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Solvolyses of Medium-Ring 2-Halocycloalkanols.

John Schneller III

Louisiana State University and Agricultural & Mechanical College

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SOLVOLYSES OF MEDIUM-RING
2-HALOCYCLOALKANOLS

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

John Schneller, III
B.S., Louisiana State University in New Orleans, 1962
May, 1965
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The author feels that this acknowledgment would be incomplete without thanking his parents, whose encouragement and assistance have always meant so much.
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Product distribution data have been obtained for solvolyses of trans-2-chloro- and -bromocyclooctanols in mixed aqueous solvents and in carboxylic acid solvents. Less extensive data have been obtained for solvolyses of cis-2-bromocyclooctanol, trans-2-chloro- and -bromocyclo- nonanols, and trans-2-bromocyclodecanol. The product mixtures contain substantial amounts of both transannular and nontransannular products. The proportions of the various products are remarkably insensitive to the identity of the halogen, the presence or absence of silver salts or sodium acetate (buffer), temperature and solvent change. Solvolyses of cis-cyclooctene oxide have been reexamined under these conditions to permit direct comparison of related reactions. The data lead to the conclusion that these halohydrin solvolyses proceed by two competing mechanisms: (1) ionization to an unbridged 2-hydroxycycloalkyl cation, and (2) formation of hydrogen- (or alkyl-) bridged species. The small shift in proportions of products with change of solvent, and the change in product distribution with the addition of sodium azide support the conclusion. Solvolyses of epoxide, glycol and amino alcohol by previous workers are compared with the halohydrin and epoxide solvolyses performed in this work; the amino alcohol and halohydrin reactions are distinguished from the others by the relative abundance of carbonyl products in the mixtures.
INTRODUCTION

Studies of solvolysis reactions have provided a wealth of information pertinent to considerations of reaction mechanisms during the past forty years.

The particular type of solvolysis reaction which is studied in this work is of the class known as pinacolic transformations (after Fittig's original observation that pinacol undergoes acid-catalyzed rearrangement to pinacolone).

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3-\text{C} & \quad \text{C}-\text{CH}_3 \\
\text{OH} & \quad \text{OH}
\end{align*}
\xrightarrow{\text{H}^+}
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3-\text{C} & \quad \text{C}-\text{CH}_3 \\
\text{OH} & \quad \text{OH}
\end{align*}
\]

Rearrangements of pinacols (1,2-glycols), olefin oxides, amino alcohols and halohydrins of corresponding structure are presumed to be closely related processes. Pocker has reported that these derivatives of tetramethylethylene all give equivalent proportions of glycol (substitution) and ketone (rearrangement) products. These and other related data have led to the claim that "the accepted mechanism for pinacolic transformations involves the prior formation of a carbonium ion intermediate."

When hydrogen rather than alkyl or phenyl migrates in the rearrangements of these olefin derivatives (for example, rearrangements
of secondary glycols), evidence concerning the nature of the intermediate is far less extensive. Acid-catalyzed rearrangement of \textit{exo-cis}-norbornene glycol yields norcamphor, not \textit{cis}-2,7-norbornanediol. \textsuperscript{5} It

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

appears that carbon migration is unable to compete with hydrogen migration in this system where carbon migration is highly favored. Traynham suggested that a carbonium ion is not involved here, but that neighboring hydrogen must migrate concurrently with the departure of water.

A more recent paper by Collins and coworkers \textsuperscript{6} reports the acid-catalyzed rearrangement of 2-phenylnorbomane-2,3-\textit{exo-cis}-dil to 3-\textit{endo}-phenyl-2-norbornanone of inverted configuration. This result, they say, can only be the result of a nonclassical type carbonium ion intermediate rather than the normal open carbonium ion structure.

Some data which exhibit little evidence for carbonium ion intermediates were submitted by Smith, Bowman and Kmet, \textsuperscript{7} who demonstrated the internal nature of deuterium migration during the rearrangement of 2-methyl-2,3-butanediol-3-d.

\[
\begin{align*}
\text{CH}_3 & \text{D} \\
\text{CH}_3 & \text{C} - \text{C-CH}_3 \\
\text{OH} & \text{OH} \\
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \\
\text{CH}_3 & \text{C} - \text{C-CH}_3 \\
\text{D} & \text{O} \\
\end{align*}
\]

Acid-catalyzed rearrangement of isobutylene glycol appears to have more carbonium ion character than the rearrangement of the isobutylene
Although numerous examples of reactions involving hydrogen migration are known, evidence for migration during departure of leaving group is meager. Even in some apparently ideally suited cases, neighboring hydrogen leads to small rate enhancement, and in some fast reactions involving hydrogen migration (for example, cyclodecyl tosylate acetolysis) anchiméric assistance has been shown to be absent.7,9,10

Medium ring (eight to twelve ring members) compounds exhibit features which set them apart from compounds of other ring sizes.10,11,12 They are extremely hard to synthesize by conventional methods (and unconventional ones, too), and in general have unusual physical and chemical properties. These differences were rationalized by assuming that unusual nonclassical strains exist in medium ring compounds. Heats of combustion data13 and x-ray diffraction measurements14 have indicated that these ring systems are unusually strained, especially the nine and ten membered systems.

Pitzer strain (lateral repulsion between atoms or orbitals attached to vicinal ring members) and Baeyer strain (deviation from optimum bond angles) are present to some extent in medium ring compounds, although the cyclodecane ring shows a conformation free of Pitzer strain.14 End-on interaction of hydrogens from opposite sides of the ring (transannular strain) is considered to be of major influence in many of the reactions of medium ring compounds.

These unusual properties make medium ring compounds useful tools in the study of reaction mechanisms. Different kinds of intermediates (or transition states) can lead to different kinds of products to an
extent seldom matched in other systems. Reaction courses seem to be particularly sensitive to carbonium ion character in intermediates. Transannular migrations (that is, reactions in which an atom or group migrates across the ring) were discovered almost simultaneously by Cope and Prelog in peroxyformic acid oxidations of cyclooctenes and cyclodecenes. These same workers have reported many further examples of transannular reactions in systems closely related to the original.

Acid-catalyzed rearrangements of epoxides and peroxy-acid oxidation of olefins normally lead to 1,2-diols as major products. However, with medium ring epoxides and olefins, the 1,2-diols are formed to minor extents or not at all, and the major substitution products become the 1,4-, 1,5- and 1,6-diols for the eight, nine and ten membered rings, respectively. Descriptions of mechanism have involved opening of the epoxide ring to give the 2-hydroxycycloalkyl cation which then can undergo a transannular hydride shift.

Some recent papers from Professor Traynham's group on the rearrangements of medium ring 2-substituted-cycloalkanols have shed new light on the intermediates involved in these type systems.

Acid-catalyzed rearrangements of medium ring glycols are highly similar to those of the corresponding epoxides and give extensive transannular rearrangement, but nitrous acid deamination of the corresponding amino alcohols leads almost exclusively to products formed.
by 1,2-shifts with very little transannular rearrangement. This great
difference in product composition leads to the belief that there is a
different mechanism operating in the amino alcohol deaminations than
in glycol or epoxide rearrangements.

The present work, a continuation of the above studies is
an evaluation of the occurrence of dual mechanisms in the reactions of
related 2-hydroxycycloalkyl derivatives and an attempt to obtain a
detailed mechanistic picture of these reactions. Solvolyses of trans-
2-bromo- and -chlorocyclooctanols, cis-2-bromocyclooctanol, trans-2-
chloro- and -bromocyclononanols and trans-2-bromocyclodecanol were investigated.
Acid-catalyzed hydrolyses of cis-cyclooctene oxide under conditions
similar to those for halohydrin solvolyses were examined for comparison.
Product distribution data for the halohydrin solvolyses, falling in
between those for epoxide and glycol reactions and those for
amino alcohol deaminations, point strongly to an influence of leaving
group not only on product formation but on gross reaction mechanism as
well.
CHAPTER II

RESULTS AND DISCUSSION

A. Solvolyses of the 2-Halocyclooctanols

1. Results

Solvolyses of the halohydrins \(1, 2t, 2c\) were carried out, both with and without added silver nitrate, in mixed aqueous solvents and in nearly anhydrous carboxylic acid solvents. Some experiments were performed to evaluate the effects of temperature, buffer and azide ion on the solvolysis reactions. Reaction mixtures were analyzed by capillary column gas chromatography (g.c.), and component identities were established by use of preparative gas chromatography, infrared spectroscopy, preparation of derivatives and comparison with authentic samples of mixtures.\(^{29,30}\) The various solvolysis products are illustrated on the following page and the numbers underneath each compound are used to designate those compounds throughout the text. Tables I, II, and III summarize the product data. The symbols THF, HOAc, and EtOH refer to tetrahydrofuran, acetic acid, and ethanol, respectively.


<table>
<thead>
<tr>
<th>Halide</th>
<th>Solvent&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Salt</th>
<th>Hours</th>
<th>2</th>
<th>4</th>
<th>5</th>
<th>6t</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10,11&lt;sup&gt;b&lt;/sup&gt;</th>
<th>12t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td>THF</td>
<td>none</td>
<td>335</td>
<td>15</td>
<td>8</td>
<td>0</td>
<td>7</td>
<td>4</td>
<td>28</td>
<td>9</td>
<td>15</td>
<td>3.5</td>
</tr>
<tr>
<td>Cl</td>
<td>THF</td>
<td>AgNO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>27</td>
<td>16</td>
<td>0</td>
<td>8</td>
<td>1</td>
<td>2</td>
<td>38</td>
<td>4</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>Br</td>
<td>THF</td>
<td>none</td>
<td>44</td>
<td>21</td>
<td>3</td>
<td>.4</td>
<td>7</td>
<td>5</td>
<td>32</td>
<td>7</td>
<td>17</td>
<td>3.5</td>
</tr>
<tr>
<td>Br</td>
<td>THF</td>
<td>AgNO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>4</td>
<td>24</td>
<td>0</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>34</td>
<td>2</td>
<td>28</td>
<td>1</td>
</tr>
<tr>
<td>Br</td>
<td>THF</td>
<td>NaOAc</td>
<td>54</td>
<td>24</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>4</td>
<td>30</td>
<td>10</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Br</td>
<td>HOAc</td>
<td>AgNO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>6</td>
<td>23</td>
<td>11</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>26</td>
<td>4</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Br</td>
<td>HOAc&lt;sup&gt;d&lt;/sup&gt;</td>
<td>AgNO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>52</td>
<td>25</td>
<td>11</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>36</td>
<td>2</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Br</td>
<td>1M H&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt;&lt;sup&gt;e&lt;/sup&gt;</td>
<td>AgNO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>22</td>
<td>24</td>
<td>0</td>
<td>10</td>
<td>1</td>
<td>0</td>
<td>9</td>
<td>3.5</td>
<td>47</td>
<td>1</td>
</tr>
<tr>
<td>Br</td>
<td>EtOH&lt;sup&gt;f&lt;/sup&gt;</td>
<td>NaN&lt;sub&gt;3&lt;/sub&gt;</td>
<td>60</td>
<td>20</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>2.5</td>
<td>0</td>
</tr>
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</table>

<sup>a</sup>Organic solvent indicated was mixed with water in the following proportions by volume: 2THF/1HOH; 1HOAc/1 HOH; 2 EtOH/1HOH. Reaction temperature 66° unless otherwise noted. <sup>b</sup>Mixture on bases of infrared spectrum; not resolved on g.c. <sup>c</sup>Product mixture also contained 13.5% of cis-cyclooctene oxide; product distribution data reported are calculated for remainder of the mixture. <sup>d</sup>Reaction temp. 0°. <sup>e</sup>Reaction temp. 100°. <sup>f</sup>Reaction temp. 78°. Product mixture also contained 16% of cis-cyclooctene oxide; product distribution data reported are calculated for remainder of the mixture and include 58% of an unidentified basic fraction.
## TABLE II

PRODUCT DISTRIBUTION DATA FROM SOLVOLYSES OF 
\textit{cis}-2-BROMOCYCLOOCTANOL IN AQUEOUS 
TETRAHYDROFURAN

<table>
<thead>
<tr>
<th>Solvent (^a)</th>
<th>Salt</th>
<th>Hours</th>
<th>2</th>
<th>4</th>
<th>6t</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10,11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>THF (^b)</td>
<td>none</td>
<td>72</td>
<td>16</td>
<td>3</td>
<td>6</td>
<td>4</td>
<td>8</td>
<td>14</td>
<td>6</td>
<td>2.5</td>
</tr>
<tr>
<td>THF (^c)</td>
<td>AgNO(_3)</td>
<td>17</td>
<td>14</td>
<td>2</td>
<td>2</td>
<td>8</td>
<td>12</td>
<td>2</td>
<td>28</td>
<td>2</td>
</tr>
</tbody>
</table>

\(^a\) 2\text{THF}/1\text{HOH} by volume. \(^b\) Reaction temp. 66\(^\circ\). \(^c\) Reaction temp. 38\(^\circ\).

## TABLE III

PRODUCT DISTRIBUTION DATA FROM SOLVOLYSES OF \textit{trans}-2-BROMOCYCLOOCTANOL IN CARBOXYLIC ACID SOLVENTS

<table>
<thead>
<tr>
<th>Solvent (^d)</th>
<th>Salt</th>
<th>Hours</th>
<th>2</th>
<th>4</th>
<th>5</th>
<th>6t</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10,11</th>
<th>12t</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH(_3)COOH (^a)</td>
<td>CH(_3)COOAg</td>
<td>35</td>
<td>0.2</td>
<td>1</td>
<td>15</td>
<td>1</td>
<td>11</td>
<td>4</td>
<td>1</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>CF(_3)COOH (^b)</td>
<td>CF(_3)COOAg</td>
<td>20</td>
<td>2</td>
<td>4</td>
<td>tr(^c)</td>
<td>0</td>
<td>29</td>
<td>4</td>
<td>15</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>HCOOH (^d)</td>
<td>CH(_3)COOAg</td>
<td>10</td>
<td>1.5</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>37</td>
<td>4</td>
<td>3</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>HCOOH (^e)</td>
<td>CH(_3)COOAg</td>
<td>10</td>
<td>tr(^c)</td>
<td>4</td>
<td>4.5</td>
<td>0</td>
<td>37</td>
<td>4</td>
<td>2</td>
<td>37.5</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Glacial acetic acid, 10\(^\circ\), 24 hr. \(^b\) Anhydrous acid, 0\(^\circ\), 3.5 hr. \(^c\) Trace detected by g.c. \(^d\) Commercial 97-100\% formic acid, 0\(^\circ\), 10 hr. \(^e\) Commercial 97-100\% formic acid, 38\(^\circ\), 6.5 hr.
2. Discussion of Results

a. Aqueous Solvents

The data for the several runs are remarkably similar. About two-thirds to three-fourths of each product mixture consists of diols, unsaturated alcohols and bicyclic ethers. These products are mainly transannular in nature and obtained in acid-catalyzed rearrangements of cyclooctene oxides and glycols. The change from chloro to bromo as leaving group, the presence or absence of silver nitrate, or the change of solvent from aqueous THF to aqueous acetic acid affects the composition of the product mixtures but little. Also the two geometrical isomers, cis- and trans-2-bromocyclooctanol give highly similar product mixtures.

