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# Stereospecificity of organomercurial ozonolysis

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# STEREOSPECIFICITY OF ORGANOMERCURIAL OZONOLYSIS

by

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for the degree of

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UNIVERSITY OF MONTANA

1973

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# ACKNOWLEDGEMENTS

I wish to express my gratitude to my advisor, Dr. W. L. Waters for his patience, understanding, and advice in this research.

I also wish to express gratitude to my colleagues Philip G. Marsh, Robert J. Moody, and Anthony Rollin for their helpful discussions. I would like to thank Mr. George Wolfe for his aid in kinetic calculations and the processing of the data.

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# CHAPTER I

# INTRODUCTION

## Background

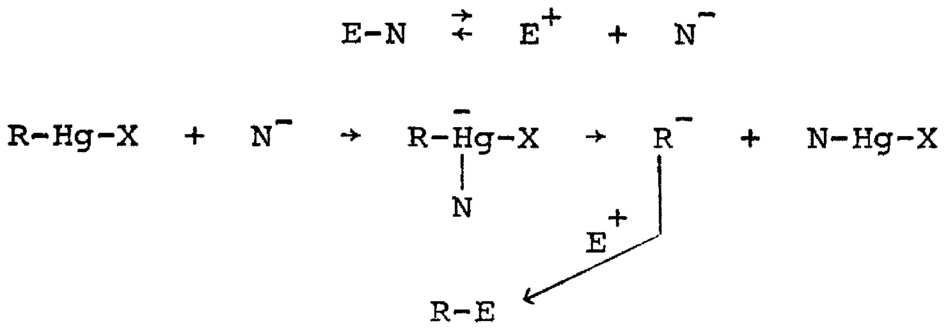
*Reactions of Organomercurials.* It has long been established that organomercurials are prone to electrophilic substitution.[1] Some of the better studied electrophilic reagents are protic acids, mercuric salts, and the halogens.

| Substrate | | Reactant | | Products | |
|---|---|---|---|---|---|
| R-Hg-R | + | HX | → | R-H + RHgX | (1) |
| R-Hg-X | + | HX | → | R-H + $HgX_2$ | (2) |
| R-Hg-R | + | $HgX_2$ | → | 2R-Hg-X | (3) |
| R-Hg-R | + | $X_2$ | → | R-X + RHgX | (4) |
| R-Hg-X | + | $X_2$ | → | R-X + $HgX_2$ | (5) |

In each case above, the reactant dissociates or becomes polarized and attacks the substrate. This can be accomplished by any of four mechanisms.

*Mechanisms in electrophilic substitution of organomercurials.* Currently there are four mechanisms normally associated with electrophilic substitution of organomercurials. These are as follows:

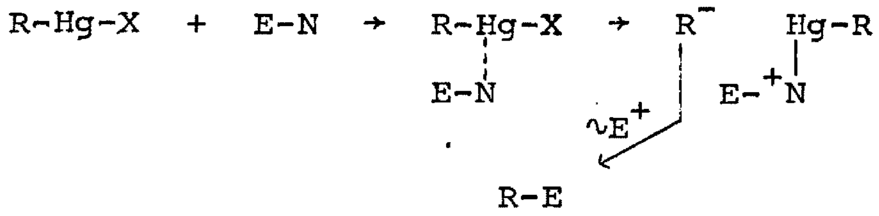
$S_E1$



(6)

The $S_E1$ reaction above involves ionization of the reactant followed by nucleophilic attack on the mercury by $N^-$. This complex releases the free carbanion $R^-$ which can then couple with the electrophile $E^+$.

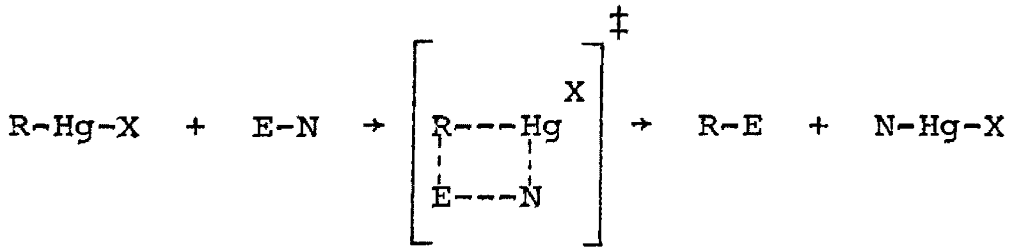
$S_Ei$



(7)

The $S_Ei$ mechanism above is exactly analogous to the $S_E1$ mechanism except that no ionization of E-N is necessary. The molecule E-N attacks the mercury, a free carbanion is formed, and then transfer of the electrophile $E^+$ occurs.

