75. Found: C, 61.14; H, 7.79.
4. cis-1,2-Cyclooctanediol

A solution of cis-cyclooctene (22.0 g, 0.20 mole), tert-butyl alcohol (700 ml), and water (700 ml) was cooled to -5°. A separate solution of potassium permanganate (46.4 g, 0.30 mole), water (1 liter) and sodium hydroxide (10 g) was cooled to 0°. The permanganate solution was then added all at once to the olefin solution. Immediate precipitation of manganese dioxide occurred. The mixture was stirred magnetically for 1 hr. The cold solution was filtered by suction through a bed of glass wool, Celite filter aid, and filter paper to remove the manganese dioxide. The volume of solution was reduced from 2000 ml to 500 ml by rotary evaporation. The water-alcohol solution was then extracted with five 100 ml portions of water and dried with anhydrous magnesium sulfate. Removal of the ether solvent gave 10 g of crude yellow crystals. Recrystallization from ethyl acetate gave 8 g (29%) of cis-1,2-cyclooctanediol, white plates, mp 78-79° (lit. mp, 77.5-79°).

5. cis-2-Methoxycyclooctanol

cis-1,2-Cyclooctanediol (9.35 g, 0.065 mole) was dissolved in 400 ml of dry tetrahydrofuran (THF; predried over calcium hydride and distilled under nitrogen from lithium aluminum hydride). A slurry of 100 ml of THF and 2.84 g of sodium hydride as a 57% oil dispersion (1.62 g, 0.065 mole) was rapidly stirred with a mechanical stirrer in a 250 ml pressure equalized addition funnel. This slurry was added to the diol solution during one hour, and the mixture was stirred for an additional hour. Redistilled methyl iodide (8.5 g, 0.065 mole) was
added to the mixture, which was then heated at 60° for 1 hr. The THF solution was transferred to a 1 liter round bottom flask and was vacuum evaporated to a volume of about 100 ml. This solution was poured into 500 ml of water and extracted four times with 100 ml portions of ethyl ether. The ether extract was washed with two 100 ml portions of water and was dried over sodium sulfate overnight (about 12 hrs). The ether solution was removed by vacuum evaporation, and the solution was distilled to give four impure fractions, bp 48-70° (0.1 mm). Redistillation of this mixture gave four impure fractions, bp 80-98° (5 mm). The first two fractions (bp 80-83°) were largely cis-1,2-dimethoxycyclooctane. The latter fractions (bp 94-98°) were largely (73% glpc purity) cis-2-methoxycyclooctanol. Pure monoether was obtained by chromatographing the latter fractions through a 3' X 1/2" Silica Gel "G" column with petroleum ether-ethyl acetate (90/10 v/v%) and was used in this form without further purification for subsequent reactions. There was obtained 3.62 g (38.7%) of cis-2-methoxycyclooctanol; nmr (CDCl₃) δ 3.91 (m, 1, H-COR), 3.35 (s, 3, -OCH₃), 3.35 (m, 1, H-COR), 2.58 (s, 1, OH), 1.58 (m, 12, CH₂ ring envelope). Anal. Calcd. for C₉H₁₈O₂: C, 68.27; H, 11.47. Found: C, 67.93; H, 11.50.

6. cis-2-Methoxycyclooctyl p-Toluenesulfonate

cis-2-Methoxycyclooctanol (2.34 g, 0.015 mole) was dissolved in 50 ml of dry pyridine. To this clear, colorless solution was added, all at once, 5.7 g (0.03 mole) of p-toluenesulfonyl chloride. The mixture was swirled for five minutes to dissolve the solid, allowed to
stand for one hour at room temperature, and stored in a freezer at -10° overnight. The next morning the solution, which contained crystals of pyridine hydrochloride, was poured into 300 g of ice water. The viscous oil which separated was agitated with a stirring rod for 30 minutes, but crystallization did not occur. The oil was dissolved in two 50 ml portions of chloroform. The chloroform solution was washed with two cold 20 ml portions of 10% hydrochloric acid, with three 50 ml portions of water, with 25 ml of 10% sodium bicarbonate solution, and finally with 50 ml of water. It was dried (Na₂SO₄) overnight in a refrigerator and then was concentrated at 50° with a vacuum pump attached to the rotary evaporator through a dry ice-acetone cold trap. In this way the chloroform was rapidly stripped off before thermal decomposition of the sulfonate ester could occur. There was obtained 3.0 g (65%) of cis-2-methoxycyclooctyl tosylate: nmr (CDCl₃) δ 7.58 (m, 4, aromatic ring protons), 4.80 (m, 1, H-C-O₃SO₂⁻), 3.45 (m, 1, H-COCH₃), 3.27 (s, 3, OCH₃), 2.43 (s, 3, -C₈H₄CH₃), 1.50 (m, 12, CH₂ ring envelope).

