# THE FORMATION OF 1-METHYL-6,7-BENZOBICYCLO[3.2.2]NON-6-ENE FROM THE FRIEDEL-CRAFTS REACTION OF 1,1-BIS(BROMOMETHYL)CYCLOHEXANE WITH BENZENE

by

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A Dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York.

1976

This manuscript has been read and accepted for the Graduate Faculty in Chemistry in satisfaction of the dissertation for the degree of Doctor of Philosophy.

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## DEDICATION

This thesis is dedicated to my wife Hinda, my son Shmuel, and my daughter Tzipporah.

This work is also dedicated to the memory of Rabbi Dr. Samuel Soloveichik, whose inspiration led many students through the path of synthesis of religion and science. To this end I wish to incorporate the following poem written by him.

# I SEE HIM

by Rabbi Dr. Samuel Soloveichik, ztl

I see Him in a sick's recovery,
In a scientific discovery.
I see Him in creative tension,
Realization, materialization, and invention.

I see Him in the voice of our Tanoim,
In the discussion of the Amoroim.
I see Him in the Rishonim's debate,
And in my ancestors' faith.

I see Him in my mother's devotion,
In a little girl's emotion.
I see Him in Beethoven's inspiration
And in Dr. Schweitzer's devotion.

I see Him in the gale's soar,
In the sea's mighty roar.
I see Him in heaven's silence,
And in nature's thundering violence.

I see Him in Jewish History,
Highly complex and full of mystery.
I see the Great Sire
Even in Treblinka's and Oswicim's fire.

On a rainy day I see Him on the cloud's roof,
Cold, far, distant, aloof.
And on a warm day, in prayer I see Him clear,
Glorious, majestic and yet close and near.

I see G-d the Universe Creator,
In science, the innovator.
I see G-d the Great Judge,
In human misery and grudge.

I believe in the uniqueness of our religion and race,
I believe in the righteousness of our case.
When I see the weak's survival,
I am sure of the Messiah's ultimate arrival.

I believe that all people are of one stock,
Yet I am aware that I am of the minority block,
A lost sheep of Jacob's flock,
And G-d is my fortress and rock.

ACKNOWLEDGEMENTS

The author wishes to thank Professor Leonard H. Schwartz for his continued guidance and encouragement throughout this research.

I would also like to thank Mr. Joe LaRubbio and Mr. Jack Landis for the many hours they spent assisting me in determining the mass spectra incorporated in this thesis.

I would also like to thank the Chemistry Department of City College for their financial support during the work on this project.

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# THE FORMATION OF 1-METHYL-6,7-BENZOBICYCLO[3.2.2]NON-6-ENE FROM THE FRIEDEL-CRAFTS REACTION OF 1,1-BIS(BROMOMETHYL)CYCLOHEXANE WITH BENZENE

## Abstract

The Friedel-Crafts reaction of 1,1-bis(bromomethyl)-cyclohexane with benzene in the presence of aluminum chloride produces more than twenty products. Studies at various reaction times show that the relative concentration of one product increases with time to as much as 40% of the mixture, and then decreases, while the concentrations of many of the other products grow slowly, even after the starting material is consumed. This indicates that this one product is the major primary product which, after it is formed, reacts further to form many of the secondary products. This primary product is isolated by preparative gas chromatography and its structure established by spectroscopy and a comparison of its properties with a synthetically prepared sample to be 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene.

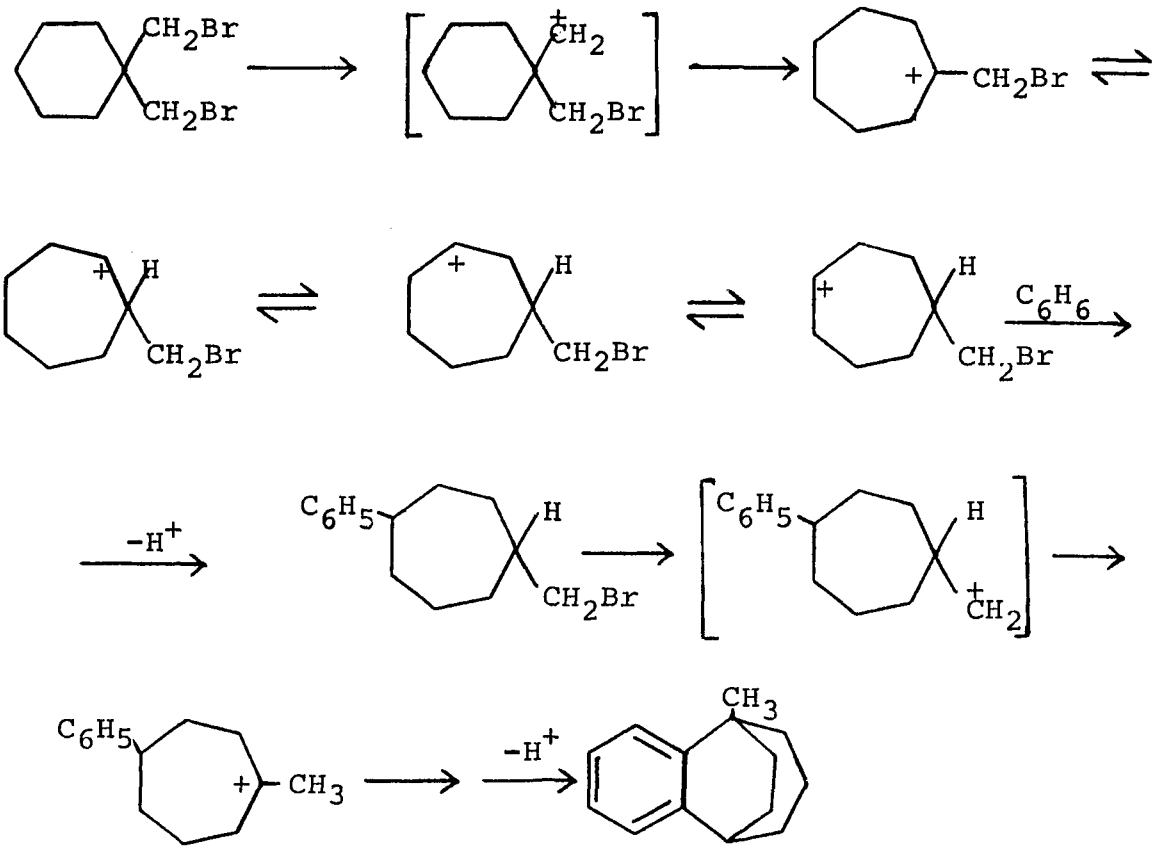
Many possible mechanisms for this reaction are proposed and examined. Gas chromatographic analyses of aliquots during the Friedel-Crafts reaction of 1-bromo-1-bromomethylcycloheptane show that the increase and later decrease of the primary product and the increase of the other products are essentially the same as for 1,1-bis-(bromomethyl)cyclohexane. This is interpreted to mean that the 1-bromomethylcycloheptyl cation, possibly formed from a ring expansion of the incipient 1-bromomethylcyclohexylmethyl cation, is an intermediate in the reaction.

That 1-bromo-1-methyl-4-phenylcycloheptane and/or the corresponding 1-methyl-4-phenylcycloheptyl cation is an intermediate in the reaction is suggested by the fact that the major product of the Friedel-Crafts reaction of this bromide is the primary product.

The fact that the product of the reaction of 1,1-bis-(bromomethyl)cyclohexane in benzene-$d_6$ gives no aliphatic deuterium incorporation is interpreted to mean that deprotonation-protonation steps do not intervene in the reaction pathway.

Analyses of the P - methyl regions of the mass spectra of primary products formed from the Friedel-Crafts reactions of 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane, 1,1-bis(bromodideuteriomethyl)cyclohexane, 2,2,3,3,5,5,6,6-octadeuterio-1,1-bis(bromomethyl)cyclohexane, and 2,2,6,6-tetradeuterio-1,1-bis(bromodideuteriomethyl)cyclohexane show that a large proportion of the third hydrogen (deuterium) of the methyl group originates from the 2-position of the 1-bromomethylcycloheptyl cation, with lesser amounts from further removed positions.

The mechanism suggested which best fits all the evidence is as follows:




This mechanism is tested by studying the Friedel-Crafts reaction of 1-bromomethyl-4-phenylcycloheptane, a possible intermediate in this mechanism. It is found that this bromide gives almost exclusively primary product.

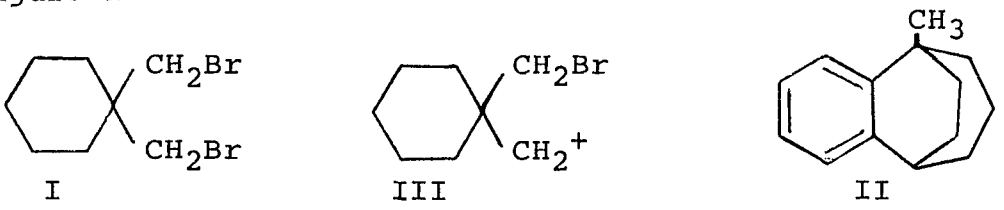
# INTRODUCTION

## Definition of the Problem

Previous work in these laboratories[1] has been carried out on the Friedel-Crafts reaction of 1,1-bis(bromomethyl)-cyclohexane (I) with benzene in the presence of aluminum chloride. This system is interesting because, upon ionization under the reaction conditions, it can produce an incipient 1-bromomethylcyclohexylmethyl cation (III)* with the combined elements of (a) a neopentyl system which is very prone to β-alkyl shifts and (b) a cycloalkylcarbinyl system which should show competition between ring expansion and hydride shifts from various positions on the ring and the side chain. This reaction was studied in order to investigate the relative importance of the various rearrangements that cation III can undergo (Figure I).

*It is generally accepted that Friedel-Crafts reactions proceed by way of carbonium ion or carbonium ion-like intermediates.[2] It would be expected that the tendency to form free ions would decrease as the stability of the potential ion decreased. Thus, tertiary halides would tend more towards the formation of free ions than would primary halides. A range of situations can exist from complete dissociation to form free ions to only a slight bond stretching before alkylation occurs. We would expect the Friedel-Crafts reactions of primary halides to be closer to the latter case or perhaps to involve tight ion-pairs. In this thesis, for simplicity of presentation and in order to avoid cumbersome wording, no attempt is made to specify the exact structures of the intermediates. Less stable intermediates such as those arising from a primary halide will be referred to as incipient ions, while more stable intermediates, as from tertiary halides, will be referred to only as ions.

Figure I




It was shown[1] by gas chromatography that the reaction produces more than twenty products. Studies at various reaction times showed that the concentration of one product increased with time and then decreased, whereby the concentrations of many of the other products grew slowly, even after the starting material was consumed. This seemed to indicate that this one product is the major primary product which, after it is formed, reacts further to form many of the other secondary products. By carefully controlling the reaction conditions (relative concentrations of dibromide (I), benzene, and aluminum chloride; reaction temperature; and reaction time), the relative concentration of this primary product could be maximized to about 40% of the total mixture.

This primary product (II) was isolated by preparative gas chromatography and its structure shown by spectroscopy and a comparison of its properties with a synthetically prepared sample, to be 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene (II). A very extensive rearrangement has occurred during the reaction. It is the purpose of the present work to examine this rearrangement and to ascertain what mechanism or mechanisms are involved in the formation of the

primary product (II), thereby obtaining some insight as to the relative importance of the possible rearrangement pathways.

The initial intermediate from 1,1-bis(bromomethyl)cyclohexane would be the incipient 1-bromomethylcyclohexylmethyl cation (III). Before we can propose any specific mechanisms for the formation of primary product, it is necessary to examine this carbocation in the light of previous work reported in the chemical literature. The unstable primary carbocation could rearrange via (a) a 1,2-shift of the bromomethyl group, (b) a 1,3-hydride shift of a bromomethyl hydrogen, (c) a hydride shift from any of the positions on the ring, (d) ring expansion, or (e) it could alkylate benzene directly. Each of these possibilities will now be examined separately. General analogies to similar rearrangements in similar systems will be cited.

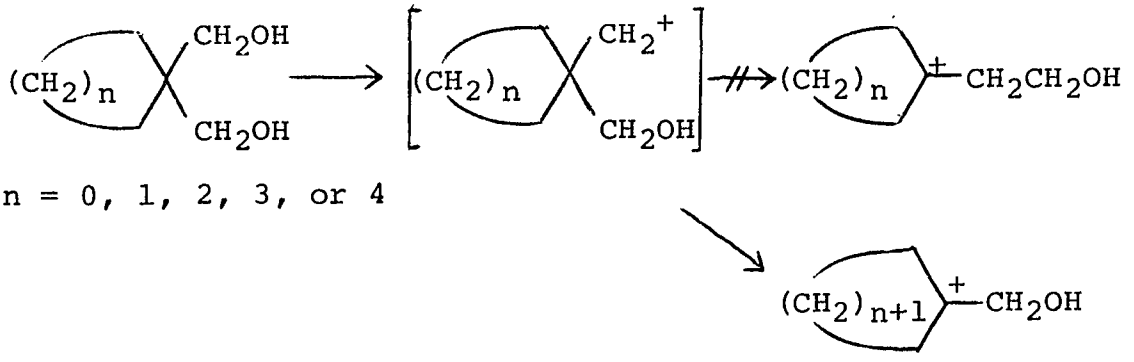
It should be noted that no attempt is being made here to establish direct proof of the possibility of a particular step occurring. Differences in solvents, reaction conditions, structure of the substrates, catalysts, etc., make this impossible. The examples cited are only meant to provide some insight to the various pathways. Specific mechanisms along with arguments for and against specific steps within these mechanisms will be discussed in the Results and Discussion Section of this thesis.

## Possible Rearrangements Involving the Incipient 1-Bromomethylcyclohexylmethyl Cation (III)

### (A) A Shift of the Bromomethyl Group

The first possibility of rearrangement of the 1-bromomethylcyclohexylmethyl cation (III) is the migration of the bromomethyl group. This group is more electronegative than an alkyl group. A comparison can be made with the acid catalyzed rearrangement of 1,1-bis(hydroxymethyl)cycloalkanes of three- to seven-membered rings which gave no products consistent with migration of a hydroxymethyl group to the primary incipient carbocation (Scheme i).[3]

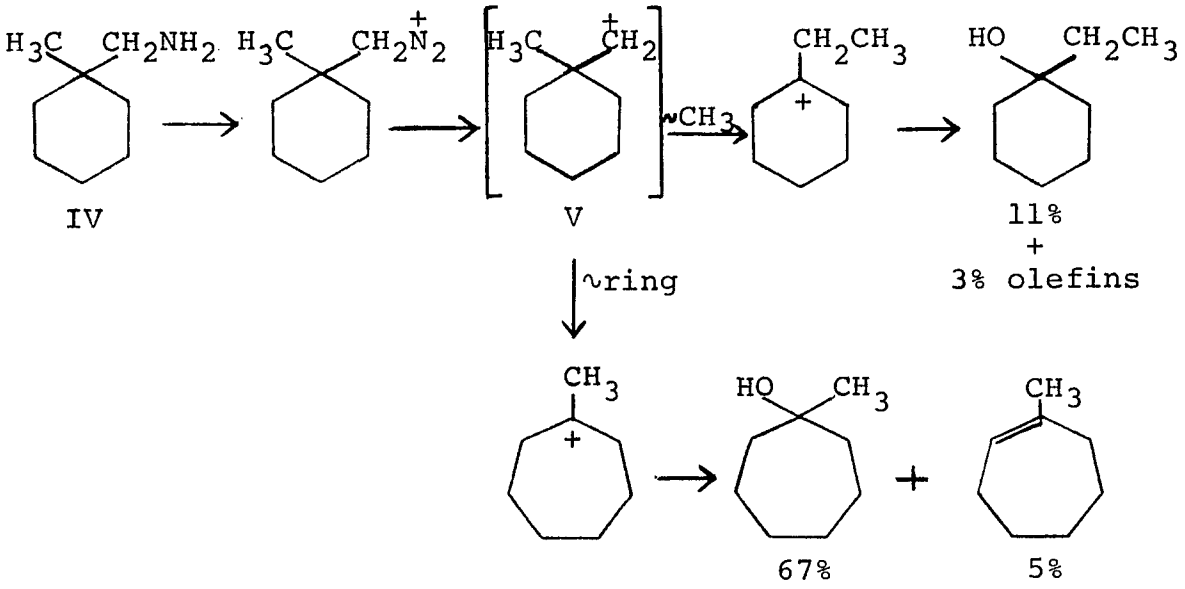
Scheme i




In the diazotization of 1-methylcyclohexylmethylamine (IV), the rearrangement of the resulting incipient 1-methylcyclohexylmethyl cation (V) involves a competition between 1,2-migration of a methyl group to form the ethylcyclohexyl cation and ring expansion to the methylcycloheptyl cation.

Each pathway involves a rearrangement from a primary to a tertiary carbocation. The ratio of the latter pathway to the former is 72:14 (Scheme ii).[4]

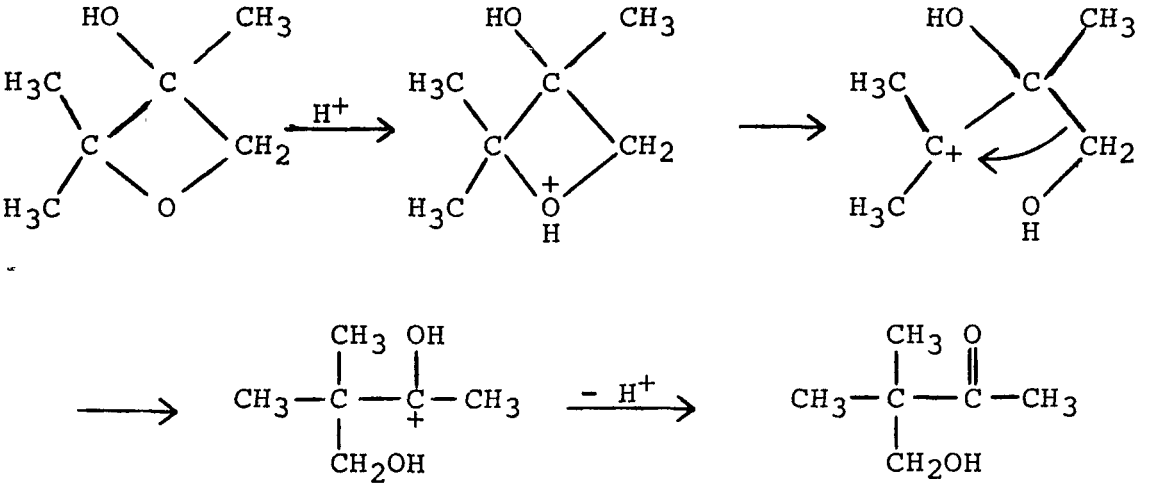
Scheme ii




It seems reasonable to assume that the electronegative bromomethyl group should compete less favorably with the ring expansion. The methyl group of V migrates only to the extent of 14%; the bromomethyl group migration should be even less important.

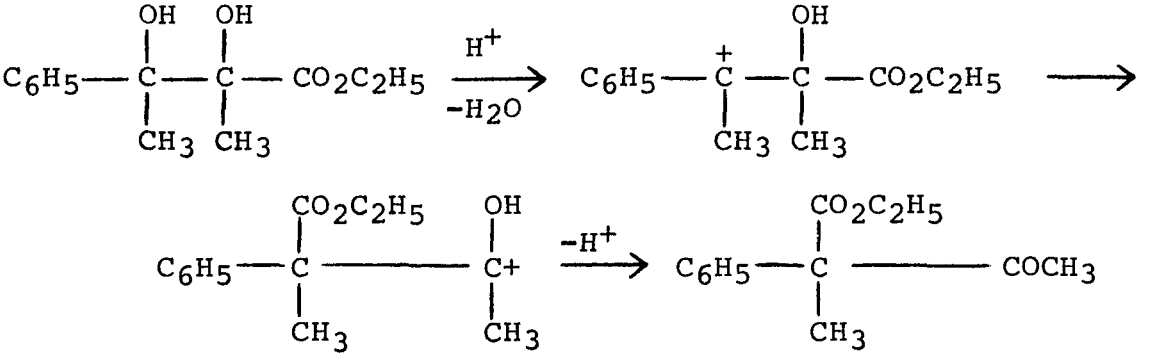
Although relatively rare, there are a few cases reported of electronegative groups migrating toward a carbocation center.[5] Such a case is the conversion of 2,2,3-trimethyl-3-oxetanol to 3-methyl-3-hydroxymethyl-2-butanone via the shift of a hydroxymethyl group (Scheme iii).[6]

Scheme iii



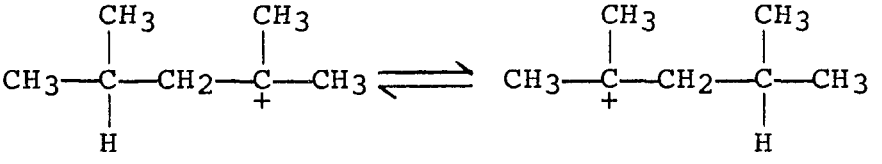
Another example is the migration of an ethoxycarbonyl group in the pinacol rearrangement (Scheme iv).[7]

Scheme iv



(B) A 1,3-Hydride Shift from the Bromomethyl Group

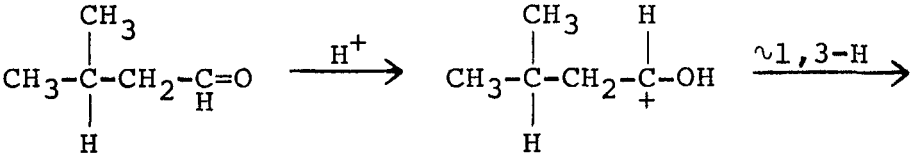
Another possibility for rearrangement of the incipient 1-bromomethylcyclohexylmethyl cation (III) involves a 1,3-hydride shift of a hydrogen from the bromomethyl group. 1,3-Hydride shifts, direct or through a protonated cyclopropane, have been shown to occur in acyclic systems.[8-15] Saunders and Stofko have reported the direct observance of 1,3-hydride shifts in super acids (Eq. 1).[16]

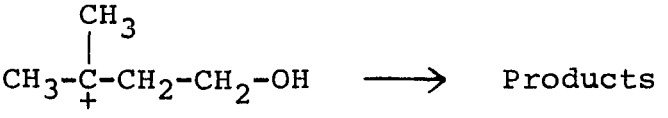


(1)

Brouwer and Kiffen have shown that a 1,3-hydride shift occurs in the acid catalyzed rearrangement of 3-methylbutyraldehyde (Scheme v).[17]

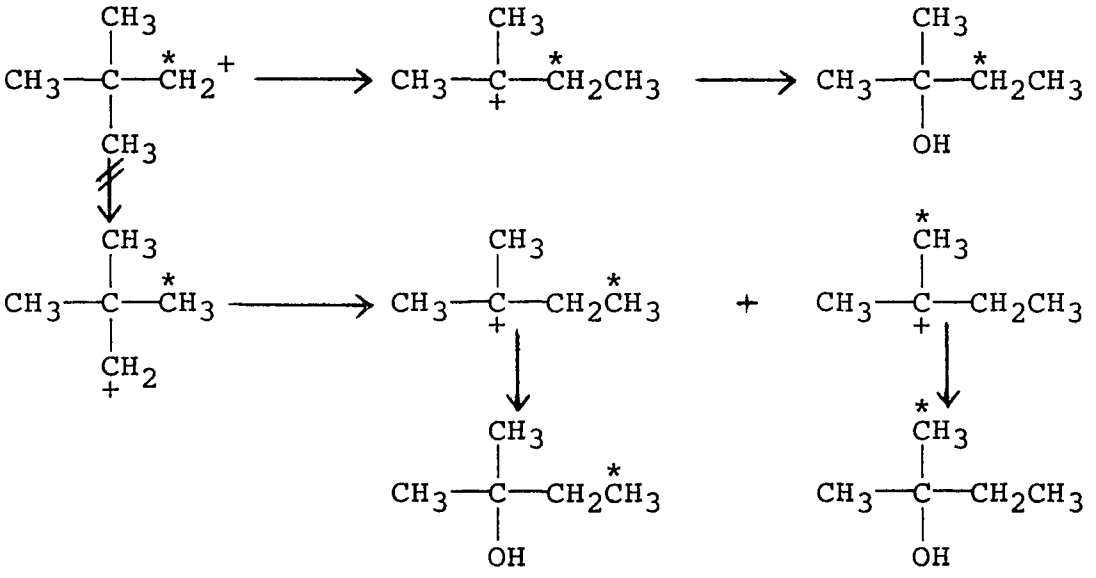
Scheme v





However, 1,3-hydride shifts in neopentyl systems have not been detected. The t-amyl alcohol, obtained from the deamination of neopentyl-1-$^{13}$C and 1,1-dideuterioneopentylamine and from the hydrolyses of neopentyl-1-$^{13}$C and 1,1-dideuterioneopentyl tosylate and neopentyl-1-$^{13}$C iodide, showed the label only at C-3.[18] This is illustrated by Scheme vi.

Scheme vi



The deoxidation of 1,1-dideuterioneopentyl alcohol to give 2-methyl-2-butene and 2-methyl-1-butene[19] and the reaction of neopentyl-1-$^{13}$C alcohol with hydrogen bromide to give 2-methyl-2-butene, 2-methyl-1-butene, and t-amyl bromide[20] both gave products labeled only at C-3.

A shift of a bromomethyl hydrogen in III would yield a cation with a charge on the carbon α to the bromine. Heteroatoms have been shown to stabilize the charge by donation

of unshared pairs of electrons. For bromine this can be demonstrated by the addition of HCl to vinyl bromide to give 1-bromo-1-chloroethane,[21] and by the fact that the rates of hydrolysis of benzyl halides under $S_N1$ conditions are increased by the presence of an α-chlorine or bromine atom via resonance stabilization of the intermediate cation.[22]

Under Friedel-Crafts conditions 1,3-dihalides have been shown not to react via a 1,3-hydride shift. Tsukervanik et al.[23] have shown that 1-bromo-3-chloropropane yields 1-bromo-3-phenylpropane, which reacts further to yield 1,3-diphenylpropane, but no 1-bromo-1-phenylpropane. Reppe et al.[24] and Ransley[25] have found that 1,3-dibromobutane yields only 1-bromo-3-phenylbutane, which reacts further. 1,3-Dichloro-3-methylbutane initially yields only 1-chloro-3-phenyl-3-methylbutane.[26]

(C) A Transannular Hydride Shift

The next possibility is the migration of a hydrogen from any of the positions of the ring to the exomethylene group. For a transannular hydride shift to occur two major criteria must be met - (a) a close proximity of the migrating hydrogen to the carbon bearing the positive or incipient positive charge and (b) a favorable geometric arrangement which meets the stereoelectronic requirements of the transition state for the shift by allowing a maximum overlap of electron density of the migrating hydrogen with the empty p-orbital of the migration terminus.

The simplest and most frequently observed hydride shift is the 1,2-hydride shift to a positive carbon atom. Here, the migrating atom is quite close and easily interacts with the positive center. In addition, especially in acyclic systems, this β-hydrogen can relatively easily align itself so that there is a favorable stereochemistry (dihedral angle of 0° or 180°) between the C-H bond and the empty p-orbital.

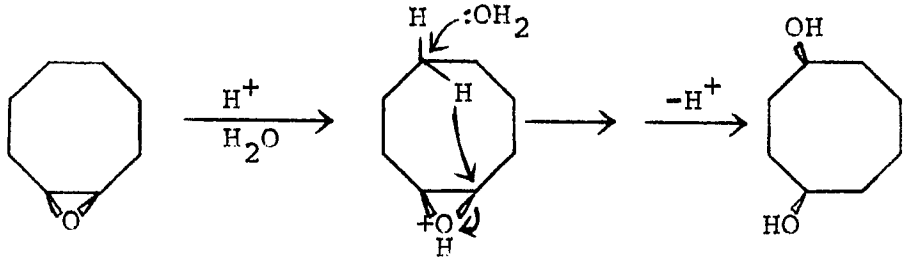
Intramolecular hydride shifts of higher orders, 1,3-, 1,4-, 1,5-, and even 1,6-hydride shifts, can also occur if the stereochemistry is such that the criteria of proximity of the hydrogen to the empty p-orbital and of maximum electron overlap in the transition state are met. For 1,3- and 1,4-hydride shifts the ring strain in the formation of this transition state is greater than for the corresponding

1,5-shift. For higher order shifts there is a greater entropy loss in forming the ring. In acyclic systems a 1,5-hydride shift can occur more easily than a 1,3-shift, a 1,3-shift more easily than a 1,4-shift, and longer range shifts are rare.[27]

In cyclic systems, hydrogens many bonds away from the cation center may be held in position to be in close proximity to the empty p-orbital. Long range transannular hydride shifts are especially favorable in medium rings with eight, nine, ten, eleven, or twelve carbons.[28-30] These systems are flexible enough and of the right size so that they can relatively easily attain a favorable transition state conformation.

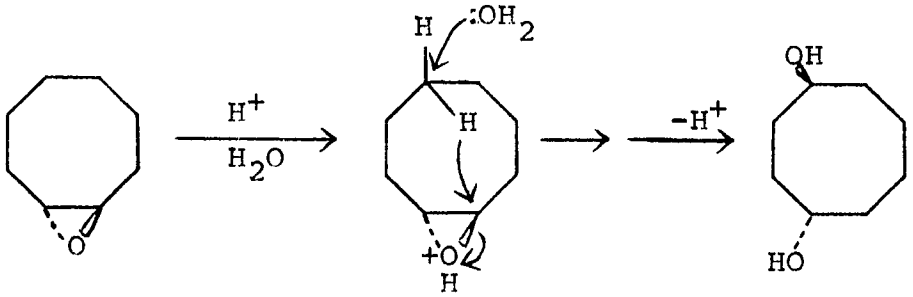
One of the earliest studies of the relationship of geometry to the ability of a system to undergo transannular hydride shifts was carried out by Cope and co-workers.[31,32] The peroxyformic acid oxidation of cis-cyclooctene and the acid hydrolysis of cis-cyclooctene oxide (VI) gave 25-30% cis-1,4-dihydroxycyclooctane (VII) due to a transannular 1,5-hydride shift and 20% of the normal product, trans-1,2-dihydroxycyclooctane.[31] The corresponding trans isomers gave 33% trans-1,4-dihydroxycyclooctane (IX), 1% trans-1,3-dihydroxycyclooctane, and no trans-1,2-dihydroxycyclooctane.[32] The 1,5-hydride shifts in the reactions of the oxides (VI and VIII) are shown in Schemes vii and viii.

Scheme vii



VI VII

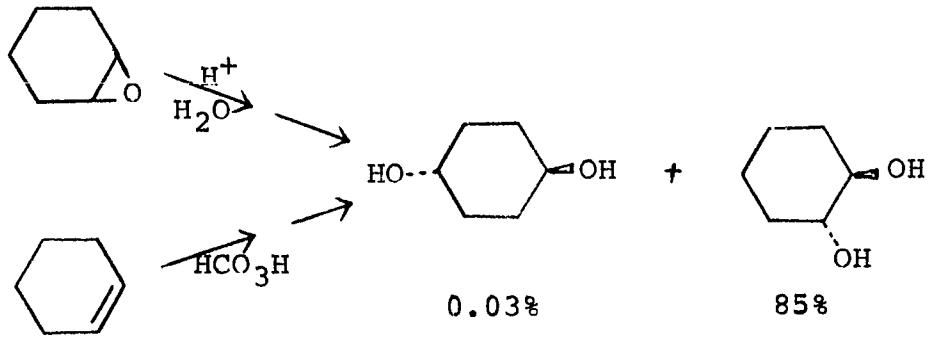
Scheme viii



VIII IX

Cope[33,34] also showed that under the same conditions the cyclohexyl analogs gave only traces of transannular shift products (Scheme ix).

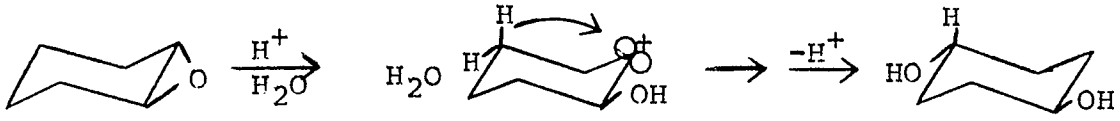
Scheme ix



0.03% 85%

The transannular hydride shift probably occurs via a 1,3-diaxial interaction (Scheme x).

Scheme x



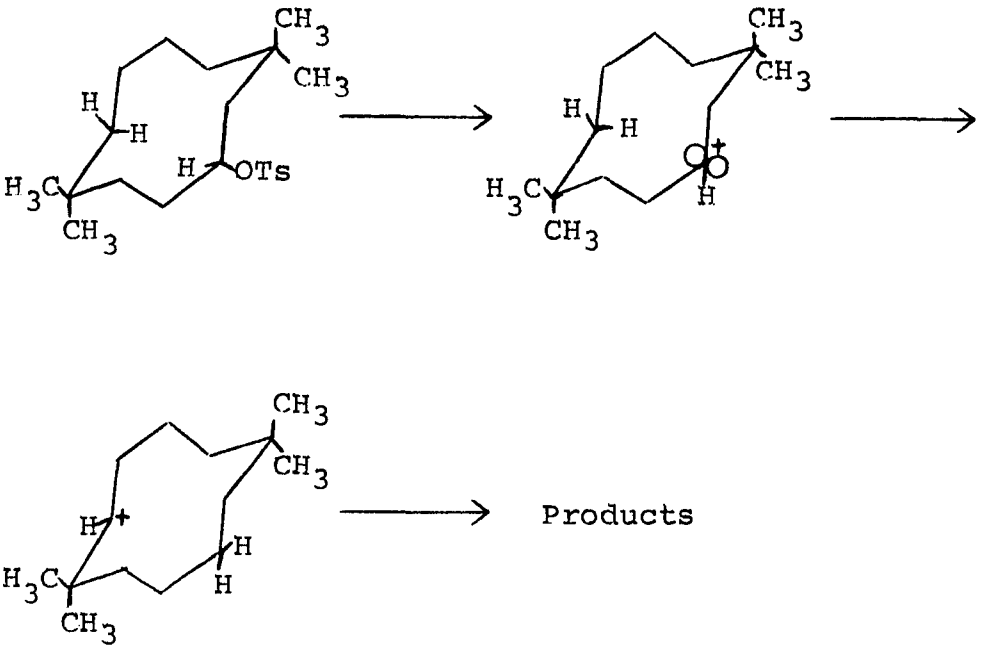
Under the same reaction conditions cis-cycloheptene oxide gave 2.4% trans-1,4-dihydroxycycloheptane via a transannular hydride shift.[35]

Transannular 1,5-hydride shifts have also been reported in the formolysis of cis-5-t-butylcyclooctyl tosylate[36] and cyclooctyl brosylate.[37] In nine- to 12-membered rings, due to the added flexibility, it is possible for several hydrogens to align themselves properly with the p-orbital of the cation center leading to several different transannular shifts.[29]

The proper geometric requirements for the relationship between the hydrogen and the p-orbital for a transannular shift to occur were shown by Prelog et al.[38] in a study of the acetolysis of 3,3,8,8-tetramethylcyclodecyl p-toluenesulfonate. This compound rearranges to the extent of about 13% via a transannular hydride shift. Prelog approximated the structure of the carbonium ion to be close to the most stable conformation of the tosylate. It was pointed out that the hydrogen on C-7 in the preferred conformation is

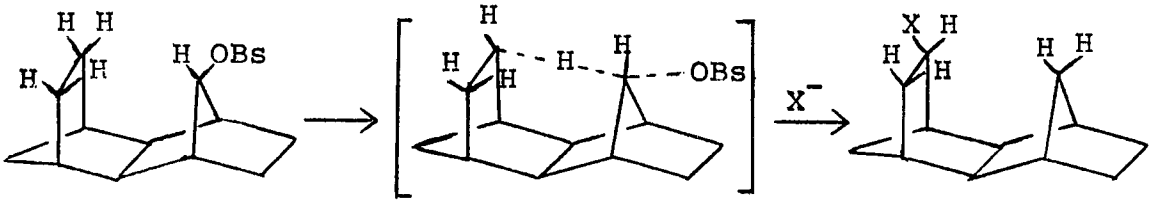
perfectly in line with the p-orbital of the ionized tosylate (Scheme xi).

Scheme xi



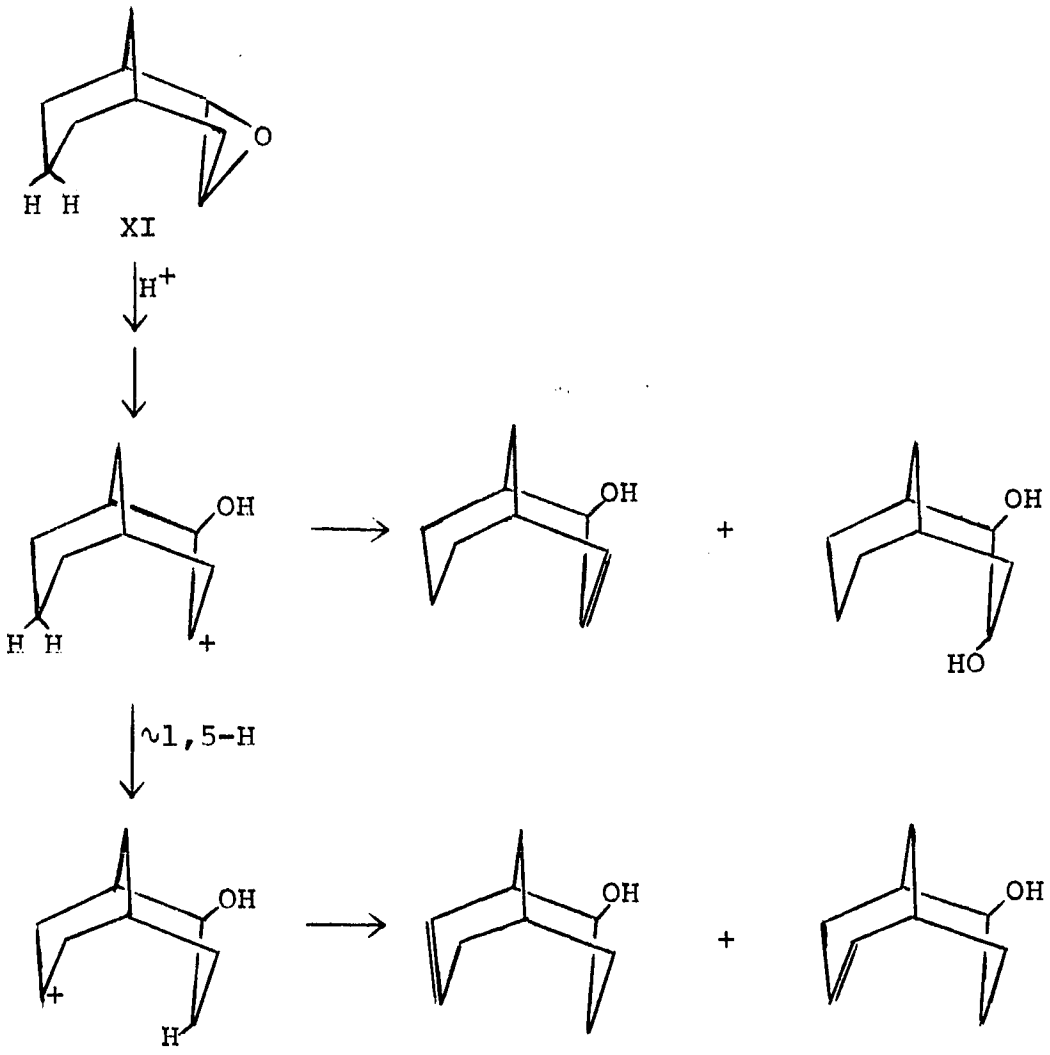

The most favorable case for a transannular shift would be a rigid framework, e.g., a bicyclic system, with the hydrogen across from the developing orbital fixed in a position directly in line with it. Examples include exo-12-brosyloxydecahydrodimethanonaphthalene (X) (Scheme xii),[39] bicyclo[3.3.1]nonan-2β,3β-oxide (XI) (Scheme xiii),[40] and 3α-bromo(7β-H)longifolane (XII) (Scheme xiv).[41]

Scheme xii

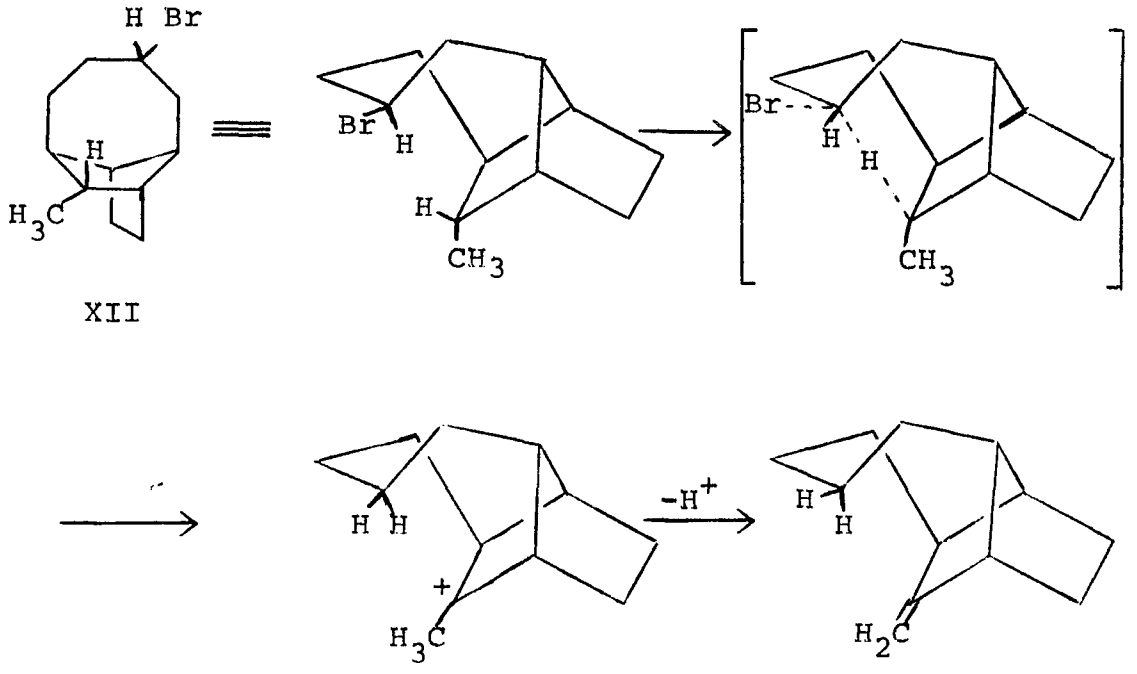



X

Scheme xiii



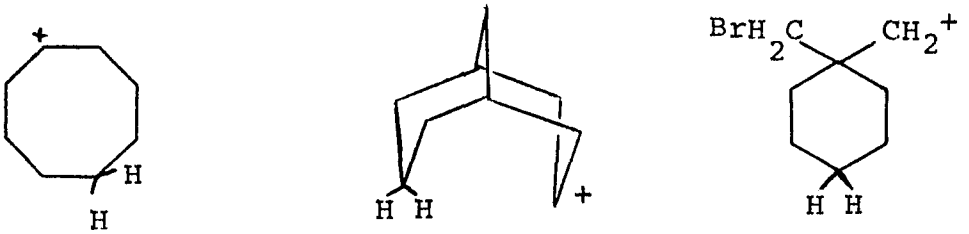
Scheme xiv



XII

We have examined Drieding models of the 1-bromomethylcyclohexylmethyl cation (III) and a variety of compounds that undergo transannular hydride shifts in order to compare the relative proximity of the migrating hydrogens and the p-orbitals of the migration termini. The distance for a 1,5-hydride shift in the incipient carbocations XIII, XIV, and III are 0.6-1.5 Å, 1.9 Å, and 1.8-2.5 Å respectively (Figure II).

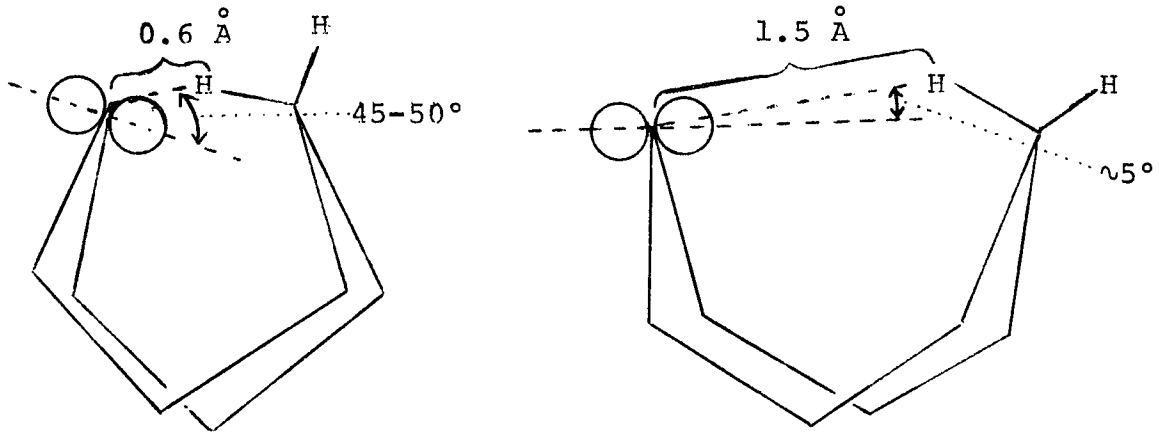
Figure II



XIII XIV III

The ranges for XIII and III reflect a range of conformations that can represent each case. For XIII the conformation that leads to the smallest distance between the hydrogen on C-5 and the migration terminus (conformation $XIII_1$, Figure III) leads to an unfavorable geometric arrangement involving the angle between the incipient p-orbital and a line drawn from the hydrogen to C-1. The importance of these two factors has been discussed on p. 15. In $XIII_1$ the H---$C^+$ distance is about 0.6 Å, but the angle is about 45-50°.

Figure III

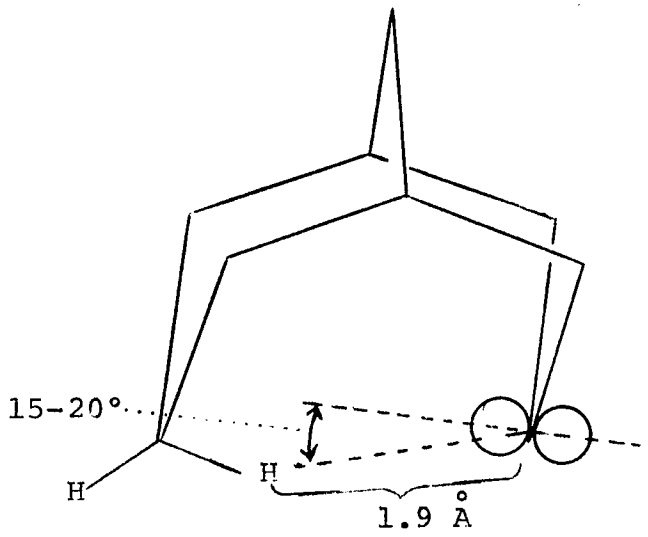



$XIII_1$ $XIII_2$

The conformation by which the best angle, about 5°, can be achieved is $XIII_2$, but the distance between the hydrogen atom and the positive center is about 1.5 Å. The relative stabilities and therefore the relative populations of these and intermediate conformations are not known.

In the chair-chair conformation of the more rigid bicyclic system XIV the distance between the migrating hydrogen atom and the positive center is about 1.9 Å with an angle of about 15-20° (Figure IV). The importance of this conformation relative to other conformations, i.e., the chair-boat or chair-twist boat conformations, is not known.

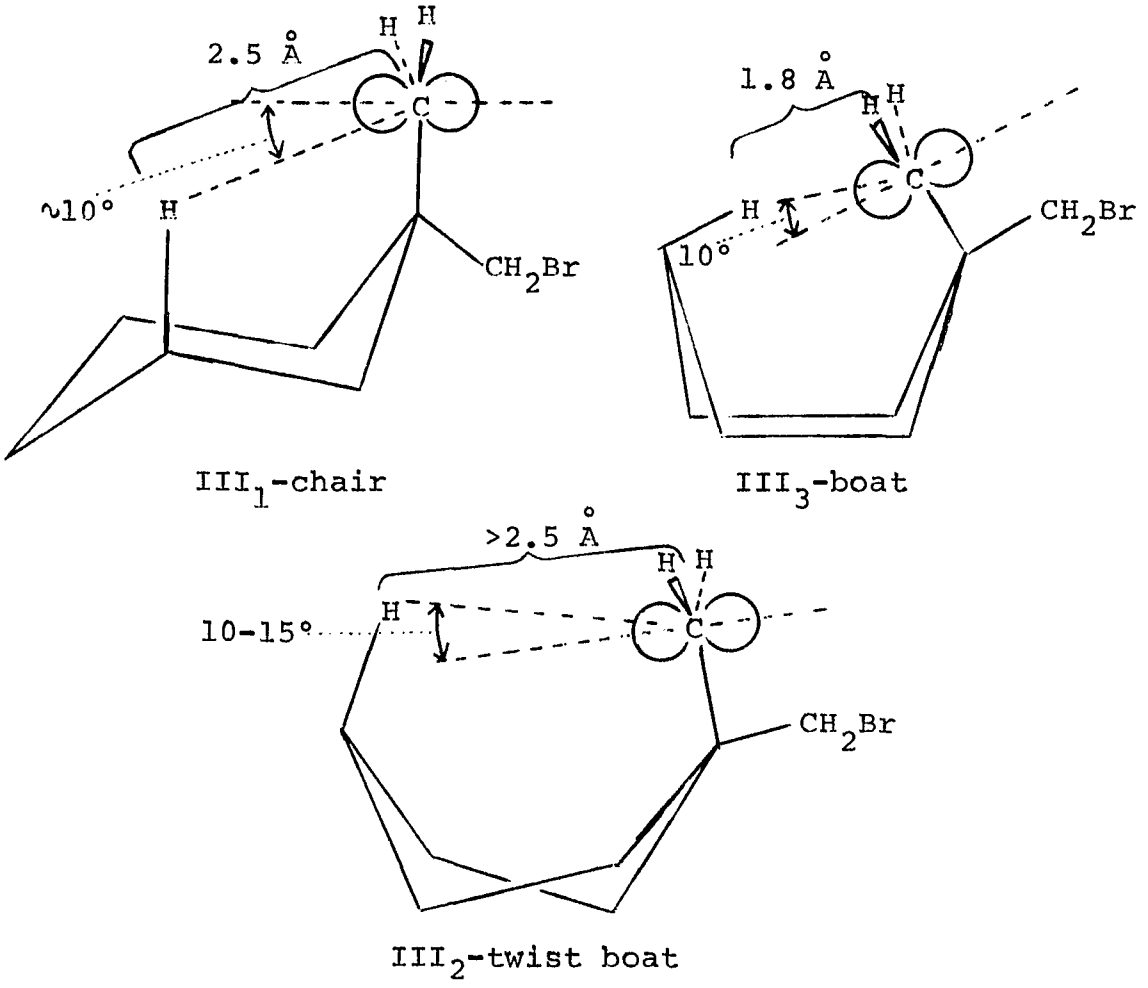
Figure IV




XIV

In the chair conformation of the 1-bromomethylcyclohexyl cation ($III_1$) the hydrogen atom on C-3 (for a 1,4-hydride shift) is 2.5 Å away from the positive carbon and makes an angle of about 10° with the p-orbital (Figure V). This is appreciably greater than the distances between the migrating hydrogen atoms and the positive centers of XIII and XIV. The hydrogens on C-4 (for a 1,5-hydride shift) are not at all in the proximity of the p-orbital.

Figure V




In the twist boat conformation ($III_2$), the hydrogen atom at C-4 is over 2.5 Å away from the exomethylene group with an angle of 10-15°. The hydrogen on C-3 is not at all in the proximity of the positive center.

In the least stable boat conformation the hydrogen atom on C-3 is still too far away from the positive center to be considered for migration. The hydrogen atom on C-4 is approximately 1.8 Å from the cationic center with an angle of about 10° to the p-orbital.

The different conformations of each cation have dif-

fering stabilities and, therefore, different relative populations in the overall picture of each case. If the energy barrier between conformations is small relative to the energy barrier of the rearrangement, then the equilibrium between conformers will not appreciably affect the rearrangement.[42]

For a transannular hydride shift to occur there must be a reasonably small H---$C^+$ distance, the geometric arrangement of the hydrogen atom and the p-orbital must be proper, and the relative energies of the conformers and their rate of interconversion compared to the rate of reaction must be considered. The relative importance of these factors in XIII and XIV is not known.

We cannot estimate the relative importance of these factors in our system (III), which may or may not have the same balance as XIII and XIV. It is, therefore, not possible for us to reach a firm conclusion on the likelihood of a 1,5- or a 1,4-transannular hydride shift in the 1-bromomethylcyclohexylmethyl cation (III), other than to point out that the distances and the geometries involved do not appear unreasonable.

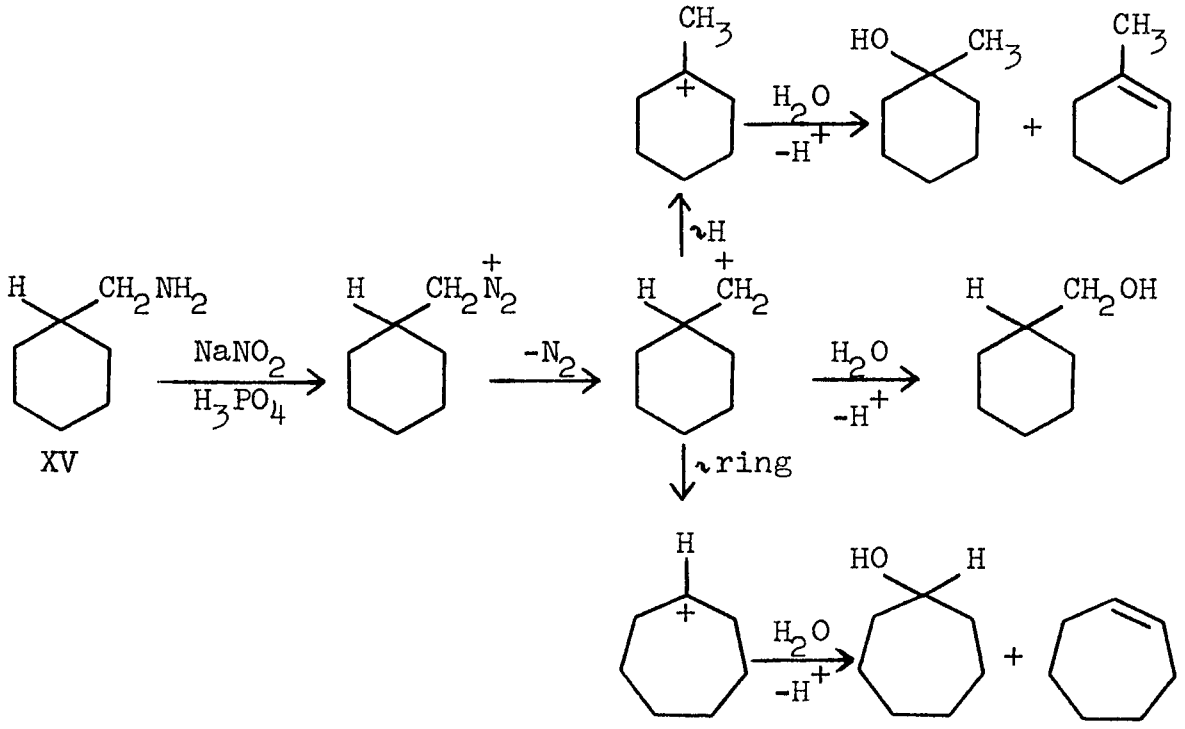
(D) Ring Expansion

Ring expansion of the cycloalkylmethyl system is usually very favorable. Studies of cyclohexylmethyl substrates under a variety of conditions have shown that the preferred mode of rearrangement is ring expansion to the cycloheptyl system, thus converting the relatively unstable incipient primary carbocation to a more stable one.