The major differences between experiments with silver nitrate and those without it are in the relative proportions \( A \) of 4 to 5, and \( B \) of diols (6 and 12) to bicyclic ethers (10,11). The shift from 4 to 5 with addition of silver nitrate probably represents secondary processes unassociated with the halohydrin solvolyses themselves. In studies of deaminations of 2-hydroxycyclooctylamines, the surprising transformation of cycloheptanecarboxaldehyde (4) into cycloheptanone (5) was detected under acidic conditions. Apparently silver ion, or silver halide is an unusually effective catalyst for this degradation. For present considerations, the solvolysis reactions, products 4 and 5 should be considered as 4 alone. The shift from diols to bicyclic ethers (10,11) may reflect influences of salt on the lifetime and consequent fate of intermediate carbonium ions. A similar, though less extensive, shift was found for solvolysis of cis-cyclooctene oxide in 50% acetic acid.
containing either silver nitrate or sodium nitrate (Table IV), although sodium acetate did not cause such a shift with bromohydrin solvolysis (Table I).

Although cyclooctene oxide and glycol, and 3- and 4-cyclooctenols all yield small amounts of cyclooctanone (2) in hot aqueous sulfuric acid solutions, none of these materials is changed by the solvolysis reaction conditions. Cyclooctanone must then be a primary reaction product in the solvolyses. Cycloheptanecarboxaldehyde (4) is not formed in the acid-catalyzed rearrangements of cyclooctene oxide and glycol and cyclooctenols. The relatively high proportion of cyclooctanone together with cycloheptanecarboxaldehyde in all of the solvolysis reaction mixtures is significant for description of mechanism. These are the products which are formed almost exclusively during nitrous acid deaminations of 2-hydroxycyclooctylamines. Although one can attribute such products to the intervention of a "hot" carbonium ion in deamination, it is extremely unlikely that anything like a "hot" carbonium ion is formed during solvolysis of the halohydrins, most particularly in aqueous solvent without added silver salt (no less 2 and 4 than with silver nitrate). Since the products that distinguish amino alcohol deaminations and halohydrin solvolyses from acid-catalyzed rearrangements of glycols and epoxides are the same, the temptation is indeed strong to blame their appearance on the same mechanistic feature, in the absence of any evidence to the contrary.

Even with the similarity of products, however, certain features distinguish the amino alcohol deaminations and halohydrin solvolyses. trans-2-Hydroxycyclooctylamine leads mainly to cycloheptanecarboxaldehyde
(ratio of 2 to 4, 1:5.5), but trans-2-hydroxycyclooctyl halides give
mainly cyclooctanone (ratio of 2 to 4, 2-3:1). cis-2-Hydroxycyclo-
octylamine does give mainly cyclooctanone (ratio of 2 to 4, 2.5:1),
but cis-2-hydroxycyclooctyl bromide gives a much higher ratio of 2 to 4
(5-7:1). If these carbonyl products are indeed formed by essentially the
same process in the different reactions, the differences in product
ratios may be associated with ring conformational preferences.\textsuperscript{35,36}

Alternately, halide may leave mostly from one constituent conformation
(favoring ketone formation), while deamination of amine can involve
intermediates with a different substituent conformation.\textsuperscript{36}

Sodium azide is reputed to be able to trap some carbonium ion
intermediates.\textsuperscript{37,38} When this reagent is used in the solvolysis of
trans-2-bromocyclooctanol (Table I), the relative amounts of cyclooctanone
(\textsuperscript{2}) and cycloheptanecarboxaldehyde (\textsuperscript{4}) are changed but little from their
values without sodium azide but the transannular products are considerably
diminished (They are only about one-fourth as much as when there is no
azide present). There is also formed a basic compound (58\% of the
mixture), which, although it has not been identified so far, indicates
combination of azide with some intermediate in the solvolysis. (S\textsubscript{N}\textsubscript{2}
attack can not be completely ruled out here but this possibility has
been ruled out in previous solvolysis work using azide ion\textsuperscript{37,38} and
S\textsubscript{N}\textsubscript{2} attack is very slow in medium ring systems).\textsuperscript{12} The data from the
above reaction strongly indicate that the azide is trapping the
intermediate leading to transannular products but not the one leading to
carbonyl products.

In some cases, a major influence of incompletely departed leaving
group on the reactions of a carbonium ion have been reported. It does not seem reasonable, however, to ascribe very similar influences to associated halide being removed by solvent alone, to halide being removed by silver ion and the removal of nitrogen from diazonium cation.

The product data from these related reactions demand two distinct, competing mechanisms, alternate descriptions of which are as follows:

(I) (a) Formation of a 2-hydroxycyclooctyl cation (14) which gives products almost exclusively after a transannular shift (to 15 for example) and (b) concurrent migration of hydrogen or alkyl during departure of the leaving group, before substantial carbonium development has occurred (16).

(II) (a) Direct formation of a hydrogen-bridged carbonium ion (such as 17) which gives mostly or exclusively transannular products, and (b) formation of a 2-hydroxycyclooctyl cation (14) in which combination with solvent and 1,2-shifts rather than transannular shifts lead to products.

\[
\begin{array}{c}
\text{OH} \\
\text{14} \\
+ \\
\text{OH} \\
\text{12} \\
\text{OH} \\
\text{16} \\
\text{H} \\
\text{X} \\
\text{17} \\
\end{array}
\]

The stereochemistry of 1,4-diol formation from trans-halohydrins (it has not been established for the cis-isomers) favors, but does not demand, path IIa for a major part of these reactions. The stereoselective formation of cis-1,4-diol from cis-epoxide and of trans-1,4-diol from trans-halohydrins is precisely what an ion such as 17 leads one to expect, but, in these crowded eight-membered rings, such stereoselectivity with unbridged carbonium ions is entirely reasonable.
Complete stereoselectivity of product formation merely signals asymmetric combination of intermediate with reagent. It does not appear able to distinguish open carbonium ions from alternate descriptions of the reaction intermediates.

These alternate descriptions (Paths I and II) clearly assign completely different roles to intermediate 2-hydroxycyclooctyl cations (14) and to hydrogen bridged species (16 and 17). Cyclooctene oxide and glycol rearrange almost completely by path Ia or IIa, amino alcohol almost completely by path IIa or IIb, and halohydrins by both path Ia and Ib or IIa and IIb.

Path Ib would favor concurrent trans migration of hydrogen or alkyl with departure of leaving group. Models strongly suggest that trans migration will favor carbon rather than hydrogen migration for the trans-halohydrin and hydrogen migration for the cis isomer. Thus, the above data would lead us to expect that the trans isomer would give on solvolyis less ketone (2) and more aldehyde (4) than the cis isomer.

The trans-bromohydrin actually gives more of both compounds than the cis-bromohydrin (for 2, ratio of trans to cis is 3:2; for 4 ratio of trans to cis is 2:1). Trans-bromohydrin, also contrary to expectations (path Ib), gives more ketone than aldehyde (ratio of 2 to 4, 5:1). The experimental product distribution data seem to be in complete disagreement with path Ib. Models also suggest that the intermediate 2-hydroxycyclooctyl cation derived from trans-halohydrin would be more likely to lead to ketone formation than that derived from cis-halohydrin. This is, of course, the experimentally observed fact. Thus the comparison of the product distribution data from cis- and
trans-2-hydroxycyclooctyl bromide points toward Mechanism II rather than Mechanism I as the actual path of solvolysis.

The formation of trans-1,2-diol (6t) from trans-halohydrin excludes an $S_N^2$ type replacement and signals a stereoselective combination of intermediate cation with solvent. The same stereoselective formation of 1,2-diol is observed in acid-catalyzed reactions of the corresponding epoxide and glycol: cis-epoxide gives only trans-1,2-diol, and trans-1,2-diol is not isomerized to cis-1,2-diol. Formation of trans-1,2-diol from trans-halohydrin has far more mechanistic significance than formation of trans-1,2-diol from cis-epoxide: the epoxide can react by $S_N^2$ displacement or by 2-hydroxycyclooctyl cations to give the same 1,2-diol, but all trans-1,2-diol from halohydrin must come from intermediate cations. A comparison of the relative proportions of various products from epoxide and halohydrin reactions reveals that very little 1,2-diol is formed from 2-hydroxycyclooctyl cations, and nearly all of the 1,2-diol formed from epoxide is an $S_N^2$ displacement product. If we choose mechanism description I, which would couple 1,2-diol and transannular product formation through intermediate 2-hydroxycyclooctyl cations (14), comparison of the ratio of 1,2-diol to transannular products (3-12) obtained from bromohydrin and from epoxide under comparable conditions indicates that only 2-10% of the 1,2-diol from epoxide is formed from 14. If we choose the alternate description, II, which would couple 1,2-diol and carbonyl products through 14, appropriate comparison of epoxide and bromohydrin rearrangements indicates that less than 0.5% of the 1,2-diol obtained from epoxide is formed through 2-hydroxycyclooctyl cations (14). Formation of 1,2-diol from an intermediate like 17 is apparently unlikely, since that...
path should lead to cis-1,2-diol and not the trans-1,2-diol actually obtained from cis-epoxide. Before these data for halohydrin solvolysis became available, no good estimation of the proportions of transannular and nontransannular reactions for the cation $\text{I}_4$ was possible.

Kinetic data offer little promise of aiding in the choice of mechanisms at this time. In the absence of anchimeric assistance, a vicinal OH group is strongly rate retarding in solvolysis reactions, and a comparison of rates of reaction of bromocyclooctane and the 2-bromocyclooctanols should reveal the effect of the hydroxyl substituent. If the major parts of the solvolyses of these three bromides are alike in mechanism, for intermediates like $\text{I}_4$ and $\text{I}_7$ the effect of the hydroxyl group should be strongly rate retarding. Only for an intermediate such as $\text{I}_6$, possibly favored for the bromohydrins but not for the bromide, should the electrostatic effect of the hydroxyl be offset to some degree by a rate enhancement due to assistance by migrating hydrogen (or alkyl). When the rates of solvolysis of the three compounds in refluxing THF were compared, only small retardations (factor of 0.82 for the trans, 0.70 for the cis) were found. Such a result clearly implies some actual rate acceleration and tends to implicate mechanism I rather than II. Since mechanism I would ascribe $\text{I}_6$ to only 24.5% of the total reaction for the trans bromohydrin and 19% for the cis isomer (see Tables I and II, mole % of carbonyl products), combination of experimental rate retardation factors of 0.82 and 0.70 with an expected one of $10^{-2}$ indicates that the actual rate acceleration factor for $\text{I}_6$ is 325 for the trans and 364 for the cis (The factors calculated from each of the isomers are in quite close
agreement). One cannot account for the acceleration as a result of participation of hydroxyl itself, leading to epoxide which then reacts further, because the distributions of even the non-carbonyl products from epoxide and bromohydrin are quite different (compare entries in Tables I and IV) and epoxide rearranges too slowly under these conditions.31 The kinetic data seem to imply that carbonyl formation is by path Ib because of an acceleration in rate over that expected for the solvolyses of the bromohydrins. The key point here is whether or not we can accept the estimate of a rate retarding factor of $10^{-2}$ for a vicinal OH in this system. This estimate was made for a six membered ring40 rather than a medium ring system and as was strongly pointed out in the beginning of this work, medium ring systems with their different geometry do not in general behave like other ring systems. It could well be that the small observed retardation in the bromohydrin solvolyses was not due to a compensating acceleration by concerted carbonyl formation but was a result of the normal combined stereo and electrostatic effect of a vicinal OH in a medium ring system. If there is no actual acceleration, then there would be no need to invoke mechanism I to explain it. This would be much more in accord with the product distribution data which indicate mechanism II as the solvolysis path.

b. Carboxylic Acid Solvents

Solvolyses of trans-bromohydrin in three nearly anhydrous carboxylic acid solvents show more solvent influence than do the reactions in the aqueous solvents. Even so, the general pattern of the aqueous solvolyses is followed except that the relative proportions of 1,4-diol (12t) to other transannular products (8-11) are reversed.
Substantial but differing proportions of carbonyl compounds are found in the product mixtures.

High proportions of 1,4-diol in carboxylic acid solvents have also been reported for cyclooctene oxide solvolyses. Since either $\text{(15 or 17)}$ is a reasonable precursor for all the transannular products $\text{(8, 2, 11, and 12t)}$, it is unexpected that the less nucleophilic carboxylic acid solvents favor $\text{12t}$ more than do the more nucleophilic aqueous solvents. In view of the great number of studies of effects of solvent change on rates of solvolysis of various compounds, the paucity of data which reveal effects of solvent change on composition of product mixtures from solvolyses is surprising. Data particularly pertinent to the present considerations—namely, change from aqueous to carboxylic acid solvents—are not readily available, but two studies may be cited. Solvolysis of t-butyl chloride in aqueous methanol is reported to yield, along with substitution products, small proportions of olefin which increase with decreasing water content in the mixed solvent. In solvents containing substantial amounts of bases ($\text{CaCO}_3$ in aqueous
acetone, \( \text{RCO}_2\text{Na} \) in acetic and formic acid), \( \text{4-t-butylcyclohexyl tosylate} \) undergoes solvolysis to yield product mixtures containing slightly increasing amounts of olefin with change from aqueous acetone to acetic acid to formic acid.\(^{42} \) In both these cases, which show a trend opposite to that shown by the present work, the shift from substitution to elimination product is most probably determined mainly or wholly by the relative nucleophilicities of the solvents used. Abstraction of proton (to give olefin) will be a function of basicity, which is about the same in the solvents compared in each of the above studies. In the present solutions however, with substantial differences in basicity of solvent molecules and with no other good base present, the alternate fates of 15 or 17, once formed, will depend on both the relative nucleophilicities and relative basicities of the solvents. Water is a better nucleophile than carboxylic acid, but it is also a far better base. The competing roles of solvent molecules (combination with cation and abstraction of proton) then can account for the relative proportions of diol and enol products in these different solvent systems.