B. Synthesis of cis- and trans-2-Methoxycyclooctyl Acetates

1. 2-Methoxycyclooctanone

The procedure used was adapted from Organic Synthesis, 1528 (1966), which describes the chromic acid oxidation of cyclooctanol to cyclooctanone in acetone. One change in the procedure was made. The addition of the chromate solution had to be terminated after the calculated stoichiometric amount was added. Since the reagent continued
to react with the methoxy ketone to produce an organic acid, (as yet uncharacterized), a color change (green to yellow) was not produced until this unwanted secondary reaction was complete. The rest of the procedure was followed exactly to yield 4.9 g (63%) of a clear, colorless liquid, bp 50-51° (0.4 mm), ir (neat) 1710 (C=O) and 1100 cm⁻¹ (ether C-O-C asymmetric stretch); nmr (CDCl₃) δ 3.82 (dd, 1, H-COCH₃), 3.38 (s, 3, OCH₃), 2.50 (m, 2, O=C-CH₂), 1.75 (m, 10, CH₂ envelope).

2. Lithium Aluminum Hydride Reduction of 2-Methoxycyclooctanone

Absolute ethyl ether (100 ml) was charged into a 300 ml three-neck round bottom flask equipped with magnetic stirrer bar, condenser with drying tube, gas inlet adapter and dropping funnel. A slow nitrogen flow through the flask was employed while lithium aluminum hydride, (LAH, 1.98 g, 0.052 mole) was introduced into the flask and stirred for 30 minutes. 2-Methoxycyclooctanone (5.47 g, 0.035 mole) was dissolved in 30 ml of absolute ether and was added dropwise to the LAH solution during 30 minutes. The mixture was refluxed for two hrs after which the slurry was decomposed by adding 100 ml of 3 M hydrochloric acid and decanting the ether layer. The aqueous layer was extracted with two 50 ml portions of ether which were combined with the original ether solution. The total ether solution was washed with cold saturated sodium bicarbonate solution, dried (MgSO₄), and concentrated in a rotary vacuum evaporator to give an oil whose infrared spectrum indicated hydroxyl and carbonyl stretching frequencies. A glpc analysis made by comparing authentic 2-methoxycyclooctanone and
trans-2-methoxycyclooctanol with the oil sample from LAH reduction indicated that the sample consisted of unreacted ketone and both 2-methoxycyclooctanols (2 cis/1 trans). Further separation of this mixture was not attempted after the successful synthesis of cis-2-methoxycyclooctanol via the sodium hydride Williamson synthesis already described. The mixture was found to be useful as a glpc reference in solvolysis reactions of cis- and trans-2-methoxycyclooctyl tosylates in 80% ethanol.

3. Acetylation of Mixture of cis- and trans-2-Methoxycyclooctanols:
Preparation of cis- and trans-2-Methoxycyclooctyl Acetates

The reaction product mixture of cis- and trans-2-methoxycyclooctanols and 2-methoxycyclooctanone (3.75 g of this mixture was used) was dissolved in 20 ml of acetic anhydride in which 3.0 g of sodium acetate had been previously dissolved. This mixture was refluxed for 24 hrs after which it was rinsed with water into a separatory funnel containing 100 ml of water. The mixture was extracted with three 50 ml portions of pentane. The combined pentane extract was extracted with two 20 ml portions of water, dried (MgSO₄), and concentrated by rotary vacuum evaporation to give a pleasant smelling oil which was used without further purification. Glpc analysis of this oil revealed cis- and trans-2-methoxycyclooctyl acetates in a 2/1 ratio and unreacted 2-methoxycyclooctanone. Comparison of the mixture of acetylated alcohols to authentic trans-2-methoxycyclooctyl acetate showed that cis-2-methoxycyclooctyl acetate had a shorter retention time on the 10' Carbowax 20M column than did the trans-isomer.
Glpc analysis of the isomeric cis- and trans-2-methoxycyclooctanols revealed that the trans alcohol had a slightly shorter retention time than did the cis alcohol.