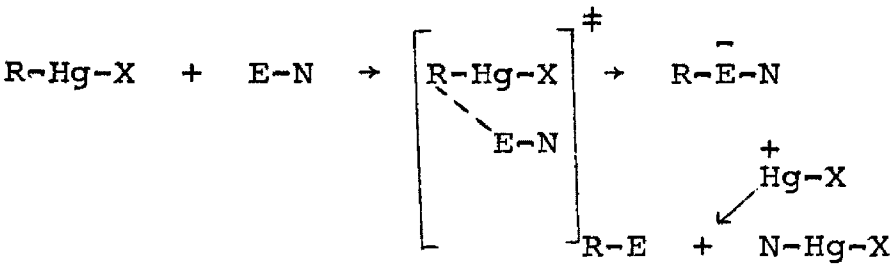
Four Center



(8)

The four center mechanism is a concerted reaction with an attack from the front side. As the bond R-Hg breaks, the R-E bond forms. The attack here is on the electrons between the R-Hg bond, and not on the mercury. There is no carbanion formed.

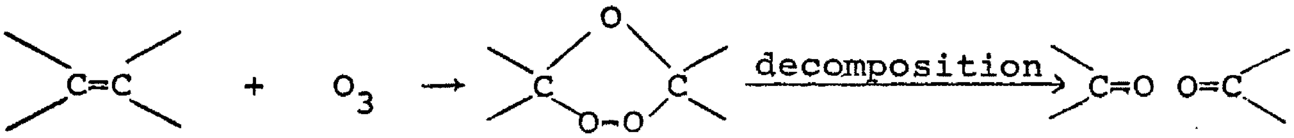
$S_E2$



(9)

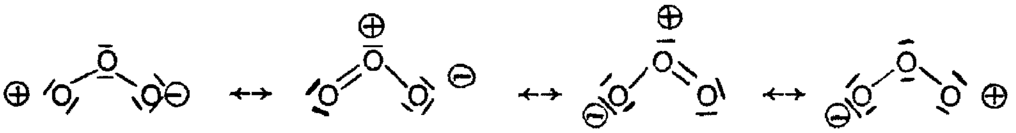
With the $S_E2$ mechanism, again, an attack on the electrons occurs. The difference between this mechanism and the four center mechanism is that here a tight ion pair exists that collapses into products. In other words, bond breaking and bond making do not occur simultaneously in the $S_E2$ mechanism as in the four center mechanism. Both mechanisms are alike in that they involve front side attack and lead to products with a retained configuration.

Reactions of Ozone. Early organic chemists working with ozone and olefins often found themselves characterizing readily exploding intermediates which were later found to be ozonides.[2,3] Ozone has been most widely used for the oxidative cleavage of double bonds.[4]



(10)

Since a double bond is an area of high electron density, attack by ozone is probably electrophilic. Its electrophilic nature can be explained by looking at some of its resonance structures.

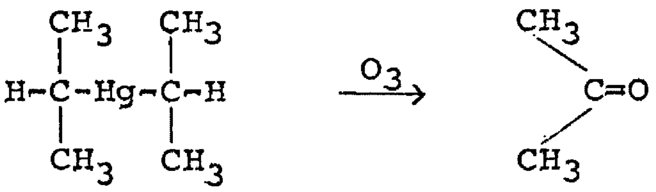


(11)

Other uses of ozone in organic chemistry have been reviewed by Long[5] and Bailey.[6]

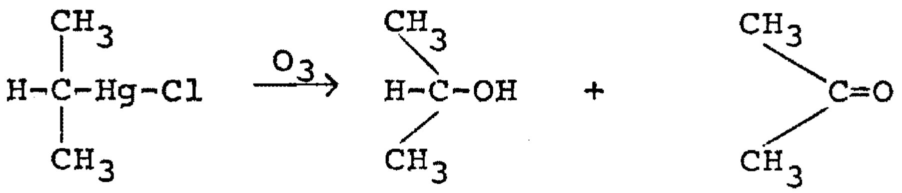
Reactions of Ozone with Organomercurials. It has been shown by various workers that many carbon-metal bonds react with ozone to produce products in which oxygen has replaced the metal.[7-13] This subject has been discussed by Waters, Pike, and Rivera.[14]

In 1939 it was shown by Böchmueller that diisopropyl mercury produced acetone upon ozonolysis.[15]



(12)

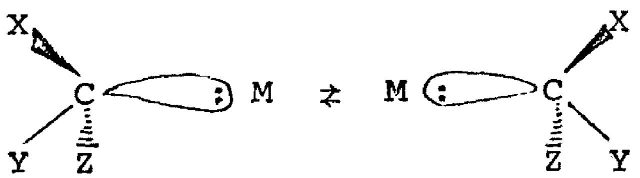
More recently it was reported by Waters, Pike, Erickson, and Marsh that isopropyl mercuric chloride underwent the same reaction.[16] However, studies performed by Rivera and Waters indicated that ozonolysis of isopropyl mercuric chloride yielded isopropanol as well as acetone.[17]



(13)