The major difference among the carboxylic acid solvents themselves, a difference more salient to considerations of solvolysis mechanisms, lies in the relative abundance of carbonyl and transannular products formed during reaction. The highest proportion of 2 + 4 is obtained in acetic acid, the lowest in formic acid. These relative proportions support the inference of duality of mechanism in these halohydrin solvolyses, but do not point to a clean choice between mechanism descriptions I and II (page 13). For description I, the competitive
pathways involve a carbonium ion (14) and a hydrogen-bridged, neutral species (16). As the ionizing power of the solvent increases, the carbonium ion-pathway is augmented at the expense of the carbonyl-forming one. For description II, the competition is between cationic intermediate formation with and without transannular hydrogen participation. For solvolysis of 1-phenyl-2-propyl tosylate, to which has been attributed competition between neighboring phenyl participation and more conventional carbonium ion formation, change of solvent from ethanol to acetic acid to formic acid was found to favor phenyl participation. Similarly, a shift to more limiting conditions (metal ion catalysis) favored phenyl-assisted solvolysis over unassisted processes with
The same kind of shift, toward bridged ions at the expense of unbridged ones, can be read into the small solvent effects observed here. However, these data offer no firm choice for the mechanism of halohydrin solvolysis.

Some reports have indicated an unusually strong promotion of ionic reactions by trifluoroacetic acid solvent. For example, solvolysis of cis-cyclooctene oxide with trifluoroacetic acid gives transannular products more extensively than does acetic or formic acid.25,31 Contrasting with these reports, the data in this work on halohydrin solvolysis place trifluoroacetic acid in between acetic and formic acid in promoting ion-forming reactions in competition with concerted ones and suggest strongly that the epoxide reactions are best accounted for by differences in nucleophilicity of trifluoroacetic and formic acid solvents.

As has already been pointed out, the bulk of 1,2-diol formed from cyclooctene oxide most likely comes from an S_N2-type reaction between solvent and epoxide and not from an intermediate 2-hydroxycyclooctyl cation. Formic acid, weakly nucleophilic though it may be, is a far better nucleophile and will react more by displacement on epoxide than will trifluoroacetic acid. The relative proportions of 1,2-diol and transannular products from epoxide solvolysis with these two solvents appear to be poor measures of the relative ionizing power of the solvents. The cautionary note about claiming maximum ionizing power for trifluoroacetic acid46 is supported by the above data.

B. Solvolyses of cis-Cyclooctene Oxide

Rearrangements of cyclooctene oxides in carboxylic acid solvents have been investigated elegantly by Cope and coworkers.16,23-26 However,
in order that the rearrangements of epoxide and 2-substituted-cyclooctanols might be compared more directly, rearrangement of cis-cyclooctene oxide was reexamined under the aqueous conditions chosen for the other studies.\textsuperscript{29-31}

Some uncertainty figures in the comparison: We can only presume that the preferred conformation of a leaving group is one which will lead to relief of intraannular strain; we are further uncertain about the preferred conformation of the ring\textsuperscript{14,35} for reaction and what changes (if any) in that conformation occur during cation formation. Models alone do not indicate convincingly whether trans-amino alcohol and trans-halohydrin should be compared more appropriately with cis- or trans-epoxide, but reaction products clearly favor cis-epoxide. Although the 1,4-diols obtained from trans-halohydrin and cis-epoxide, respectively, are geometrical isomers, the other components of the two reaction mixtures are quite similar and are unlike those obtained from formolysis of trans-epoxide.\textsuperscript{23} Therefore, the far more accessible cis-cyclooctene oxide was used.

Just as was found in carboxylic solvents,\textsuperscript{16,23-25} transannular rearrangements dominate the reactions of cis-cyclooctene oxide in the mixed aqueous solvents, and cyclooctanone is a minor component in the product mixtures (Table IV). In addition to the relative importance of carbonyl products from the two reactions, these halohydrin and epoxide solvolyses are distinguished from each other by the relative proportions of different transannular products: from epoxide, small amounts of bicyclic ethers (10,11) and large amounts of 1,4-diols (12) are obtained, while from the halohydrin the opposite is true. This difference,
## TABLE IV

PRODUCT DISTRIBUTION DATA FROM ACID-CATALYZED REARRANGEMENTS OF **cis**-CYCLOOCTENE OXIDE

<table>
<thead>
<tr>
<th>Solvent</th>
<th>2</th>
<th>6t</th>
<th>8</th>
<th>9</th>
<th>10,11</th>
<th>12c</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>2THF/LHOH^a</td>
<td></td>
<td>tr^b</td>
<td>39</td>
<td>16</td>
<td>8</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>50% HOAc^e</td>
<td>1.5</td>
<td>33</td>
<td>28</td>
<td>9</td>
<td>1.5</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>50% HOAc^d</td>
<td>1.5</td>
<td>34</td>
<td>29</td>
<td>9</td>
<td>6</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>50% HOAc^e</td>
<td>2</td>
<td>33</td>
<td>29</td>
<td>9</td>
<td>4.5</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>90% HOAc^f</td>
<td>1</td>
<td>23</td>
<td>22</td>
<td>14</td>
<td>4</td>
<td>27</td>
<td>7.5</td>
</tr>
<tr>
<td>1 M H₂SO₄^g</td>
<td>7</td>
<td>10</td>
<td>4</td>
<td>2</td>
<td>30</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>HCOOH^h</td>
<td>8</td>
<td>20</td>
<td>23</td>
<td>8</td>
<td>0</td>
<td>39</td>
<td>0</td>
</tr>
<tr>
<td>CF₃COOH^i</td>
<td>2</td>
<td>4</td>
<td>40</td>
<td>3</td>
<td>0.5</td>
<td>48</td>
<td>1</td>
</tr>
</tbody>
</table>

*20 mmoles of epoxide in 150 ml. of solvent, 6 drops of concentrated H₂SO₄, refluxing for 5 da.; product mixture also contained 1% of 7.*

^bTrace detected by g.c. ^c0.1 mole of epoxide in 300 ml. of solvent, refluxing for 72 hr. ^dSame as d but with 0.1 mole of AgNO₃ added.

^eSame as d but with 0.1 mole of NaNO₃ added. ^f0.1 mole of epoxide in 50 ml. of solvent, steam bath for 3.5 hr. ^g24 mmoles of epoxide in 100 ml. of solvent, refluxing for 15 hr. ^h10 mmoles of epoxide in 35 ml. of commercial 97-100% solvent, refluxing for 3 hr. ^i0.1 mole of epoxide in 65 g. of solvent, 3 hr. at 0°.
together with the opposite stereoselectivity in 1,4-diol formation, indicates that the interpretation of these reactions in terms of rather simple carbonium ions suffers some inadequacy.

Added silver nitrate or sodium nitrate does not affect significantly the product distribution from epoxide in 50% acetic acid solution. A change in proportions of isomeric enols (8 and 2) in going from acidified aqueous THF or 50% acetic acid to 90% formic acid and a slight decrease in proportions of glycols (6t and 12c) with change to less nucleophilic solvent occur, but the general patterns of product distribution for the three solvents are notably similar. A higher proportion of trans-1,2-diol (6t) is formed in each of these solvents than in nearly anhydrous carboxylic acid solvents. As already pointed out, this result probably stems from a competition between direct displacement (on epoxide by solvent) and formation (and subsequent rearrangement) of cationic intermediates. Better competition by the displacement path is expected with the more nucleophilic water present than with the less nucleophilic carboxylic solvents alone.

The product distribution in 1 M sulfuric acid solution is similar to that found for rearrangement of glycol (6) in the same solvent. The shift of product distribution from 8 and 2 to 2, 10, 11, and 13 simply reflects the reactions of 8 and 2 in sulfuric acid, secondary effects not germane to the rearrangement of the epoxide.

These results clearly show that the major course of acid-catalyzed reaction of the epoxide is not particularly solvent dependent. Some $S_N^2$ type displacement by solvent does occur, to extents affected by the relative nucleophilicity of the solvent, but the main reaction is
transannular rearrangement, with solvent playing a minor role in shifting exact product proportions. Except in hot, strongly acidic solutions favoring secondary reactions, cyclooctanone is formed in hardly more than detectable amounts from the epoxide, and cycloheptanecarboxaldehyde was not even detected in any of the epoxide or glycol rearrangements. The appearance then of both of these carbonyl products in substantial amounts among the products from amino alcohol deamination and halohydrin solvolysis must necessarily denote a change in mechanism of rearrangement.

C. Solvolyses of the trans-2-Halocyclonanols

Both the bromo- and chlorohydrin were solvolyzed in aqueous THF with silver nitrate present. The mole percentage of each component of the product mixtures is given here. The product mixture from trans-2-chlorocyclononanol contained cyclooctanone, 5.3%; a bicyclic ether \( (C_9H_{16}O) \), 14.8% cyclononanone, 31.3%; a mixture of cyclononenols \( (C_9H_{16}O) \), 40.4% (consisting of 3-isomers in ratio 1:1:6.2). The product mixture from trans-2-bromocyclononanol contained: cyclooctanone, trace; a bicyclic ether \( (C_9H_{16}O) \), 12.1%; cyclooctanecarboxaldehyde (tentative identification), 5.6%; cyclononanone, 36.1%; a mixture of cyclononenols \( (C_9H_{16}O) \), 29.1% (consisting of 3 isomers in ratio 1:1:2:8.4); and 1,2-cyclononanediol, 12.4%.

![Chemical Structures]

It is to be noted that the types of compounds found here are
highly similar to those found in the solvolyses of the 2-hydroxycyclooctyl halides. Also the high percentages of carbonyl products (36.6%, chloro; 41.8%, bromo) which are present in these mixtures is in direct contrast to the peroxyformic acid oxidation of cis- and trans-cyclononanols which yielded only very small amounts of cyclononanone (2% for the cis, none for the trans) and no other carbonyl products. Acid-catalyzed rearrangement of cis-cyclononanone-diol gave a 40% yield of cyclononanone, but it has not been established how much of the ketone is primary reaction product and how much is formed by acid-catalyzed rearrangement of the enols and ethers which may be the primary products. Thus the evidence in this case (incomplete though it may be) indicates a duality in mechanism for the solvolyses of the trans-2-halocyclonanols similar to that found in the solvolyses of the 2-halocyclooctanols.

D. Solvolysis of trans-2-Bromocyclodecanol

trans-2-Bromocyclodecanol was solvolyzed at 36°C in aqueous THF with silver nitrate present. The product mixture contained a bicyclic ether, 4.2%; cyclodecanone, 18.5%; a mixture containing mostly cis- and trans-5-cyclodecenols, 59.1%; 1,2-cyclodecanediol, 9.9%; 1,1-cyclodecane-diol, 8.1%.

cis- and trans-Cyclodecene on peroxyformic acid oxidation give very little cyclodecanone (0% and 10%, respectively). Again it would
seem that the idea of a dual mechanism for halohydrin solvolysis is supported by these data. There is a real need, however, for more data on the nine- and ten-carbon systems. More halohydrin solvolyses must be run and the total product mixture must be characterized. Also the epoxide rearrangements must be reexamined under a variety of conditions.
Gas Chromatographic (g.c.) analyses were carried out with a Barber-Colman Model 20 instrument equipped with a hydrogen-flame detector and a 100 ft. capillary column coated with either GE-96 silicone (GE-96) or poly (propylene glycol) (P(PG)). An Aerograph Autoprep Model A-700 instrument equipped with a 3/8 in. x 20 ft. SE-30 silicone column or a 3/8 in. x 10 ft. Carbowax 20-M column was used for preparative gas chromatography. Capillary melting points were obtained with a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were obtained mainly with a Beckman IR-5 spectrophotometer. Microanalyses designated (S) were performed in these laboratories by Mr. R. Seab, and those designated (G) were obtained from Galbraith Laboratories, Inc., Knoxville, Tennessee.

A. The Preparation of the trans-2-Halocyclooctanols

The trans-2-halocyclooctanols were prepared from the commercially available cis-cyclooctene by the scheme shown below:

Although the reactions of medium ring epoxides with aqueous acid proceed with extensive transannular rearrangement,\textsuperscript{23,24,26,10} the 1,2 product is obtained in non-polar solvent.\textsuperscript{53} Confidence in the simplicity of this reaction is supported by the reformation of cis-cyclooctene oxide
### TABLE V

G. C. RETENTION TIMES OF SOME IMPORTANT COMPOUNDS

<table>
<thead>
<tr>
<th>Compound</th>
<th>Temp. (°C)</th>
<th>Retention Times (Min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>cis-Cyclooctene oxide</strong>(^{16})</td>
<td>100</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>3.1</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>2.3</td>
</tr>
<tr>
<td>Cycloheptanone</td>
<td>100</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>trans-2-Vinylcyclohexanol</strong>(^{29,47})</td>
<td>100</td>
<td>3.5</td>
</tr>
<tr>
<td>-TMS derivative</td>
<td>100</td>
<td>7.8</td>
</tr>
<tr>
<td><strong>1,4- and 1,5-epoxycyclooctane</strong>(^{29,47})</td>
<td>100</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>2.3</td>
</tr>
<tr>
<td>Cycloheptanecarboxaldehyde(^{30})</td>
<td>100</td>
<td>4.3</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>2.6</td>
</tr>
<tr>
<td>Cyclooctanone(^{49})</td>
<td>100</td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>3.4</td>
</tr>
<tr>
<td>2-cyclooctenol(^{50})</td>
<td>100</td>
<td>5.6</td>
</tr>
<tr>
<td>-TMS derivative</td>
<td>120</td>
<td>11.5</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>6.5</td>
</tr>
<tr>
<td>3-cyclooctenol(^{26,29})</td>
<td>100</td>
<td>5.6</td>
</tr>
<tr>
<td>-TMS derivative</td>
<td>120</td>
<td>11.5</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>6.5</td>
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<td>Temp. (°C)</td>
<td>Retention Times (Min.)</td>
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<td>Cyclodecanone</td>
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in high yields from the halohydrins and base.

1. cis-Cyclooctene Oxide
   a. Peroxyacid Method
   A solution of 55 g. (1.5 mole) of cis-cyclooctene in 60 ml. of ethyl acetate was placed in a 1 l. 3-neck flask equipped with a stirrer and dropping funnel and surrounded by a cold water bath. Then 101 g. (0.5 mole) of 85% m-chloroperoxybenzoic acid in 400 ml. of ethyl acetate was added over a period of ½ hour. The resulting mixture was stirred for 11 hr. at 15-29°. The m-chlorobenzoic acid was filtered off, and the acetate solution was washed 3 times with dilute sodium bicarbonate and 2 times with water and then dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue was distilled under reduced pressure to yield 43 g. (67%) of cis-cyclooctene oxide, b.p. 108-110° (63mm.).

b. Peroxide-Benzonitrile Method
   To a mixture of 15.7 g. of potassium bicarbonate, 93.9 g.
(0.92 mole) of benzonitrile, 116 g. (1.05 mole) of cis-cyclooctene and 500 ml. of methanol; 177.8 g. (0.96 mole) of 30% hydrogen peroxide was added with continuous stirring over a period of 2 hr. The mixture was stirred at 25° for 54 hr. after the addition was complete, diluted with 700 ml. of water and extracted with three 200-ml. portions of chloroform. The combined chloroform extracts were washed twice with water and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to yield 108 g. (93%) of cis-cyclooctene oxide, b.p. 110-112° (65 mm.).