With other cycloalkylmethyl systems, the three-, four-, and five-membered rings give almost exclusively ring expansion products. The six-membered ring seems to be a borderline case, depending upon the reaction conditions and the leaving group. Here there is a competition between ring expansion and alkyl or hydrogen migrations.

The diazotization of cyclohexylmethylamine (XV)[43,44,45] yields cycloheptanol as the major product, despite the fact that it is formed through a secondary carbocation while a 1,2-hydride shift would give a more stable tertiary ion (Scheme xv).

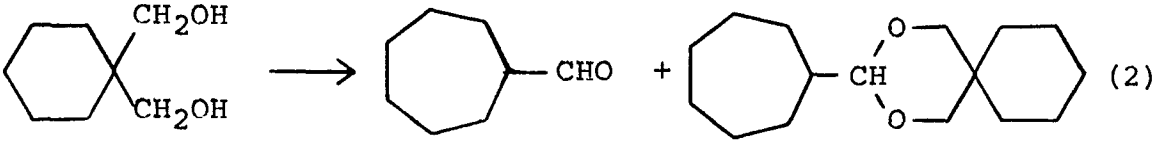
Scheme xv




Substitution at C-1 which leads to the formation of a more stable cycloheptyl cation compared to the situation with XV, relative to ions formed from other rearrangements of the primary ion, increases the amount of ring expansion. It has already been pointed out (p. 10) that 1-methylcyclohexylmethylamine (IV) gives 72% ring-expanded products.[4]

It seems reasonable to expect that where there is a substituent which could better stabilize the ring expanded cation, that the ring expansion would become even more favorable. Therefore, upon diazotization 1-aminomethylcyclohexanol gives almost exclusively cycloheptanone.[46]

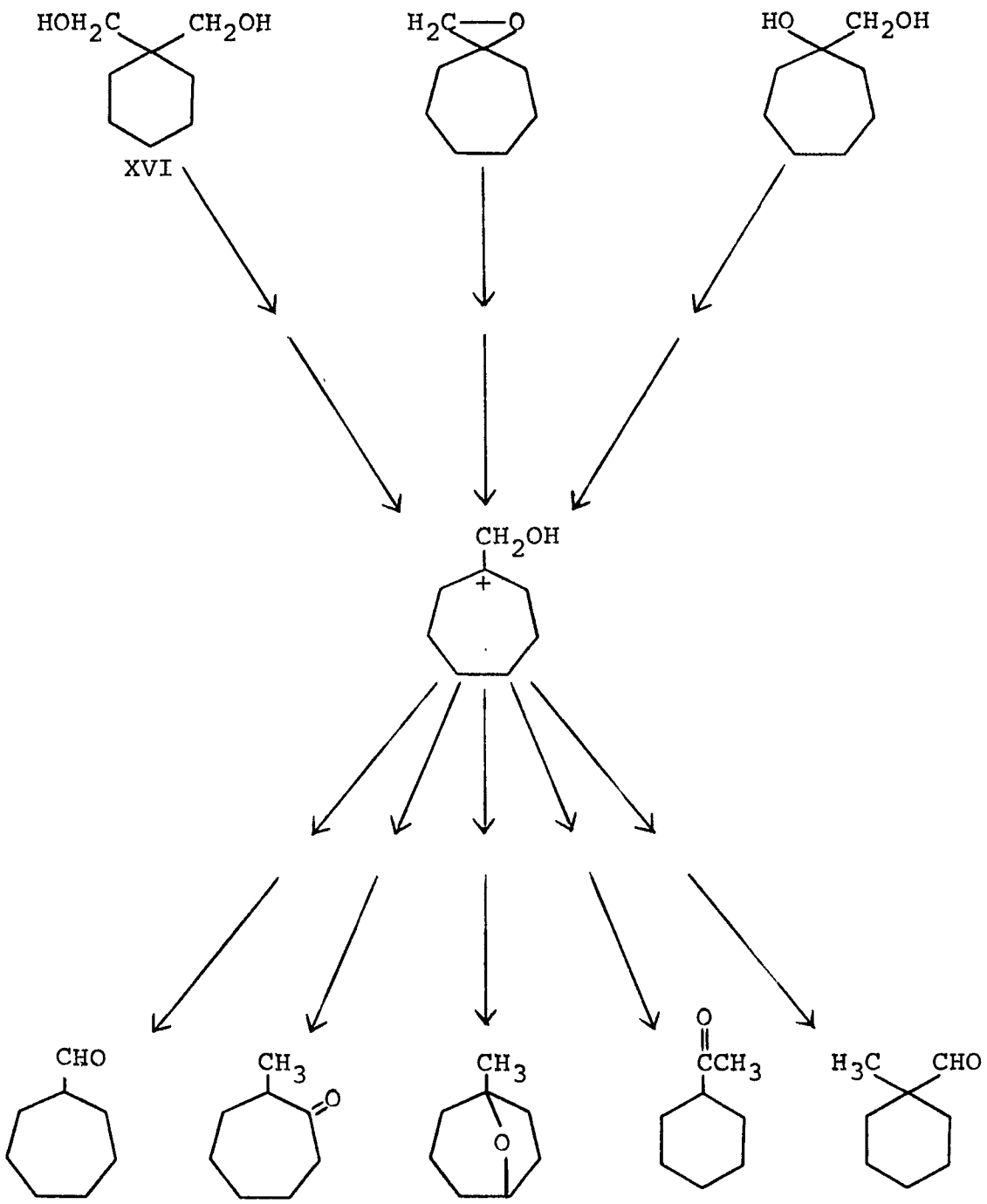
The dehydration with sulfuric acid of 1,1-bis(hydroxymethyl)cyclohexane (XVI) proceeds by ring expansion to give cycloheptane carboxaldehyde and the acetal of this aldehyde and the starting diol (Eq. 2).[3]




XVI (2)

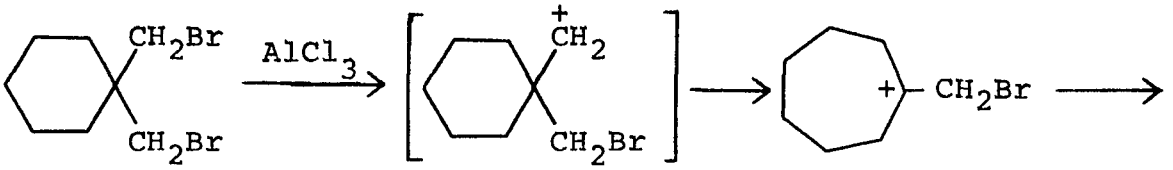
Under greater acidity and higher temperature the dehydration of 1,1-bis(hydroxymethyl)cyclohexane (XVI) has been shown to produce five major products, three of which involve a ring expansion. The possibility of the intermediacy of the 1-hydroxymethylcycloheptyl cation was suggested by the fact that 1-oxaspiro[2.6]nonane and 1-hydroxymethylcycloheptanol give the same five major products (Scheme xvi).[47,48]

Scheme xvi


HOH2C
CH2OH
XVI
H2C
O
HO
CH2OH
CH2OH
+
CHO
CH3
O
CH3
O
O
CCH3
H3C
CHO

From the preceding examples, it seems probable that the incipient 1-bromomethylcyclohexylmethyl cation (III) should undergo ring expansion to the 1-bromomethylcycloheptyl ion (XVII) (Scheme xvii).

Scheme xvii




I III XVII

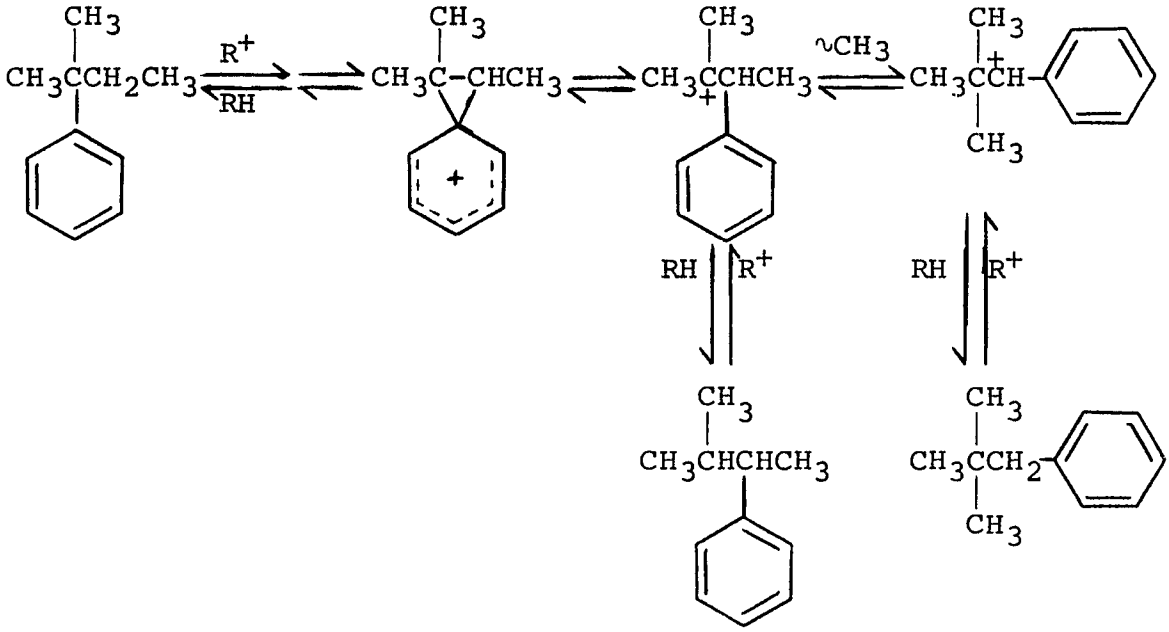
(E) Direct Alkylation of Benzene

The last possibility to be considered for reaction of the 1-bromomethylcyclohexylmethyl cation (III) is direct alkylation of benzene. Dibromide I can be considered as a substituted neopentyl system. Under a variety of conditions neopentyl systems rearrange almost exclusively to the t-pentyl ion before yielding final products.[9-11,18-20]

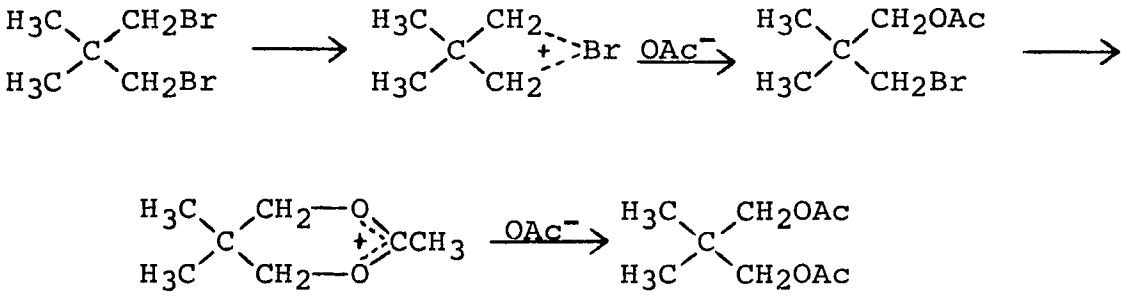
When treated under Friedel-Crafts conditions, neopentyl alcohol yields t-pentylbenzene as the major[9] or almost exclusive product.[49,50] More recently it has been shown that the small amount of neopentylbenzene formed in these Friedel-Crafts reactions is not produced by direct reaction with a neopentyl precursor.[51] The initial product is t-pentylbenzene, which rearranges under the reaction conditions to form neopentylbenzene and sec-pentylbenzene (Scheme xviii).

Yet, the reaction of 2,2-dimethyl-1,3-dibromopropane with silver acetate yields 2,2-dimethyl-1,3-diacetoxypropane.[52] A mechanism involving neighboring group participation has been proposed to explain this lack of rearrangement (Scheme xix).[53] It is possible that the bromine of the incipient 1-bromomethylcyclohexylmethyl cation (III) may participate similarly to allow alkylation at the primary center directly without rearrangement. Therefore, this possible pathway cannot be dismissed out of hand.

Scheme xviii



Scheme xix



# RESULTS

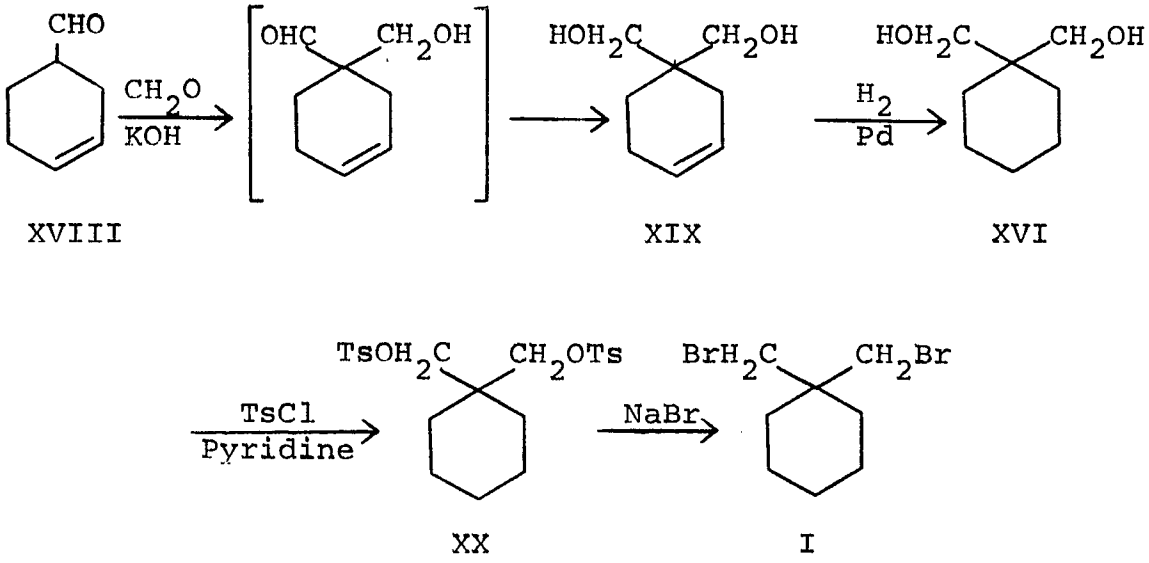
# AND

# DISCUSSION

Preparation of Starting Material (I) and Primary Product (II)

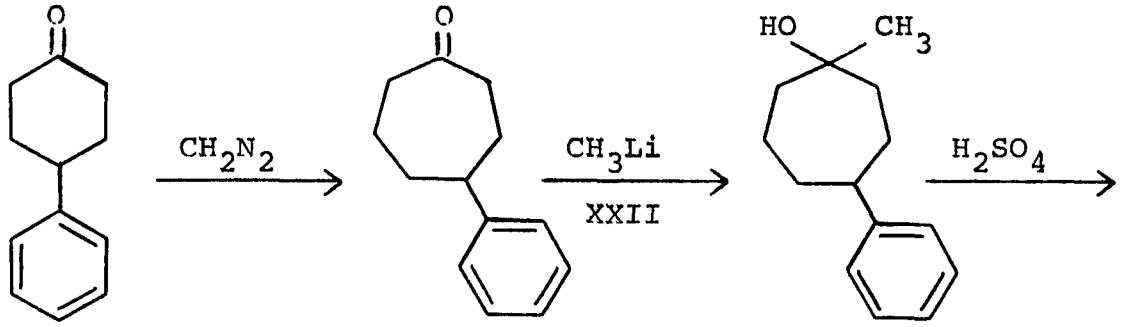
1,1-Bis(bromomethyl)cyclohexane (I) was prepared by the sequence of steps described in Scheme xx.[1]

Scheme xx

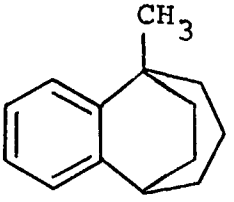



The primary product of the reaction of 1,1-bis(bromomethyl)cyclohexane (I) with benzene and aluminum chloride was isolated by preparative glc as described in the Experimental Section, p. 228. The structure was established by synthesis as 1-methyl-6,7-benzobicyclo[3.2.2]non-6-ene (II) using the sequence of steps shown in Scheme xxi.[1]

Scheme xxi




XXI XXIII




II

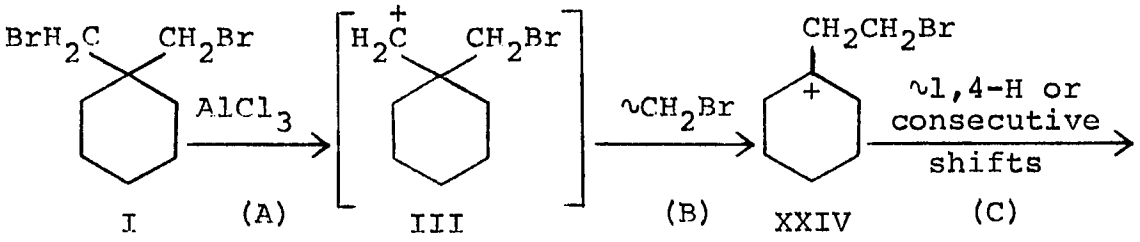
## Consideration of General Mechanistic Schemes

A rather extensive rearrangement apparently occurs in the conversion of 1,1-bis(bromomethyl)cyclohexane (I) to the primary product (II). A hydrogen migrates to a methylene carbon to form the methyl group, the six-membered ring expands to a seven-membered ring, and a positive charge from the reaction of at least one of the bromines with the Lewis acid migrates across the ring, via one or more hydride shifts before or after the ring expansion, to allow the benzene to be alkylated by widely separated ring positions.

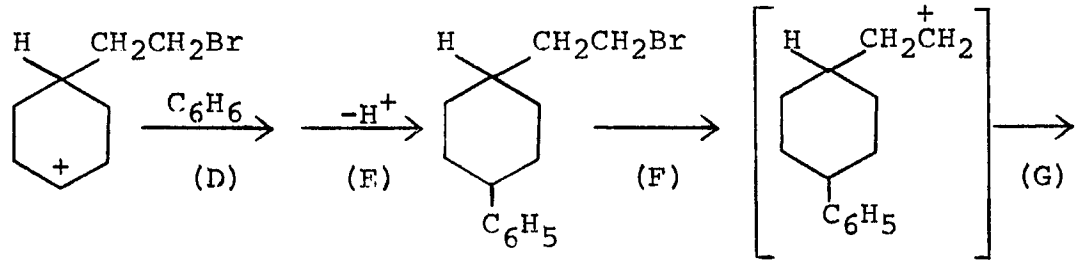
We have considered many possible mechanisms for this reaction. These may be grouped into a few general types according to what happens to the incipient 1-bromomethylcyclohexylmethyl cation (III). They are: (a) a 1,2-shift of the bromomethyl group, (b) a 1,3-hydride shift of a bromomethyl hydrogen, (c) a hydride shift from any of the positions of the ring, (d) ring expansion, or (e) direct alkylation of benzene. Representative examples of these general types of mechanisms are given in Scheme xxii.

Scheme xxii

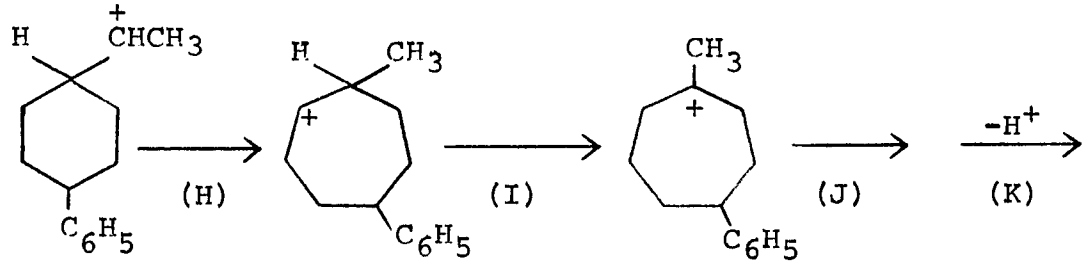
Mechanism I - A 1,2-Hydride Shift of a Bromomethyl Group



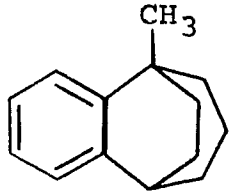

I III XXIV




XXV XXVI XXVII



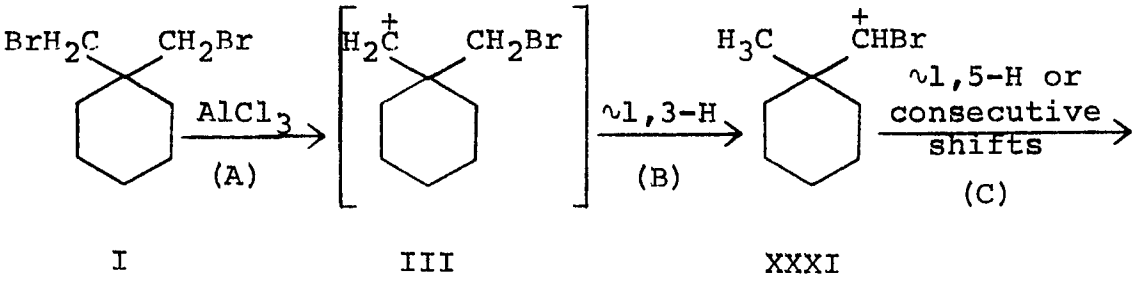

XXVIII XXIX XXX



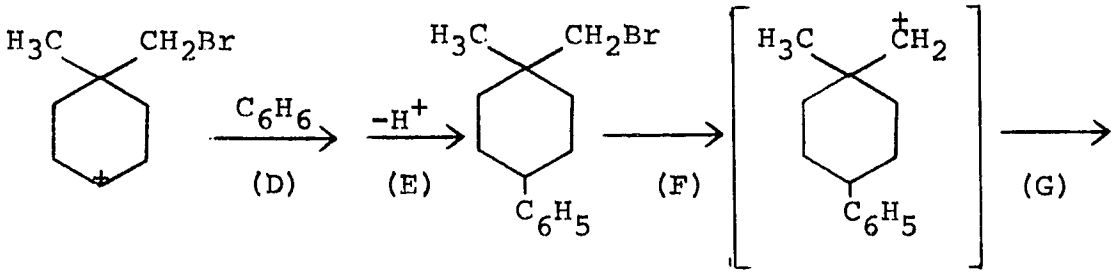

II

Scheme xxii (cont'd.)

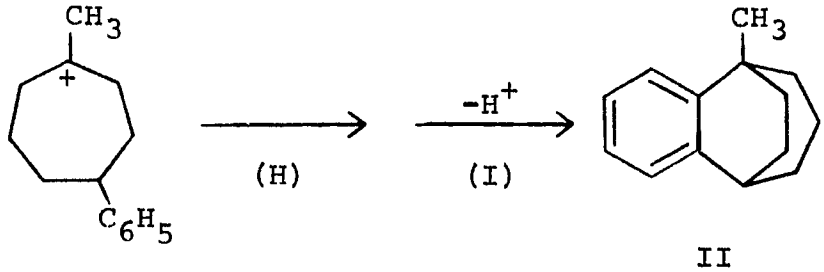
Mechanism II - A 1,3-Hydride Shift of a Bromomethyl Hydrogen




I III XXXI



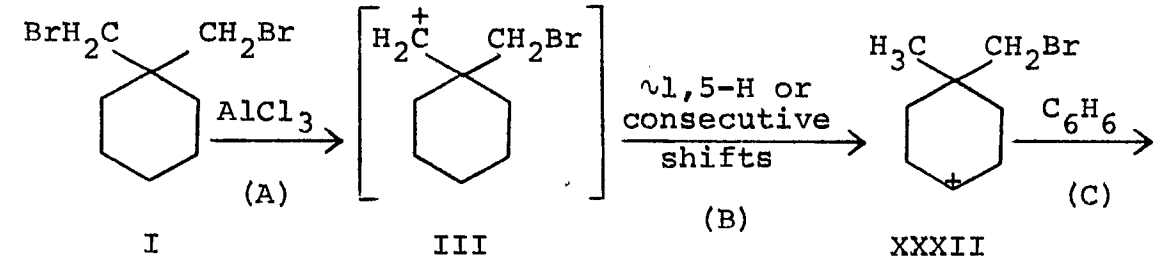

XXXII XXXIII XXXIV



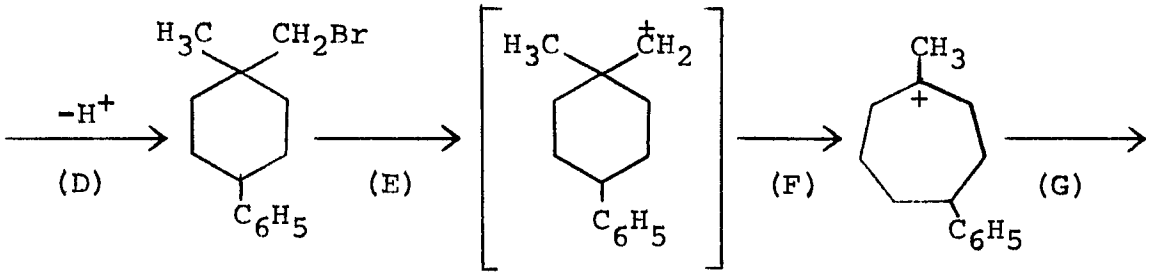

II

Scheme xxii (cont'd.)

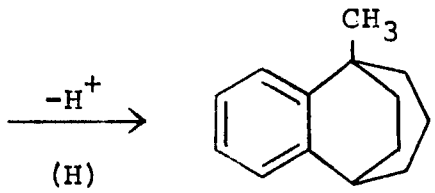
Mechanism III - A Hydride Shift from the Ring




I III XXXII



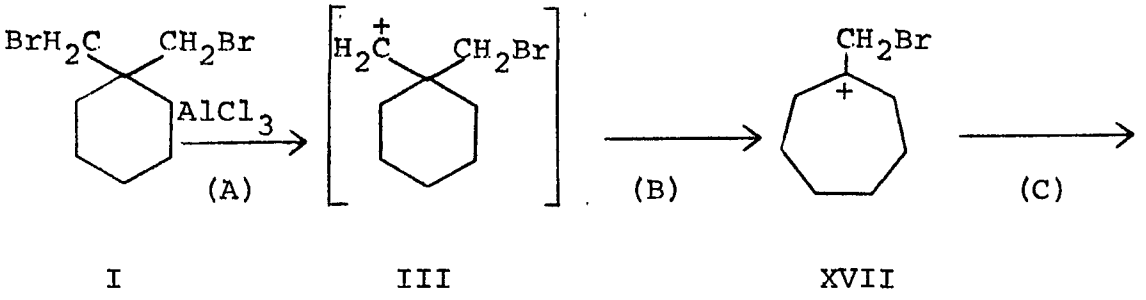

XXXIII XXXIV XXX



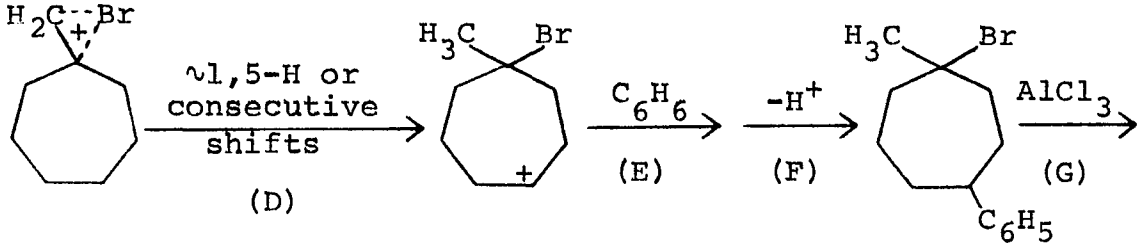

II

Scheme xxii (cont'd.)

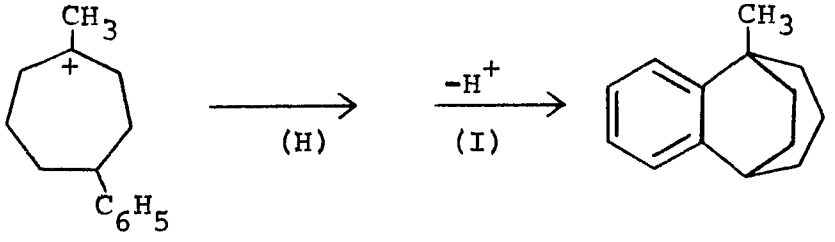
Mechanism IV - Ring Expansion, a Methylenecycloheptane Bromonium Ion




I III XVII



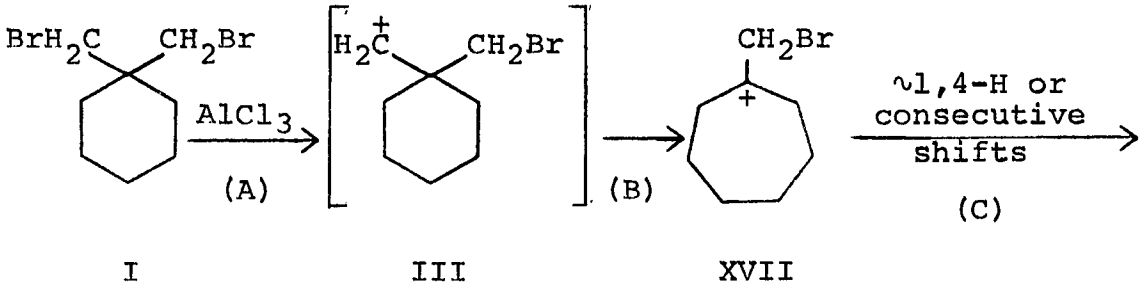

XXXV XXXVI XXXVII



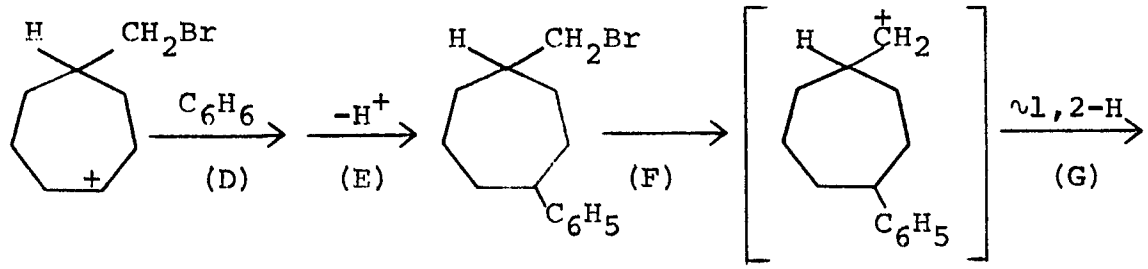

XXX II

Scheme xxii (cont'd.)

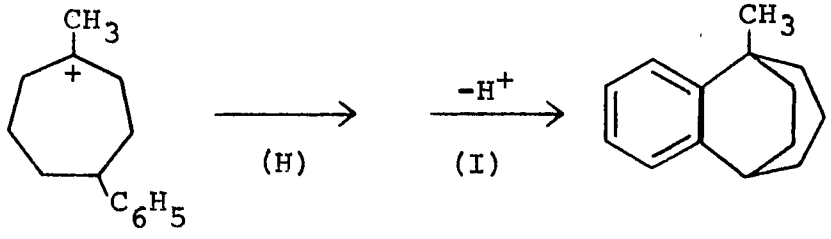
Mechanism V - Ring Expansion, a Hydride Shift from C-1 of the Incipient 4-Phenylcycloheptylmethyl Cation (XL)




I III XVII



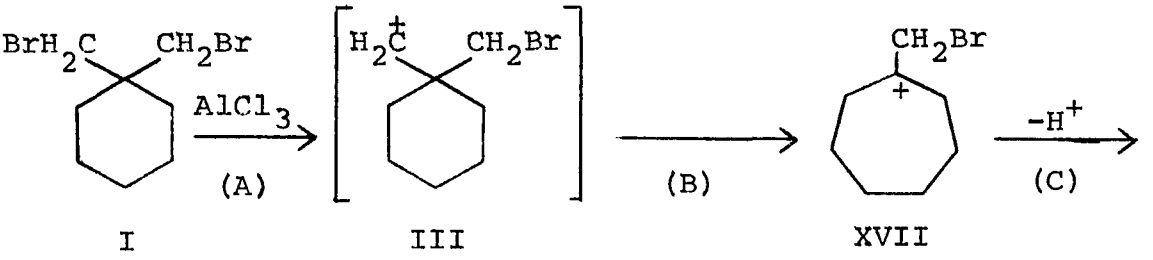

XXXVIII XXXIX XL



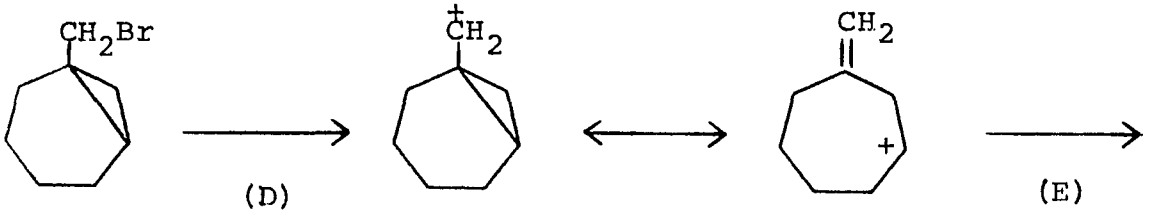

XXX II

Scheme xxii (cont'd.)

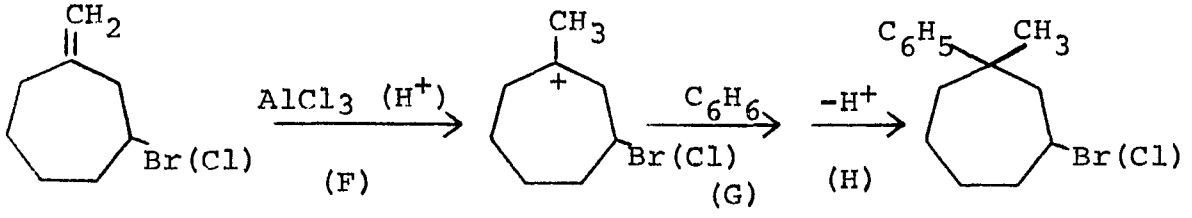
Mechanism VI - Ring Expansion, Solvent Hydrogen Incorporation



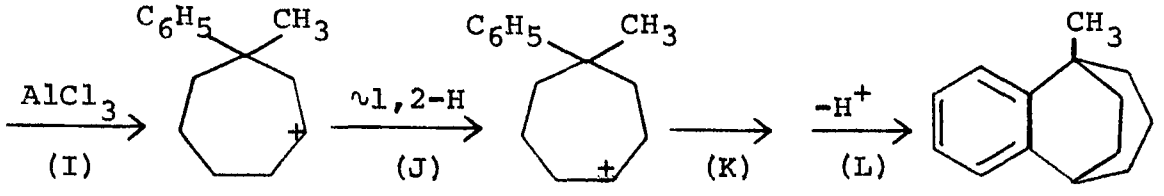

I III XVII




XLI XLII XLIII



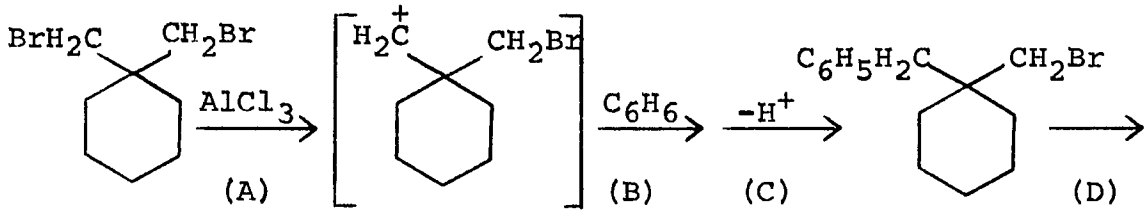

XLIV XLV XLVI



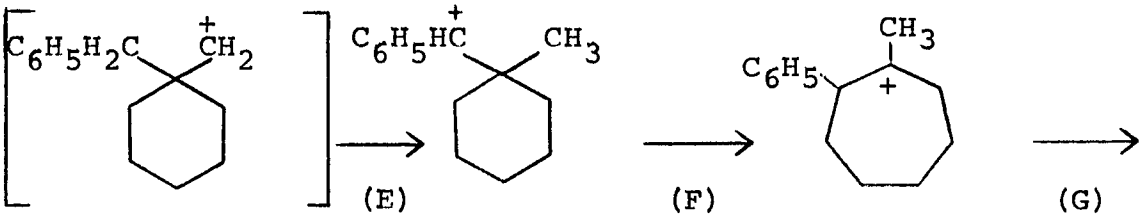

XLVI XLVIII II

Scheme xxii (cont'd.)

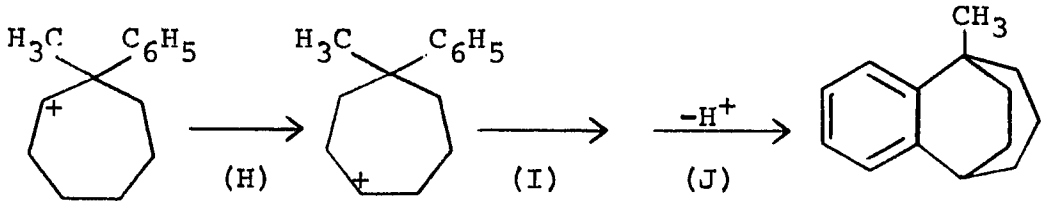
Mechanism VII - Direct Alkylation of Benzene




I III XLIX




L LI LII

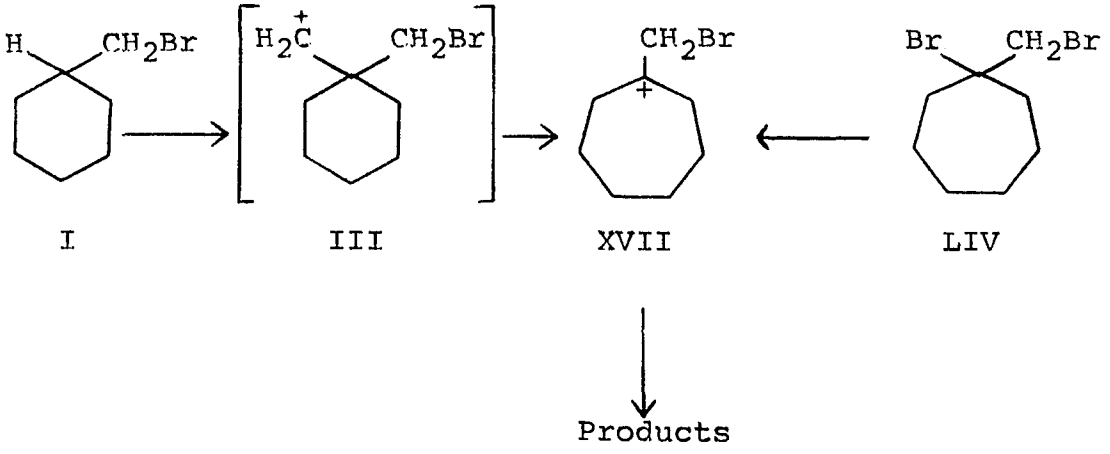



LIII XLVIII II

The 1-Bromomethylcycloheptyl Cation (XVII)

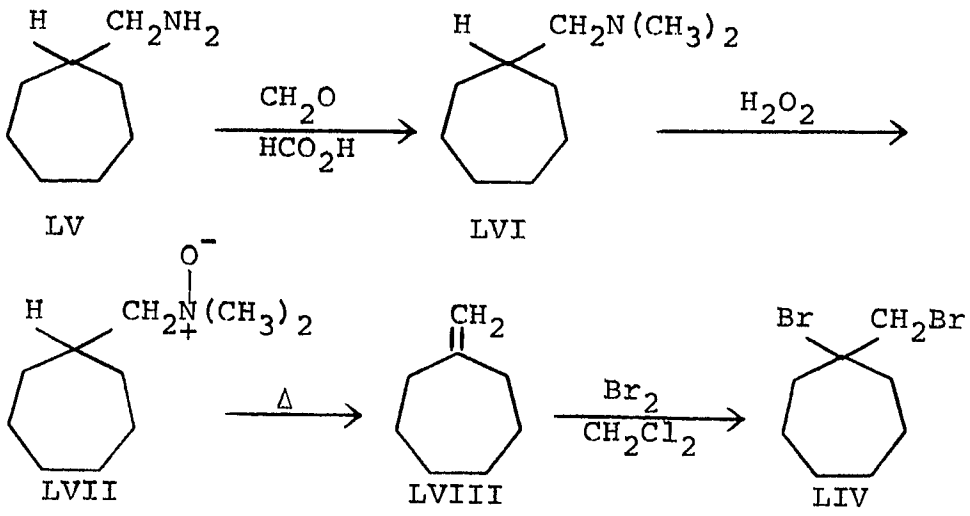
From what has already been discussed (pp. 9-32), ring expansion is the most likely route for the rearrangement of the incipient 1-bromomethylcyclohexylmethyl cation (III). This would lead to the 1-bromomethylcycloheptyl cation (XVII). The possible intermediacy of this carbocation was investigated by studying the reaction of 1-bromo-1-bromomethylcycloheptane (LIV) under the Friedel-Crafts conditions. In this approach it was assumed that the tertiary bromine would be much more labile than the primary one, and therefore, the dibromide, by initial ionization, would lead to the 1-bromomethylcycloheptyl cation (XVII) (Scheme xxiii).

Scheme xxiii



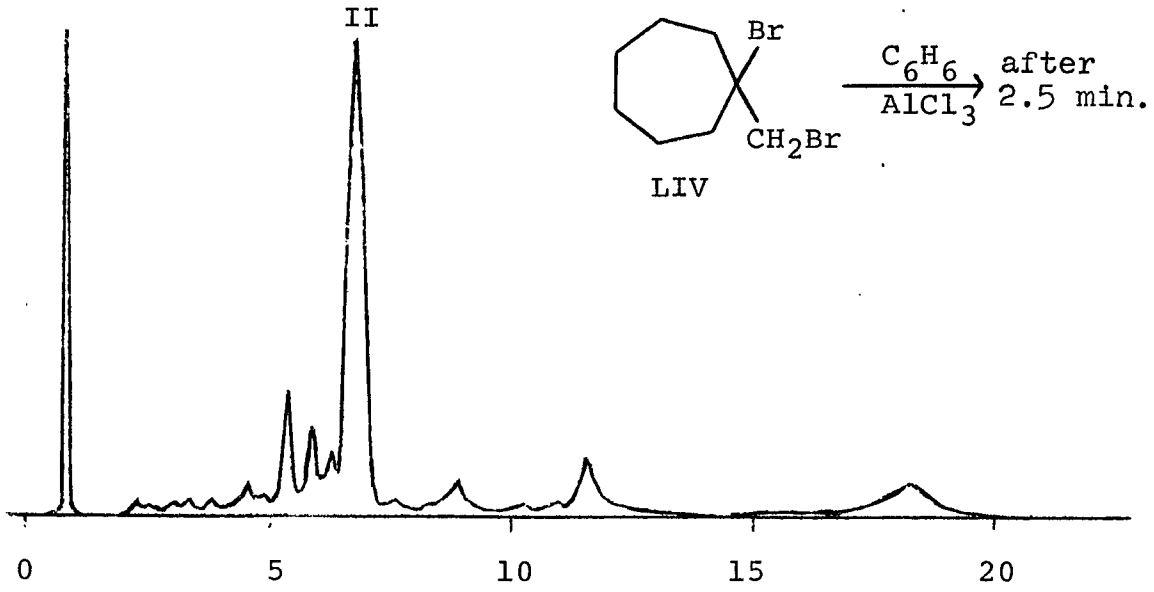

Dibromide LIV was synthesized by addition of molecular bromine to methylenecycloheptane (LVIII), which in turn was made by the method of Cope et al.[54] (Scheme xxiv).

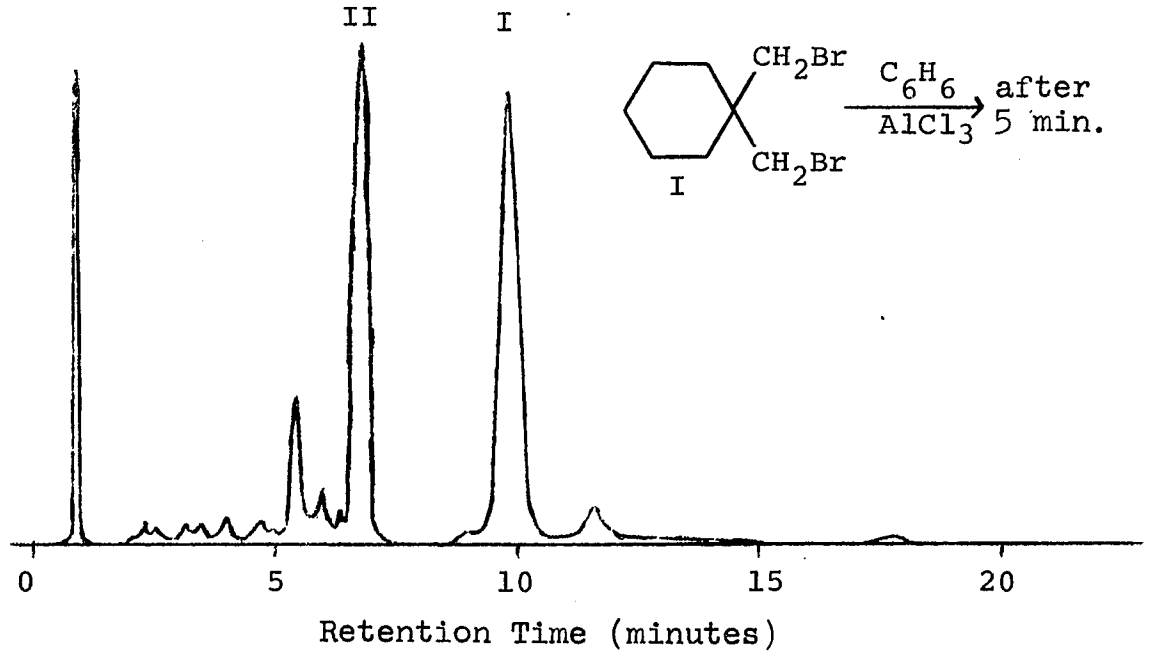
Scheme xxiv




Parallel reactions of 1,1-bis(bromomethyl)cyclohexane (I) and 1-bromo-1-bromomethylcycloheptane (LIV) with benzene and aluminum chloride were carried out. Aliquots were removed at times 2.5, 5.0, 10.0, 15.0 and 30.0 min., worked up, and gas chromatograms taken of each (See Exp. Section p. 230). The chromatograms from the two reaction mixtures showed the same components. The increase and decrease of the concentration of primary product (II) and the increase of other products were essentially the same. Typical gas chromatograms, after 2.5 min. for the reaction of LIV and after 5 min. for the reaction of I, are shown in Figure VI.

Figure VI


II
Br
$CH_2Br$
LIV
$C_6H_6$
$AlCl_3$
after
2.5 min.
0
5
10
15
20
Retention Time (minutes)


II
I
$CH_2Br$
$CH_2Br$
I
$C_6H_6$
$AlCl_3$
after
5 min.
0
5
10
15
20
Retention Time (minutes)

Glc-mass spectra of selected peaks in the region of the primary product of both chromatograms showed that peaks of corresponding retention times from both reactions were the same compounds. This is a strong indication that the 1-bromomethylcycloheptyl cation (XVII) is an intermediate in the Friedel-Crafts reaction of 1,1-bis(bromomethyl)-cyclohexane (I) to form primary product (II), and argues against pathways of the type shown as Mechanisms I, II, III, and VII (Scheme xxii, pp. 37-43).

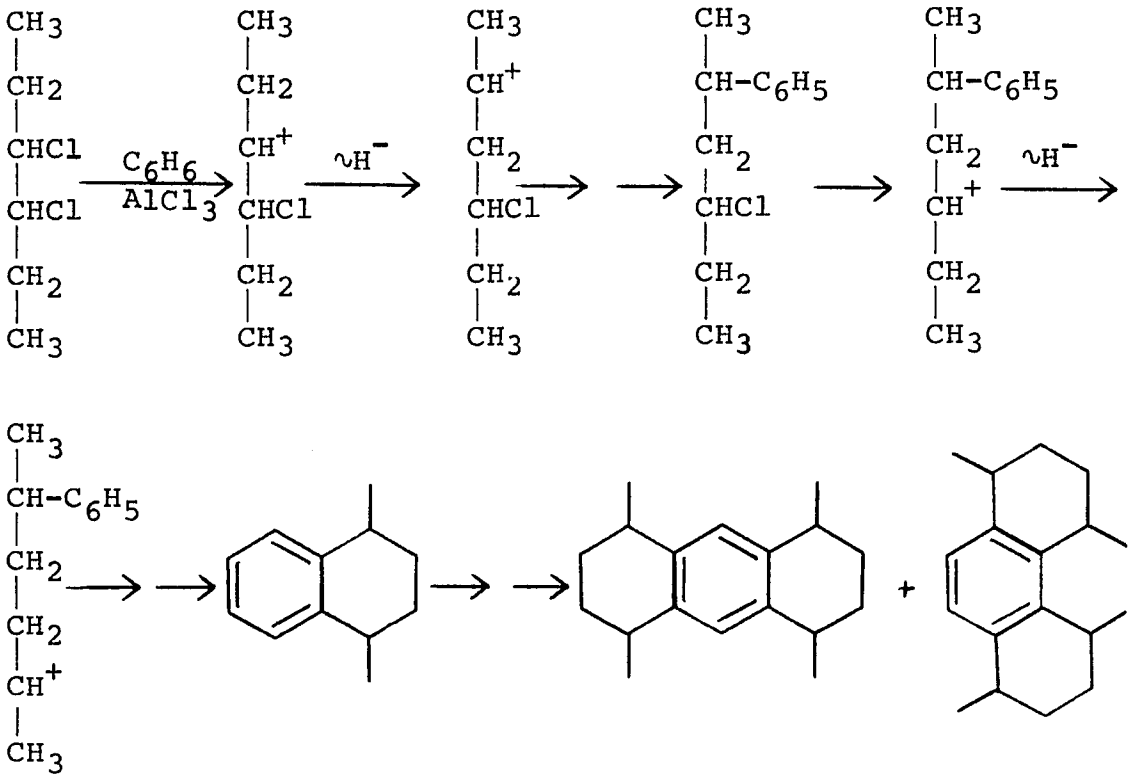
## The 1-Methyl-4-phenylcycloheptyl Cation (XXX)

1-Bromo-1-methyl-4-phenylcycloheptane (XXXVII) is present as an intermediate in a number of the postulated general mechanisms. The corresponding 1-methyl-4-phenylcycloheptyl cation (XXX) is also an intermediate in a number of mechanisms even where the bromide (XXXVII) is not. It was felt that the Friedel-Crafts reaction of the bromide would, therefore, provide valuable mechanistic information.

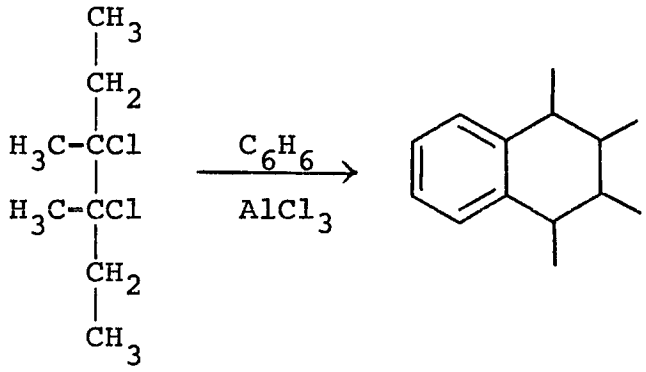
That the 1-bromo-1-methyl-4-phenylcycloheptane (XXXVII) and/or its corresponding cation (XXX) should react to give product is expected. The formation of the six-membered ring upon Friedel-Crafts alkylation has been shown to be a very favorable intramolecular path, even if the alkylation must proceed through a rearrangement from a more stable to a less stable carbocation intermediate. Indeed, the cation here is tertiary and any hydride shift would tend not only to prevent the system from forming the more stable six-membered ring upon intramolecular alkylation, but would also lead to a less stable secondary or primary carbocation.

Sisido and Nozaki[55] have shown that 3,4-dichlorohexane when treated with benzene and aluminum chloride gives a mixture of products, all with six-membered rings, involving rearrangements which put the charge in position for the formation of six-membered rings (Scheme xxv).