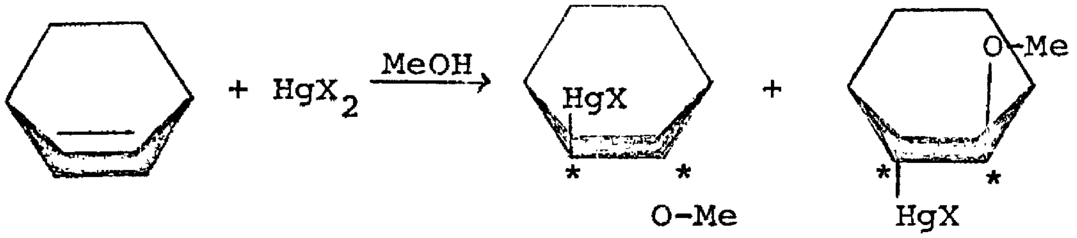
Since ozone has often been shown to act as an electrophile,[18] coupled with the fact that organomercurials undergo electrophilic substitution,[1] an electrophilic mechanism seems probable.

<u>Stereoisomerism in Organomercuric Halides</u>. For most organometallic compounds, optical activity derived from the carbon-metal bond has rarely been claimed. Because of the high degree of ionic character of the C-Mg, C-Na, and C-Li bonds,[19] their synthesis in optically active form where the asymmetric carbon atom is bonded to the metal can be difficult, due to facile inversion at carbon.



(14)

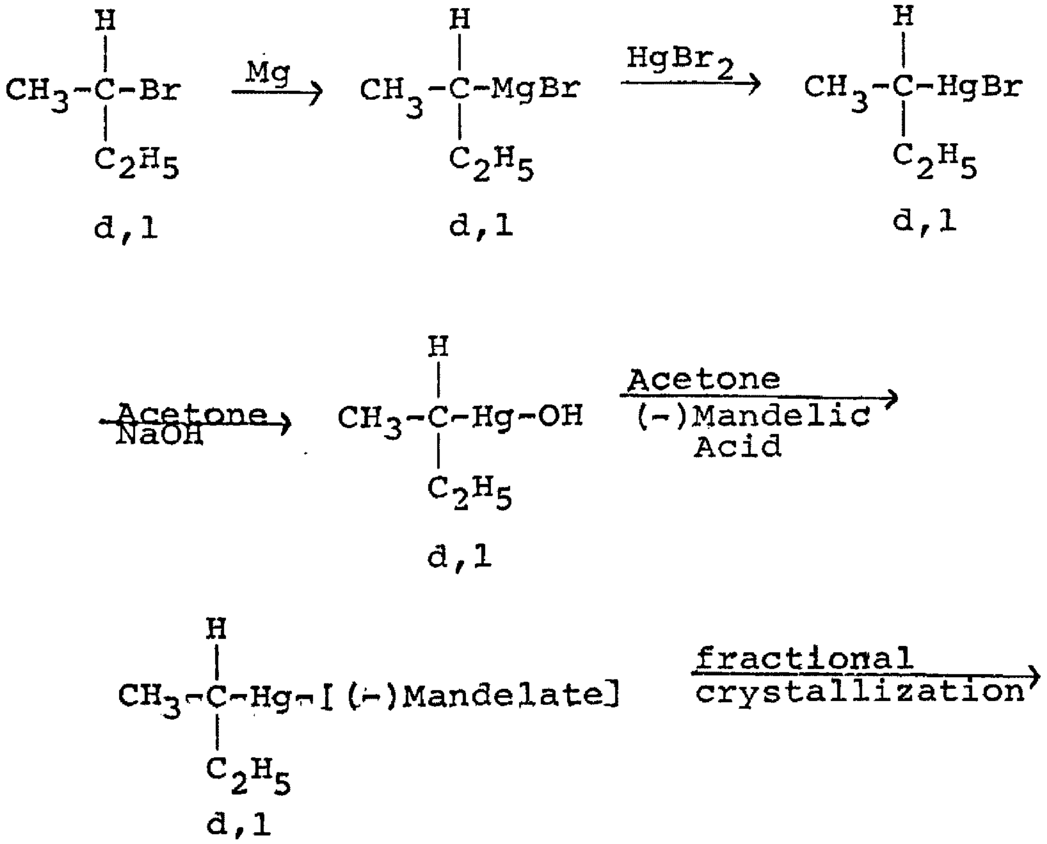
Unlike many carbon-metal bonds, the C-Hg bond is more covalent than ionic.[20] Marvel,[21] Wright,[22] and Nesmeyanov[23] found that optical activity in some organomercurials was not only dependent on other asymmetric carbons in the molecule, but also dependent on the carbon mercury bond as well. Specifically, Wright used a mercuric salt in methyl alcohol as a reagent, and added the groups "HgX" and "O-Me" across cyclohexene, thus creating two centers of asymmetry.