2. trans-2-Chlorocyclooctanol

Dry hydrogen chloride gas was passed into a solution of 12.6 g. (0.1 mole) of cis-cyclooctene oxide in 100 ml. of carbon tetrachloride at 10° until the solution became saturated with hydrogen chloride (80 min.). The carbon tetrachloride solution was washed with water, dilute sodium bicarbonate and water, and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue was distilled under reduced pressure to give 12.3 g. (75%) of trans-2-chlorocyclooctanol, b.p. 61° (1.06mm.). The silver nitrate test for halogen and the permanganate test for secondary alcohols were positive. Gas chromatographic analysis showed a single product in greater than 98% purity, and the infrared spectrum agreed with that expected for trans-2-chlorocyclooctanol. A subsequent experiment with duplicate quantities gave chlorohydrin in 85% yield.

Anal. (S) Calc. for C₈H₁₅ClO: C, 59.1%; H, 9.29%. Found: C, 58.8%; H, 9.54%.

The chlorohydrin was converted to solid ester derivatives:
benzoate, m.p. 60-61° (lit. 58 61°); 3,5 dinitrobenzoate, m.p. 96-97°
(Anal. (G) Calc. for C_{15}H_{17}ClN_{2}O: C, 50.5%; H, 4.81%. Found: C, 50.6%;
H, 4.84%); \( p \)-nitrobenzoate, m.p. 86-87° (Anal. (S) Calc. for C_{15}H_{18}ClNO_{3}:
C, 57.6%; H, 5.82%. Found: C, 57.8%; H, 6.15%).

\textbf{cis- Cyclooctene oxide (1.1 g., 87%) was reformed by stirring
1.63 g. (0.01 mole) of trans-2-chlorocyclooctanol with 0.5 g. of
sodium hydroxide in 5 ml. of water at room temperature for 5 hr.}

3. \textbf{trans-2-Bromocyclooctanol}^{53}

Anhydrous hydrogen bromide was bubbled through a mixture of
12.6 g. (0.1 mole) of \textit{cis}-cyclooctene oxide in 100 ml. of carbon
tetrachloride at 0° until the solution was saturated with hydrogen
bromide (5 hr.). The carbon tetrachloride solution was washed with
water, dilute sodium bicarbonate, and water and dried over magnesium
sulfate. The solvent was removed by rotary evaporation, and the residue
distilled under reduced pressure to yield 17.7 g. (85%) of trans-2-
bromocyclooctanol,$^{53}$ b.p. 75-76° (0.2 mm.). Gas chromatographic
analysis showed one component in greater than 99% purity. An infrared
spectrum agreed with that expected for trans-2-bromocyclooctanol.
Subsequent experiments with duplicate quantities of reagents produced
bromohydrin in yields of between 88% and 91%.

\textbf{Anal. (S) Calc. for C_{8}H_{15}BrO: C, 46.4%; H, 7.46%. Found: C,
46.4%; H, 7.30%.}

The bromohydrin (0.5 g.) was esterified$^{57}$ by heating it for 5
minutes with 0.5 g. of 3,5-dinitrobenzoic acid, 1.0 g. of \( p \)-
toluenesulfonyl chloride and 4 ml. of anhydrous pyridine to give
\textbf{trans-2-bromocyclooctyl 3,5-dinitrobenzoate}, which was recrystallized
from ethanol-water; m.p. 94-96° (lit. 53 95-96°).

cis-Cyclooctene oxide (0.25 g., 78%) was reformed by stirring 0.51 g. (2.5 mmole) of trans-2-bromocyclooctanol with 0.2 g. of sodium hydroxide in 5 ml. of water for 8 hr. at 38°.

4. trans-2-Bromocyclooctyl Acetate53

To 5.0 g. of trans-2-bromocyclooctanol was added 5 ml. of acetic anhydride and 1 drop of sulfuric acid. The solution was refluxed for 5 minutes and then allowed to stand overnight. It was then poured onto crushed ice and extracted with four 75-ml. portions of ethyl ether. The combined ether extracts were washed with water, dilute sodium bicarbonate, and water. The aqueous washings were extracted once with ethyl ether, and the total ether fraction was dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue was distilled under reduced pressure to yield 4.5 g. (75%) of trans-2-bromocyclooctyl acetate,53 b.p. 80-81° (0.1 mm.).

Anal. (S) Calc. for C_{10}H_{17}BrO_{2}: C, 48.3%; H, 6.88%. Found: C, 48.3%; H, 6.94%.

B. The Preparation of cis-2-Bromocyclooctanol53

cis-2-Bromocyclooctanol53 was prepared from cis-cyclooctene by the following reaction sequence. The isomerization of cis-cyclooctene to trans-cyclooctene follows the work of Cope and co-workers.59

1. Cyclooctylamine60,61

A generator62 for diborane63 was set up consisting of a 300 ml. distilling flask equipped with a pressure-equalized dropping funnel, an inlet for nitrogen, and outlet for the diborane, and a magnetic stirrer.
A solution of 53.8 g. (0.38 mole) of freshly distilled boron trifluoride-etherate in 100 ml. of diglyme (diglyme distilled from sodium under nitrogen) was placed in the flask and 10.6 g. (0.28 mole) of sodium borohydride in 80 ml. of diglyme was placed in the dropping funnel. Stirring was initiated, the system was flushed with nitrogen and the borohydride was added to the boron trifluoride solution in the flask (addition time 1 hr.). Diborane evolution began immediately. A slow stream of nitrogen was maintained to carry the diborane out of the flask and into a second flask connected by Tygon tubing to the generator, equipped with a magnetic stirrer and a condenser, and containing 110 g. (1.0 mole) of cis-cyclooctene in 400 ml. of tetrahydrofuran (distilled from sodium under nitrogen). The mixture was stirred for 3 hr. after
the generation of diborane had ceased. Then 30 ml. of water was added to destroy the residual hydride, followed by 500 ml of 3 M aqueous sodium hydroxide. The amination was accomplished by adding a solution of chloramine (0.7 mole), prepared by mixing 1 kg. of 5.25% sodium hypochlorite (Chlorox) and 1 l. of 0.7 M ammonia at 0°. After 1 hr. of stirring at room temperature, the mixture was acidified and extracted 4 times with ethyl ether. The ether extract was discarded, the aqueous mixture was made strongly basic with sodium hydroxide, and the amine was extracted with ethyl ether. This ether extract was dried over magnesium sulfate. Removal of the solvent by rotary evaporation gave 44 g. (35%) of crude cyclooctylamine, which was used without further purification in the next step.

2. N,N,N-Trimethylcyclooctylammonium Iodide

A solution of 44 g. (0.347 mole) of crude cyclooctylamine in 250 ml. of methanol was prepared in a 3 l. round bottom flask fitted with a magnetic stirrer, condenser and two dropping funnels. The solution was cooled in ice-water during the addition of reactants and for one additional hr. Methanolic potassium hydroxide (78 g. of solution, 25% potassium hydroxide by weight) was added through one funnel and 100 g. of a solution of methyl iodide in methanol (50% by weight) through the other. When the reaction became neutral to litmus (1.5 hr.), duplicate quantities of base and methyl iodide solutions were added, and then a third equivalent portion each of base and methyl iodide solutions was added 1.5 hr. after the second portion. The mixture was allowed to warm to room temperature and stirred overnight, after which 75 g. of methyl iodide and 30 g. of 25% by weight potassium hydroxide in methanol was
added (final solution neutral to litmus). The methanol was removed by rotary evaporation and the methiodide was precipitated by the addition of concentrated sodium hydroxide. The product was collected by suction filtration and washed with a mixture of water, methanol and acetone. The N,N,N-trimethylcyclooctylammonium iodide after drying weighed 84 g. (81%) and had m.p. 266-269° (lit. 270-271°).

3. trans-Cyclooctene

A solution of 84 g. of N,N,N-trimethylcyclooctylammonium iodide in 430 ml. of water was stirred for 5 hr. with moist silver oxide (which had been freshly precipitated from 98 g. of silver nitrate and washed free of base with water). The mixture was filtered, the solid was washed with 200 ml. of water, and the filtrate was concentrated on a rotary evaporator. The residual quarternary base was decomposed by heating in a nitrogen atmosphere at 7-9 mm. with a bath temperature of 105-120°. The distillate was collected in a trap cooled by Dry Ice and acetone. The distillate was acidified with dilute sulfuric acid and then extracted with four 60-ml. portions of pentane. The pentane solution was extracted with five 75-ml. portions of aqueous silver nitrate (20% by weight). The aqueous solution was washed once with pentane and then poured into 350 ml. of concentrated aqueous ammonia containing cracked ice. The hydrocarbon that separated was extracted with five 200-ml. portions of pentane. The pentane extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 5.5 g. (17.7%) of crude trans-cyclooctene. An infrared spectrum agreed with one previously published (trans-alkene absorption at 10.3 microns).
4. cis-2-Bromocyclooctanol

To a 125 ml. erlenmeyer flask equipped with a magnetic stirrer was added 5.5 g. (0.05 mole) of trans-cyclooctene, 5.3 g. (0.052 mole) of benzonitrile, 0.9 g. of potassium bicarbonate and 30 ml. of methanol. Then 10.2 g. (0.056 mole) of 30% hydrogen peroxide was added, and the resulting mixture was stirred at 30° for 23 hr. and at 60° for 11 hr. It was then diluted with 70 ml. of water and extracted 4 times with chloroform. The chloroform extract was washed twice with water and dried over magnesium sulfate. Rotary evaporation of solvent left a mixture of trans-cyclooctene oxide and benzamide. Most of the benzamide was removed by filtration and the filtrate was dissolved in 60 ml. of carbon tetrachloride which had been first used to wash the benzamide. Hydrogen bromide gas was bubbled into the solution until it became saturated (40 min.) and then the carbon tetrachloride solution was washed with water, twice with dilute sodium bicarbonate and water. The aqueous portion was extracted one time with carbon tetrachloride, and the total carbon tetrachloride solution was dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to give 1.93 g. (19%) of cis-2-bromocyclooctanol, b.p. 84-87° (0.25 mm.). A small portion of the bromohydrin was esterified in the usual manner with 3,5 dinitrobenzoic acid to give cis-2-bromocyclooctyl 3,5-dinitrobenzoate, m.p. 116-117° (lit. 117-117.5°).

A mixture of 0.21 g. of cis-2-bromocyclooctanol, 0.5 g. of sodium hydroxide and 10 ml. of water was stirred at 38° for 5 hr. Extraction with ethyl ether and removal of solvent (after drying) gave a residue of 0.12 g. (95%) which was shown by g.c. analysis to be made up of trans-
cyclooctene oxide$^{23}$ (85%) and a mixture of 1,4- and 1,5-epoxycyclooctane (15%).$^{29}$

C. Preparation of Cyclooctyl Bromide$^{65a}$

Hydrogen bromide gas was bubbled through a mixture of 20 g. of cis-cyclooctene in 100 ml. of petroleum ether and 2 g. of zinc wool until the solution was saturated with hydrogen bromide (1 hr.). The petroleum ether solution was decanted from the zinc and washed 4 times with dilute sodium bicarbonate solution and one time with water. The aqueous portion was extracted one time with petroleum ether and the combined ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to give 8.0 g. (23%) of cyclooctyl bromide,$^{65a}$ b.p. 51-52° (0.2 mm.).

D. Solvolyses of trans-2-Chlorocyclooctanol

1. Refluxing Aqueous Tetrahydrofuran

A mixture of 3.25 g. (0.02 mole) of trans-2-chlorocyclooctanol, 100 ml. of tetrahydrofuran and 50 ml. of water was refluxed (66°) under nitrogen for 14 days (samples were injected periodically into the g.c. to determine the extent of the reaction). It was then diluted with 500 ml. of water and extracted 4 times with ethyl ether. The ether extract was washed once with water and dried over magnesium sulfate. Rotary evaporation of solvent left a residue of 2.2 g. The residue was analyzed by gas chromatography (Barber-Colman instrument, GE-96 silicone column); the chromatogram showed the presence of 4 major and several minor components. By comparison with authentic samples, the 4 major peaks were associated with cycloheptanecarboxaldehyde,$^{30}$ a mixture of 1,4- and 1,5-epoxycyclooctane,$^{29,42}$ cyclooctanone,$^{49}$ and a
mixture of 2-,3- and 4-cyclooctenols. Cycloheptanecarboxaldehyde was identified by a comparison of its retention times on the silicone and the poly (propylene glycol) columns with those of an authentic sample. Cyclooctanone was isolated from the crude mixture as its 2,4-dinitrophenylhydrazone, m.p. 168-170° (mixed melting point with authentic cyclooctanone 2,4-dinitrophenylhydrazone showed no depression). A portion of the reaction mixture was treated in pyridine solution to convert alcohol components to their trimethylsilyl ether derivatives. With the exception of cis- and trans-1,4-cyclooctanediols, the isomeric enols and the isomeric diols were resolved on the silicone column when converted to their trimethylsilyl derivatives. trans-1,4-Cyclooctanediol was isolated from formic and trifluoroacetic acid solvolyses of trans-2-bromocyclooctanol, and it was assumed that the 1,4-cyclooctanediol found in the other solvolyses of the trans-2-halocyclooctanols was also the trans isomer. A calculation of the relative amounts of the various products was made. The relative response of the instrument (Barber-Colman) to the various compounds was determined by injecting series of known amounts of pure compounds and noting the area produced on the graph by each. From this and the relative areas of the peaks in the product mixture, it was possible to calculate the relative amounts of each product with the exception of the diol products. The 1,2-diol present was determined quantitatively by periodic acid oxidation and iodometric titration of a portion of the product mixture. The 1,4-diol was estimated from the value determined for the 1,2 diol together with the relative g.c. peak areas of the isomeric trimethylsilyl derivatives and the assumption that they
gave equivalent responses in the detector. As a check, the amount of cyclooctanone in the mixture was determined independently by an internal standard method in which a sample of a carefully weighed mixture of cyclooctanone and cyclohexanone was injected into the g.c. and a relative weight-response ratio determined. A portion of another carefully weighed mixture of cyclohexanone and the solvolysis product mixture was also injected into the g.c. and from the relative areas of the cyclohexanone and cyclooctanone peaks in this mixture and in the standard mixture, the amount of cyclooctanone present in the solvolyses mixture was calculated. The value was found to agree within 0.7% of the value found by the other method. The products and their relative amounts are given here. The first number following the compound represents the mole percent in the mixture and the second number is the percentage yield of that particular component. This same scheme will be followed throughout unless otherwise noted. Cycloheptanecarboxaldehyde, 7.9% (6.9%); 1,4- and 1,5-epoxycyclooctane, 14.5% (12.8%); cyclooctanone, 15.4% (13.4%); 2-cyclooctenol, 4.5% (3.9%); 3-cyclooctenol, 28.0% (24.3%); 4-cyclooctenol, 9.1% (7.9%); trans-1,2-cyclooctanediol, 8.2% (7.1%); trans-1,4-cyclooctanediol, 4.1% (3.5%); total identified components, 91.7% (78.7%).

