Study of Rearrangements in Medium Ring Organometallic Compounds.

Richard L. Frye

Louisiana State University and Agricultural & Mechanical College

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ORGANOMETALLIC COMPOUNDS.

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and Mechanical College, Ph.D., 1971
Chemistry, organic

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STUDY OF REARRANGEMENTS IN
MEDIUM RING ORGANOMETALLIC COMPOUNDS

A Dissertation

Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of

Doctor of Philosophy

in

The Department of Chemistry

by

Richard L. Frye
B.S., University of Tennessee, 1962
M.S., University of Tennessee, 1965

December, 1971
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To my wife, Glynis
ACKNOWLEDGEMENT

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The sincere concern and help of Sister Alice Theine smoothed over many rough places in the road during this last year.

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGEMENT</td>
<td>ii</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>v</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>vi</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>vii</td>
</tr>
<tr>
<td>I.  INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>II. RESULTS AND DISCUSSION OF RESULTS</td>
<td>10</td>
</tr>
<tr>
<td>III. CONCLUSIONS</td>
<td>35</td>
</tr>
<tr>
<td>IV. EXPERIMENTERAL</td>
<td>37</td>
</tr>
<tr>
<td>A. Preparation of α-Deuteriocycloalkyl Halides</td>
<td>38</td>
</tr>
<tr>
<td>1(a) Preparation of α-Deuteriocyclooctane-carboxylic Acid</td>
<td>38</td>
</tr>
<tr>
<td>1(b) Preparation of α-Deuteriocyclooctyl Chloride</td>
<td>38</td>
</tr>
<tr>
<td>2(a) Preparation of Cyclohexanol-1-d</td>
<td>39</td>
</tr>
<tr>
<td>2(b) Preparation of α-Deuteriocyclohexyl Chloride</td>
<td>40</td>
</tr>
<tr>
<td>2(c) Preparation of α-Deuteriocyclohexyl Bromide</td>
<td>41</td>
</tr>
<tr>
<td>B. Preparation and Reactions of α-Deuteriocyclooctylmagnesium Halides</td>
<td>42</td>
</tr>
<tr>
<td>1(a) Preparation of α-Deuteriocycloctyl-magnesium Chloride</td>
<td>42</td>
</tr>
<tr>
<td>1(b) Exchange of α-Deuteriocycloctylmagnesium Chloride with Mercuric Bromide</td>
<td>43</td>
</tr>
<tr>
<td>1(c) Oxygenation of α-Deuteriocycloctylmagnesium Chloride</td>
<td>44</td>
</tr>
<tr>
<td>2(a) Preparation of α-Deuteriocyclohexyl-magnesium Bromide</td>
<td>44</td>
</tr>
<tr>
<td>2(b) Exchange of α-Deuteriocyclohexylmagnesium Bromide with Mercuric Bromide</td>
<td>44</td>
</tr>
<tr>
<td>3(a) Preparation of α-Deuteriocyclohexyl-magnesium Chloride</td>
<td>45</td>
</tr>
</tbody>
</table>
3(b) Exchange of α-Deuteriocyclohexyl-
magnesium Chloride with Mercuric Bromide...... 46

C. Preparation and Reactions of α-Deuteriocycloalkyl-
alkali Metal Compounds........................................... 47

1(a) Preparation of α-Deuteriocyclooctyllithium
from the Chloride...................................................... 47
1(b) Preparation of α-Deuteriocyclooctylmercury.... 48
1(c) Preparation of α-Deuteriocyclooctyllithium
from the Dialkylmercury.......................................... 49
1(d) Preparation of α-Deuteriocyclooctylsodium.... 50
2(a) Preparation of α-Deuteriocyclohexylmercury.... 51
2(b) Preparation of α-Deuteriocyclohexylsodium.... 51

D. Reactions of Cyclooctyl Chloride with Organo-
lithium Compounds.................................................. 52
1(a)-(i) Reaction with Cyclooctyllithium................. 52
2(a) Reaction with sec-Butyllithium in Ethyl
Ether Solvent............................................................. 57
2(b) Reaction with sec-Butyllithium Complexed
with TMEDA............................................................... 57
3 Reaction with Butyllithium Complexed with
TMEDA........................................................................... 58

E. Miscellaneous Control Experiments...................... 58
1. Preparation of Cyclooctylmagnesium Chloride..... 58
2. Preparation of Cyclooctylmagnesium Bromide..... 59
3(a)-(d) Preparation of Cyclooctyllithium by
Exchange with Dicyclooctylmercury....................... 60

V. SUMMARY.............................................................................. 62

REFERENCES............................................................................. 64

SELECTED BIBLIOGRAPHY......................................................... 68

APPENDIX I.................................................................................. 69

APPENDIX II................................................................................. 75

VITA.............................................................................................. 79
## LIST OF TABLES

| Table I. Types of Transannular Interactions.......................... | 2 |
| Table II. Hydrocarbon Products from Cycloalkylmetal Compounds...... | 16 |
| Table III. Analysis of Neutral Fraction of Reactions 1.(a)-(i)..... | 53 |
LIST OF FIGURES

1. Rearrangement in α-Deuteriocyclohexylsodium by Single 1,2 Shift .............................................. 22
2. Rearrangement in α-Deuteriocyclooctylsodium by 100% 1,2 Shift ...................................................... 22
3. Carbanionic versus Radical Pathways for Olefin Formation in Exchange Reactions ....................... 24
4. Reaction of Organolithium Compounds with Cyclooctyl Chloride ................................................. 31
ABSTRACT

Transannular reactions occur in medium ring (8-11 carbon atoms) carbonium ion, radical, and carbene processes. By use of several deuterium labelled cyclooctylmetal compounds, the possibility of transannular rearrangement or elimination resulting from a carbanionic intermediate has been investigated. Derivatives were prepared from α-deuteriocyclooctyl chloride through the alkylmagnesium chloride and alkyllithium without loss of deuterium from the alpha position. Reaction of α-deuteriocyclooctyllithium in pentane results in formation of cyclooctene-1-d, but α-deuteriocyclooctylsodium in pentane solvent gives cyclooctene-d, in which the deuterium has been scrambled from the alpha position. Thus, increasing ionic character of the carbon metal bond in the series Mg < Li < Na finally leads to carbanionic rearrangement in the case of cyclooctylsodium. A smaller amount of rearrangement was found in the case of cyclohexylsodium. Comparison of the amounts of rearrangement found in six- and eight-membered rings shows the former is best explained by 1,2 proton shifts and the latter by transannular proton shifts. Transannular elimination from cyclooctylmetal compounds was not found.

Organolithium compounds react with cyclooctyl chloride to form bicyclo[3.3.0]octane by α-elimination of the halide. The ratio of bicyclooctane:cyclooctene formation was found to be a measure of the tendency of the organolithium compound toward carbanionic and radical reaction. The ratio of bicyclo[3.3.0]octane:cyclooctene
decreases from 0.12 to 0.03 when cyclooctyllithium is substituted for sec-butyllithium. The decrease in relative amount of bicyclooctane formed indicates that cyclooctyllithium has greater tendency for radical reaction than does sec-butyllithium.
I. INTRODUCTION

Organic compounds of rings of 8-11 carbon atoms (medium-ring compounds) have across the ring (transannular) interactions which can lead to transannular reactions. Products from these reactions have a substituent or functional group remote from the original reaction site. Transannular reactions were first discovered in medium ring reactive intermediates of carbonium ion systems and have since been found for radical and carbene intermediates. This Dissertation extends the knowledge of medium ring reactive intermediates to include carbanionic ones. Transannular rearrangement apparently occurs in reactive carbanion or carbanoid intermediates formed from saturated, unsubstituted medium ring organometallic compounds. In the course of this investigation, it became apparent that reaction of cyclooctyl halides with organolithium compounds also provided a means of detecting carbanionic intermediates formed from the carbon-metal bond.

The types of transannular reactions which may occur with unsubstituted, medium-ring compounds vary with the type of intermediate produced, as illustrated in Table I. With unsubstituted carbonium ion intermediates, the occurrence of transannular hydride shifts and elimination depends upon the mode of formation of the intermediate. For example, transannular hydride shifts but not transannular elimination were detected in chlorinolysis of deuterium-labelled cycloalkyl sulenate esters; both processes were found to occur from carbonium ions produced by the anodic oxidation of cycloalkanecarboxylic acids.

The formation of a carbene intermediate results in transannular carbon-hydrogen insertion reactions to form bicyclic products.
### TABLE I: Types of Transannular Interactions

<table>
<thead>
<tr>
<th>Type Intermediate</th>
<th>Transannular Interaction</th>
<th>Resultant Product or Intermediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonium Ion</td>
<td>1,3 Hydride Shift</td>
<td><img src="image1" alt="Carbonium Ion" /></td>
</tr>
<tr>
<td></td>
<td>1,5 Hydride Shift</td>
<td><img src="image2" alt="1,5 Hydride Shift" /></td>
</tr>
<tr>
<td></td>
<td>1,3 Elimination</td>
<td><img src="image3" alt="1,3 Elimination" /></td>
</tr>
<tr>
<td></td>
<td>1,5 Elimination</td>
<td><img src="image4" alt="1,5 Elimination" /></td>
</tr>
<tr>
<td>Carbene</td>
<td>1,3 C-H Insertion</td>
<td><img src="image5" alt="1,3 C-H Insertion" /></td>
</tr>
<tr>
<td></td>
<td>1,5 C-H Insertion</td>
<td><img src="image6" alt="1,5 C-H Insertion" /></td>
</tr>
<tr>
<td>Free Radical</td>
<td>None</td>
<td><img src="image7" alt="None" /></td>
</tr>
<tr>
<td>Destabilized Free Radical</td>
<td>1,5 Hydrogen Atom Shift</td>
<td><img src="image8" alt="1,5 Hydrogen Atom Shift" /></td>
</tr>
</tbody>
</table>

Z = Destabilizing Group
The base catalyzed decomposition of cyclooctanone p-toluenesulfonyl-hydrazone results in 1,2-, 1,3- and 1,5 C-H insertion to form cyclooctene, bicyclo[5.1.0]octane and bicyclo[3.3.0]octane, respectively. The proportions of products depend upon the base and solvent used as shown below.

<table>
<thead>
<tr>
<th>Base and Solvent</th>
<th>cis-Cyclo- [3.3.0]-Bicyclo-[5.1.0]-1-Methyl-cyclo-octene</th>
<th>Products, %</th>
<th>heptene</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na in HOCH₂CH₂OH</td>
<td>83.3</td>
<td>6.4</td>
<td>10.3</td>
<td>0</td>
</tr>
<tr>
<td>NaOCH₃ in Diethyl Carbitol</td>
<td>43.3</td>
<td>50</td>
<td>6.5</td>
<td>0</td>
</tr>
</tbody>
</table>

Transannular carbon-hydrogen insertion reactions also result from treatment of medium-ring epoxides with phenyllithium or lithium di-ethylamide. A similar transannular insertion reaction resulting from treatment of 2,3-epoxybicyclo[2.2.1]heptane with lithium diethylamide was attributed to carbonoid formation.

Although transannular hydrogen atom shift to a radical center adjacent to a destabilizing group is a known process, transannular shift or elimination to form bicyclic compounds has not been found in reactions of unsubstituted radicals from medium ring compounds. Reactions investigated in the 8-membered system include the photolysis and pyrolysis of dicyclooctylmercury compounds and pyrolysis of t-butyl α-deuteriocyclooctaneperoxycarboxylate. The Hunsdiecker reaction of α-deuteriocyclooctanecarboxylic acid results in bromide formation without loss of deuterium at the alpha position. Other examples of reactions proceeding through radical intermediates without transannular interaction have been found in the present study.
Rearrangement of a metalalkyl was discovered by Schlenk\textsuperscript{10a} and Ziegler\textsuperscript{10b} in the reaction of sodium with 1,3,3-triphenylindene shown below.*

\[
\begin{array}{c}
\text{Ph} & \text{Ph} & \text{Ph} \\
\text{H} & \text{Na} & \rightarrow \\
\text{Ph} & \text{Ph} & \text{Ph} \\
\text{Ph} & \text{Ph} & \text{Na}
\end{array}
\]

Another example of carbanoid rearrangement was discovered independently by Zimmerman\textsuperscript{11a} and by Grovenstein\textsuperscript{11b} in the study of 2,2,2-triarylethylmetal compounds. The effect of the metal upon the tendency for this isomerization was found to be $K \sim Na > Li > Mg, Hg$

\[
R_3CCH_2-M \quad \rightarrow \quad M \quad R_2C-CH_2R
\]

indicating that weakening of the carbon-metal bond favors isomerization. The substitution of different groups in the 2-position gave a migratory order of benzyl $>$ phenyl $>$ p-tolyl $>$ methyl for sodium- and potassiumalkyls.\textsuperscript{12a,b} The same order was initially found for lithium-alkyl; however, later work by Grovenstein\textsuperscript{13} showed that different mechanisms operate in the case of the benzyl and phenyl moieties. The benzyl group in 2,2,3-triphenylpropyllithium undergoes 1,2-migration by an elimination-readdition pathway involving formation of benzyl-lithium and 2,2-diphenylethene or possibly by a radical-radical anion

*Throughout this Dissertation, the symbol $\quad \rightarrow \quad$ means "rearrangement".
pathway. The migration of the phenyl group in 2,2,2-triphenylethyl-
lithium was shown to follow an intramolecular pathway. Evidence was
presented by Grovenstein\textsuperscript{14} for the probable formation of a bridged
carbonionic species \( \ddagger \), as either an intermediate or a transition
state, by nucleophilic addition to the migrating phenyl group. How­
ever, the possibility of rearrangement by the corresponding radical
intermediate \( \mathcal{J} \) could not be excluded.

\[
\begin{align*}
\text{Ph}_2C-CH_2 & \quad \text{Ph}_2C-CH_2 \\
\ddagger & \quad \mathcal{J}
\end{align*}
\]

The norbornene system provides another example of carbonionic
isomerization by electron acceptance at an unsaturated center. For
lithium\textsuperscript{15,16} and sodium\textsuperscript{17} derivatives, anions \( \ddagger \) and \( \ddagger \) were found to be
in equilibrium with each other. Presumably, the electron-withdrawing

\[
\begin{align*}
\ddagger & \quad \ddagger \quad \ddagger
\end{align*}
\]

(anion stabilizing) effect of the cyclopropyl ring (\( \ddagger \)) may provide a
driving force for the rearrangement.
The more ionic character of sodiumalkyl causes a fragmentation of 8 to give 10, the precursor of 3-vinylcyclopentene and 4-vinylcyclopentene, as shown below.\(^{18}\) Fragmentation did not occur in the absence of a double bond or a potential double bond (the cyclopropyl ring of 8). Norbornylsodium formed from the chloride did not undergo fragmentation but produced only norbornane, norbornene, and nortricyclene. The last compound probably resulted from a carbene intermediate formed by α-elimination of the chloride rather than 2,6-elimination by the carbanion. The possibility of a radical pathway for cleavage was excluded on the basis that 5-norbornen-2-yl and nortricyclyl radicals have not undergone cleavage reactions similar to those found for the organosodium compounds.