(15)

X=ℓ(+) Lactic Acid
* denotes asymmetric centers

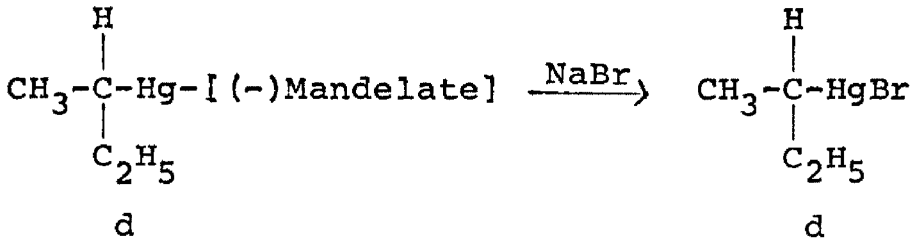
In order to elucidate the mechanism of electrophilic cleavages, Charman, Hughes and Ingold[24] synthesised an optically active organomercuric halide from sec-butyl bromide by the following scheme.



$$\underset{d,l}{CH_3-\underset{C_2H_5}{\overset{H}{C}}-Br} \xrightarrow{Mg} \underset{d,l}{CH_3-\underset{C_2H_5}{\overset{H}{C}}-MgBr} \xrightarrow{HgBr_2} \underset{d,l}{CH_3-\underset{C_2H_5}{\overset{H}{C}}-HgBr}$$

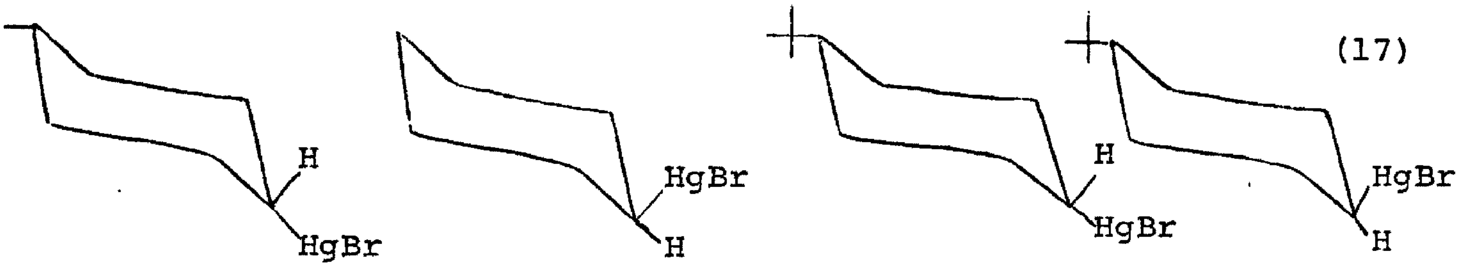
$$\xrightarrow[NaOH]{Acetone} \underset{d,l}{CH_3-\underset{C_2H_5}{\overset{H}{C}}-Hg-OH} \xrightarrow[\text{(-)Mandelic Acid}]{Acetone}$$

$$\underset{d,l}{CH_3-\underset{C_2H_5}{\overset{H}{C}}-Hg-[(-)Mandelate]} \xrightarrow[\text{crystallization}]{\text{fractional}}$$



$$\underset{\text{d}}{CH_3-\overset{\displaystyle H}{\underset{\displaystyle C_2H_5}{C}}-Hg-[(-)\text{Mandelate}]} \xrightarrow{NaBr} \underset{\text{d}}{CH_3-\overset{\displaystyle H}{\underset{\displaystyle C_2H_5}{C}}-HgBr} \qquad (16)$$

More recently the cis and trans-4-methyl or cis and trans-4-tert-butylcyclohexane systems have been utilized for mechanistic studies of organomercurials.[25,26,27]



(17)

trans cis

1-bromomercuri-4-methyl cyclohexane

cis trans

1-bromomercuri-4-tert-butylcyclohexane

All of these compounds are stable under normal conditions, and do not interconvert.