2. Refluxing Aqueous Tetrahydrofuran with Silver Nitrate

A mixture prepared by adding 20.4 g. (0.12 mole) of silver nitrate in 250 ml. of water to 16.2 g. (0.1 mole) of trans-2-chlorocyclooctanol in 500 ml. of tetrahydrofuran was refluxed (66°) for 27 hr. under nitrogen, filtered to remove the silver chloride, diluted with 1 l. of water and extracted with several portions of ethyl ether which had
been used to wash the filter cake. The ether extract was washed once with water and dried over magnesium sulfate. The solvent was removed by rotary evaporation to yield 13 g. of product mixture which was analyzed in the same manner as before. One new product, cycloheptanone, was found and it was distinguished from trans-2-vinylcyclohexanol which has an identical retention time on the silicone column, by injecting samples of both compounds into the Aerograph Autoprep instrument (Carbowax column) which separated the two compounds. The composition of the product mixture is given here (the mole percent and the actual yield are identical in this case). Cycloheptanone, 7.7%; 1,4- and 1,5-epoxycyclooctane, 25.3%; cyclooctanone, 16.0%; 2-cyclooctenol, 1.6%; 3-cyclooctenol, 38.1%; 4-cyclooctenol, 4.4%; trans-1,2-cyclooctanediol, 1%; trans-1,4-cyclooctanediol, 1%; total identified products, 96.1%.

E. Solvolyses of trans-2-Bromocyclooctanol

1. Refluxing Aqueous Tetrahydrofuran with Silver Nitrate

To 4.14 g. (0.02 mole) of trans-2-bromocyclooctanol in 100 ml. of tetrahydrofuran was added 4.08 g. (0.024 mole) of silver nitrate in 50 ml. of water, and, after refluxing (66°) for 4 hr. under nitrogen, the mixture was allowed for convenience to stand overnight at room temperature. The mixture was diluted with 500 ml. of water and filtered to remove the silver bromide. The silver bromide was then washed 4 times with ethyl ether and each ether portion was used in turn to extract the filtrate. The ether extracts were then washed once with water and dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 2.2 g. of products. The product mixture was analyzed as before to give the following product distribution:
cycloheptanone, 6.4% (5.6%); 1,4- and 1,5-epoxycyclooctane, 28.0% (24.4%); cyclooctanone, 23.7% (20.6%); 2-cyclooctenol, 0.8% (0.7%); 3-cyclooctenol, 34.1% (29.6%); 4-cyclooctenol, 2.4% (2.1%); trans-1,2-cyclooctanediol, 1% (0.9%); trans-1,4-cyclooctanediol, 1% (0.9%); total identified components, 97.4% (84.8%).

2. Refluxing Aqueous Tetrahydrofuran without Silver Salt

A mixture of 4.14 g. (0.01 mole) of trans-2-bromocyclooctanol, 100 ml. of tetrahydrofuran and 50 ml. of water was refluxed (66°) under nitrogen for 44 hr. The mixture was then diluted with 300 ml. of water and extracted 4 times with ethyl ether. The ether extract was washed once with water and dried over magnesium sulfate. The solvent was removed by rotary evaporation to yield 2.4 g. of products. Analysis of this residue gave the following results: cycloheptanone, 0.4% (0.4%); cycloheptanecarboxaldehyde, 3.3% (3.3%); 1,4- and 1,5-epoxycyclooctane, 16.8% (16.0%); cyclooctanone, 21.3% (20.3%); 2-cyclooctenol, 4.5% (3.9%); 3-cyclooctenol, 32.1% (30.5%); 4-cyclooctenol, 7.0% (6.7%); trans-1,2-cyclooctanediol, 8.1% (7.7%); trans-1,4-cyclooctanediol, 4.0% (3.5%); total identified components, 97.8% (92.6%).

3. Refluxing Aqueous Tetrahydrofuran with Sodium Acetate

A solution of 3.2 g. (0.04 mole) of sodium acetate in 500 ml. of water was added to 4.14 g. (0.02 mole) of trans-2-bromocyclooctanol in 100 ml. of tetrahydrofuran, and this mixture was refluxed under nitrogen for 54 hr. The reaction mixture was then diluted with 200 ml. of water and extracted 4 times with ethyl ether. The ether extract was washed once with water and dried over magnesium sulfate. Rotary evaporation of solvent left 2.52 g. of residue, for which the following composition
was determined by g.c. analysis: Cycloheptanone, trace: cycloheptane-carboxaldehyde, 5.5% (5.4%); 1,4- and 1,5-epoxycyclooctane, 8.0% (7.9%); cis-cyclooctene oxide, 13.5% (13.3%); cyclooctanone, 20.8% (20.6%); 2-cyclooctenol, 3.7% (3.6%); 3-cyclooctenol, 26.3% (25.9%); 4-cyclooctenol, 7.3% (7.2%); trans-1,2-cyclooctanediol, 6.4% (5.9%); trans-1,4-cyclooctanediol, 5.0% (4.6%); total identified components, 96.7% (92.8%).

4. 50% Acetic Acid with Silver Nitrate at 66°

A mixture of 4.14 g. (0.02 mole) of trans-2-bromocyclooctanol, 4.08 g. (0.024 mole) of silver nitrate and 100 ml. of 50% aqueous acetic acid was stirred at 66° for 6 hr. under nitrogen. The mixture was then filtered to remove silver bromide, diluted with 200 ml. of water and extracted 5 times with ethyl ether (each ether portion having been used to wash the silver bromide). The ether extract was washed with water, dilute sodium bicarbonate and water. The aqueous washings were extracted once with ethyl ether, and the total ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation. The product mixture (2.5 g.) was analyzed as before to give the following results: cycloheptanone, 2.9% (2.8%); 1,4- and 1,5-epoxycyclooctane, 24.1% (23.4%); cycloheptanecarboxaldehyde, 11.4% (11.1%); cyclooctanone, 22.9% (22.2%); 2-cyclooctenol, 0.8% (0.8%); 3-cyclooctenol, 25.9% (25.1%); 4-cyclooctenol, 4.2% (4.1%); trans-1,2-cyclooctanediol, 1% (1%); trans-1,4-cyclooctanediol, 1% (1%); total identified components, 97.3% (91.5%).

5. 50% Acetic Acid with Silver Nitrate at 0°

A mixture of 4.14 g. (0.02 mole) of trans-2-bromocyclooctanol,
4.08 g. (0.024 mole) of silver nitrate, and 100 ml. of aqueous acetic acid (50% by volume) was stirred at 0° under nitrogen for 24 hr. The mixture was then filtered to remove silver bromide, diluted with 200 ml. of water, and extracted 5 times with the ethyl ether which had been first used to wash the silver bromide. The ether extract was then washed with water, dilute sodium bicarbonate and water. The aqueous washings were extracted once with ethyl ether, and the total ether extract was dried over magnesium sulfate. Rotary evaporation of solvent left 2.4 g. of mixture which was analyzed as before to give the following results: cycloheptanone, 0.7% (0.7%); 1,4- and 1,5-epoxycyclooctane, 21.3% (20.3%); cycloheptanecarboxaldehyde, 11.1% (10.6%); cyclooctanone, 24.6% (23.4%); 2-cyclooctenol, 1.1% (1.0%); 3-cyclooctenol, 36.0% (34.4%); 4-cyclooctenol, 2.0% (1.9%); trans-1,2-cyclooctanediol, 1% (1%); trans-1,4-cyclooctanediol, 1% (1%); total identified components, 96.8% (94.2%).

6. **Refluxing 1 M Sulfuric Acid with Silver Nitrate**

A solution of 2.5 g. (0.012 mole) of trans-2-bromocyclooctanol and 2.4 g. (0.012 mole) of silver nitrate in 50 ml. of 1 M sulfuric acid was refluxed (100°) under nitrogen for 22 hr. The mixture was filtered to remove silver bromide and then extracted 5 times with the ethyl ether which had been used to wash the silver bromide. The ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation to yield 1.3 g. of products. The product mixture was analyzed as before with the following results: cycloheptanone, 10.5% (9.0%); 1,4- and 1,5-epoxycyclooctane, 47.2% (40.8%); cyclooctanone, 23.6% (20.5%); 3-cyclooctenol, 8.7% (7.6%); 4-cyclooctenol, 3.5% (3.0%);
trans-1,2-cyclooctanediol, 1% (1%); trans-1,4-cyclooctanediol, 1% (1%); total identified products, 95.5% (82.7%).

7. Glacial Acetic Acid with Silver Acetate at 10°

To 2.7 g. (0.013 mole) of trans-2-bromocyclooctanol in 30 ml. of glacial acetic acid was added 2.5 g. (0.015 mole) of silver acetate, and this mixture was stirred at 10° under nitrogen for 24 hr. The reaction mixture was then filtered to remove silver bromide, and the filtrate was stirred at room temperature with 70 g. of sodium hydroxide in 200 ml. of water for 8 hr. It was then extracted 4 times with ethyl ether. The total ether extract was dried over magnesium sulfate. Rotary evaporation of solvent gave a residue of 1.7 g. of product mixture. Analysis of this mixture indicated the following composition:
cycloheptanone, 1.0% (0.8%); 1,4- and 1,5-epoxycyclooctane, 1.2% (1.2%); cycloheptanecarboxaldehyde, 0.2% (0.2%); cyclooctanone, 35.1% (32.8%); 2-cyclooctenol, 0.8% (0.8%); 3-cyclooctenol, 11.0% (10.5%); 4-cyclooctenol, 3.8% (3.5%); trans-1,2-cyclooctanediol, 15.6% (15.5%); trans-1,4-cyclooctanediol, 28.1% (25.5%); total identified products, 96.8% (89.8%).

8. 99% Trifluoroacetic Acid at 0° with Silver Trifluoroacetate

Silver trifluoroacetate was prepared by suspending dried silver oxide in benzene and adding trifluoroacetic acid until the silver oxide just dissolved. The benzene was stripped off and the residue was recrystallized from fresh benzene.

A mixture of 7.8 g. (0.036 mole) of silver trifluoroacetate, 6.1 g. (0.03 mole) of trans-2-bromocyclooctanol and 36 g. of commercial 99% trifluoroacetic acid was stirred under nitrogen at 0° for 3.5 hr.
The reaction mixture was filtered to remove silver bromide, stirred overnight with 54 g. of sodium hydroxide in 180 ml. of water to saponify esters, and then extracted 5 times with ethyl ether. The total ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 3.9 g. of product mixture, which was analyzed as before to give the following results: cycloheptanone, 3.2% (2.7%); 1,4- and 1,5-epoxycyclooctane, 11.9% (11.3%); cycloheptanecarboxaldehyde, 4.2% (3.9%); cyclooctanone, 18.2% (17.6%); 3-cyclooctenol, 23.7% (22.3%); 4-cyclooctenol, 6.2% (5.9%); trans-1,2-cyclooctanediol, 3.7% (3.6%); trans-1,4-cyclooctanediol, 25.9% (25.1%); total identified products, 97% (92%).

9. Anhydrous Trifluoroacetic Acid at 0° with Silver Trifluoroacetate

A solution of 4.4 g. of silver trifluoroacetate and 3.5 g. of trans-2-bromocyclooctanol in 30 g. of anhydrous trifluoroacetic acid (distilled under nitrogen from phosphorus pentoxide) was stirred under nitrogen at 0° for 4 hr. It was then mixed with 30 g. of sodium hydroxide in 100 ml. of water and stirred for 6 hr. at 38°. This mixture was extracted 5 times with ethyl ether, and the total ether extract was dried over magnesium sulfate. Rotary evaporation of solvent gave 2.1 g. of residue in which 1,2-diol was not detected.\(^5^7\) trans-1,4-Cyclooctanediol, m.p. 90-91° (lit.\(^2^4\) 90-91°), was isolated directly from the reaction mixture by crystallization from ethyl acetate. It was converted into two derivatives,\(^5^7\) the bis-p-nitrobenzoate, m.p. 154-155° (lit.\(^2^4\) 156.2-156.7°) and the bis-phenylurethan, m.p. 179-179.5° (lit.\(^2^4\) 180.2-181.7°). Melting points of samples of cis-1,4-
cyclooctanediol (isolated from epoxide solvolyses) and its derivatives mixed with the corresponding trans isomer (from halohydrin solvolyses) and its derivatives were strongly depressed. Diol isolated from halohydrin solvolyses in formic and 99% trifluoroacetic acids proved also to be the trans-1,4-isomer by mixed melting points. The remainder of the product mixture was analyzed as before to give the following results: cyclooctanone, 20.2% (19.6%); cycloheptanone, 2.3% (2.2%); cycloheptanecarboxaldehyde, 4.1% (4.0%); 3-cyclooctenol, 28.6% (26.6%); 4-cyclooctenol, 4.1% (4.0%); 1,4- and 1,5-epoxycyclooctane, 14.7% (14.1%); trans-1,4-cyclooctanediol, 20.5% (20.0%); total identified products, 94.5% (90.0%).

10. Formic Acid at 0° with Silver Acetate

A mixture of 5.2 g. (0.025 mole) of trans-2-bromocyclooctanol, 5.0 g. (0.030 mole) of silver acetate and 40 ml. of commercial 97—100% formic acid was stirred at 0° under nitrogen for 10 hr. It was then filtered to remove silver bromide, stirred for 10 hr. with 75 g. of sodium hydroxide and 200 ml. of water, and extracted 5 times with ethyl ether. The total ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 3.3 g. of crude products. The mixture was analyzed with the following results: cycloheptanone, 2.5% (2.1%); 1,4- and 1,5-epoxycyclooctane, 3.3% (3.1%); cycloheptanecarboxaldehyde, 1.5% (1.4%); cyclooctanone, 9.8% (9.1%); 3-cyclooctenol, 36.6% (34.1%); 4-cyclooctenol, 4.2% (3.9%); trans-1,2-cyclooctanediol, 4.2% (3.9%); trans-1,4-cyclooctanediol, 36.9% (35.5%); total identified products, 98.8% (92.9%).
11. Formic Acid at 38° with Silver Acetate

A solution of 5.2 g. (0.025 mole) of trans-2-bromocyclooctanol and 5.0 g. (0.030 mole) of silver acetate in 40 ml. of commercial 97-100% formic acid was stirred under nitrogen at 38° for 5 hr. It was then filtered to remove the silver bromide, stirred with 75 g. of sodium hydroxide and 200 ml. of water, and extracted 5 times with ethyl ether. The total ether extract was dried over magnesium sulfate. Rotary evaporation of solvent left a residue of 3.1 g. This crude mixture was analyzed as before to give the following results: cycloheptanone, 3.7% (3.6%); 1,4- and 1,5-epoxycyclooctane, 2.4% (2.3%); cycloheptancarboxaldehyde, trace; cyclooctanone, 10.2% (10.0%); 3-cyclooctenol, 36.9% (34.2%); 4-cyclooctenol, 4.0% (3.7%); trans-1,2-cyclooctanediol, 4.5% (3.7%); trans-1,4-cyclooctanediol, 37.4% (34.2%); total identified products, 99.0% (91.5%).