Scheme xxv

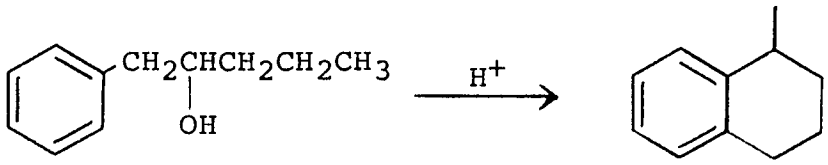


Even when the rearrangement is from a tertiary to a secondary ion, the formation of the six-membered ring tetralin predominates (Eq. 3).[56]



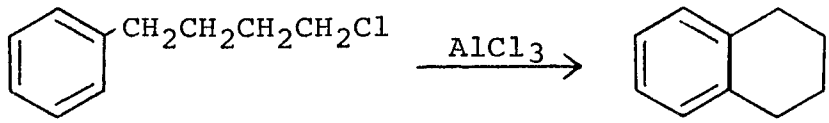
(3)

When multiple shifts are necessary to put the charge in the proper position, a six-membered ring product still predominates. Thus, 2-hydroxy-1-phenylpentane gives 1-methyltetralin (Eq. 4).[57]



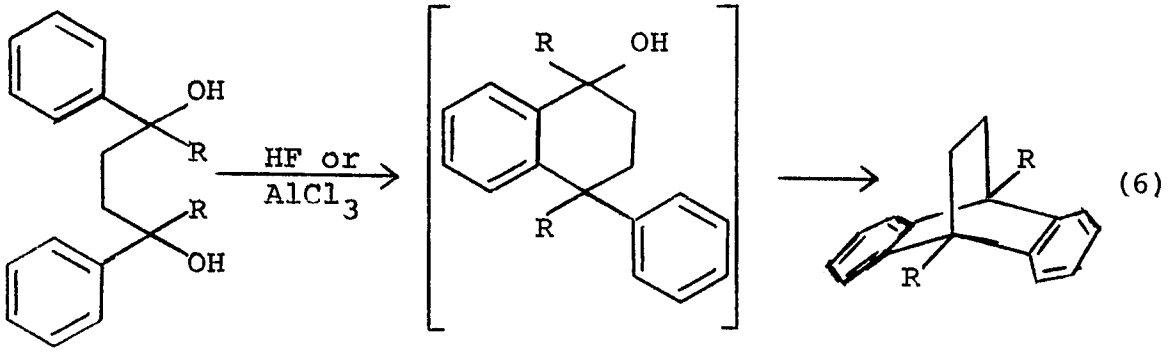

(4)

Sometimes, even if the alkylation would involve a primary site, the six-membered ring tetralin is still the major product (Eq. 5).[58]




(5)

Bicyclic compounds containing six-membered rings are also readily formed (Eq. 6).[59]

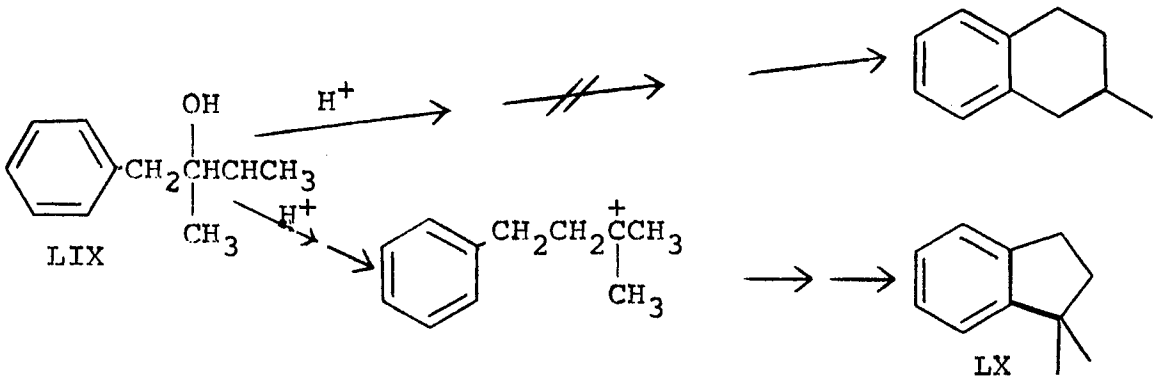



(6)

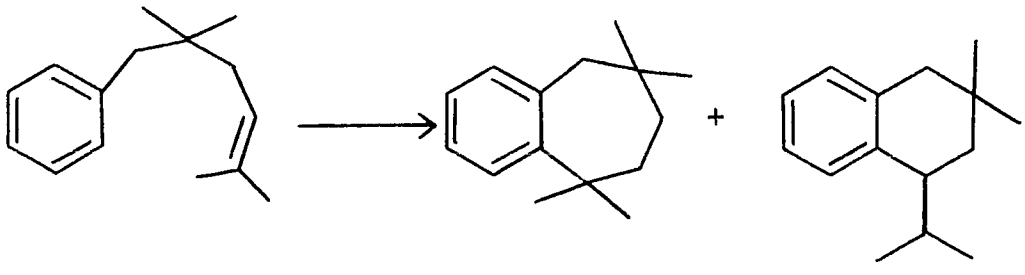
R = $C_6H_5$, $CH_3$

Five- or seven-membered rings, i.e., indanes and benzosuberanes, may be formed if the intermediate carbocation leading to them is relatively more stable than the one leading to the tetralin. Hydroxyisopentylbenzene (LIX) gives 1,1-dimethylindane (LX) (Scheme xxvi).[57]

Scheme xxvi




The relatively mild catalyst boron trifluoride etherate converts 6-phenyl-2,5,5-trimethyl-2-hexene (LXI) to 1,1,4,4-tetramethyl-6,7-benzocycloheptene (LXII) and 1-isopropyl-3,3-dimethyltetralin (LXIII) in a 2:1 ratio (Eq. 7).[60]



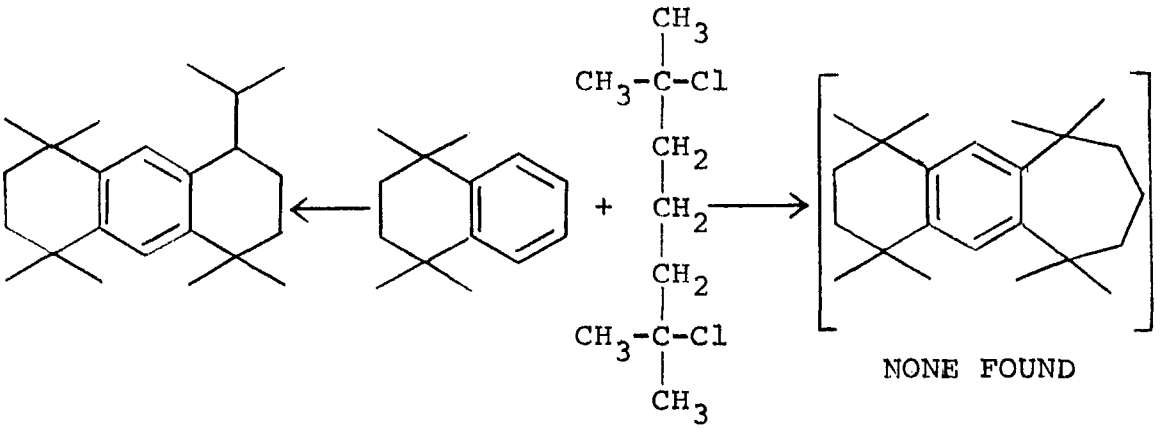

(7)

LXI LXII LXIII

Reaction with aluminum chloride, however, gives no benzosuberane (LXII). If any did form, it would have rapidly isomerized.[60]

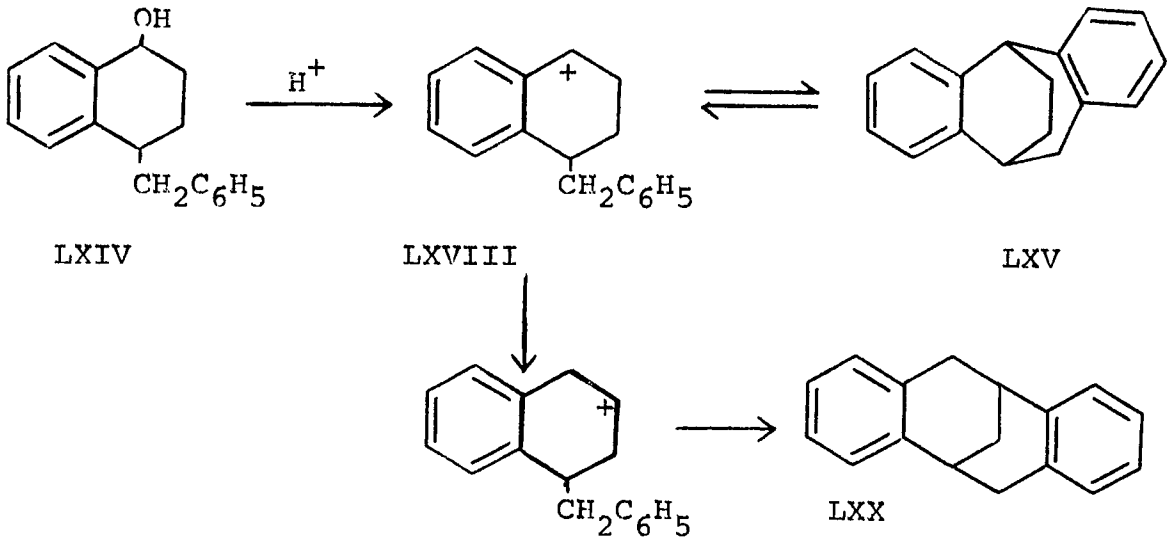
This may explain why no benzosuberane derivative is found in the aluminum chloride catalyzed reaction of 1,1,4,4-tetramethyltetralin and 2,6-dichloro-2,6-dimethylheptane (Scheme xxvii).[61]

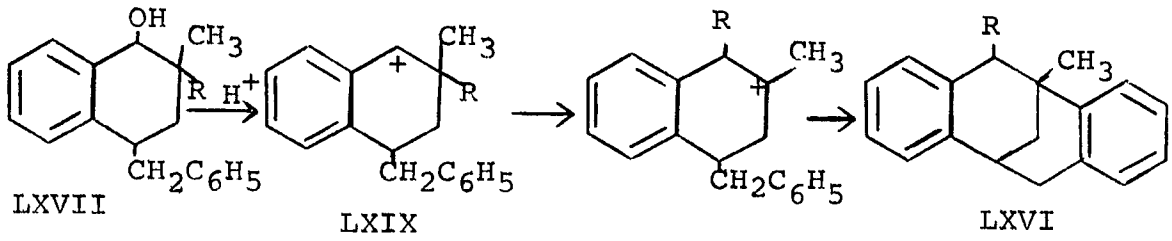
Scheme xxvii




Roberts and Low[62] have shown that 4-benzyl-1-tetralol (LXIV) reacts with sulfuric or phosphoric acid to form dibenzobicyclo[3.2.2]nona-2,6-diene (LXV), a system with a six- and a seven-membered ring, as the major product. When there is at least one methyl group at C-2, then rearrangement of the intermediate carbocation occurs, leading to a product with two six-membered rings (LXVI) (Scheme xxviii).

Scheme xxviii



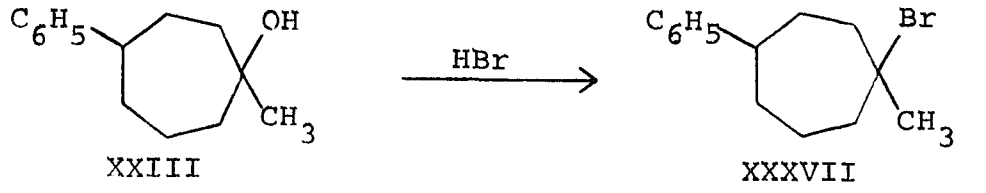




R = H, $CH_3$

Compound LXIV does not follow the pattern of LXVII, since the latter can rearrange to relatively stable tertiary ions, while LXIV would form only a secondary ion. Thus, the benzylic ion LXVIII has a longer lifetime than LXIX and direct ring closure occurs. Evidence that the benzosuberane system, particularly a bicyclic system, cannot survive strong Friedel-Crafts conditions is given by the reactions of 4-benzyl-1-tetralol (LXIV) and dibenzobicyclo[3.2.2]nona-2,6-diene (LXV) with the stronger catalyst aluminum chloride. The major product is LXX, from the

analogous rearrangement of LXVIII which can be formed from the alcohol (LXIV) or from the ring opening of the bicyclic compound (LXV). Our primary product (II) is a bridged benzosuberane. Such a pathway would explain why it is unstable to the conditions of the Friedel-Crafts reaction that leads to its formation (p. 7 and p. 228).

The 1-bromo-1-methyl-4-phenylcycloheptane (XXXVII) was synthesized by the reaction of hydrobromic acid and the previously mentioned 1-methyl-4-phenylcycloheptanol (XXIII) (p. 35) (Eq. 8).




XXIII XXXVII (8)

Reaction of XXXVII* with aluminum chloride in benzene resulted in the formation of two major products, one, over 90% of the mixture, with the same glc retention time as the primary product (II). By use of preparative glc an oil was isolated. It had virtually identical mass, ir, and nmr spectra to those of the primary product (II). This indicates that 1-bromo-1-methyl-4-phenylcycloheptane or its

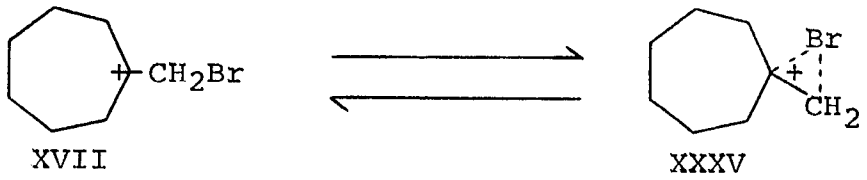
*The synthetic product contained approximately 20% (by nmr) of 1-methyl-4-phenylcycloheptene. Vacuum distillation did not appreciably improve the purity of the bromide (XXXVII). Since both the bromide and the olefin should initially give the 1-methyl-4-phenylcycloheptyl cation (XXX), it was decided to use this mixture for the Friedel-Crafts reaction.

corresponding cation can be an intermediate in the conversion of 1,1-bis(bromomethyl)cyclohexane (I) to primary product (II) as in General Mechanisms IV, V and VI (Scheme xxii, pp. 40-42).

## Routes from the 1-Bromomethylcycloheptyl Cation (XVII) to Primary Product (II)

### (A) The Methylenecycloheptane Bromonium Ion (XXXV)

There are a number of mechanistic pathways from the 1-bromomethylcycloheptyl cation (XVII) to the 1-methyl-4-phenylcycloheptyl cation (XXX). The most reasonable direct route is through the methylenecycloheptane bromonium ion (XXXV) (Eq. 9).



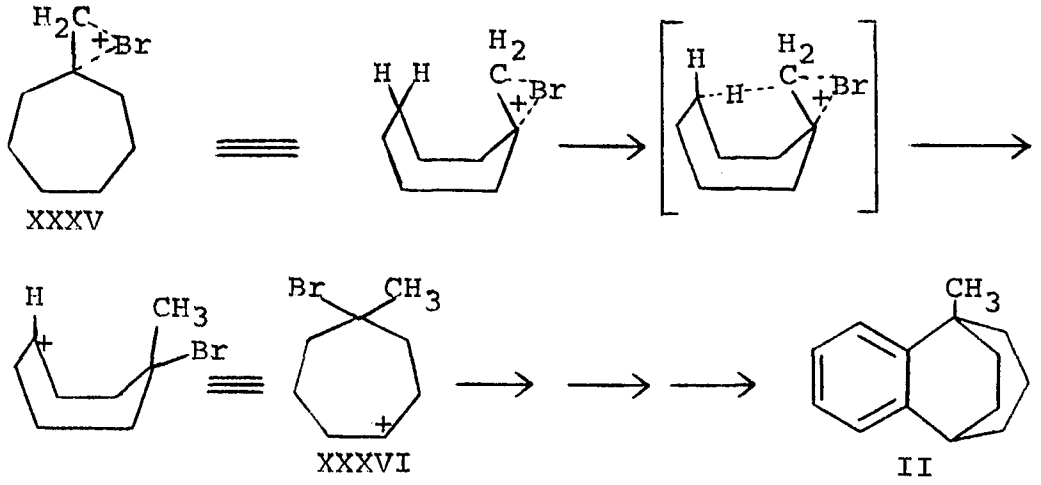

XVII XXXV (9)

A transannular 1,5-hydride shift to the exomethylene group of XXXV would form the methyl group present in the final product and would place a positive charge at C-4 of the cycloheptyl ring (XXXVI) (Scheme xxii, Mechanism IV, p. 40). Benzene could then be alkylated by this cation to give 1-bromo-1-methyl-4-phenylcycloheptane (XXXVII), which, as we have seen, can react further to form primary product (II). The interconversion of XVII to XXXVI through XXXV could also occur by consecutive 1,2-, 1,3-, and/or 1,4-hydride shifts.

Molecular models show that the bromonium ion can adopt a conformation which allows the hydrogen on C-4 of the ring to approach directly behind the exomethylene group. This is a perfect situation for a transannular 1,5-hydride

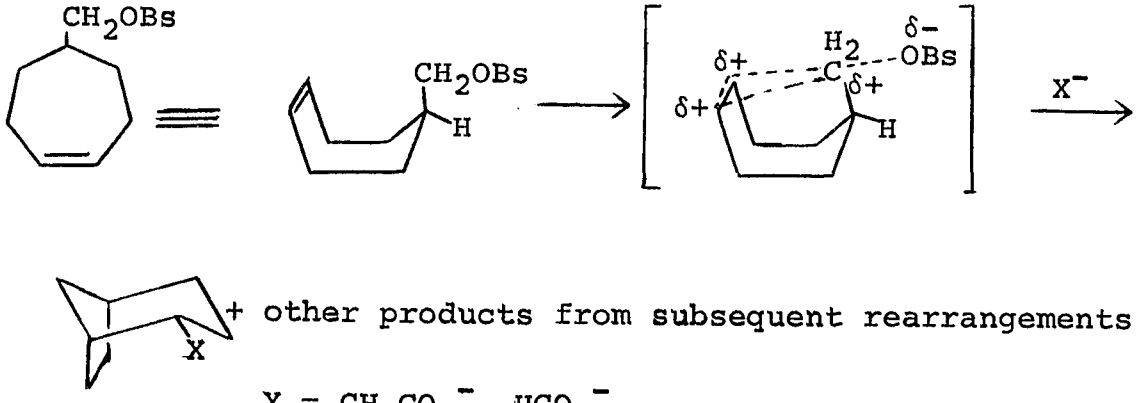
shift (Scheme xxix) (see pp. 15-25).

Scheme xxix



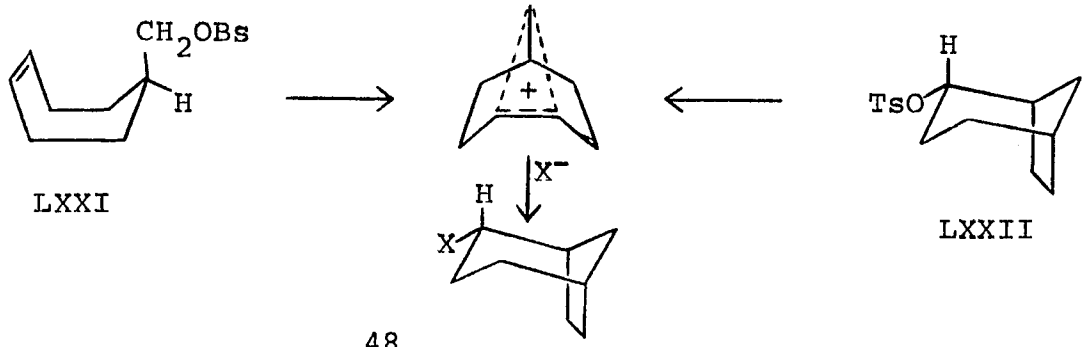

There is precedent for transannular 1,5-effects in the cycloalkylmethyl and cycloalkenylmethyl systems. Many groups of workers have demonstrated the formation of bicyclic products in the solvolyses of cycloalkenylmethyl brosylates.[63-67] An example with the cycloheptenylmethyl system (LXXI) is shown in Scheme xxx.[67-70]

Scheme xxx



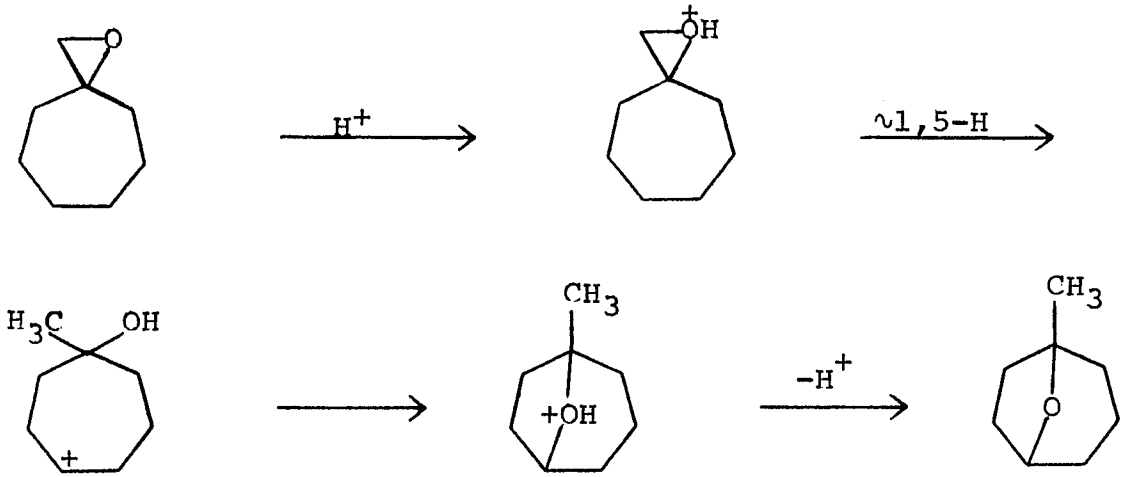
A transannular nonclassical effect was demonstrated by a number of groups[71-75] by the comparison of the solvolyses of cyclohept-4-enylmethyl brosylate (LXXI) and endo-bicyclo[3.2.1]oct-2-yl tosylate (LXXII). The formation of substituted endo-bicyclo[3.2.1]oct-2-yl compounds as over 90% of the product mixtures from both starting materials was cited as proof that both reactions proceed via a symmetrical bridged ion (Scheme xxxi).

Scheme xxxi



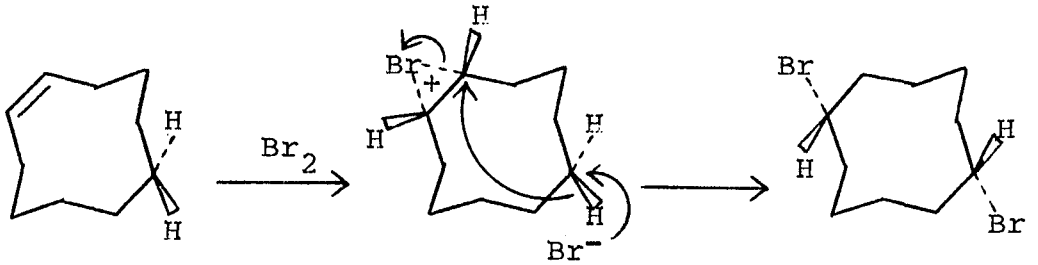

Schwartz et al.[48] have postulated a transannular 1,5-hydride shift in the reaction of 1-oxaspiro[2.6]nonane with aqueous sulfuric acid (Scheme xxxii).

Scheme xxxii



The ability of a bromonium ion to undergo a transannular 1,5-hydride shift has been demonstrated by the formation of cis- and trans-1,6-dibromocyclodecane on addition of molecular bromine to cis- and trans-cyclodecene, respectively.[76] The cis case, proceeding through bromonium ion LXXIII, is shown in Scheme xxxiii.

Scheme xxxiii

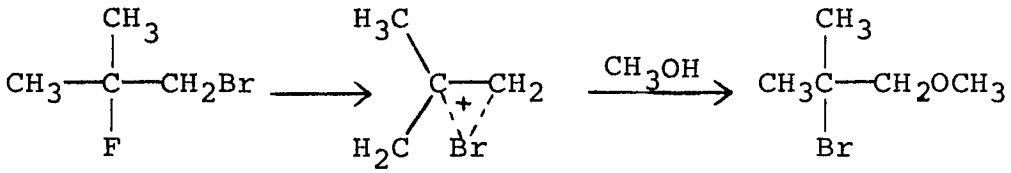



LXXIII

The fact that a bromonium ion between primary and tertiary atoms is more stable than the corresponding tertiary carbocation, despite the fact that the primary carbon of the bromonium ion (LXXIV) has a partial positive charge, was demonstrated by Olah et al.[77] in a study of the ionization of 1-bromo-2-fluoro-2-methylpropane in antimony pentafluoride-sulfur dioxide solution. The fact that the nmr spectrum showed no allylic coupling was taken as evidence that the bromonium ion was almost pure σ complexed. The reaction of the ion with methanol gave exclusively 1-methoxy-2-bromomethylpropane via attack at the less hindered primary carbon in a $S_N2$ manner (Scheme xxxiv). Bromonium ion XXXV would be a similar situation with the bromine atom bridged between a primary and a tertiary center, and having

been formed via XVII, a tertiary ion.

Scheme xxxiv

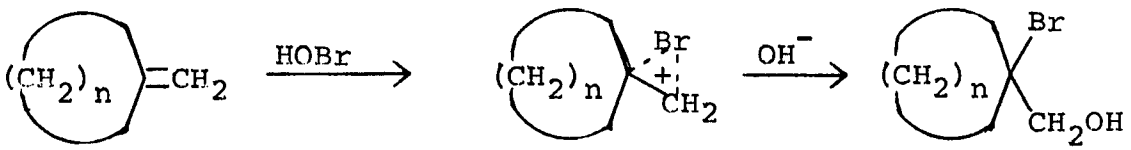


LXXIV

Bromonium ion XXXV could be expected to favor nucleophilic attack at the less hindered exomethylene group, possibly via a transannular hydride shift.

$S_N2$ attack on a bromonium ion was also shown in the reaction of a series of methylenecycloalkanes with hypobromous acid to give almost exclusively 1-bromo-1-(hydroxymethyl)cycloalkanes (Scheme xxxv).[78] The case of n=4 corresponds to bromonium ion XXXV postulated in Mechanism IV, p. 40, and shows the ability of such an intermediate bromonium ion (LXXV) to undergo $S_N2$ attack at the exomethylene group.

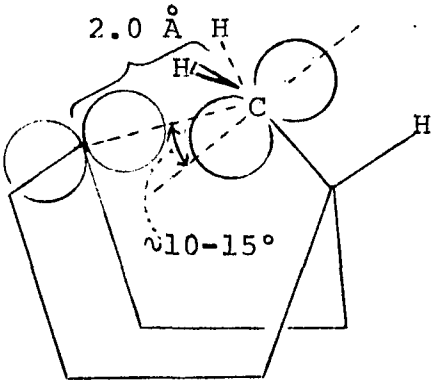
Scheme xxxv



n = 1, 2, 3, 4 LXXV

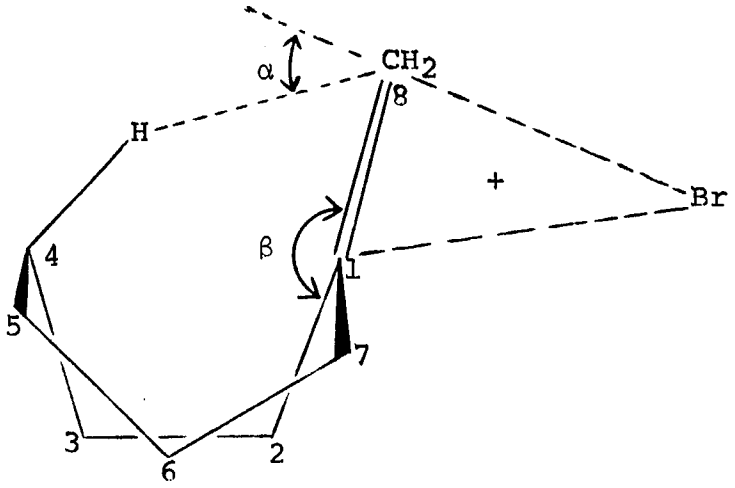
A comparison between Dreiding models of bromonium ion XXXV and the 4-cycloheptenylmethyl system (LXXI), where transannular effects have been demonstrated, is instructive. An exact comparison of models of the transition states of the transannular effects is impossible since the exact structures of the transition states are not known, and available models do not portray partially bonded structures. Therefore, we have crudely approximated the transition states by using models of the cations leading to them. In the 4-cycloheptenylmethyl cation, C-4 and the positive center can approach within 2.0 Å of each other with the two p-orbitals oriented towards each other with an angle of 10-15°. This appears to allow a direct overlap of the two orbitals without any large distortion (Figure VII).

Figure VII

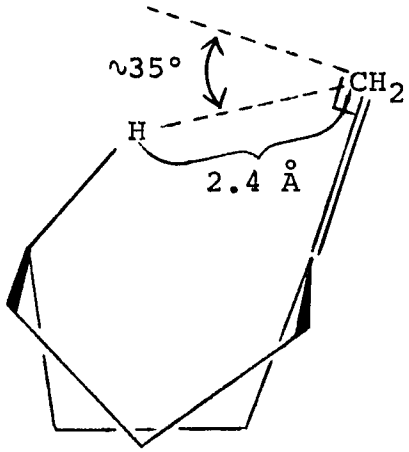



The exact structure of the methylenecycloheptane bromonium ion (XXXV) is not known. This ion could conceivably have σ- and/or π-complex character.[79] On one extreme, the π-complex (Figure VIII, structure $XXXV_1$), with the bromine

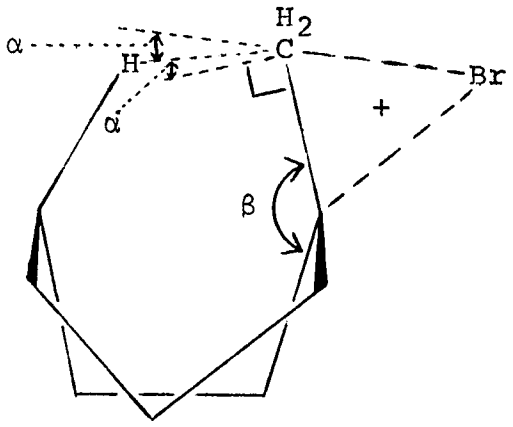
Figure VIII



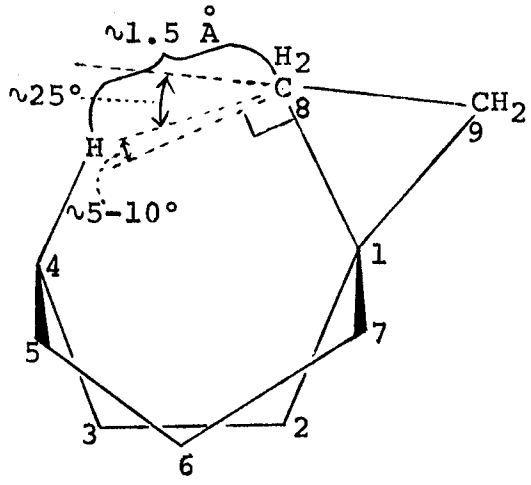

XXXV1




LVII




XXXV2




LXXVI

atom loosely coordinated with the carbon-carbon π-bond, and thus at a relatively large distance from the $sp^2$ hybridized carbon atoms, can be approximated by the olefin itself (Figure VIII, structure LVII). In this case, C-1 would be $sp^2$ hybridized, and the (C-1)-(C-8) bond length would be close to that of a typical carbon-carbon double bond. Angle β (between the (C-1)-(C-2)-(C-7) plane and the (C-1)-(C-8) bond) would be close to 180° and angle α (between the p-orbital on C-8 and a line drawn from C-8 to the hydrogen on C-4) would be about 35°. The distance from C-8 to the hydrogen on C-4 would be about 2.4 Å.

On the other extreme, the σ-complex (Figure VIII, structure $XXXV_2$), angle β would be about 120°, and the distance between C-8 and the hydrogen on C-4 much less than in $XXXV_1$. This structure can be crudely approximated by spiro[2.6]nonane (LXXVI). The approximation is a crude one because in the pure σ-complex the carbon-bromine bond would be larger than the (C-1)-(C-9) bond of LXXVI.

Based upon examples of the bromonium ions already cited, LXXIV and LXXV (p. 60), the geometry of bromonium ion XXXV is probably close to the σ-complex ($XXXV_2$). If either of ions LXXIV or LXXV had a structure close to the π-complex, $S_N1$-type attack at the more substituted tertiary carbon (C-1) would have been expected. But this was not observed for either case.

In spiro[2.6]nonane (LXXVI) the distance between C-8 and the hydrogen on C-4 is about 1.5 Å. Angle α would be

estimated as the angle between the incipient p-orbital on C-8 perpendicular to the (C-1)-(C-8) bond, formed as the (C-8)-Br bond is broken, and a line drawn from C-8 to the hydrogen on C-4. This would be about 5-10°. We could also estimate α as the angle between the line between C-8 and the hydrogen on C-4 and the (C-8)-(C-9) bond, since the best approach for direct $S_N2$ displacement of the (C-8)-Br bond would be at a 0° angle. This angle α would be about 25°. In the σ-complex bromonium ion ($XXXV_2$) the distance between C-8 and the hydrogen on C-4 would be somewhat larger. As explained previously for III, XIII and XIV (pp. 21-25), exactly where the balance exists between the H---C-8 distances, the geometrical requirements of the transition states, and the relative populations of the various conformers of bromonium ion XXXV is not known. Therefore, no firm conclusion can be reached using a comparison of models. However, the distance between C-8 and the potential migrating hydrogen atom, and the angle α, in what seems to be the best conformation for the migration are within the values shown by the cyclooctyl (XIII) and bicyclo[3.3.1]nonane (XIV) systems. Therefore, it does not seem unreasonable to consider the possibility of a transannular 1,5-hydride shift of the hydrogen on C-4 to the exomethylene group of bromonium ion XXXV.*

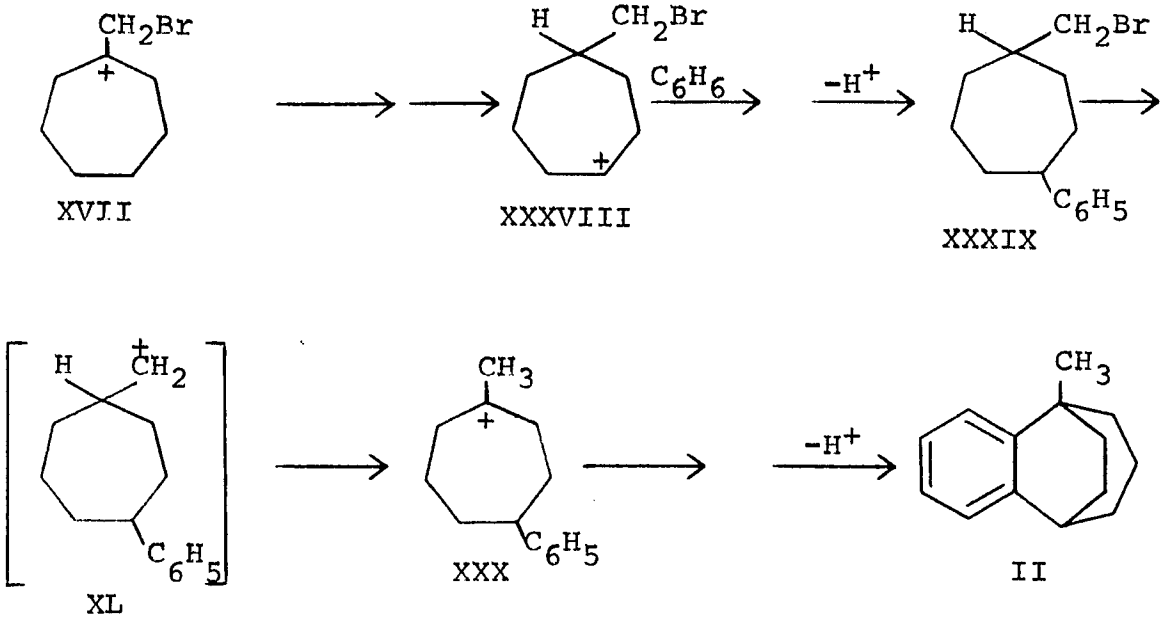
*For, perhaps, a somewhat better comparison of distances, the values for XIII and XIV would have to be decreased somewhat to correct for the size of the p-orbitals on the migration terminus.

(B) A Hydride Shift from C-1 of the Incipient 4-Phenylcycloheptylmethyl Cation (XL)

As can be seen from Scheme xxii, Mechanisms IV and V (pp. 40-41), there are several routes, other than a direct transannular H shift, from the 1-bromomethylcycloheptyl cation (XVII) to 1-bromo-1-methyl-4-phenylcycloheptane (XXXVII) or its corresponding ion (XXX). These all include stepwise migration of the positive charge from one side of the ring to the other via some combination of 1,2-, 1,3-, and 1,4-hydride shifts and protonated cyclopropane intermediates.

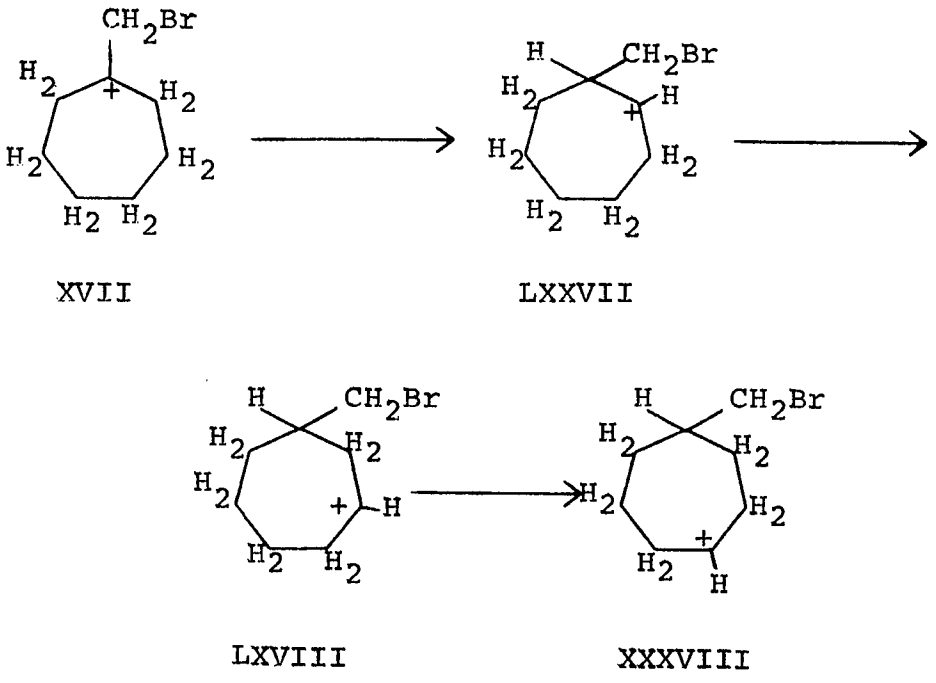
A hydrogen could migrate directly to the exocyclic methylene group as shown in Mechanism IV, Step D, or it could migrate first to C-1 as in Mechanism V, Step C. In the latter case the positive charge could then migrate to the 4-position where the benzene would be alkylated to form 1-bromomethyl-4-phenylcycloheptane (XXXIX). Ionization of this bromide (Step F) could be followed by a 1,2-hydride shift of the tertiary hydrogen on C-1 (Step G), the same one that first migrated in Step C, to form cation XXX, the same cation which would be formed by the ionization of 1-bromo-1-methyl-4-phenylcycloheptane (XXXVII) as described on p. 48. This pathway is illustrated again in Scheme xxxvi.

Scheme xxxvi



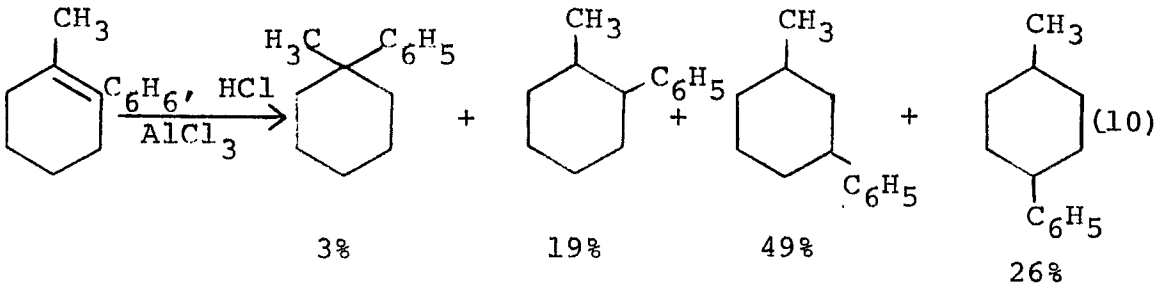

The most likely route from XVII to XXXVIII is through a series of 1,2-hydride shifts (Scheme xxxvii).

Scheme xxxvii



Precedent exists for the migration of a positive charge around a ring by a series of sequential hydride shifts. In the Demjanov ring expansion of cyclopentylmethyl-1-t-amine to form cyclohexanol the label was found at all positions of the cyclohexyl ring.[80] In the isomerization of cyclopentylmethyl-1-$^{13}C$ chloride to cyclohexyl chloride with aluminum chloride the label was found to be distributed almost uniformly throughout the product.[81]

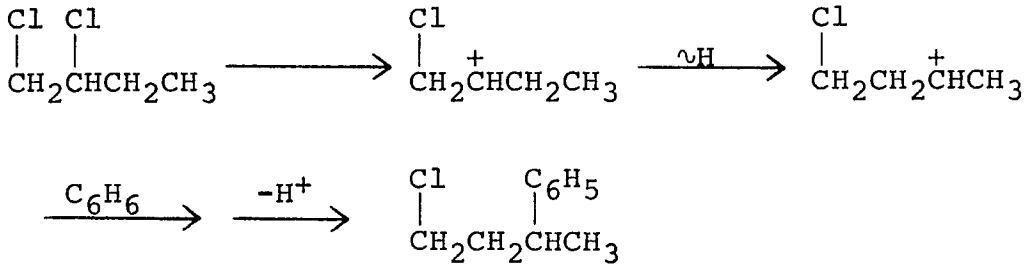
In the alkylation of benzene with 1-methylcyclohexene the majority of the products are 3- and 4-phenylated materials, showing that alkylation occurs furthest away from the existing side chain (Eq. 10).[82] The simplest way to rationalize these results is by a series of 1,2-hydride shifts.



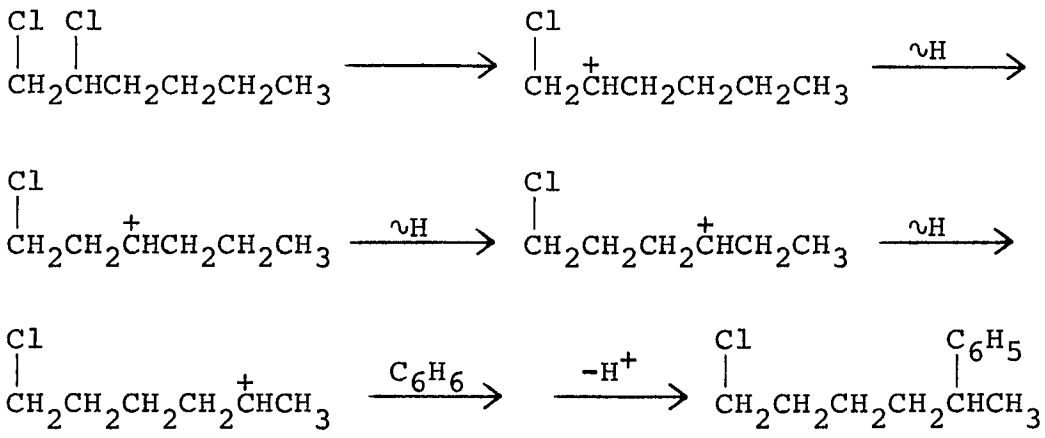

A strong driving force for the series of shifts in Scheme xxxvii is the movement of the positive center away from an electronegative halogen. It has been shown that the preferred mode of reaction of dihalides under Friedel-Crafts conditions is a migration of the charge in the intermediate cation away from the remaining halogen before alkylation. Reactions of 1,2-dichlorobutane and 1,2-di-

chlorohexane with benzene in the presence of aluminum chloride yield as the major products the species formed by alkylation of the cation furthest from the halogen (Schemes xxxviii and xxxix).[25]

Scheme xxxviii



Scheme xxxix



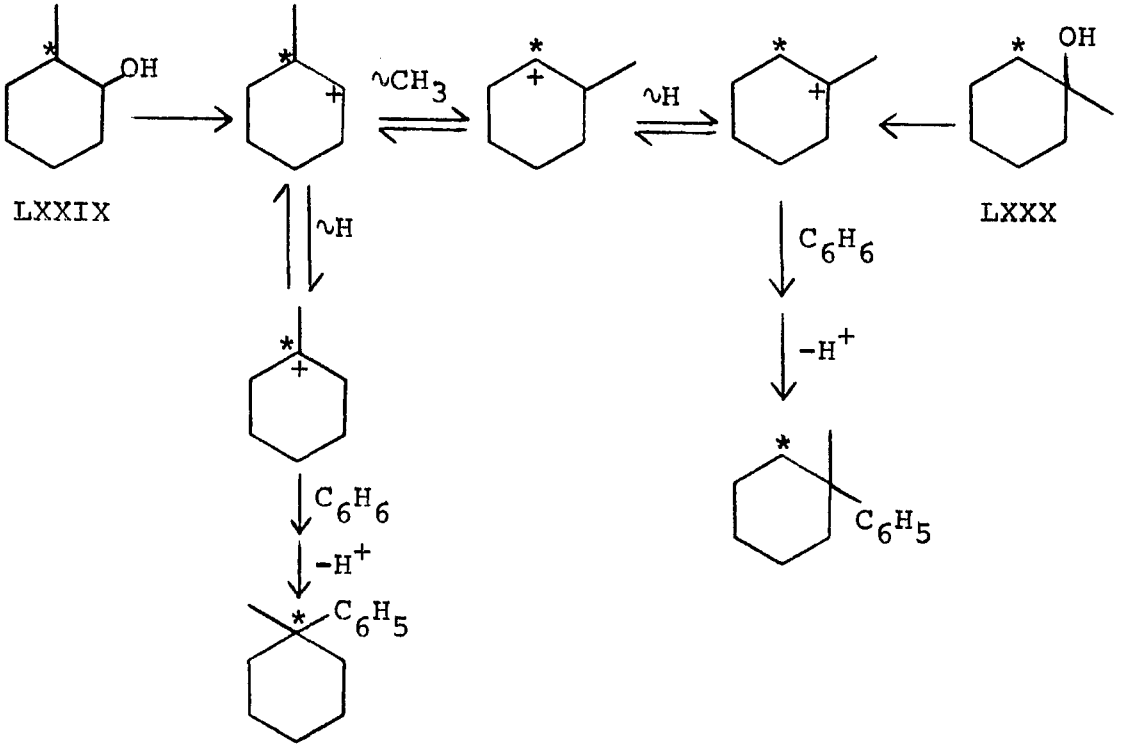
3,4-Dichlorohexane also reacts via hydride migration which moves the positive charge away from the halogen as discussed on p. 48.[55]

The first hydride shift of Scheme xxxvii that converts a tertiary cation to a secondary ion is not unreasonable, since the difference in energy is probably less than the 11 kcal. per mole difference between simple secondary and tertiary ions,[83-85] due to the added stabilization of

moving the charge away from the halogen.

Alkylation of benzene with cis-2-methylcyclohexanol-2-$^{14}$C (LXXIX) or 1-methylcyclohexanol-2-$^{14}$C (LXXX) gives 1-methyl-1-phenylcyclohexane labeled to the same extent at C-1 and C-2. This indicates that these reactions involve secondary shifts which equilibrate secondary and tertiary cations (Scheme xl).[86]

Scheme xl




The combination of both factors, conversion of a tertiary to a secondary carbocation and migration of the positive charge away from a halogen, can be illustrated by the Friedel-Crafts alkylation of 3,4-dichloro-3,4-dimethylhexane shown on p. 49.[56]

(C) Solvent Hydrogen Incorporation

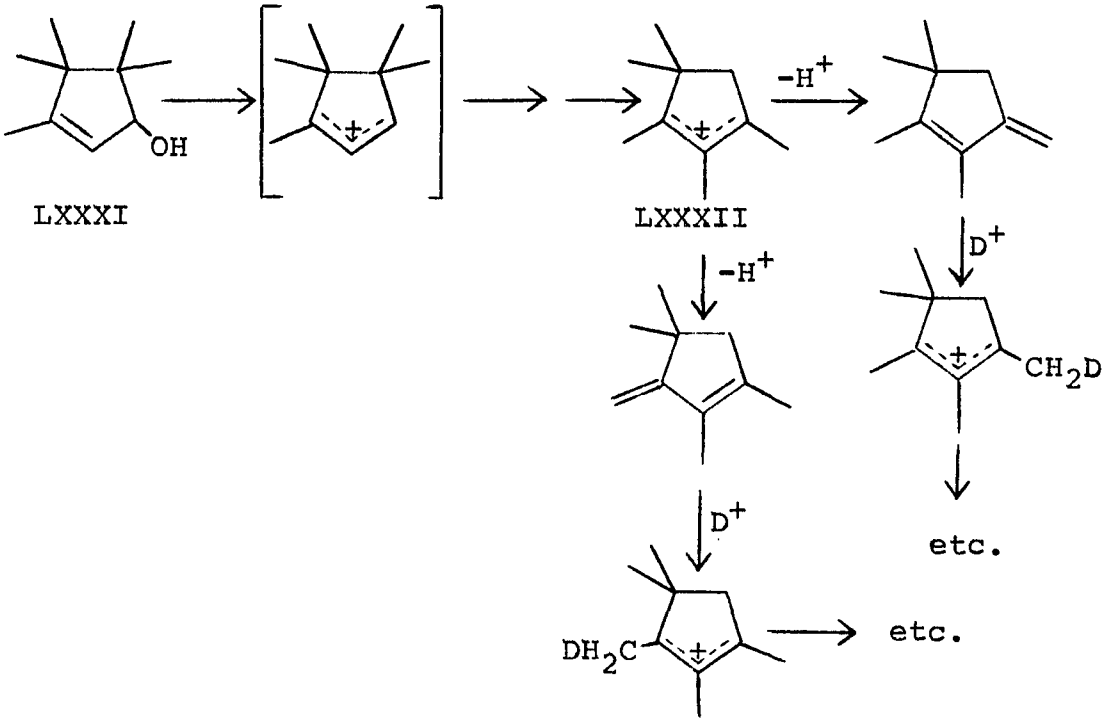
A variety of pathways can be envisioned for the formation of primary product (II) which would involve incorporation of hydrogen from the solvent into the molecule. Mechanisms that involve an olefin, a protonated cyclopropane, or an allylic or homoallylic shift are of this type. Mechanism VI (p. 42) is an example. Below, a number of studies are described in which incorporation of deuterium from the solvent yielded valuable mechanistic information.

3,4,4,5,5-Pentamethyl-2-cyclopentene-1-ol (LXXXI) was isomerized in 96% sulfuric acid to products arising via a 1,2,3,4,4-pentamethylcyclopentenyl cation (LXXXII).[87] In deuteriosulfuric acid the products showed deuterium-hydrogen exchange only on carbon atoms α to the allylic cation system. This was explained by loss of $H^+$ to form a diene and addition of $D^+$ to go back to the original ion (Scheme xli).

The same type of exchange was found for the 1,2,3,4,4-pentamethylcyclobutenyl cation (LXXXIII).[88]

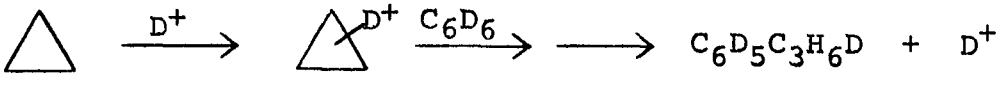
The possible intermediacy of a protonated cyclopropane in the acid catalyzed interconversion of cyclopropane to propanol was demonstrated by the reaction of cyclopropane in deuteriosulfuric acid. The propanol isolated from the product mixture contained deuterium at the 1-, 2-, and 3-positions. This was explained by the formation of a protonated cyclopropane in which the deuterium scrambles before attack by water.[89]

Scheme xli




When cyclopropane was allowed to react with benzene-$d_6$ in the presence of aluminum chloride moistened with heavy water, both the 2-propylbenzene and the 1-propylbenzene formed contained one deuterium statistically distributed throughout the alkyl group. This was explained by the formation of a deuterio-protonated cyclopropane which isomerizes to scramble the deuterium and then alkylates the benzene-$d_6$. Each alkylation ejects a $D^+$ which reacts with another cyclopropane to form another deuterio-protonated cyclopropane (Scheme xlii).[90]

Scheme xlii



## Deuterium Labeling Studies

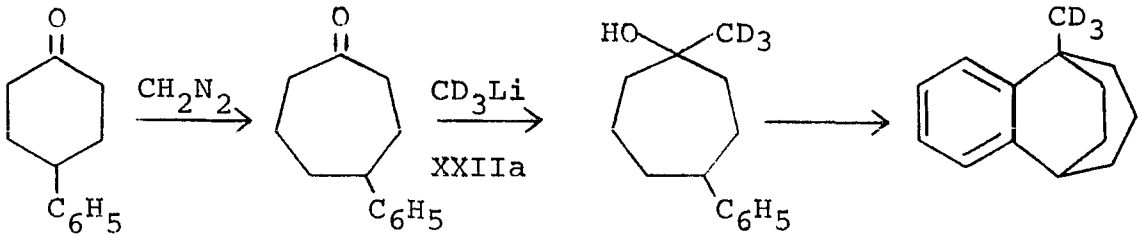
### (A) The Synthesis of Trideuteriomethyl Primary Product (IIa)

The methyl group of the primary product (II) is formed either by a hydrogen migration from the solvent or from one or more positions of the substrate to an exocyclic methylene group. We suspected that the formation of the methyl group would provide the key to the mechanism of the formation of the primary product (II). Possible D labeling on specific sites of the starting material (I) could be used as a tracer to determine from where the hydrogens of the methyl group originate, thereby providing evidence about the step or steps of the mechanism involving the hydrogen migration. Any proposed mechanism whereby the migration would originate from a position other than that which is indicated by the labeling experiments would thereby be eliminated.

Examination of the mass spectrum of the primary product (II) shows a prominent peak at m/e 171, about 35% of the height of the parent peak, corresponding to $C_{13}H_{15}^{+}$, possibly from the loss of the bridgehead methyl group. The only other appreciable peak in the vicinity is at m/e 172 with an intensity corresponding to P + 1 for $C_{13}H_{15}^{+}$. If the m/e 171 peak were due to the loss of the bridgehead methyl group, we would have a simple method for detecting deuterium migration to form this group.

To check this interpretation of the mass spectrum we attempted to synthesize the primary product with a trideuteriomethyl group at the bridgehead position. If this compound exhibited only a m/e 171 peak, and not m/e 172, 173, or 174 peaks, the origin of the m/e 171 peak in the primary product (II) would be confirmed as originating from loss of the bridgehead methyl group. The synthesis of 1-trideuteriomethyl-6,7-benzobicyclo[3.2.2]non-6-ene (IIa) is outlined in Scheme xliii.

Scheme xliii




XXI XXIIIa IIa

1-Trideuteriomethyl-4-phenylcycloheptanol (XXIIIa) was prepared containing an isotope composition of 90% $d_3$, 10% $d_2$. Ring closure of XXIIIa was initially carried out with 85% sulfuric acid. The parent peak and P - methyl regions of IIa from this reaction are shown in Table I. For comparison, the mass spectrum of II is also shown.*

*Because of deviations in the relative peak heights in the mass spectrum of primary product from day to day, it was necessary to run a sample of primary product (II) at the same time as deuterated primary product in order to be able to make direct comparisons. Each peak height was measured to a precision of ±.5% of the base peak. Within a series of scans the reproducibility of the relative ratios of peak heights in successive scans was ±5%.

Table I. Parent and P - Methyl Peaks of the Mass Spectra of Primary Product (II) and Primary Product-$d_3$ (IIa)

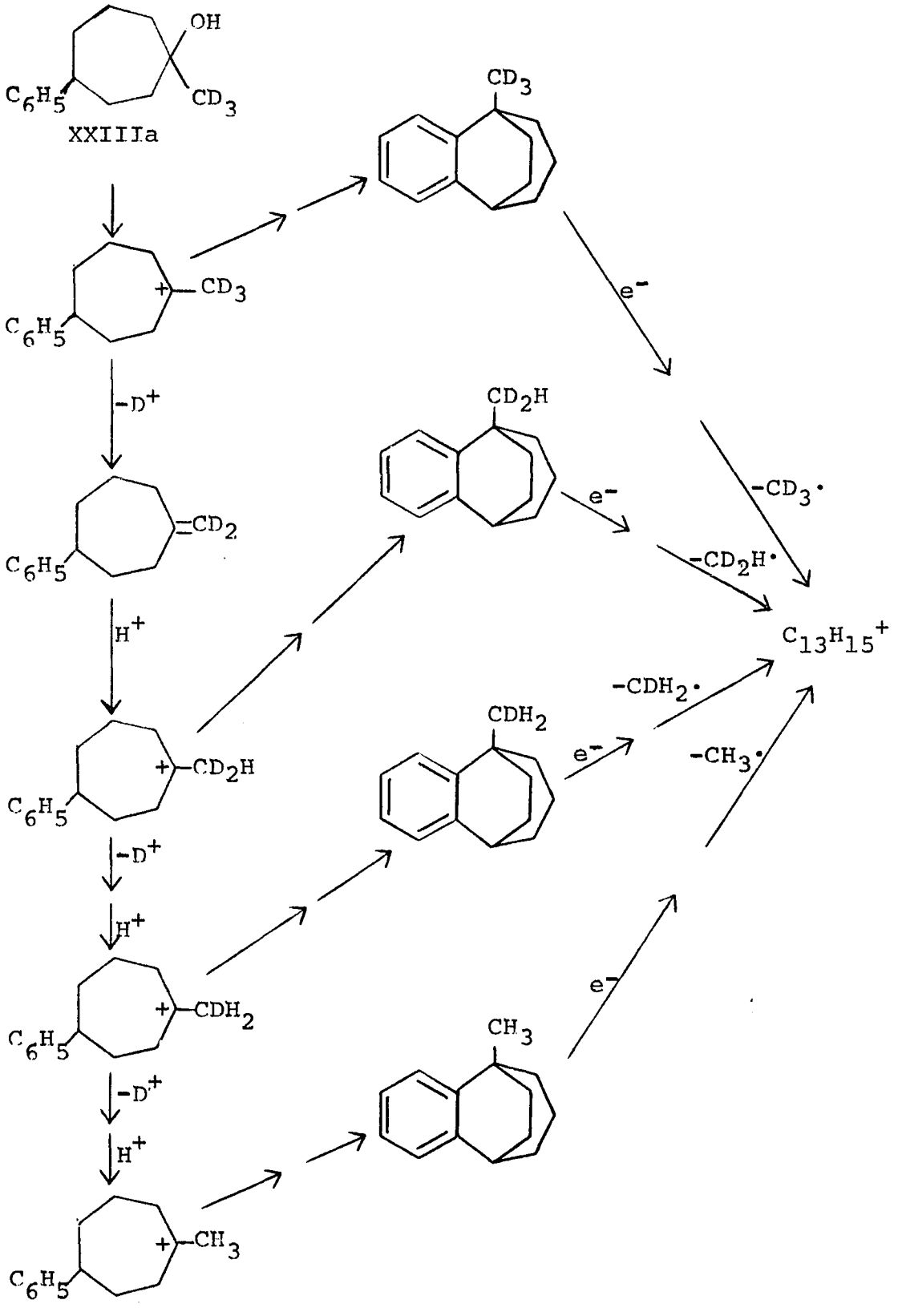
| Primary Product | 171 Peak Region m/e relative peak height | | | | Parent Peak Region m/e relative peak height | | | | |
|---|---|---|---|---|---|---|---|---|---|
| IIa | 170 1 | 171 39 | 172 9 | 173 1 | 186 10 | 187 32 | 188 75 | 189 100 | 190 22 |
| II | 170 1 | 171 36 | 172 6 | 173 1 | | | 185 6 | 186 100 | 187 16 |

These results indicated that in the highly acidic protic medium there was appreciable deuterium-hydrogen exchange, probably at the cation stage. Yet, the only appreciable peaks in the region around m/e 171 are m/e 171 and m/e 172, corresponding to $C_{13}H_{15}^+$ and its P + 1. There are no other appreciable peaks which would correspond to fragments with one or more deuteriums on them.