Unlike the sodium compounds, butyl- and pentylpotassium compounds undergo fragmentation reactions without the necessity of a double bond.\(^{19}\) Besides facile fragmentation, the excessively high charge density at carbon leads to hydride elimination (unusual at room temperature for a primary alkylsodium or potassium compound) and metation of the hydrocarbon solvent to give an array of organopotassium products. Intramolecular proton shifts in concert with (see below) or prior to fragmentation may account for fragments containing
an odd number of carbons being produced from starting materials containing only even numbers of carbons in the molecules, e.g., butyl-potassium in hexane. However, products containing an odd number of

1.5 Proton Shift

\[ \text{H}_3\text{C}-\text{CH}_2 \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{K}^+ \rightarrow \text{CH}_3\text{CH}=	ext{CH}_2 + \text{CH}_3\text{CH}_2\text{CH}_2^-\text{K}^+ \]

1.2 Proton Shift

\[ \text{CH}_3\text{CH}_2\text{CH}_2^-\text{CH}-\text{CH}_2 \quad \text{K}^+ \]

carbon atoms could also be explained by intermolecular exchange reactions leading to secondary carbanions.

A review of these cases of carbanionic rearrangement in hydrocarbons indicates that only the cases of bond rearrangement in norbornyl systems can be definitely established as proceeding by a carbanionic pathway. The proton rearrangements suggested in the alkyl-potassium system are only tentative. In the cases of rearrangement by a migrating group studied by Zimmerman and Grovenstein, none of the examples could exclude the possibility of a radical pathway although a carbanionic pathway does seem reasonable for the more electropositive sodium and potassium compounds. The possibility of an elimination-readdition mechanism was excluded only in the case of 2,2,2-triphenyl-ethyl lithium, but the possibility of phenyl migration by a radical process still remains.
The purpose of this work was to investigate the possibility of a transannular hydrogen shift or other transannular process in a carbanion intermediate. Since transannular processes have not been found in unsubstituted cyclooctyl radicals, the occurrence of these processes in organometallic compounds would clearly indicate the presence of a carbanionic intermediate. To accomplish this goal, several deuterium-labelled cyclooctylmetallic compounds were prepared and investigated to determine transannular rearrangement or elimination.

In the course of this study, another method was found to distinguish between carbanionic and free radical behavior in the reaction of cyclooctyl halides with organolithium reagents. The reaction resulted in formation of bicyclo[3.3.0]octane, probably by a C-H insertion reaction of the cyclic carbene intermediate. Eastham investigated the mechanism of reaction of alkyl halides with organolithium compounds. The reaction of 2-tritiobutyllithium with chlorocyclohexane, resulting in the incorporation of tritium into the cyclohexane product, was initially explained by a concerted mechanism involving a quasi-ring complex. The possibility of carbene formation from the alkyl halide was also suggested. However, further work indicated the reaction proceeded by charge transfer from the lithium reagent to the alkyl halide to form a radical anion which could then decompose to give an alkyl radical. Normal disproportionation and coupling products could then be formed from the resultant radicals. The charge transfer mechanism was given strong support by electron spin resonance (esr) spectral identification of radical anions.
generated by organolithium reagents.\textsuperscript{22} Direct esr techniques detected the organic radicals generated by reaction of organolithium compounds with alkyl iodides.\textsuperscript{23} Chemically induced dynamic nuclear polarization (CIDNP) has also been used to establish the intermediacy of radicals in the reaction of organolithium compounds with alkyl halides.\textsuperscript{24,25}

The presence of a radical pathway in the reaction has been firmly established. However, the possibility of a competing carbanionic process functioning by alpha and beta elimination of the halide still exists. The detection of such a process could be accomplished by the identification of products from carbene intermediates, but previous attempts by Kirmse to generate such products from the action of organolithium compounds on alkyl halides were unsuccessful.\textsuperscript{26} The detection of carbene products from cyclooctyl halides provided a method of comparing the tendency of organolithium compounds for carbanionic reaction and will be discussed in the following section.
II. RESULTS AND DISCUSSION OF RESULTS

The work of Traynham and Green on the generation of deuterium-labelled, medium-ring cycloalkyl radicals indicates that cyclooctyl radical intermediates do not undergo transannular rearrangement or elimination. In contrast, the generation of correspondingly-labelled carbonium ion intermediates revealed that rearrangement occurs readily with these species.\(^5,6\) The present work dealt with the possibility of rearrangement in medium ring carbanionic intermediates. To detect the occurrence of rearrangement, several alpha-deuterated cyclooctyl-metallic compounds were prepared and reacted to provide suitable derivatives whose alpha deuteration could be measured by proton nuclear magnetic resonance (nmr) methods as described in Appendix I. When loss of deuterium from the alpha position occurred, the compounds were examined by mass spectrometer (ms) to detect any loss of deuterium from the molecule. Hydrocarbon products resulting from the organo-metallic species were also examined by gas chromatography (gc) for the presence of bicyclo[5.1.0]octane and bicyclo[3.3.0]octane to check for the occurrence of transannular elimination in the intermediate.

Rearrangements of organometallic compounds can be interpreted by means of radical or carbanionic intermediates as exemplified\(^13,14\) by the discussion in the Introduction of 1,2 migration of phenyl in 2,2,2-triphenylethylithium. Cyclooctyl radicals generated from peroxo esters\(^9\) or cyclooctylmercury compounds\(^6,8\) do not give rearranged products. An additional example of the stability of the cyclooctyl radical...
to rearrangement was provided by halodecarboxylation of α-deuteriocyclooctanecarboxylic acid by use of lead tetraacetate in combination with lithium chloride. Kochi\textsuperscript{27} conducted the halodecarboxylation of a number of carboxylic acids and proposed a mechanism involving alkyl radicals as intermediates. Evidence for participation of radical intermediates was provided by reaction of 3,3-dimethylbutanoic acid or cyclobutanecarboxylic acid which results in formation of only the corresponding unrearranged neopentyl or cyclobutyl chloride. The reaction also was found to be strongly inhibited by the presence of oxygen. In accord with a radical pathway, halodecarboxylation of α-deuteriocyclooctanecarboxylic acid results in the formation of the chloride without loss of deuterium from the alpha position.

The first medium ring organometallic system chosen for study was the Grignard system. Previous work\textsuperscript{28} had shown that the cyclopropylmethyl Grignard and allylmethyl Grignard reagents undergo facile interconversion at room temperature, resulting in exchange in position of the alpha and beta carbons of the allylmethyl Grignard reagent as shown below.

\[
\text{CH}_2=\text{CH}-\text{CH}_2-\text{CH}_2\text{MgX} \xrightarrow{\text{H}} \text{CH}_2=\text{CH}-\text{CH}_2-\text{CH}_2\text{MgX} \]

The reaction may proceed by a radical pathway through intermediate 1,\textsuperscript{28} or by a carbanionic pathway through intermediate 2.\textsuperscript{14,28}
Radical intermediates similar to \( 1 \) are known to rearrange to the open chain form,\(^{30} \) whereas reactions proceeding through the anionic species, \( 2 \), do not give rearrangement products.\(^{28,29} \) Therefore, a radical pathway seems more reasonable overall than an anionic one for rearrangement of the Grignard reagent.

The facile rearrangement of the cyclopropylmethyl radical by bond isomerization contrasts sharply with the stability to rearrangement by hydrogen atom shift found in the cyclooctyl radical. The preparation of the \( \alpha \)-labeled cyclooctyl Grignard reagent and measurement of any scrambling of deuterium due to intramolecular proton shifts provides a means of distinguishing between radical and anionic rearrangement. \( \alpha \)-Deuteriocyclooctylmagnesium chloride in ethyl ether was shown to be stable to rearrangement by preparation of the alcohol and mercuric bromide derivatives; nmr analysis of these derivatives showed no loss of deuterium from the \( \alpha \) position. Of course, the stability of the organomercury compound to rearrangement would be expected from the stability of its Grignard precursor.

Although the non-rearrangement of the medium ring Grignard reagent may have been caused by its having an essentially radical character, it was recognized that the organometallic reagent may not have been sufficiently basic to effect the hydrogen abstraction.
necessary for rearrangement. The lithium reagent seemed a more likely species to undergo rearrangement on the basis that 2,2-diphenylpropyl-lithium, $_3$, undergoes phenyl migration to provide 2-methyl-2,3-diphenylpropanoic acid upon carbonation, whereas the corresponding Grignard and mercury compounds do not rearrange.$^{31}$ Besides undergoing phenyl migration, $_3$ gives $\alpha$-(2,2-dimethylbenzyl)-benzoic acid, $\frac{4}{5}$, as a minor product, possibly by the intramolecular hydrogen abstraction illustrated below.

\[
\begin{align*}
\text{Ph} & \quad \text{CH}_3 \\
b & \quad \text{CH}_2 \\
\text{H} & \quad \text{Li}^+ \\
\text{Ph} & \quad \text{CH}_3 \\
\text{Ph} & \quad \text{CH}_3 \\
\text{Ph} & \quad \text{CH}_3 \\
\text{Ph} & \quad \text{CH}_3 \\
\text{Ph} & \quad \text{CH}_3 \\
\end{align*}
\]

The preparation of cyclooctyllithium revealed the compound to be quite reactive toward ethyl ether, even at temperatures below $-30^\circ$; in contrast, cyclohexyllithium is stable in the presence of ethyl ether below $-10^\circ$. The formation of cyclooctyllithium in ethyl ether at $-35^\circ$, followed by reaction with dry ice, resulted in the formation of a mixture of cyclooctanecarboxylic acid and 3-cyclooctyl-propionic acid. The propionic acid derivative was apparently formed by reaction of the lithium reagent with ether to yield ethylene,$^{33}$ which added to a second molecule of cyclooctyllithium to give 2-cyclooctylethyllithium. In THF at $-15^\circ$, a 20% yield of 3-cyclooctyl-propionic acid was obtained with apparently little, if any, formation
of cyclooctanecarboxylic acid. However, at \(-78^\circ\) the acid product iso-
lated was found to be cyclooctanecarboxylic acid, the lower tempera-
ture either preventing reaction of the lithium reagent with THF or
stopping the addition step to ethylene.

The formation of cyclooctanecarboxylic acid at \(-78^\circ\) provided
a derivative by which rearrangement of cyclooctyllithium could be de-
tected. Thus, \(\alpha\)-deuteriocyclooctyllithium was prepared from the
deuterated chloride by reaction with lithium wire in THF at \(-78^\circ\).
Unrearranged \(\alpha\)-deuteriocyclooctanecarboxylic acid was recovered in 5% yield whether the reaction was run for 18 or 48 hours. Gc analysis
of the hydrocarbon products and recovered chloride (shown below) re-
vealed cyclooctyllithium to be quite reactive despite its lack of

<table>
<thead>
<tr>
<th>Reaction Time, hours</th>
<th>18</th>
<th>48</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mole Ratio</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclooctene</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Cyclooctane</td>
<td>11.2</td>
<td>4.4</td>
</tr>
<tr>
<td>Cyclooctyl chloride</td>
<td>24.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Bicyclo[3.3.0]octane</td>
<td>0.02</td>
<td>0.04</td>
</tr>
</tbody>
</table>

rearrangement. The yield of acid from the reaction did not improve,
although the ratio of chloride to hydrocarbon products after 48 hours
was much less. Once formed, the cyclooctyllithium apparently reacted
with THF to yield cyclooctane or with starting chloride to give cyclo-
octene and cyclooctane. Also, unimolecular decomposition to cyclo-
octene and lithium hydride may have occurred. The formation of
bicyclo[3.3.0]octane, which resulted from reaction of the lithium re-
agent with the starting chloride rather than from transannular elimina-
tion, will be discussed later.
Since side reactions with ether solvent and starting chloride are troublesome in the preparation of cyclooctyllithium, these side reactions were eliminated by preparation of lithium reagent from the dialkylmercury compound. Sodium stannite reduction of α-deuterio-cyclooctylmercuric bromide was used to prepare α-deuteriocyclooctylmercury. α-Deuteriocyclooctyllithium, formed by exchange of the dialkylmercury compound with lithium in pentane solvent, reacted to give cyclooctene-1-d and cyclooctane-d in 78% and 7% yields, respectively (see Table II, No. 1). Carbonation of the reaction mixture did not yield any cyclooctanecarboxylic acid. Analysis by nmr showed retention of deuterium at the 1-position for cyclooctene-1-d, and the nmr analysis was supported by ms which indicated a corresponding amount of deuterium in the molecule. The deuteration at the one position was also indicated by the line shape of the olefinic nmr absorption of cyclooctene-1-d, which differed considerably from that for cyclooctene because of coupling between vinyl hydrogen and deuterium.