12. Refluxing Aqueous Ethanol with Sodium Azide

A mixture consisting of 8.28 g. (0.04 mole) of trans-2-bromocyclooctanol, 26 g. (0.4 mole) of sodium azide, 112 ml. of water and 228 ml. of ethanol was refluxed for 60 hr. The mixture was diluted with water and extracted 5 times with ethyl ether. The ether extracts were washed with water and dried over magnesium sulfate. Removal of solvent by rotary evaporation left a residue of 5.1 g. A small portion of this residue (0.5 g.) was analyzed as previously. The remainder was dissolved in 50 ml. of methanol, 200 mg. of Adam's catalyst was added and the mixture was placed on the Parr low pressure hydrogenator for 24 hr. The hydrogen uptake was 1 lb. (0.012 mole). The solution was filtered to remove the catalyst, acidified with dilute
hydrochloric acid, and extracted 4 times with ethyl ether. The ether extract was dried over magnesium sulfate, and the aqueous portion was made strongly basic with sodium hydroxide. The basic solution was then extracted 4 times with ethyl ether and the ether extract dried over magnesium sulfate. Removal of solvent from the acidic extract left a residue of 1.9 g. (which consisted of the reduction products of the normal solvolysis mixture). Removal of solvent from the basic extract left a residue of 2.0 g. Several attempts were made to crystallize the basic residue from a variety of common solvents (petroleum ether, ethyl acetate, methanol, ethanol, benzene, methanol-water, and ethanol-water). None of these attempts were successful. The infrared spectrum of the basic fraction did not show azide absorption at 4.63-4.72 microns nor did the spectrum match that of cis- or trans-2-hydroxycyclooctylamine. Two attempts were made to convert this material to an N-benzoyl derivative without success. The components of the reaction mixture and their relative mole percentages are: cycloheptanone, 0.9%; cycloheptanecarboxaldehyde, 2.3%; cyclooctanone, 16.9%; cis-cyclooctene oxide, 16.0%; 2-cyclooctenol, 2.1%; 3-cyclooctenol, 6.9%; 4-cyclooctenol, 1.7%; 1,4- and 1,5-epoxycyclooctane, 2.3%; trans-1,2-cyclooctanediol, 1%; basic fraction, 49% (assuming this is an amino alcohol).

F. Solvolyses of cis-2-Bromocyclooctanol

1. Refluxing Aqueous Tetrahydrofuran with Silver Nitrate

A solution of 0.62 g. (0.003 mole) of cis-2-bromocyclooctanol in 15 ml. of tetrahydrofuran was mixed with 0.61 g. (0.0036 mole) of silver nitrate in 7.5 ml. of water and the resulting
mixture was stirred for 17 hr. at 38°. The mixture was then diluted with water and filtered to remove the silver bromide. The filter cake was washed with five 40-ml. portions of ethyl ether which were used in turn to extract the filtrate. The ether extract was washed once with water and dried over magnesium sulfate. Removal of the solvent by rotary evaporation left a residue of 0.4 g, which was analyzed in the same way as the solvolysis mixtures from trans-2-bromocyclooctanol. Most of the products were similar to those found in the solvolyses of the trans compound, with the exception that one major and four minor components of this mixture were unidentified. The infrared spectrum of the product mixture indicated the possibility of a second aldehyde being present in the mixture. This could be 2-methylcyclohexanecarboxaldehyde which is found in 25% yield in the acid-catalyzed rearrangement of trans-cyclooctene oxide. There was not enough material available to attempt an isolation of the unidentified products. The products and their relative amounts are given here (mole percent is equal to the percentage yield in this case, figures for the unknown components represent the percentage of the total g.c. peak area): four minor components, 7.7%; one major component, 8.4%; cycloheptanecarboxaldehyde, 2.3%; cyclooctanone, 13.7%; 2-cyclooctenol, 8.3%; 3-cyclooctenol, 11.9%; 4-cyclooctenol, 2.4%; cis-1,2-cyclooctanediol, 2.4%; trans-1,2-cyclooctanediol, 2.4%; 1,4-cyclooctanediol, 2.0%; 1,4- and 1,5-epoxy-cyclooctane, 28.1%; total identified products, 73.5%.

2. Refluxing Aqueous Tetrahydrofuran

A solution of 0.4147 g. (0.002 mole) of cis-2-bromocyclo-
octanol in 140 ml. of solvent (made by mixing 2 parts of tetrahydrofuran with 1 part water) was refluxed for 72 hr. During the course of the reaction, 40 ml. of solution was withdrawn in several portions for a kinetic study. The remainder of the solution was diluted with water and extracted 4 times with ethyl ether. The ether extract was washed once with water and dried over magnesium sulfate. Removal of the solvent by rotary evaporation left a residue of 0.2 g. which was analyzed as before to give the following results: four minor components, 6.2%; one major component, 9.3%; cycloheptanecarboxaldehyde, 3.1% (2.9%); cyclooctanone, 15.7% (14.9%); 2-cyclooctenol, 8.0% (7.6%); 3-cyclooctenol, 14.5% (13.7%); 4-cyclooctenol, 6.0% (5.7%); 1,4- and 1,5-epoxycyclooctane, 20.5% (19.5%); cis-1,2-cyclooctanediol, 6.0% (5.7%); trans-1,2-cyclooctanediol, 4.0% (3.8%); 1,4-cyclooctanediol, 2.5% (2.4%); total identified products, 78.3% (73.0%).

G. Kinetic Studies

Solvolyses of trans-2-bromocyclooctanol (2 runs), cis-2-bromocyclooctanol (1 run), and cyclooctyl bromide (2 runs) were studied kinetically. All of the runs were made in as similar a manner as was experimentally possible. A description of a model run will be given here and the data from all 5 runs are given in Table VI and presented graphically in Figures 1, 2, and 3.

A mixture of 200 ml. of water and 400 ml. of tetrahydrofuran was stirred at room temperature for 3 hr. in a closed vessel. In a 500 ml. round bottom flask equipped with a reflux condenser and a side arm sealed with a rubber serum cap was placed 285 ml. of the aqueous tetrahydrofuran solution. The solution was brought to reflux and
TABLE VI

KINETIC DATA

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Figure 1

**trans-2-Bromocyclooctanol Rate Data**

\[ k = \frac{-\text{slope}}{2.3} = 0.0502 \]

\[ k = \frac{-\text{slope}}{2.3} = 0.0423 \]

\[ k_{av} = 0.0463 \pm 0.020 \]

Figure 2

**cis-2-Bromocyclooctanol Rate Data**

\[ k = \frac{-\text{slope}}{2.3} = 0.0399 \]

Figure 3

**Cyclooctyl Bromide Rate Data**

\[ k = \frac{-\text{slope}}{2.3} = 0.0571 \]

\[ k = \frac{-\text{slope}}{2.3} = 0.0567 \]

\[ k_{av} = 0.40569 \pm 0.0002 \]
0.004 mole (weighed out on an analytical balance) of the bromide in 5 ml. of the solvent was added through the top of the condenser followed by two 5-ml. washings of solvent (time zero). At periodic intervals, approximately 6-ml. samples were withdrawn from the mixture by a hypodermic syringe and quenched by ejection into a test tube immersed in an ice-bath. A pipet was used to transfer a 5-ml. portion of the sample to a small erlenmeyer flask in which the liberated acid was titrated with 0.0025 M sodium hydroxide and phenol red indicator.

A plot of log. concentration versus time was made for each run. The slope of the plot is equal to the rate constant, k, divided by -2.303. These plots are shown in Figures 1, 2, and 3.

H. Solvolyses of cis Cyclooctene Oxide

1. Refluxing Aqueous Tetrahydrofuran with Silver Nitrate and Silver Chloride

A mixture of 1.26 g. (0.01 mole) of cis-cyclooctene oxide, 50 ml. of tetrahydrofuran, 0.33 g. of silver nitrate, 1.44 g. of silver chloride and 25 ml. of water was refluxed for 22 hr. The mixture was then filtered, diluted with 300 ml. of water and extracted 3 times with ethyl ether. The total ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 1.0 g. (79% recovery) of cis-cyclooctene oxide, pure by gas chromatography.

2. Refluxing Aqueous Tetrahydrofuran with Sulfuric Acid

A solution of 2.52 g. (0.02 mole) of cis-cyclooctene oxide in 100 ml. of tetrahydrofuran containing 50 ml. of water and 6 drops of concentrated sulfuric acid was refluxed for 5 days. The mixture was then diluted with 500 ml. of water and extracted 4 times with
ethyl ether. The ether extract was washed once with water and dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 2.1 g. of crude products. The crude mixture was analyzed by g.c. to give the following results: \textit{trans-2-vinylcyclohexanol}, trace; 1,4- and 1,5-epoxycyclooctane, 0.9% (0.7%); cyclooctanone, trace; 2-cyclooctenol, 1.2% (1.0%); 3-cyclooctenol, 14.2% (12.1%); 4-cyclooctenol, 7.3% (6.1%); \textit{trans-1,2-cyclooctanediol}, 40.8% (30.2%); \textit{cis-1,4-cyclooctanediol}, 31.2% (23.0%); total identified products, 95.9% (73.1%).

3. \textbf{Refluxing 50\% Acetic Acid}

A solution of \textit{cis-cyclooctene oxide} (12.6 g., 0.1 mole) in 300 ml. of 50\% acetic acid was refluxed for 72 hr., 80 g. of sodium hydroxide and 50 ml. of water were added, and the resulting mixture was stirred overnight without external heating. It was then extracted 7 times with ethyl ether. The ether extract was washed with water, dilute sodium bicarbonate, and water, and dried over magnesium sulfate. Rotary evaporation of solvent left 13.2 g. of residue which was analyzed with the following results: 1,4- and 1,5-epoxycyclooctane, 1.5% (1.4%); cyclooctanone, 1.5% (1.4%); 3-cyclooctenol, 27.9% (26.5%); 4-cyclooctenol, 9.4% (8.5%); \textit{trans-1,2-cyclooctanediol}, 33.0% (31.5%); \textit{cis-1,4-cyclooctanediol}, 19.4% (18.9%); total identified products, 92.7% (90.2%).

4. \textbf{Refluxing 50\% Acetic Acid with Silver Nitrate}

A solution of 6.3 g. (0.05 mole) of \textit{cis-cyclooctene oxide} and 10.2 g. (0.06 mole) of silver nitrate in 150 ml. of 50\% acetic acid was refluxed for 75 hr.; 80 g. of sodium hydroxide and 50 ml. of
water were added, and after being stirred overnight, the total mixture was extracted 7 times with ethyl ether. The ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 6.0 g. of crude product, which was analyzed to give the following results: trans-2-vinylcyclohexanol, 1.3% (1.1%); 1,4- and 1,5-epoxycyclooctane, 5.8% (5.1%); cyclooctanone, 1.5% (1.3%); 3-cyclooctenol, 28.7% (25.2%); 4-cyclooctenol, 9.1% (8.0%); trans-1,2-cyclooctanediol, 33.9% (30.0%); cis-1,4-cyclooctanediol, 16.6% (14.7%); total identified products, 96.9% (85.4%).

5. Refluxing 50% Acetic Acid with Sodium Nitrate

A mixture of 6.3 g. (0.05 mole) of cis-cyclooctene oxide, 5.1 g. (0.06 mole) of sodium nitrate and 150 ml. of 50% acetic acid was refluxed for 61 hr.; 80 g. of sodium hydroxide and 50 ml. of water were added, and the mixture was refluxed for 3 hr. and then extracted 5 times with ethyl ether. The total ether extract was dried over magnesium sulfate and concentrated by rotary evaporation. Analysis of the residue (6.2 g.) indicated the following composition: trans-2-vinylcyclohexanol, 1.0% (0.9%); 1,4- and 1,5-epoxycyclooctane, 4.5% (4.1%); cyclooctanone, 1.9% (1.7%); 3-cyclooctenol, 28.5% (25.6%); 4-cyclooctenol, 9.3% (8.5%); trans-1,2-cyclooctanediol, 32.5% (29.5%); cis-1,4-cyclooctanediol, 17.0% (15.6%); total identified products, 94.2% (85.9%).

6. Refluxing 90% Formic Acid

A solution of cis-cyclooctene oxide (6.3 g., 0.05 mole) in 25 ml. of commercial 90% formic acid was refluxed for 4 hr., a solution of 60 g. of sodium hydroxide in 200 ml. of water was added and the
resulting mixture was stirred for 12 hr. It was then extracted 5 times with ethyl ether. The total ether extract was dried over magnesium sulfate and concentrated by rotary evaporation to give 6.3 g. of product mixture, which was analyzed as before with the following results: 

- **trans-2-vinylcyclohexanol**, 7.5% (7.0%); 1,4- and 1,5-epoxycyclooctane, 3.7% (3.5%); cyclooctanone, 1.1% (1.0%); 3-cyclooctenol, 22.2% (20.8%); 4-cyclooctenol, 14.4% (13.5%); **trans-1,2-cyclooctanediol**, 22.7% (21.3%); **cis-1,4-cyclooctanediol**, 27.1% (25.5%); total identified products, 98.7% (92.6%).

7. **Reflexing 1 M Sulfuric Acid**

A solution of 3.0 g. of **cis-cyclooctene oxide** in 100 ml. of 1 M sulfuric acid was refluxed for 15 hr. and then extracted 4 times with ethyl ether. The total ether extract was washed once with water and dried over magnesium sulfate. The solvent was removed by rotary evaporation to leave 1.8 g. of residue which was analyzed as before with the following results: **trans-1,2-cyclooctanediol**, 9.7% (5.4%); **trans-2-vinylcyclohexanol**, 19.7% (11.2%); 1,4- and 1,5-epoxycyclooctane, 29.7% (16.7%); cyclooctanone, 7.1% (5.2%); 3-cyclooctenol, 4.2% (2.3%); 4-cyclooctenol, 1.7% (1.0%); **cis-1,4-cyclooctanediol**, 38.9% (24.5%); total identified products, 94% (54%).