4. **trans-2-Methoxycyclooctyl acetate**

2-Methoxycyclooctanol (5.0 g, 0.031 mole) was refluxed overnight in 50 ml of acetic anhydride containing 5 g of sodium acetate. The mixture was worked up as described above to give a pentane concentrate with a pleasant odor. Glpc analysis showed this concentrate to be a relatively pure sample containing less than 0.1% of the starting alcohol. Nmr (CCl₄) δ 4.83 (m, 1, H-C-OAc), 3.29 (m, 1, H-COCH₃), 3.29 (s, 3, OCH₃), 1.99 (s, 3, O-CO-CH₃), 1.68 (m, 12, CH₂ envelope).

C. **3-Acetoxy cyclooctene**

2-Cycloocten-1-ol (5.0 g, 0.03 mole) was dissolved in 25 ml of acetic anhydride containing 3.0 g of anhydrous sodium acetate. The mixture was refluxed for 24 hrs after which the procedure for the isolation of the isomeric 2-methoxycyclooctyl acetates was followed to yield a pleasant smelling oil which gas chromatography showed was essentially a single component. Nmr (CDCl₃) δ 5.58 (m, 2, -CH=CH⁻), 5.58 (m, 1, H-COAc), 2.17 (m, 2, -CH₃-CH=CH⁻), 2.00 (s, 3, -OCOCH₃), 1.58 (m, 8, CH₂ ring envelope).
D. Attempted Preparation of trans-2-Methoxycyclodecanol

1. cis-Cyclodecene Oxide (11-oxabicyclo[8.1.0]undecane)

 cis-Cyclodecene (0.09 mole, 12.0 g), benzonitrile (9.6 g, 0.09 mole), and potassium bicarbonate (1.5 g) were dissolved in 150 ml of methanol, and 11 g of 30% hydrogen peroxide was added at room temperature. The progress of the reaction was followed by gas chromatography until the consumption of cyclodecene was nearly complete. The reaction mixture was diluted with 250 ml of water and extracted with three 100 ml portions of chloroform. The chloroform extracts were combined and washed with two 75 ml portions of warm (60°) water. The chloroform extract was dried (MgSO₄) and concentrated by rotary vacuum evaporation. The crystals of benzamide which separated were filtered, and the filtrate was distilled at reduced pressure (0.4 mm) to yield 9.23 g (69%) of cis-cyclodecene oxide, bp 60° (0.4 mm), ir, (neat) 1250 cm⁻¹ (O=C); nmr (CDCl₃) δ 2.94 (m, 2, HOC=CH), 1.70 (m, 16, CH₂ envelope).


The experimental procedure followed was the same as that for the analogous reaction with cis-cyclooctene oxide; 5.0 g (0.032 mole) of cis-cyclodecene oxide was used in the reaction.

Evaporation of the dried pentane extract yielded a viscous yellow liquid, which, from gas chromatographic analysis, contained five components. The retention times and area percentages of these
components were: (1) 2.6 min., 5%; (2) 13.2 min., 64%; (3) 13.6 min., 15%; (4) 32.8 min., 6%; (5) 34.6 min., 10%. Component (3) appeared as a small shoulder on component (2). These components were partially separated by preparative gas chromatography. The component of retention time 13.2 minutes was tentatively identified as cis-2-cyclodecen-1-ol; nmr (CDCl₃) δ 5.4 (m, 2, H-C=CH), 3.8 (m, 1, H-C-OH), 3.4 (impurity, s, 1/5, OCH₃), 2.52 (s, 1, OH), 2.2 (m, 4, CH₂ C-4 and C-10), 1.55 (m, 13, CH₂ envelope). Components (4) and (5) gave the following composite nmr spectrum: (CDCl₃), δ 3.9 (m, 1, H-C-OR), 3.35 (m, 1, H-C-OR), 3.35 (s, 3, OCH₃), 2.81 (s, 1, OH), 1.50 (m, 18, CH₂ envelope).