Thus, as found previously in THF solvent, α-deuteriocyclooctyllithium does not undergo rearrangement. Also, formation of the
<table>
<thead>
<tr>
<th>Reaction Number</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<td>Ring Size</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>6</td>
</tr>
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<table>
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</thead>
<tbody>
<tr>
<td>Lithium</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complexing Agent</th>
<th></th>
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<tr>
<td>TMEDA</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
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<table>
<thead>
<tr>
<th>Products, % Yield</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycloalkene</td>
<td>78</td>
<td>45</td>
<td>55</td>
<td>38</td>
</tr>
<tr>
<td>Cycloalkane</td>
<td>7</td>
<td>37</td>
<td>39</td>
<td>22</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Deuterium, Number</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycloalkane</td>
<td>0.61*</td>
<td>0.70</td>
<td>0.65</td>
<td>0.77</td>
</tr>
<tr>
<td>Molecular</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cycloalkene</td>
<td>0.77</td>
<td>0.78</td>
<td>0.70</td>
<td>0.82</td>
</tr>
<tr>
<td>Vinyl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Found (±0.1)</td>
<td>0.8</td>
<td>0.8</td>
<td>0.1</td>
<td>0.60</td>
</tr>
<tr>
<td>No Rearrangement (±0.05)</td>
<td>0.70</td>
<td>0.70</td>
<td>0.70</td>
<td>0.88</td>
</tr>
<tr>
<td>Scrambled</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.18</td>
</tr>
<tr>
<td>Scrambling, %, Z**</td>
<td>0%</td>
<td>0%</td>
<td>100</td>
<td>40</td>
</tr>
</tbody>
</table>

*Value low because small amount present made measurement difficult.

**Calculation explained in Appendix II.
dialkylmercury compound from the alkylmercuric bromide proceeds with retention of deuterium at the alpha position.

Because the stability of α-deuteriocyclooctyllithium to rearrangement in pentane might have been due to the low ionizing power of solvent, the exchange reaction was repeated in the presence of N,N,N′,N′-tetramethylethylenediamine (TMEDA) with the results shown in Table II, No. 2. The complexation of TMEDA with the organolithium compound should have increased the amount of ionic reaction;34 however, the lithium reagent was again found not to have undergone rearrangement by analysis of cyclooctene product. The increase in yield of cyclooctane may have been due to the increased basicity of the lithium reagent or the presence of TMEDA, a more active hydrogen donor than pentane. The stability of cyclooctyllithium to rearrangement even in the presence of strongly ionizing complexing agents, e.g., THF or TMEDA, indicated that a more electropositive metal would be necessary to effect carbanionic rearrangement.

The carbanionic rearrangement of 2,2,2-triphenylethylmetal compounds proceeds approximately equally with either potassium or sodium compounds, both of which rearrange more readily than the lithium compound.12 It was decided to prepare cyclooctylsodium rather than potassium since alkylpotassium compounds are known to fragment by beta-cleavage and to metalate alkane solvents.35 Cyclooctylsodium was prepared by exchange of α-deuteriocyclooctylmercury with sodium in pentane solvent. Carbonation of the reaction mixture over dry ice did not yield any cyclooctanecarboxylic acid. Gc analysis (Table I, No. 3)
of the hydrocarbon fraction showed cyclooctane and cyclooctene in yields of 55% and 39%, respectively. Nmr analysis of the mixture revealed that the average olefinic moiety contained only 0.1 atom of deuterium per molecule while ms indicated that no significant loss of deuterium had occurred from the molecule. Thus, 100% of deuterium scrambling occurred with the cyclooctylsodium compound. Corresponding formation of α-deuteriocyclohexylsodium from the deuterated mercury compound resulted in a significantly lesser amount (40%) of scrambling as shown in Table II, No. 4. Several possible paths of intermolecular rearrangement which were considered but rejected are discussed in the following four paragraphs.

The observed rearrangement could have resulted from metala-
tion of previously formed cycloalkane-d as shown below. However, the

![Diagram showing the rearrangement process]

high yield of cyclooctene resulting from the reaction would be unlikely since metatalation of the pentane solvent would be greatly favored both on the basis of amount present and the possibility of forming a more stable, primary alkylsodium compound, e.g., pentyl-
sodium.
Apparent rearrangement resulting from removal of the deuterium by metalation directly at the vinyl position of the cycloalkene is ruled out by mass measurement which shows no significant loss of deuterium from the molecule.

Intermolecular rearrangement could occur also by allylic abstraction of hydrogen from cycloalkene-1-\textsuperscript{d} product as demonstrated below for abstraction adjacent to vinylic hydrogen. For rearrangement

\[
\text{RNA} + \begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{D} \\
\end{array} \rightarrow \begin{array}{c}
\text{R-H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{D} \\
\end{array} \rightarrow \begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{Na} \\
\text{D} \\
\end{array}
\]

by intermolecular allylic abstraction, the stability of the allylic carbanion or radical system for six- and eight-membered cycloalkenes should be of significance. Allylic stabilization for the 2-cyclooctenyl radical has been found to be poorer than the 2-cyclohexenyl radical by consideration of the ratio of radical addition to allylic abstraction \((k_{ad}/k_{ab})\) for irreversible\textsuperscript{3} and reversible\textsuperscript{37} addends. The reaction of trichloromethyl or acetyl radical (irreversible addends) with cyclooctene proceeds with less allylic abstraction than corresponding reaction with the cyclohexene system.\textsuperscript{3} The greater amount of addition to abstraction displayed by cyclooctene could have been due to a greater ease of 1,2 addition to the cyclooctene double bond or to
poorer stabilization of the 2-cyclooctenyl radical. The latter has been found to be the reason since 1,2 addition to cyclooctene occurs less readily than addition to cyclohexene as shown by study of the addition of hydrogen bromide or ethanethiol (reversible addends). Therefore, rearrangement by intermolecular allylic abstraction would be expected to be more complete with the 6-membered cyclic system than with the 8-membered system. Since the reverse occurs (compare reactions 3 and 4 in Table II), rearrangement by intermolecular allylic abstraction is ruled out. The abstraction in the metalation could occur by either radical or carbanionic pathway; however, allylic stabilization of either a radical or a carbanion intermediate in cycloalkene should be parallel processes subject to the same conformational factors since both require introduction of a third trigonal center adjacent to the double bond.

For the rearrangement of cyclooctene-1-d to occur by allylic intermolecular abstraction, metalation must occur in the allylic position. However, metalation of cycloalkenes by alkylsodium compounds can occur at either the vinylic position, in the case of cyclopentene, or the allylic position, in the case of cyclohexene. (Initial metalation at the vinylic position followed by rearrangement to the allylic position is excluded by the stability of vinylsodium compounds.) The position of metalation of cyclopentene apparently results from the difficulty of placing a third trigonal center, required for allylic stabilization of 2-cyclopentenyl carbanion, into the five-membered ring. The stabilities of allylic systems in 5-, 6-,
and 8-membered rings are in the order cyclohexene > cyclopentene >
cyclooctene, as determined by the relative rates of radical addition
of reversible and irreversible addends discussed previously.\textsuperscript{3,37}
Since allylic stability is less in the cyclooctene system than in the
cyclopentene system, it is quite reasonable that metalation of cyclo-
occene also will occur at the vinyllic rather than allylic position.
Thus, rearrangement by allylic abstraction in the cyclooctyl system is
unlikely.

Rearrangement by an intramolecular mechanism provides a more
likely path for deuterium scrambling. Transannular 1,3 and 1,5 re-
actions occur generally in cyclooctyl systems along with some 1,2 re-
action. Cyclohexyl systems undergo much less transannular reaction;\textsuperscript{39}
therefore, intramolecular rearrangement in the cyclohexyl systems is
best explained on the basis of 1,2 proton shifts. The amount of
scrambling observed in cyclooctene product from $\alpha$-deuteriocyclooctyl-
sodium (Table II, No. 4) can be accounted on the basis of single 1,2
shifts as shown in Figure 1 (calculations explained in Appendix II).
Thus, to account for the amount of scrambling observed approximately
one half of the cyclohexylsodium molecules undergo rearrangement. In
contrast, the amount of scrambling observed in cyclooctene from the re-
action of $\alpha$-deuteriocyclooctylsodium (Table II, No. 3) cannot be ex-
plained on the basis of single 1,2 shifts. As shown in Figure 2, the
maximum amount of scrambling obtained from 100\% 1,2 shift is 81\%, too
low a value to account for the 100\% scrambling observed. It seems
likely that, unlike the cyclohexyl system, the cyclooctyl system
FIGURE 1*

Rearrangement in α-Deuteriocyclohexylsodium by Single 1,2 Shift

FIGURE 2*

Rearrangement in α-Deuteriocyclooctylsodium by 100% 1,2 Shift

*Legend
E means elimination.
S means shift.
1,2 specifies positions involved in shift or elimination.
undergoes a mode of rearrangement in which the deuterium cannot be incorporated into the olefinic region upon formation of the olefin. This condition is met by occurrence of 1,3 or 1,5 tranannular proton shifts in the cyclooctyl system as shown below. Thus,

![Diagram showing tranannular rearrangement in cyclooctyl system](image)

the greater amount of scrambling observed in the cyclooctyl system compared to cyclohexyl can be satisfactorily explained by use of tranannular reactions similar to those found in the 8-membered system with carbonium ions and carbone intermediates.

The tranannular rearrangement found in medium ring carbanionic intermediates provides a useful tool for distinguishing between carbanionic and radical processes in organometallic compounds. For example, olefin formation by exchange of a dialkylmercury compound with an alkali metal can proceed by radical or carbanion paths, as outlined in Figure 3.\(^{19}\) Although radical intermediates can be assigned a role in the reaction of a metal with an alkylmercury, virtually complete reduction by sodium to the carbanion, as illustrated in path b, has been assumed. The formation of product by path a in significant
FIGURE 3

Carbanionic versus Radical Pathways for Olefin Formation in Exchange Reactions

\[ \text{olefin or alkane} \leftarrow^a R^* + RHg^{\text{Na}^+} \rightarrow R^{\text{Na}^+} + Hg \]

\[ \text{Na} \]

\[ \text{olefin or alkane}^* \]

*Formed by abstraction of solvent proton.
amounts has been thought unlikely on the basis that radical coupling products have not been detected in exchange reaction of dialkylmercury with sodium or potassium. However, direct evidence for olefin formation principally from carbanionic species has been lacking. The 100% scrambling of deuterium by intramolecular rearrangement observed with cyclooctylsodium combined with the observed non-rearrangement of the cyclooctyl radical provides direct evidence that at least 90% of the olefin formed in the exchange reaction resulted from an originally carbanionic species. Likewise, major formation of olefin product from pathways involving (1) reaction of a radical with sodium metal before formation of the organosodium compound, or (2) reaction of the alkylmercury with an alkylpotassium is ruled out. Since the tendency

\[ \text{1) } R^* + \text{Na}^- \rightarrow \text{alkene} + \text{NaH} \]
\[ \text{2) } R_2\text{Hg} + R^K \rightarrow R^*\text{H} + \text{olefin} + R^K + \text{Hg} \]

found for radical formation is cyclooctane > cycloheptane > cyclopentane > cyclohexane,\textsuperscript{40,41} it seems reasonable that the 7-, 6-, and 5-membered alkyl moieties as well as secondary, primary, and methyl alkyl groups will follow a carbanionic path to olefin formation.

The detection of carbanionic intermediates by rearrangement in medium ring compounds gives results in general agreement with the expectation that ionic character increases with increasing electropositivity of the metal cation. Rearrangement occurs with the strongly ionic carbon-sodium bond, but the carbon-lithium bond, which is reported to undergo carbanionic rearrangement in other systems,\textsuperscript{12,13,14} does not rearrange. A method of distinguishing the ionic character
of the carbon-lithium bond from the more covalent carbon-magnesium bond is desirable. Such a method can be drawn from the reaction of organolithium compounds with cyclooctyl halides.

The reaction of Grignard reagents with alkyl halides proceeds principally by heterolytic pathways in good solvating media (THF, 1,2-dimethoxyethane)\(^{42a}\) or by radical pathways in poor solvating media (hydrocarbon).\(^{42b}\) In ethyl ether, a weakly solvating medium, both radical and heterolytic pathways can occur\(^{42b}\) to a major extent. An example of solvent effect upon the ratio of heterolytic and radical reactions of Grignard reagents is provided by data on the preparation of cyclooctanecarboxylic acid from cyclooctylmagnesium halides shown below.