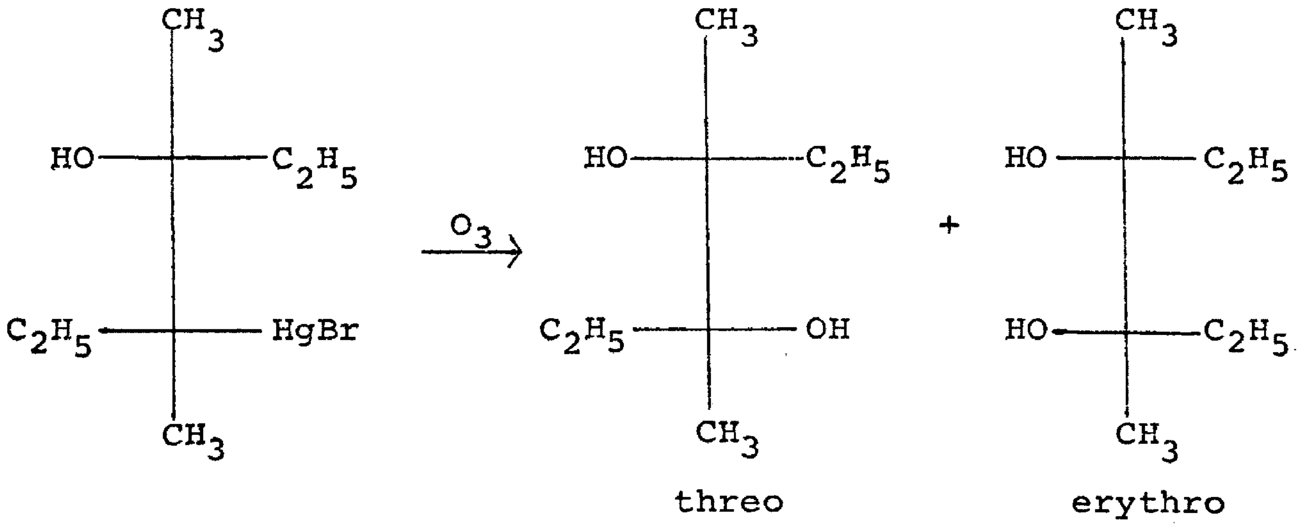
## Objective of the Research

The objective of this research was to establish a plausable mechanism for the reaction of ozone with organomercurials. This was to be achieved by ozonolysis of compounds that would show the stereochemical course of the reaction. Should the reaction be stereospecific, this would be the first step in a stereoselective synthesis of alcohols using mercuric salts and ozone, thus expanding the synthetic utility of organomercurial ozonolysis.

## Approaches to the Problem

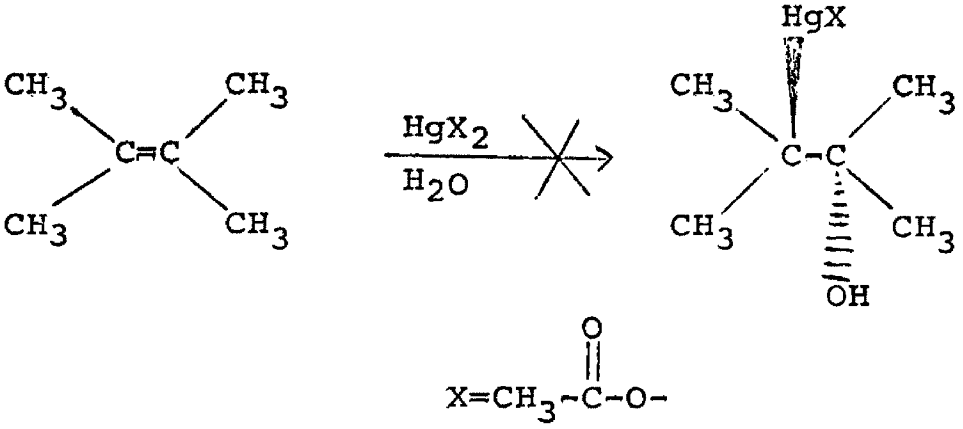
The overall approach was to take advantage of the fact that secondary and tertiary organomercuric halides yield alcohols as well as ketones. By ozonizing either geometrical or optical isomers of a specific organomercuric halide and subsequently identifying the resulting alcohol, the stereochemical pathway of the reaction could be deduced.

The first approach was to ozonize threo-2-bromomercuri-2,3-dimethyl-2-hexanol.



(18)

Ozonolysis proceeding with retention of configuration would yield the threo isomer, and ozonolysis proceeding with inversion would yield the erythro isomer. This approach was abandoned after attempted hydroxymercuration of tetramethyl ethylene. The desired adduct was not obtained.

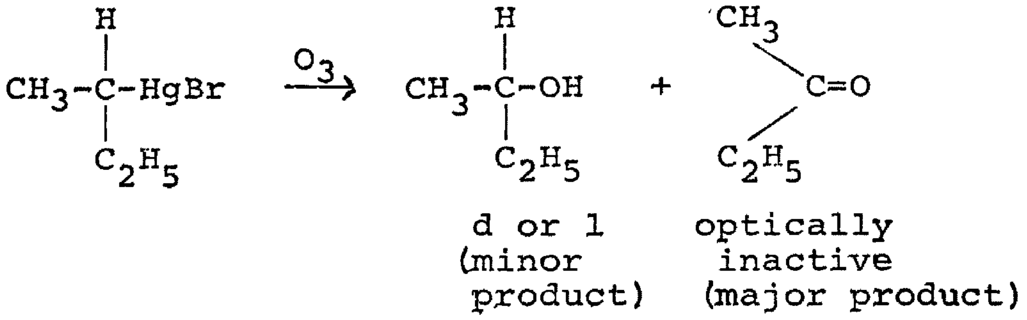


$$X{=}CH_3{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}O{-}$$

(19)