E. Solvolyses

1. Solvolysis of trans-2-Methoxycyclooctyl Tosylate in 80% Aqueous Ethanol at 60°

In a 50 ml round bottom flask, a mixture of 24 ml of absolute ethanol, 6 ml of distilled water, and 0.33 g (0.032 mole) of reagent grade calcium carbonate was heated to 60° while being stirred magnetically. After temperature equilibrium was established, trans-2-methoxycyclooctyl tosylate (1.00 g, 0.032 mole) was added. One reaction was monitored by gas chromatography at time intervals of 10, 35, 55, and 360 minutes. These analyses showed that all products formed simultaneously and were in the same proportions at all times. The solvolysis was terminated after six hours, and the mixture was poured into 250 ml of water. The mixture was tested with pHydron paper and found to be slightly basic. This mixture was extracted with three 40 ml portions
of water. The pentane extracts were dried (Na₂SO₄) and were concentrated by rotary evaporation. (Distillation of one solvolysis mixture to remove pentane gave product percentages which were not significantly different from those in which rotary vacuum evaporation was used to remove extracting solvent.) The concentrates were analyzed by infrared spectroscopy and nmr spectrometry; ir (neat) 1700 (C=O) and 1100 cm⁻¹ (C-O-C asymmetric stretch); nmr (neat δ 5.58 (m, H₃C=CH), 4.35 (m, H₃C-O-C₄H), 3.38 (q, J = 7Hz, CH₃CH₂O-), 3.15 (s, OCH₃), 3.17 (s, OCH₃), 1.70 (m, CH₂ envelope), 1.01 (t, J = 7Hz, CH₃CH₂O-).

This experiment was repeated five times more, twice without calcium carbonate. The results obtained from runs without calcium carbonate were identical in all respects with those with added calcium carbonate. One solvolysis was done on a preparative scale with 6.0 g (0.019 mole) of tosylate, 192 ml of 80% aqueous ethanol and 4 g (excess) of calcium carbonate. After 6 hrs, the mixture was worked up as described previously, and the pentane concentrate was separated on a 9.7' x 1/4" stainless steel Carbowax 20M column (10% on 60/80 Chromosorb) at a column temperature of 140°C. Each injection was 0.05 ml for a total of four injections. Four fractions were collected and identified from nmr spectra as (1) a mixture of 4-methoxycyclooctene and 9-oxabicyclo[4.2.1]nonane (39% and 6%, respectively); nmr (CCl₄) δ 5.58 (m, 2, H₃C=CH), 4.35 (m, 0.15, H₃C-O-C₄H), 3.23 (m, 1, H-COCH₃), 1.75 (m, 10.75, CH₂ envelope); (2) cyclooctanone (12%); nmr (CCl₄) exactly matched that of an authentic commercial sample; (3) ethyl 2-methoxycyclooctyl ether (39%); nmr (CCl₄) δ 3.38 (q, 2, J = 7Hz, CH₃CH₂O-), 3.20 (s, 3, OCH₃), 1.50 (m, 12, CH₂ envelope), 1.01 (t, 3,
2. Solvolysis of trans-2-Methoxycyclooctyl Tosylate in 80% Aqueous Ethanol with Lithium Perchlorate

trans-2-Methoxycyclooctyl tosylate (1.0 g, 0.032 mole) was solvolyzed in 30 ml of 80% ethanol at 60° containing calcium carbonate (1.00 g) and 0.16 g of lithium perchlorate (0.05 M). Workup of this mixture in the manner previously described for trans-2-methoxycyclooctyl tosylate yielded an oil which gave an infrared spectrum identical in all respects to that of solvolysis mixtures from trans-2-methoxycyclooctyl tosylate without lithium perchlorate. Analyses by gas chromatography and by nmr also verified the infrared spectral indications.