8. **Hot 97-100% Formic Acid**

A mixture of 11.0 g. of **cis-cyclooctene oxide** and 35 ml. of commercial 97-100% formic acid was heated on a steam bath for 3 hr., 70 g. of sodium hydroxide and 200 ml. of water were added, and this mixture was stirred overnight to saponify esters. The mixture was extracted 4 times with ethyl ether, and the total ether extract was
dried over magnesium sulfate. Rotary evaporation of solvent left 7.3 g. of residue, which was analyzed with the following results: cyclooctanone, 8.5% (5.2%); 3-cyclooctenol, 23.2% (14.1%); 4-cyclooctenol, 7.8% (4.8%); trans-1,2-cyclooctanediol, 20.5% (13.0%); cis-1,4-cyclooctanediol, 38.9% (24.5%); total identified products, 98.9% (61.6%).

9. **Trifluoroacetic Acid at 0°**

An ice chilled solution of cis-cyclooctene oxide (12.6 g., 0.1 mole) in 65 g. of trifluoroacetic acid was stirred under nitrogen for 3 hr., a solution of sodium hydroxide (100 g.) in 200 ml. of water was added, and after being stirred overnight at room temperature the alkaline mixture was extracted 5 times with ethyl ether. The total ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation to give 11.0 g. of crude products. cis-Cyclooctanediol, identified by m.p. 84-84.5° (lit. 85-86.5°) and derivatives (bis-p-nitrobenzoate, m.p. 156.6-157.5° (lit. 161.5-162.7°), bis-phenylurethan, m.p. 182-183° (lit. 186-186.7°)), was isolated directly from the product mixture by crystallization from ethyl acetate; no evidence for trans-1,4-diol was obtained. The crude mixture from the solvolysis was analyzed as before with the following results: trans-2-vinylcyclohexanol, 1.0% (0.9%); 1,4- and 1,5-epoxycyclooctane, 0.5% (0.5%); cyclooctanone, 2.3% (2.0%); 3-cyclooctenol, 40.1% (35.3%); 4-cyclooctenol, 2.9% (2.6%); trans-1,2-cyclooctanediol, 4.0% (3.5%); cis-1,4-cyclooctanediol, 47.5% (41.9%); total identified products, 98.3% (86.7%).
I. Attempted Solvolyses of Cyclooctenols

1. 2-Cyclooctenol

A mixture of 1.26 g. (0.01 mole) of 2-cyclooctenol, 2.04 g. (0.012 mole) of silver nitrate, 6.5 ml. (0.008 mole) of 38% hydrochloric acid, 50.5 ml. of tetrahydrofuran and 18.5 ml. of water was refluxed for 4 hr. and then filtered to remove the silver chloride. The filtrate was diluted with 100 ml. of water and extracted 3 times with ethyl ether. The total extract was washed once with water and dried over magnesium sulfate. Rotary evaporation of solvent left 1.20 g. (95% recovery) of 2-cyclooctenol, pure by gas chromatography.

2. 3-Cyclooctenol

A mixture of 0.55 g. (0.0044 mole) of 3-cyclooctenol, 0.9 g. (0.0052 mole) of silver nitrate, 2.8 g. (0.0035 mole) of 37% hydrochloric acid, 22 ml. of tetrahydrofuran and 8 ml. of water was refluxed for 4 hr. and then filtered to remove silver chloride. The filtrate, after being dried over magnesium sulfate and concentrated, was diluted with 100 ml. of water and extracted 3 times with ethyl ether. The total ether extract was dried over magnesium sulfate. After concentration by rotary evaporation, the total ether extract yielded 0.52 g. (95% recovery) of 3-cyclooctenol, pure by gas chromatography.

J. The preparation of the trans-2-Halocyclonanols

The trans-2-halocyclonanols were prepared starting from readily available cyclooctene by the following sequence of reactions:
To 1500 ml. of dry t-butyl alcohol (distilled from sodium metal under nitrogen) in a 3 l. 3-neck flask equipped with stirrer, dropping funnel and condenser, was added 168 g. (1.5 moles) of potassium t-butoxide (K and K Labs). After all of the butoxide had dissolved, 495 g. (4.5 moles) of cis-cyclooctene was added. The reaction vessel was cooled in an ice bath and 379 g. (1.5 moles) of bromoform was added dropwise over a period of 1 hr. through the dropping funnel. The entire reaction was run under a nitrogen atmosphere. The reaction mixture was allowed to warm to room temperature while it was stirred for an additional 2 hr. After addition of 1300 ml. of water, the mixture was extracted with four 300-ml. portions of pentane, and the combined pentane extracts were washed with three 150-ml. portions of water. The total pentane extract was dried with magnesium sulfate, the solvent was removed by rotary evaporation, and the residue was distilled under reduced pressure to yield 249 g. (60%) of 9,9-dibromobicyclo(6.1.0)nonane, b.p. 87-89° (0.2 mm.) (lit. 92-93° (0.9 mm.)); 29 45° (0.15 mm.)73. Analysis by gas chromatography indicated
only one component. An infrared spectrum was obtained and compared with ones previously obtained.29,30

2. 1,2-Cyclononadiene29,73,74

A 2 l. 3-neck flask equipped with stirrer, dropping funnel, and ice-water cooled condenser was dried and swept out with nitrogen. A slight positive pressure of nitrogen was maintained throughout the preparation of methyllithium and 1,2-cyclononadiene. A solution of 274 g. (2 moles) of methyl iodide and 800 ml. of dry ethyl ether was added dropwise during a 3 hr. period to 28 g. (4 moles) of lithium shot and 250 ml. of dry ethyl ether in the flask. In order to insure complete reaction, the mixture was stirred for an additional hr. By use of phenolphthalein indicator and a standard solution (0.1 N) of hydrochloric acid, titrations were made with aliquots of the methyllithium-ether solution in water. The titrations indicated that the solution was 1.8 mM. There were approximately 1000 ml. of solution or a total yield of 1.8 mole (90%) of methyllithium. The methyllithium solution was transferred into an addition funnel by pouring it quickly while maintaining a nitrogen atmosphere in the immediate area of the transfer. In a 2 l. 3-neck flask fitted with an addition funnel, Dry-Ice condenser, low-temperature thermometer and stirrer was placed 213 g. (0.76 mole) of 9,9-dibromobicyclo(6.1.0)nonane and 500 ml. of dry ether. The reaction vessel and its contents were cooled between -35 and -40° by use of a Dry Ice-acetone bath, and this temperature was maintained throughout the dropwise addition of methyllithium-ether solution. After an additional hr. of stirring, the reaction mixture was allowed to warm to room temperature. Small pieces of ice
were cautiously added to destroy any excess methyllithium. The reaction mixture was transferred to a separatory funnel and washed with three 200-ml. portions of water. The combined water extract was washed twice with 200-ml. portions of ethyl ether. The total ether extract was dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to yield 77 g. (84%) of 1,2-cyclononadiene, b.p. 82-85° (30 mm.) (lit. 73 94° (44 mm.)). The allene structure was confirmed by infrared absorption at 5.13 microns. 74

3. cis-Cyclononene 76

A Parr low pressure hydrogenator was used to hydrogenate 39 g. of 1,2-cyclononadiene. Because of limited solubility of the allene in methanol and capacity of apparatus, it was necessary to hydrogenate in two portions. After hydrogenation, the methanol-cyclononene solutions were combined for isolations of the cyclononene.

A heavy-walled 500 ml. bottle containing 27 g. of 1,2-cyclononadiene, 200 mg. of Pd/C catalyst and 200 ml. of absolute methanol was flushed with nitrogen and then with hydrogen. Hydrogenation, which occurred over a 35 minute period, required 19 lb. of hydrogen (corresponding to 0.25 mole of hydrogen). The second portion, 12 g. of 1,2-cyclononadiene, required 8.5 lbs. (0.1 mole) of hydrogen and 15 minutes. The catalyst was removed from both solutions by use of a fritted-glass filter and rinsed with 50 ml. of methanol. The combined solutions were added to 300 ml. of ethyl ether and 250 ml. of water in a large separatory funnel. The ether layer was separated and washed with 3 portions of water. The combined aqueous solution
was washed with 3 portions of ether, and the total ether extract was
dried over magnesium sulfate. The solvent was removed by rotary
evaporation, and the residue distilled under reduced pressure to yield
34.4 g. (87%) of cis-cyclononene, b.p. 92-94° (60 mm.) (lit. 85-86°
(45 mm.),73 84-86° (60 mm.),18 157-169° (740 mm.)).76 An infrared
spectrum agreed with one previously published.76 An apparatus adapted
from one described by Story and DePuy77 was also used for hydrogenation
at atmospheric pressure. The procedure was essentially identical to
the one above with the exception that small amounts had to be used
because of the smaller capacity of the reaction vessel.

4. cis-Cyclononene Oxide

A solution of 34.4 g. (0.267 mole) of cis-cyclononene in 40
ml. of ethyl acetate was placed in a 1 l. 3-neck flask equipped with a
stirrer and dropping funnel and surrounded by a cold water bath. Then
60 g. (0.29 mole) of 85% m-chloroperbenzoic acid54 in 250 ml. of ethyl
acetate was added dropwise in 0.5 hr. The resulting mixture was stirred
for 2 additional hr. and then filtered to remove the m-chlorobenzoic
acid. The filtrate was washed 5 times with dilute sodium bicarbonate
and one time with water. The aqueous washings were extracted once
with ethyl acetate, and the total ethyl acetate extract was dried over
magnesium sulfate. The solvent was removed by rotary evaporation, and
the residue distilled under reduced pressure to yield 29.3 g. (77%) of
cis-cyclononene oxide b.p. 60° (0.2 mm.). The infrared spectrum was
similar to those for cis-cyclooctene oxide16 and cis-cyclodecene oxide.17

Anal. (S) Calc. for C_{9}H_{16}O; C, 77.0%; H, 11.4%. Found: C,
76.7%, 76.3%; H, 11.41%, 11.51%.
5. trans-2-Chlorocyclononanol

Dry hydrogen chloride gas was passed into a solution of 14.0 g. (0.1 mole) of cis-cyclononene oxide in 100 ml. of carbon tetrachloride at 0° until the solution became saturated with hydrogen chloride (1 hr.). The carbon tetrachloride solution was washed with water, dilute sodium bicarbonate and water and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to yield 12.9 g. (73%) of trans-2-chlorocyclononanol, b.p. 74° (0.05 mm.).

**Anal.** (S) Calc. for C_{9}H_{17}ClO: C, 61.1%; H, 9.62%. Found: C, 61.8%; 61.3%; H, 9.90%, 9.94%.

The chlorohydrin was converted to its p-nitrobenzoate, m.p. 84-85°.

**Anal.** (S) Calc. for C_{16}H_{20}ClNO_{4}: C, 59.1%; H, 6.15%. Found: C, 59.6%, 59.5%; H, 6.62%, 6.70%.

cis-cyclononene oxide (0.6 g., 89%) was reformed by stirring 0.88 g. of chlorohydrin with 0.5 g. of sodium hydroxide in 10 ml. of water for 5 hr. at 38°.

6. trans-2-Bromocyclononanol

Anhydrous hydrogen bromide was passed through a solution of 14.0 g. (0.1 mole) of cis-cyclononene oxide in 100 ml. of carbon tetrachloride at 0° until the solution became saturated with hydrogen bromide (2.5 hr.). The carbon tetrachloride solution was washed with water, dilute sodium bicarbonate and water and then dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to yield 17.8 (80%) of trans-2-bromocyclononanol, b.p. 93° (0.35 mm.).
Anal. (G) Calc. for C\textsubscript{6}H\textsubscript{17}BrO: C, 48.8%; H, 7.68%. Found: 
C, 49.5%; H, 7.81%. This compound decomposed on standing, turning dark brown within a few days of distillation. This probably accounts for the high carbon and hydrogen values in the analysis.

The bromohydrin was converted into its p-nitrobenzoate, m.p. 81-82°.

Anal. (S) Calc. for C\textsubscript{16}H\textsubscript{20}BrNO\textsubscript{4}: C, 51.8%; H, 5.41%. Found: 
C, 52.1%, 52.0%; H, 5.86%, 5.77%.

cis-cyclononene oxide (0.68 g., 97%) was reformed by stirring 1.1 g. of bromohydrin with 0.5 g. of sodium hydroxide in 10 ml. of water at 38° for 7 hr.

K. Solvolyses of the trans-2-Halocyclonanols

1. trans-2-Bromocyclonanol

A solution of 11.2 g. (0.05 mole) of trans-2-bromocyclonanol in 300 ml. of tetrahydrofuran was stirred at room temperature with 10.2 g. (0.06 mole) of silver nitrate in 150 ml. of water for 22 hr. The mixture was then diluted with water and filtered to remove the silver bromide. The silver bromide was washed with five portions of ethyl ether which were used in turn to extract the filtrate. The ether extract was washed with water and dried over magnesium sulfate. Removal of solvent by rotary evaporation gave a residue of 7.4 g.

G.C. analysis showed the presence of 5 components. Titration\textsuperscript{68} for 1,2-diol showed that there was 13.4% 1,2-diol present in the mixture. The product mixture (except for the diol fraction) was separated on the Aerograph Autoprep instrument (carboxax column). The first fraction was identified as cyclooctanone by its 2,4-dinitrophenyl-
hydrazone, m.p. 168-170° (lit. 169-170°). A mixed melting point with an authentic sample showed no depression. The second fraction had an infrared spectrum consistent with a bicyclic ether. The third component was not isolated. Spectral and other indirect evidence indicated that it was cyclooctanecarboxaldehyde.

The fourth component was identified as cyclononanone by its 2,4-dinitrophenylhydrazone, m.p. 140-141° (lit. 140-141°). A mixed melting point with an authentic sample showed no depression. The fifth fraction was a mixture of isomeric cyclononenols. The infrared spectrum indicates unsaturated alcohol, and this component was readily converted to a mixture of three different trimethylsilyl ether derivatives with relative g.c. peak areas of 1:1:2:8:4. A portion of this mixture was converted to a p-nitrobenzoate, m.p. 85-92°. Two crystallizations from ethanol-water gave a material with melting point 94-95°.

The fourth component was identified as cyclononanone by its 2,4-dinitrophenylhydrazone, m.p. 140-141° (lit. 140-141°). A mixed melting point with an authentic sample showed no depression. The fifth fraction was a mixture of isomeric cyclononenols. The infrared spectrum indicates unsaturated alcohol, and this component was readily converted to a mixture of three different trimethylsilyl ether derivatives with relative g.c. peak areas of 1:1:2:8:4. A portion of this mixture was converted to a p-nitrobenzoate, m.p. 85-92°. Two crystallizations from ethanol-water gave a material with melting point 94-95°.

Based on the responses of analogous cyclooctyl derivatives in the g.c., the relative mole percentages of the components in the product mixture are: cyclooctanone, trace; 1,2-epoxycyclononanone, 12.1%; cyclooctanecarboxaldehyde, 5.7%; cyclononanone, 36.1%; cyclononenols, 29.1%; 1,2-cyclononanediol, 12.4%.