We interpret this as meaning that the deuterium-hydrogen exchange took place almost exclusively between the methyl group and the solvent, and not between the methyl group and another part of the molecule, and that the loss, in the mass spectrum, of a one carbon fragment corresponds to the loss of the bridgehead methyl group (Scheme xliv).

To check this interpretation we repeated the ring closure using an aprotic catalyst and medium, aluminum chloride in dry benzene, in order to minimize the deuterium-hydrogen exchange. The following mass spectrum of the trideuteriomethyl primary product was obtained:

Scheme xliv

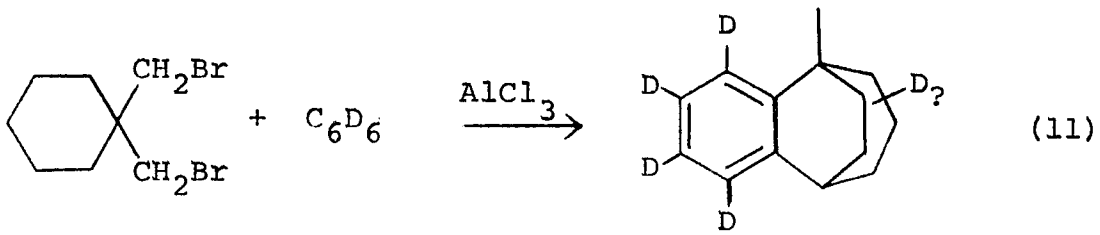

OH
$C_6H_5$
$CD_3$
XXIIIa
$CD_3$
$CD_2H$
$CDH_2$
$CH_3$
$=CD_2$
$-D^+$
$H^+$
e⁻
$-CD_3\cdot$
$-CD_2H\cdot$
$-CDH_2\cdot$
$-CH_3\cdot$
$C_{13}H_{15}^+$

| 170 | 171 | 172 | 173 | | 188 | 189 | 190 |
|---|---|---|---|---|---|---|---|
| 1 | 35 | 6 | 1 | | 17 | 100 | 17 |

The relative abundances may be explained as follows. The 189 peak is due to the parent peak of IIa and the P + 1 peak of the $d_2$ material. The 190 peak is due to the P + 1 of IIa. The 188 peak represents an expected P - 1 peak height of 6 (by comparison with the undeuterated primary product) plus a contribution of 10 due to the 10% $d_2$ in the 1-methyl-4-phenylcycloheptanol-$d_3$ (XXIIIa) from which the product was formed. The only appreciable peaks in the P - methyl region are m/e 171 and 172, showing that the fragment lost is only the bridgehead methyl group.

(B) The Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)-cyclohexane (I) with Hexadeuteriobenzene

The possibility of a hydrogen of the bridgehead methyl group of II originating from the solvent was tested by running the reaction in benzene-$d_6$ as solvent. As we have previously explained (p. 72), mass spectral analysis of primary product from this reaction was expected to be very informative. The parent peak of the primary product was expected to indicate how much, if any, deuterium is incorporated, other than the four remaining on the aromatic ring (Eq. 11). Also, if there were any deuterium incorporation in the primary product (IIb), the P - methyl region would be expected to indicate if there were any incorporation into the methyl group.




I IIb (11)

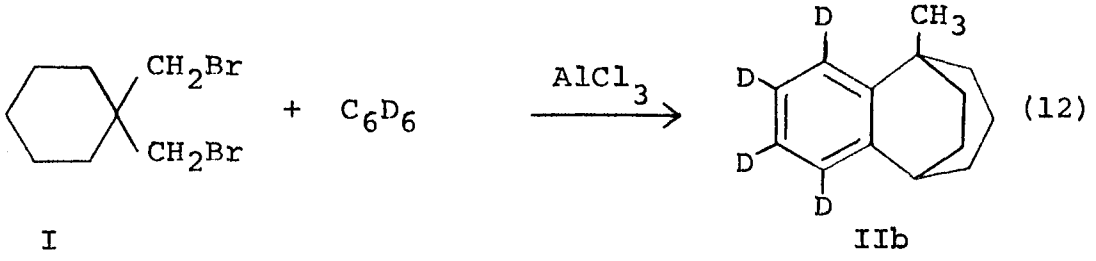
1,1-Bis(bromomethyl)cyclohexane (I) was allowed to react with benzene-$d_6$ in the presence of aluminum chloride as described in the Experimental Section, p. 235, and the primary product (IIb) was isolated. The parent peak and P - methyl regions of the mass spectrum of the primary

product (IIb) are shown in Table II.*

Table II. Parent and P - Methyl Regions of the Mass Spectra of Primary Product (II) and Primary Product from Benzene-$d_6$ (IIb)

| Reaction | P - Methyl Region m/e relative peak height | | | | Parent Peak Region m/e relative peak height | | |
|---|---|---|---|---|---|---|---|
| I → II | 170 1 | 171 36 | 172 6 | 173 1 | 185 6 | 186 100 | 187 16 |
| I → IIb | 174 1 | 175 36 | 176 6 | 177 1 | 189 6 | 190 100 | 191 17 |

The ratios of the peaks in the parent peak region of the two primary products are almost identical. This indicates that there was no appreciable incorporation of deuterium in the product at any alkyl position. There are four deuteriums on the aromatic ring from the reaction in benzene-$d_6$ (Eq. 12).




I IIb (12)

The ratios of peak heights in the P - methyl region are also almost identical. The mass spectrum shows only the loss of 15, indicating that there has not been any scrambling of deuterium into the methyl group. This es-

*See footnote on p. 73.

tablishes the fact that the third hydrogen on the bridgehead methyl group of the primary product (II) originates from somewhere on the substrate through some form of hydride shift or combination of shifts, and eliminates mechanisms involving olefins or protonated cyclopropanes, and allylic or homoallylic shifts, such as Mechanism VI, p. 42.

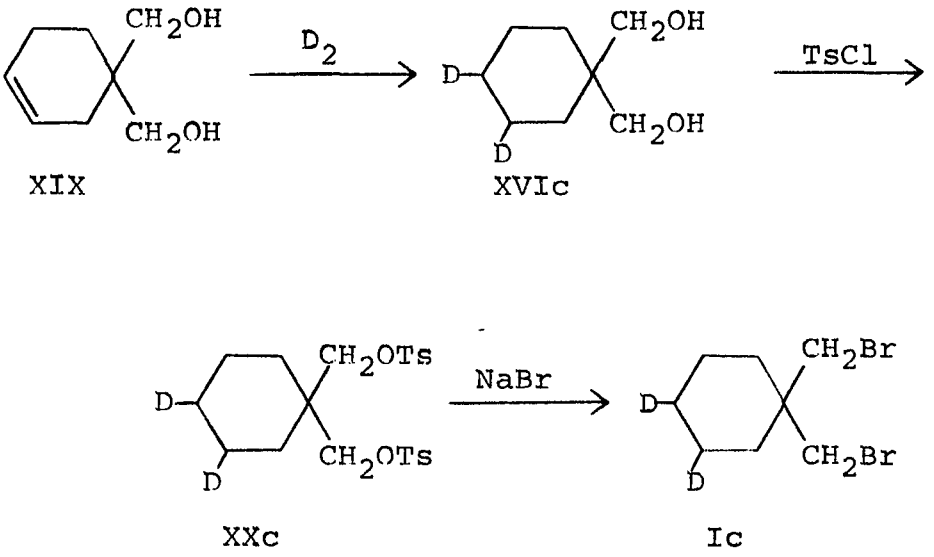
(C) The Friedel-Crafts Reaction of 3,4-Dideuterio-1,1-bis(bromomethyl)cyclohexane (Ic) with Benzene

After establishing the fact that the third hydrogen of the bridgehead methyl group of the primary product (II) originates from the starting dibromide (I), we investigated the possibility of a 1,5-hydride shift via the methylenecycloheptane bromonium ion (XXXV) (Mechanism IV, p. 40). Our plan was to place a deuterium label at a position which, after the transannular shift, would result in a deuterated methyl group. A comparison of the mass spectrum of the deuterated primary product with the spectrum of unlabeled material in the P - methyl region would indicate whether or not a 1,5-shift had occurred.

The first compound we chose to study was one that we suspected could easily be synthesized, 3,4-dideuterio-1,1-bis(bromomethyl)cyclohexane (Ic). Since 1,1-bis(bromomethyl)cyclohexane (I) was synthesized by catalytic hydrogenation of 4,4-bis(hydroxymethyl)cyclohexene (XIX), it was felt that the synthesis of Ic could be accomplished by the addition of molecular deuterium across the double bond, followed by the usual steps to form the dideuteriodibromide (Ic) (Scheme xlv).

The reduction of the double bond was accomplished using deuterium gas and a tris(triphenylphosphine)rhodium(I) chloride soluble catalyst in order to minimize scrambling by deuterium-hydrogen exchange at other sites in the mole-

Scheme xlv



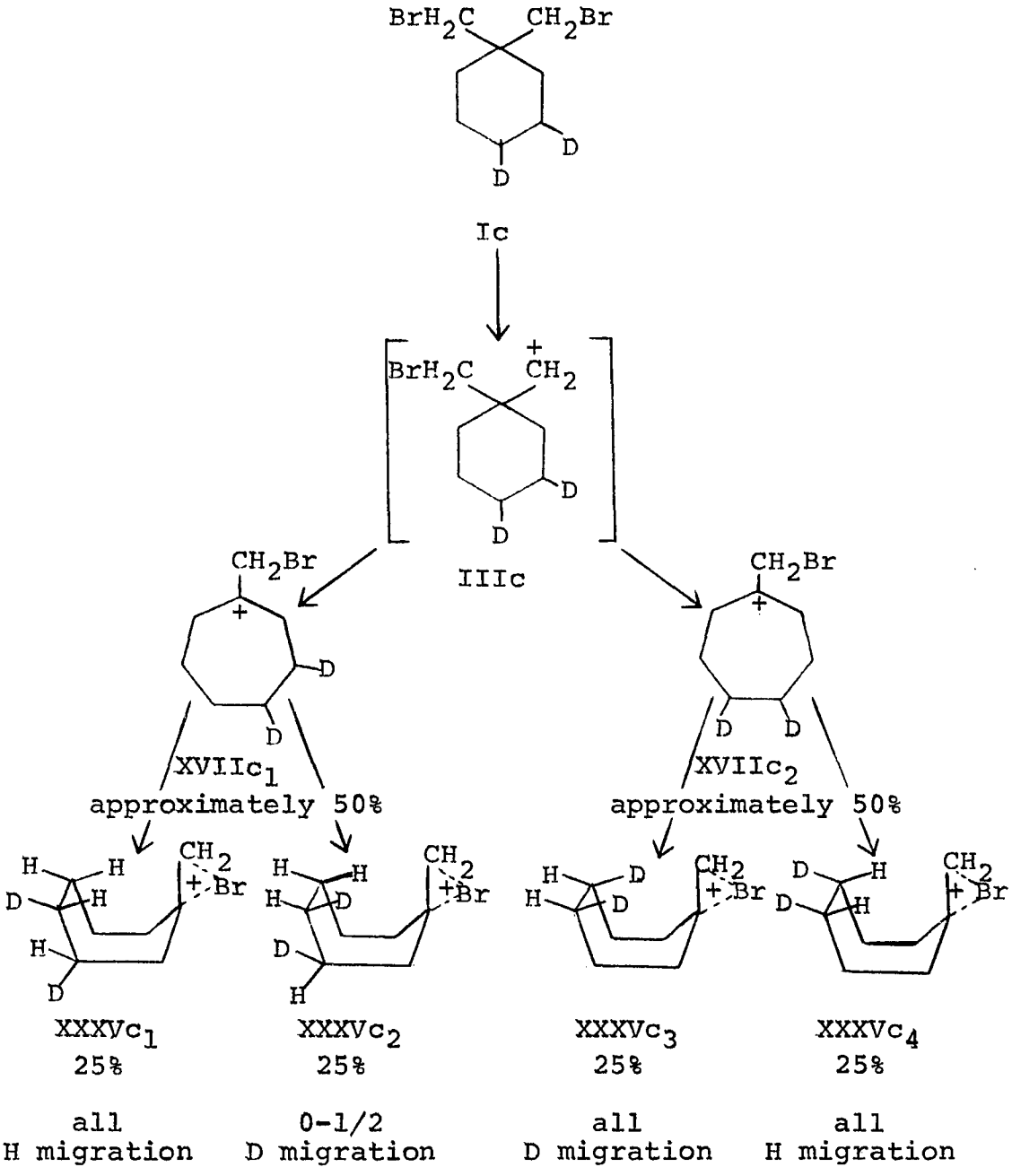

XIX XVIc XXc Ic

cule as is observed with metallic catalysts.[91,92] This reagent has been shown to produce appreciable scrambling in cycloheptene and cyclooctene but very little in cyclohexene.[93] The reagent is known to catalyze the addition of deuterium stereospecifically cis across a double bond.[94] The sequence of reactions shown in Scheme xlv was shown by mass spectral analysis to give dibromide Ic with 85% $d_2$ and 15% $d_1$.

It was expected that if there is a transannular 1,5-hydride shift the product would show 25 to 37.5% $CH_2D$ depending upon the isotope effect in the migration step. Initial ionization and ring expansion (Scheme xlvi) can lead to two ions, $XVIIc_1$ and $XVIIc_2$, each of which can form two bromonium ions, $XXXVc_1$ and $XXXVc_2$, and $XXXVc_3$ and $XXXVc_4$, respectively. Since only the inner hydrogens or

deuteriums on C-4 and C-5 of $XXXVc_1$, $XXXVc_2$, $XXXVc_3$, and $XXXVc_4$ can migrate, it was expected that no isotope effect would be present except perhaps in the case $XXXVc_2$ where a hydrogen and a deuterium compete in the migration.

Scheme xlvi



A very large $k_H/k_D$ would be expected to produce 25% deuterium in the methyl group. A very small isotope effect, i.e., not very different from 1.0, would result in 37.5% D migration.

The Friedel-Crafts reaction was run with 3,4-dideuterio-1,1-bis(bromomethyl)cyclohexane (Ic), under identical conditions to the undeuterated dibromide (I), and the primary product (IIc) was isolated. The parent peak region of the mass spectrum was expected to show a m/e 189 peak (P + 1 for $d_2$ material), a m/e 188 peak (P for $d_2$ material plus P + 1 for $d_1$ material), and a m/e 187 peak (P - 1 for $d_2$ material plus P for $d_1$ material), assuming no appreciable loss of deuterium to the solvent. The latter seems reasonable based on the lack of exchange in the reaction of dibromide I carried out in benzene-$d_6$. The presence of $CH_3$ and $CH_2D$ groups in the primary product (IIc) would be reflected by m/e 173 and 172 peaks in the mass spectrum. Primary product formed from the monodeuterated dibromide would give corresponding peaks at m/e 172 and 171.

The mass spectrum of the parent and P - methyl regions is shown in Table III.*

The spectrum was interpreted as follows. The m/e 188 and 189 peaks are the normal parent and P + 1 peaks. Based on the mass spectrum of unlabeled primary product m/e 187 (P - 1) should be about 6.** But the starting dideuterated

*See footnote on p. 73.
**However, see pp. 159-160.

Table III. Parent and P - Methyl Mass Spectral Peaks for Primary Product (II) and Primary Product-$d_2$ (IIc)

| Reaction | | P - Methyl Region m/e relative peak height | | | | | Parent Peak Region m/e relative peak height | | |
|---|---|---|---|---|---|---|---|---|---|
| I | II | | 170 1 | 171 36 | 172 6 | 173 1 | 185 6 | 186 100 | 187 16 |
| Ic | IIc | 171 1 | 172 8 | 173 37 | 174 6.5 | 175 1 | 187 22 | 188 100 | 189 18 |

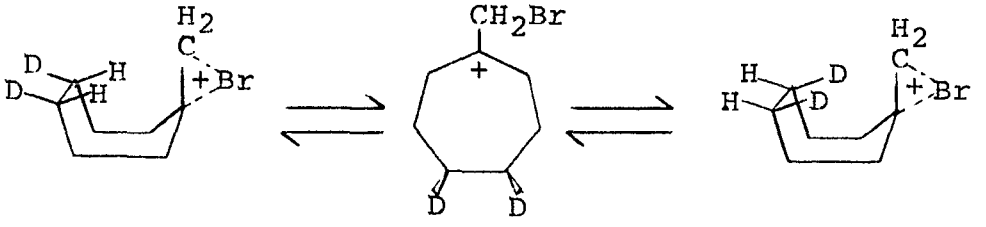
dibromide (Ic) contained about 15% $d_1$, thus accounting for a peak of 22. This shows, as expected, that there was very little, if any, hydrogen-deuterium exchange in the reaction.

The m/e 173 and 174 peaks correspond to m/e 188 - 15 (P - $CH_3$) and the P + 1 for the fragment. We would expect a P - $CH_3$ for the 15% of the monodeuterated dibromide at m/e 172, in proportion to the P - $CH_3$ from dideuterated dibromide, of approximately 5.5 and a contribution of 1 from the dideuterio primary product. Because of the fact that the monodeuterated dibromide has more hydrogens available for migration, the H migration would lead to a somewhat larger m/e 172 peak. The relative peak height of 8 is not unreasonable.

These results can be explained by the formation of the methyl group by migration of hydrogen from a site other than the 4-position of the 1-bromomethylcycloheptyl cation (XVII).

An alternative rationalization for the lack of deuterium in the methyl group is the rapid establishment of an equilibrium between the two stereoisomeric bromonium ions, $XXXVc_3$ and $XXXVc_4$, and the bromomethylcycloheptyl cation ($XVIIc_2$) (Scheme xlvii), together with an appreciable isotope effect in the H migration step.

Scheme xlvii



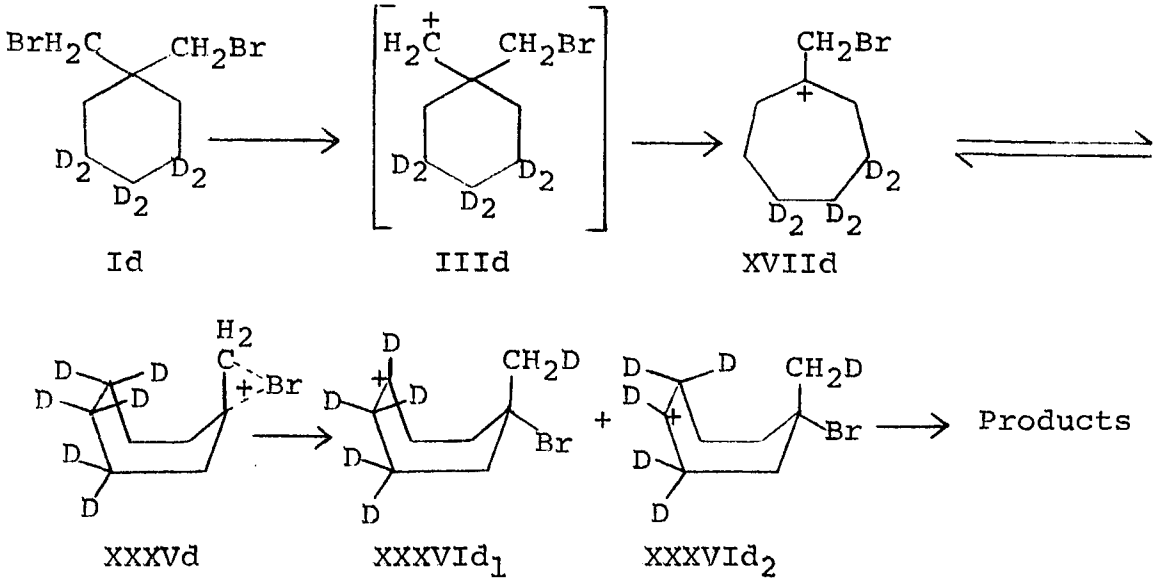

$XXXVc_4$ $XVIIc_2$ $XXXVc_3$

Bromonium ions $XXXVc_1$ and $XXXVc_4$ would give almost exclusively H migration. Ion $XXXVc_3$ would react much more slowly than $XXXVc_4$, allowing the equilibrium to continually shift towards $XXXVc_4$, resulting in only hydrogen migration. Any kinetic isotope effect could also cause the deuterium migration to be slow enough relative to possible side reactions to allow these side reactions to be more important for $XXXVc_3$, thus removing it from the pathway to primary product (II).

(D) The Friedel-Crafts Reaction of 3,3,4,4,5,5-Hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id) with Benzene

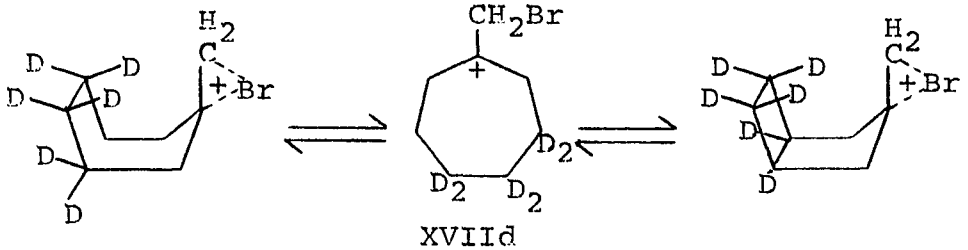
We next studied the reaction of 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id). Our purpose was to use a starting dibromide which was completely labeled with deuterium at all the 1,5-transannular migration origins. If a 1,5-hydride shift occurred, we would expect only deuterium migration to occur, in contrast to Ic (Scheme xlvi, p. 82). The situation with Id is shown in Scheme xlviii.

Scheme xlviii




An equilibrium (Scheme xlix) as described on p. 85 for XVIIc$_2$ would not affect the transannular shift of deuterium, since in this case only deuterium is available for migration.

Scheme xlix



XVIId

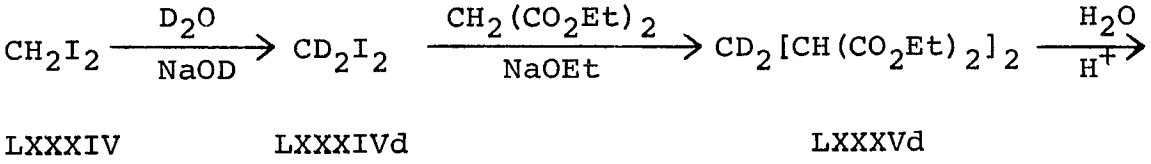
3,3,4,4,5,5-Hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id) was synthesized by the route outlined in Scheme 1. The deuterium content was checked after each step by comparison of the mass spectrum of each product with the spectra of undeuterated materials. Since the spectrum of glutaric acid showed no parent peak, the p-phenylphenacyl derivatives (XCII) were compared.

If the 1,5-hydride shift in the bromonium ion (XXXV) to form the bridgehead methyl group is appreciable, the deuterium shift in the bromonium ion-$d_6$ (XXXVd) should be reflected in a loss of 16 ($CH_2D$) in the mass spectrum of the primary product (IId). Hydrogen migration to form the methyl group would be discernible by loss of 15 ($CH_3$) in the mass spectrum. The expected mass spectral peaks for primary product-$d_6$ (IId) are summarized in Table IV.

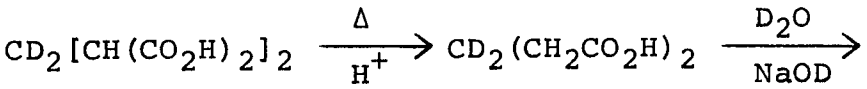
Table IV. Expected Parent and P - Methyl Mass Spectral Peaks for Primary Product (II) and Primary Product-$d_6$ (IId)

| Starting Material | Bromonium Ion | Parent Peak of Primary Product | P - Methyl | |
|---|---|---|---|---|
| | | | H Migration | D Migration |
| I | XXXV | 186 | 171 | - |
| Id | XXXVd | 192 | 177 | 176 |

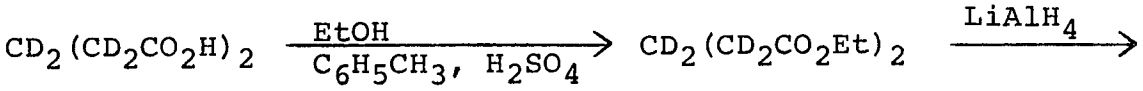
Scheme 1



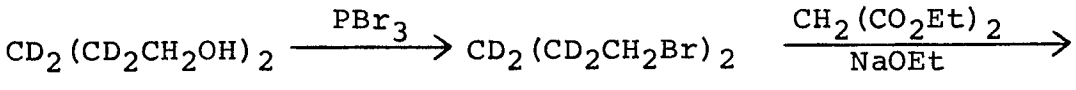

LXXXIV LXXXIVd LXXXVd



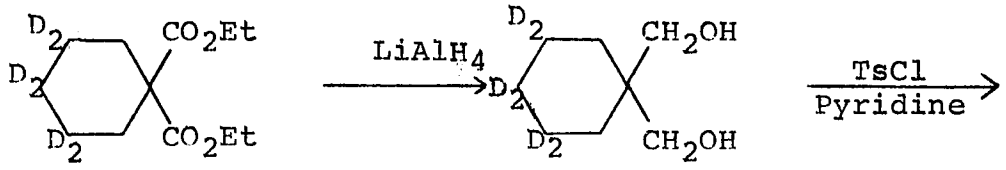

LXXXVId $LXXXVIId_1$



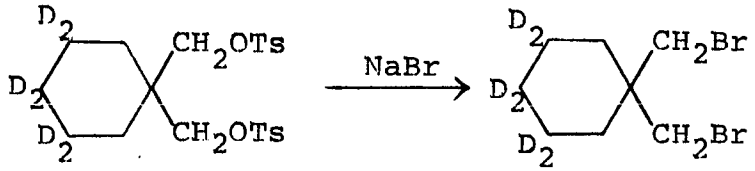

$LXXXVIId_2$ LXXXVIIId




LXXXIXd XCd




XCId XVId




XXd Id

The primary product (IId) from the reaction of 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id) was isolated by preparative glc and its mass spectrum determined as described in the Experimental Section on p. 230. The ratios of peak heights were adjusted to account for differences due to changing amounts of sample (changing pressure) within the mass spectrometer during a spectrum scan. A sample calculation is described in Appendix I, p. 125.

The adjusted mass spectral peak heights of primary products II and IId are summarized in Table V.*

Table V. Adjusted Parent and P - Methyl Peaks of the Mass Spectra of Primary Product (II) and Primary Product-$d_6$ (IId)

| Reaction | | P - Methyl Region m/e (relative peak height) | | | | Parent Peak Region m/e (relative peak height) | | | |
|---|---|---|---|---|---|---|---|---|---|
| I | II | 170 (1) | 171 (30.3) | 172 (4.4) | 173 (1) | 185 (4.6) | 186 (100) | 187 (15.6) | |
| Id | IId | 175 (1.4) | 176 (9.9) | 177 (36.8) | 178 (5.0) | 190 (3.0) | 191 (22.3) | 192 (100) | 193 (17.0) |

Using these experimental peak heights and taking into account equalization of the extents of fragmentation in the formation of P - methyl fragments for the undeuterated and deuterated species, the corrections for $^{13}C$-contributions, and the corrections for incomplete deuteration of IId, the

*See footnote on p. 73.

percentages of hydrogen and deuterium migration in the formation of the bridgehead methyl group of the primary product IId were calculated to be 96.0% and 4.0% respectively. The calculation is described in Appendix II, p. 129.

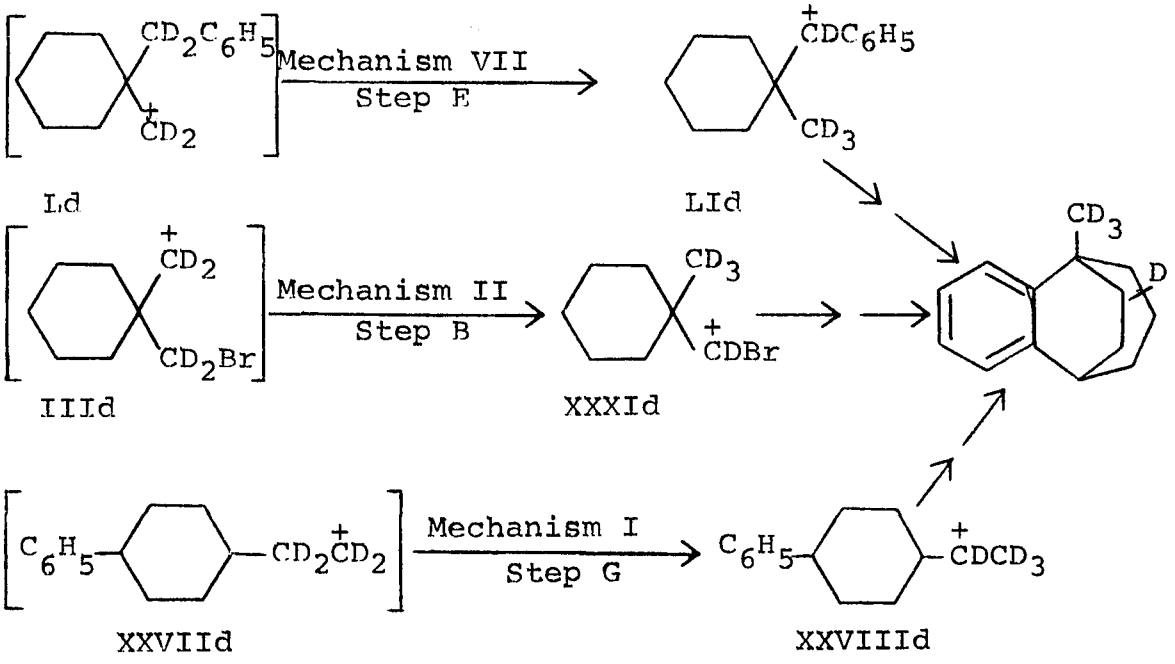
The results show that the large majority of the bridgehead methyl groups are not formed by a hydrogen migration from the 3- or 4-positions of Id. This, therefore, excludes the possibility of the 1,5-transannular hydride shift in the methylenecycloheptane bromonium ion (XXXV) (Mechanism IV, Step D, p. 40) as a major reaction pathway.

(E) The Friedel-Crafts Reaction of 1,1-Bis(bromodideuteriomethyl)cyclohexane (Ie) with Benzene

We next studied the reaction of 1,1-bis(bromodideuteriomethyl)cyclohexane (Ie). This compound was expected to provide information concerning Mechanisms I, II, and VII (Scheme xxii, pp. 37-43). Each of these mechanisms involves a step which would lead to the formation of a trideuteriomethyl group.

The specific steps which would account for this result are summarized in Scheme li.

Scheme li

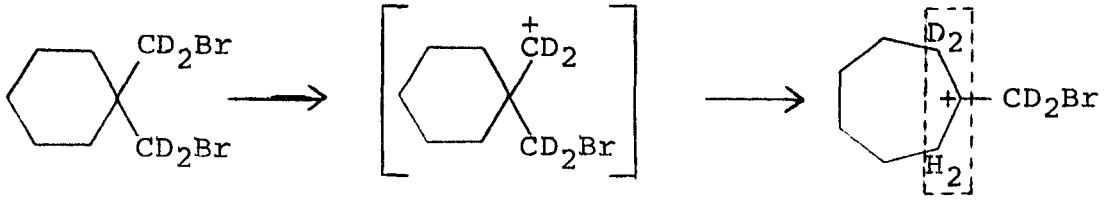



If any of these mechanisms is occurring, the deuterium incorporation in the bridgehead methyl group should be reflected by the loss of 18 ($CD_3$) in the mass spectrum of

primary product IIe. Any hydrogen migration to form the methyl group would be reflected by loss of 17 ($CD_2H$) in the mass spectrum.

Reaction of Ie was not expected to provide direct information about the mechanisms that proceed through the bromomethylcycloheptyl cation (XVII), Mechanisms IV, V, and VI (Scheme xxii, pp. 40-42). Any migration of a deuterium in the 2-position of the bromomethylcycloheptyl ion (XVII) would be subject to competition from the 7-hydrogen. This competition is shown by Scheme lii.

Scheme lii




Ie IIIe XVIIe

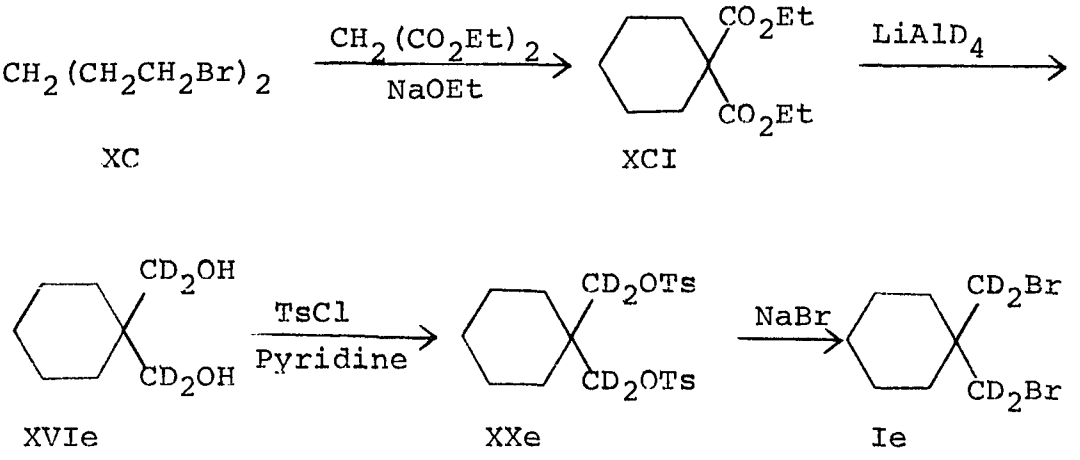
The expected mass spectral peaks for primary product (IIe) produced from Ie are summarized in Table VI.

Table VI. Expected Parent and P - Methyl Mass Spectral Peaks for Primary Product (II) and Primary Product-$d_4$ (IIe)

| Starting Material | Parent Peak of Primary Product | P - Methyl | |
|---|---|---|---|
| | | H Migration | D Migration |
| I | 186 | 171 | - |
| Ie | 190 | 173 | 172 |

1,1-Bis(bromodideuteriomethyl)cyclohexane (Ie) was synthesized by the same general route as 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id). The deuterium atoms were incorporated by the reduction of 1,1-dicarbethoxycyclohexane (XCI) with lithium aluminum deuteride. The synthetic route is outlined in Scheme liii.

Scheme liii




The primary product from the reaction of 1,1-bis(bromodideuteriomethyl)cyclohexane (Ie) was isolated by preparative glc and its mass spectrum determined as described in the Experimental Section, p. 231.

The ratios of peak heights were adjusted as described in Appendix I, p. 125.

The adjusted peak heights of the mass spectrum of primary product formed from I and Ie, II and IIe respectively, are summarized in Table VII.*

*See footnote on p. 73.

Table VII. Adjusted Parent and P - Methyl Mass Spectral Peaks for Primary Product (II) and Primary Product-$d_4$ (IIe)

| Reaction | | P - Methyl Region m/e relative peak height | | | | | | Parent Peak Region m/e relative peak height | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I | II | | 170 1 | 171 30.3 | 172 4.4 | 173 1 | | | 185 4.6 | 186 100 | 187 15.6 | | |
| Ie | IIe | 171 1 | 172 6.6 | 173 23.4 | 174 3.4 | 175 1 | | 188 1 | 189 10.0 | 190 100 | 191 17.0 | | |

The percentages of hydrogen and deuterium migration in the formation of the methyl group of IIe were calculated to be 79.9% and 20.1% respectively. The calculation is described in Appendix II, p. 141.

These results show that Ie leads to product with much less deuterium migration than would be expected if Mechanism I, II, or VII were the major reaction pathway.

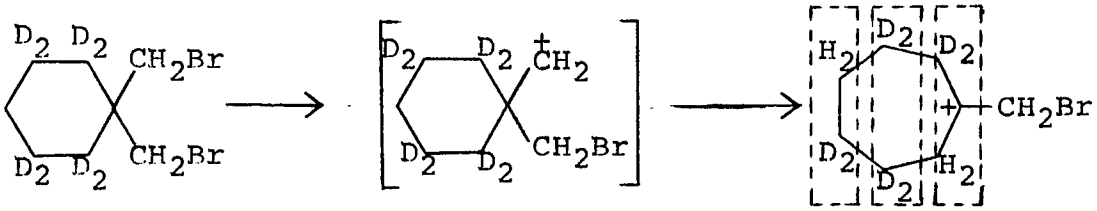
(F) The Friedel-Crafts Reactions of 2,2,3,3,5,5,6,6-Octadeuterio-1,1-bis(bromomethyl)cyclohexane (If) and 2,2,6,6-Tetradeuterio-1,1-bis(bromodideuteriomethyl)cyclohexane (Ig) with Benzene

We then studied the reactions of 2,2,3,3,5,5,6,6-octadeuterio-1,1-bis(bromomethyl)cyclohexane (If) and 2,2,6,6-tetradeuterio-1,1-bis(bromodideuteriomethyl)cyclohexane (Ig). These were expected to provide probes into the possibilities of hydride migration from the 3- and/or the 2-positions of the bromomethylcycloheptyl cation (XVII).

If would lead to a bromomethylcycloheptyl cation (XVIIf) completely deuterated at the 3-position (Scheme liv). If the 3-hydrogen of the starting dibromide (I) eventually becomes part of the bridgehead methyl group, If would give primary product with a $CH_2D$ at the bridgehead position. This would be reflected by loss of 16 in the mass spectrum of primary product IIf. A migration from the 2- or 4-positions would lead to deuterium and hydrogen incorporation and would be reflected by loss of both 16 and 15 in the mass spectrum. This is demonstrated by Scheme liv.

Ig would lead to a bromomethylcycloheptyl cation (XVIIg) completely deuterated at the 2-position (Scheme lv). If the 2-hydrogen of the starting dibromide (I) eventually becomes part of the bridgehead methyl group,

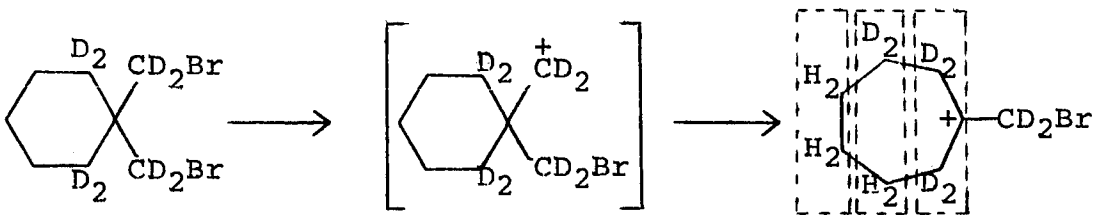
Scheme liv



If IIIf XVIIf

Ig would give primary product with a $CD_3$ at the bridgehead position. This would be reflected by loss of 18 in the mass spectrum of the primary product IIg. A migration from the 3-position of XVIIg would lead to deuterium and hydrogen incorporation and would be reflected by the loss of 18 and 17 in the mass spectrum. A migration from the 4-position of XVIIg would lead to hydrogen incorporation at the bridgehead methyl group and would be reflected by loss of 17 in the mass spectrum. This is demonstrated by Scheme lv.

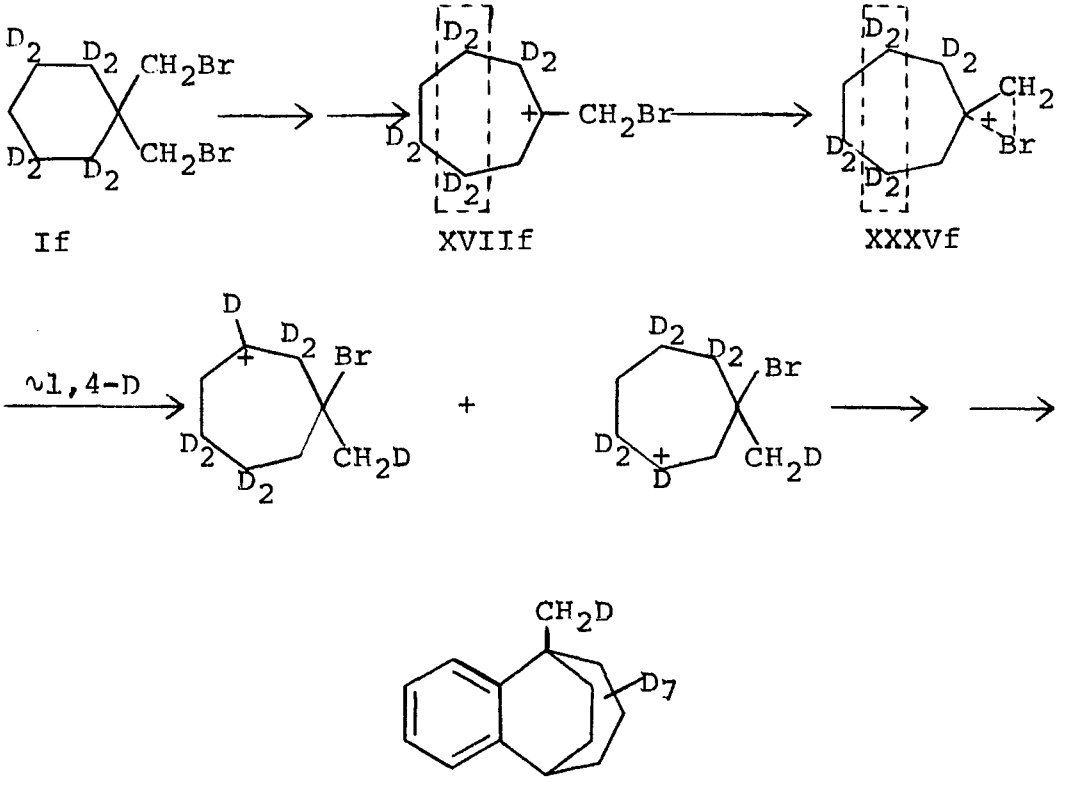
Scheme lv



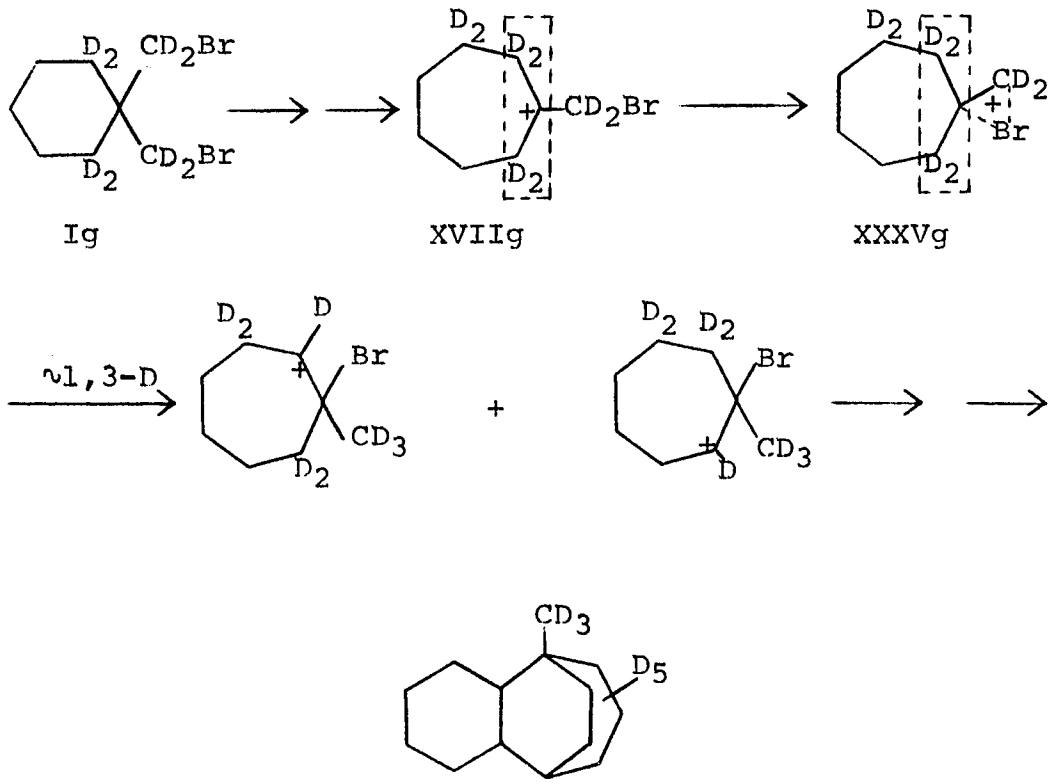
Ig IIIg XVIIg

Two general mechanisms (Scheme xxii, pp. 40-41), in particular, can be checked by examination of the products from If and Ig, Mechanisms IV and V. Step D of Mechanism IV involves a direct hydride shift from the 2-, 3-, or 4-position of the ring of XXXV to the exocyclic methylene group. A shift from the 3-position should be manifested by a deuterium shift in ion XXXVf formed from If. A shift from the 2-position should be manifested by a deuterium shift in ion XXXVg formed from Ig. A shift from the 4-position has already been ruled out (p. 90). These are demonstrated by Schemes lvi and lvii, respectively.

Scheme lvi

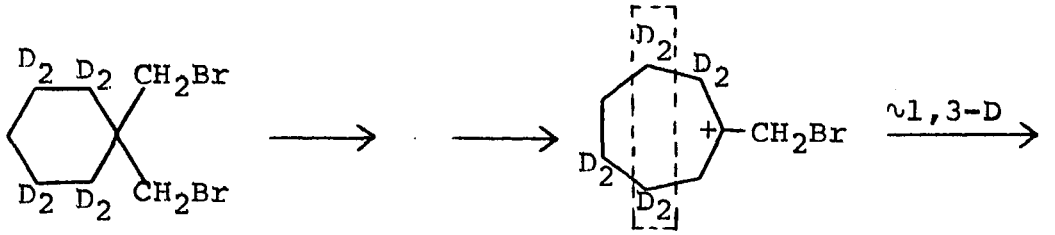


Scheme lvii

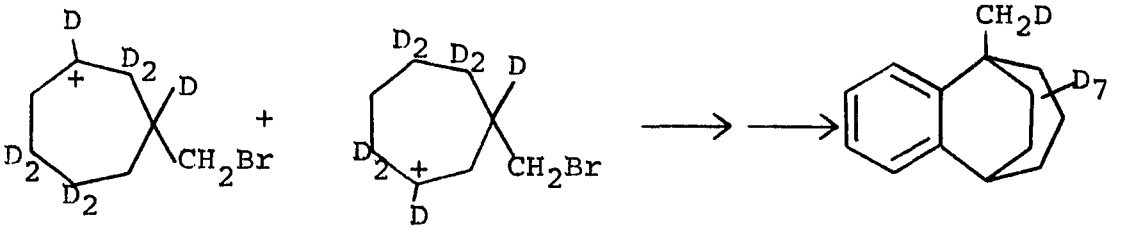



If one of the possibilities of Mechanism V is occurring, If would be expected to provide a check for a 1,3-hydride shift from the 3-position of the 1-bromomethylcycloheptyl cation (XVII) (Step C). Ig would be expected to provide a check for a 1,2-hydride shift from the 2-position of XVII. The 1,4-shift possibility is eliminated by the lack of a significant deuteride shift in the reaction of 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id) (p. 90). These are demonstrated by Schemes lviii and lix, respectively.

Scheme lviii

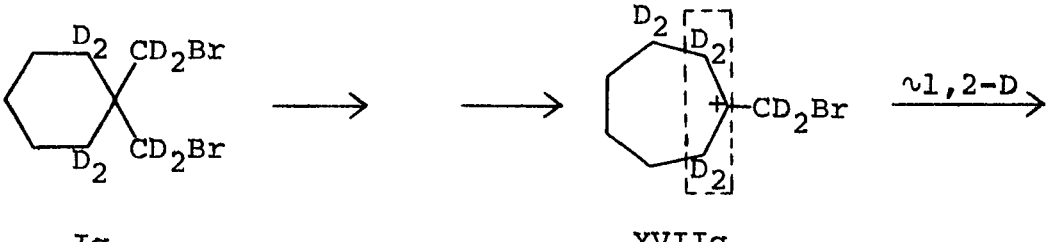


If XVIIf

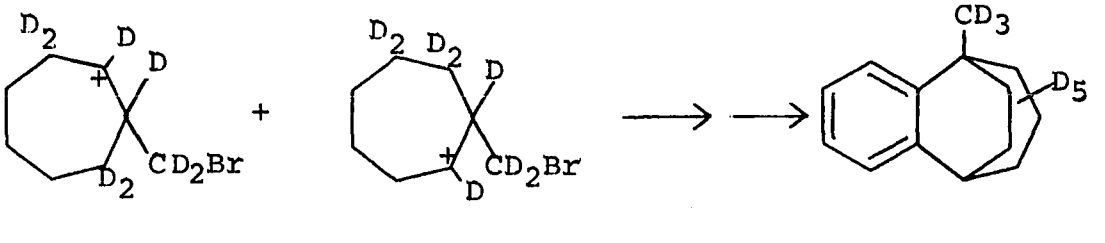


LXXVIIIf$_1$ LXXVIIIf$_2$

Scheme lix



Ig XVIIg



LXXVIIg$_1$ LXXVIIg$_2$

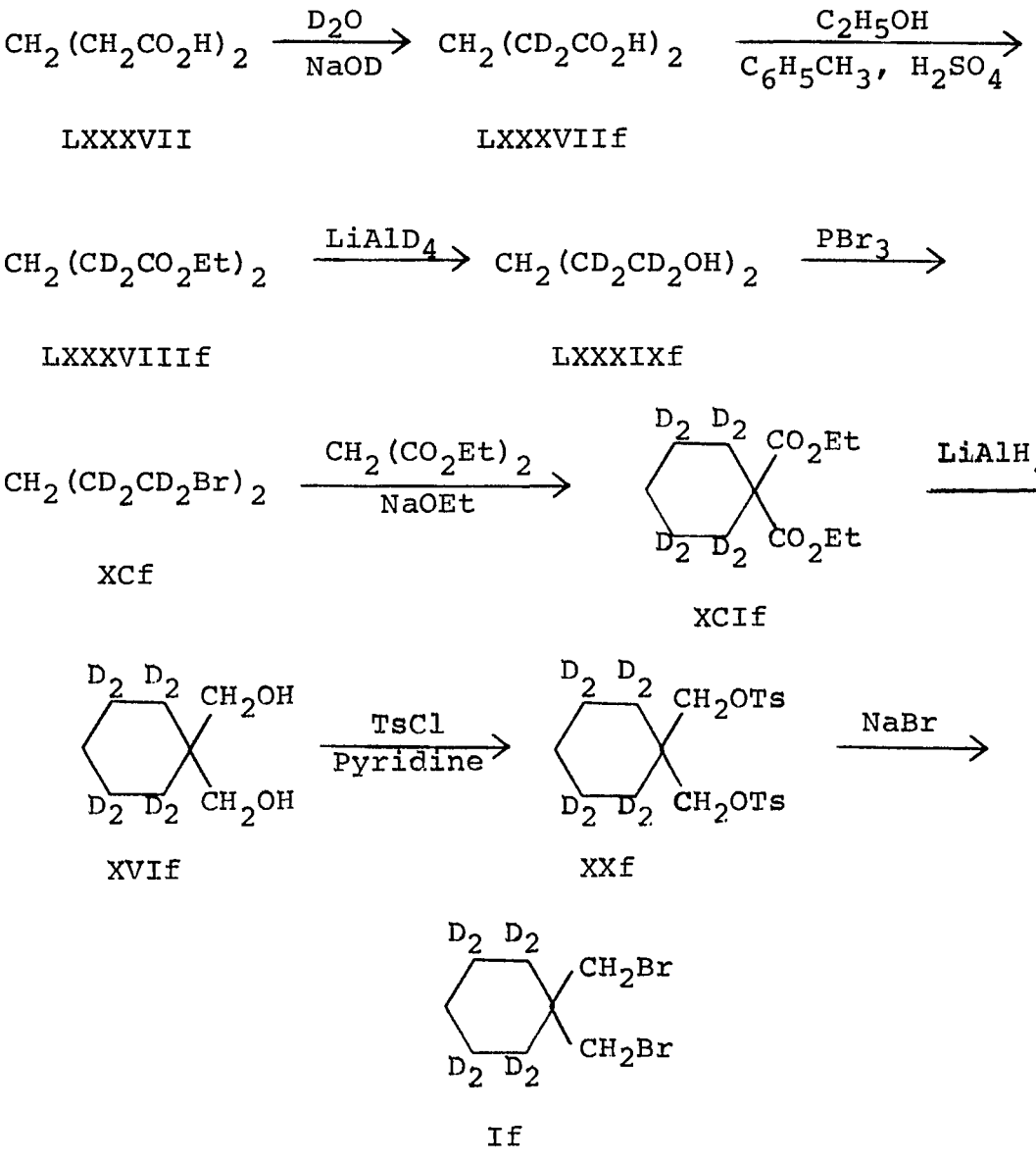
The expected mass spectral peaks for primary product produced from 2,2,3,3,5,5,6,6-octadeuterio-1,1-bis(bromomethyl)cyclohexane (If) and 2,2,6,6-tetradeuterio-1,1-bis-(bromodideuteriomethyl)cyclohexane (Ig) are summarized in Table VIII.