3. Solvolysis of cis-2-Methoxycyclooctyl Tosylate in 80% Aqueous Ethanol at 60°

cis-2-Methoxycyclooctyl tosylate (0.5 g, 0.016 mole), and calcium carbonate (0.5 g) were dissolved in 15 ml of 80% aqueous ethanol which had been heated to 60°. After 6 hrs, the mixture was poured into 250 ml of water and worked up as previously described for 80% aqueous ethanol solvolyses. The resulting oil was analyzed by gas chromatography and nmr techniques. Glpc analysis revealed seven components of retention times (1) 5.2, (2) 7.0, (3) 9.8, (4) 13.6, (5) 14.8, (6) 19.6, and (7) 20.3 minutes. An unknown component of retention time 9.4 minutes was also detected. The first seven components were separated on a preparative 9' X 3/8" Carbowax 20M gas
chromatographic column and subsequently identified by comparison of their nmr or gas chromatographic data with those of authentic samples. The components were identified as (1) 5-methoxycyclooctene (54%), [nmr (CDCl3) δ 5.65 (m, 2, HC-CH), 3.25 (m, 1, H-COCH3), 3.25 (s, 3, OCH3), 1.85 (m, 10, CH2 envelope; this pattern is split into a 3/2 ratio, the allylic protons, CH2CH=CH-CH2, appearing farthest downfield)]; (2) cycloheptanecarboxaldehyde (11%), identified by glpc comparison with an authentic sample on Carbowax 20M and XF-1150 columns (Nmr analysis of the reaction mixture revealed a broad doublet absorption at δ 9.65, which is attributed to CHCHO); (3) cyclooctane (3%) identified by comparison of its glpc retention time and nmr spectrum with those of an authentic sample; (4) ethyl trans-2-methoxycyclooctyl ether (0.7%), identified by glpc comparison with an authentic sample obtained from solvolysis of trans-2-methoxycyclooctyl tosylate in 80% ethanol; (5) ethyl cis-2-methoxycyclooctyl ether (24%), identified by comparison of glpc retention time with that of an authentic sample prepared from cis-2-methoxycyclooctanol, sodium hydride and ethyl iodide; (6) trans-2-methoxycyclooctanol (1%), identified by comparison of glpc retention time with that of an authentic sample; (7) cis-2-methoxycyclooctanol (3%), identified by comparison of glpc retention time with that of an authentic sample. All comparisons were made on both Carbowax 20M and XF-1150 columns.

4. Solvolysis of trans-2-Methoxycyclooctyl Tosylate in Acetic Acid

Solvolysis of this tosylate without lithium perchlorate was carried out seven times; the only variation in procedure was the amount
of tosylate used. All solvolyses were 0.1 M with respect to tosylate. A typical solvolysis and workup procedure is described.

A mixture of glacial acetic acid (60 ml) and acetic anhydride (0.1 ml) was heated to 60° in a 100 ml single neck round bottom flask equipped with a 1/2" magnetic stirrer bar and a condenser with drying tube (CaCl₂). After one hour, trans-2-methoxycyclooctyl tosylate (2.0 g, 0.064 mole) was introduced into the flask and was solvolyzed with stirring for six hours. The colorless mixture was poured into 500 ml of distilled water, and the cloudy aqueous solution was extracted with four 40 ml portions of pentane. The combined pentane extracts were washed with two 50 ml portions of water after which the pentane extract was dried (Na₂SO₄). The pentane was removed by rotary vacuum evaporation to yield a colorless oil which was analyzed by gas chromatography with a 10' X 1/8" Carbowax 20M column (10% on 60/80 Chromosorb). Six major components which made up > 99% of the total product mixture were detected. Separation of these components on a 9' X 3/8" Carbowax 20M preparative column, followed by nmr analysis of each component, revealed that the first component peak consisted of two discrete compounds with identical retention times on the Carbowax column under the conditions used. (See nmr spectrum No. 14.) The components were identified as (1) 4-methoxycyclooctene (25%), nmr (CCl₄) δ 5.60 (m, 2, HC=CH), 3.21 (s, 3, OCH₃), 3.18 (m, 1, H-COCH₃), 2.20 (m, 4, CH₂CH=CHCH₂), 1.55 (m, 6, CH₂ envelope); (2) 9-oxabicyclo[4.2.1]nonane (12%), ir, identical to that of A. C. Cope's sample of same; nmr (CDCl₃) δ 4.35 (m, 2, H-C¹-O-C²H), 1.72 (m, 12, CH₂ envelope); (3)
cyclooctanone (15%), identified by glpc and nmr comparisons with an 
authentic commercial sample; (4) 4-acetoxy-cyclooctene (5%), nmr 
(CDCl₃) δ 5.65 (m, 2, H=CH), 4.88 (m, 1, H-COAc), 2.40 (m, 2, C-3 
methylene; this multiplet appears as a superimposed doublet of 
doublets and has been found to be characteristic of the [OX]
structure for eight-membered rings where X is methyl or acyl) 
2.15 (m, 2, CH=CHCH₂), 2.00 (s, 3, O-COCH₃), 1.65 (m, 6, CH₂ envelope); 
(5) trans-2-methoxycyclooctyl acetate (3%), nmr (CCl₄) δ 4.85 (m, 1, 
H-COAc), 3.30 (s, 3, OCH₃), 3.30 (m, 1, H-C-OCH₃), 1.98 (s, 3, O-COCH₃), 
1.65 (m, 12, CH₂ envelope); (6) 4-methoxycyclooctyl acetate (39%), nmr 
(CCl₄) δ 4.81 (m, 1, H-C-OAc), 3.20 (s, 3, OCH₃), 3.20 (m, 1, H-C-OCH₃), 
1.90(s, 3, O-COCH₃), 1.65 (m, 12, CH₂ envelope).