2. trans-2-Chlorocyclononanol

A mixture of 8.8 g. (0.05 mole) of trans-2-chlorocyclononanol,
10.2 g. (0.06 mole) of silver nitrate, 300 ml. of tetrahydrofuran and 150 ml. of water was refluxed for 28 hr. It was then diluted with 500 ml. of water and filtered to remove the silver chloride. The filtrate was extracted 4 times with ethyl ether which had been first used to wash the filter cake. The ether extract was washed once with water and dried over magnesium sulfate. Rotary evaporation of solvent left a residue of 7.5 g. which was analyzed in the same manner as the solvolysis product mixture from trans-2-bromocyclonananol. The products were similar except that no 1,2-diol was detected and the component presumed to be cyclooctanecarboxaldehyde in the bromohydrin solvolysis was not found in this mixture. There was, however, a larger amount of cyclooctanone in this mixture, indicating an aldehyde to ketone transformation in this series as well. The components of the product mixture and their relative mole percentages (based on the g.c. responses of the analogous cyclooctyl compounds) are given here: cyclooctanone, 5.3%; 1,3-epoxycyclonanone, 14.8%; cyclonanone, 31.3%; cyclonanenols, 40.4% (the g.c. trace of the TMS derivative of this last fraction showed the same three components as found in the bromohydrin solvolysis in ratio 1:1:6.2).

L. The Preparation of the trans-2-Halocyclodecanols

The trans-2-halocyclodecanols were prepared from a mixture rich in cis-cyclodecene by the following sequence of reactions. The first step illustrates the selective reduction of trans-cyclodecene by diimide.
A mixture containing 8.1% trans-cyclodecene, 12.2% cyclodecane, 73.4% cis-cyclodecene and 5.7% light ends was reduced selectively with diimide (HN = NH). A solution containing 50 g. of the hydrocarbon mixture (0.029 mole of trans-cyclodecene), 8.7 g. (0.15 mole) of 85% hydrazine hydrate, 0.20 g. of cupric sulfate and 400 ml. of ethanol was stirred at room temperature for 35 hr. with a stream of air passing through the reaction mixture (a condenser minimized loss of material in the air stream). The mixture was then diluted with 600 ml. of water and extracted 4 times with petroleum ether. The petroleum ether extract was washed with 2 M hydrochloric acid and water. The aqueous washings were extracted once with petroleum ether and the total
petroleum ether extract was dried over magnesium sulfate. Removal of the solvent by rotary evaporation left 50 g. of product mixture which, by gas chromatography, contained cyclodecane, no trans-cyclodecene and 70% cis-cyclodecene.

2. **cis-Cyclodecene Oxide**

A solution of 60 g. (0.29 mole) of 85% m-chloroperoxybenzoic acid\(^5\) in 250 ml. of ethyl acetate was added dropwise to a stirred solution of the above cyclodecane-cyclodecene mixture (70% cis-cyclodecene, 0.253 mole) in 40 ml. of ethyl acetate over a period of 35 minutes. The reaction vessel was kept in a cold water bath, and the reaction mixture was stirred for 9 hr. after the addition was complete. The mixture was washed with sodium carbonate and water and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to yield 36 g. (92%) of cis-cyclodecene oxide,\(^1\) b.p. 58-60° (0.3 mm.). An infrared spectrum agreed with one previously published.\(^1\)

3. **trans-2-Bromocyclodecanol**

Anhydrous hydrogen bromide was passed through a solution of 36 g. (0.234 mole) of cis-cyclodecene oxide in 200 ml. of carbon tetrachloride until the solution became saturated (1.5 hr.). The carbon tetrachloride solution was then washed with water, dilute sodium bicarbonate, and water and dried over magnesium sulfate. The solvent was removed by rotary evaporation, and the residue distilled under reduced pressure to yield 53 g. (96%) of trans-2-bromocyclodecanol, b.p. 107-108° (0.7 mm.).

A small portion of the bromohydrin was converted\(^5\) to its
3,5-dinitrobenzoate, m.p. 88-89°.

Anal. (S) Calc. for C₁₇H₂₁N₂O₆Br: C, 47.6%; H, 4.89%. Found: C, 47.6%, 47.6%; H, 5.20%, 5.12%.

A mixture of 1.0 g. of trans-2-bromocyclodecanol, 1.0 g. of sodium hydroxide and 15 ml. of water was stirred at room temperature for 6 hr. It was then extracted with ethyl ether and the ether extract dried over magnesium sulfate. Removal of the solvent left 0.6 g. (90%) of cis-cyclodecene oxide, pure by gas chromatography.

4. trans-2-Chlorocyclodecanol

A solution of 70 g. (0.454 mole) of cis-cyclodecene oxide in 400 ml. of carbon tetrachloride was placed in a flask immersed in an ice-bath and dry hydrogen chloride gas was passed through the solution until it became saturated (1.6 hr.). The solution was then washed with water, dilute sodium bicarbonate and water. The aqueous washings were extracted once with carbon tetrachloride and the total carbon tetrachloride solution was dried over magnesium sulfate. Rotary evaporation of the solvent gave 86 g. (92%) of crude trans-2-chlorocyclodecanol.

A p-nitrobenzoate derivative was prepared, m.p. 74-76°.

Anal. (S) Calc. for C₁₇H₂₂ClNO₄: C, 60.1%; H, 6.48%. Found: C, 60.4%, 60.3%; H, 6.77%, 6.86%.

cis-Cyclodecene oxide (1.3 g., 85%) was reformed by stirring 1.9 g. of trans-2-chlorocyclodecanol with 2.0 g. of sodium hydroxide and 20 ml. of water for 6 hr. at room temperature.

M. Solvolysis of trans-2-Bromocyclodecanol

A mixture of 14 g. (0.06 mole) of trans-2-bromocyclodecanol,
12.2 g. (0.07 mole) of silver nitrate, 300 ml. of tetrahydrofuran and 150 ml. of water was stirred under nitrogen for 24 hr. at 38°. The mixture was diluted with water, filtered, and extracted 6 times with ethyl ether that had been used to wash the filter cake. The ether extract was washed once with water and dried over magnesium sulfate. Rotary evaporation of solvent left a residue of 8.5 g. A small portion of this mixture was subjected to periodic acid oxidation and iodometric titration and this showed the presence of 9.9% of 1,2-diol in the mixture. The lighter components of the mixture were distilled to give a fraction, b.p. 60-80° (0.4 mm.) showing 3 peaks in the g.c. This fraction (weighing 6.5 g.) was separated by preparative gas chromatography into three fractions.

Fraction I (0.3 g.) had an infrared spectrum consistent with a bicyclic ether.

\[ \text{Anal. (G) Calc. for } \text{C}_{10}\text{H}_{18}O: \text{C, } 77.8\%; \text{H, } 7.66\%. \text{ Found: } \text{C, } 49.6\%; \text{H, } 7.81\%. \]

The analysis is not at all consistent with an epoxycyclodecane or any readily conceivable formula for this material.

Fraction II (1.0 g.) was identified as cyclodecanone by its 2,4-dinitrophenylhydrazone, m.p. 162-163° (lit. 165°). A mixed melting point with an authentic sample showed no depression.

Fraction III (4.1 g.) was a mixture containing two major and at least one minor component (g.c.). Infrared and n.m.r. spectra indicated cis- and trans-5-cyclodecenols as the major components. A 1.5 g. portion of this mixture was separated by column chromatography (absorbant prepared by slowly adding with shaking, 5.25 g. of silver
nitrate in 25 ml. of water to 75 g. of Davidson "thru 325" silica gel.\textsuperscript{84a} Two fractions were eluted, one with 1 l. of benzene in petroleum ether (1:1 by volume, solution previously saturated with 5% aqueous silver nitrate) and the other with 500 ml. of benzene in ethyl ether (1:1 by volume). The first fraction was mostly trans-5-cyclodecenol\textsuperscript{84a} which was identified by conversion\textsuperscript{57} into two of its derivatives: the p-nitrobenzoate, m.p. 105-107° (lit.\textsuperscript{84a} 108.4-109.4°) and the phenylurethan, m.p. 81-83° (lit.\textsuperscript{84a} 80.8-81.6°). The second fraction was mainly trans-5-cyclodecenol\textsuperscript{84a} which was identified by conversion\textsuperscript{57} into two of its derivatives; the p-nitrobenzoate, m.p. 150-152° (lit.\textsuperscript{84a} 154.5-155°) and the phenylurethan, m.p. 108-110° (lit.\textsuperscript{84a} 111.0-111.7°).

The diol fraction (2 g.) was crystallized from benzene. The solid product (0.9 g.) had m.p. 116.5-117.5° and the 1,2-diol test\textsuperscript{57} was negative.

\textbf{Anal. (S)} Calc. for C\textsubscript{10}H\textsubscript{20}O\textsubscript{2}: C, 70.0%; H, 11.62%. Found: C, 70.0%, 70.0%; H, 12.12%, 11.95%.

A bis-p-nitrobenzoate was prepared\textsuperscript{57} from this material, m.p. 152-153°.

\textbf{Anal. (S)} Calc. for C\textsubscript{24}H\textsubscript{26}N\textsubscript{2}O\textsubscript{6}: C, 61.3%, H, 5.53%. Found: C, 61.8%, 61.6%; H, 5.89%, 5.95%.

The only cyclodecanediols that are known are the isomeric 1,2- and 1,6-cyclodecanediols.\textsuperscript{83} The melting point of the diol isolated from the solvolysis mixture and the melting point of its p-nitrobenzoate derivative are both about 30° lower than those of either of the isomeric 1,6-diols.\textsuperscript{83} Thus it would seem that the diol from bromo-
hydrin solvolysis is either the 1,3-, 1,4-, or the 1,5-cyclodecanediol (there is also the possibility that there is a mixture of more than one diol, but the probability that both the diol mixture and the \( p \)-nitrobenzoate mixture would both have sharp melting points is indeed small). The filtrate from the original diol crystallization was evaporated to give a viscous liquid (1.1 g.) which gave a positive 1,2-diol test. Attempts to crystallize this material from various solvents and by vacuum sublimation all failed.

The mole percentages (assuming similar g.c. responses to the analagous cyclooctyl compounds) of the components of the solvolysis mixture are: 1,\( X \)-epoxycyclodecane, 4.2\%; cyclodecanone, 18.5\%; cyclodecenols, 59.1\%; 1,2-cyclodecanediol, 9.9\%; 1,\( X \)-cyclodecanediol, 8.1\%.
CHAPTER IV

SUMMARY

Acid-catalyzed rearrangements of medium ring glycols are highly similar to those of the corresponding epoxides and give extensive transannular rearrangement, but nitrous acid deamination of the corresponding amino alcohols leads almost exclusively to products formed by 1,2-shifts with very little transannular rearrangement. This great difference in product composition leads to the belief that there is a different mechanism operating in the amino alcohol deaminations than in glycol or epoxide rearrangements.

The present work is a continuation of the above studies and is an evaluation of the occurrence of dual mechanisms of related 2-hydroxy-cycloalkyl derivatives and an attempt to obtain a detailed mechanistic picture of these reactions.

There can be no doubt from the data in this work that the medium ring 2-halocycloalkanols react in solvolysis reactions by a combination of two mechanisms. The exact description of these two mechanisms is still in doubt but at this moment the available evidence seems to point in the direction of mechanism II; that is, (a) direct formation of a hydrogen-bridged carbonium ion (such as 17) which gives mostly or exclusively transannular products, and (b) formation of a 2-hydroxycycloalkyl cation (14) in which combination with solvent and 1,2-shifts rather than transannular shifts lead to products. The product distribution from cis- and trans-2-bromocyclooctanol strongly support this idea, and all of the other data, at the very least, allow
In order for the complete picture of these solvolysis reactions to be known, there must be a considerable amount of additional work. It is hoped that those who come after me and perform this work will enjoy and learn from it as much as I have.
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33. cis-Cyclooctene oxide is rearranged under the solvolysis conditions but so slowly that it cannot figure in the halohydrin reactions.
34. For a list of pertinent references, see footnote 6 in ref. 30.
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47Grateful acknowledgement is made of the helpful cooperation of Professor A. C. Cope, who lent us spectra of trans-2-vinylcyclohexanol, 1,4-epoxycyclooctane and 1,5-epoxycyclooctane for comparison.

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50 Grateful acknowledgement is made of generous gifts of cis-
cyclooctene, cyclooctanol and 2-cyclooctenol from the Columbian Carbon Co., Lake Charles, La.

51 This work.


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supplied.

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Acknowledgment is made to Mr. G. Franzen at these laboratories for providing a sample of this compound.


This procedure is supposed to reduce any alkyl azide formed to the primary amine.


J. G. Traynham and M. T. Yang, unpublished work.

This mixture was chosen to approximate the halohydrin solvolysis conditions; silver nitrate, silver chloride, and nitric acid in refluxing aqueous tetrahydrofuran.


Ref. 70, p. 34.


It was similar to those for 1,4- and 1,5-epoxycyclo-octane.

Mixture analysis generously provided by Dr. J. R. Olechowski, Columbian Carbon Co., Lake Charles, La.


This separation as well as the infrared and n.m.r. spectra of fraction III were generously provided by the analytical group working under Dr. William Hamilton, Continental Oil Co., Ponca City, Okla.

84 (a) H. L. Goering, W. D. Closson and A. C. Olson, *J. Am. Chem. Soc.*, 83, 3507 (1961): (b) I also wish to thank Professor H. L. Goering for lending spectra of both cis-5-cyclodecenol and trans-5-cyclodecenol.
SELECTED BIBLIOGRAPHY


VITA

John Schneller, III was born in New Orleans, Louisiana, on September 9, 1941. He attended public school in New Orleans, Louisiana, and graduated from Warren Easton High School in June, 1958. He entered Louisiana State University in New Orleans the following September and was awarded the Bachelor of Science degree from that institution in June, 1962.

He entered Louisiana State University that same month. He was employed by the University as a teaching and research assistant, being supported partly by funds from a National Science Foundation grant (G 14461). He was later the recipient of two fellowships, a Cities Service Honor Fellowship for 1963-64 and a National Science Foundation Cooperative Graduate Fellowship for 1964-65. In June, 1964 he was married to Sylvia Mary Johns. He is a member of the American Chemical Society, Phi Lambda Upsilon Honorary Chemical Fraternity, and the Society of the Sigma Xi. He has the distinction of being the first graduate of Louisiana State University in New Orleans to be awarded the degree of Doctor of Philosophy.
EXAMINATION AND THESIS REPORT

Candidate: John Schneller, III

Major Field: Chemistry (Organic chemistry)

Title of Thesis: Solvolyses of Medium Ring 2-Halocycloalkanols

Approved:

[Signatures]

Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

[Signatures]

Date of Examination:

May 7, 1965