Table VIII. Expected Mass Spectral Peaks for Parent and P - Methyl Peaks of Primary Product (II) and Primary Products-$d_8$ (IIf and IIg)

| Starting Material | Parent Peak of Primary Product | P - Methyl | |
|---|---|---|---|
| | | H Migration | D Migration |
| I | 186 | 171 | - |
| If | 194 | 179 | 178 |
| Ig | 194 | 177 | 176 |

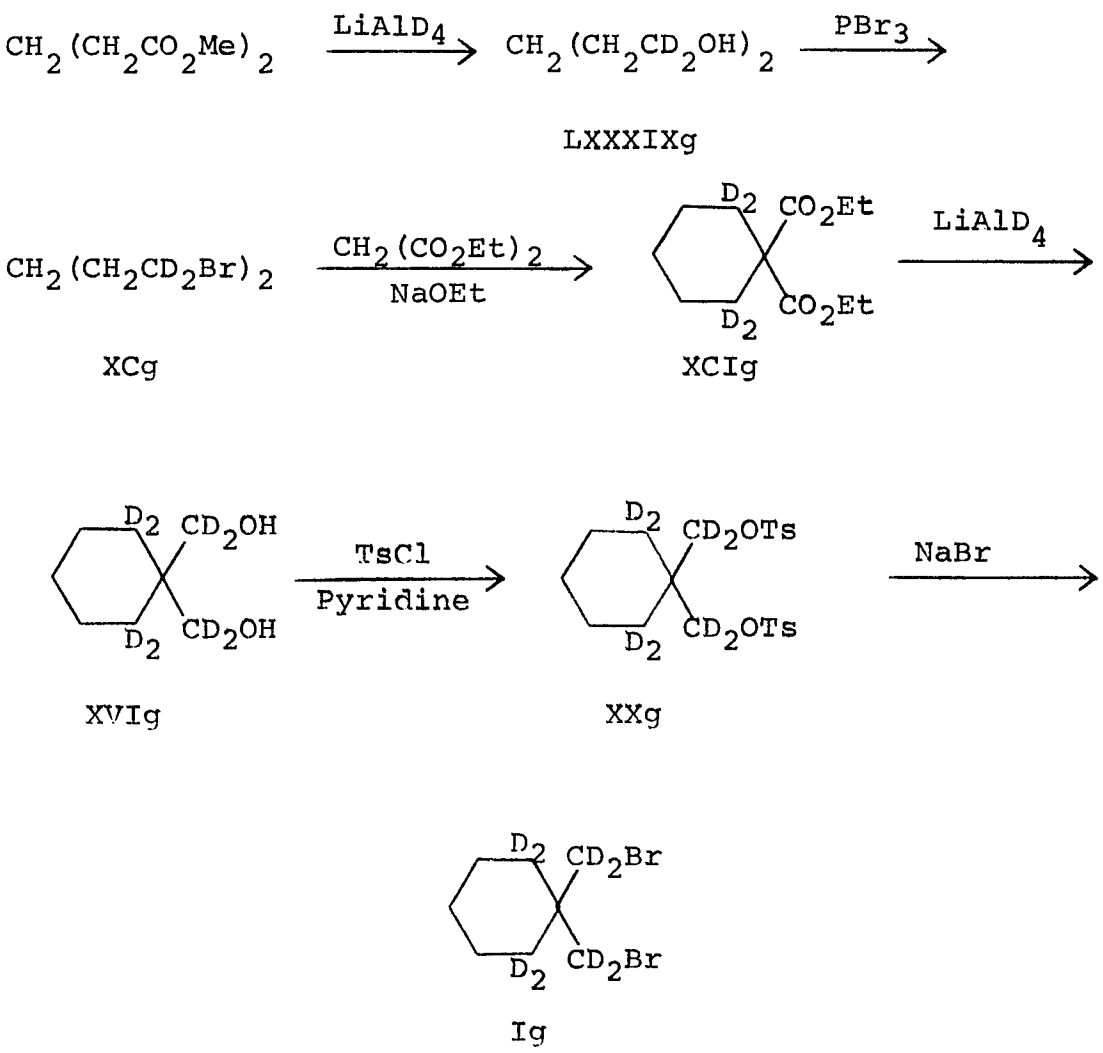
2,2,3,3,5,5,6,6-Octadeuterio-1,1-bis(bromomethyl)cyclohexane (If) was prepared by the same general route as 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id). The 3- and 5-deuterium atoms were incorporated by the base catalyzed exchange of the 2- and 4-hydrogens of glutaric acid (LXXXVII). The 2- and 6-deuterium atoms were incorporated by the reduction of diethyl 2,2,4,4-tetradeuterioglutarate (LXXXVIIIf) with lithium aluminum deuteride (Scheme lx).

Scheme lx




2,2,6,6-Tetradeuterio-1,1-bis(bromodideuteriomethyl)-cyclohexane (Ig) was prepared by the same general route. The 2- and 6-deuterium atoms and the bromomethyl deuterium atoms were incorporated by the reduction of dimethyl glutarate and 2,2,6,6-tetradeuterio-1,1-dicarbethoxycyclohexane (LXXXIXg), respectively, with lithium aluminum deuteride (Scheme lxi).

Scheme lxi




The primary products from the reactions of If and Ig were isolated by preparatory glc and their mass spectra determined as described in the Experimental Section, p. 231 and p. 232. The ratios of peak heights were adjusted as described in Appendix I, p. 125.

The adjusted mass spectral peak heights of primary products II, IIf, and IIg are summarized in Table IX.*

*See footnote on p. 73.

Table IX. Adjusted Parent and P - Methyl Peaks of the Mass Spectra of Primary Product (II) and Primary Products-$d_8$ (IIf and IIg)

| Reaction | | P - Methyl Region m/e relative peak height | | | | Parent Peak Region m/e relative peak height | | | |
|---|---|---|---|---|---|---|---|---|---|
| I | II | 170 1 | 171 30.3 | 172 4.4 | 173 1 | 185 4.6 | 186 100 | 187 15.6 | |
| If | IIf | 177 3.8 | 178 19.1 | 179 22.0 | 180 3.1 | 192 1.9 | 193 16.5 | 194 100 | 195 16.2 |
| Ig | IIg | 175 1.7 | 176 24.5 | 177 12.2 | 178 2.8 | 192 2.0 | 193 17.3 | 194 100 | 195 17.3 |

The percentages of hydrogen and deuterium migration to form the bridgehead methyl group were calculated as described in Appendix II, pp. 146 and 151. For If there was 55.3% H migration and 44.7% D migration. For Ig there was 28.6% H migration and 71.4% D migration.

From these results alone no specific conclusion as to the origin of the third hydrogen of the bridgehead methyl group of the primary product (I) can be reached. In both cases there is a mixture of hydrogen and deuterium migration, showing that none of the aforementioned possibilities can be the only operating mechanism.

## (G) The Mechanism as Derived by Comparison of the Mass Spectra of All Deuterated Primary Products

A comparison of the hydrogen-deuterium migration ratios of all four deuterated dibromides (Id, Ie, If, and Ig) is given in Table X.

Table X. Percent Hydrogen and Deuterium Migration to the Exomethylene Group in the Formation of Primary Product

| Starting Material | Initial Ionization Intermediate | Ring-Expanded Intermediate | Migration to the Exomethylene | |
|---|---|---|---|---|
| | | | Percent H | Percent D |
| Id | IIId | XVIId | 96.0 | 4.0 |
| Ie | IIIe | XVIIe | 79.9 | 20.1 |
| If | IIIf | XVIIf | 55.3 | 44.7 |
| Ig | IIIg | XVIIg | 28.6 | 71.4 |

With this information we are able to examine the possibility of Mechanism III (p. 39) more closely than before (p. 47). Previously this mechanism had been dismissed on the basis of circumstantial evidence - the fact that the 1-bromomethylcycloheptyl cation (XVII) (from 1-bromo-1-bromomethylcycloheptane (LIV)) yielded a reaction mixture virtually identical to that from 1,1-bis(bromomethyl)cyclohexane (I). The possibility of a transannular migration taking place before ring expansion (Step III-B, p. 39) should be discernible from a comparison of the mass spectra of the primary products formed from the four deuterated dibromides. If the predominating mechanism involves an initial 1,4-

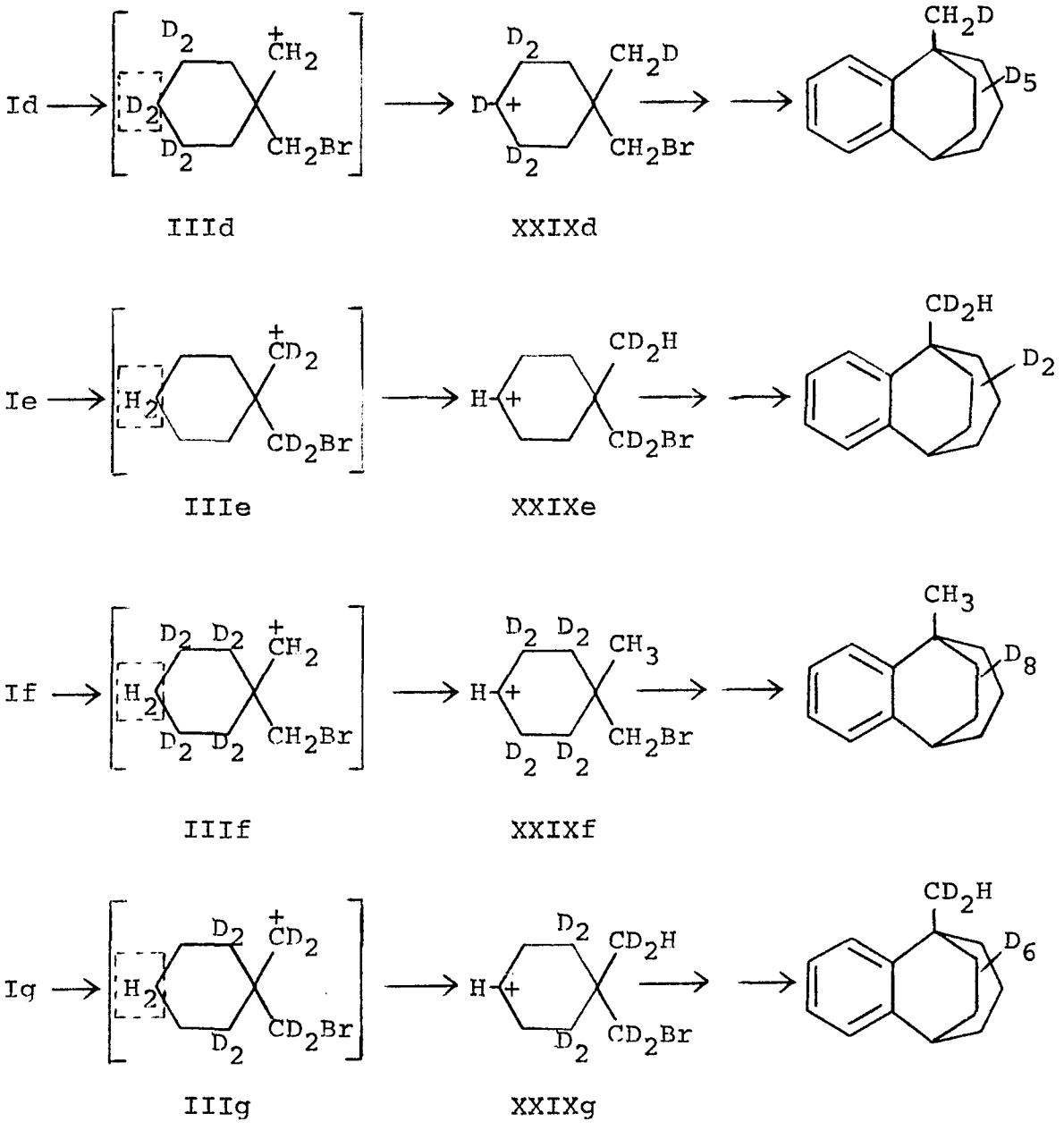
hydride shift in Step III-B, compounds Id and If should give primary products via a deuterium atom shift, and Ie and Ig via a hydrogen shift. If a 1,5-shift is involved, Id should rearrange via migration of deuterium, whereas Ie, If, and Ig should rearrange via migration of hydrogen. A 1,3-shift would result in a hydrogen atom shift from Id and Ie and a deuterium atom shift from If and Ig.

For example, the 1,5-shift is summarized by Scheme lxii.

The results summarized in Table X show that the third hydrogen (deuterium) atom of the bridgehead methyl group does not come from only one position, unless there is some significant scrambling before the migration. In order for there to be scrambling, hydrogens must migrate back and forth toward a cation center. If the bridgehead methyl group is formed by a hydride migration from the ring of the incipient 1-bromomethylcyclohexylmethyl cation (III) (Step III-B), subsequent shifts around the ring could occur. However, since a primary cation is about 33 kcal/mole and 22 kcal/mole less stable than a tertiary ion and a secondary ion, respectively,[83-85] it seems extremely unlikely that a hydrogen would shift from the methyl group back to the ring, thereby regenerating the unstable primary cation. It is only through this kind of shift that scrambling could occur at the methyl group being formed by Mechanism III.

The possibility that the scrambling could occur via protonated cyclopropane intermediates (e.g. Scheme lxiii),

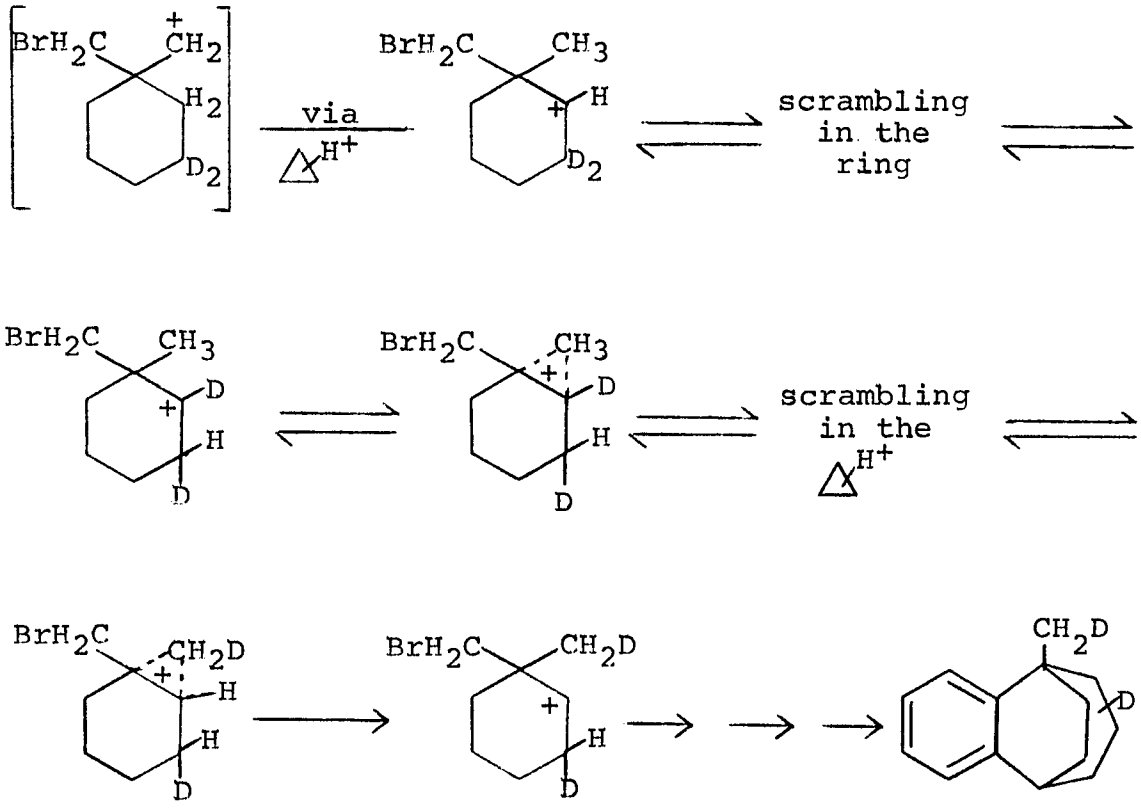
Scheme lxii




thereby eliminating the problem of a primary cation intermediate, is also very unlikely in light of the fact that in many neopentyl systems, under a variety of reaction conditions no such intermediates are formed (pp. 12-14).

If formation of a protonated cyclopropane intermediate to allow the equilibration of two primary cations of a neopentyl system does not occur, then in our system where a more stable secondary ion would have to equilibrate with a primary ion, e.g. Scheme lxiii, it should be even less likely.

Scheme lxiii




On the other hand, if the ring expansion to the 1-bromomethylcycloheptyl cation (XVII) occurs before the hydride migration, the positive charge would now reside in the ring. This would make the possibility that hydride shifts occur before the shift which forms the methyl group more

likely. The information and arguments presented to this point strongly favor this possibility compared to methyl group formation before ring expansion. Therefore, we believe it highly unlikely that Mechanism III is the major pathway in the conversion of dibromide I to primary product (II).

The possibility of a number of different shifts occurring which would account for the ratios of hydrogen-deuterium migration observed was examined in more detail. Various calculations were performed to determine the fraction of hydrogen migration (the ratio of the relative amount of hydrogen migration divided by the total relative migration of hydrogen and deuterium) from each position of the 1-bromomethylcycloheptyl cation (XVII). It was considered that all hydrogen (deuterium) atoms on all the positions of the 1-bromomethylcycloheptyl cation (XVII) could give rise to the third atom of the bridgehead methyl group. Also taken into account was the possibility of an isotope effect in the competition between hydrogen and deuterium in each of the deuterated materials. Isotope effects in the range 1.0 to 3.5 were considered, as would be expected for intramolecular hydride shifts.[95-97] Different isotope effects for shifts from different positions were examined. Also included in the calculations was the possibility that migration from the various positions of XVII were occurring to different extents.

The relative amount of deuterium migration from a given position of the 1-bromomethylcycloheptyl cation (XVII) can be defined as the number of deuterium atoms at the position (D). The relative amount of hydrogen migration is defined as the number of hydrogens at the position (H) times a kinetic isotope effect factor (I). Therefore, we can express the fraction of H migration from position 2 as:

$$\frac{(H_2 \times I_2)}{(H_2 \times I_2) + D_2}$$

When more than one position is being considered, new variables are introduced. First, there is the kinetic isotope effect (I) for each position. Second, if there is an inherent difference in migrating ability of hydrogens at the different positions, then ratio factors (F) must be included. Position 2 would then be represented by:

$$\frac{(H_2 \times I_2 \times F_2)}{(H_2 \times I_2 \times F_2) + (D_2 \times F_2)}$$

To consider the 2-, 3-, and 4-positions together, we must consider the total hydrogen migration and the total deuterium migration from all three positions. The fraction of hydrogen migration can be expressed as:

$$\frac{\Sigma H \text{ migration}}{\Sigma H \text{ migration} + \Sigma D \text{ migration}} =$$

$$\frac{(H_2 \times I_2 \times F_2) + (H_3 \times I_3 \times F_3) + (H_4 \times I_4 \times F_4)}{(H_2 \times I_2 \times F_2) + (H_3 \times I_3 \times F_3) + (H_4 \times I_4 \times F_4) + (D_2 \times F_2) + (D_3 \times F_3) + (D_4 \times F_4)}$$

A computer program for calculating the fraction of hydrogen migration for different values of the variables is described in Appendix III, p. 164. A summary of some of the results of these calculations is given in Table XI.

Table XI. Calculated Fractions of Migration of Hydrogen to the Exomethylene Group in the Formation of Deuterated Primary Products - Competition Between the 2-, 3-, and 4-Positions of the Deuterated 1-Bromomethylcycloheptyl Cations

| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg |
| 1 | 1 | 1 | 1 | 1 | 0 | .75 | .75 | .25 | .25 |
| | | | 1 | 1 | .50 | .60 | .80 | .30 | .40 |
| | | | 1 | 1 | 1 | .50 | .83 | .33 | .50 |
| | | | 2 | 1 | 0 | .83 | .67 | .33 | .17 |
| | | | 2 | 1 | .50 | .71 | .71 | .36 | .29 |
| | | | 2 | 1 | 1 | .63 | .75 | .38 | .38 |
| | | | 3 | 1 | 0 | .88 | .63 | .38 | .13 |
| | | | 3 | 1 | .50 | .78 | .67 | .39 | .22 |
| | | | 3 | 1 | 1 | .70 | .70 | .40 | .30 |
| | | | 3 | 1 | 2 | .58 | .75 | .42 | .42 |
| | | | 3 | 1.5 | 1 | .68 | .73 | .36 | .32 |
| | | | 3 | 2 | 1 | .67 | .75 | .33 | .33 |
| | | | 4 | 1 | 0 | .90 | .60 | .40 | .10 |
| | | | 4 | 1 | .50 | .82 | .64 | .41 | .18 |
| | | | 4 | 1 | 1 | .75 | .67 | .42 | .25 |
| | | | 4 | 1 | 2 | .64 | .71 | .43 | .36 |
| | | | 4 | 2 | 1 | .71 | .71 | .36 | .29 |
| | | | 4 | 3 | 1 | .69 | .75 | .31 | .31 |
| | | | 5 | 1 | 0 | .92 | .58 | .42 | .08 |
| | | | 5 | 1 | .50 | .85 | .62 | .42 | .15 |
| | | | 5 | 1 | 1 | .79 | .64 | .43 | .21 |
| | | | 5 | 1 | 2 | .69 | .69 | .44 | .31 |
| | | | 5 | 2 | 1 | .75 | .69 | .38 | .25 |
| | | | 5 | 3 | 1 | .72 | .72 | .33 | .28 |
| | | | 6 | 1 | 0 | .93 | .57 | .43 | .07 |
| | | | 6 | 1 | .50 | .87 | .60 | .43 | .13 |
| | | | 6 | 1 | 1 | .81 | .63 | .44 | .19 |
| | | | 6 | 1 | 2 | .72 | .67 | .44 | .28 |
| | | | 6 | 2 | 1 | .78 | .67 | .39 | .22 |
| | | | 6 | 3 | 1 | .75 | .70 | .35 | .25 |
| | | | 7 | 1 | 0 | .94 | .56 | .44 | .06 |
| | | | 7 | 1 | .50 | .88 | .59 | .44 | .12 |
| | | | 7 | 1 | 1 | .83 | .61 | .44 | .17 |

Table XI. (cont'd.)

| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg |
| 1 | 1 | 1 | 7 | 1 | 2 | .75 | .65 | .45 | .25 |
| | | | 7 | 2 | 1 | .80 | .65 | .40 | .20 |
| | | | 7 | 3 | 1 | .77 | .68 | .36 | .23 |
| | | | 8 | 1 | 0 | .94 | .56 | .44 | .05 |
| | | | 8 | 1 | .50 | .89 | .58 | .45 | .11 |
| | | | 8 | 1 | 1 | .85 | .60 | .45 | .15 |
| | | | 8 | 1 | 2 | .77 | .64 | .45 | .23 |
| | | | 8 | 2 | 1 | .82 | .64 | .41 | .18 |
| | | | 8 | 3 | 1 | .79 | .67 | .38 | .21 |
| | | | 9 | 1 | 0 | .95 | .55 | .45 | .05 |
| | | | 9 | 1 | .50 | .90 | .57 | .45 | .09 |
| | | | 9 | 1 | 1 | .86 | .59 | .45 | .14 |
| | | | 9 | 1 | 2 | .79 | .63 | .46 | .21 |
| | | | 9 | 2 | 1 | .83 | .63 | .42 | .17 |
| | | | 9 | 3 | 1 | .81 | .65 | .38 | .19 |
| | | | 9 | 4 | 1 | .79 | .68 | .36 | .21 |
| | | | 10 | 1 | 0 | .95 | .55 | .45 | .04 |
| | | | 10 | 1 | .50 | .91 | .57 | .46 | .08 |
| | | | 10 | 1 | 1 | .88 | .58 | .46 | .13 |
| | | | 10 | 1 | 2 | .81 | .62 | .46 | .19 |
| | | | 10 | 2 | 1 | .85 | .62 | .42 | .15 |
| | | | 10 | 3 | 1 | .82 | .64 | .39 | .18 |
| | | | 10 | 4 | 1 | .80 | .67 | .37 | .20 |
| 1.5 | 1.5 | 1.5 | 1 | 1 | 0 | .82 | .82 | .33 | .33 |
| | | | 1 | 1 | .50 | .69 | .86 | .39 | .50 |
| | | | 1 | 1 | 1 | .60 | .88 | .43 | .60 |
| | | | 2 | 1 | 0 | .88 | .75 | .43 | .23 |
| | | | 2 | 1 | .50 | .79 | .79 | .45 | .38 |
| | | | 2 | 1 | 1 | .71 | .82 | .47 | .47 |
| | | | 3 | 1 | 0 | .91 | .71 | .47 | .18 |
| | | | 3 | 1 | .50 | .84 | .75 | .49 | .30 |
| | | | 3 | 1 | 1 | .78 | .78 | .50 | .39 |
| | | | 3 | 1 | 2 | .68 | .82 | .52 | .52 |
| | | | 3 | 1.5 | 1 | .76 | .80 | .46 | .41 |
| | | | 3 | 2 | 1 | .75 | .82 | .43 | .43 |
| | | | 4 | 1 | 0 | .93 | .69 | .50 | .14 |
| | | | 4 | 1 | .50 | .87 | .72 | .51 | .25 |
| | | | 4 | 1 | 1 | .82 | .75 | .52 | .33 |
| | | | 4 | 1 | 2 | .73 | .79 | .53 | .45 |
| | | | 4 | 2 | 1 | .79 | .79 | .45 | .38 |
| | | | 4 | 3 | 1 | .77 | .82 | .41 | .41 |
| | | | 5 | 1 | 0 | .94 | .68 | .52 | .12 |
| | | | 5 | 1 | .50 | .89 | .71 | .52 | .21 |
| | | | 5 | 1 | 1 | .85 | .73 | .53 | .29 |
| | | | 5 | 1 | 2 | .77 | .77 | .54 | .41 |

Table XI. (cont'd.)

| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg | |
| 1.5 | 1.5 | 1.5 | 5 | 2 | 1 | .82 | .77 | .47 | .33 | |
| | | | 5 | 3 | 1 | .80 | .80 | .43 | .37 | |
| | | | 6 | 1 | 0 | .95 | .67 | .53 | .10 | |
| | | | 6 | 1 | .50 | .91 | .69 | .53 | .19 | |
| | | | 6 | 1 | 1 | .87 | .71 | .54 | .26 | |
| | | | 6 | 1 | 2 | .80 | .75 | .55 | .37 | |
| | | | 6 | 2 | 1 | .84 | .75 | .49 | .30 | |
| | | | 6 | 3 | 1 | .82 | .78 | .45 | .33 | |
| | | | 7 | 1 | 0 | .96 | .66 | .54 | .09 | |
| | | | 7 | 1 | .50 | .92 | .68 | .54 | .17 | |
| | | | 7 | 1 | 1 | .88 | .70 | .55 | .23 | |
| | | | 7 | 1 | 2 | .82 | .74 | .55 | .33 | |
| | | | 7 | 2 | 1 | .86 | .74 | .50 | .27 | |
| | | | 7 | 3 | 1 | .84 | .76 | .46 | .31 | |
| | | | 8 | 1 | 0 | .96 | .65 | .55 | .08 | |
| | | | 8 | 1 | .50 | .93 | .67 | .55 | .15 | |
| | | | 8 | 1 | 1 | .89 | .69 | .55 | .21 | |
| | | | 8 | 1 | 2 | .84 | .72 | .56 | .31 | |
| | | | 8 | 2 | 1 | .87 | .72 | .51 | .25 | |
| | | | 8 | 3 | 1 | .85 | .75 | .47 | .28 | |
| | | | 9 | 1 | 0 | .97 | .65 | .55 | .07 | |
| | | | 9 | 1 | .50 | .93 | .67 | .55 | .14 | |
| | | | 9 | 1 | 1 | .90 | .68 | .56 | .19 | |
| | | | 9 | 1 | 2 | .85 | .71 | .56 | .28 | |
| | | | 9 | 2 | 1 | .88 | .71 | .52 | .23 | |
| | | | 9 | 3 | 1 | .86 | .74 | .48 | .26 | |
| | | | 9 | 4 | 1 | .85 | .76 | .45 | .29 | |
| | | | 10 | 1 | 0 | .97 | .64 | .56 | .06 | |
| | | | 10 | 1 | .50 | .94 | .66 | .56 | .13 | |
| | | | 10 | 1 | 1 | .91 | .68 | .56 | .18 | |
| | | | 10 | 1 | 2 | .86 | .71 | .56 | .26 | |
| | | | 10 | 2 | 1 | .89 | .71 | .52 | .21 | |
| | | | 10 | 3 | 1 | .87 | .73 | .49 | .25 | |
| | | | 10 | 4 | 1 | .86 | .75 | .46 | .27 | |
| 2 | 2 | 2 | 1 | 1 | 0 | .86 | .86 | .40 | .40 | |
| | | | 1 | 1 | .50 | .75 | .89 | .46 | .57 | |
| | | | 1 | 1 | 1 | .67 | .91 | .50 | .67 | |
| | | | 2 | 1 | 0 | .91 | .80 | .50 | .29 | * |
| | | | 2 | 1 | .50 | .83 | .83 | .53 | .44 | |
| | | | 2 | 1 | 1 | .77 | .86 | .55 | .55 | |
| | | | 3 | 1 | 0 | .93 | .77 | .55 | .22 | |

*All numbers in this set lie within ±.05 of the experimental value (see Appendix II, p. 129).

Table XI. (cont'd.)

| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg | |
| 2 | 2 | 2 | 3 | 1 | .50 | .88 | .80 | .56 | .36 | |
| | | | 3 | 1 | 1 | .82 | .82 | .57 | .46 | |
| | | | 3 | 1 | 2 | .74 | .86 | .59 | .59 | |
| | | | 3 | 1.5 | 1 | .81 | .84 | .53 | .48 | |
| | | | 3 | 2 | 1 | .80 | .86 | .50 | .50 | |
| | | | 4 | 1 | 0 | .95 | .75 | .57 | .18 | |
| | | | 4 | 1 | .50 | .90 | .78 | .58 | .31 | |
| | | | 4 | 1 | 1 | .86 | .80 | .59 | .40 | |
| | | | 4 | 1 | 2 | .78 | .83 | .60 | .53 | |
| | | | 4 | 2 | 1 | .83 | .83 | .53 | .44 | |
| | | | 4 | 3 | 1 | .81 | .86 | .48 | .48 | |
| | | | 5 | 1 | 0 | .96 | .74 | .59 | .15 | |
| | | | 5 | 1 | .50 | .92 | .76 | .59 | .27 | * |
| | | | 5 | 1 | 1 | .88 | .78 | .60 | .35 | |
| | | | 5 | 1 | 2 | .81 | .81 | .61 | .48 | |
| | | | 5 | 2 | 1 | .86 | .81 | .55 | .40 | |
| | | | 5 | 3 | 1 | .84 | .84 | .50 | .43 | |
| | | | 6 | 1 | 0 | .96 | .73 | .60 | .13 | |
| | | | 6 | 1 | .50 | .93 | .75 | .60 | .24 | * |
| | | | 6 | 1 | 1 | .90 | .77 | .61 | .32 | |
| | | | 6 | 1 | 2 | .84 | .80 | .62 | .43 | |
| | | | 6 | 2 | 1 | .88 | .80 | .56 | .36 | |
| | | | 6 | 3 | 1 | .86 | .82 | .52 | .40 | |
| | | | 7 | 1 | 0 | .97 | .72 | .61 | .12 | |
| | | | 7 | 1 | .50 | .94 | .74 | .61 | .21 | |
| | | | 7 | 1 | 1 | .90 | .76 | .62 | .29 | |
| | | | 7 | 1 | 2 | .86 | .79 | .62 | .40 | |
| | | | 7 | 2 | 1 | .89 | .79 | .57 | .33 | |
| | | | 7 | 3 | 1 | .87 | .81 | .53 | .37 | |
| | | | 8 | 1 | 0 | .97 | .71 | .62 | .11 | |
| | | | 8 | 1 | .50 | .94 | .73 | .62 | .19 | |
| | | | 8 | 1 | 1 | .92 | .75 | .62 | .26 | |
| | | | 8 | 1 | 2 | .87 | .78 | .63 | .37 | |
| | | | 8 | 2 | 1 | .90 | .78 | .58 | .31 | |
| | | | 8 | 3 | 1 | .88 | .80 | .55 | .34 | |
| | | | 9 | 1 | 0 | .97 | .71 | .62 | .09 | |
| | | | 9 | 1 | .50 | .95 | .73 | .62 | .17 | |
| | | | 9 | 1 | 1 | .93 | .74 | .63 | .24 | |
| | | | 9 | 1 | 2 | .88 | .77 | .63 | .34 | |
| | | | 9 | 2 | 1 | .91 | .77 | .59 | .29 | |
| | | | 9 | 3 | 1 | .89 | .79 | .56 | .32 | |

*All numbers in this set lie within ±.05 of the experimental value (see Appendix II, p. 129).

Table XI. (cont'd.)

| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg | |
| 2 | 2 | 2 | 9 | 4 | 1 | .88 | .81 | .53 | .35 | |
| | | | 10 | 1 | 0 | .98 | .71 | .63 | .08 | |
| | | | 10 | 1 | .50 | .95 | .72 | .63 | .16 | |
| | | | 10 | 1 | 1 | .93 | .74 | .63 | .22 | |
| | | | 10 | 1 | 2 | .89 | .76 | .63 | .32 | |
| | | | 10 | 2 | 1 | .92 | .76 | .59 | .27 | * |
| | | | 10 | 3 | 1 | .90 | .78 | .56 | .30 | |
| | | | 10 | 4 | 1 | .89 | .80 | .54 | .33 | |
| 2.5 | 2.5 | 2.5 | 1 | 1 | 0 | .88 | .88 | .45 | .45 | |
| | | | 1 | 1 | .50 | .79 | .91 | .52 | .63 | |
| | | | 1 | 1 | 1 | .71 | .93 | .56 | .71 | |
| | | | 2 | 1 | 0 | .93 | .83 | .56 | .33 | * |
| | | | 2 | 1 | .50 | .86 | .86 | .58 | .50 | |
| | | | 2 | 1 | 1 | .81 | .88 | .60 | .60 | |
| | | | 3 | 1 | 0 | .95 | .81 | .60 | .26 | * |
| | | | 3 | 1 | .50 | .90 | .83 | .61 | .42 | |
| | | | 3 | 1 | 1 | .85 | .85 | .63 | .52 | |
| | | | 3 | 1 | 2 | .78 | .88 | .64 | .64 | |
| | | | 3 | 1.5 | 1 | .84 | .87 | .59 | .54 | |
| | | | 3 | 2 | 1 | .83 | .88 | .56 | .56 | |
| | | | 4 | 1 | 0 | .96 | .79 | .63 | .22 | |
| | | | 4 | 1 | .50 | .92 | .81 | .63 | .36 | |
| | | | 4 | 1 | 1 | .88 | .83 | .64 | .45 | |
| | | | 4 | 1 | 2 | .82 | .86 | .65 | .58 | |
| | | | 4 | 2 | 1 | .86 | .86 | .58 | .50 | |
| | | | 4 | 3 | 1 | .85 | .88 | .53 | .53 | |
| | | | 5 | 1 | 0 | .96 | .78 | .64 | .19 | |
| | | | 5 | 1 | .50 | .93 | .80 | .65 | .31 | |
| | | | 5 | 1 | 1 | .90 | .82 | .65 | .41 | |
| | | | 5 | 1 | 2 | .85 | .85 | .66 | .53 | |
| | | | 5 | 2 | 1 | .88 | .85 | .60 | .45 | |
| | | | 5 | 3 | 1 | .87 | .87 | .56 | .49 | |
| | | | 6 | 1 | 0 | .97 | .77 | .65 | .16 | |
| | | | 6 | 1 | .50 | .94 | .79 | .66 | .28 | |
| | | | 6 | 1 | 1 | .92 | .81 | .66 | .37 | |
| | | | 6 | 1 | 2 | .87 | .83 | .67 | .49 | |
| | | | 6 | 2 | 1 | .90 | .83 | .61 | .42 | |
| | | | 6 | 3 | 1 | .88 | .85 | .57 | .45 | |
| | | | 7 | 1 | 0 | .97 | .76 | .66 | .14 | |
| | | | 7 | 1 | .50 | .95 | .78 | .66 | .25 | |
| | | | 7 | 1 | 1 | .93 | .80 | .67 | .33 | |

*All numbers in this set lie within ±.05 of the experimental value (see Appendix II, p. 129).

Table XI. (cont'd.)

| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg |
| 2.5 | 2.5 | 2.5 | 7 | 1 | 2 | .88 | .82 | .67 | .45 |
| | | | 7 | 2 | 1 | .91 | .82 | .63 | .38 |
| | | | 7 | 3 | 1 | .89 | .84 | .59 | .42 |
| | | | 8 | 1 | 0 | .98 | .76 | .67 | .13 |
| | | | 8 | 1 | .50 | .96 | .77 | .67 | .23 |
| | | | 8 | 1 | 1 | .93 | .79 | .67 | .31 |
| | | | 8 | 1 | 2 | .89 | .81 | .68 | .42 |
| | | | 8 | 2 | 1 | .92 | .81 | .63 | .36 |
| | | | 8 | 3 | 1 | .90 | .83 | .60 | .40 |
| | | | 9 | 1 | 0 | .98 | .75 | .67 | .12 |
| | | | 9 | 1 | .50 | .96 | .77 | .67 | .21 |
| | | | 9 | 1 | 1 | .94 | .78 | .68 | .28 |
| | | | 9 | 1 | 2 | .90 | .81 | .68 | .40 |
| | | | 9 | 2 | 1 | .93 | .81 | .64 | .33 |
| | | | 9 | 3 | 1 | .91 | .83 | .61 | .37 |
| | | | 9 | 4 | 1 | .90 | .84 | .58 | .41 |
| | | | 10 | 1 | 0 | .98 | .75 | .68 | .11 |
| | | | 10 | 1 | .50 | .96 | .76 | .68 | .19 |
| | | | 10 | 1 | 1 | .95 | .78 | .68 | .26 |
| | | | 10 | 1 | 2 | .91 | .80 | .68 | .37 |
| | | | 10 | 2 | 1 | .93 | .80 | .65 | .31 |
| | | | 10 | 3 | 1 | .92 | .82 | .62 | .35 |
| | | | 10 | 4 | 1 | .91 | .83 | .59 | .38 |
| 3 | 3 | 3 | 1 | 1 | 0 | .90 | .90 | .50 | .50 |
| | | | 1 | 1 | .50 | .82 | .92 | .56 | .67 |
| | | | 1 | 1 | 1 | .75 | .94 | .60 | .75 |
| | | | 2 | 1 | 0 | .94 | .86 | .60 | .38 |
| | | | 2 | 1 | .50 | .88 | .88 | .63 | .55 |
| | | | 2 | 1 | 1 | .83 | .90 | .64 | .64 |
| | | | 3 | 1 | 0 | .95 | .83 | .64 | .30 |
| | | | 3 | 1 | .50 | .91 | .86 | .66 | .46 |
| | | | 3 | 1 | 1 | .88 | .88 | .67 | .56 |
| | | | 3 | 1 | 2 | .81 | .90 | .68 | .68 |
| | | | 3 | 1.5 | 1 | .87 | .89 | .63 | .58 |
| | | | 3 | 2 | 1 | .86 | .90 | .60 | .60 |
| | | | 4 | 1 | 0 | .96 | .82 | .67 | .25 |
| | | | 4 | 1 | .50 | .93 | .84 | .68 | .40 |
| | | | 4 | 1 | 1 | .90 | .86 | .68 | .50 |
| | | | 4 | 1 | 2 | .84 | .88 | .69 | .63 |
| | | | 4 | 2 | 1 | .88 | .88 | .63 | .55 |
| | | | 4 | 3 | 1 | .87 | .90 | .58 | .58 |
| | | | 5 | 1 | 0 | .97 | .81 | .68 | .21 |
| | | | 5 | 1 | .50 | .94 | .83 | .69 | .35 |
| | | | 5 | 1 | 1 | .92 | .84 | .69 | .45 |
| | | | 5 | 1 | 2 | .87 | .87 | .70 | .58 |

Table XI. (cont'd.)

| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg |
| 3 | 3 | 3 | 5 | 2 | 1 | .90 | .87 | .64 | .50 |
| | | | 5 | 3 | 1 | .89 | .89 | .60 | .54 |
| | | | 6 | 1 | 0 | .98 | .80 | .69 | .19 |
| | | | 6 | 1 | .50 | .95 | .82 | .70 | .32 |
| | | | 6 | 1 | 1 | .93 | .83 | .70 | .41 |
| | | | 6 | 1 | 2 | .89 | .86 | .71 | .54 |
| | | | 6 | 2 | 1 | .91 | .86 | .66 | .46 |
| | | | 6 | 3 | 1 | .90 | .88 | .62 | .50 |
| | | | 7 | 1 | 0 | .98 | .79 | .70 | .17 |
| | | | 7 | 1 | .50 | .96 | .81 | .70 | .29 |
| | | | 7 | 1 | 1 | .94 | .83 | .71 | .38 |
| | | | 7 | 1 | 2 | .90 | .85 | .71 | .50 |
| | | | 7 | 2 | 1 | .92 | .85 | .67 | .43 |
| | | | 7 | 3 | 1 | .91 | .87 | .63 | .47 |
| | | | 8 | 1 | 0 | .98 | .79 | .71 | .15 |
| | | | 8 | 1 | .50 | .96 | .80 | .71 | .26 |
| | | | 8 | 1 | 1 | .94 | .82 | .71 | .35 |
| | | | 8 | 1 | 2 | .91 | .84 | .71 | .47 |
| | | | 8 | 2 | 1 | .93 | .84 | .68 | .40 |
| | | | 8 | 3 | 1 | .92 | .86 | .64 | .44 |
| | | | 9 | 1 | 0 | .98 | .79 | .71 | .14 |
| | | | 9 | 1 | .50 | .97 | .80 | .71 | .24 |
| | | | 9 | 1 | 1 | .95 | .81 | .71 | .32 |
| | | | 9 | 1 | 2 | .92 | .83 | .72 | .44 |
| | | | 9 | 2 | 1 | .94 | .83 | .68 | .38 |
| | | | 9 | 3 | 1 | .93 | .85 | .65 | .42 |
| | | | 9 | 4 | 1 | .92 | .86 | .63 | .45 |
| | | | 10 | 1 | 0 | .98 | .78 | .71 | .13 |
| | | | 10 | 1 | .50 | .97 | .80 | .72 | .22 |
| | | | 10 | 1 | 1 | .95 | .81 | .72 | .30 |
| | | | 10 | 1 | 2 | .93 | .83 | .72 | .42 |
| | | | 10 | 2 | 1 | .94 | .83 | .69 | .35 |
| | | | 10 | 3 | 1 | .93 | .84 | .66 | .39 |
| | | | 10 | 4 | 1 | .92 | .86 | .63 | .43 |
| 3.5 | 3.5 | 3.5 | 1 | 1 | 0 | .91 | .91 | .54 | .54 |
| | | | 1 | 1 | .50 | .84 | .93 | .60 | .70 |
| | | | 1 | 1 | 1 | .78 | .95 | .64 | .78 |
| | | | 2 | 1 | 0 | .95 | .88 | .64 | .41 |
| | | | 2 | 1 | .50 | .90 | .90 | .66 | .58 |
| | | | 2 | 1 | 1 | .85 | .91 | .68 | .68 |
| | | | 3 | 1 | 0 | .96 | .85 | .68 | .33 |
| | | | 3 | 1 | .50 | .92 | .88 | .69 | .50 |
| | | | 3 | 1 | 1 | .89 | .89 | .70 | .60 |
| | | | 3 | 1 | 2 | .83 | .91 | .71 | .71 |
| | | | 3 | 1.5 | 1 | .88 | .90 | .67 | .62 |

Table XI. (cont'd.)

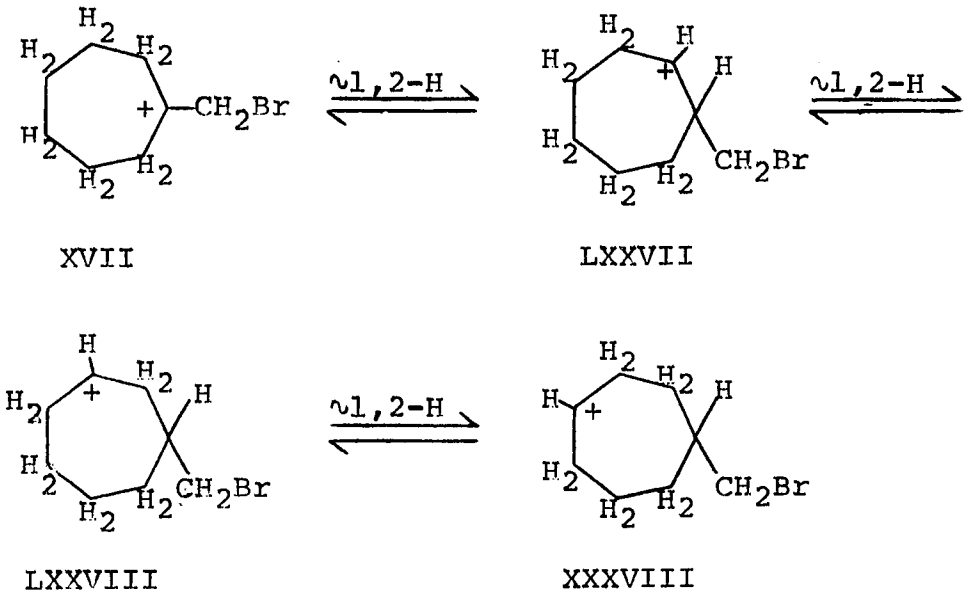
| Isotope Effects (I) | | | Ratio Factors (F) | | | Fractions of H Migration | | | |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 4 | 2 | 3 | 4 | IId | IIe | IIf | IIg |
| 3.5 | 3.5 | 3.5 | 3 | 2 | 1 | .88 | .91 | .64 | .64 |
| | | | 4 | 1 | 0 | .97 | .84 | .70 | .28 |
| | | | 4 | 1 | .50 | .94 | .86 | .71 | .44 |
| | | | 4 | 1 | 1 | .91 | .88 | .71 | .54 |
| | | | 4 | 1 | 2 | .86 | .90 | .72 | .66 |
| | | | 4 | 2 | 1 | .90 | .90 | .66 | .58 |
| | | | 4 | 3 | 1 | .89 | .91 | .61 | .61 |
| | | | 5 | 1 | 0 | .97 | .83 | .71 | .24 |
| | | | 5 | 1 | .50 | .95 | .85 | .72 | .39 |
| | | | 5 | 1 | 1 | .93 | .86 | .72 | .49 |
| | | | 5 | 1 | 2 | .89 | .89 | .73 | .61 |
| | | | 5 | 2 | 1 | .91 | .89 | .68 | .54 |
| | | | 5 | 3 | 1 | .90 | .90 | .64 | .57 |
| | | | 6 | 1 | 0 | .98 | .82 | .72 | .21 |
| | | | 6 | 1 | .50 | .96 | .84 | .73 | .35 |
| | | | 6 | 1 | 1 | .94 | .85 | .73 | .45 |
| | | | 6 | 1 | 2 | .90 | .88 | .74 | .57 |
| | | | 6 | 2 | 1 | .92 | .88 | .69 | .50 |
| | | | 6 | 3 | 1 | .91 | .89 | .65 | .54 |
| | | | 7 | 1 | 0 | .98 | .82 | .73 | .19 |
| | | | 7 | 1 | .50 | .96 | .83 | .73 | .32 |
| | | | 7 | 1 | 1 | .95 | .85 | .74 | .41 |
| | | | 7 | 1 | 2 | .91 | .87 | .74 | .54 |
| | | | 7 | 2 | 1 | .93 | .87 | .70 | .47 |
| | | | 7 | 3 | 1 | .92 | .88 | .67 | .51 |
| | | | 8 | 1 | 0 | .98 | .81 | .74 | .17 |
| | | | 8 | 1 | .50 | .97 | .83 | .74 | .29 |
| | | | 8 | 1 | 1 | .95 | .84 | .74 | .38 |
| | | | 8 | 1 | 2 | .92 | .86 | .74 | .51 |
| | | | 8 | 2 | 1 | .94 | .86 | .71 | .44 |
| | | | 8 | 3 | 1 | .93 | .88 | .68 | .48 |
| | | | 9 | 1 | 0 | .99 | .81 | .74 | .16 |
| | | | 9 | 1 | .50 | .97 | .82 | .74 | .27 |
| | | | 9 | 1 | 1 | .96 | .83 | .74 | .36 |
| | | | 9 | 1 | 2 | .93 | .85 | .75 | .48 |
| | | | 9 | 2 | 1 | .95 | .85 | .71 | .41 |
| | | | 9 | 3 | 1 | .94 | .87 | .69 | .45 |
| | | | 9 | 4 | 1 | .93 | .88 | .66 | .49 |
| | | | 10 | 1 | 0 | .99 | .81 | .74 | .14 |
| | | | 10 | 1 | .50 | .97 | .82 | .75 | .25 |
| | | | 10 | 1 | 1 | .96 | .83 | .75 | .33 |
| | | | 10 | 1 | 2 | .94 | .85 | .75 | .45 |
| | | | 10 | 2 | 1 | .95 | .85 | .72 | .39 |
| | | | 10 | 3 | 1 | .94 | .86 | .69 | .43 |
| | | | 10 | 4 | 1 | .93 | .88 | .67 | .47 |

The calculated results that best correspond to the experimental data (Table X, p. 104), those sets of Table XI marked with an asterisk, involve an isotope effect of 2.0 and a migration ratio, $F_2:F_3:F_4$, of 2-6:1:0-.50, or an isotope effect of 2.5 and a migration ratio 2-3:1:0. This indicates that approximately 67-80% of the third hydrogen (deuterium) of the methyl group of the primary product comes from the 2-position of the 1-bromomethylcycloheptyl cation (XVII) with lesser amounts from the further removed positions, mostly the 3-position. It seems that the further removed the position the smaller the contribution to the hydrogens (deuteriums) that migrate to the exomethylene group.

These results may be explained by invoking Mechanism V, p. 41. Hydrogen would migrate to C-1 of the 1-bromomethylcycloheptyl cation (XVII) by a series of reversible 1,2-hydride shifts (Step V-C) as shown in Scheme lxiv. The further removed a hydrogen (deuterium) is from C-1, the greater the number of shifts necessary for it to reach C-1.

Alkylation of benzene (Step V-D) would occur by species XXXVIII (Scheme lxv), where the positive charge is far-removed from the halogen atom. (See pp. 67-68 for examples of a positive charge migrating away from a halogen atom.) Further reaction would lead to a hydride shift of the tertiary hydrogen on C-1 to form the 1-methyl-4-phenylcycloheptyl cation (XXX), which, as was shown on p. 48,

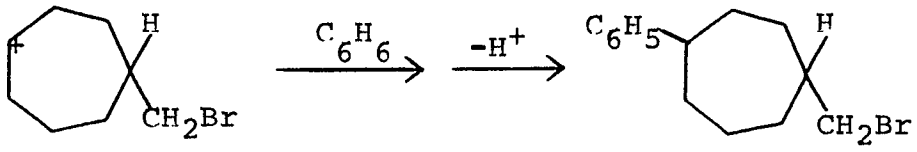
Scheme lxiv




XVII LXXVII

LXXVIII XXXVIII

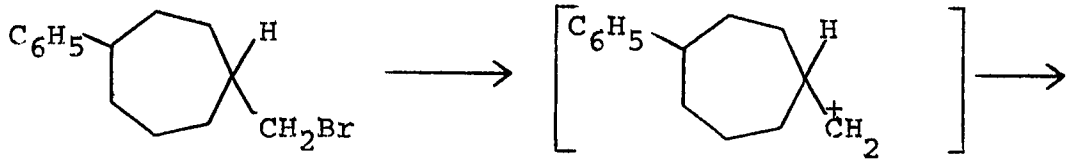
Scheme lxv



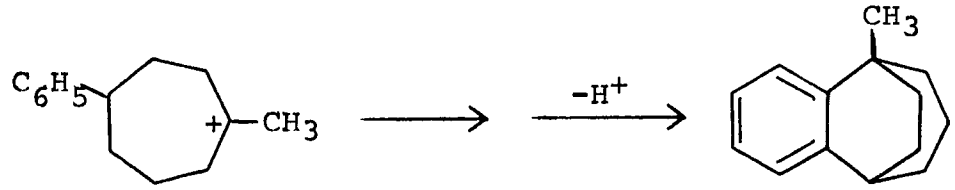

XXXVIII XXXIX

would undergo intramolecular alkylation to form the primary product (II), as in Scheme lxvi.

Scheme lxvi




XXXIX XL




XXX II

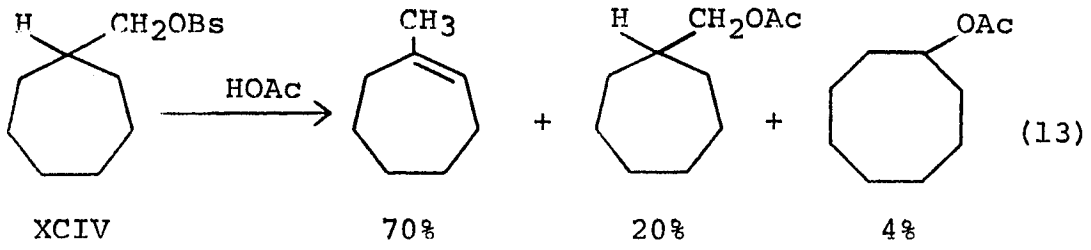
## The Friedel-Crafts Reaction of 1-Bromomethyl-4-phenylcycloheptane (XXXIX) with Benzene

In the previous section we saw how the results of the mass spectra of the deuterated primary products from Id, Ie, If, and Ig could be understood in terms of Mechanism V (p. 41). We were able to put this mechanism to a further test by studying the reaction of 1-bromomethyl-4-phenylcycloheptane (XXXIX) with benzene and aluminum chloride under the usual conditions.

That 1-bromomethyl-4-phenylcycloheptane (XXXIX) should react to give the 1-methyl-4-phenylcycloheptyl cation (XL), followed by intramolecular alkylation to form the primary product, is not unexpected. The major rearrangement pathway for the cycloheptylmethyl cation (XCIII) has been found to involve a 1,2-hydride shift to form the methylcycloheptyl ion which reacts further.

Prunier[98] and Chuit and co-workers[67] have shown that, upon acetolysis, cycloheptylmethyl brosylate (XCIV) reacts four times as fast as isobutyl brosylate which they suggested is due to anchimeric assistance by the migrating tertiary hydrogen. The overall reaction is summarized in Eq. 13.

The driving force for this concerted hydrogen migration includes the rearrangement from a primary to a tertiary cation and the release of steric strain by the change of C-1 from a coordination number of four to three.[99]

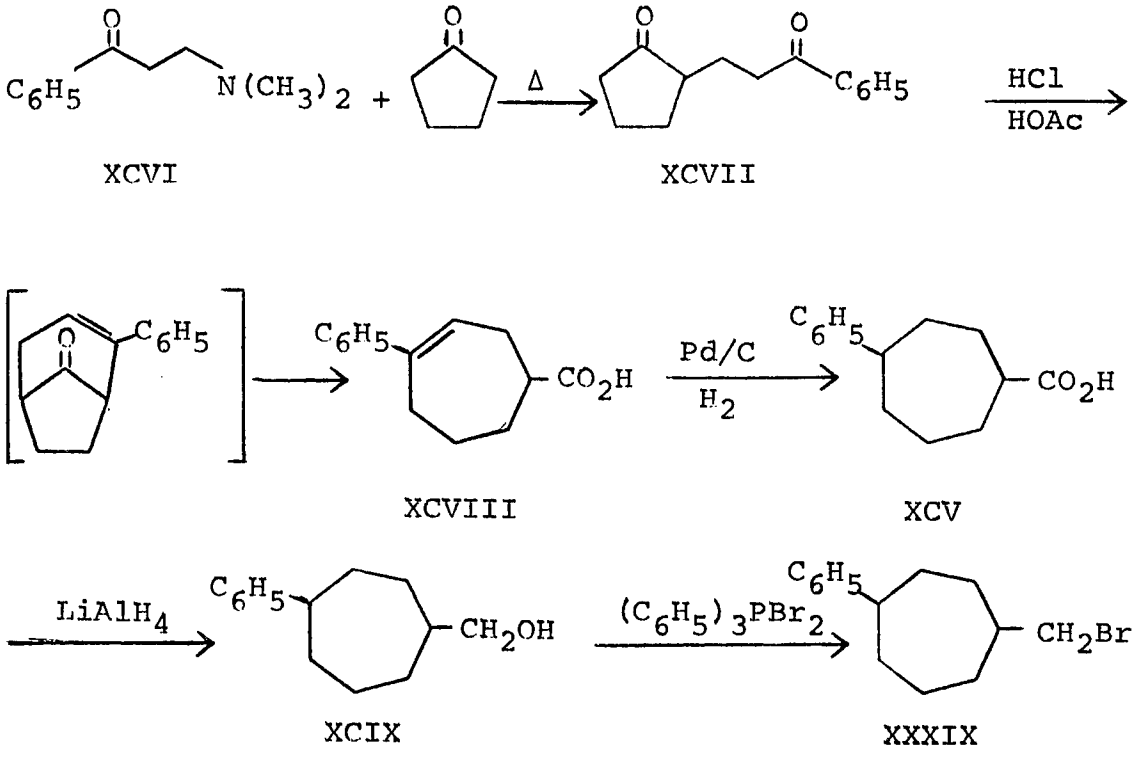



XCIV 70% 20% 4%

Thus, 1-bromomethyl-4-phenylcycloheptane (XXXIX) would not be an unreasonable intermediate in the formation of primary product (II).