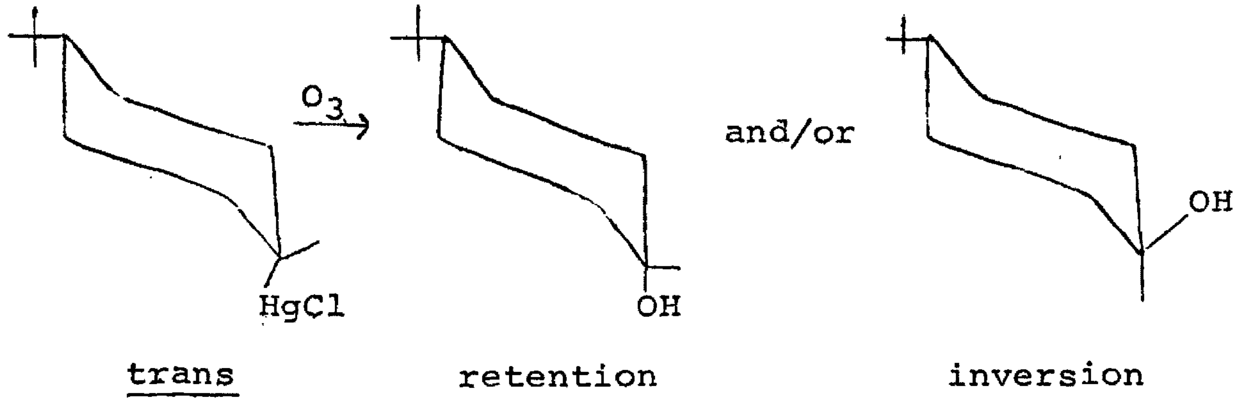
It had been shown earlier that other oxymercuration reactions of tetrasubstituted alkenes do not go well.[28] Therefore it seemed unlikely that <u>cis</u>-2,3-dimethyl-2-hexene would undergo hydroxymercuration, and other schemes were considered.

The plan to synthesize an optically active organomercuric halide similar to the one previously mentioned on pages 5 and 6 was also abandoned for the following reason. The secondary alcohol formed would be a minor product and separation and isolation of a large enough amount of it for an optical rotation determination would be an exceedingly formidable task.

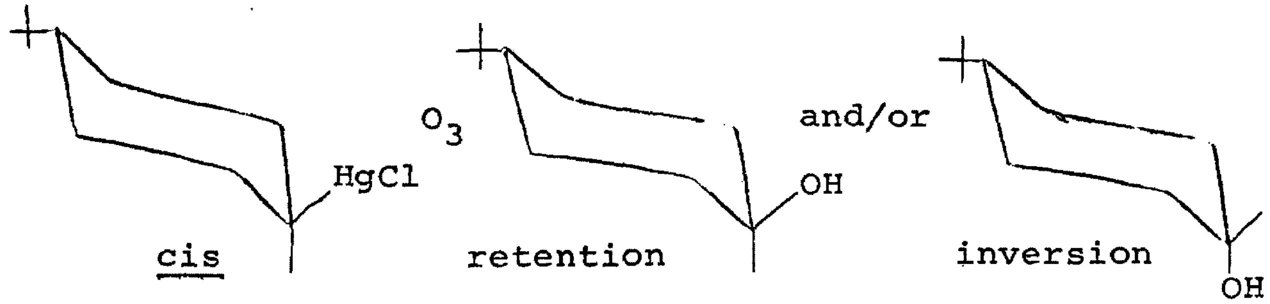


(20)

A new system was devised. Since secondary alkyl mercuric halides are readily oxidized to ketones as well as alcohols, a tertiary system was desired. The 4-tert-butylmethylcyclohexyl system seemed promising, and could react as shown below.