<table>
<thead>
<tr>
<th>Halide*</th>
<th>Solvent</th>
<th>% Acid</th>
<th>Mole Ratio Cyclooctane/Cyclooctene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloride</td>
<td>Ethyl Ether</td>
<td>45</td>
<td>0.9</td>
</tr>
<tr>
<td>Bromide</td>
<td>Ethyl Ether</td>
<td>7</td>
<td>1.7</td>
</tr>
<tr>
<td>Bromide</td>
<td>THF</td>
<td>38</td>
<td>2.8</td>
</tr>
</tbody>
</table>

*Starting halide was not found after reaction.

The increased amount of acid product from reaction of cyclooctylmagnesium bromide in THF compared to that formed in ethyl ether solvent results from stabilization of the carbon-magnesium bond in a more ionic form preventing consumption of the organometallic in radical reaction with the starting halide. If formation of cyclooctane proceeded by a heterolytic pathway, a smaller yield of acid would be expected in THF solvent rather than a larger one. The better yield obtained from cyclooctylmagnesium chloride in ethyl ether compared to the corresponding
bromide probably reflects the greater stability of the alkyl chloride to further reaction with alkylmagnesium halides as compared to the alkyl bromide. The ratio of cyclooctane/cyclooctene of 0.9 for cyclooctyrmagnesium chloride apparently indicates heterolytic reaction or radical reaction in a cage process in which diffusion from the cage to react with solvent was unlikely before disproportionation or coupling took place. The greater proportion of cyclooctane found in reactions with cyclooctyl bromide probably results from greater opportunity for radical reaction with solvent.

The formation of cyclooctyllithium from the chloride resulted in the appearance of a hydrocarbon product, bicyclo[3.3.0]octane, which was not found in formation of the Grignard reagent. Unlike cyclooctane and cyclooctene, the bicyclo[3.3.0]octane does not arise directly from reaction of the cyclooctyl radical. Several methods of formation of the compound can be postulated as discussed in the following paragraphs.

Transannular 1,5 elimination of lithium hydride from cyclooctyllithium was eliminated as a pathway to the bicyclic compound as follows: (a) exchange of dicyclooctylmercury with lithium, which did not result in the formation of bicyclic product, demonstrated the necessity of cyclooctyl chloride for bicyclic formation; (b) the ratio of bicyclooctane:cyclooctene was decreased from 0.12 to 0.03 when α-deuteriocyclooctyl chloride was used in place of unlabeled halide in THF solvent. Such an isotope effect would not have been expected in the transannular elimination pathway; (c) reaction of butyllithium in the presence of TMEDA upon cyclooctyl chloride produced
bicyclo[3.3.0]octane. Formation of cyclooctyllithium by exchange of
the lithium reagent with the chloride would be unlikely since it would
be necessary to form a secondary carbanion from a primary one.

The formation of bicyclooctane product by a carbenoid inter-
mediate is considered unlikely on the basis that α-haloalkyllithium
compounds generally do not insert into a carbon-hydrogen bond of a
saturated hydrocarbon. In postulated cases of carbenoid insertion
into C-H bonds, oxygen is either bound to the carbenoid or alpha to
the C-H bond undergoing insertion.

In contrast to the lack of C-H insertion found in α-haloalkyll-
lithium compounds, carbenes formed by α-elimination of primary alkyl
halides yield C-H insertion into saturated portions of the molecule. In the case of secondary alkyl halides, α-elimination has been found
only in 2-chloronorbornane. The α-eliminations discussed above
were usually carried out using an organosodium base. Although
a previous attempt to achieve α-elimination with alkyl halides by use
of an organolithium base was not successful, a carbene mechanism
with an organolithium base seems the most reasonable mechanism for bi-
cyclooctane formation as discussed below.

a) The effectiveness of an organolithium base in achieving
α-elimination from cyclooctyl chloride is accounted for by the relief
of steric strain in the cyclooctyl system upon removal of the α-
hydrogen. This steric effect is particularly important because in
unstrained systems the energy required for hydrogen removal is com-
pensated only by energy of the new bond to the attacking base. In
the competing process of $\beta$-elimination, additional energy is also
gained by formation of the new C-C bond of the product olefin.  Thus,
the effect of steric strain relief should favor both $\alpha$- and $\beta$-
elimination, but the effect should be more influential on $\alpha$-elimination.

b) The ratio of bicyclooctane to olefin formation in the
reaction of cyclooctyllithium with the chloride increases with the
order of promotion of ionic reaction, i.e., THF > ethyl ether > pentane, as shown below.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Bicyclo[3.3.0]octane/Cyclooctene</th>
</tr>
</thead>
<tbody>
<tr>
<td>THF</td>
<td>0.12</td>
</tr>
<tr>
<td>Ethyl Ether</td>
<td>0.03</td>
</tr>
<tr>
<td>Pentane</td>
<td>0.006</td>
</tr>
</tbody>
</table>

c) A deuterium isotope effect, $k_H/k_D \geq 4$, is observed in
reactions of $\alpha$-deuteriocyclooctyl chloride. The value of the isotope
effect found indicates a considerable amount of breaking of the C-H(D)
bond in the transition state of the rate determining step. Such a
finding is in accord with basic abstraction of the $\alpha$-hydrogen with
concurrent departure of the halide resulting in formation of carbene
which undergoes rapid transannular C-H insertion. Of course, C-H in-
sertion may conceivably occur in a concerted manner with $\alpha$-elimination
before production of a free carbene intermediate.

d) In the preparation of cyclooctyllithium in ethyl ether
at $-35^\circ$, the following ratios of hydrocarbon products were obtained
by use of cyclooctyl chloride or bromide.
<table>
<thead>
<tr>
<th>Products, Relative Molar Amounts</th>
<th>Chloride</th>
<th>Bromide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclooctene</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Bicyclo[3.3.0]octane</td>
<td>0.030</td>
<td>0.0085</td>
</tr>
<tr>
<td>Cyclooctane</td>
<td>1.5</td>
<td>2.0</td>
</tr>
</tbody>
</table>

The decrease in bicyclooctane/olefin ratio observed with cyclooctyl bromide is in accord with previous decrease in $\alpha$- compared to $\beta$-elimination when one changes from the chloride to the bromide. However, the decrease in bicyclooctane/olefin ratio also could result from more extensive formation of olefin by disproportionation of cyclooctyl radicals generated more easily from cyclooctyl bromide.

The formation of bicyclo[3.3.0]octane as a result of the action of a carbanionic species provides an example of the greater ionic character of the C-Li bond as compared to that of the C-Mg bond. Since, unlike alkane or olefin, bicyclooctane product is not formed by a radical pathway, a carbanionic pathway in the reaction of alkyl halides with organolithium compounds can be established on the basis of product studies. As discussed in the Introduction, several studies employing esr have demonstrated the existence of radical pathways in the reaction of alkylhalides with organolithium compounds. Consideration of the reaction paths available for the reaction of organolithium compounds with cyclooctyl chloride shown in Figure 3 reveals that measurement of the bicyclooctane/olefin ratio can provide insight into the tendency for radical versus ionic reaction of an organolithium compound. The ratio of bicyclooctane to olefin should increase with the increasing ionic character of the compound since a stronger base favors $\alpha$- over...
FIGURE 4

Reaction of Organolithium Compounds with Cyclooctyl Chloride

Reaction: RLi +

<table>
<thead>
<tr>
<th>Reaction Type</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disproportionation</td>
<td>alkane + alkane</td>
</tr>
<tr>
<td>Coupling</td>
<td></td>
</tr>
<tr>
<td>β-elimination</td>
<td></td>
</tr>
<tr>
<td>α-elimination</td>
<td></td>
</tr>
</tbody>
</table>

Reaction: RLi + Ether → alkane + ethylene
\[\beta\text{-elimination.}^{43}\] Also, the greater ionic character of the lithium reagent should give a lesser amount of radical formation and hence of olefin production by disproportionation reaction. For example, olefin products obtained from the reaction of cyclooctyllithium and of sec-butyllithium with cyclooctyl chloride are tabulated below.

<table>
<thead>
<tr>
<th>Products, Relative Molar Amounts</th>
<th>Cyclooctyl-Lithium</th>
<th>sec-Butyllithium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclooctene</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Bicyclo[3.3.0]octane</td>
<td>0.030</td>
<td>0.12</td>
</tr>
<tr>
<td>Cyclooctane</td>
<td>1.5</td>
<td>0.55</td>
</tr>
</tbody>
</table>

Due to the similarity of structure of the two secondary organolithium compounds the ratio of disproportionation to coupling was considered approximately equal; therefore, measurement of coupling products was not necessary for determination of the relative ionic character of the compounds. Likewise, the ratio of 1,2- to 1,5-C-H insertion in \(\alpha\)-elimination of the chloride resulting from reaction with lithium reagents was considered approximately equal. The bicyclooctane:cyclooctene ratio for the sec-butyllithium was approximately four times larger than that for reaction with the cyclooctyllithium, which indicates a considerably lesser ionic character for the latter compound. The decreased ionic character of cyclooctyllithium seems caused by acceleration of dissociation to a free radical by relief of steric strain. This effect has been documented previously in the radical abstraction of hydrogen from medium ring compounds and dissociation of azobisnitriles.\(^{40,41}\) In contrast to its lessened basic activity, at \(-35^\circ\) cyclooctyllithium is exceptionally reactive with ethyl ether yielding
a 1:1 ratio of 3-cyclooctylpropionic acid:cyclooctanecarboxylic acid. Since unstrained secondary organolithium compounds, e.g., cyclohexyl-
lithium, are stable to ethyl ether below $-10^\circ$, the reaction of ethers with secondary organolithium compounds apparently follows a radical reaction pathway.

The ratio of $\alpha$-$\beta$-elimination in the case of one reaction can be calculated from the ratio of hydrocarbon products (tabulated below) obtained from the reaction of butyllithium complexes with TMEDA in pentane solvent. Butyllithium-TMEDA has been reported to react

<table>
<thead>
<tr>
<th>Products</th>
<th>Relative Molar Amounts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclooctene</td>
<td>1.0</td>
</tr>
<tr>
<td>Bicyclo[3.3.0]octane</td>
<td>0.10</td>
</tr>
<tr>
<td>Cyclooctane</td>
<td>0.06</td>
</tr>
</tbody>
</table>

with alkyl halides by an ionic pathway, and predominant ionic reaction is indicated by the small amount of cyclooctane formation. Assuming that the amounts of cyclooctane and cyclooctene formed by disproportionation are approximately equal, the amount of cyclooctene produced by radical pathway is negligible compared to the total amount. If one takes the ratio of bicyclooctane:cyclooctene as the ratio of $\alpha$-$\beta$-elimination, approximately 10% $\alpha$-elimination must occur. Since cyclooctene is formed in $\alpha$-elimination by 1,2 insertion and the ratio of 1,2:1,5 insertion previously found in the cyclooctyl system is at least one, a minimum value of 20% $\alpha$-elimination is probably a more accurate estimate.
The formation of bicyclo[3.3.0]octane by α-elimination from cyclooctyl halides by organolithium compounds is evidence for the greater ionic character of the C-Li bond compared to the C-Mg bond. The relative amounts of bicyclo[3.3.0]octane and cyclooctene formed provide insight into solvent and steric effects upon the carbanionic versus the radical reaction paths of organolithium compounds. Particular emphasis has been placed upon the reaction of cyclooctyllithium. Thus, the information derived from the formation of bicyclo[3.3.3]-octane is a valuable supplement to the study of carbanionic intermediates in medium ring compounds.

The main purpose of the Dissertation was to extend the knowledge of transannular processes in medium ring compounds to carbanionic intermediates. Transannular rearrangement apparently does occur in cyclooctylsodium, which contains a highly ionic carbon-metal bond. Rearrangement was not observed in cyclooctylmetal compounds of lithium, magnesium, or mercury, which have a lesser amount of ionic character. Transannular elimination was not observed for any of the cyclooctylmetal compounds investigated, but bicyclooctane was identified as a carbene insertion product formed by reaction of the organolithium with the cyclooctyl chloride from which the organolithium was being prepared.
III. CONCLUSIONS

Transannular reactions occur in medium ring carbonium ion, carbene, and radical processes. This Dissertation shows that rearrangement occurs in the cyclooctyl carbanion and is best explained on the basis of 1,3 and 1,5 transannular proton shifts corresponding to the 1,3 and 1,5 reactions found in other types of intermediates. A smaller amount of rearrangement, which could be accounted for by single 1,2 proton shifts, was found in the cyclohexyl carbanion.

Since the cyclooctyl radical is known not to undergo rearrangement, the shifts found in the cyclooctyl system can be ascribed solely to a carbanionic mechanism. Alternative radical mechanisms have been possible explanations for carbanionic shifts recorded in other systems.

The tendency for rearrangement is controlled by the electropositive character of the cation which determines the ionic character of the carbon-metal bond. Rearrangement occurs with cyclooctylsodium, but cyclooctylmetal compounds having less electropositive cations (lithium, magnesium, or mercury) do not rearrange.