5. Solvolysis of trans-2-Methoxycyclooctyl Tosylate in Acetic 
Acid at 60°C with Added Lithium Perchlorate.

trans-2-Methoxycyclooctyl tosylate (2.0 g, 0.064 mole), 
lithium perchlorate (0.64 g, 0.1 M in 60 ml) and acetic anhydride 
(0.1 ml) were dissolved in 60 ml of glacial acetic acid previously 
heated to 60°C in a heating bath. After six hrs, the mixture was 
worked up following the standard method described previously for the 
trans-tosylate. The brown oil obtained was analyzed as described 
before. The compounds identified were (1) 4-methoxycyclooctene (7%), 
(2) 9-oxabicyclo[4.2.1]nonane (43%), (3) cis-cyclooctene oxide (3%), 
identified by glpc and nmr comparisons with an authentic commercial 
sample, (4) cyclooctanone (11%), (5) 4-acetoxy-cyclooctene (27%), (6) 
trans-2-methoxycyclooctyl acetate (2%), and (7) 4-methoxycyclooctyl 
acetate (7%).
6. Solvolysis of \textit{cis}-2-Methoxycyclooctyl Tosylate in Acetic Acid at 60°

A mixture of glacial acetic acid (30 ml, previously heated to 60°), \textit{cis}-2-methoxycyclooctyl tosylate (1.0 g, 0.032 mole) and acetic anhydride (0.1 ml) was heated at 60° for six hours. The mixture was worked up by the standard method described for the \textit{trans}-tosylate. There was obtained a colorless oil which consisted of the following components: (1) 5-methoxycyclooctene (47%), (2) cycloheptanecarboxyaldehyde (3%), (3) cyclooctanone (2.6%), (4) 4-acetoxyoctooclooctene (2.2%), (5) \textit{cis}-2-methoxycyclooctyl acetate (5%), (6) \textit{trans}-4-methoxycyclooctyl acetate (2%) and (7) \textit{cis}-4-methoxycyclooctyl acetate (35%), tentatively identified on the basis of glpc retention time and nmr spectral data:

\textit{nmr} (CDCl$_3$) $\delta$ 4.85 (m, 1, H-O-OAc), 3.27 (s, 3, OCH$_3$), 3.27 (m, 1, H-C-OCH$_3$), 1.99 (s, 3, O-COCH$_3$), 1.72 (m, 12, CH$_3$ envelope), 3.66 (s, 1, unassigned peak). The unassigned peak makes the identification tentative. Otherwise, glpc and nmr data indicate this to be the \textit{cis} isomer of 4-methoxycyclooctyl acetate.

7. Solvolysis of \textit{cis}-2-Methoxycyclooctyl Tosylate in Acetic Acid with Added Lithium Perchlorate at 60°

A mixture of glacial acetic acid (30 ml, previously heated to 60°), \textit{cis}-2-methoxycyclooctyl tosylate (1.0 g, 0.032 mole), acetic anhydride (0.1 ml), and lithium perchlorate (0.32 g, 0.1 mole) was heated at 60° for six hours. The mixture was worked up following the standard method described for the workup of the solvolysis mixture of
the trans-tosylate. There was obtained a brown oil with the following components: (1) 5-methoxycyclooctene (17%), (2) cycloheptanecarboxyaldehyde (13%), (3) cis-cyclooctene oxide (1.0%), (4) cyclooctanone (3%), (5) 4-acetoxyoctene (23%), (6) cis-2-methoxycyclooctyl acetate (14%), (7) trans-4-methoxycyclooctyl acetate (1.4%), and (8) cis-4-methoxycyclooctyl acetate (14%). All components have been described previously.
Solvolysis reactions of cis- and trans-2-methoxycyclooctyl p-toluenesulfonates (tosylates) have been investigated in two solvents to determine product distributions and the roles of different ion pair intermediates in the reactions. The rearrangement products can be directly correlated with the stereochemistry of the starting tosylates. Product distribution data have shown that the compounds arising from cis- and trans-tosylates are quite different and imply that the reactive intermediates from each stereoisomer do not undergo conformational changes to give identical species.