1-Bromomethyl-4-phenylcycloheptane (XXXIX) was synthesized from 4-phenylcycloheptanecarboxylic acid (XCV), which was prepared by the method of Buchanan et al. (Scheme lxvii).[100]

Scheme lxvii



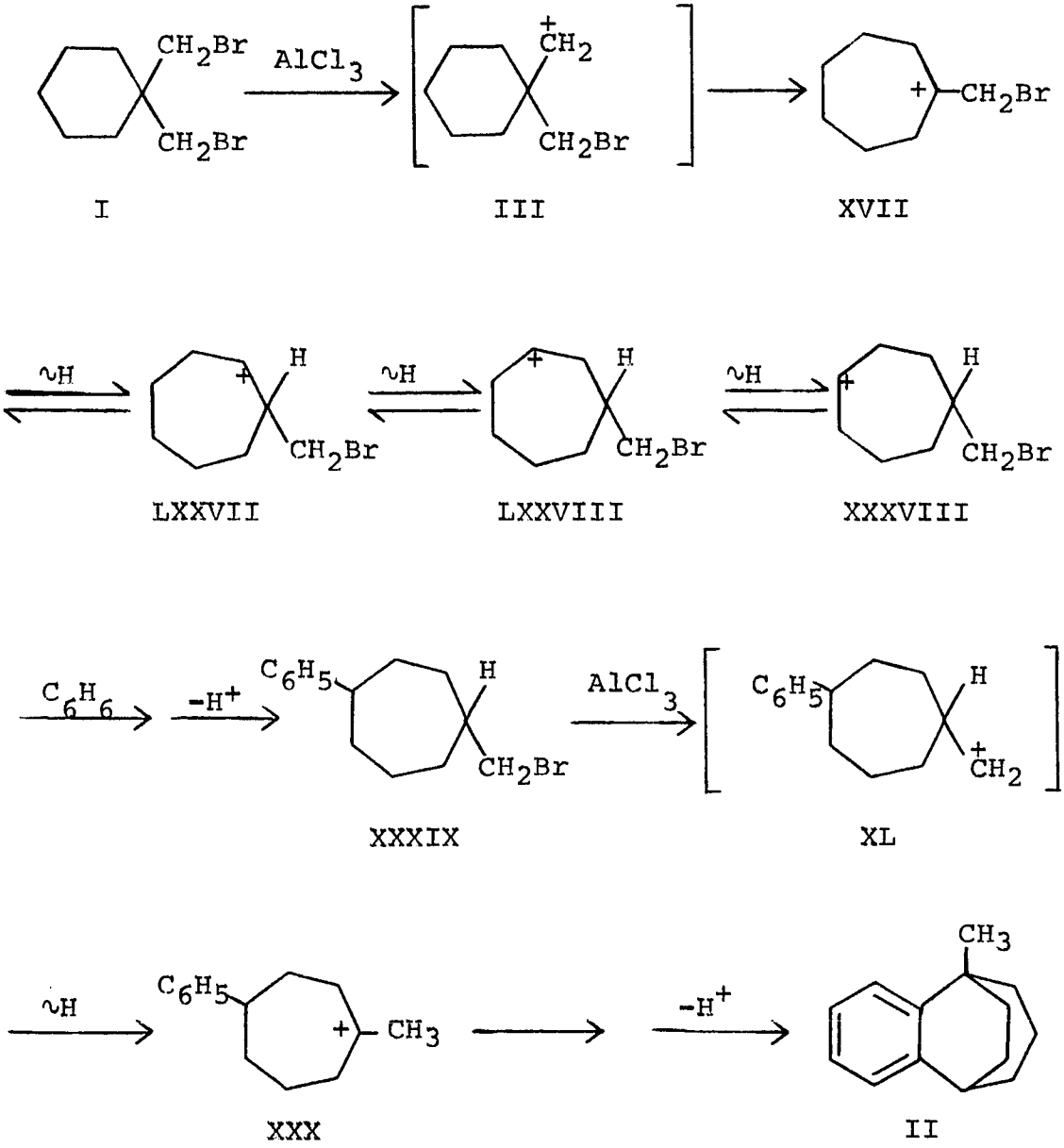
Reaction of 1-bromomethyl-4-phenylcycloheptane (XXXIX) with benzene and aluminum chloride under the usual conditions for one min. yielded a mixture with one product, which was over 90% of the total, having the same glc retention time (Column I) as the primary product. This material was isolated by preparative glc, and its ir, nmr, and mass spectra were found to be virtually identical to the spectra of primary product (II). This suggests that 1-bromomethyl-4-phenylcycloheptane is an intermediate in the conversion of 1,1-bis(bromomethyl)cyclohexane (I) to primary product (II).

In order to check whether the major secondary products in the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane (I) were truly products of further reaction of the primary product and not the initial products formed directly from the dibromide, a study of the reaction products of 1-bromomethyl-4-phenylcycloheptane (XXXIX) as a function of time was carried out. The reaction was run and aliquots were taken at 5, 10, and 15 min. The glc analysis of these aliquots showed a decrease in the concentration of the primary product and the formation of most of the secondary products observed from I. This is a strong indication that these products result from reaction of the primary product and not directly from 1,1-bis(bromomethyl)cyclohexane (I).

In line with the results presented in this dissertation, Mechanism V (p. 41), with multiple reversible hydride shifts in Step V-C, is suggested as the pathway for the

Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane (I) with benzene in the presence of aluminum chloride. This is summarized in Scheme lxviii.

Scheme lxviii



## Appendix I - Calculation of Corrected Peak Heights of Mass Spectra of Deuterated Primary Products

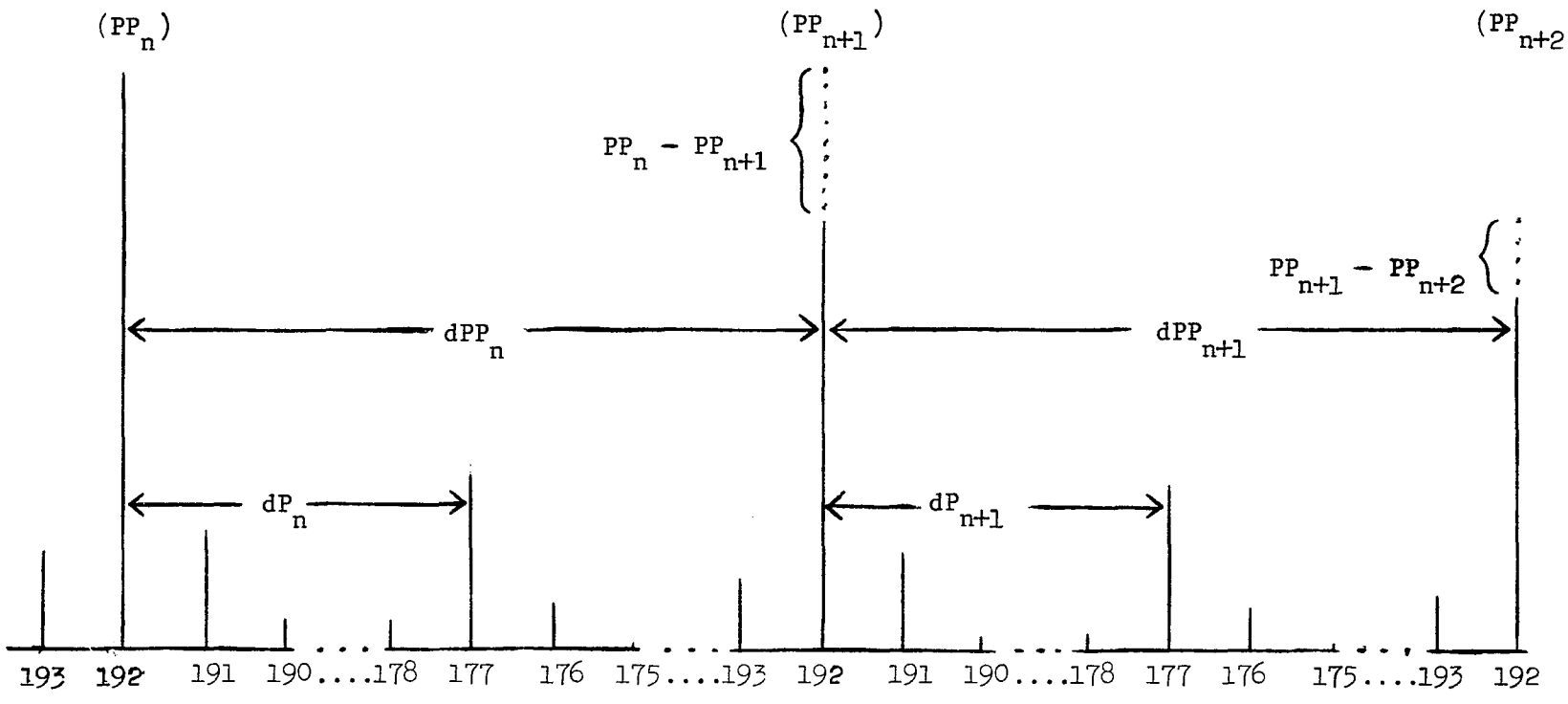
Since during a scan the total pressure in the analyzer is constantly changing, the relative concentrations of ions, and thus the peak heights, are also changing. After introduction of a sample into the analyzer, the total pressure increases quickly to a maximum, then decreases exponentially because of analyzer differential pumping.[101]

The following procedure to correct for changing pressure was devised. The mass spectrometer was adjusted to scan backwards, exponentially, through automatic repetitive scans over the desired range - from about 10 m/e units above the parent peak (P) to about 10 m/e units below the P - methyl region. This assured a constant time interval between a peak on one scan and the corresponding peak on the next scan.

The heights of peaks corresponding to the same m/e on successive scans decrease as the pressure decreases. Also, heights of peaks within a scan decrease from their true values, relative to each other. The further a peak is along a given scan, the more the decrease in pressure, and, therefore, the larger the correction needed.

For a small time span, e.g., between two successive scans, the exponential pressure change can be approximated as linear. Since the chart paper is moving at a constant rate, the pressure change is linear with length of chart

Figure IX




| m/e | 193 | 192 | 191 | 190 | ....178 | 177 | 176 | 175 | ....193 | 192 | 191 | 190 | ....178 | 177 | 176 | 175 | ....193 | 192 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $P_e$ (scan n) | 17.2 | 100 | 22.0 | 4.3 | | 4.9 | 32.0 | 8.5 | 1.0 | | 74.5 | | | | | | | |
| $P_e$ (scan n+1) | | | | | | | | | | 16.5 | 100 | 23.2 | 3.2 | | 4.7 | 38.1 | 10.5 | 1.3 | | 82.4 |
| $\frac{dP_n}{dPP_n}$ | -.022 | 0 | .022 | .045 | | .355 | .381 | .409 | .435 | | 1.0 | | | | | | | | | |
| $\frac{dP_{n+1}}{dPP_{n+1}}$ | | | | | | | | | | -.022 | 0 | .022 | .045 | | .355 | .381 | .409 | .435 | | 1.0 |

paper. Figure IX shows two successive scans for the primary product formed from the reaction of 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane.

The distance between the parent peak on scan n being analyzed and the peak being measured we define as $dP_n$.

The distance between the parent peak of scan n and the parent peak of the next scan (scan n + 1) we define as $dPP_n$.

The fractional decrease in the height of the parent peak from scan n to scan n + 1 is defined as $\Delta PP_n$. This is equal to the height of the parent peak ($PP_n$) minus the height of the parent peak of the next scan ($PP_{n+1}$) divided by the height of $PP_n$:

$$\Delta PP_n = \frac{PP_n - PP_{n+1}}{PP_n}$$

The fractional height loss of a given peak within a scan ($\Delta P_n$) can be calculated by multiplying the ratio of $dP_n$ over $dPP_n$ by $\Delta PP$:

$$\Delta P_n = \frac{dP_n}{dPP_n} \times \Delta PP_n = \frac{dP_n}{dPP_n} \times \frac{PP_n - PP_{n+1}}{PP_n}$$

If $P_e$ and $P_c$ are, respectively, the experimental (measured) and corrected relative peak heights of peak $P_n$ (for scan n) the experimental peak height can be described as follows:

$$P_e = P_c - (P_c \text{ X fraction height loss of } P_n)$$

$$= P_c - (P_c \text{ X } \Delta P_n)$$

$$= P_c \ (1 - \Delta P_n)$$

The corrected peak height would be given by:

$$P_c = \frac{P_e}{1 - \Delta P_n}$$

$$= \frac{P_e}{1 - \frac{dP_n}{dPP_n} X \frac{PP_n - PP_{n+1}}{PP_n}}$$

For example, the corrected relative peak heights of the P - methyl region of the spectrum just outlined would be:

$$P_c \ (178) = \frac{4.9}{1 - (.355 \text{ X } .255)} = 5.4$$

$$P_c \ (177) = \frac{32.0}{1 - (.381 \text{ X } .255)} = 35.5$$

$$P_c \ (176) = \frac{8.5}{1 - (.409 \text{ X } .255)} = 9.5$$

$$P_c \ (175) = \frac{1.0}{1 - (.435 \text{ X } .255)} = 1.1$$

The relative intensities reported in the Results and Discussion Section of this thesis are averages of values calculated from a number of spectra for each compound.

## Appendix II - Calculation of Ratios of Incorporation of Hydrogen and Deuterium into the Methyl Groups of the Deuterated Primary Products (IId, IIe, IIf, and IIg)

### Id→IId

The calculations of the relative amounts of hydrogen and deuterium incorporation into the bridgehead methyl groups of the primary products formed from the various deuterated dibromides (Id, Ie, If, and Ig) involve several corrections of the mass spectral peak heights in the P - methyl region. These include the equalization of the extents of fragmentation in the formation of the P - methyl fragments, for all deuterated primary products, with the amount of fragmentation exhibited by the undeuterated primary product; the corrections for the P + 1 ($^{13}C$) contributions of fragments on the m/e value one larger than the m/e value of the fragment itself; and the corrections for the contributions of the incompletely deuterated materials on the intensities of the parent and P - methyl regions of the spectra of the completely deuterated materials.

Table XIII shows the various 1-bromomethylcycloheptyl cations that may arise from Id, Ie, If, and Ig and the corresponding incompletely deuterated analogues, and the contributions of these species to the P - methyl regions of the mass spectra of the respective primary products.

The relative extents of fragmentation of the molecular ions of the deuterated primary products, with respect to

Table XIII. Mass Spectral Peaks Expected for P - Methyl Fragments of Primary Products from Completely and Incompletely Deuterated Dibromide (I)

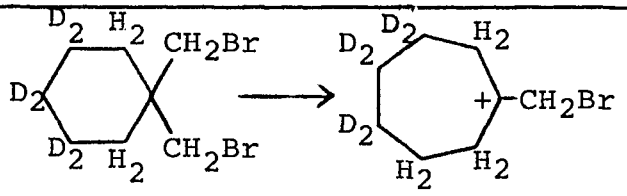
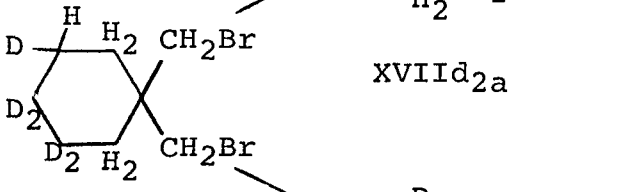
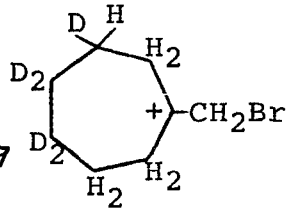
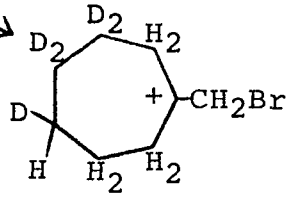
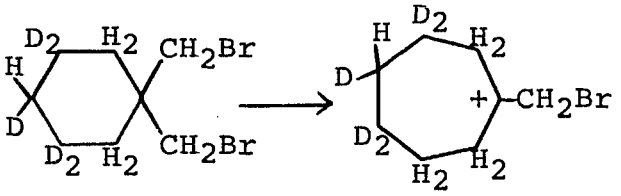
| Starting Material | Ring-Expanded Intermediate | Parent Peak of Primary Product | P - Methyl Fragments | |
|---|---|---|---|---|
| | | | H migration | D migration |
| | | m/e | | |
|  $Id_1$ |  $XVIId_1$ | 192 | 177 | 176 |
|  $Id_2$ |  $XVIId_{2a}$ | 191 | 176 | 175 |
| |  $XVIId_{2b}$ | 191 | 176 | 175 |
|  $Id_3$ |  $XVIId_3$ | 191 | 176 | 175 |

Table XIII (cont'd.)

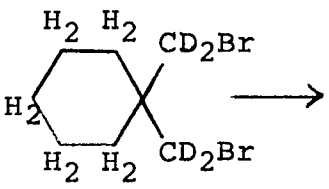
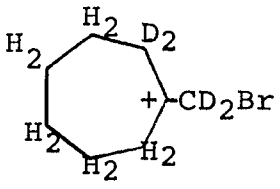
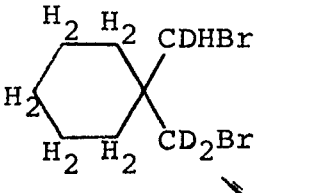
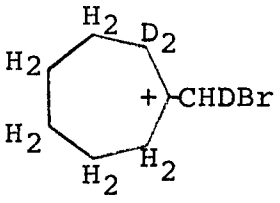
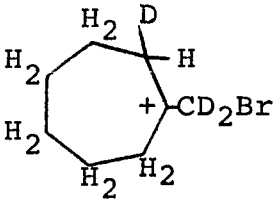
| Starting Material | Ring-Expanded Intermediate | Parent Peak of Primary Product | P - Methyl Fragments | |
|---|---|---|---|---|
| | | | H migration | D migration |
| | | m/e | | |
|  $Ie_1$ |  $XVIIe_1$ | 190 | 173 | 172 |
|  $Ie_2$ |  $XVIIe_{2a}$ | 189 | 173 | 172 |
| |  $XVIIe_{2b}$ | 189 | 172 | 171 |

Table XIII (cont'd.)

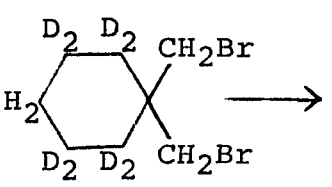
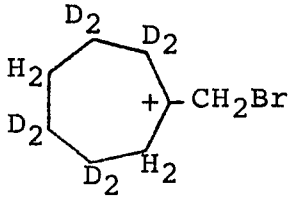
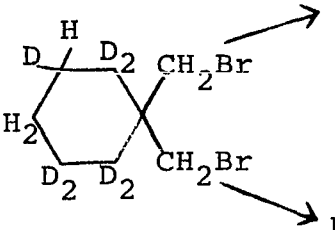
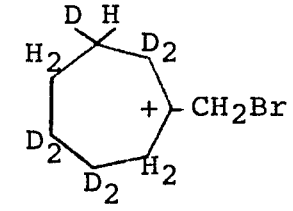
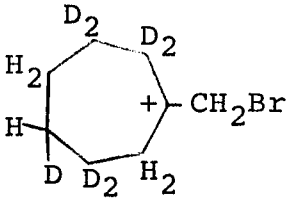
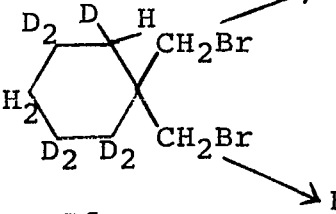
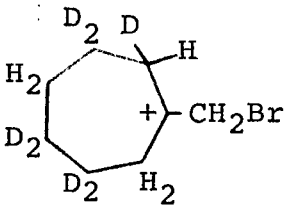
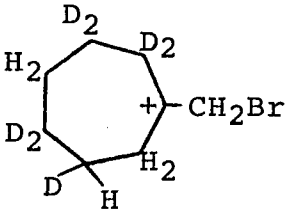
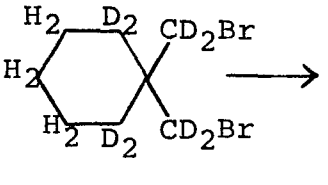
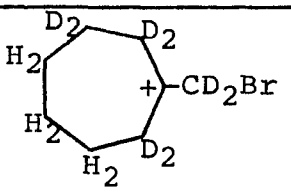
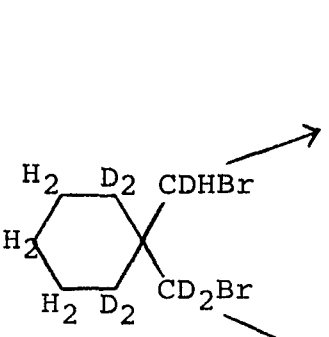
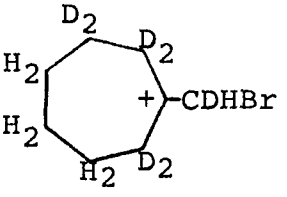
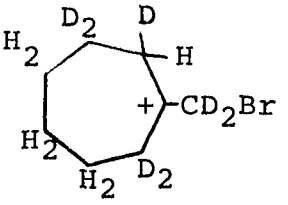
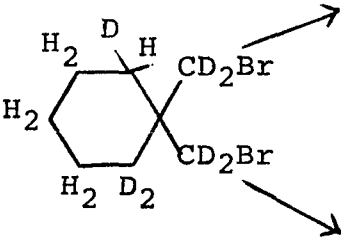
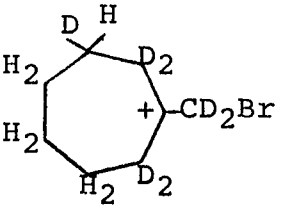
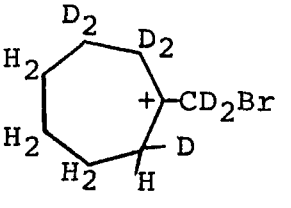
| Starting Material | Ring-Expanded Intermediate | Parent Peak of Primary Product | P - Methyl Fragments | |
|---|---|---|---|---|
| | | | H migration | D migration |
| | | m/e | | |
|  $If_1$ |  $XVIIf_1$ | 194 | 179 | 178 |
|  $If_2$ |  $XVIIf_{2a}$ | 193 | 178 | 177 |
| |  $XVIIf_{2b}$ | 193 | 178 | 177 |
|  $If_3$ |  $XVIIf_{3a}$ | 193 | 178 | 177 |
| |  $XVIIf_{3b}$ | 193 | 178 | 177 |

Table XIII (cont'd.)

| Starting Material | Ring-Expanded Intermediate | Parent Peak of Primary Product | P - Methyl Fragments | |
|---|---|---|---|---|
| | | | H migration | D migration |
| | | m/e | | |
|  $Ig_1$ |  $XVIIg_1$ | 194 | 177 | 176 |
|  $Ig_2$ |  $XVIIg_{2a}$ | 193 | 177 | 176 |
| |  $XVIIg_{2b}$ | 193 | 176 | 175 |
|  $Ig_3$ |  $XVIIg_{3a}$ | 193 | 176 | 175 |
| |  $XVIIg_{3b}$ | 193 | 176 | 175 |

the intensities of the peaks in the respective molecular ion regions, are different due to isotope effects in the fragmentation processes. In order to be able to calculate the extents of H and D incorporation into the bridgehead methyl groups of the various deuterated primary products, it is necessary to correct the P - methyl regions for these isotope effects. The reason for this will become apparent from the calculations which follow. These corrections will only change the magnitudes of the individual peaks in the P - methyl regions. The relative ratios of these peaks within each compound, which are determined by the extents of the H and D migrations, will not be affected.

The first step in the analyses of the mass spectral data involves the equalization of the ratios of the summation of the intensities of all peaks in the P - methyl region to the summation of the intensities of all peaks in the parent peak region. This is illustrated below, by the correction for IId.

In Table V (p. 89) the parent and P - methyl peaks of the mass spectra of II and IId are compared. The relative intensities of these peaks are reproduced below:

| | m/e / rel intensity | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | P - Methyl Region | | | | Parent Peak Region | | | |
| II | 170 / 1 | 171 / 30.3 | 172 / 4.4 | 173 / 1 | 185 / 4.6 | 186 / 100 | 187 / 15.6 | |
| IId | 175 / 1.4 | 176 / 9.9 | 177 / 36.8 | 178 / 5.0 | 190 / 3.0 | 191 / 22.3 | 192 / 100 | 193 / 17.0 |

The ratio of the summation of the intensities of all peaks in the P - methyl region to the summation of the intensities of all peaks in the parent peak region of II is:

$$\frac{1 + 30.3 + 4.4 + 1}{4.6 + 100 + 15.6} = \frac{36.7}{120.2}$$

In order to equalize the extents of fragmentation of the molecular ions of II and IId, we begin by using the above ratio to determine what the summation of the peak intensities (x) in the P - methyl region of IId should be.

$$\frac{36.7}{120.2} = \frac{x}{142.3}$$

$$x = 43.4$$

The value 142.3 represents the summation of the peak heights of the parent peak region of IId (3.0 + 22.3 + 100 + 17.0). However, the summation of the peak heights of the P - methyl region of IId is:

$$1.4 + 9.9 + 36.8 + 5.0 = 53.1$$

The individual peak heights of the P - methyl region of the spectrum of IId must, therefore, be adjusted by the factor 43.4/53.1. The adjusted peak heights of the P - methyl region of the spectrum of IId are:

$$\frac{\text{m/e } 175}{1.1} \quad \frac{\text{m/e } 176}{8.1} \quad \frac{\text{m/e } 177}{30.1} \quad \frac{\text{m/e } 178}{4.1}$$

Consider now the corrections for the P + 1 ($^{13}C$) contributions. The relative height of the peak of lowest m/e value in the P - methyl region is multiplied by 0.14, the theoretical ratio of the P + 1 to parent peak for $C_{13}H_{15}$ (molecular ion ($C_{14}H_{18}$) - methyl ($CH_3$)).[102] The resulting

quantity is subtracted from the relative height of the peak of the next highest m/e value. The resulting corrected height is then multiplied by 0.14 and the procedure repeated. This is done for the entire P - methyl range. The P + 1 corrections for II are:

1 (m/e 170 peak) X 0.14 = 0.14

30.3 (m/e 171 peak) - 0.14 = 30.2

30.2 X 0.14 = 4.2

4.4 (m/e 172 peak) - 4.2 = 0.2 ≃ 0

The P + 1 corrections for the parent peak region of II are made in the same way, using 0.15, the theoretical ratio of the P + 1 to the parent peak for $C_{14}H_{18}$.[102]

4.6 (m/e 185 peak) X 0.15 = 0.69

100 (m/e 186 peak) - 0.69 = 99.3

99.3 X 0.15 = 14.9

15.6 (m/e 187 peak) - 14.9 = 0.7 ≃ 0

The corrected peak heights of the spectrum of II are:

| m/e 170 | m/e 171 | m/e 172 | m/e 185 | m/e 186 | m/e 187 |
|---|---|---|---|---|---|
| 1 | 30.2 | ≃0 | 4.6 | 99.3 | ≃0 |

These numbers indicate that in II the ratio of the intensity of the parent peak (m/e 186) to the intensity of the P - $CH_3$ peak (186 - 15 = 171) is 99.3:30.2. Normalization of this ratio to 100 for the parent peak yields 100:30.4. It is uncertain whether the P + 1 peak of the P - 1 fragment (equal to 0.69) will make any appreciable contribution to the m/e 171 peak height, since it is not known whether or not this species fragments by the loss of

a methyl group. We have chosen to neglect this peak. The possible error involved in this procedure is discussed on pp. 158-159. It turns out to be very small.

The adjusted P - methyl region of IId is corrected for the P + 1 contributions in a similar manner to II, above:

1.1 (m/e 175 peak) X 0.14 = 0.15

8.1 (m/e 176 peak) - 0.15 = 8.0

8.0 X 0.14 = 1.1

30.1 (m/e 177 peak) - 1.1 = 29.0

29.0 X 0.14 = 4.1

4.1 (m/e 178 peak) - 4.1 = 0

The corrected P - methyl region of the spectrum of IId is:

| m/e 175 | m/e 176 | m/e 177 | m/e 178 |
|---|---|---|---|
| 1.1 | 8.0 | 29.0 | 0 |

Consider now the correction for the presence of a $d_5$ species in IId. The experimental parent peak region of the spectrum of IId is corrected as follows. First we subtract 4.6 from the m/e 191 relative peak height:

$$\begin{array}{r} 22.3 \\ -4.6 \\ \hline 17.7 \end{array}$$

The value 4.6 is the relative peak intensity of the P - 1 peak of II. In subtracting this same value from the P - 1 peak of IId, we are assuming that the molecular ion of IId loses a hydrogen atom to the same extent as does the molecular ion of II. Because of isotope effects and the presence of deuterium in IId, this is not necessarily the case. However, as discussed on pp. 159-160, the error involved in

the calculated percentages of H and D migration, if this assumption is incorrect, is very small and does not significantly affect our conclusions. The value 17.7 represents the contribution of the molecular ion of the $d_5$ species to the P - 1 region of IId. The m/e 192 peak height is next corrected for the P + 1 peak of the $d_5$ material. The theoretical P:P + 1 ratio for a $C_{14}$ species is 100:15.[102]

$$17.7 \times 0.15 = 2.6$$

$$100 - 2.6 = 97.4$$

The P - 1 peak of the $d_6$ material is readjusted in proportion to a value of 97.4 for the parent peak.

$$\frac{97.4}{100} = \frac{x}{4.6}$$

$$x = 4.5$$

The process described in the preceding paragraph is now repeated once in order to get a better corrected value for the parent peak height of IId. The adjusted P - 1 value (4.5) is subtracted from the m/e 191 peak height and the resulting value used to readjust the m/e 192 peak height for the P + 1 peak of the $d_5$ material.

$$22.3 - 4.5 = 17.8$$

$$17.8 \times 0.15 = 2.7$$

$$100 - 2.7 = 97.3$$

The contributions of $d_6$ and $d_5$ materials to the parent peak region are:

| | m/e 191 | m/e 192 | m/e 193 |
|---|---|---|---|
| $d_6$ | 4.5 | 97.3 | 17.0 |
| $d_5$ | 17.8 | 2.7 | ____ |
| total | 22.3 | 100.0 | 17.0 |

The m/e 177 peak (corrected rel intensity 29.0) originates from the loss of 15 units (bridgehead $CH_3$, which arises from H migration in the formation of primary product (Table XIII, p. 130)) from the m/e 192 peak. The latter peak, as shown above, contains contributions from the parent peak of the $d_6$ species (97.3) and the P + 1 peak of the $d_5$ species (2.7). The contribution from the $d_6$ species to the m/e 192 peak can be broken down into two components, from the parent peak and from the P + 1 peak of the P - 1 fragment (4.5). This latter quantity is estimated as:

$$4.5 \times 0.15 = 0.68$$

The contribution of the parent peak of $IId_1$ to the m/e 192 peak is then:

$$97.3 - 0.68 = 96.6$$

It is uncertain whether the P + 1 peak of the P - 1 fragment will make any appreciable contribution to the m/e 177 peak height, since it is not known whether this species fragments by the loss of a methyl group. We have chosen to neglect this peak. The possible error involved in this procedure is discussed on p. 161. It turns out to be very small.

To continue the calculation, it is now necessary to know the extent of H and D migration in the $d_5$ species.

This information is not available. We have assumed that the extent of H and D migration in the $d_5$ and $d_6$ species are the same. This assumption, if incorrect, leads to only a small error (discussed on pp. 161-162). The ratio of the parent peak of the $d_6$ material plus the P + 1 peak of the $d_5$ material (96.6 + 2.7 = 99.3) to the P - $CH_3$ fragment (from H migration) (represented by the m/e 177 peak) is 99.3:29.0. Normalization leads to the value 100:29.2. If only H migration had occurred in the formation of IId, we would have expected the latter ratio to be 100:30.4, i.e., identical to the ratio of the parent peak intensity to the P - methyl peak intensity observed for II (p. 136). The difference, 30.4 - 29.2 = 1.2, is due to deuterium migration which leads to a P - $CH_2D$ fragment.

The percentage of H migration can, therefore, be calculated as:

$$\frac{29.2}{30.4} \times 100 = 96.0\%$$

Ie→IIe

To determine the percentage of hydrogen migration in the reaction of Ie, the same general procedure described for the reaction of Id is followed. In Table VII (p. 94) the parent and P - methyl peaks of the mass spectra of II and IIe are compared. The relative intensities of these peaks are reproduced below:

| | m/e / rel intensity | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | P - Methyl Region | | | | | Parent Peak Region | | | |
| II | 170 / 1 | 171 / 30.3 | 172 / 4.4 | 173 / 1 | | 185 / 4.6 | 186 / 100 | 187 / 15.6 | |
| IIe | 171 / 1 | 172 / 6.6 | 173 / 23.4 | 174 / 3.4 | 175 / 1 | 188 / 1 | 189 / 10.0 | 190 / 100 | 191 / 17.0 |

The summation of the peak heights of the parent peak region of the spectrum of IIe is:

$$1 + 10.0 + 100 + 17.0 = 128.0$$

The ratio of the summation of the intensities of all peaks in the P - methyl region to the summation of the intensities of all the peaks in the parent peak region in the spectrum of II is 36.7:120.2 (p. 135).

Using this ratio, the extents of fragmentation of the molecular ions of II and IIe can be equalized. The summation of the peak intensities (x) in the P - methyl region of IIe should be:

$$\frac{36.7}{120.2} = \frac{x}{128.0}$$

$$x = 39.1$$

The summation of the peak heights of the P - methyl region of the spectrum of IIe is:

$$1 + 6.6 + 23.4 + 3.4 + 1 = 35.4$$

The fragmentations for II and IIe are equalized by multiplying the individual peak heights of the P - methyl region of the spectrum of IIe by the factor 39.1/35.4. The adjusted peak heights of the P - methyl region of the spectrum of IIe are:

| m/e 171 | m/e 172 | m/e 173 | m/e 174 | m/e 175 |
|---|---|---|---|---|
| 1.1 | 7.3 | 25.7 | 3.7 | 1.1 |

The adjusted relative intensities of the peaks of the P - methyl region of the mass spectrum of IIe are first corrected for P + 1 contributions. The relative height of the peak of lowest m/e value is multiplied by 0.14, the theoretical ratio of the P + 1 to the parent peak for $C_{13}H_{15}$ (molecular ion ($C_{14}H_{18}$) - methyl ($CH_3$)).[102] The resulting quantity is subtracted from the relative height of the peak of the next highest m/e value. The resulting corrected height is then multiplied by 0.14 and the procedure repeated. This is done for the entire P - methyl region:

1.1 (m/e 171 peak) X 0.14 = 0.15

7.3 (m/e 172 peak) - 0.2 = 7.2

7.2 X 0.14 = 1.0

25.7 (m/e 173 peak) - 1.0 = 24.7

24.7 X 0.14 = 3.5

3.7 (m/e 174 peak) - 3.5 = 0.2 ≈ 0

The corrected peak heights for the P - methyl region

of the spectrum of IIe are:

| m/e 171 | m/e 172 | m/e 173 | m/e 174 |
|---|---|---|---|
| 1.1 | 7.2 | 24.7 | ≃0 |

Next the presence of a $d_3$ species in IIe is considered. The experimental parent peak region is corrected in the same manner as IId (pp. 137-139). First the value 4.6 (the relative peak intensity of the P - 1 peak of II) is subtracted from the m/e 189 peak height. The result represents the contribution of the molecular ion of the $d_3$ species to the P - 1 region of IIe.

$$\begin{array}{r} 10.0 \\ -4.6 \\ \hline 5.4 \end{array}$$

The m/e 190 peak height is corrected for the presence of the P + 1 peak from the $d_3$ material using the theoretical P:P + 1 ratio for $C_{14}H_{18}$, 100:15, in the same manner as the correction of the m/e 192 peak height of IId (p. 138).

$$5.4 \times 0.15 = 0.81$$

$$100 - 0.81 = 99.2$$

The P - 1 peak of the $d_4$ material is readjusted in proportion to a value of 99.2 for the parent peak.

$$\frac{99.2}{100} = \frac{x}{4.6}$$

$$x = 4.6$$

This indicates that no readjustment of the m/e 190 peak height for the P + 1 peak of the $d_3$ material is necessary.

These calculations give a ratio of $d_4$ to $d_3$ material of 99.2:5.4. The ratio of intermediates $XVIIe_1$, $XVIIe_{2a}$, and $XVIIe_{2b}$ should be 99.2:2.7:2.7. If we examine Table

XIII (p. 131), we see that hydrogen migration from $XVIIe_{2a}$ leads to a peak of m/e 173, the same as from the completely deuterated material $XVIIe_1$. Since secondary isotope effects are generally small,[103] we can assume that the percentages of hydrogen migration in $XVIIe_1$ and $XVIIe_{2a}$ will be essentially the same. The parent peak region broken down into the contributions from the primary products formed from the $d_4$ and $d_3$ dibromides is:

| | m/e 189 | m/e 190 |
|---|---|---|
| $IIe_1$ | 4.6 | 99.2 |
| $IIe_{2a}$ | 2.7 | 0.4 |
| $IIe_{2b}$ | 2.7 | 0.4 |
| Total | 10.0 | 100.0 |

The m/e 173 peak (corrected rel intensity 24.7) originates from the loss of 17 units (bridgehead $CD_2H$, which arises from H migration in the formation of primary product from $XVIIe_1$ (Table XIII, p. 131)) from the m/e 190 peak, the loss of 16 units (bridgehead $CDH_2$, which arises from H migration in the formation of primary product from $XVIIe_{2a}$) from the m/e 189 peak, and the P + 1 peak of the fragment which arises from the loss of 17 units (bridgehead $CD_2H$, from H migration in the formation of primary product from $XVIIe_{2b}$) from the m/e 189 peak.

The m/e 190 peak, as shown above, contains contributions from the parent peak of the $d_4$ species ($IIe_1$) (99.2) and the P + 1 peaks of the two $d_3$ species ($IIe_{2a}$ and $IIe_{2b}$) (0.4 + 0.4). The contribution from the $d_4$ species to the

m/e 190 peak can be further broken down into two components, from the parent peak, and from the P + 1 peak of the P - 1 fragment (4.6). The latter quantity is estimated as:

$$4.6 \times 0.15 = 0.69$$

The contribution of the parent peak of $IIe_1$ to the m/e 190 peak is:

$$99.2 - 0.69 = 98.5$$

As with $IId_1$ (p. 140), it is assumed that any contribution of the P + 1 peak of the P - 1 fragment to the P - methyl region is negligible. It is also assumed, as above (p. 140), that the extents of H and D migrations in the $d_4$ and $d_3$ species are the same.

The ratio of the summation of the intensities of the parent peak of $IIe_1$, the parent peak of $IIe_{2a}$, and the P + 1 peak of $IIe_{2b}$ (98.5 + 2.7 + 0.4) to the height of the m/e 173 peak is 101.6:24.7. Normalization leads to the ratio 100:24.3.

If only H migration had occurred in the formation of IIe, we would have expected this ratio to be 100:30.4, i.e., identical to the ratio of the parent peak intensity to the P - methyl peak intensity observed for II (p. 136). The difference, 30.4 - 24.3 = 6.1, is due to deuterium migration which leads to a P - $CD_3$ fragment in $IIe_1$ and $IIe_{2a}$ and a P - $CHD_2$ fragment in $IIe_{2b}$.

The percentage of H migration can, therefore, be calculated as:

$$\frac{24.3}{30.4} \times 100 = 79.9\%$$

If→IIf

In Table IX (p. 103) the parent and P - methyl peaks of the mass spectra of II and IIf are compared. The relative intensities of these peaks are reproduced below:

| | m/e / rel intensity | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | P - Methyl Region | | | | Parent Peak Region | | | |
| II | 170 / 1 | 171 / 30.3 | 172 / 4.4 | 173 / 1 | 185 / 4.6 | 186 / 100 | 187 / 15.6 | |
| IIf | 177 / 3.8 | 178 / 19.1 | 179 / 22.0 | 180 / 3.1 | 192 / 1.9 | 193 / 16.5 | 194 / 100 | 195 / 16.2 |

In order to equalize the extents of fragmentation for II and IIf, the same procedure as described for II and IId (pp. 134-135) is followed.

The summation of the peak heights of the parent peak region of the spectrum of IIf is:

$$1.9 + 16.5 + 100 + 16.2 = 134.6$$

The ratio of the summation of the intensities of all peaks in the P - methyl region to the summation of the intensities of all the peaks of the parent peak region in the spectrum of II is 36.7:120.2 (p. 135). The expected summation of the peak heights (x) of the P - methyl region of IIf is calculated from the following proportion:

$$\frac{36.7}{120.2} = \frac{x}{134.6}$$

$$x = 41.1$$

The summation of the peak heights of the P - methyl region of the spectrum of IIf is:

$$3.8 + 19.1 + 22.0 + 3.1 = 48.0$$

The fragmentations for II and IIf are equalized by multiplying the individual peak heights of the P - methyl region of the spectrum of IIf by the factor 41.1/48.0. The adjusted peak heights of the P - methyl region of the spectrum of IIf are:

| m/e 177 | m/e 178 | m/e 179 | m/e 180 |
|---|---|---|---|
| 3.3 | 16.4 | 18.9 | 2.7 |

The adjusted relative intensities of the peaks of the P - methyl region of the spectrum of IIf are corrected for P + 1 contributions. The relative height of the peak of lowest m/e value in the P - methyl region is multiplied by 0.14, the theoretical ratio of the P + 1 to parent peak for $C_{13}H_{15}$ (molecular ion ($C_{14}H_{18}$) - methyl ($CH_3$)).[102] The resulting quantity is subtracted from the relative height of the peak of the next highest m/e value. The resulting corrected height is then multiplied by 0.14 and the procedure repeated. This is done for the entire P - methyl region:

3.3 (m/e 177 peak) X 0.14 = 0.46

16.4 (m/e 178 peak) - 0.46 = 15.9

15.9 X 0.14 = 2.2

18.9 (m/e 179 peak) - 2.2 = 16.7

16.7 X 0.14 = 2.3

2.7 (m/e 180 peak) - 2.3 = 0.4 ≃ 0

The corrected peak heights for the P - methyl region of IIf are:

| m/e 177 | m/e 178 | m/e 179 | m/e 180 |
|---|---|---|---|
| 3.3 | 15.9 | 16.7 | ≃0 |

Next the presence of a $d_7$ species in IIf is considered.

The experimental parent peak region is corrected in the same manner as IId (pp. 137-139). First the value 4.6 (the relative peak intensity of the P - 1 peak of II) is subtracted from the m/e 193 peak height. The result represents the contribution of the molecular ion of the $d_7$ species to the P - 1 region of IIf.

$$\begin{array}{r} 16.5 \\ -4.6 \\ \hline 11.9 \end{array}$$

The m/e 194 peak height is corrected for the presence of the P + 1 peak from $d_7$ material, using the theoretical P:P + 1 ratio for $C_{14}H_{18}$, 100:15, in the same manner as the correction of the m/e 192 peak height of IId (p. 138).

$$11.9 \times 0.15 = 1.8$$

$$100 - 1.8 = 98.2$$

The P - 1 peak of the $d_8$ material is readjusted in proportion to a value of 98.2 for the parent peak.

$$\frac{98.2}{100} = \frac{x}{4.6}$$

$$x = 4.5$$

The process described in the preceding paragraph is now repeated once in order to get a better corrected value for the parent peak height of IIf. The adjusted P - 1 value (4.5) is subtracted from the m/e 193 peak height and the resulting value used to readjust the m/e 194 peak height for the P + 1 peak of the $d_7$ material.

$$16.5 - 4.5 = 12.0$$

$$12.0 \times 0.15 = 1.8$$

$$100 - 1.8 = 98.2$$

This gives a ratio of $d_8$ to $d_7$ material of 98.2:12.0. The contributions of $d_8$ and $d_7$ materials to the parent peak region are:

| | m/e 193 | m/e 194 |
|---|---|---|
| $d_8$ | 4.5 | 98.2 |
| $d_7$ | 12.0 | 1.8 |
| total | 16.5 | 100.0 |

The m/e 179 peak (corrected rel intensity 16.7) originates from the loss of 15 units (bridgehead $CH_3$, which arises from H migration in the formation of primary product (Table XIII, p. 132)) from the m/e 194 peak. The latter peak, as shown above, contains contributions from the parent peak of the $d_8$ species (98.2) and the P + 1 peak of the $d_7$ species (1.8). The contribution from the $d_8$ species to the m/e 194 peak can be further broken down into two components, from the parent peak and from the P + 1 peak of the P - 1 fragment (4.5). This latter quantity is estimated as:

$$4.6 \times 0.15 = 0.69$$

The contribution of the parent peak of $IIf_1$ to the m/e 194 peak is then:

$$98.2 - 0.69 = 97.5$$

As with $IId_1$ (p. 140), it is assumed that any contribution of the P + 1 peak of the P - 1 fragment to the P - methyl region is negligible. It is also assumed, as above (p. 140), that the extents of H and D migration in the $d_8$

and $d_7$ species are the same.

The ratio of the parent peak of the $d_8$ material plus the P + 1 peak of the $d_7$ material (97.5 + 1.8) to the P - $CH_3$ fragment (from H migration, represented by the m/e 179 peak) is 99.3:16.7. Normalization leads to the value 100:16.8.

If only H migration had occurred in the formation of IIf, we would have expected this ratio to be 100:30.4, i.e., identical to the ratio of the parent peak intensity to the P - methyl peak intensity observed for II (p. 136). The difference, 30.4 - 16.8 = 13.6, is due to deuterium migration which leads to a P - $CH_2D$ fragment.

The percentage of H migration can, therefore, be calculated as:

$$\frac{16.8}{30.4} \times 100 = 55.3\%$$

Ig→IIg

In Table IX (p. 103), the parent and P - methyl peaks of the mass spectra of II and IIg are compared. The relative intensities of these peaks are reproduced below:

| | m/e / rel intensity | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | P - Methyl Region | | | | Parent Peak Region | | | |
| II | 170 / 1 | 171 / 30.3 | 172 / 4.4 | 173 / 1 | 185 / 4.6 | 186 / 100 | 187 / 15.6 | |
| IIg | 175 / 1.7 | 176 / 24.5 | 177 / 12.2 | 178 / 2.8 | 192 / 2.0 | 193 / 17.3 | 194 / 100 | 195 / 17.3 |

In order to equalize the extents of fragmentation for II and IIg, the same procedure as described for II and IId (pp.134-135) is followed.

The summation of the peak heights of the parent peak region of IIg is:

$$2.0 + 17.3 + 100 + 17.3 = 136.6$$

The ratio of the summations of the intensities of all peaks in the P - methyl region to the summation of the intensities of all the peaks of the parent peak region in the spectrum of II is 36.7:120.2 (p. 135). The expected summation of the peak heights (x) of the P - methyl region of IIe is calculated from the following proportion:

$$\frac{36.7}{120.2} = \frac{x}{136.6}$$

$$x = 41.7$$

The summation of the peak heights of the P - methyl region of the spectrum of IIg is:

$$1.7 + 24.5 + 12.2 + 2.8 = 41.2$$

The fragmentations for II and IIe are equalized by multiplying the individual peak heights of the P - methyl region of the spectrum of IIg by the factor 41.7/41.2. The adjusted peak heights of the P - methyl region of the spectrum of IIg are:

| m/e 175 | m/e 176 | m/e 177 | m/e 178 |
|---|---|---|---|
| 1.7 | 24.7 | 12.3 | 2.8 |

The relative intensities of the peaks of the P - methyl region of the spectrum of IIg are corrected for P + 1 contributions. The relative height of the peak of lowest m/e value in the P - methyl region is multiplied by 0.14, the theoretical ratio of the P + 1 to parent peak for $C_{13}H_{15}$ (molecular ion ($C_{14}H_{18}$) - methyl ($CH_3$)).[102] The resulting quantity is subtracted from the relative height of the peak of next highest m/e value. The resulting corrected height is then multiplied by 0.14 and the procedure repeated. This is done for the entire P - methyl region:

1.7 (m/e 175 peak) X 0.14 = 0.24

24.7 (m/e 176 peak) - 0.24 = 24.5

24.5 X 0.14 = 3.4

12.3 (m/e 177 peak) - 3.4 = 8.9

8.9 X 0.14 = 1.2

2.8 (m/e 178 peak) - 1.2 = 1.6

The corrected peak heights for the P - methyl region of the spectrum of IIg are:

| m/e 175 | m/e 176 | m/e 177 | m/e 178 |
|---|---|---|---|
| 1.7 | 24.5 | 8.9 | 1.6 |

Next the presence of a $d_7$ species in IIg is considered. The experimental parent peak region is corrected in the same manner as IId (pp. 137-139). First the value 4.6 (the relative peak intensity of the P - 1 peak of II) is subtracted from the m/e 193 peak height. The result represents the contribution of the molecular ion of the $d_7$ species to the P - 1 region of IIg.

$$\begin{array}{r} 17.3 \\ -4.6 \\ \hline 12.7 \end{array}$$

The m/e 194 peak height is corrected for the presence of the P + 1 peak from the $d_7$ material, using the theoretical P:P + 1 ratio for $C_{14}H_{18}$, 100:15, in the same manner as the correction of the m/e 192 peak height of the spectrum of IId (p. 138).

$$12.7 \times 0.15 = 1.9$$

$$100 - 1.9 = 98.1$$

The P - 1 peak of the $d_8$ material is readjusted in proportion to a value of 98.1 for the parent peak.

$$\frac{98.1}{100} = \frac{x}{4.6}$$

$$x = 4.5$$

The process described in the preceding paragraph is now repeated once in order to get a better corrected value for the parent peak height of IIg. The adjusted P - 1 value (4.5) is subtracted from the m/e 193 peak and the resulting value used to readjust the m/e 194 peak height for the P + 1 peak of the $d_7$ material.

$$17.3 - 4.5 = 12.8$$

$$12.8 \times 0.15 = 1.9$$

$$100 - 1.9 = 98.1$$

This gives a ratio of $d_8$ to $d_7$ material of 98.1:12.8, corresponding to 11.5% $d_7$ species.

We next consider the contributions of $IIg_1$, $IIg_{2a}$, $IIg_{2b}$, $IIg_{3a}$, and $IIg_{3b}$ to the parent peak region of the spectrum of IIg. The ratio of $d_4$ to $d_3$ species in 2,2,6,6-tetradeuterio-1,1-dicarbethoxycyclohexane (XCIg) was 100:6 (Scheme lxi, p. 102). This corresponds to 5.7% trideuteration in the 2- and 6-positions of Ig. After the remaining four deuterium atoms had been incorporated (compound Ig), the percentage of incomplete deuteration was 11.5%. Thus, 5.8% of the incomplete deuteration was present in the exo-methylene groups of Ig. The ratio of intermediates $XVIIg_1$, $XVIIg_{2a}$, $XVIIg_{2b}$, $XVIIg_{3a}$, and $XVIIg_{3b}$ would, therefore, be 98.1:3.2:3.2:3.2:3.2.

The contributions of the completely and incompletely deuterated materials to the parent peak region are:

| | m/e 193 | m/e 194 | m/e 195 |
|---|---|---|---|
| $IIg_1$ | 4.5 | 98.1 | 17.3 |
| $IIg_{2a}$ | 3.2 | 0.5 | |
| $IIg_{2b}$ | 3.2 | 0.5 | |
| $IIg_{3a}$ | 3.2 | 0.5 | |
| $IIg_{3b}$ | 3.2 | 0.5 | |
| total | 17.3 | 100.1 | 17.3 |

If we examine Table XIII (p. 133), we see that hydro-

gen migration from $XVIIg_{2a}$ leads to a peak at m/e 177, the same as that from the completely deuterated material $XVIIg_1$. Since secondary isotope effects are generally small,[103] we can assume that the percentage of hydrogen migration in $XVIIg_1$ and $XVIIg_{2a}$ will be essentially the same.

The m/e 177 peak (corrected rel intensity 8.9) originates from the loss of 17 units (bridgehead $CD_2H$, which arises from H migration in the formation of primary product from $XVIIg_1$ (Table XIII, p. 133)) from the m/e 194 peak, the loss of 16 units (bridgehead $CDH_2$, which arises from H migration of primary product from $IIg_{2a}$) from the m/e 193 peak, and the P + 1 peaks of the fragments which arise from the loss of 17 units (bridgehead $CD_2H$, which arise from H migration in the formation of primary product from $XVIIg_{2b}$, $XVIIg_{3a}$, and $XVIIg_{3b}$) from the m/e 193 peak.

The m/e 194 peak, as shown above, contains contributions from the parent peak of the $d_8$ species (98.1) and the P + 1 peaks of the four $d_7$ species (0.5 + 0.5 + 0.5 + 0.5). The contribution of the $d_8$ species can be further broken down into two components, from the parent peak and from the P + 1 peak of the P - 1 fragment (4.5). The latter quantity is estimated as:

$$4.5 \times 0.15 = 0.68$$

The contribution of the parent peak of $IIg_1$ to the m/e 194 peak is:

$$98.1 - 0.68 = 97.4$$

As with $IId_1$ (p. 140), it is assumed that any contri-

bution of the P + 1 peak of the P - 1 fragment to the P - methyl region is negligible. It is also assumed, as above (p. 140), that the extents of H and D migrations in the $d_8$ and $d_7$ species are the same.

The ratio of the summation of the intensities of the parent peaks of $IIg_1$ (97.4) and $IIg_{2a}$ (3.2) and the P + 1 peaks of $IIg_{2b}$, $IIg_{3a}$, and $IIg_{3b}$ (0.5 + 0.5 + 0.5) to the height of the m/e 177 peak is 102.1:8.9. Normalization leads to the ratio 100:8.7.

If only H migration had occurred in the formation of IIg, we would have expected the ratio to be 100:30.4, i.e., identical to the ratio of the parent peak intensity to the P - methyl peak intensity observed for II (p. 136). The difference, 30.4 - 8.7 = 21.7, is due to deuterium migration which produces a P - $CD_3$ fragment from $IIg_1$ and $IIg_{2a}$ and a P - $CHD_2$ fragment from $IIg_{2b}$, $IIg_{3a}$, and $IIg_{3b}$.

The percentage of H migration can, therefore, be calculated as:

$$\frac{8.7}{30.4} \times 100 = 28.6\%$$

Error Analysis

In the calculation of the percentages of hydrogen migration to the methyl groups of the deuterated primary products, IId, IIe, IIf, and IIg, a number of assumptions have been made. An analysis of these assumptions is necessary in order to determine whether the possible errors caused by them could appreciably alter the final percentages and, therefore, the conclusions that have been reached.

Since we do not know the actual errors caused by our assumptions, we will consider the extreme cases in order to determine the worst possible errors in our calculations. If the resulting calculations of the percentages of H migrations do not deviate appreciably from our calculated results, then our assumptions are valid. The case of IId is used as an example.

The calculation of the relative amounts of hydrogen migration and deuterium migration in the formation of IId depended upon the ratio of the adjusted height of the m/e 177 peak to the adjusted height of the parent peak (m/e 192) in the mass spectrum of IId. The m/e 177 peak represents a P - $CH_3$ fragment resulting from hydrogen migration. This ratio was divided by the ratio of the height of the m/e 171 peak to the height of the parent peak (m/e 186) in the spectrum of undeuterated primary product II. The resulting fraction, i.e., 29.2/30.4 (see p. 140), multiplied by 100 gave the percent hydrogen migration.

The methods for obtaining the two numerals of this fraction, the numerator, the ratio of the intensity of the m/e 177 peak to the intensity of the parent peak (m/e 192) of the spectrum of IId, and the denominator, the ratio of the intensity of the m/e 171 peak to the intensity of the parent peak (m/e 186) of the spectrum of II, will be analyzed separately. From a consideration of the errors involved in the four peak intensities, we will then estimate the uncertainty in our calculation of the percent of H migration.

First, let us consider the possible errors in the denominator, the ratio of the heights of the P - methyl and parent peaks of the spectrum of II. The parent peak height (m/e 186) was set at 100%. A reasonable estimate of the error in the measurement of this peak height is about ±0.5. Therefore, the experimental value would be 100 ± 0.5.