Organolithium compounds were found to react with cyclooctyl chloride to form bicyclo[3.3.0]octane by $\alpha$-elimination of the chloride. Previous attempts to obtain $\alpha$-elimination of alkyl halides by organolithium compounds have not been successful. The formation of bicyclo[3.3.0]octane apparently is the result of carbanionic rather than radical reaction of the organometallic. Therefore, the measurement of the relative amounts of bicyclooctane to radical products can
provide a measure of the tendency of the organolithium compound for
carbanionic and radical reactions. Such a comparison of sec-butyl-
lithium with cyclooctyllithium shows the latter compound to have a
greater tendency for radical reaction. The greater tendency for
radical reaction found with cyclooctyllithium seems to be directly re-
lated to a greater relief of steric strain by formation of a radical
intermediate compared to a carbanion intermediate.

An opportunity to estimate the ratio of $\alpha:\beta$ elimination
occurred in the reaction of cyclooctyl chloride with butyllithium
complexed by TMEDA. A minimum value of 0.2 for the ratio of $\alpha:\beta$
elimination was obtained for this system.
IV. EXPERIMENTAL

The compounds used in all syntheses were reagent grade commercial chemicals and, except for solvents, required no further treatment. Alkali metal dispersions and lithium wire were obtained from Ventron. Butyl- and sec-butyllithium solutions were obtained from Foote Mineral Company. Purification procedures for solvents requiring such treatment are outlined below.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Purification Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethylformamide (DMF)</td>
<td>Distillation from calcium hydride, followed by storage over calcium hydride.</td>
</tr>
<tr>
<td>Ethyl ether</td>
<td>Storage over calcium hydride.</td>
</tr>
<tr>
<td>Pentane</td>
<td>Washing with concentrated sulfuric acid until acid layer was colorless; washing with water; storage over calcium hydride.</td>
</tr>
<tr>
<td>Tetrahydrofuran (THF)</td>
<td>Preliminary drying with calcium hydride, followed by distillation from lithium aluminum hydride; storage in sealed ampoules.</td>
</tr>
</tbody>
</table>

All reaction mixtures were stirred by magnetic or motor driven stirrer unless otherwise stated.

The infrared (ir) spectra were obtained with a Perkin-Elmer Infracord Model 137 infrared spectrometer; samples of compounds were examined as thin films on sodium chloride plates.

Except for decoupling experiments, the nuclear magnetic resonance (nmr) spectra were obtained with a Varian Associates Model A60A
nmr spectrometer; samples were dissolved in carbon tetrachloride with
tetramethylsilane (TMS) as internal reference. Deuteration of com-
ounds was determined by nmr to within ±5% unless otherwise stated.
A detailed discussion of methods used is given in Appendix I.

Gas chromatographic (gc) data were obtained with Beckman
Model GC5 and Hewlett-Packard Model 700 instruments, both equipped
with hydrogen flame ionization detectors and 1/8" aluminum columns.

Mass spectra (ms) were obtained from a Consolidated Electrodynamics Corporation Model 21-130 instrument by Dr. H. T. Bickley of
the Louisiana State University Chemistry Department technical staff.

A. Preparation of α-Deuteriocyloalkyl Halides
1. (a) α-Deuteriocylooctanecarboxylic Acid

α-Deuteriocylooctanecarboxylic acid was prepared by dis-
solving the acid in D2SO4. The published procedure of E. E. Green6
was used, except that the mole ratio of cyclooctanecarboxylic acid to
D2SO4 was changed from 1.0:1.6 to 1.0:2.0, and bromoform was used in-
stead of pentane to extract the carboxylic acid from the reaction mix-
ture. The method resulted in the incorporation of 0.67 ± 0.05 mole
fraction of deuterium in the alpha position as shown by nmr analysis.

1. (b) Preparation of α-Deuteriocylooctyl Chloride27

α-Deuteriocylooctanecarboxylic acid (40.0 g, 0.255 mole, 67% α-D) was added to 200 ml of benzene in a three-neck, 1000 ml flask
equipped with a stirrer and condenser. Lead tetraacetate (38.2 g, 0.0763 mole) was added, and after fifteen minutes the stirrer was
stopped for the addition of lithium chloride (7.2 g, 0.17 mole). The reaction vessel was placed in a water bath at 75°, the stirrer was restarted, and nitrogen was passed through the reaction mixture. A vigorous evolution of carbon dioxide began after a few minutes, and the nitrogen flow was stopped. Reaction was complete after twenty minutes as shown by cessation of carbon dioxide evolution and loss of the bright yellow color of the reaction mixture. The water bath was removed, the reaction mixture was allowed to cool to room temperature, and glacial acetic acid (41 g, 0.71 mole) was added. After fifteen minutes the reaction mixture was poured into a separatory funnel and extracted with three 75-ml portions of a mixture of 75% dilute aqueous perchloric acid (7%) and 25% saturated sodium chloride solution, three 100-ml portions of water, three 75-ml portions of 1 M sodium hydroxide, and four 75-ml portions of water. Acidification of the basic washings gave 20 g (50%) of recovered α-deuteriocyclooctanecarboxylic acid which showed no loss of α-deuterium upon analysis by nmr. The organic layer was dried over MgSO₄ and concentrated with the water aspirator. Distillation of the residue gave 8.0 g (22% yield) of α-deuteriocyclooctyl chloride (bp 63-66° at 7 mm). The ir spectrum showed a peak at 4.60 μ (C-D stretching region) but otherwise was similar to that of the undeuterated compound. Nmr analysis indicated 77% deuteration at the alpha position.

2.(a) Preparation of cyclohexanol-1-d

Lithium aluminum deuteride (2.4 g, 0.057 mole) was added to 375 ml of ethyl ether in a 500 ml three-neck flask, and, after 20 minutes, a solution of cyclohexanone (19.5 g, 0.200 mole) in 50 ml of
ether was added slowly. The reaction mixture was refluxed for 20 hours. To it was added dropwise and successively 2.5 ml of water, 2.5 ml of 15% sodium hydroxide solution, and 7.5 ml of water. The reaction mixture was filtered, dried by MgSO₄-Drierite, concentrated by rotary evaporation, and distilled to give 16 g (80%) of cyclohexanol-1-d (bp 160-162°C; lit 161.1°C). Its ir spectrum showed a peak at 4.70 μ (lit 4.64 μ) for C-D stretch, and nmr analysis indicated 100% deuteration at the 1-position.

2. (b) Preparation of α-Deuteriocyclohexyl Chloride

α-Deuteriocyclohexyl chloride was prepared by reaction of the deuterated alcohol with phosphorus pentachloride in chloroform. The procedure of Goering and McCarron was followed except that cyclohexanol-1-d from 2.(a) was used in place of cyclohexanol, calcium carbonate was not added, and the work-up was modified as described below. The reaction mixture was washed with water followed by saturated aqueous sodium bicarbonate, dried over CaCl₂, and concentrated by rotary evaporation. Distillation gave 7.0 g (47%) of α-deuteriocyclohexyl chloride: bp 49-51°C (30 mm) [lit 48-50°C (30 mm) of undeuterated material] and 3 g (17%) of trans-1,2-dichlorocyclohexane-1-d: bp 63-65°C (4 mm) [lit 80-85°C (27 mm)]. The monochloride showed the C-D stretching absorption at 4.5 μ (lit 4.55 μ) and C-Cl stretching frequencies at 14.0 μ and 14.9 μ (13.6 μ and 14.6 μ for D-free chloride). Nmr analysis indicated 92% deuteration for both the monochloride and the dichloride at the 1-position.
2.(c) Preparation of α-Deuteriocyclohexyl Bromide

Freshly-distilled cyclohexanol-1-d (12 g, 0.12 mole) was mixed with triphenylphosphine (36.4 g, 0.139 mole) in 125 ml of dimethylformamide in a nitrogen atmosphere. Bromine was added to the mixture while the flask temperature was maintained below 10°C by use of an ice bath, and addition was stopped when the bromine color persisted in the solution. The reaction mixture was allowed to warm to room temperature, and all volatile material was removed by distillation at 10 mm. The distillate was poured into 500 ml of water, and the crude cyclohexyl bromide was separated. The water layer was extracted with three 100-ml portions of pentane, which were then combined with the cyclohexyl bromide. The organic material was washed with water, dried over MgSO₄, concentrated by rotary evaporation, and distilled to give 2.5 g (25%) of cyclohexene-1-d [bp 53-56°C (300 mm), lit₄₈ bp 82.98°C (760 mm) for cyclohexene] and 2.5 g (15% of α-deuteriocyclohexyl bromide [bp 63-65°C (30 mm), lit₄₈ bp 163-165°C (760 mm) for cyclohexyl bromide].

The olefin IR spectrum showed the C-D stretch at 4.48 μ and nmr analysis indicated 100% deuteriation at the 1-position. The olefinic nmr absorption at δ 5.6 was a considerably broadened eight peak multiplet rather than the uneven triplet recorded for cyclohexene. Although decoupling of this multiplet by irradiation of the β-hydrogen region at δ 2.1 was not complete, sharpening of the multiplet at δ 5.6 to give a crudely formed triplet with J_{D-H} = 1.2-1.4 Hz occurred. By use of J_H/J_D = 6 - 7,₅₂ the HC=CH₂ vicinal coupling constant, J_{HH₂},
was calculated to be 7.2 - 9.8 Hz (lit 8.8 - 11 Hz). (Decoupling experiments were conducted on a 100 MHz Varian Associates NMR Spectrometer Model HA-100.) Additional peaks of cyclohexene-1-d at δ 2.1 (beta hydrogens) and δ 1.6 (gamma hydrogens) did not show any major change from cyclohexene. Integration gave the ratio of beta and gamma hydrogens as 8.7:1 (theoretical 8.0:1). Gas chromatographic analysis showed the same retention times for the deuterated and undeuterated compounds on Apiezon L, 10.5 ft, 90° and Carbowax 20M, 6 ft., 70°.

Nmr analysis of α-deuteriocyclohexyl bromide indicated 89% deuteration in the alpha position. The nmr spectrum showed a diminished, poorly-resolved multiplet at δ 4.1, the position of the alpha hydrogen in cyclohexyl bromide. The remainder of the ring protons were grouped in a broad envelope from δ 1.1-2.4.

B. Preparation and Reactions of α-Deuteriocycloalkylmagnesium Halides

1. (a) Preparation of α-Deuteriocyclooctylmagnesium Chloride

A 500 ml, three-neck round bottom flask was equipped with a nitrogen inlet, reflux condenser, 250 ml addition funnel, and a magnetic stirring bar. The equipment was dried in an oven before assembly, then flamed out in a nitrogen stream before use. α-Deuteriocyclooctyl chloride (1 g, 0.006 mole, 76% deuterated) was mixed in the 500 ml flask under slight nitrogen pressure with magnesium turnings (3.1 g, 0.13 g-atom) in 25 ml of ethyl ether. The reaction was initiated by addition of a small crystal of iodine, after which the solution began to reflux slowly. Reflux was maintained by addition of
α-deuteriocyclooctyl chloride (8.5 g, 0.058 mole) in 150 ml of ethyl ether. Reflux was maintained by use of a heating mantle if necessary. The nitrogen pressure was released, the reaction mixture was protected by use of a calcium chloride drying tube, and reflux was continued for 12 hours by use of a heating mantle.

1.(b) Exchange of α-Deuteriocyclooctylmagnesium Chloride with Mercuric Bromide

The reaction mixture from 1.(a) was transferred under nitrogen pressure to a dry three-neck 1-liter flask equipped with a motor driven stirrer. Unreacted magnesium turnings were left in the original flask. When a heterogeneous mixture of mercuric bromide (22.0 g, 0.064 mole) in 400 ml of ethyl ether was added to the Grignard solution from a dry 1-liter dropping funnel, a white precipitate formed. The mixture was stirred for 6 hours after which 140 ml of 0.5 M acetic acid was added. The organic layer was washed several times with water, dried over magnesium sulfate, and concentrated by rotary evaporation. The crude crystals of α-deuteriocyclooctylmercuric bromide were recrystallized from acetone-water to give 12.5 g of white needles, mp 97-98° (lit 99.2-99.9°, 98-99° 8). The nmr spectrum showed broad unresolved multiplets at δ 2.2 (β-hydrogens) and δ 1.6 (remainder of ring hydrogens as found previously 8); however, the broad multiplet at δ 3.2 (α-hydrogens) was greatly reduced in size. Calculations based on an external standard showed the compound to be 71% deuterated at the α position.
1. (c) Oxygenation of α-Deuteriocyclooctylmagnesium Chloride

Cyclooctylmagnesium chloride was prepared from 1.3 g of α-deuteriocyclooctyl chloride (54% deuterated) according to the procedure of 1. (a) with a 7-hour rather than a 12-hour reflux period. Oxygen was bubbled through the reaction mixture for 10 minutes, causing the solution to lose its green color. After dropwise addition of 1.8 ml of saturated ammonium chloride solution, the ether layer was decanted from the precipitated salts, washed with water, dried over magnesium sulfate, and concentrated by rotary evaporation. After being heated at 40° under vacuum (2.5 mm) for several hours, the residue was found to contain 94% cyclooctanol-1-d (0.3 g, 30% yield) by gc analysis. The nmr spectrum indicated 59% deuteration by internal standard and 61% by external standard.