The outstanding differences in product distribution for the isomeric tosylates were (a) the formation of cycloheptanecarboxaldehyde, an alkyl migration product, from cis-tosylate and cyclooctanone, a hydrogen migration product, from trans-tosylate; and (b) the formation of 5-methoxycyclooctene as the chief olefinic product from cis-tosylate and 4-methoxycyclooctene from trans-tosylate.

The effect of lithium perchlorate in acetic acid solvolyses revealed the existence of several discrete ionic species. Addition of lithium perchlorate in the acetolysis of trans-tosylate increased the amount of 9-oxabicyclo[4.2.1]nonane (4) from 12% to 43%, and the amount of 4-acetoxyoctyloctene (10) from 5% to 27% at the expense of 4-methoxycyclooctene (2) and 4-methoxycyclooctyl acetate (12t), respectively. This result indicates that the products (4 and 10) which increased in amount are most likely formed from solvent-separated ion
pairs, while those \((2 \text{ and } 12t)\) which decreased in amount are most likely formed from intimate ion pairs. The \textit{cis}-tosylate responded in a fashion similar to the \textit{trans}-isomer towards added lithium perchlorate. The amounts of cycloheptanecarboxaldehyde and 4-acetoxyoctoactene were increased at the expense of 4-methoxycyclooctyl acetate and 5-methoxycyclooctene.

Although I have attempted to define this system in as much detail as possible, there are some unanswered questions. If this problem is scrutinized further, I hope that the next investigator will find this project as challenging and as rewarding as I have.
REFERENCES


20. This explanation based on a discussion in "Solvolytic Displacement Reactions" by Andrew Streitweiser, Jr., McGraw-Hill, New York, pp. 167-170.


24. For an example of the use of calcium carbonate to prevent the accumulation of product acid during solvolysis, see Winstein, S., and Ingraham, L. L., J. Amer. Chem. Soc., 74, 1160 (1952).


34. Adapted from Payne, G. B., Tetrahedron, 18, 763 (1962).


APPENDIX I

NMR SPECTRA
SPECTRUM NO. 1

cis-2-Methoxycyclooctanol

60 MHz in CDCl₃
SPECTRUM NO. 2

trans-2-Methoxycyclooctanol

60 MHz in CDCl₃
This spectrum was included because of the interesting pattern obtained for the methylene portion of the ethyl group at δ 3.50. This pattern (which should be a quartet) is due to either "W" coupling between the methine hydrogen on C-2 and the methylenes of the ethyl group or to unequal coupling of the two methylene hydrogens of the ethyl group to the C-2 methine hydrogen.
SPECTRUM NO. 4

* cis-2-Methoxycyclooctyl p-Toluenesulfonate *

60 MHz in CDCl₃

The offset portion of the spectrum at δ 7.58 represents the symmetrical AA'BB' pattern of the p-disubstituted benzene ring of the p-toluenesulfonate ester group. There is a chloroform impurity peak at δ 7.35. The methoxy singlet (δ 3.27) has shifted 0.08 ppm upfield with respect to the parent alcohol.
trans-2-Methoxycyclooctyl p-Toluenesulfonate

60 MHz in CDCl₃

The methoxy singlet (3.02) has shifted 0.31 ppm upfield with respect to the parent alcohol.
SPECTRUM NO. 6

**trans-2-Methoxycyclooctyl p-Toluenesulfonate**

100 MHz in CDCl₃

Decoupling Experiment

The bottom spectrum is unperturbed. The middle spectrum represents amplification of the methine hydrogens Hₐ and Hₐ. Irradiation at the point designated by the arrow causes the quintet pattern to collapse to a doublet with J = 8 Hz. This experiment proved that the **trans**-tosylate obtained from the **trans**-methoxy alcohol was a 1,2-disubstituted isomer (as opposed to 1,4-disubstituted).
SPECTRUM NO. 7

\textbf{trans-2-Methoxycyclooctyl Acetate}

60 MHz in CDCl$_3$

A slight pentane impurity appears at $\delta$ 1.4 and 1.0.
SPECTRUM NO. 8

4-Methoxycyclooctyl Acetate

Compound 12t

60 MHz in CCl₄

The stereochemistry of this compound is not known with certainty, but is believed to be

trans.
SPECTRUM NO. 9

3-Acetoxycyclooctene

60 MHz in CDCl₃

Pentane impurities appear just upfield from the methylene envelope. The area at δ 5.58 represents three hydrogens, the acetoxymethine and the two of the carbon-carbon double bond.
SPECTRUM NO. 10