There is an error of about ±0.5 in the measurement of the height of the m/e 171 peak. Therefore, the experimental value would be 30.3 ± 0.5. After the P + 1 correction is made (p. 136), the peak height would be 30.2 ± 0.5.

After the correction for the P + 1 contribution of the P - 1 fragment to the m/e 186 peak, the m/e 186 peak height was 99.3 (p. 136). It was assumed that this P + 1 contribution (0.69) does not make any appreciable contribution to the m/e 171 peak height. The ratio of the height of the m/e 171 peak to the height of the m/e 186 peak, 30.2:99.3, was then normalized to 30.4:100. If this P + 1 contribu-

tion is included in the m/e 186 peak height the ratio would be 30.2:100. Thus, the inclusion of this factor would give a value of up to 0.2 less than the value in our calculation.

Incorporation of these factors into the ratio of the intensity of the P - methyl peak to the intensity of the parent peak of II (the denominator of the H migration fraction) gives a range of:

$$\frac{29.7\ (30.4 - 0.5 - 0.2) \text{ to } 30.9\ (30.4 + 0.5)}{99.5\ (100 - 0.5) \text{ to } 100.5\ (100 + 0.5)} = .296 \text{ to } .310$$

Next, we consider the possible errors in the numerator of the fraction, the ratio of the adjusted P - $CH_3$ peak (m/e 177) height to the parent peak (m/e 192) height of IId. The parent peak height (m/e 192) was set at 100%. There is a probable error of about ±0.5 in the measurement of this peak height. Therefore, the experimental value would be 100 ± 0.5.

The experimental value for the intensity of the m/e 177 peak is 36.8. There is an error in this measurement of about ±0.5. Therefore, the experimental value would be 36.8 ± 0.5. After the correction for equalizing the fragmentations of II and IId (p. 135) the value would be 30.1 ± 0.5. After the correction for P + 1 contributions (p. 137) the value would be 29.0 ± 0.5.

To determine the contribution of the $d_5$ species (pp. 137-139) we subtracted a value of 4.5 from the m/e 191 peak height. In doing this it was assumed that the deuterated

material, IId, fragments by a loss of a hydrogen to give a P - 1 (m/e 191) peak to the same extent as loss of H occurs from II. However, IId could give an appreciable P - 2 fragment (P - deuterium), instead of just the P - 1 peak. Then the contribution of the P - 1 fragment to the m/e 191 peak would be less than 4.5. To test the effect of appreciable P - 2 fragmentation in IId we will use as an example the assumption that half of the fragmentation leads to a P - 2 peak. The peak heights of the m/e 191 and 192 peaks would be affected as follows (see p. 139 for a comparison of values):

| | m/e 191 | m/e 192 |
|---|---|---|
| $d_6$ | 2.3 (0.5 X 4.5) | 97.0 (100 - 3.0) |
| $d_5$ | 20.0 (22.3 - 2.3) | 3.0 (20.0 X 0.15) |
| total | 22.3 | 100.0 |

The P + 1 contribution of the m/e 191 fragment of the $d_6$ material would be 2.3 X 0.15 = 0.3. The contribution of the parent peak of the $d_6$ material to the m/e 192 peak height would be 97.0 - 0.3 = 96.7.

The parent peak of the $d_6$ material and P + 1 peak of the $d_5$ material together would be 96.7 + 3.0 = 99.7. This would correspond to a m/e 177 peak height of 29.0. With the m/e 192 peak height normalized to 100 the ratio of the height of the m/e 177 peak to the height of the m/e 192 peak would be 29.1:100. Our calculation (p. 140) gave this ratio as 29.2:100. Therefore, this factor could contribute as much as -0.1 to the ratio of the height of the m/e 177 peak

to the height of the m/e 192 peak, the numerator of the H migration fraction.

After the correction for the contributions to the parent peak region by the $d_5$ material (p. 140) the ratio of the height of the m/e 177 peak to the height of the m/e 192 peak of the $d_6$ material was 29.0:97.3. The value 97.3 was broken down into a contribution of 96.6 from the parent peak and 0.68 from the P + 1 of the P - 1 fragment. It was assumed that the latter contribution would not make any appreciable contribution to the m/e 177 peak height. With this value ignored the ratio of the m/e 177 peak height to the m/e 192 peak height was calculated as 29.0:99.3 (96.6 from the parent peak plus 2.7 from the P + 1 of the $d_5$ material). Normalization led to the ratio of 29.2:100. If we were to incorporate the P + 1 contribution from the P - 1 fragment (0.68), the ratio would be 29.0:100 (96.6 + 0.68 + 2.7). Thus, including this factor could cause a difference of up to -0.2 in the numerator of the fraction.

We also assumed (p. 140) that the $d_5$ material gives the same percent of hydrogen migration as the $d_6$ material. Therefore, the parent peak (m/e 192) of the $d_6$ material and the P + 1 of the $d_5$ material were treated equally in their contribution to the m/e 177 peak (P - $CH_3$) height. We added the heights of the parent peak of the $d_6$ material (96.6) and the P + 1 of the $d_5$ material (2.7) to get the total height of the m/e 192 peak to be used in comparison to the m/e 177 peak as shown below:

$$96.6 + 2.7 = 99.3$$

$$\frac{99.3}{100} = \frac{29.0}{x}$$

$$x = 29.2$$

If the H migration of the $d_5$ starting material were appreciably greater than that of the $d_6$ starting material, then the contribution of the $d_5$ product to the P - $CH_3$ fragments of the spectrum of IId would be greater by the amount of the increased H migration. We would have to adjust the 2.7 contribution to the ratio of m/e 192 to 177 peak heights. Let us use as an example an extreme case whereby the one extra hydrogen present in the $d_5$ starting material leads to 1.5 times as much hydrogen migration as the $d_6$ material. The weight of the P + 1 peak of the $d_5$ product (contribution to the m/e 192 peak height) would be 2.7 X 1.5 ≃ 4.0.

The calculation of the expected m/e 177 peak height would be:

$$\frac{96.6 + 4.0}{100} = \frac{100.6}{100} = \frac{29.0}{x}$$

$$x = 28.8$$

This could contribute a difference of up to -0.4 in the numerator of the H migration fraction.

Incorporation of all the possible errors into the ratio of the m/e 177 to the m/e 192 peak heights (the numerator of the hydrogen migration fraction) gives a range of:

$$\frac{28.0\ (29.2 - 0.5 - 0.2 - 0.1 - 0.4)\ \text{to}\ 29.7\ (29.2 + 0.5)}{99.5\ (100 - 0.5)\ \text{to}\ 100.5\ (100 + 0.5)} =$$

$$.279\ \text{to}\ .298$$

Thus, the range of the percentage of hydrogen migration in the formation of IId is:

$$\frac{.279\ \text{to}\ .298}{.296\ \text{to}\ .310} \times 100 = 90.0\ \text{to}\ 100.6\%$$

These calculations indicate that the assumptions made in the calculation of the percent hydrogen migration in the formation of IId (96.0%) probably affect the calculation by only a few percent. Therefore, the assumptions made in this calculation and, therefore, in the calculations of the percentages of hydrogen migration in the formation of IIe, IIf, and IIg are reasonable and would not affect the final conclusions drawn from these numbers.

## Appendix III - Computer Program for the Calculation of the Percentages of Hydrogen Migration from Different Positions of the Deuterated 1-Bromomethylcycloheptyl Cations (XVIId, XVIIe, XVIIf, and XVIIg)

The following computer program in BASIC language was used for calculating the percentages of hydrogen migration from the 2-, 3-, and 4-positions of the deuterated 1-bromomethylcycloheptyl cations (XVIId, XVIIe, XVIIf, and XVIIg). The program allows changes in the relative migrating ability of hydrogen atoms from the three positions respectively (F2, F3, and F4). Kinetic isotope effects for all positions are set at 1.0, 1.5, 2.0, 2.5, 3.0, and 3.5. The output consists of I2, I3, I4, F2, F3, and F4, which are set by the program, and D, E, F, and G, the percentages of H migration from XVIId, XVIIe, XVIIf, and XVIIg respectively.

```
010 PRINT "I2","I3","I4","F2","F3","F4","D","E","F","G"
020 READ F2, F3, F4
021 I2 = 1
022 I3 = 1
023 I4 = 1
025 M = 0
030 LET H2 = 4
040 LET H3 = 2
050 LET H4 = 0
070 LET L = 0
080 D2 = 4 - H2
090 D3 = 4 - H3
100 D4 = 4 - H4
110 H = (H2 * I2 * F2) + (H3 * I3 * F3) + (H4 * I4 * F4)
120 D = (D2 * F2) + (D3 * F3) + (D4 * F4)
130 A = H / (H + D)
140 L = L + 1
150 IF L = 2 GOTO 230
160 IF L = 3 GOTO 280
170 IF L = 4 GOTO 330
180 D5 = A
190 LET H2 = 2
200 LET H3 = 4
```

```
210 LET H4 = 4
220 GOTO 80
230 E = A
240 LET H2 = 2
250 LET H3 = 0
260 LET H4 = 2
270 GOTO 80
280 F = A
290 LET H2 = 0
300 LET H3 = 2
310 LET H4 = 4
320 GOTO 80
330 G = A
340 PRINT I2, I3, I4, F2, F3, F4, D5, E, F, G
350 M = M + 1
360 IF M = 2 GOTO 430
370 IF M = 3 GOTO 470
380 IF M = 4 GOTO 510
381 IF M = 5 GOTO 550
382 IF M = 6 GOTO 10
390 LET I2 = 1.5
400 LET I3 = 1.5
410 LET I4 = 1.5
420 GOTO 30
430 LET I2 = 2
440 LET I3 = 2
450 LET I4 = 2
460 GOTO 30
470 LET I2 = 2.5
480 LET I3 = 2.5
490 LET I4 = 2.5
500 GOTO 30
510 I2 = 3
520 I3 = 3
530 I4 = 3
540 GOTO 30
550 I2 = 3.5
560 I3 = 3.5
570 I4 = 3.5
580 GOTO 30
700 END
```

For calculations with other values for the isotope effects at any of the three positions these changes are made:

```
020 READ I2, I3, I4, F2, F3, F4
021 erased
022 erased
023 erased
350 GOTO 10
```

The input data needed are I2, I3, I4, F2, F3, and F4.

## EXPERIMENTAL SECTION

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. 37921. Melting points were determined using a Thomas-Hoover apparatus in open capillary tubes and are corrected. Boiling points are uncorrected. Infrared spectra were taken using a Beckman IR-20A spectrophotometer. Proton magnetic resonance spectra were taken using a Joelco JNM-MH-100 spectrometer. Unless otherwise indicated, chemical shifts are expressed in ppm ($\delta$) downfield from internal tetramethylsilane. Integration experimental values within ±5% of the expected values are recorded as integers. Mass spectra were taken using a Varian CH-5 Mass Spectrometer at 70 ev under direct sample inlet conditions and, unless otherwise indicated, linear mass scan was used. Within a series of scans the reproducibility of the relative ratios of mass spectral peak heights in successive scans was ±5%. Analytical gas chromatography was performed on 10' x 1/8" 10% OV-225 on 80/100 mesh Varaport #30 (Varian Aerograph, Springfield, N.J.) (Column I) or 6' x 1/8" 10% UC-W98 on 80/100 mesh WHP (Supelco, Inc., Bellefonte, Pa.) (Column II) columns using a Hewlett-Packard 5750B chromatograph with flame ionization detection. Preparative gas chromatography was performed on a 10' x 1/4" 25% cyclohexanedimethanol succinate on 60/80 mesh CPAW-DMCS column using a Varian A-700 chromatograph with a thermal conductivity detector. An electrostatic

precipitator[104] was used to increase the collection efficiency.

(A) Preparation of 1-Methyl-6,7-benzobicyclo[3.2.2]non-6-ene (II)

(1) Preparation of 4-Phenylcycloheptanone Semicarbazone (C)[105-108]

To a 100-ml. three-necked flask, equipped with an addition funnel, a mechanical stirrer, and a reflux condenser with a suspended thermometer, immersed in an ice bath in a ventilated hood behind a safety shield, were added 10.0 g. (57.4 mmole.) of 4-phenylcyclohexanone (Gallard-Schlesinger Chemical Manufacturing Corp., Carle Place, Long Island, N.Y.) and 50 ml. of 95% ethanol. p-Tolylsulfonylmethyl nitrosoamide (Diazald, Aldrich Chemical Co., Inc., Cedar Knolls, N.J.) (14.0 g., 67.8 mmole.) and 20 ml. of 95% ethanol were then added. Only a little dissolved to give a pale orange solution.

The stirrer was adjusted so that it would stir the solution slowly and disturb the surface of the solid only slightly. Six ml. of a solution of 15 g. of potassium hydroxide in 50 ml. of water was added at a rate of about one drop per min. The temperature of the solution remained at about 10-15°. After the first few drops were added, the evolution of gas began. After the addition which took 65 min., the reaction mixture was a deep orange. The stirring was then accelerated and continued for a half hr. at which time the gas evolution had stopped.

Hydrochloric acid (2 N) was added slowly until the

solution became acid to litmus, the solution turning pale yellow. About 7-8 ml. were needed. With stirring, a solution of 11.5 g. of sodium bisulfite in 20 ml. of water was added. After a few min. a thick white solid began to separate. The mixture was warmed to room temperature and stirred for 17 hr.

The mixture was filtered through a fritted glass funnel, and the thick semi-solid was washed twice with 25-ml. portions of cold ether.

Six additional samples (10.0, 10.1, 10.1, 10.1, 10.1, and 10.1 g.) of 4-phenylcyclohexanone were treated as described above.

The bisulfite adducts were combined in a 1000-ml. Erlenmeyer flask with a solution of 101.5 g. of sodium carbonate in 500 ml. of water. The mixture was warmed to 50-60° and stirred for a half hr. The solid melted to give two layers which, after about 15 min., became one liquid layer with a fine solid suspension. One hundred ml. of ether was added to dissolve the solid.

The aqueous layer was extracted with five 200-ml. portions of ether. The organic layers were combined, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to yield 45.05 g. (83.4%) of an orange oil.

The oil was dissolved in 50 ml. of 95% ethanol and added slowly to a one-l. three-necked flask containing a solution of 65.5 g. (0.89 mole) of semicarbazide hydrochlo-

ride and 100 g. of sodium acetate trihydrate in 500 ml. of water. Upon heating in a 75° water bath, a white fluffy solid precipitated. The mixture was heated for half an hr., then stirred at room temperature for 48 hr.

The solid was separated by filtration and recrystallized from ethanol to yield 45.4 g. of a white fluffy solid; m.p. 171-173° (lit.[107] m.p. 175-177°). Two successive concentrations of the mother liquor yielded 7.6 g. (m.p. 171-172°) and 2.04 g. (m.p. 171-172°) of white crystalline solids. The total yield was 55.0 g. (78.3% based on 4-phenylcyclohexanone); m.p. 171-173°; ir (KBr) 3400 (m, N-H), 3030 (m, aromatic-H), 2900, 2850 (m, alkyl-H), 1675 (s, carbonyl), 1635 (s, prim. amide), 1580, 1485 (s, phenyl), 1550 (s, sec. amide), 1450 (m, methylene), 1420 (m, prim. amide), 755, 695 (m, monosub. phenyl) $cm.^{-1}$

(2) Preparation of 4-Phenylcycloheptanone (XXI)[106,107]

4-Phenylcycloheptanone semicarbazone (C) (50.18 g., 0.204 mole) was mixed with 500 ml. of 20% phosphoric acid in a one-l. flask with a reflux condenser and a large magnetic stirring bar and was heated to reflux with stirring. The solid slowly melted and remained as oil globules suspended in the aqueous solution. After two hr. the mixture was cooled and allowed to stir overnight.

The mixture, an aqueous layer and a small upper oil layer, was extracted six times with 250-ml. portions of chloroform. The extracts were combined, dried over magne-

sium sulfate, and filtered. The solvent was evaporated under reduced pressure to yield an orange oil. Upon standing in a refrigerator for two days the oil became a pale orange-yellow solid which was recrystallized from pentane. Successive crops of white crystals were obtained by filtration, followed by partial evaporation of the filtrate. These crops weighed 3.74 g. (m.p. 59-60°), 1.34 g. (m.p. 59.5-60.5°), 2.08 g. (m.p. 58-58.8°), 2.26 g. (m.p. 57-58°), 3.80 g. (m.p. 60.5-61°), and 3.97 g. (m.p. 60-61°) (lit.[107] m.p. 52-53°); nmr ($CDCl_3$) δ 1.37-2.30 (m, 6 H, 3-, 5-, and 6-methylenes), 2.30-2.80 (m, 5 H, 2- and 7-methylenes and 4-H), 3.13 (s, 5 H, phenyl-H); ir (KBr) 3080, 3020 (s, phenyl-H), 2910, 2850 (m, alkyl-H), 1690 (s, carbonyl), 1600, 1490 (m, phenyl), 1440 (m, methylene), 760, 695 (s, monosub. phenyl) $cm.^{-1}$

(3) Preparation of Methyllithium (XXII)[109]

A 300-ml. three-necked flask containing a fritted glass filter with a stopcock was equipped with a condenser containing a drying tube, a mechanical stirrer, and a pressure-equalizing addition funnel containing a helium inlet. The glassware had previously been dried in an oven overnight and brought to room temperature under a helium atmosphere. A helium atmosphere was maintained throughout the reaction.

To the flask were added 100 ml. of dry ether (refluxed over lithium aluminum hydride for one hr., then distilled)

and lithium metal wire (2.25 g., 0.311 mole) in small pieces. While stirring 17.30 g. (0.122 mole) of methyl iodide was added dropwise through the addition funnel. After a few min., a white precipitate began to form. After the addition which took one hr., the mixture was stirred an additional 15 min.

A 250-ml. flask was attached to the bottom stopcock through a Claisen adaptor, evacuated, and filled with helium. The reaction mixture was allowed to filter into this flask. Some ether evaporated during the filtration.

The flask was stoppered and stored in a refrigerator. The solution was found to contain 1.27 mequiv. of methyllithium per ml. by titration against hydrochloric acid.

(4) Preparation of 1-Methyl-4-phenylcycloheptanol (XXIII)

In a Glove Bag ($I^2R$, Chettenham, Pa.) filled with nitrogen, 18 ml. of an ether solution of 1.27 mequiv. of methyllithium (XXII) per ml. (23 mmole.) and 50 ml. of dry ether (refluxed over lithium aluminum hydride for one hr., then distilled) were added to a 250-ml. three-necked flask, which was then stoppered. To a pressure-equalizing addition funnel was added a solution of 1.41 g. (7.5 mmole.) of 4-phenylcycloheptanone (XXI) in 40 ml. of dry ether. The flask was removed from the bag and equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and the addition funnel containing a nitrogen inlet. A nitrogen atmosphere was maintained throughout the reaction.

The ketone solution was added dropwise over one hr. The resulting cloudy solution, which contained a small amount of white fluffy solid, was stirred for an additional three hr.

The flask was immersed in an ice-water bath and 100 ml. of water was added dropwise. Much gas evolved and the solid dissolved. The aqueous layer was extracted with three 50-ml. portions of ether. The organic layers were combined, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 1.20 g. (77.2%) of a slightly yellowish solid. Four recrystallizations from hexane gave white needles; m.p. 100-102°; (lit.[1] m.p. 102.5-103.2°); nmr ($CDCl_3$) δ 1.00-2.30 (broad m with a singlet at 1.28, 14 H, methyl, ring methylenes, and hydroxyl), 2.30-3.00 (broad m, 1 H, benzyl), 7.27 (s, 5 H, phenyl-H); ir (KBr) 3400 (s, alcohol), 3080, 3030 (w, aromatic-H), 2920, 2860 (s, alkyl-H), 1600, 1485 (m, phenyl), 1470, 1450, 1430 (m, methylene), 1365 (m, methyl), 1130 (s, tert. alcohol), 755, 700 (s, monosub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 205 (15), 204 (100), 203 (4). The ratio of the base peak, 91, to 204 is 100:22.

(5) Preparation of 1-Methyl-6,7-benzobicyclo[3.2.2]non-6-ene (II)[1]

One ml. of 85% sulfuric acid was added to a 5-ml. flask equipped with a magnetic stirring bar and a reflux condenser containing a drying tube. The flask was immersed

in an ice-water bath. While stirring 0.096 g. (0.47 mmole.) of 1-methyl-4-phenylcycloheptanol (XXIII) was added in small portions over a half hr. A small upper layer separated. After complete addition, the mixture was stirred at room temperature for two hr., poured into 30 ml. of water, and extracted with three 25-ml. portions of benzene. The extracts were combined, washed with two 25-ml. portions of 10% sodium carbonate and 25 ml. of 10% sodium sulfate, dried over sodium sulfate, and filtered. The solvent was evaporated under reduced pressure to yield a pale yellow oil; nmr ($CDCl_3$) $\delta$ 0.60-2.18 (broad m with a singlet at 1.31, 13 H, methyl and ring methylenes), 2.82-3.15 (broad m, 1 H, methine), 6.8-7.2 (complex m, 4 H, aromatic); ir (liquid film) 3090, 3030 (w, phenyl-H), 2920, 2860 (s, alkyl-H), 1600 (w), 1490 (m, phenyl), 1450 (m, methylene), 1375 (m, methyl), 750 (vs, orthosub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 188 (2), 187 (17), 186 (100), 185 (6), 173 (1), 172 (6), 171 (35), 170 (1). The ratio of the base peak, 143, to 186 is 100:48.

(B) Preparation of 1-Trideuteriomethyl-6,7-benzo[3.2.2]-non-6-ene (IIa)

(1) Preparation of Trideuteriomethyllithium (XXIIa)

The procedure for preparing methyllithium (XXII) given on p. 171 was followed using 14.98 g. (0.103 mole) of trideuteriomethyl iodide (Stohler Isotope Chemicals, Rutherford, N. J.) and 2.20 g. (0.315 mole) of lithium metal, to give an ether solution containing 0.81 mequiv. per ml.

(2) Preparation of 1-Trideuteriomethyl-4-phenylcycloheptanol (XXIIIa)

The procedure given on p. 172 for preparing 1-methyl-4-phenylcycloheptanol (XXIII) was followed using 1.20 g. (6.4 mmole.) of 4-phenylcycloheptanone (XXI) and 25.5 ml. of an ether solution containing 0.81 mequiv. (20.7 mmole.) of trideuteriomethyllithium (XXIIa) per ml. to give 1.00 g. (75.5%) of an off-white solid. Recrystallization from hexane gave a white solid; m.p. 98-100°; nmr ($CDCl_3$) $\delta$ 1.15-2.30 (broad m, 11 H, ring methylenes and hydroxyl-H), 2.30-3.00 (broad m, 1 H, benzyl), 7.27 (s, 5 H, phenyl-H); ir (KBr) 3400 (s, alcohol), 3080, 3030 (w, phenyl-H), 2920, 2860 (s, alkyl-H), 2220 (m, alkyl-D), 1600, 1485 (m, phenyl), 1460, 1450, 1440 (m, methylenes), 1130 (tert. alcohol), 750, 695 (s, monosub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 208 (12), 207 (100), 206 (14). This corresponds to 90% $d_3$, 10% $d_2$. The ratio of the base peak, 91,

to 207 is 100:8.

(3) Preparation of 1-Trideuteriomethyl-6,7-benzo[3.2.2]-non-6-ene (IIa)

A 100-ml. three-necked flask was equipped with a stopper, a reflux condenser containing a drying tube, and a nitrogen inlet. The glassware had been previously dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

Thirty-five ml. of dry benzene (dried over Dri-Na, J. T. Baker Chemical Co., Phillipsburg, N. J.), 0.076 g. (0.57 mmole.) of aluminum chloride and a magnetic stirring bar were added. 1-Trideuteriomethyl-4-phenylcycloheptanol (XXIIIa) (0.101 g., 0.486 mmole.) was dissolved in five ml. of benzene and added. The mixture was stirred for ten min. During this time it became slightly cloudy.

The mixture was poured into 25 ml. of 10% hydrochloric acid. The organic layer was washed with 10 ml. of sat'd. sodium carbonate solution and 10 ml. of sat'd. sodium chloride solution, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 0.094 g. of a pale yellow liquid. Gas chromatography (Column I) showed the sample to consist of mainly one component with the same retention time as 1-methyl-6,7-benzobicyclo-[3.2.2]non-6-ene (II). The material was purified by preparative glc to give 0.025 g. (27.1%) of a colorless

liquid; nmr ($CDCl_3$) $\delta$ 0.83-2.17 (complex m, 10 H, alkyl-H), 2.83-3.17 (m, 1 H, methine), 6.87-7.42 (complex m, 4 H, aromatic); ir (liquid film) 3090, 3030 (w, phenyl-H), 2920, 2860 (s, alkyl-H), 2200 (m, alkyl-D), 1600 (w), 1490 (m, phenyl), 1450 (m, methylene), 752 (s, orthodisub. phenyl) $cm.^{-1}$ The mass spectrum is described on p. 76.

(C) Preparation of 1-Bromo-1-methyl-4-phenylcycloheptane (XXXVII)

Twenty-five ml. (39 g., 24 mmole.) of 48% hydrobromic acid in a 50-ml. flask containing a magnetic stirring bar was cooled in an ice bath. While stirring, 0.761 g. (3.73 mmole.) of 1-methyl-4-phenylcycloheptanol (XXIII) was added in portions over a few min.

The mixture was stirred at room temperature for one hr., poured into 50 ml. of water, the layers separated, and the aqueous layer extracted with three 10-ml. portions of benzene. The organic layers were combined, washed with 10 ml. of sat'd. sodium bicarbonate and 10 ml. of sat'd. sodium bromide, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give a yellow liquid which was distilled through a short-path apparatus (oil bath temp. 80°, 0.05 mm.) to yield a colorless liquid which consisted of 80% 1-bromo-1-methyl-4-phenylcycloheptane and 20% of an olefin impurity; nmr ($CDCl_3$) $\delta$ 1.02-2.90 (m, 14 H, aliphatic ring hydrogens and methyl), 5.6 (broad s, vinyl-H of impurity), 7.17 (s, 5 H, phenyl-H); ir (liquid film) 3065, 3030 (m, phenyl-H), 2930 (s), 2865 (m, alkyl-H), 1600, 1490 (m, phenyl), 1460, 1440 (m, methylene), 1380 (m, methyl), 753, 698 (s, monosub. phenyl $cm.^{-1}$

(D) Preparation of 1-Bromo-1-bromomethylcycloheptane (LIV)

(1) Preparation of N,N-Dimethylcycloheptylmethylamine (LVI)[54,110]

To a 500-ml. flask immersed in an ice bath was added 50 g. (1 mole) of 88% formic acid. Cycloheptylmethylamine (24.89 g., 0.196 mole, Aldrich Chemical Company, Inc., Cedar Knolls, N. J.) was added slowly in small portions, with much fuming. After the fuming subsided, a few boiling chips and 45 ml. (0.6 mole) of 36-38% formalin were added to give a colorless solution.

The ice bath was replaced by an oil bath at 95-100°. The solution began to reflux vigorously with the evolution of gas and slowly turned yellow. The heat was removed until the gas evolution subsided and the refluxing slowed. The heating was then continued for eight hr. The mixture was allowed to cool overnight. One hundred ml. of 4 N hydrochloric acid was added, and the solution was concentrated under reduced pressure to yield a semisolid. This was dissolved in 60 ml. of 4 N hydrochloric acid. The solution was made basic to precipitate the free amine by the slow addition of 50 ml. of 18 N sodium hydroxide. Two layers formed, a colorless aqueous bottom layer and a yellow oily organic layer. The aqueous layer was extracted with five 100-ml. portions of benzene. The organic layers were combined, dried over anhydrous potassium carbonate, and filtered. The solvent was evaporated under reduced pres-

sure to yield a viscous yellow-orange liquid which was distilled to yield 20.09 g. (68%) of a colorless liquid; b.p. 62-63° (5-6 mm.) (lit.[54] b.p. 102-103° (35 mm.)); nmr ($CDCl_3$) δ 0.80-2.10 (m, 15 H, methylenes and methine), 2.17 (s, 6 H, methyls).

(2) Preparation of N,N-Dimethylcycloheptylmethylamine Oxide (LVII)[54,111]

N,N-Dimethylcycloheptylmethylamine (LVI) (10.8 g., 69.7 mmole.) was dissolved in 20 ml. of methanol and placed in a 125-ml. Erlenmeyer flask containing a small magnetic stirring bar. The flask was cooled in an ice-water bath in a hood behind a safety shield. With stirring, 21.5 g. (189 mmole.) of 30% hydrogen peroxide (Matheson, Coleman, and Bell, East Rutherford, N. J.) was added dropwise over 45 min. to give a cloudy mixture which separated into two layers. The ice bath was removed and the mixture was allowed to stir at room temperature for 48 hr. The mixture, now one colorless layer, gave a negative phenolphthalein spot test and a positive test with starch-iodide paper.

About 25 mg. of 5% platinum on carbon powder (Engelhard Industries, Inc., Newark, N. J.) was carefully added to the solution with a microspatula, behind the shield. The mixture began to fizz, burst into flame, and then extinguished itself almost instantly. Two additional portions were added with the same results. After allowing the mixture to stand about an hr., another microspatula tip of

5% platinum on carbon was added with no reaction. At that point the solution gave a negative starch-iodide test.

The mixture was filtered through a fritted glass funnel, and the solvent was evaporated under vacuum to give a semisolid, which upon standing became an oily solid. The material was dried overnight using a vacuum pump to yield 12.0 g. (100%) of a slightly oily solid; nmr ($CDCl_3$) $\delta$ 1.55 (very broad s, 13 H, ring methylenes and methine), 3.08-3.38 (m with s at 3.18, 8 H, N-methylene and methyls), 4.45 (s, water impurity).

(3) Preparation of Methylenecycloheptane (LVIII)[54,111]

Slightly wet N,N-dimethylcycloheptylmethylamine oxide (LVII) (19.9 g., 0.116 mole) was put into a one-l. three-necked flask equipped with a magnetic stirring bar, a stopper, a nitrogen inlet, and a Claisen distilling head connected in series to a condenser, two dry ice traps, and a vacuum pump. The flask had been rinsed with a few ml. of conc. ammonia and dried in an oven overnight. The system with the nitrogen inlet closed was adjusted to a pressure of 22-23 mm. The nitrogen flow was then adjusted so the total pressure was 30-31 mm.

The reaction flask was heated slowly in an oil bath. At 95° a slow distillation began. Heating was continued until 130° at which time the distillation stopped. A small amount of deep red material remained in the reaction flask. The contents of the two traps were combined and washed with

three 50-ml. portions of water. The material was dissolved in 100 ml. of methylene chloride, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to yield a slightly yellow liquid which was distilled to yield 3.1 g. (21% based on N,N-dimethylcycloheptylmethylamine) of a colorless liquid; b.p. 139-140° (lit. b.p. 134°[54], 138-140°[112], 136-138°[113-115]); nmr ($CDCl_3$) δ 1.53 (broad s, 8 H, ring methylenes), 2.10-2.50 (m, 4 H, allylic methylenes), 4.67-4.80 (m, 2 H, vinyl); ir (liquid film) 3060 (w, vinyl-H), 2880, 2860 (s, alkyl-H), 1645 (m, olefin), 1450 (s, methylene), 880 (s, terminal methylene) $cm.^{-1}$ 1-Methylcycloheptene was shown to be absent by the absence of a peak at δ 5.48 in the nmr spectrum.

(4) Preparation of 1-Bromo-1-bromomethylcycloheptane (LIV)[116]

A 250-ml. three-necked flask was equipped with a mechanical stirrer, a Claisen adapter containing a suspended thermometer and a condenser with a drying tube, and a 150-ml. pressure-equalizing addition funnel containing a nitrogen inlet. The glassware had been dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

The flask was immersed in a dry ice-acetone bath and covered with aluminum foil. To the flask were added 2.82

g. (25.7 mmole.) of methylenecycloheptane (LVIII), 2.05 g. (26.3 mmole.) of pyridine (dried over potassium hydroxide), and 100 ml. of methylene chloride (dried over calcium sulfate). To the addition funnel was added 4.1 g. (25.6 mmole.) of bromine in 75 ml. of dry methylene chloride. The bromine solution was added dropwise with stirring, at such a rate as to keep the reaction temperature below -65°. The addition took one hr. Upon stirring for an additional fifteen min., the yellow solution became a little lighter.

The solution was allowed to warm to room temperature, and was washed with three 50-ml. portions of 5% sodium bisulfite (after the first wash, the solution became colorless) followed by three 50-ml. portions of water, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give a colorless liquid which was distilled through a heated, jacketed column of porcelain saddles to give 2.21 g. (51%) of a colorless liquid; b.p. 75-78° (3.8-4.1 mm.); nmr ($CDCl_3$) $\delta$ 1.65 (broad s, 8 H, 3-, 4-, 5-, and 6-methylenes), 2.0-2.5 (broad m, 4 H, 2- and 7-methylenes), 3.89 (s, 2 H, bromomethylene); ir (liquid film) 2930, 2860 (s, alkyl-H), 1455, 1445, 1440 (m, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 191 (12), 189 (13), 109 (100), 95 (11), 87 (14).

Anal. Calc'd. for $C_8H_{14}Br_2$: C, 35.58; H, 5.23; Br, 59.19. Found: C, 35.61; H, 5.25; Br, 59.17.

(E) Preparation of 3,4-Dideuterio-1,1-bis(bromomethyl)-cyclohexane (Ic)

(1) Preparation of 4,4-Bis(hydroxymethyl)cyclohexene (XIX)[117-119]

A three-l. three-necked flask, equipped with a mechanical stirrer, a reflux condenser, and a Claisen adapter containing an addition funnel and a reflux condenser containing a suspended thermometer to measure the temperature within the reaction flask, was immersed in a water bath thermostated at 40°. A cloudy mixture of 120 g. (1.2 moles) of 3-cyclohexene-1-carboxaldehyde (Aldrich Chemical Co., Inc., Cedar Knolls, N. J.), 260 ml. (3.04 moles) of 36-38% formalin and 320 ml. of methanol was added.

A solution of 90 g. (1.75 moles) of potassium hydroxide in 68 ml. of water was added dropwise with stirring. After the addition of the first few drops, the solution turned clear yellow. During the addition, which took 70 min., the temperature of the solution rose to 65° and became increasingly darker. The solution was heated at reflux for two hr.

The cooled solution was poured into 400 ml. of water and extracted with four 500-ml. portions of ether. The organic layers were combined and washed with three 300-ml. portions of water, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 110 g. of an off-white solid. The solid was re-

crystallized from 1:1 benzene:hexane to give 101 g. (62%) of white needles; m.p. 90.5-91.5° (lit. m.p. 92.5°[117], 92.0°[118]); nmr ($CDCl_3$) δ 1.70-2.20 (complex m, 6 H, 2-, 5-, and 6-methylenes), 2.55 (broad s, 2 H, hydroxyl-H), 3.58 (s, 4 H, hydroxymethylenes), 5.68 (m, 2 H, vinyl-H); ir (KBr) 3250 (s, alcohol), 3010 (m, vinyl-H), 2900, 2840 (s, alkyl-H), 1645 (w, olefin), 1460, 1430 (s, methylene), 1035 (s, prim. alcohol), 705 (s, cis olefin) $cm.^{-1}$

(2) Preparation of 3,4-Dideuterio-1,1-bis(hydroxymethyl)-cyclohexane (XVc)

Tris(triphenylphosphine)rhodium(I) chloride (Alfa Inorganics, Inc., Beverly, Mass.) (2.39 g., 2.58 mmole.) was mixed with 125 ml. of benzene. Almost all of the solid dissolved, giving a brownish orange solution containing a few specks of an orange solid. 4,4-Bis(hydroxymethyl)-cyclohexene (XIX) (50 g., 0.352 mole) was dissolved in a mixture of 250 ml. of ethanol and 50 ml. of benzene.

The olefin solution and the catalyst mixture were combined in a 1000-ml. Erlenmeyer flask. A large magnetic stirring bar was added, and the flask was attached to an atmospheric pressure hydrogenation apparatus containing a 500-ml. buret and a deuterium gas tank.

The apparatus was successively evacuated and flushed with deuterium five times. A slightly negative pressure, which was put on the system for ten minutes, remained constant, showing that there were no leaks.

The buret was filled with deuterium. A slight positive pressure, about 50-70 mm., was put on the system, and vigorous stirring was then begun.

The gas buret was refilled twenty-four times, each time after about 400 to 450 ml. of gas had been used up. During the reaction, the time necessary to use up a buret of deuterium slowed from fifteen min. to about forty min. The total volume of deuterium used was 9136 ml. (The theoretical volume of deuterium needed was 8560 ml.) The system was then stirred overnight under a small negative pressure. The fact that the pressure increased slightly overnight indicated the presence of a slow leak.

The reaction mixture, now a black solution, was concentrated under reduced pressure, to give a mixture of two solids, one black and the other light brown. The solids were washed with three 200-ml. portions of methylene chloride, which dissolved most of the black solid and some of the other.

The remaining solid was recrystallized from 1:1 benzene:hexane to give 30.2 g. of a white fluffy solid; m.p. 97.5-98.5° (lit.[93] for the undeuterated analog m.p. 98.5°).

The mother liquor and the methylene chloride solution were combined and evaporated to give a dark brown solid. The recrystallization of this material from 1:1 benzene: hexane gave 7.3 g. of a fluffy white solid; m.p. 97.5-98.1°. The solids were combined (72.5%); nmr ($CDCl_3$) $\delta$ 1.40 (broad s, 8 H, ring hydrogens), 2.99 (s, 2 H, hydroxyl), 3.63 (s,

4 H, hydroxymethylenes); ir (KBr) 3300 (s, alcohol), 2930, 2860 (s, alkyl-H), 2180 (m, alkyl-D), 1485, 1470, 1450 (s, methylene), 1050 (s, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 128 (2), 97 (100).

(3) Preparation of 3,4-Dideuterio-1,1-bis(tosyloxymethyl)-cyclohexane (XXc)

To a 500-ml. three-necked flask equipped with a Claisen adapter containing a stopper and a reflux condenser containing a drying tube, a mechanical stirrer, and a thermometer extending to the bottom of the flask, was added 30.16 g. (0.200 mole) of 3,4-dideuterio-1,1-bis(hydroxymethyl)cyclohexane (XVIc) in 200 ml. of pyridine (dried over potassium hydroxide).

The solution was cooled in a salt-ice water bath and 99.47 g. (0.52 mole) of p-toluenesulfonyl chloride was added in portions over a one and a half hr. period, to give a white precipitate and a yellow solution. The ice bath was removed, and the mixture stirred for another hr.

The mixture was poured into a solution of 400 ml. of concentrated hydrochloric acid and 400 ml. of ice water. The resulting tan oil slowly changed to a semi-solid upon standing for two hr. The mixture was filtered and the semi-solid was washed with five 100-ml. portions of dilute hydrochloric acid and five 100-ml. portions of water, until the washes were neutral to litmus.

The solid was air dried and recrystallized from metha-

nol to give 67.39 g. (72%) of a white solid; m.p. 85.5-86.5°; (lit.[120] for the nondeuterated analog m.p. 84-84.5°); nmr ($CDCl_3$) δ 1.26 (broad s, 8.5 H, ring hydrogens), 2.45 (s, 6 H, aromatic methyls), 3.81 (s, 4 H, hydroxymethylenes), 7.30, 7.44, 7.70, 7.84 (AA'BB', 8 H, aromatic hydrogens); ir (KBr) 3030 (vw, aromatic-H), 2920, 2860 (m, alkyl-H), 2180 (w, alkyl-D), 1595 (m), 1495 (w, aromatic), 1460 (m, methylene), 1360 (w, methyl), 1350, 1180 (s, sulfonate ester), 820 (s, p-disub. aromatic); mass spec m/e (rel intensity) 457 (3), 456 (14), 455 (29), 454 (100), 453 (19), 452 (7). This indicated the isotope ratio of $D_2:D_1:D_0$ to be 79:15:5.

(4) Preparation of 3,4-Dideuterio-1,1-bis(bromomethyl)-cyclohexane (Ic)

To a 500-ml. three-necked flask equipped with a reflux condenser, a stopper, a suspended thermometer, and a magnetic stirring bar, was added 150 ml. of diethylene glycol (2,2'-oxydiethanol, Matheson, Coleman, and Bell, East Rutherford, N. J.) and 30.49 g. (67.46 mmole.) of 3,4-dideuterio-1,1-bis(tosyloxymethyl)cyclohexane (XXc). The mixture was heated with stirring. At 90°, the solid dissolved to give a colorless solution. At 140°, 24.63 g. (239.2 mmole.) of powdered sodium bromide was added in portions over a few min. The solution became light amber. The solution was stirred and heated at 150° (flask temperature) for six hr.

The solution was cooled to room temperature and poured

into 100 ml. of water, to give a dark brown oil and a cloudy brown aqueous layer. The oil was separated and the aqueous layer was extracted eight times with 25-ml. portions of carbon tetrachloride. The extracts were successively lighter in color; the last two were colorless. The organic layers were combined, washed once with 50 ml. of water, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 16.92 g. (92%) of a dark brown liquid. The liquid was combined with the crude product of another such reaction of the ditosylate (20 g. of ditosylate (XXc)) and distilled to give 18.47 g. (61.5%) of a colorless liquid; b.p. 103-105° (3-3.5 mm.) (lit.[120] b.p. 117° (6 mm.), 110° (5 mm.)); nmr ($CDCl_3$) δ 1.51 (s, 8.4 H, ring hydrogens), 3.48 (s, 4 H, bromomethylenes); ir (liquid film) 2920, 2860 (s, alkyl-H), 2160 (m, alkyl-D), 1450, 1420 (s, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 275 (5), 274 (49), 273 (17), 272 (100), 271 (22), 270 (55), 269 (10), 268 (3). This indicated the isotope ratio of $D_2:D_1$ to be 86.8:13.2. The ratio of the base peak, 97, to the parent peak is 100:22.

(F) Preparation of 1-Bromomethyl-4-phenylcycloheptane (XXXIX)

(1) Preparation of 3-(2-Oxocyclopentyl)propiophenone (XCVII)[121,122]

β-Dimethylaminopropiophenone hydrochloride (Aldrich Chemical Co., Cedar Knolls, N. J.) (106.58 g., 0.500 mole) was neutralized with a solution of 20 g. (0.50 mole) of sodium hydroxide to give 86.34 g. of β-dimethylaminopropiophenone (XCVI).

The amine and 245.86 g. (1.461 moles) of cyclopentanone were heated at reflux for 20 min. The orange mixture was transferred to a one-l. flask equipped for distillation. The excess cyclopentanone was removed by a simple distillation (b.p. 33-36° (3.8-4.0 mm.)). The remaining viscous red liquid was distilled through a Claisen distillation head to give 80.74 g. (74.8%) of a yellow liquid which solidified upon standing; b.p. 150-152° (1.3 mm.); m.p. 39-42° (lit.[121] m.p. 40°); nmr ($CDCl_3$) δ 1.20-2.60 (m, 9 H, ring and 3-methylenes), 3.80 (t, J = 7 Hz, 2 H, 2-methylene), 7.28-8.30 (m, 5 H, phenyl-H); ir (KBr) 3070 (w, phenyl-H), 2965, 2880 (m, alkyl-H), 1745 (s, aliph. ketone), 1675 (s, aryl ketone), 1595, 1480 (m, aromatic), 1445 (m, methylene), 750, 685 (m, monosub. phenyl) $cm.^{-1}$

(2) Preparation of 4-Phenylcyclohept-3-enecarboxylic Acid (XCVIII)[100]

A mixture of 37.00 g. (0.170 mole) 3-(2-oxocyclopentyl)propiophenone (XCVII), 300 ml. of glacial acetic acid, and 74 ml. of conc. hydrochloric acid was heated at reflux for eight hr., after which the solvent was removed by distillation under aspirator pressure. The viscous, brown residue was dissolved in 500 ml. of ether. Cold 6 N sodium hydroxide (250 ml.) was added to give a white precipitate in the interface which dissolved on addition of 200 ml. of water. The water layer was separated and a solution of 16.5 g. of sulfuric acid in 200 ml. of water was added with cooling, followed by conc. hydrochloric acid until pH 1. The resulting mixture was extracted with 200 ml. of ether. The ether solution was washed with two 400-ml. portions of sat'd. sodium chloride solution, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 27.00 g. of a viscous oil which was distilled under reduced pressure to give 23.71 g. (64.1%) of a very pale, lemon-colored liquid; b.p. 179-182° (2.5 mm.) (lit.[100] b.p. 150-154° (0.15 mm.)); nmr ($CDCl_3$) δ 1.10-2.96 (m, 9 H, aliphatic ring-H), 5.98 (broad, 1 H, vinyl), 7.20 (broad s, 5 H, phenyl), 12.04 (s, 1 H, acid-H); ir (liquid film) 3600-2400 (s, carboxylic acid), 3040 (s, phenyl-H), 2950, 2880 (s, alkyl-H), 1705 (s, carbonyl), 1600, 1490 (m, aromatic), 1450, 1430 (m, methylene), 750, 700

(monosub. phenyl) cm.$^{-1}$

(3) Preparation of 4-Phenylcycloheptanecarboxylic Acid (XCV)[100,122]

A solution of 8.64 g. (0.040 mole) of 4-phenylcyclohept-3-enecarboxylic acid (XCVIII) in 100 ml. of ethyl acetate and 1.44 g. of 5% paladium on carbon were shaken with hydrogen in a Parr apparatus for three hr. The mixture was then filtered and the catalyst rinsed with an additional 50 ml. of ethyl acetate. The solvent was evaporated under reduced pressure to give a white solid which was recrystallized from hexane to yield 7.77 g. (89.1%) of white crystals; m.p. 65.3-67° (lit.[100] m.p. 57-59°); nmr ($CDCl_3$) $\delta$ 1.00-2.28 (m, 10 H, ring methylenes), 2.56 (broad, 2 H, methines), 7.09 (broad s, 5 H, phenyl), 13.11 (s, 1 H, acid); ir (liquid film) 3400-2400 (s, carboxylic acid), 3090, 3040 (m, phenyl-H), 2940, 2880 (s, alkyl-H), 1705 (s, carbonyl), 1605, 1495 (m, aromatic), 1450 (m, methylene) 758, 700 (m, monosub. phenyl) cm.$^{-1}$

(4) Preparation of 1-Hydroxymethyl-4-phenylcycloheptane (XCIX)

To a 300-ml. flask, equipped with a magnetic stirring bar and a reflux condenser with a drying tube, was added 7.77 g. (0.0356 mole) of 4-phenylcycloheptanecarboxylic acid (XCV) and 75 ml. of dry tetrahydrofuran (dried over potassium hydroxide). Lithium aluminum hydride (2.98 g.,

0.0784 mole) was added in small portions with much gas evolution, and an additional 25 ml. of tetrahydrofuran was used to wash it in. The mixture was heated at reflux for 17 hr.

The flask was immersed in an ice bath and 20 ml. of water, followed by 20 ml. of conc. hydrochloric acid, was added dropwise. There was gas evolution. The mixture was stirred for 10 min. to give two colorless layers which were extracted with two 300-ml. portions of ether. The ether solutions were combined, washed with two 300-ml. portions of sat'd. sodium chloride solution, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 6.32 g. (87.0%) of a light yellow liquid which was distilled to give 5.09 g. of a colorless liquid; b.p. 138-140° (1.2 mm.); nmr ($CDCl_3$) δ 0.80-2.10 (m, 11 H, ring methylenes and 1-methine), 2.40-2.80 (broad m, 1 H, 4-methine), 3.20 (s, 1 H, hydroxyl), 3.38 (d, J = 6 Hz, 2 H, hydroxymethylene), 7.16 (broad s, 5 H, phenyl); ir (liquid film) 3400 (broad s, hydroxyl), 3100, 3080, 3050 (m, phenyl-H), 2930, 2865 (s, alkyl-H), 2000-1660 (four bands, overtones-monosub. phenyl), 1602, 1490 (m, aromatic), 1450 (s, methylene), 1060 (prim. alcohol), 755, 698 (s, monosub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 205 (10), 204 (73), 186 (48), 171 (21), 147 (99), 91 (100).

Anal. Calc'd. for $C_{14}H_{20}O$: C, 82.30; H, 9.87; O, 7.38. Found: C, 82.31; H, 9.96.

(5) Preparation of 1-Bromomethyl-4-phenylcycloheptane (XXXIX)

A 100-ml. three-necked flask, equipped with a reflux condenser containing a drying tube, a stopper, a pressure-equalizing addition funnel containing a nitrogen inlet, and a magnetic stirring bar, was immersed in an ice bath. The apparatus had been dried overnight in an oven and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

To the flask was added a solution of 1.428 g. (5.45 mmole.) of triphenylphosphine in 10 ml. of dry benzene (dried over sodium). A solution of 0.905 g. (5.66 mmole.) of bromine in 15 ml. of benzene was added dropwise with stirring over a half hr. The resulting yellow solution was stirred for an additional half hr. during which time most of the color disappeared. The ice bath was removed and a solution of 0.966 g. (4.73 mmole.) of 1-hydroxymethyl-4-phenylcycloheptane (XCIX) and 0.435 g. (5.51 mmole.) of dry pyridine (dried over potassium hydroxide) in 25 ml. of benzene was added dropwise with vigorous stirring over a half hr. The resulting slurry was heated for one hr. at 50-60°. The mixture was filtered through a fritted glass funnel, and the off-white solid was washed with two 10-ml. portions of hexane. The washes and filtrate were combined, and the solvent evaporated under reduced pressure to give a mixture of solid and oil.

Twenty-five ml. of hexane was added, and the mixture stirred for one hr. The mixture was filtered through a fritted glass funnel, and the solid was washed with two 10-ml. portions of hexane. The washes and filtrate were combined, and the solvent evaporated under reduced pressure to give 0.90 g. of an orange oil, which was distilled under reduced pressure to give 0.730 g. (57.8%) of a colorless liquid; b.p. 155° (1.7 mm.); nmr δ 0.88-2.10 (m, 11 H, ring methylenes and 1-methine), 2.40-2.80 (broad, 1 H, 4-methine), 3.29 (d, J = 6 Hz, 2 H, bromomethylene), 7.16 (broad s, 5 H, phenyl-H); ir (liquid film) 3095, 3085, 3025, 3005 (m, phenyl-H), 2930, 2860 (s, alkyl-H), 2000-1660 (four bands, overtones-monosub. phenyl), 1600, 1490 (m, aromatic), 1450 (m, methylene), 750, 695 (s, monosub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 269 (2), 268 (16), 267 (2), 266 (17), 186 (10), 117 (100), 91 (91).

Anal. Calc'd. for $C_{14}H_{19}Br$: C, 62.93; H, 7.17; Br, 29.90. Found: C, 63.08; H, 7.17; Br, 29.79.

(G) Model Experiments for the Preparation of Deuterated 1,1-Bis(bromomethyl)cyclohexanes (Id, Ie, If, Ig)

(1) Preparation of 1,1,3,3-Tetracarbethoxypropane (LXXXV)[123,124]

A 100-ml. three-necked flask was equipped with a reflux condenser containing a drying tube, a stopper, a pressure-equalizing addition funnel containing a nitrogen inlet, and a magnetic stirring bar. The glassware was dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

Sodium (1.68 g., 0.073 mole), in small pieces, was added to 60 ml. of absolute ethanol with rapid stirring. The sodium dissolved slowly with the evolution of hydrogen gas and heat. Diethyl malonate (12.54 g., 0.0756 mole) was added dropwise over a few min. The resulting cloudy solution was stirred for an additional few min.

The nitrogen atmosphere was removed. Methylene iodide (10.41 g., 0.0388 mole) was added dropwise. The yellow solution, which was basic to litmus, was heated at reflux for three hr., at which time it was neutral.

The slightly cloudy mixture was concentrated under reduced pressure to give a mixture of a white solid and a light yellow liquid. The addition of ten ml. of water caused the white solid to dissolve. The aqueous layer was extracted with four 25-ml. portions of ether. The organic

layers were combined, washed with ten ml. of water and two ten-ml. portions of a 5% sodium bisulfite solution, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 10.32 g. (85.1%) of a yellow liquid which was distilled through a vacuum-jacketed Vigreux column to give a colorless liquid; b.p. 155-157° (0.8-1.0 mm.) (lit.[123] b.p. 192° (12 mm.)); nmr ($CDCl_3$) δ 1.25 (t, J = 7.0 Hz, 12 H, methyls), 2.39 (t, J = 7.5 Hz, 2 H, 2-methylene), 3.42 (t, J = 7.5 Hz, 2 H, 1- and 3-methylenes), 4.17 (q, J = 7.0 Hz, 8 H, ethyl methylenes) (lit.[123] 1.24, 2.36, 3.43, 4.17); ir (liquid film) 2980, 2940, 2900 (s, alkyl-H), 1730 (s, carbonyl), 1460, 1440 (m, methylene), 1365 (m, methyl), 1020 (s, carbon-oxygen) $cm.^{-1}$ (lit.[123] (liquid film) 2980, 2930, 2900, 1750, 1730 $cm.^{-1}$); mass spec m/e (rel intensity) 333 (27), 332 (100). The ratio of the base peak, 287, to 332 is 100:10.5.

(2) Preparation of Glutaric Acid (LXXXVII)[125]

To a ten-ml. flask was added 0.997 g. (3.00 mmole.) of 1,1,3,3-tetracarbethoxypropane (LXXXV), one ml. of conc. hydrochloric acid, one ml. of water, and a magnetic stirring bar. The flask was fitted with a reflux condenser and the two-layer mixture was heated at reflux for 20 hr. After about five hr. the two layers had become one. The reaction mixture was evaporated under reduced pressure to yield 0.371 g. (93.7%) of a slightly off-white solid; m.p. 95.5-96.6° (lit.[125] m.p. 96-97°); nmr ($D_2O$) δ 1.85 (p, J =

7.5 Hz, 2 H, 3-methylene), 2.36 (t, J = 7.5 Hz, 4 H, 2- and 4-methylenes), 4.67 (s, hydroxyl and HDO of solvent); ir (KBr) 3600-2100 (m, carboxylic acid), 1700 (s, carbonyl), 1465 (m, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 114 (43), 86 (100), 85 (30).

(3) Preparation of Di-p-phenylphenacyl Glutarate (XCII)[126-128]

Glutaric acid (LXXXVII) (0.101 g., 0.765 mmole.) was dissolved in one ml. of water in a 25-ml. flask containing a magnetic stirring bar. One half drop of 1% phenolphthalein solution was added. While stirring, a few drops of 10% sodium hydroxide were added until the solution just turned pink. One drop of 10% hydrochloric acid solution was added to discharge the color.

p-Phenylphenacyl bromide (0.391 g., 1.43 mmole.) was dissolved in 15 ml. of warm ethanol and added, causing a precipitate to form. The mixture was heated at reflux for two hr., during which time most of the solid dissolved. Upon cooling, a white crystalline precipitate formed. The solid was filtered and air dried to give 0.194 g. of an off-white crystalline solid. A few mg. were recrystallized from acetone to give white crystals; m.p. 152-153° (lit.[126] m.p. 152°); mass spec m/e (rel intensity) 522 (8), 521 (37), 520 (100), 519 (1).

(4) Preparation of Diethyl Glutarate (LXXXVIII)

To a 250-ml. flask containing a magnetic stirring bar were added a solution of 14.97 g. (0.113 mole) of glutaric acid (LXXXVII) in 45 ml. of absolute ethanol, 22 ml. of toluene and 0.15 ml. of conc. sulfuric acid. The flask was set up for simple distillation and the mixture was heated by raising an oil bath at 115° slowly over the flask. A water, toluene, ethanol mixture distilled at 75-76°. When the distillation stopped, 45 ml. of absolute ethanol was added. Distillation began at 75°. When the distillation slowed, the oil bath temperature was raised to 160° until the distillation stopped. The residual liquid was distilled through a vacuum jacketed Vigreux column to give 19.94 g. (93.5%) of a colorless liquid; b.p. 90-96° (4 mm.); nmr ($CDCl_3$) $\delta$ 1.26 (t, J = 7.0 Hz, 6 H, methyls), 1.92 (p, J = 7.0, 2 H, 3-methylene), 2.34 (t, J = 7.0, 4 H, 2- and 4-methylenes), 4.17 (q, J = 7.0, 4 H, oxymethylenes); ir (liquid film) 2990, 2950, 2920 (s, alkyl-H), 1735 (s, carbonyl), 1470, 1450 (m, methylene), 1365 (m, methyl) $cm.^{-1}$; mass spec m/e (rel intensity) 189 (14), 188 (100). The ratio of the base peak, 143, to 188 is 100:0.6.