2. (a) Preparation of α-Deuteriocyclohexylmagnesium Bromide

α-Deuteriocyclohexyl bromide (0.5 g, 0.003 mole, 84% deuterated) was mixed with magnesium turnings (0.6 g, 0.03 g-atom) in 5 ml of THF under a nitrogen atmosphere in a dry three-neck 50-ml flask equipped with magnetic stirrer, dropping funnel, and thermometer. After initiation of the reaction by addition of an iodine crystal, more bromide (1.8 g, 0.011 mole) in 20 ml of THF was gradually added while the reaction temperature was maintained below 30°. The reaction mixture was then stirred at room temperature for 5 hours.

2. (b) Preparation of α-Deuteriocyclohexylmercuric Bromide

The solution of α-deuteriocyclohexylmagnesium bromide in THF was transferred by syringe to another 50-ml 3-neck flask protected
from moisture by a nitrogen atmosphere. Mercuric bromide (5.1 g, 0.014 mole) dissolved in 10 ml of THF was slowly added over a 45-minute period. The reaction mixture was stirred overnight and then poured into 220 ml of 0.75 M acetic acid in a separatory funnel. The mixture was extracted four times with 20-ml portions of chloroform. The chloroform extracts were washed with water, dried over magnesium sulfate, and filtered. Chloroform was removed by rotary evaporation, and the crude crystals were recrystallized from acetone-water to give 0.8 g (20%) of a-deuteriocyclohexylmercuric bromide (mp 138-140°, lit54 141-142° for cyclohexylmercuric bromide). Nmr analysis showed broad unresolved absorptions at δ 2.0 (beta hydrogens) and δ 1.6 (gamma and delta hydrogens) as found in the undeuterated compound. However, the multiplet at δ 3.2 (alpha hydrogens) was almost absent, and the compound was calculated to be 92% deuterated.

3.(a) Preparation of α-Deuteriocyclohexylmagnesium Chloride

α-Deuteriocyclohexyl chloride from reaction 2.(b) was diluted with pentane, washed with saturated aqueous sodium bicarbonate and water, dried over calcium chloride, concentrated by rotary evaporation, and distilled at 15 mm to remove any traces of hydrogen chloride. The same equipment was used as in reaction 1.(a) except that a motor driven stirrer was substituted for the magnetic stirrer. α-Deuteriocyclohexyl chloride (0.5 g, 0.004 mole, 92% deuterated) was mixed with magnesium turnings (3.0 g, 0.12 g-atom) in 20 ml of ethyl ether under a nitrogen atmosphere. The reaction was initiated by addition of a few drops of methyl iodide after which the solution turned
green, followed by formation of a gray precipitate. The reaction mixture was refluxed by use of a heating mantle during addition of the remaining chloride (4.5 g, 0.037 mole) in 100 ml of ethyl ether. The nitrogen pressure was released, the reaction mixture was protected with a calcium chloride drying tube, and reflux was continued for 6 hours.

3.(b) Exchange of α-Deuteriocyclohexylmagnesium Chloride with Mercuric Bromide

The reaction mixture from 3.(a) was transferred under nitrogen pressure to a dry three-neck 1-liter flask equipped with a motor driven stirrer. Unreacted magnesium turnings were left in the original flask. Mercuric bromide (11.8 g, 0.33 mole) in 25 ml of THF was added dropwise, causing formation of a white precipitate. After 8 hours, 105 ml of 0.5 M acetic acid was added. The organic layer was separated from the white precipitate, washed with water, dried over calcium chloride and concentrated by rotary evaporation, leaving 1.5 g of crude crystals. The white precipitate was dissolved in 600 ml of chloroform and washed with three 500-ml portions of water. Removal of the chloroform by rotary evaporation left 7 g of crude crystals. The crude crystals were combined and recrystallized from water-acetone to give 6 g (40%) of 88% deuterated α-deuteriocyclohexyl-mercuric bromide, almost colorless leaflets, mp 141-142°C (lit 141-142°C for cyclohexylmercuric bromide); nmr (DCCl₃) δ 3.2 (bm, 0.12 alpha hydrogens), 2.0 (bm, 3.9 beta hydrogens), 1.6 (bm, 6.1 gamma and delta hydrogens).
C. Preparation and Reactions of α-Deuteriocycloalkylalkali Metal Compounds

1.(a) Preparation of α-Deuteriocyclooctyllithium from the Chloride

(i) Eighteen-hour Reaction Period

α-Deuteriocyclooctyl chloride (1.4 g, 0.0095 mole, 75% deuterated) was mixed with lithium wire (0.14 g, 0.020 g-atom) in THF (20 ml)-pentane (10 ml) at -70° under an argon atmosphere. The reaction mixture was allowed to warm to room temperature to initiate the reaction, which was indicated by the yellow coloration with a slight cloudiness. After rapid recooling to -70° by immersion in Dry Ice-acetone, the reaction was continued at -70° for 18 hours. The reaction mixture was drawn into a syringe and expelled over Dry Ice. Ethyl ether (25 ml) and then 3 M HCl (20 ml) were added to the mixture. The aqueous layer was extracted with 20 ml of ether, which was combined with the organic layer. The organic layer was separated into neutral and acidic components by extraction. The acidic component (0.1 g) showed the NMR spectrum of α-deuteriocyclooctane carboxylic acid without any significant change in deuteration compared to the precursor acid from which the deuterated chloride had been prepared. The neutral fraction (1 g) was analyzed by GC (Hewlett-Packard 700, 10 ft Carbowax 20M column at 70° and 6 ft Ucon B column at 110°). Cyclooctene, cyclooctane, bicyclo[3.3.0]octane, and cyclooctyl chloride were detected in molar ratios of 1.0:11.2:0.02:24.8, respectively. A trace amount of 1-methylcycloheptene was also detected.
(ii) Forty-hour Reaction Period

Reaction procedure (i) was repeated except the reaction period at -70° was extended from 18 to 40 hours. The acidic fraction (0.1 g) was found again to have no significant change in deuteration from the precursor acid. Gc analysis of the neutral fraction (1 g) detected cyclooctene, cyclooctane, bicyclo[3.3.0]octane, and α-deuteriocyclooctyl chloride in molar ratios of 1.0:4.4:0.04:1.7. A trace of 1-methylcycloheptene was detected.

1.(b) Preparation of α-Deuteriocyclooctylmercury

α-Deuteriocyclooctylmercury was obtained by sodium stannite reduction by use of the published procedure of E. E. Green. Following reduction of α-deuteriocyclooctylmercuric bromide (10 g, 0.022 mole, 76% deuterated), the reaction mixture was extracted with pentane. The extract was washed with water, dried over MgSO₄-Drierite, and concentrated by rotary evaporation. After the residue was placed under vacuum (1 mm) for 30 minutes, 4 g (90%) of α-deuteriocyclooctylmercury was obtained. A portion (0.5 g) was recrystallized from acetone-ethyl acetate to yield a white powder, mp 47-49° (lit mp 48-50°, mp 50-51°). The dry powder decomposed to a black semisolid within twenty minutes in the presence of air. The remainder of the original product (3.5 g) was diluted to 20 ml with dry pentane and stored over Drierite in the freezer. Nmr analysis showed an absorption at δ 1.6 with a shoulder at δ 1.9 (lit δ 1.6 peak, δ 1.9 shoulder). No absorption was found in the olefin region of the spectrum, even upon increasing amplitude by a factor of five.
I.(c) Preparation of α-Deuteriocyclooctyllithium from the Dialkylmercury

(i) No Complexing Agent

α-Deuteriocyclooctylmercury (0.75 g, 0.0017 mole) in 3.3 ml of pentane was mixed with dispersed lithium (0.06 g, 0.009 g-atom) in 10 ml of pentane under an argon atmosphere. Cyclodecane (48 mg, 0.34 mmole) in 2 ml of pentane was added to the reaction mixture as an internal standard. After 18 hours, the reaction mixture was removed by syringe, expelled over Dry Ice, and then decomposed with 10 ml of 3 M HCl. The organic layer was separated into acidic and neutral fractions by extraction. An acid product was not found. Gc analysis (Hewlett-Packard 700, 6 ft Ucon B column at 110°) of the neutral fraction with cyclodecane internal standard detected cyclooctene and cyclooctane in 78% and 7% yields, respectively. No bicyclooctane products were found. Nmr analysis, by use of an external standard with gc determination of standard:cyclooctene mole ratio, indicated 1.1-1.3 hydrogen/molecule at the olefinic positions. This value corresponded to retention of deuterium at the alpha position and furthermore indicated that little or no loss of deuterium had occurred in the preparation of α-deuteriocyclooctylmercury. In accord with these data for the presence of cyclooctene-1-d, the line shape of the olefinic absorption at δ 4.6 was different from that in the spectrum for undeuterated cyclooctene, probably because of vicinal deuterium-hydrogen coupling. Ms measurement of the peak ratio at 110 and 111 mass units indicated that the cyclooctene-1-d was 77% deuterated. The small
amount of cyclooctane-d present in the sample made an accurate determination of its deuteration difficult, but a value of 61% was obtained by measurement of the peaks at 112 and 113 mass units.

(ii) Tetramethylethylenediamine (TMEDA) Complexing Agent

The procedure of (i) was followed except that TMEDA (1.1 g, 0.0095 mole), dried by storage over calcium hydride, was added to the reaction mixture just before addition of α-deuteriodicyclooctylmercury. Extraction did not furnish an acid derivative. GC, NMR, and MS analyses of the neutral fraction were conducted as described previously for (i). Cyclooctene and cyclooctane were found in yields of 45%, and 37%, respectively. Again, absorption equivalent to 1.1-1.3 hydrogens/molecule was present in the olefinic region of the NMR spectrum. MS indicated 78% deuteration for cyclooctene-1-d and 70% deuteration of cyclooctane-d.

1.(d) Preparation of α-Deuteriocyclooctylsodium

The procedure of 1.(c)(i) was followed except that dispersed sodium (0.2 g, 0.009 g-atom) was used instead of lithium. Acid was not obtained by the extraction procedure. The neutral fraction was analyzed in the same manner as in 1.(a). GC analysis detected cyclooctene and cyclooctane in 55% and 39% yields, respectively. The NMR spectrum included absorptions in the olefinic region at δ 4.6 equivalent to 1.8-2.0 hydrogens/molecule. Correspondingly, the line shape of the olefinic absorption matched that of an authentic sample of cyclooctene. MS analysis indicated 70% deuteration for cyclooctene-d and 65% deuteration for cyclooctane-d.
2.(a) Preparation of α-Deuteriocyclohexylmercury

The procedure of E. E. Green\(^6\) was followed except that α-deuteriocyclohexylmercuric bromide was used in place of the cyclo-octyl compound. After reduction of α-deuteriocyclohexylmercuric bromide (3.8 g, 0.01 mole, 88\% deuterated) by sodium stannite, the reaction mixture was extracted with pentane. The pentane extract was washed with water, dried over MgSO\(_4\)-Drierite, and concentrated by rotary evaporation. The residue was then placed under a vacuum (1 mm) for 30 minutes to give 1.4 g (78\%) of 88\% deuterated α-deuteriocyclohexylmercury; nmr (C\(_6\)H\(_6\)) \(\delta\) 1.6 (bm with shoulder sloping to \(\delta\) 1.8). The deuteration of the compound was determined by exchange of the dialkylmercury with mercuric bromide in hot ethanol\(^5\) to form α-deuteriocyclohexylmercuric bromide which was found to have the same nmr spectrum as the precursor alkylmercuric bromide.

2.(b) Preparation of α-Deuteriocyclohexylsodium

α-Deuteriocyclohexylmercury (0.65 g, 0.18 mole) in 5 ml of pentane was mixed with dispersed sodium (0.2 g, 0.009 g-atom) in 15 ml of pentane under a nitrogen atmosphere. Cyclooctane (0.024 g, 0.12 mmole) was added to the reaction mixture as an internal standard. After 18 hours, the reaction mixture was removed by syringe, expelled over Dry Ice, and then decomposed by ice and 3 M HCl. The organic layer was extracted with base, but no acid product was found. Gc analysis (Hewlett-Packard 700, 9.5 ft Apiezon L column at 55\(^\circ\) and 130\(^\circ\)) of the neutral fraction with cyclooctane internal standard found cyclohexene and cyclohexane in 38\% and 22\% yields, respectively. Nmr
analysis (toluene external standard with gc determination of toluene: cyclohexene mole ratio) indicated 1.30-1.50 hydrogens/molecule present in the olefinic position. Ms measurement of peaks at 82 and 83 mass units indicated 82% deuteration of cyclohexene-d. Similarly by measurement of peaks at 84 and 85 mass units the cyclohexane-d was found to be 77% deuterated.

D. Reactions of Cyclooctyl Halides with Organolithium Compounds

1. Reaction with Cyclooctyllithium

Cyclooctyllithium was prepared from the chloride in several solvent systems under argon atmosphere, and the mole ratios of hydrocarbon products were determined by gc analysis (Hewlett-Packard 700, 6 ft Ucon B column at 100° and 75°; 9.5 ft Carbowax 20M column at 65° and 75°; 6 ft Carbowax 20M column at 95°; 9.5 ft Apiezon L column at 90°). Cyclooctyl chloride, cyclooctane, cyclooctene, 1-methylocycloheptene, and bicyclo[3.3.0]octane were identified by comparison with authentic samples either purchased or available from previous work in these laboratories. Results of gc analyses and products obtained from reactions 1. (a) through 1. (i) are given in Table III. The experimental procedures for these reactions are described below.