4-Acetoxy cyclooctene

60 MHz in CDCl₃

The acetoxy methine hydrogen at δ 4.88 is not shifted as far downfield as in 3-
acetoxy cyclooctene (Spectrum No. 9).
SPECTRUM NO. 11

4-Acetoxycyclooctene

100 MHz in Benzene

Decoupling Experiment

The bottom spectrum is unperturbed. The middle spectrum represents irradiation at 484 Hz, the acetoxyc methine. Irradiation at this point collapses the triplet pattern at 237 to a broad doublet, and leaves the vinyl hydrogen pattern at 565 unperturbed. Irradiation at 237 perturbs the patterns at 565 and 484. This experiment is interpreted as showing that the allylic hydrogens at 237 lie between the vinyl hydrogens at 565 and the methine hydrogen at 484, thereby fixing the position of the double bond relative to the acetoxyc group.
SPECTRUM NO. 12

4-Methoxycyclooctene

60 MHz in CCl₄

The spectrum is quite similar to that of 4-acetoxycyclooctene (Spectrum No. 10).
This sample was one of the olefinic products isolated from solvolyses of cis-2-methoxycyclooctyl tosylate. The difference between the vinyl hydrogen pattern of this methoxy olefin and that of 4-methoxycyclooctene (Spectrum No. 12) is quite striking.
This experiment was designed to fix the position of the double bond relative to the methoxy group. The effect on the methoxy methine hydrogen was not observed since this absorption is obscured by the methoxy methyl singlet absorption. The upfield and downfield irradiations produced the same type perturbances as were observed in decoupling 4-acetoxycyclooctene. The conclusion was that the double bond is separated from the methoxy group by the methylene indicated on the spectrum.
SPECTRUM NO. 15

Mixture of 9-Oxabicyclo[4.2.1]nonane and 4-Methoxycyclooctene

60 MHz in CCl₄

This spectrum was taken of component one obtained by preparative glpc, from the acetolysis of trans-2-methoxycyclooctyl tosylate without lithium perchlorate added. The two-component nature of component was suggested by this spectrum.
mixture of

CH₃ + CH₃OCH₃
SPECTRUM NO. 16

9-0xabicyclo[4.2.1]nonane

60 MHz in CCl₄

This spectrum was taken of component one obtained by preparative gipc, from acetolysis of trans-2-methoxycyclooctyl tosylate with added lithium perchlorate. The singlet at δ 3.25 is due to the methoxy group of 4-methoxycyclooctene. The sample is > 85% bicyclic ether.
A SELECTED BIBLIOGRAPHY


VITA

Richard Arthur Evans was born in Gulfport, Mississippi, November 20, 1938, to Louis A. and Hannah M. Evans. He attended public school in Gulfport and graduated from 33rd Avenue High School in May of 1955. He entered Tougaloo College in Tougaloo, Mississippi, the following September and was awarded the Bachelor of Science Degree in Chemistry from that institution in June of 1959. In that same month, he entered Western Michigan University, Kalamazoo, Michigan. In August of 1960, he was married to Gloria Anne Bolton of Greenville, Mississippi. After completing a Master of Arts Degree in Chemistry at Western Michigan in 1962, he taught for one year at Morgan State College, Baltimore, Maryland. During that year, a son, Gregory, was born. In September of 1963, he began employment at Alabama A. and M. University in Huntsville, Alabama. During his tenure there a second son, Christopher, was born. He began his studies at Louisiana State University in the Summer of 1965 in a National Science Foundation supported Summer Institute for College Teachers of Chemistry. These summer studies continued through 1968, when he took a leave of absence from Alabama A. and M. to finish his doctoral studies. During the three years in residence, he was a National Science Foundation Science Faculty Fellow (1968-69), a Southern Fellowships Fund Fellow (1969-70), and a Ford Foundation Fellow (1970-71). He is a member of Alpha Phi Alpha Fraternity, Inc., Beta Kappa Chi National Scientific Honorary Society, The American Chemical Society, and The Society of Sigma Xi.

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Candidate: Richard Arthur Evans

Major Field: Chemistry

Title of Thesis: The Influence of a Neighboring Methoxy Group on Solvolyses of Cyclooctyl p-Toluenesulfonates

Approved:

[Signatures]

Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

[Signatures]

Date of Examination:

July 16, 1971