(5) Preparation of 1,5-Pentanediol (LXXXIX)

A one-l. three-necked flask was equipped with a mechanical stirrer, a reflux condenser containing a drying tube, and a pressure-equalizing addition funnel containing

a nitrogen inlet. The glassware had been dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

Four hundred ml. of dry ether and 11.80 g. (0.310 mole) of lithium aluminum hydride were added to the flask. Diethyl glutarate (LXXXVIII) (19.60 g., 0.104 mole) was dissolved in 150 ml. of ether and added dropwise, with stirring, at a rate sufficient to maintain a slow reflux. The mixture was heated at reflux for six hr. The mixture was then stirred at room temperature overnight.

The flask was immersed in an ice bath, and 50 ml. of ice water was added dropwise with vigorous stirring, to give a white precipitate. Sulfuric acid (125 ml., 25%) was added slowly over a few min. to dissolve the solid.

The aqueous layer was continuously extracted with ether for five days. The organic layers were combined, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 9.42 g. (87%) of a colorless liquid; nmr ($D_2O$) $\delta$ 1.08-2.00 (m, 6 H, 2-, 3-, and 4-methylenes), 3.60 (t, J = 7.5 Hz, 4 H, 1- and 5-methylenes), 4.65 (s, hydroxyl); ir (liquid film) 3300 (s, hydroxyl), 2930, 2870 (s, alkyl-H), 1450, 1430 (m, methylene), 1060 (s, carbon-oxygen) $cm.^{-1}$; mass spec m/e (rel intensity) 85 (23), 74 (34), 68 (67), 67 (37), 57 (83), 56 (100), 55 (72).

(6) Preparation of 1,5-Dibromopentane (XC)

A 100-ml. three-necked flask was equipped with a magnetic stirring bar, a stopper, a reflux condenser containing a drying tube, and a pressure-equalizing addition funnel containing a nitrogen inlet. The apparatus was dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

Phosphorous tribromide (26.93 g., 99.5 mmole.) was added to the flask. With rapid stirring, 8.98 g. (86.2 mmole.) of 1,5-pentanediol (LXXXIX) was added dropwise over a half hr. As the first few drops were added, the mixture became warm, turned orange, and gave off some white fumes. The mixture, consisting of two layers, was heated for 24 hr. at 60-65°.

The light orange mixture was cooled in an ice bath and the nitrogen atmosphere was removed. With rapid stirring, 20 ml. of water was added very slowly resulting in the profuse evolution of white fumes. The light aqueous layer was extracted with four 25-ml. portions of methylene chloride. The organic layers were combined, washed with two 25-ml. portions of a sat'd. sodium carbonate solution, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 15.99 g. (80.8%) of a slightly yellowish liquid which was shown by glc (Column II) to be one compound; nmr ($CDCl_3$) $\delta$ 1.20-2.06 (m, 6 H,

2-, 3-, and 4-methylenes), 3.40 (t, J = 7 Hz, 4 H, 1- and 5-methylenes); ir (liquid film) 2930, 2870 (s, alkyl-H), 1460, 1430 (m, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 232 (50), 231 (7), 230 (100), 229 (6), 228 (47). The ratio of the base peak, 150, to 230 is 100:19.

(7) Preparation of 1,1-Dicarbethoxycyclohexane (XCI)[129,130]

A 1000-ml. three-necked flask was equipped with a magnetic stirring bar, a reflux condenser containing a drying tube, and two pressure-equalizing addition funnels, one containing a drying tube, the other a nitrogen inlet. The glassware was dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

To a stirred solution of 2.10 g. (91.3 mmole.) of sodium metal in 200 ml. of absolute ethanol was added 7.017 g. (43.86 mmole.) of diethyl malonate in small portions over ten min. The resulting cloudy solution was added to one of the dropping funnels. The other dropping funnel was charged with a solution of 10.04 g. (43.67 mmole.) of 1,5-dibromopentane (XC) in 200 ml. of absolute ethanol. To the flask was added 25 ml. of ethanol which was maintained at reflux. The two mixtures were added simultaneously over five hr. The resulting white solid and cloudy suspension was heated at reflux for 17 hr.

The ethanol was evaporated under reduced pressure

leaving a white solid and yellowish liquid. Twenty-five ml. of water was added to dissolve the solid. The mixture was extracted with four 50-ml. portions of benzene. The organic layers were combined, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 8.727 g. of a yellow oil. The material was distilled through a heated jacketed Vigreux column containing a partial takeoff total reflux distillation head. Fractions were analyzed by glc (Column II). Retention times were compared to authentic samples.

| Fraction | B.P. (mm.) | Wt. | Comments (GLC Analysis) |
|---|---|---|---|
| 1 | 76-82° (9.5-10.2) | 0.974 g. | no XCI present, all low boiling material |
| 2 | 82-106° (9.5-9.8) | 1.101 g. | contains approximately 10% XCI |
| 3 | 118-124° (8.8-9.0) | 1.976 g. | contains 90-95% XCI |
| 4 | 125-126° (8.8) | 1.136 g. | contains over 95% XCI |
| 5 | 122° (7.5) | 0.337 g. | contains over 95% XCI |
| 6 | 118° (5.2) | 0.086 g. | contains 75% XCI, 25% high boiling material |
| 7 | 142° (3.5) | 0.457 g. | contains 10% XCI, 90% high boiling material |

Fractions 3, 4, and 5 were combined to give 3.44 g. (34.6%) of a colorless liquid; nmr ($CDCl_3$) $\delta$ 1.06-1.80 (broad m with a triplet, J = 7.0 Hz, at 1.25, 12 H, methyls and 3-, 4-, and 5-methylenes), 1.80-2.20 (m, 4 H, 2-, and

6-methylenes), 4.16 (q, J = 7.0 Hz, 4 H, ethyl methylenes); ir (liquid film) 2930, 2870 (s, alkyl-H), 1725 (s, carbonyl), 1460, 1450 (m, methylene), 1365 (m, methyl) cm.$^{-1}$; mass spec m/e (rel intensity) 229 (17), 228 (100). The ratio of the base peak, 173, to 228 is 100:8.

(8) Preparation of 1,1-Bis(hydroxymethyl)cyclohexane (XVI)[120]

A 50-ml. three-necked flask was equipped with a magnetic stirring bar, a reflux condenser containing a drying tube, a stopper, and a pressure-equalizing addition funnel containing a nitrogen inlet. The glassware was dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. A nitrogen atmosphere was maintained throughout the reaction.

Ten ml. of dry ether and 0.336 g. (8.85 mmole.) of lithium aluminum hydride were added to the flask.

A solution of 1.008 g. (4.42 mmole.) of 1,1-dicarbethoxycyclohexane (XCI) in 10 ml. of ether was added dropwise. The resulting mixture was heated at reflux for three hr. and then stirred at room temperature overnight.

The flask was cooled in an ice bath and five ml. of water was added dropwise. Ten ml. of 10% hydrochloric acid was added to dissolve the resulting solid. The aqueous layer was extracted with four 25-ml. portions of ether. The organic layers were combined, dried over magnesium sulfate, and filtered. The solvent was evaporated to give

0.500 g. (78.4%) of a white solid which was recrystallized from 1:1 benzene:hexane; m.p. 97.5-98.5° (lit.[120] m.p. 98.5°); nmr ($CDCl_3$) δ 1.42 (broad s, 12 H, ring hydrogens), 3.08 (broad s, 2 H, hydroxyl), 3.60 (s, 4 H, hydroxymethylenes); ir (KBr) 3300 (s, hydroxyl), 2930, 2860 (s, alkyl-H), 1485, 1470, 1450 (s, methylene), 1040 (s, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 126 (8), 95 (100), 96 (76), 97 (54).

(H) Preparation of 3,3,4,4,5,5-Hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id)

(1) Preparation of Dideuteriomethylene Iodide (LXXXIVd)[131,132]

A solution of 5.74 g. (0.250 mole) of sodium metal in 100 ml. of 99.8% deuterium oxide (10% sodium deuterioxide) and 50.10 g. (0.187 mole) of methylene iodide were placed in a dry flask containing a magnetic stirring bar and a reflux condenser containing a drying tube, and the mixture was heated at 80-85°.

After 48 hr., the aqueous layer was replaced by a fresh solution of 2.94 g. (0.128 mole) of sodium in 50 ml. of deuterium oxide and the mixture heated at 80-85° for an additional 48 hr. The organic layer was dissolved in 100 ml. of ether, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 42.0 g. (84%) of a slightly yellow liquid which was combined with 12.05 g. of dideuteriomethylene iodide from another reaction and distilled through a vacuum-jacketed Vigreux column to give 51.4 g. (79%) of a slightly pink liquid; b.p. 73-76° (4.5-5.0 mm.); ir (liquid film) 2150 (m, alkyl-D) $cm.^{-1}$; mass spec m/e (rel intensity) 271 (2), 270 (100), 269 (4). This indicated the isotope ratio of $D_2:D_1$ to be 96:4.

(2) Preparation of 1,1,3,3-Tetracarbethoxy-2,2-dideuteriopropane (LXXXVd)

The procedure on p. 196 for the preparation of 1,1,3,3-tetracarbethoxypropane (LXXXV) was followed, using 8.58 g. (0.373 mole) of sodium metal, 60.70 g. (0.361 mole) of diethyl malonate, and 50.5 g. (0.187 mole) of dideuteriomethylene iodide (LXXXIVd) in 300 ml. of absolute ethanol, to yield 50.1 g. (80.5%) of a colorless liquid; b.p. 128-132° (0.10-0.12 mm.); nmr ($CDCl_3$) δ 1.24 (t, J = 7.0 Hz, 12 H, methyls), 3.42 (s, 2 H, 1- and 3-methines), 4.15 (q, J = 7.0 Hz, 8 H, ethyl methylenes); ir (liquid film) 2980, 2940, 2900 (s, alkyl-H), 2150 (m, alkyl-D), 1730 (s, carbonyl), 1460, 1440 (m, methylene), 1365 (m, methyl) $cm.^{-1}$; mass spec m/e (rel intensity) 336 (5), 335 (22), 334 (100), 333 (8). This indicated the isotope ratio of $D_2:D_1$ to be 92.5:7.5. The ratio of the base peak, 289, to the parent peak, 334, was 100:11.

(3) Preparation of 3,3-Dideuterioglutaric Acid (LXXXVIId)

The procedure on p. 197 for the preparation of glutaric acid (LXXXVII) was followed, using 44.8 g. (0.134 mole) of 2,2-dideuterio-1,1,3,3-tetracarbethoxypropane (LXXXVd), 50 ml. of conc. hydrochloric acid, and 50 ml. of water, to give 17.00 g. (95.0%) of a slightly off-white solid; m.p. 95.5-96.5°; nmr ($D_2O$) δ 2.36 (s, 2- and 4-methylenes), 4.67 (s, hydroxyl and HDO of solvent); ir (KBr) 3600-2100 (m,

carboxylic acid), 2150 (m, alkyl-D), 1700 (s, carbonyl), 1460 (m, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 117 (13), 116 (67), 88 (100), 87 (20).

(4) Preparation of Di-p-phenylphenacyl 3,3-Dideuterioglutarate ($XCIId_1$)[133-135]

The procedure on p. 198 for the preparation of di-p-phenylphenacyl glutarate (XCII) was followed, using 0.021 g. (0.153 mmole.) of 3,3-dideuterioglutaric acid ($LXXXVIId_1$) and 0.077 g. (0.280 mmole.) of p-phenylphenacyl bromide, to yield 0.043 g. (34.5%) of a white solid; m.p. 150-151°; mass spec m/e (rel intensity) 524 (8), 523 (37), 522 (100), 521 (9). This indicated the isotope ratio of $D_2$:$D_1$ to be 92:8.

(5) Preparation of 2,2,3,3,4,4-Hexadeuterioglutaric Acid ($LXXXVIId_2$)

3,3-Dideuterioglutaric acid ($LXXXVIId_1$) (17.00 g., 0.127 mole) was dissolved in a solution of 13.65 g. (0.129 mole) anhydrous sodium carbonate in 40 ml. of deuterium oxide. The solvent was evaporated under reduced pressure to give a slightly off-white solid. The solid was dissolved in a solution of 9.29 g. (0.216 mole) of sodium metal in 100 ml. of deuterium oxide (20% sodium deuterioxide). A sample was taken for monitoring the H:D ratio of the 2- and 4-positions at constant concentration. The solution was heated at slow reflux for three days. After each 24 hr.

period, the mixture was cooled and a sample removed. An nmr spectrum was taken, and the peak area was compared to the peak area of the first sample. The solvent was evaporated under reduced pressure, 100 ml. of fresh deuterium oxide was added and the mixture heated for another three days. The solvent was evaporated and the procedure repeated. The mixture, a cloudy solution with some solid (silicon dioxide), was filtered. Conc. hydrochloric acid was added to the filtrate until a pH of 1. A solid precipitated which dissolved on the addition of 300 ml. of water. The solution was continuously extracted with ether for one week. The ether solution was dried over magnesium sulfate and filtered. The solvent was evaporated under reduced pressure to give 14.1 g. (80.5%) of a slightly off-white solid; m.p. 91-93°; ir (KBr) 3600-2000 (carboxylic acid), 2150 (m, alkyl-D), 1700 (s, carbonyl) $cm.^{-1}$; mass spec m/e (rel intensity) 120 (29), 119 (45), 92 (57), 91 (100).

(6) Preparation of Di-p-phenylphenacyl 2,2,3,3,4,4-Hexadeuterioglutarate ($XCIId_2$)

The procedure on p. 198 for the preparation of di-p-phenylphenacyl glutarate (XCII) was followed, using 0.103 g. (0.742 mmole.) of 2,2,3,3,4,4-hexadeuterioglutaric acid ($LXXXVIId_2$) and 0.385 g. (1.413 mmole.) of p-phenylphenacyl bromide, to yield 0.299 g. (80.5%) of a yellow solid which was recrystallized to give white crystals; m.p. 152-152.8°; mass spec m/e (rel intensity) 528 (5), 527 (43),

526 (100), 525 (20), 524 (2). This indicated the isotope ratio of $D_6$:$D_5$:$D_4$ to be 81:17:2.

(7) Preparation of Diethyl 2,2,3,3,4,4-Hexadeuterioglutarate (LXXXVIIId)

The procedure on p. 199 for the preparation of diethyl glutarate (LXXXVIII) was followed, using 11.53 g. (83.7 mmole.) of 2,2,3,3,4,4-hexadeuterioglutaric acid (LXXXVIId$_2$), 35 ml. of absolute ethanol, 17 ml. of toluene, and 0.1 ml. of conc. sulfuric acid, to give 14.29 g. (88.3%) of a colorless liquid which was pure by glc analysis (Column II); b.p. 85-88° (2.6-2.8 mm.); nmr ($CDCl_3$) δ 1.25 (t, J = 7.5 Hz, 6 H, methyls), 4.14 (q, J = 7.5 Hz, 4 H, ethyl methylenes); ir (liquid film) 2990, 2950, 2920 (s, alkyl-H), 2240, 2130 (w, alkyl-D), 1735 (s, carbonyl), 1470, 1450 (m, methylene), 1365 (m, methyl) $cm.^{-1}$; mass spec m/e (rel intensity) 195 (14), 194 (100), 193 (15), 192 (2). This indicated the isotope ratio of $D_6$:$D_5$:$D_4$ to be 85:13:2. The ratio of the base peak, 149, to 194 is 100:2.

(8) Preparation of 2,2,3,3,4,4-Hexadeuterio-1,5-pentanediol (LXXXIXd)

The procedure on p. 199 for the preparation of 1,5-pentanediol (LXXXIX) was followed using 13.83 g. (0.072 mole) of diethyl 2,2,3,3,4,4-hexadeuterioglutarate (LXXXVIIId) and 8.338 g. (0.219 mole) of lithium aluminum

hydride in 400 ml. of ether, to give 7.355 g. (89.8%) of a slightly yellow liquid which was over 90% pure by glc analysis (Column II); nmr ($D_2O$) δ 3.54 (s, hydroxymethylenes), 4.64 (s, hydroxyl and HDO of solvent); ir (liquid film) 3300 (s, hydroxyl), 2930, 2870 (s, alkyl-H), 2200, 2100 (m, alkyl-D), 1470, 1430 (m, methylene), 1040 (s, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 89 (15), 77 (40), 76 (32), 69 (64), 68 (33), 58 (86), 57 (100), 56 (66).

(9) Preparation of 2,2,3,3,4,4-Hexadeuterio-1,5-dibromopentane (XCd)

The procedure on p. 201 for the preparation of 1,5-dibromopentane (XC) was followed, using 6.956 g. (63.24 mmole.) of 2,2,3,3,4,4-hexadeuterio-1,5-pentanediol (LXXXIXd) and 23.20 g. (83.60 mmole.) of phosphorus tribromide, to give 11.09 g. (74.3%) of a slightly yellow liquid which was 95% pure by glc analysis (Column II); nmr ($CDCl_3$) δ 3.39 (s, bromomethylenes); ir (liquid film) 2960 (s), 2860 (m, alkyl-H), 2200, 2100 (s, alkyl-D), 1435 (s, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 238 (51), 237 (15), 236 (100), 235 (19), 234 (56), 232 (9). This indicated the isotope ratio of $D_6$:$D_5$:$D_4$ to be 85:14:1. The ratio of the base peak, 155, to 236 is 100:17.

(10) Preparation of 3,3,4,4,5,5-Hexadeuterio-1,1-dicarbethoxycyclohexane (XCId)

The procedure on p. 202 for the preparation of 1,1-di-

carbethoxycyclohexane (XCI) was followed, using 9.013 g. (38.1 mmole.) of 2,2,3,3,4,4-hexadeuterio-1,5-dibromopentane (XCd), 6.321 g. (39.2 mmole.) of diethyl malonate, and 1.91 g. (83.0 mmole.) of sodium metal in 425 ml. of absolute ethanol, to yield 2.904 g. (30.8%) of a colorless liquid which was 80-85% pure by glc analysis (Column II); b.p. 120-123° (6.9-7.0 mm.); nmr ($CDCl_3$) δ 1.24 (t, J = 7.0 Hz, 6.9 H, methyls and hydrogens on methylene groups of C-3, C-4, and C-5), 1.94 (s, 4 H, 2- and 6-ring methylenes), 4.16 (q, J = 7.0 Hz, 4 H, ethyl methylenes); ir (liquid film) 2990, 2950, 2920 (m, alkyl-H), 2210, 2110 (m, alkyl-D), 1725 (s, carbonyl), 1470, 1450 (m, methylene), 1365 (m, methyl) $cm.^{-1}$; mass spec m/e (rel intensity) 236 (3), 235 (17), 234 (100), 233 (19), 232 (2). This indicated the isotope ratio of $D_6:D_5:D_4$ to be 81:17:2. The ratio of the base peak, 174, to 234 is 100:23.

(11) Preparation of 3,3,4,4,5,5-Hexadeuterio-1,1-bis(hydroxymethyl)cyclohexane (XVId)

The procedure on p. 204 for the preparation of 1,1-bis(hydroxymethyl)cyclohexane (XVI) was followed, using 2.614 g. (11.15 mmole.) of 3,3,4,4,5,5-hexadeuterio-1,1-dicarbethoxycyclohexane (XCId) and 0.896 g. (23.5 mmole.) of lithium aluminum hydride in 60 ml. of dry ether, to yield 1.242 g. (74.3%) of white crystals; m.p. 96-97°; nmr ($CDCl_3$) δ 1.37 (s, 4.3 H, 2- and 6-methylenes and hydrogens on methylene groups of C-3, C-4, and C-5), 2.84 (broad s, 2 H,

hydroxyl), 3.60 (s, 4 H, hydroxymethylenes); ir (KBr) 3300 (s, hydroxyl), 2920, 2860 (m, alkyl-H), 2200, 2100 (m, alkyl-D), 1480, 1460, 1440 (m, methylene), 1040 (m, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 132 (7), 119 (13), 118 (13), 102 (91), 101 (100), 100 (96).

(12) Preparation of 3,3,4,4,5,5-Hexadeuterio-1,1-bis-(tosyloxymethyl)cyclohexane (XXd)

The procedure on p. 187 for the preparation of 3,4-dideuterio-1,1-bis(tosyloxymethyl)cyclohexane (XXc) was followed, using 1.225 g. (8.14 mmole.) of 3,3,4,4,5,5-hexadeuterio-1,1-bis(hydroxymethyl)cyclohexane (XVId) 3.900 g. (19.8 mmole.) of p-toluenesulfonyl chloride, and 10 ml. of pyridine, to yield 2.983 g. (80.2%) of a white crystalline solid; m.p. 84.5-86.0°; nmr ($CDCl_3$) δ 1.32 (s, 4 H, 2- and 6-methylenes), 2.45 (s, 6 H, aromatic methyls), 3.86 (s, 4 H, oxymethylenes), 7.30, 7.38, 7.70, 7.78 (AA'BB', 8 H, phenyl); ir (KBr) 3090, 3050, 3030 (vw, aromatic-H), 2970, 2930, 2950 (m, alkyl-H), 2200, 2100 (m, alkyl-D), 1595, 1490 (m, aromatic), 1455 (m, methylene), 1370 (m, methyl), 1345, 1175 (s, sulfonate ester), 815 (s, p-disub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 461 (3), 460 (13), 459 (29), 458 (100), 457 (20), 456 (2). This indicated the isotope ratio of $D_6$:$D_5$:$D_4$ to be 82:16:2.

(13) Preparation of 3,3,4,4,5,5-Hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id)

The procedure on p. 188 for the preparation of 3,4-dideuterio-1,1-bis(bromomethyl)cyclohexane (Ic) was followed, using 2.517 g. (5.48 mmole.) of 3,3,4,4,5,5-hexadeuterio-1,1-bis(tosyloxymethyl)cyclohexane (XXd) and 2.399 g. (23.3 mmole.) of sodium bromide in 15 ml. of diethylene glycol, to yield 0.713 g. (46.5%) of a colorless liquid, which was shown to be over 95% pure by glc (Column I); b.p. 94-98° (1.0-1.5 mm.); nmr ($CDCl_3$) δ 1.53 (s, 4 H, 2- and 6-methylenes), 3.49 (s, 4 H, bromomethylenes); ir (liquid film) 2930, 2860 (s, alkyl-H), 2210, 2115 (s, alkyl-D), 1450, 1430 (s, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 279 (5), 278 (50), 277 (20), 276 (100), 275 (26), 274 (55), 273 (12), 272 (2). This indicated the isotope ratio of $D_6:D_5:D_4$ to be 82:16:2. The ratio of the base peak, 101, to 276 was 100:10.

(I) Preparation of 1,1-Bis(bromodideuteriomethyl)cyclohexane (Ie)

(1) Preparation of 1,1-Bis(hydroxydideuteriomethyl)cyclohexane (XVIe)

The procedure on p. 204 for the preparation of 1,1-bis(hydroxymethyl)cyclohexane (XVI) was followed, using 2.903 g. (12.8 mmole.) of 1,1-dicarbethoxycyclohexane (XCI) and 1.154 g. (27.4 mmole.) of lithium aluminum deuteride (Merck, Sharpe, and Dohme of Canada, Montreal, Quebec, Canada) in 60 ml. of ether, to give 1.575 g. (84.2%) of white crystals; m.p. 97.5-98.2°; nmr ($CDCl_3$) δ 1.42 (broad s, 10 H, ring methylenes), 2.96 (broad s, 2 H, hydroxyl); ir (KBr) 3300 (s, alcohol), 2920, 2860 (s, alkyl-H), 2210, 2100 (m, alkyl-D), 1460, 1440 (s, methylene), 1045 (s, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 130 (4), 115 (9), 98 (98), 97 (100).

(2) Preparation of 1,1-Bis(tosyloxydideuteriomethyl)cyclohexane (XXe)

The procedure on p. 187 for the preparation of 3,4-dideuterio-1,1-bis(tosyloxymethyl)cyclohexane (XXc) was followed, using 1.437 g. (9.67 mmole.) of 1,1-bis(hydroxydideuteriomethyl)cyclohexane (XVIe), 4.568 g. (24.0 mmole.) of p-toluenesulfonyl chloride, and 10 ml. of pyridine, to yield 3.79 g. (85.8%) of white crystals; m.p. 85-86°; nmr ($CDCl_3$) δ 1.31 (s, 10 H, ring methylenes), 2.44 (s, 6 H,

aromatic methyl), 7.30, 7.38, 7.70, 7.78 (AA'BB', 8 H, aromatic-H); ir (KBr) 3090, 3050, 3030 (vw, aromatic-H), 2930, 2860 (s, alkyl-H), 2170 (w, alkyl-D), 1595, 1495 (m, aromatic), 1450 (m, methylene), 1360 (m, methyl), 1350, 1180 (s, sulfonate ester), 820 (s, p-disub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 459 (4), 458 (13), 457 (30), 456 (100), 455 (7). This indicated the isotope ratio of $D_4$:$D_3$ to be 93:7.

(3) Preparation of 1,1-Bis(bromodideuteriomethyl)cyclohexane (Ie)

The procedure on p. 188 for the preparation of 3,4-dideuterio-1,1-bis(bromomethyl)cyclohexane (Ic) was followed, using 3.225 g. (7.10 mmole.) of 1,1-bis(tosyloxydideuteriomethyl)cyclohexane (XXe) and 3.113 g. (30.6 mmole.) of sodium bromide in 15 ml. of diethylene glycol, to yield 1.285 g. (66.0%) of a colorless liquid which was shown to be over 97% pure by glc analysis (Column I); b.p. 103-104° (2.8 mm.); nmr ($CDCl_3$) $\delta$ 1.49 (broad s, ring methylenes); ir (liquid film) 2940, 2870 (s, alkyl-H), 2200, 2180 (w, alkyl-D), 1460 (m), 1450 (s, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 277 (5), 276 (52), 275 (13.5), 274 (100), 273 (12.5), 272 (55), 271 (4). This indicated the isotope ratio of $D_4$:$D_3$ to be 93.9:6.1.

(J) Preparation of 2,2,3,3,5,5,6,6-Octadeuterio-1,1-bis-(bromomethyl)cyclohexane (If)

(1) Preparation of 2,2,4,4-Tetradeuterioglutaric Acid (LXXXVIIf)

The procedure on p. 208 for the preparation of 2,2,3,3,4,4-hexadeuterioglutaric acid (LXXXVII$d_2$) was followed, using 20.06 g. (0.152 mole) of glutaric acid (LXXXVII), 16.83 g. (0.159 mole) of sodium carbonate, 11.51 g. (0.500 mole) of sodium metal, and three 100-ml. portions of deuterium oxide (Stohler Isotope Chemicals, Rutherford, N. J.), to yield 14.7 g. (69.7%) of a white solid; m.p. 91-93°; nmr ($D_2O$) δ 1.76 (s, 3-methylene), 4.67 (s, hydroxyl and HDO of solvent); ir (KBr) 3600-2000 (m, carboxylic acid), 2100 (alkyl-D), 1700 (s, carbonyl) $cm.^{-1}$; mass spec m/e (rel intensity) 119 (12), 118 (24), 117 (33), 90 (78), 89 (100).

(2) Preparation of Di-p-phenylphenacyl 2,2,4,4-Tetradeuterioglutarate (XCIIf)

The procedure on p. 198 for the preparation of di-p-phenylphenacyl glutarate (XCII) was followed, using 0.106 g. (0.779 mmole.) of 2,2,4,4-tetradeuterioglutaric acid (LXXXVIIf) and 0.386 g. (1.40 mmole.) of p-phenylphenacyl bromide, to yield 0.245 g. (67.1%) of a slightly off-white solid; m.p. 151.0-152.8°; mass spec m/e (rel intensity) 526 (9.5), 525 (39), 524 (100), 523 (10). This indicated the

isotope ratio of $D_4$:$D_3$ to be 91:9.

(3) Preparation of Diethyl 2,2,4,4-Tetradeuterioglutarate (LXXXVIIIf)

The procedure on p. 199 for the preparation of diethyl glutarate (LXXXVIII) was followed, using 12.11 g. (89.09 mmole.) of 2,2,4,4-tetradeuterioglutaric acid (LXXXVIIf), 35 ml. of absolute ethanol, 17 ml. of toluene, and 0.1 ml. of conc. sulfuric acid, to yield 15.36 g. (90.1%) of a colorless liquid; b.p. 83° (1.7-1.8 mm.); nmr ($CDCl_3$) δ 1.25 (t, J = 7.0 Hz, 6 H, methyls), 1.88 (s, 2 H, 3-methylene), 4.17 (q, J = 7.0 Hz, 4 H, ethyl methylenes); ir (liquid film) 2990, 2950, 2920 (s, alkyl-H), 2240, 2130 (w, alkyl-D), 1735 (s, carbonyl), 1470, 1450 (m, methylene), 1365 (m, methyl) $cm.^{-1}$; mass spec m/e (rel intensity) 193 (10), 192 (100), 191 (10). This indicated the isotope ratio of $D_4$:$D_3$ to be 91:9. The ratio of the base peak, 147, to 192 is 100:10.

(4) Preparation of 1,1,2,2,4,4,5,5-Octadeuterio-1,5-pentanediol (LXXXIXf)

The procedure on p. 199 for the preparation of 1,5-pentanediol (LXXXIX) was followed, using 14.83 g. (77.3 mmole.) of diethyl 2,2,4,4-tetradeuterioglutarate (LXXXVIIIf) and 8.612 g. (205.1 mmole.) of lithium aluminum deuteride (Merck, Sharpe, and Dohme of Canada, Montreal, Quebec, Canada), to yield 7.90 g. (91.2%) of a colorless

liquid which was pure by glc analysis (Column II); nmr ($D_2O$) δ 1.28 (s, 3-methylene), 4.64 (s, hydroxyl and HDO of solvent); ir (liquid film) 3300 (s, alcohol), 2920, 2860 (m, alkyl-H), 2200, 2100 (m, alkyl-D), 1450 (w, methylene), 1040 (s, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 91 (5), 78 (28), 73 (43), 60 (100), 59 (86).

(5) Preparation of 1,1,2,2,4,4,5,5-Octadeuterio-1,5-dibromopentane (XCf)

The procedure on p. 201 for the preparation of dibromopentane (XC) was followed, using 6.54 g. (60.6 mmole.) of 1,1,2,2,4,4,5,5-octadeuterio-1,5-pentanediol (LXXXIXf) and 25.92 g. (95.65 mmole.) of phosphorus tribromide, to yield 8.880 g. (62.8%) of a slightly yellow liquid which was approximately 98% pure by glc analysis (Column II); nmr ($CDCl_3$) δ 1.56 (s, 3-methylene); ir (liquid film) 2930, 2870 (s, alkyl-H), 2200, 2120 (s, alkyl-D), 1450 (m, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 241 (3), 240 (50), 239 (14), 238 (100), 237 (16), 236 (48), 235 (6). This indicated the isotope ratio of $D_8$:$D_7$ to be 94:6. The ratio of the base peak, 153, to 238 is 100:20.

(6) Preparation of 2,2,3,3,5,5,6,6-Octadeuterio-1,1-dicarbethoxycyclohexane (XCIf)

The procedure on p. 202 for the preparation of 1,1-dicarbethoxycyclohexane (XCI) was followed, using 8.809 g. (37.62 mmole.) of 1,1,2,2,4,4,5,5-octadeuterio-1,5-dibromo-

pentane (XCf), 6.099 g. (38.12 mmole.) of diethyl malonate, and 1.83 g. (79.57 mmole.) of sodium metal in 425 ml. of absolute ethanol, to yield 3.088 g. (35.3%) of a colorless liquid which was 80-85% pure by glc analysis (Column II); b.p. 110-112° (4.3-5.0 mm.); nmr ($CDCl_3$) δ 1.18 (s, 2 H, 4-methylene), 1.25 (t, J = 7.0 Hz, 6 H, methyls), 4.15 (q, J = 7 Hz, 4 H, ethyl methylenes); ir (liquid film) 2980, 2920, 2860 (m, alkyl-H), 2200, 2110 (m, alkyl-D), 1725 (s, carbonyl), 1465, 1445 (m, methylene), 1365 (m, methyl) $cm.^{-1}$; mass spec m/e (rel intensity) 238 (2), 237 (12), 236 (100), 235 (13). This indicated the isotope ratio of $D_8:D_7$ to be 88:12. The ratio of the base peak, 176, to 236 is 100:13.

(7) Preparation of 2,2,3,3,5,5,6,6-Octadeuterio-1,1-bis-(hydroxymethyl)cyclohexane (XVIf)

The procedure on p. 204 for the preparation of 1,1-bis(hydroxymethyl)cyclohexane (XVI) was followed, using 2.929 g. (12.4 mmole.) of 2,2,3,3,5,5,6,6-octadeuterio-1,1-dicarbethoxycyclohexane (XCIf) and 1.256 g. (33.1 mmole.) of lithium aluminum hydride, to yield 1.250 g. (66.2%) of white crystals; m.p. 96-97°; nmr ($CDCl_3$) δ 1.42 (s, 2 H, 4-methylene), 2.96 (s, 2 H, hydroxyl), 3.60 (s, 4 H, hydroxymethylenes); ir (KBr) 3350 (s, alcohol), 2940, 2920, 2880, 2860 (s, alkyl-H), 2200, 2130, 2100 (m, alkyl-D), 1480, 1465, 1440 (m, methylene), 1040 (m, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 135 (5), 121 (10), 104

(100), 103 (44), 102 (96), 101 (38).

(8) Preparation of 2,2,3,3,5,5,6,6-Octadeuterio-1,1-bis-(tosyloxymethyl)cyclohexane (XXf)

The procedure on p. 187 for the preparation of 3,4-dideuterio-1,1-bis(tosyloxymethyl)cyclohexane (XXc) was followed, using 1.168 g. (7.02 mmole.) of 2,2,3,3,5,5,6,6-octadeuterio-1,1-bis(hydroxymethyl)cyclohexane (XVIf), 3.529 g. (18.6 mmole.) of p-toluenesulfonyl chloride and nine ml. of pyridine, to yield 2.354 g. (72.5%) of white crystals; m.p. 84.0-86.0°; nmr ($CDCl_3$) δ 1.32 (s, 2 H, 4-methylene), 2.45 (s, 6 H, aromatic methyls), 3.86 (s, 4 H, hydroxymethylenes), 7.30, 7.38, 7.70, 7.78 (AA'BB', 8 H, aromatic-H), ir (KBr) 3100, 3060, 3030 (vw, aromatic-H), 2980, 2955, 2930, 2890, 2965 (w, alkyl-H), 2200, 2130, 2100 (m, alkyl-D), 1595, 1490 (m, methylene), 1370 (m, methyl), 1345, 1180 (s, sulfonate ester), 820 (s, p-disub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 463 (3), 462 (16), 461 (29), 460 (100), 459 (12). This indicated the isotope ratio of $D_8:D_7$ to be 89:11.

(9) Preparation of 2,2,3,3,5,5,6,6-Octadeuterio-1,1-bis-(bromomethyl)cyclohexane (If)

The procedure on p. 188 for the preparation of 3,4-dideuterio-1,1-bis(bromomethyl)cyclohexane (Ic) was followed, using 2.253 g. (4.89 mmole.) of 2,2,3,3,5,5,6,6-octadeuterio-1,1-bis(tosyloxymethyl)cyclohexane (XXf) and

2.092 g. (10.2 mmole.) of sodium bromide in 10 ml. of diethylene glycol to yield 0.641 g. (47.2%) of a colorless liquid; b.p. 103-104° (3.0 mm.); nmr ($CDCl_3$) δ 1.40 (s, 2 H, 4-methylene), 3.46 (s, 4 H, bromomethylenes); ir (liquid film) 2930, 2860 (s, alkyl-H), 2210, 2140, 2110 (m, alkyl-D), 1445 (m), 1425 (s, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 281 (6), 280 (49), 279 (16.6), 278 (100), 277 (16.7), 276 (55), 275 (7.6). This indicated the isotope ratio of $D_8$:$D_7$ to be 90.3:9.7. The ratio of the base peak, 103, to 278 is 100:5.

(K) Preparation of 2,2,6,6-Tetradeuterio-1,1-bis(bromodideuteriomethyl)cyclohexane (Ig)

(1) Preparation of 1,1,5,5-Tetradeuterio-1,5-pentanediol (LXXXIXg)

The procedure on p. 199 for the preparation of 1,5-pentanediol (LXXXIX) was followed, using 13.36 g. (83.35 mmole.) of dimethyl glutarate and 8.122 g. (193.4 mmole.) of lithium aluminum deuteride (Merck, Sharpe, and Dohme of Canada, Montreal, Quebec, Canada) to yield 5.861 g. (65.1%) of a colorless liquid which was pure by glc analysis (Column II); nmr ($D_2O$) $\delta$ 1.04-2.00 (m, 2-, 3-, and 4-methylenes), 4.65 (s, hydroxyl and HDO of solvent); ir (liquid film) 3300 (s, alcohol), 2930, 2870 (s, alkyl-H), 2200, 2100 (m, alkyl-D), 1460, 1430 (w, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 88 (4), 76 (18), 72 (33), 71 (24), 58 (100), 57 (43).

(2) Preparation of 1,1,5,5-Tetradeuterio-1,5-dibromopentane (XCg)

The procedure on p. 201 for the preparation of 1,5-dibromopentane (XC) was followed, using 5.506 g. (54.0 mmole.) of 1,1,5,5-tetradeuterio-1,5-pentanediol (LXXXIXg) and 23.32 g. (86.2 mmole.) of phosphorous tribromide to yield 8.508 g. (68.3%) of a slightly yellow liquid which was approximately 85% pure by glc analysis (Column II); nmr ($CDCl_3$) $\delta$ 1.30-2.20 (m, 2-, 3-, and 4-methylenes); ir

(liquid film) 2930, 2870 (s, alkyl-H), 2170 (m, alkyl-D), 1450, 1430 (m, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 237 (3), 236 (49), 235 (24), 234 (100), 233 (18), 232 (52), 231 (3). This indicated the isotope ratio of $D_4$:$D_3$ to be 91:9. The ratio of the base peak, 152, to 234 was 100:5.

(3) Preparation of 2,2,6,6-Tetradeuterio-1,1-dicarbethoxycyclohexane (XCIg)

The procedure on p. 202 for the preparation of 1,1-dicarbethoxycyclohexane (XCI) was followed, using 6.510 g. (27.2 mmole.) of 1,1,5,5-tetradeuterio-1,5-dibromopentane (XCg), 4.565 g. (28.5 mmole.) of diethyl malonate, and 1.41 g. (61.5 mmole.) of sodium dissolved in 425 ml. of absolute alcohol, to yield 1.553 g. (23.2%) of a colorless liquid which was 80-85% pure by glc analysis (Column II); nmr ($CDCl_3$) $\delta$ 1.23 (t, J = 7.0 Hz, 6 H, methyls), 1.46 (s, 6 H, 3-, 4-, and 5-methylenes), 4.13 (q, J = 7.0 Hz, 4 H, ethyl methylenes); ir (liquid film) 2990, 2940, 2860 (s, alkyl-H), 2020, 2130 (w, alkyl-D), 1725 (s, carbonyl), 1460, 1445 (m, methylene), 1365 (m, methyl) $cm.^{-1}$; mass spec m/e (rel intensity) 234 (2), 233 (16), 232 (100), 231 (6). This indicated the isotope ratio of $D_4$:$D_3$ to be 94:6. The ratio of the base peak, 175, to 232 is 100:8.

(4) Preparation of 2,2,6,6-Tetradeuterio-1,1-bis(hydroxydideuteriomethyl)cyclohexane (XVIg)

The procedure on p. 204 for the preparation of 1,1-bis(hydroxymethyl)cyclohexane (XVI) was followed, using 1.391 g. (61.8 mmole.) of 2,2,6,6-tetradeuterio-1,1-dicarbethoxycyclohexane (XCIg) and 1.098 g. (26.6 mmole.) of lithium aluminum deuteride (Merck, Sharpe, and Dohme of Canada, Montreal, Quebec, Canada), to yield 0.579 g. (62.4%) of white crystals; m.p. 96-97°; nmr ($CDCl_3$) δ 1.42 (s, 6 H, 3-, 4-, and 5-methylenes), 3.15 (s, 2 H, hydroxyl); ir (KBr) 3350 (s, alcohol), 2920, 2860 (s, alkyl-H), 2200, 2100 (m, alkyl-D), 1455, 1435 (m, methylene), 1040 (m, prim. alcohol) $cm.^{-1}$; mass spec m/e (rel intensity) 134 (5), 119 (6), 117 (9), 102 (100), 101 (77), 100 (52).

(5) Preparation of 2,2,6,6-Tetradeuterio-1,1-bis(tosyloxydideuteriomethyl)cyclohexane (XXg)

The procedure on p. 187 for the preparation of 3,4-dideuterio-1,1-bis(tosyloxymethyl)cyclohexane (XXc) was followed, using 0.543 g. (0.357 mmole.) of 2,2,6,6-tetradeuterio-1,1-bis(hydroxydideuteriomethyl)cyclohexane (XVIg), 1.649 g. (0.861 mmole.) of p-toluenesulfonyl chloride, and 5 ml. of pyridine, to yield 1.236 g. (75.6%) of white crystals; m.p. 84.0-86.0°; nmr ($CDCl_3$) δ 1.32 (s, 6 H, 3-, 4-, and 5-methylenes), 2.45 (s, 6 H, aromatic methyls), 7.30, 7.38, 7.70, 7.78 (AA'BB', 8 H, aromatic-H), ir (KBr) 3100,

3060, 3030 (vw, aromatic-H), 2930, 2865 (m, alkyl-H), 2200, 2110 (m, alkyl-D), 1595, 1490 (m, aromatic), 1455 (m, methylene), 1370 (m, methyl), 1350, 1175 (s, sulfonate ester), 815 (s, p-disub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 463 (3), 462 (17), 461 (31), 460 (100), 459 (14). This indicated the isotope ratio of $D_8$:$D_7$ to be 87:13.

(6) Preparation of 2,2,6,6-Tetradeuterio-1,1-bis(bromodideuteriomethyl)cyclohexane (Ig)

The procedure on p. 188 for the preparation of 3,4-dideuterio-1,1-bis(bromomethyl)cyclohexane (Ic) was followed, using 1.166 g. (0.25 mmole.) of 2,2,6,6-tetradeuterio-1,1-bis(tosyloxydideuteriomethyl)cyclohexane (XXg) and 1.250 g. (1.21 mmole.) of sodium bromide in 5 ml. diethylene glycol, to yield 0.498 g. (70.8%) of a colorless liquid which was shown to be approximately 95% pure by glc analysis (Column I); b.p. 103-105° (3.0 mm.); nmr ($CDCl_3$) δ 1.42 (s, 3-, 4-, and 5-methylenes); ir (liquid film) 2930, 2870 (s, alkyl-H), 2200, 2110 (m, alkyl-D), 1460, 1445 (m, methylene) $cm.^{-1}$; mass spec m/e (rel intensity) 281 (5), 280 (51), 279 (16), 278 (100), 277 (18.7), 276 (54), 275 (9). This indicated the isotope ratio of $D_8$:$D_7$ to be 89.5:10.5. The ratio of the base peak, 101, to 278 was 100:14.

(L) Friedel-Crafts Reactions

(1) Time-monitored Friedel-Crafts Reaction of 1,1-Bis-(bromomethyl)cyclohexane (I) with Benzene

A 250-ml. three-necked flask was equipped with a stopper, an overhead stirrer, and a reflux condenser containing a drying tube. The glassware had been dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. The nitrogen atmosphere was then removed.

The flask was immersed in a water bath thermostated at 40±1°. Dry benzene (90 ml.) (dried over Dri-Na, J. T. Baker Chemical Co., Phillipsburg, New Jersey) and 0.83 g. (0.62 mmole.) of aluminum chloride were added. 1,1-Bis-(bromomethyl)cyclohexane (I) (0.251 g., 0.928 mmole.) in ten ml. of benzene was added at time zero. Five-ml. aliquots were removed at approximately five minute intervals and quenched by adding each to five ml. of 3 N hydrochloric acid. Each organic layer was washed with 2.5 ml. of sat'd. sodium bicarbonate, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. The residues were analyzed by glc (Column I). The concentration of the starting material (I) decreased steadily. The concentration of primary product (II) increased steadily, with a maximum at 15 min., then decreased steadily. The concentration of secondary products increased steadily.

(2) Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)cyclohexane (I) with Benzene

A two-l. three-necked flask was equipped with an overhead stirrer, a stopper, and a reflux condenser containing a drying tube. The glassware had been dried in an oven overnight and brought to room temperature under a nitrogen atmosphere. The nitrogen atmosphere was then removed.

The flask was immersed in a water bath thermostated at 40±1°. Dry benzene (390 ml.) (dried over Dri-Na, J. T. Baker Chemical Co., Phillipsburg, N. J.) and 0.675 g. (5.13 mmole.) of aluminum chloride were added. 1,1-Bis(bromomethyl)cyclohexane (I) (1.033 g., 3.83 mmole.) was dissolved in ten ml. of benzene and added. The mixture slowly became light orange.

After ten min. the reaction was quenched with 100 ml. of 3 N hydrochloric acid, and the light cloudy organic layer was washed with 50 ml. of sat'd. sodium bicarbonate and 50 ml. of sat'd. sodium chloride, dried over magnesium sulfate, and filtered. The solvent was evaporated under reduced pressure to give 0.776 g. of a yellow-orange liquid. Analysis by glc (Column I) showed the concentration of primary product (II) to be 30-40% of the mixture. Preparative gas chromatography was carried out on the crude reaction mixture. Three fractions of the primary product (II) peak were collected, weighing 0.028 g., 0.084 g., and 0.003 g. Analytical glc on the collected fractions showed the first

and third fractions to contain some minor impurities and the second fraction to be one peak; nmr ($CDCl_3$) δ 0.81-2.03 (broad m with a singlet at 1.31, 13 H, methyl and ring methylenes), 2.75-3.17 (broad s, 1 H, methine), 6.83-7.38 (m, 4 H, phenyl-H); ir (liquid film) 3090, 3030 (w, phenyl-H), 2920, 2860 (s, alkyl-H), 1600, 1490 (s, aromatic), 1460, 1450 (m, methylene), 1375 (m, methyl), 750 (vs, o-disub. phenyl); mass spec m/e (rel intensity) 188 (4), 187 (16), 186 (100), 185 (6), 173 (1), 172 (6), 171 (36), 170 (1).*

(3) Friedel-Crafts Reaction of 3,4-Dideuterio-1,1-bis-(bromomethyl)cyclohexane (Ic) with Benzene

The procedure on p. 228 for the reaction of 1,1-bis-(bromomethyl)cyclohexane (I) was followed, using 1.467 g. (5.39 mmole.) of 3,4-dideuterio-1,1-bis(bromomethyl)cyclohexane, 0.441 g. (3.30 mmole.) of aluminum chloride and 600 ml. of benzene to yield 1.32 g. of a yellow liquid. Preparative chromatography yielded 0.047 g. of a colorless liquid (IIc); nmr ($CDCl_3$) δ 0.81-2.06 (broad m with a singlet at 1.31, 11 H, methyl and ring methylenes), 2.80-3.12 (broad s, 1 H, methine), 6.80-7.40 (m, 4 H, phenyl-H); ir (liquid film) 3090, 3030 (w, phenyl-H), 2920, 2865 (s, alkyl-H), 2095 (m, alkyl-D), 1600, 1495 (s, aromatic), 1460, 1450 (s, methylene), 1375 (m, methyl), 760 (s, o-

*For uv spectrum and analysis see ref. 1, p. 85.

disub. phenyl) $cm.^{-1}$; mass spec m/e (rel intensity) 190 (8), 189 (18), 188 (100), 187 (22), 175 (1), 174 (65), 173 (37), 172 (8), 171 (4). This indicated the isotope ratio of $D_2$:$D_1$ to be 85:15.

(4) Friedel-Crafts Reaction of 1-Bromo-1-bromomethylcycloheptane (LIV) with Benzene

The procedure on p. 227 for the time-monitored reaction of 1,1-bis(bromomethyl)cyclohexane (I) was followed, using 0.250 g. (0.919 mmole.) of 1-bromo-1-bromomethylcycloheptane (LIV), 0.330 g. (2.47 mmole.) of aluminum chloride, and 100 ml. of benzene. After 2.5, 5, 10, 15, and 30 min., 5 ml. aliquots were removed and treated as described. Analysis of the residue by glc (Column I) showed them to be almost identical to those from the reaction of 1,1-bis-(bromomethyl)cyclohexane (I) except that this reaction proceeded at a faster rate and the relative concentration of primary product (II) was higher. The glc-mass spectrum taken on the primary product of the five min. aliquot was virtually identical to the spectrum of primary product (II) isolated from the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane.

(5) Friedel-Crafts Reaction of 3,3,4,4,5,5-Hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id) with Benzene

The procedure on p. 228 for the reaction of 1,1-bis-(bromomethyl)cyclohexane (I) was followed, using 0.111 g.

(0.403 mmole.) of 3,3,4,4,5,5-hexadeuterio-1,1-bis(bromomethyl)cyclohexane (Id), 0.077 g. (0.58 mmole.) of aluminum chloride, and 40 ml. of benzene, to give a yellow-orange liquid. Preparative gas chromatography gave a colorless liquid (IId) which gave one peak upon glc analysis (Column I); mass spec m/e (rel intensity) 194 (7), 193 (17), 192 (100), 191 (22.3), 190 (3.0), 178 (5.0), 177 (36.8), 176 (9.9), 175 (1.4). This indicated the isotope ratio of $D_6$:$D_5$:$D_4$ to be 84:15:1.

(6) Friedel-Crafts Reaction of 1,1-Bis(bromodideuteriomethyl)cyclohexane (Ie) with Benzene

The procedure on p. 228 for the reaction of 1,1-bis(bromomethyl)cyclohexane (I) was followed, using 0.109 g. (0.397 mmole.) of 1,1-bis(bromodideuteriomethyl)cyclohexane (Ie), 0.076 g. (0.57 mmole.) of aluminum chloride, and 40 ml. of dry benzene to give a yellow-orange liquid. Preparative gas chromatography gave a colorless liquid (IIe) which was shown by glc (Column I) to be 97% pure; mass spec m/e (rel intensity) 192 (18), 191 (17.0), 190 (100), 189 (10.0), 188 (1), 175 (1), 174 (3.4), 173 (23.4), 172 (6.6), 171 (1). This indicated the isotope ratio of $D_4$:$D_3$ to be 95:5.

(7) Friedel-Crafts Reaction of 2,2,3,3,5,5,6,6-Octadeuterio-1,1-bis(bromomethyl)cyclohexane (If) with Benzene

The procedure on p. 228 for the reaction of 1,1-bis-

(bromomethyl)cyclohexane (I) was followed, using 0.108 g. (0.39 mmole.) of 2,2,3,3,5,5,6,6-octadeuterio-1,1-bis(bromomethyl)cyclohexane (If), 0.084 g. (0.63 mmole.) of aluminum chloride, and 40 ml. of dry benzene, to give a yellow-orange liquid. Preparative gas chromatography gave a colorless liquid (IIf) which gave one peak upon glc analysis (Column I); mass spec m/e (rel intensity) 196 (6), 195 (16), 194 (100), 193 (16.5), 192 (1.9), 180 (3.1), 179 (22.0), 178 (19.1), 177 (3.8). This indicated the isotope ratio of $D_8$:$D_7$ to be 89:11.

(8) Friedel-Crafts Reaction of 2,2,6,6-Tetradeuterio-1,1-bis(bromodideuteriomethyl)cyclohexane (Ig) with Benzene

The procedure on p. 228 for the reaction of 1,1-bis-(bromomethyl)cyclohexane (I) was followed, using 0.094 g. (0.34 mmole.) of 2,2,6,6-tetradeuterio-1,1-bis(bromodideuteriomethyl)cyclohexane (Ig), 0.077 g. (0.58 mmole.) of aluminum chloride, and 40 ml. of dry benzene, to give a yellow-orange liquid. Preparative gas chromatography gave a colorless liquid (IIg), which was shown by glc analysis (Column I) to be over 98% pure; mass spec m/e (rel intensity) 196 (6.3), 195 (17.3), 194 (100), 193 (17.3), 192 (2.0), 178 (2.8), 177 (12.2), 176 (24.5), 175 (1.7). This indicated the isotope ratio of $D_8$:$D_7$ to be 89:11.

(9) Friedel-Crafts Reaction of 1-Bromo-1-methyl-4-phenylcycloheptane (XXXVII) with Benzene

The procedure on p. 228 for the reaction of 1,1-bis(bromomethyl)cyclohexane (I) was followed, using 0.104 g. (0.388 mmole.) of 1-bromo-1-methyl-4-phenylcycloheptane (XXXVII), 0.083 g. (0.618 mmole.) of aluminum chloride, and 40 ml. of dry benzene, except that the reaction was quenched after 90 sec. The product mixture was shown by analytical gas chromatography to be greater than 90% primary product. The product mixture was combined with that of another reaction on the same scale. Preparative glc gave approximately 33 mg. of a colorless liquid. The nmr, ir, and mass spectra were virtually identical to the spectra of primary product isolated from the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane.

(10) Friedel-Crafts Reaction of 1-Bromomethyl-4-phenylcycloheptane (XXXIX) with Benzene

The procedure on p. 228 for the reaction of 1,1-bis(bromomethyl)cyclohexane (I) was followed, using 0.201 g. (0.752 mmole.) of 1-bromomethyl-4-phenylcycloheptane (XXXIX), 0.152 g. (1.13 mmole.) of aluminum chloride and 75 ml. of dry benzene, except that the reaction was quenched after 90 sec. The product mixture was shown by analytical gas chromatography to be greater than 90% primary product. Preparative glc gave approximately 26 mg. of a colorless

liquid. The nmr, ir, and mass spectra were virtually identical to the spectra of primary product isolated from the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane.

(11) Time-monitored Friedel-Crafts Reaction of 1-Bromomethyl-4-phenylcycloheptane (XXXIX) with Benzene

The procedure on p. 227 for the reaction of 1,1-bis(bromomethyl)cyclohexane (I) was followed, using 0.053 g. (0.20 mmole.) of 1-bromomethyl-4-phenylcycloheptane (XXXIX), 0.042 g. (0.32 mmole.) of aluminum chloride, and 20 ml. of dry benzene in the same manner as 1,1-bis(bromomethyl)cyclohexane. Five ml. aliquots were removed at one, five, and ten min. and quenched by adding each to five ml. of 3 N hydrochloric acid. At 15 min. the remainder of the reaction was quenched by the addition of five ml. of acid. Each organic layer was washed with two ml. of sat'd. sodium bicarbonate solution and one ml. of sat'd. sodium chloride solution, dried over magnesium sulfate, and concentrated under reduced pressure. The residues were analyzed by glc (Column I). The concentration of products other than the primary product (II) was very low in the first aliquot and increased in the later aliquots. The retention times of many of these minor products matched those of the secondary products of the Friedel-Crafts reaction of 1,1-bis(bromomethyl)cyclohexane.

(12) Friedel-Crafts Reaction of 1,1-Bis(bromomethyl)cyclohexane (I) with Hexadeuteriobenzene

The procedure on p. 228 for the reaction of 1,1-bis(bromomethyl)cyclohexane (I) in benzene was followed, using 0.107 g. (0.394 mmole.) of 1,1-bis(bromomethyl)cyclohexane and 0.068 g. (0.51 mmole.) of aluminum chloride in 40 ml. of hexadeuteriobenzene (Merck, Sharpe, and Dohme of Canada, Montreal, Quebec, Canada), to give a yellow-orange liquid. Preparative gas chromatography gave a colorless liquid (Ib); mass spec m/e (rel intensity) 192 (2), 191 (17), 190 (100), 189 (6), 177 (1), 176 (6), 175 (36), 174 (1).

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