1. (a)-(c) Preparation of Cyclooctyllithium in THF at -70°

Cyclooctyl chloride (5.0 g, 0.034 mole) was added to lithium wire (0.49 g, 0.071 g-atom) in THF (50 ml) at -70°. Pentane (20 ml) was also added to the reaction mixture to prevent freezing of the solution. The mixture was allowed to warm to room temperature to initiate
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<th>Reaction 1.</th>
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<tr>
<td>Ethyl Ether</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Pentane</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em><em>Components</em>, Mole Ratio</em>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclooctene</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Cyclooctane</td>
<td>6.5</td>
<td>6.3</td>
<td>6.4</td>
<td>6.1</td>
<td>1.5</td>
<td>2.0</td>
<td>0.60</td>
<td>0.40</td>
<td>0.14</td>
</tr>
<tr>
<td>Bicyclo[3.3.0]octane</td>
<td>0.12</td>
<td>0.12</td>
<td>0.12</td>
<td>0.13</td>
<td>0.030</td>
<td>8.5x10^-3</td>
<td>6.9x10^-3</td>
<td>6.1x10^-3</td>
<td>2.3x10^-3</td>
</tr>
<tr>
<td>l-Methycycloheptene</td>
<td>tr.**</td>
<td>tr.</td>
<td>tr.</td>
<td>tr.</td>
<td>3.0x10^-3</td>
<td>1.2x10^-3</td>
<td>4.5x10^-3</td>
<td>1.3x10^-3</td>
<td>3.1x10^-3</td>
</tr>
<tr>
<td>Cyclooctyl Chloride</td>
<td>48.5</td>
<td>31.5</td>
<td>19.5</td>
<td>0</td>
<td>0.67</td>
<td>---</td>
<td>0.48</td>
<td>6.7</td>
<td>0</td>
</tr>
<tr>
<td>Cyclooctyl Bromide</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>---</td>
<td>0</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
</tbody>
</table>

*Bicyclo[5.1.0]octane was not found.

**Trace
the reaction, then rapidly recooled to -70°C. After 7 and 18 hours, 10-ml aliquots [designated (a) and (b), respectively] of the reaction mixture were removed by syringe, expelled over Dry Ice, and separated into acidic and neutral fractions by extraction. Results of gc analysis of the neutral fraction are given in Table III. Cyclooctanecarboxylic acid (0.03 g, 0.2 mmole, 4% yield) was recovered from each acidic fraction.

After 24 hours, another 10-ml aliquot (c) was removed from the reaction mixture, and oxygen was bubbled through the 10-ml aliquot for 10 minutes. The solution, still at -70°C, was transferred to a freezer and allowed to warm to -5°C over a one-hour period. Saturated ammonium chloride solution was added to the reaction mixture, which was then decanted from the flask, diluted with 20 ml of pentane, washed with water, dried over magnesium sulfate-Drierite, and concentrated by rotary evaporation. Gc analysis of the residue is given in Table III. Cyclooctanol was not detected.

1.(d) Preparation of Cyclooctyllithium in THF at -70°C to -15°C

Cyclooctyl chloride (0.75 g, 0.0051 mole) was mixed with lithium wire (0.079 g, 0.014 g-atom) in THF (10 ml) and pentane (2 ml) at -70°C. The reaction mixture was allowed to warm to -15°C over a one-hour period. It was removed by syringe, expelled over Dry Ice, decomposed with 3 M HCl, and separated into acidic and neutral components by extraction. The acidic fraction gave a residue of 0.15 g (~20%) of 3-cyclooctylpropionic acid: nmr (CCl4) δ 12.5 (s, 1.0, CO₂H), 2.3 (t, 2.2, J=6 Hz, CH₃CO₂), 1.6 (s, 19, C₆H₁₅CH₂). The ir spectrum was similar to, but did not match, that of cyclooctanecarboxylic acid.
1.(e) Preparation of Cyclooctyllithium in Ether from Cyclooctyl Chloride

Cyclooctyl chloride (5.0 g, 0.034 mole) in 40 ml of ethyl ether was added over a one-hour period to dispersed lithium (0.495 g, 0.0718 g-atom) in 10 ml of ethyl ether at -35°. After 5 hours, the reaction mixture was removed by syringe, expelled over Dry Ice, decomposed with ice and 3 M HCl, and separated into acidic and neutral fractions by extraction. Concentration by rotary evaporation resulted in a residue of 2.3 g for the neutral fraction (gc analysis in Table III) and 0.4 g for the acid fraction. Nmr analysis of the acid fraction indicated a mixture of cyclooctanecarboxylic acid and 3-cyclooctylpropanoic acid: nmr (CCl₄) δ 11.9 (s, 1.0), 2.36 (m, 1.5), 1.6 (s with a shoulder at 1.9, 17).

1.(f) Preparation of Cyclooctyllithium in Ethyl Ether from Cyclooctyl Bromide

Cyclooctyl bromide (2.0 g, 0.011 mole) in 20 ml of ethyl ether was added to dispersed lithium (0.17 g, 0.025 g-atom) in ethyl ether (10 ml) at -35°. Reaction and work-up procedures were the same as described in 1.(e). Results from gc analysis of the neutral fraction (1 g) are given in Table III. No acid was recovered from the reaction.

1.(g) Preparation of Cyclooctyllithium in Pentane at Room Temperature

Cyclooctyl chloride (1.5 g, 0.010 mole) in 5 ml of pentane was mixed with lithium wire (0.50 g, 0.070 g-atom) in 10 ml of pentane.
Cyclooctyl chloride (3.5 g, 0.024 mole) in pentane (35 ml) was added over a 45-minute period at room temperature. After 12 hours, the reaction mixture was removed by syringe, expelled over Dry Ice, decomposed with ice and then 3 M HCl, and separated into acidic and neutral fractions by extraction. Gc analysis of the neutral fraction (2.0 g) is summarized in Table III. An acid product was not obtained.

1.(h) Preparation of Cyclooctyllithium in Pentane at Reflux

Cyclooctyl chloride (10 g, 0.068 mole) in pentane (100 ml) was added over a 4-hour period to lithium wire (0.97 g, 0.14 g-atom) in pentane (10 ml). Reflux was maintained by a heating mantle during the addition and subsequent 18-hour reaction period. The work-up described in 1.(g) was followed. No acid was obtained. The neutral fraction (6.0 g) was analyzed by gc (Table III).

1.(i) Preparation of Cyclooctyllithium in Pentane with Lithium Dispersion

Cyclooctyl chloride (5.0 g, 0.034 mole) in pentane (50 ml) was added over a 2-hour period to dispersed lithium (0.497 g, 0.0718 g-atom) in pentane (10 ml). Reflux was maintained by a heating mantle during the addition and subsequent 6-hour reaction period. The work-up procedure described in 1.(g) was followed. An acid was not obtained. Gc analysis of the neutral fraction (1.1 g) is given in Table III.
2.(a) Reaction with sec-Butyllithium in Ethyl Ether Solvent

sec-Butyllithium (0.66 g, 0.010 mole) in pentane (8 ml) was added to 20 ml of ethyl ether at -35\(^\circ\) under an argon atmosphere. The temperature was maintained at -35\(^\circ\) during the addition of cyclooctyl chloride (1.5 g, 0.010 mole) and the subsequent 6-hour reaction period. The reaction mixture was poured over Dry Ice, decomposed with 3 M HCl, and separated into neutral and acidic fractions. Gc analysis (Hewlett-Packard 700, 9.5 ft Ucon B column at 110\(^\circ\); 9.5 ft Carbowax 20M column at 75\(^\circ\)) of the neutral fraction (1.4 g) detected cyclooctene, cyclooctane, bicyclo[3.3.0]octane, and cyclooctyl chloride in 1.0:0.55:-0.125:8.9 mole ratios, respectively.

2.(b) Reaction with sec-Butyllithium Complexed with Tetramethyl-ethylenediamine (TMEDA)

TMEDA (6.35 g, 0.055 mole) was added to sec-butyllithium (3.5 g, 0.055 mole) in hexane (30 ml) at 10\(^\circ\). Addition of cyclooctyl chloride (2.0 g, 0.014 mole) was added to the deep red solution causing it to reflux and to change color to light red and then to yellow. The reaction mixture was stirred for one hour at room temperature, poured over Dry Ice, and decomposed with 3 M HCl. Separation by extraction provided an 0.8 g neutral fraction. Gc analysis (Hewlett-Packard 700, 9.5 ft Apiezon L column at 105\(^\circ\); 9.5 ft Carbowax 20M column at 95\(^\circ\)) detected cyclooctene, cyclooctane, and bicyclo[3.3.0]octane in 1.0:0.19:-0.075 mole ratios, respectively. 1-Methylcycloheptene was present in trace amounts. Bicyclo[5.1.0]octane was not detected.
3. Reaction with Butyllithium Complexed with TMEDA

The procedure in 2.(b) was followed except that the amounts of reagents were reduced by one-half and butyllithium was used in place of sec-butyllithium. Reaction upon addition of cyclooctyl chloride was not so vigorous with butyllithium as with sec-BuLi and the mixture remained light yellow during the procedure. GC analysis [same as 2.(b)] of the neutral fraction (0.6 g) detected cyclooctene, cyclooctane, bicyclo[3.3.0]octane in 1.0:0.06:0.10 mole ratios, respectively. 1-Methylcycloheptene was present in trace amount, but bicyclo[5.1.0]octane was not detected.

E. Miscellaneous Control Experiments

1. Preparation of Cyclooctylmagnesium Chloride

Cyclooctyl chloride (20 g, 0.44 mole) was added to magnesium turnings (21 g, 0.87 g-atom) in 75 ml of ethyl ether under a nitrogen atmosphere. The mixture was stirred by a magnetic stirrer and heated to reflux. Reaction was initiated by the addition of a crystal of iodine. Cyclooctyl chloride (90 g, 0.61 mole) in 1500 ml of ethyl ether was added, and the mixture was refluxed for an additional 36 hours. The reaction mixture was poured onto excess Dry Ice and decomposed by the addition of 150 ml of 6 M HCl. The ether layer was separated and washed with water and with 0.9 M NaOH. The basic washings were extracted with ethyl ether, acidified to pH 4 with 6 M HCl, and extracted with pentane. The pentane layer was washed with water, dried over MgSO₄-Drierite, and evaporated to yield 50 g (43%) of
cyclooctanecarboxylic acid, which was identified by its nmr spectrum. The ether layer which had been washed with 0.9 M NaOH was extracted with water, dried over CaCl₂, and evaporated to give 25 g of hydrocarbon residue. Gc analysis (Beckman GC-5, 8 ft Apiezon L column at 100°) detected cyclooctene and cyclooctane in the mole ratio 1.0:0.93, respectively. bicyclooctanes were not present, and no other gc peaks appeared after the cyclooctane peak, although the column temperature was increased to 170° for 30 minutes.

2. Preparation of Cyclooctylmagnesium Bromide

Cyclooctyl bromide (7.0 g, 0.037 mole) was added to magnesium turnings (18 g, 0.74 g-atom) in 20 ml of THF. The mixture was stirred by a magnetic stirring bar, and reaction began immediately as shown by a greenish-brown color. Additional cyclooctyl bromide (43 g, 0.22 mole) in 480 ml of THF was added over a 3-hour period while the reaction temperature was maintained below 35°. The reaction mixture was cooled to 20° and, after 15 hours, was poured over an excess of Dry Ice. A solution of ammonium chloride (6 M, 100 ml) was added to the THF solution, which was then washed 4 times with 100-ml portions of ethyl ether. The ether extracts were combined and washed 4 times with 100-ml portions of water. Acidic and neutral fractions were separated by extraction. The acidic fraction was distilled to give 16 g (41%) of cyclooctane-carboxylic acid; bp 109-110° (0.6 mm). Concentration of the neutral fraction by rotary evaporation gave 2.2 g of non-acidic product. Gc analysis (Beckman GC-5 8 ft Apiezon L column at 100°) showed cyclooctene and cyclooctane present in the mole ratio 1.0:2.8.
Bicyclooctanes were not present, and no other gc peaks appeared after the one for cyclooctane, although the column temperature was raised to 130° for 40 minutes, then to 170° for 19 minutes.

3. Preparation of Cyclooctyllithium by Exchange with Dicyclooctylmercury

Reactions were conducted under an argon atmosphere, and hydrocarbon products were analyzed by gc (Hewlett-Packard 700 instrument, 9.5 ft Apiezon L column at 95°). Bicyclic and ring-contracted products were not detected in these reactions.

3.(a) Reaction in Pentane Solvent

Dicyclooctylmercury (0.80 g, 0.0019 mole) dissolved in 8 ml of pentane was added to dispersed lithium (0.08 g, 0.011 g-atom) in 5 ml of pentane, and the mixture was stirred for 3 hours. The reaction mixture was poured over Dry Ice, decomposed with ice and 3 M HCl, and separated into neutral and acidic fractions by extraction. No acid product was found. Gc analysis of the neutral fraction revealed the mole ratio of cyclooctene:cyclooctane to be 1.0:0.1.

3.(b) Reaction in Ethyl Ether

Dicyclooctylmercury (0.60 g, 0.0013 mole) in 6 ml of pentane was added to dispersed lithium (0.06 g, 0.008 g-atom) in 50 ml of ether at -70°. The mixture was stirred for 18 hours at -70°, poured over Dry Ice, and separated into acidic and neutral fractions by extraction. No acid product was found. Cyclooctene and cyclooctane were detected in a 1.0:1.4 mole ratio, respectively, by gc analysis of the neutral fraction.
3.(c) Reaction in THF-Pentane

The procedure of reaction 3.(b) was followed except that a mixed solvent of THF (10 ml) and pentane (15 ml) was used in place of ethyl ether. No acid product was isolated. Gc analysis detected cyclooctene and cyclooctane in a 1.0:1.4 mole ratio, respectively.

3.(d) Reaction in Hexamethylphosphoramide (HMPA)-Pentane

Dicyclooctylmercury (0.60 g, 0.0013 mole) in 5 ml of pentane was added to dispersed lithium (0.06 g, 0.008 g-atom) in a solution of HMPA (0.93 g, 0.0052 mole) and 10 ml pentane. The remainder of the procedure followed that of reaction 3.(a). No acid product was found. Gc analysis of the neutral fraction detected cyclooctene and cyclooctane in a 1.0:62 mole ratio, respectively.
V. SUMMARY

Transannular reactions occur in medium ring (8-11 carbon atoms) carbonium ion, radical, and carbene processes. By use of several deuterium labelled cyclooctylmetal compounds, the possibility of transannular rearrangement or elimination resulting from a carbanionic intermediate has been investigated. Derivatives were prepared from α-deuteriocyclooctyl chloride through the alkylmagnesium chloride and alkyllithium without loss of deuterium from the alpha position. Reaction of α-deuteriocyclooctyllithium in pentane results in formation of cyclooctene-1-d, but α-deuteriocyclooctylsodium in pentane solvent gives cyclooctene-d, in which the deuterium has been scrambled from the alpha position. Thus, increasing ionic character of the carbon metal bond in the series Mg < Li < Na finally leads to carbanionic rearrangement in the case of cyclooctylsodium. A smaller amount of rearrangement was found in the case of cyclohexylsodium. Comparison of the amounts of rearrangement found in six- and eight-membered rings shows the former is best explained by 1,2 proton shifts and the latter by transannular proton shifts. Transannular elimination from cyclooctylmetal compounds was not found.

Organolithium compounds react with cyclooctyl chloride to form bicyclo[3.3.0]octane by α-elimination of the halide. The ratio of bicyclooctane:cyclooctene formation was found to be a measure of the tendency of the organolithium compound toward carbanionic and radical reaction. The ratio of bicyclo[3.3.0]octane:cyclooctene decreases from 0.12 to 0.03 when cyclooctyllithium is substituted for
**sec-butyllithium.** The decrease in relative amount of bicyclooctane formed indicates that cyclooctyllithium has greater tendency for radical reaction than does sec-butyllithium.
REFERENCES


10. (a) W. Schlenk and E. Bergman, Ann. Chem., 563, 98 (1928); (b) K. Ziegler and F. Grossmann, Ber., 62, 1768 (1929).


SELECTED BIBLIOGRAPHY


APPENDIX I

Analytical Methods Used in Determination of Deuteration in Specifically Labelled Compounds

The internal standard method for nmr measurement of deuteration of a specifically labelled compound and determination of possible rearrangement in products has been employed previously by workers in these laboratories. The method is described in detail in the Dissertation of E. E. Green and was followed in this work. For example, in the case of α-deuteriocyclooctanecarboxylic acid, the integrated intensity of the absorption of the alpha hydrogen ($N_\alpha$) at δ 2.4 is compared to that of the hydroxyl absorption ($N_{OH}$) at δ 12.1 to give the amount of hydrogen remaining in the alpha position. The percentage of deuteration ($\% D$) is then

$$\text{\% D} = 100 - \frac{N_\alpha}{N_{OH}} \times 100.$$  \hspace{1cm} 1

The use of an external standard in nmr as an analytical method has been reviewed by G. A. Ward. The amount of hydrogen in a molecular position may be calculated by

$$N_s = N_r \left( \frac{M_r}{M_s} \right) \left( \frac{R_s}{R_r} \right)$$  \hspace{1cm} 2

where $N_s$ and $N_r$ are the number of hydrogens at a given absorption of the sample and reference compounds, respectively, $M_r/M_s$ is the molar ratio of the reference to the sample, and $R_r$ and $R_s$ are the areas of the absorptions as determined by integration. Then

$$\text{\% D} = 100 - \frac{N_s}{N_{s^*}} \times 100$$  \hspace{1cm} 3

where $N_{s^*}$ is the number of hydrogens at the position of interest in
TABLE A-1

Deuteration Values of Labelled Compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>Int. Std.</th>
<th>%D</th>
<th>Ext. Std.</th>
<th>%D</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Deuteriocyclooctyl-carboxylic Acid</td>
<td>Hydroxyl H</td>
<td>68</td>
<td>HCBr₃</td>
<td>68</td>
</tr>
<tr>
<td>α-Deuteriocyclooctyl Chloride</td>
<td>Ring H</td>
<td>76</td>
<td>HCBr₃</td>
<td>75</td>
</tr>
<tr>
<td>α-Deuteriocyclooctyl-mercuric Bromide</td>
<td>Beta H</td>
<td>71</td>
<td>HCBr₃</td>
<td>70</td>
</tr>
</tbody>
</table>
the undeuterated compound. Examples of compounds for which I have calculated $\delta D$ by both internal and external standards are given in Table A-1. The mole ratio, $M_r/M_s$, was determined by weighing the pure compounds into an nmr tube. The sample was then diluted with CCl$_4$, and TMS was added. In general, the accuracy of the method has been found to be within $\pm 3\%$, and is chiefly limited by the integration measurement. For this work, a figure of $\pm 5\%$ has been used as a good but conservative estimate of the accuracy of the measurement.

An external standard is necessary to determine the amount of deuteriation of compounds in a reaction mixture if an internal standard is not available. For example, in the decomposition of $\alpha$-deuteriocyclooctylalkali metal compounds to olefin and alkane [Reaction IV.C.1.(c), pages 49-50], an internal standard is not available for measurement of the deuteration of cyclooctene product in the olefinic position. However, the number of hydrogens in the olefinic region, $N_s$, was measured by addition of an external standard (m-dichlorobenzene), determination of the $M_r/M_s$ ratio by gc analysis (Hewlett-Packard 700, 6 ft Ucon B column at 110$^\circ$), and use of equation 2. Values for the number of hydrogens in the olefinic region for the products from the reaction of $\alpha$-deuteriocyclooctylmercury (70$\%$ D) with lithium [IV.C.1.(a)] and from a control reaction (undeuterated material) are shown below.

<table>
<thead>
<tr>
<th>Starting Reagent</th>
<th>Product</th>
<th>Number of H's in Olefinic Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-deuteriocyclo-</td>
<td>cyclooctene-1-d</td>
<td>1.1-1.3</td>
</tr>
<tr>
<td>octylmercury</td>
<td>cyclooctylmercury</td>
<td>1.8-2.0</td>
</tr>
</tbody>
</table>
FIGURE A-1

Olefinic Absorption of Deuterated and Undeuterated Olefins

Cyclooctene-1-d/cyclooctene
3:1 Ratio

Cyclohexene-1-d

Cyclooctene

Cyclohexene
A qualitative measure of the deuteration of a compound may be obtained by the effect of deuterium-hydrogen coupling upon the line shape of the nmr absorption. This effect is found in both cyclohexene-1-d and cyclooctene-1-d, as shown in Figure A-1.
FIGURE A-2

Rearrangement in α-Deuteriocyclohexylsodium by Single 1,2 Shift

FIGURE A-3

Rearrangement in α-Deuteriocyclooctylsodium by 100% 1,2 Shift

*Legend
E means elimination.
S means shift.
1,2 specifies positions involved in shift or elimination.
APPENDIX II.

Calculation of Intramolecular Rearrangement

I. Calculation of % Scrambling

If deuterium is scrambled in a compound the fraction of the deuterium at any one bond site, X, will be

\[ X = \frac{\text{No. D}_{\text{original}}}{\text{No. Bond Sites Available}} \]

For cyclohexene 88% deuterated

\[ X = \frac{0.88}{10} = 0.088 \]

For a particular molecular region the amount of deuterium present, Y, after scrambling is

\[ Y = X \cdot V \]

where \( V \) = number of bond sites in the molecular region.

For olefin region of cyclohexene

\[ Y = 0.088 \cdot 2 = 0.18. \]

The % scrambling, Z, is defined as

\[ Z = \frac{\text{No. D}_{\text{original}} - \text{No. D}_{\text{found}}}{\text{No. D}_{\text{original}} - Y} \]

Corresponding calculations for 70% deuterated cyclooctane give \( Y = 0.10 \).

II. Calculation for Rearrangement of Cyclohexylsodium, Figure A-2.

A. Assumptions
1. Only single 1,2 shifts occur.

2. $k_H/k_D = 3.5$ for elimination of sodium hydride. $k_H/k_D = 3.4$ for elimination of lithium hydride.\(^{58}\)

3. The ratio of elimination between two positions is proportional to the number of hydrogen atoms at each position.

   If a deuterium atom is present, a ratio of $k_H/k_D = 3.5$ is used to correct for the isotope effect.

B. Data

<table>
<thead>
<tr>
<th>Deuterium</th>
<th>No.</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular</td>
<td>0.82</td>
<td>ms</td>
</tr>
<tr>
<td>Olefinic, found</td>
<td>0.60</td>
<td>nmr, gc</td>
</tr>
<tr>
<td>Olefinic, original</td>
<td>0.88</td>
<td>nmr</td>
</tr>
</tbody>
</table>

C. Calculations

1. Relationships between Cyclohexene Products, Figure A-3.

   (1) $c + f = 68\%$ contribute to unscrambled value
   (2) $e + d = 32\%$* contribute to scrambled value
   (3) $c/d = 3.5$ deuterium isotope effect
   (4) $c/e = 0.5$ No. H available for elimination

2. % Rearrangement, $R$

   $$R = \frac{\text{No. } D_{\text{original}} - \text{No. } D_{\text{found}}}{\text{No. } D_{\text{original}}} \times 100 = \frac{(0.88 - 0.60)(100)}{0.88} = 32$$

3. Olefinic Products

   (2) $e + d = 32$
   (3) $c/d = 3.5$
   (4) $c/e = 1/2$
   (5) $e/d = 7$

*Calculated from C.2.
Substituting \( \text{\textcircled{5}} \) into \( \text{\textcircled{2}} \)

\[
d + 7d = 32
\]

\[
d = \frac{32}{8} = 4.0
\]

and from \( \text{\textcircled{5}} \)

\[
e = 28
\]

\( \text{\textcircled{3}} \) \( \frac{c}{d} = 3.5 \)

and \( d = 4.0 \) (above).

Therefore, \( c = (3.5)(4.0) \)

\[
c = 14
\]

\( \text{\textcircled{1}} \) \( c + f = 68 \)

\[
c = 14
\]

\[
f = 54
\]

III. Calculation for 1,2 Rearrangement of Cyclooctylsodium, Figure A-3.

A. Assumptions

1. 100% single 1,2 shifts occur, \( R = 100\% \)

2. Same as IIA2 for cyclohexane system

3. Same as IIA3 for cyclohexane system

B. Calculations

1. Relationships between cyclooctene products

\( \text{\textcircled{1}} \) \( d + e + c = 100 \)

\( \text{\textcircled{2}} \) \( d/e = 3.5 \)

\( \text{\textcircled{3}} \) \( d/c = 0.5 \)

2. Olefinic Products

Substituting \( \text{\textcircled{2}} \) and \( \text{\textcircled{3}} \) into \( \text{\textcircled{1}} \)

\[
 d + \frac{d}{3.5} + \frac{d}{0.5} = 100
\]

\[
3.28d = 100
\]

\[
d = 30.5
\]
\[ d/e = 3.5 \]
\[ e = 9 \]
\[ d/c = 0.5 \]
\[ c = 61.0 \]

3. Scrambling

X, Y, and Z are defined as in section IA. For cyclo-octane system, 1.0 deuterium, \( X = 0.071 \) and \( Y = 0.14 \).

\[ \text{No. D}_{\text{found}} = \% \text{ d}/100 = 0.30 \]

\[
Z = \frac{\text{No. D}_{\text{original}} - \text{No. D}_{\text{found}}}{\text{No. D}_{\text{original}} - Y} = \frac{1.0 - 0.3}{0.86} = 81\%
\]
VITA

Richard L. Frye was born on February 20, 1941, at Knoxville, Tennessee. He completed his elementary and secondary education in Knoxville and entered the University of Tennessee in 1959. He was awarded the Degrees of Bachelor of Science (1962) and Master of Science (1965) in Chemistry. He accepted a position in 1965, with Texaco, Inc., Research and Technical Department, Port Arthur, Texas. In 1966 he married Glynis Land of Beaumont, Texas, and with her faith and encouragement began graduate study at Louisiana State University in 1968. He is now the father of Keith (33 months) and Kristin (6 months) and a candidate for the Doctor of Philosophy Degree with a major in organic chemistry and a minor in physical chemistry.
EXAMINATION AND THESIS REPORT

Candidate: Richard L. Frye

Major Field: Chemistry

Title of Thesis: Study of Rearrangements in Medium Ring Organometallic Compounds

Approved:

James D. Fraynham
Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

James Dale Maconie

E. J. Mecke

Erwin B. Badger

Fred J. Hake

Date of Examination:

November 22, 1971