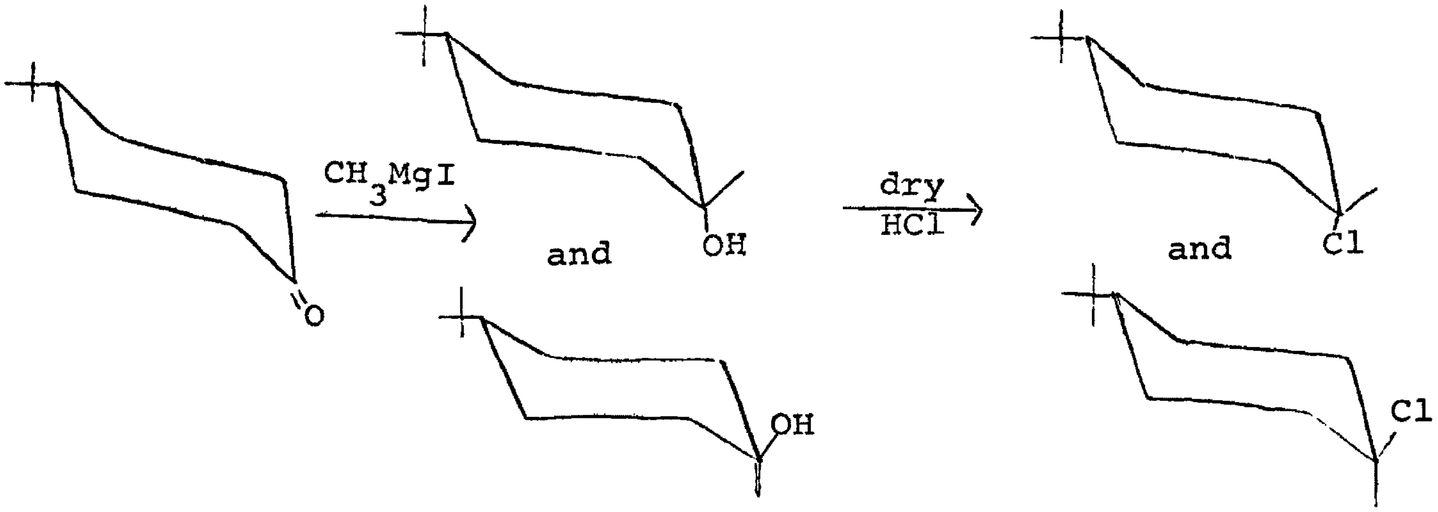


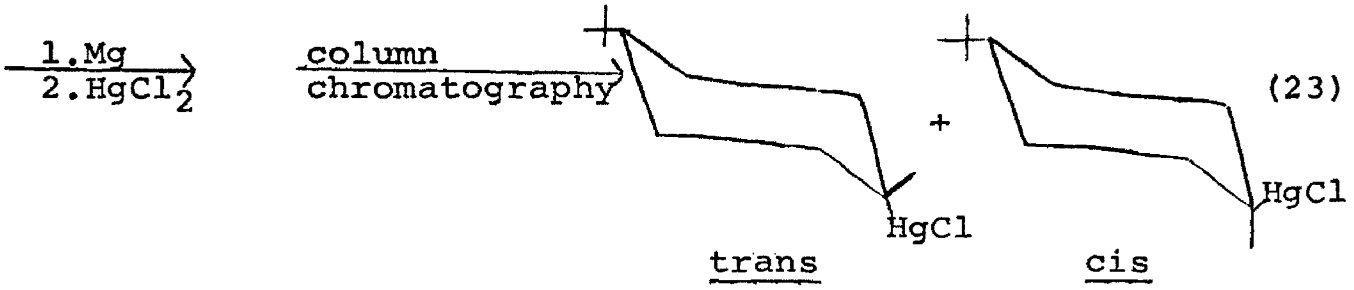
(21)



(22)

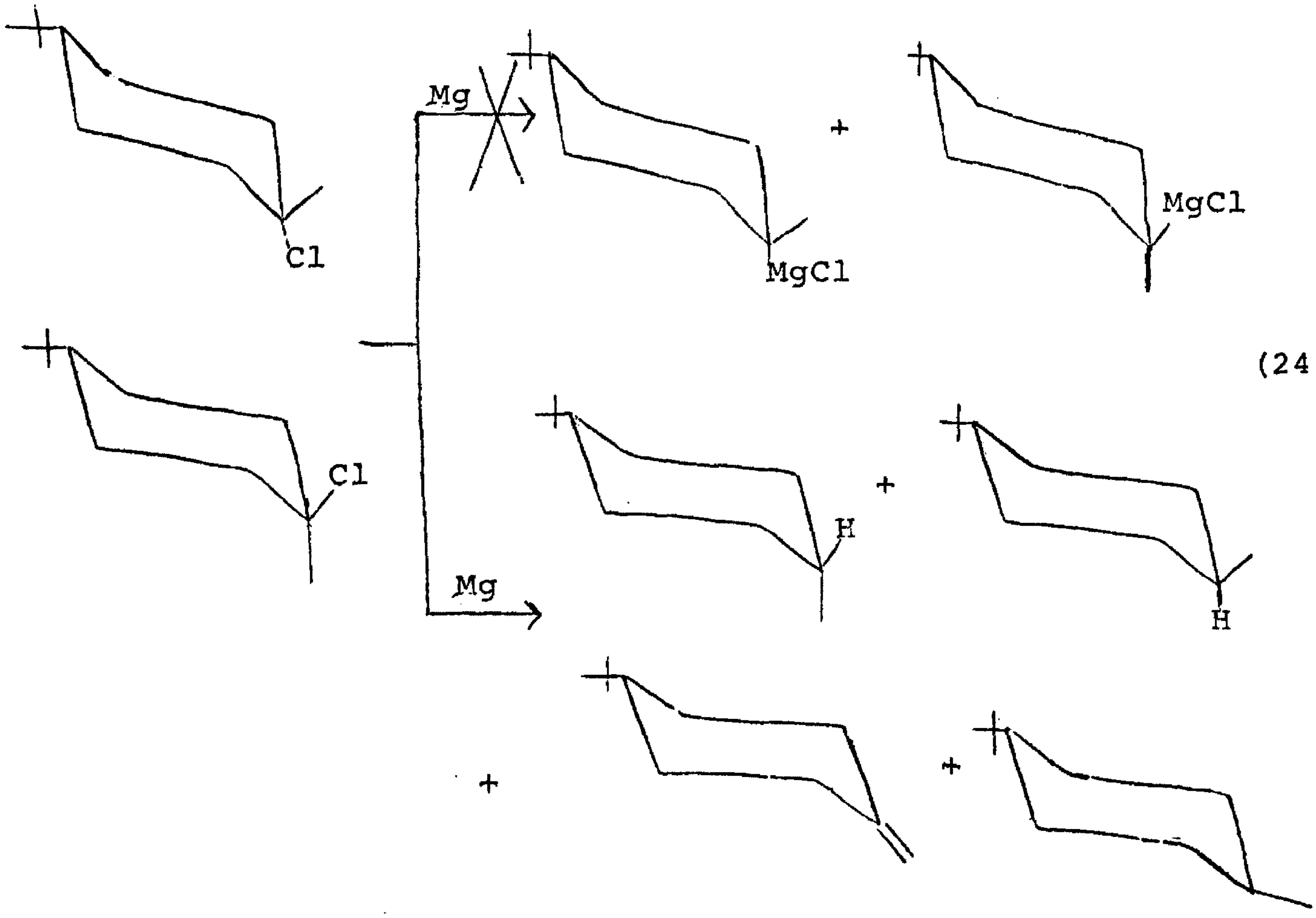
This was a new compound and the following scheme was devised for its synthesis:





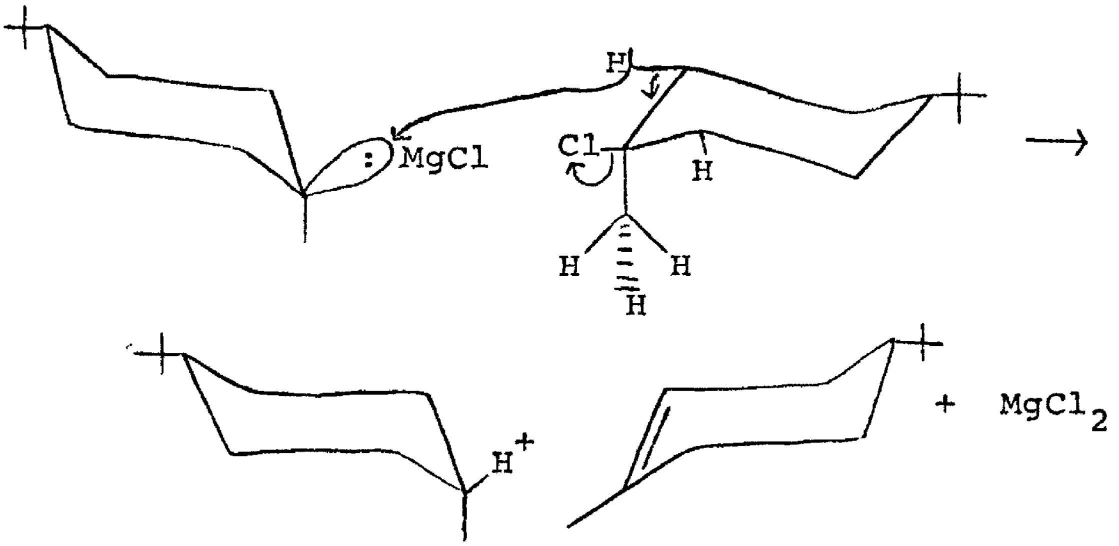
(23)

The alcohols that would be formed by ozonolysis were found to separate readily by gas chromatography. The synthesis proceeded smoothly until the formation of the Grignard. It was found that large concentrations of the Grignard were not formed, but rather elimination reactions were taking place.



(24)

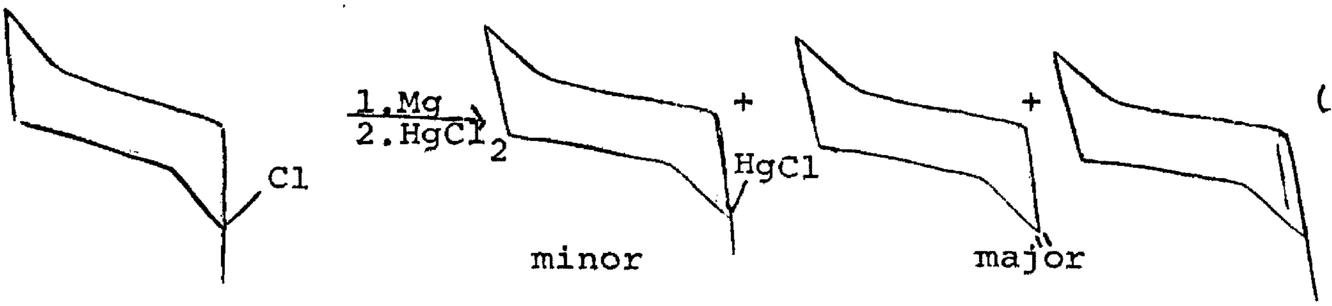
It was assumed that since a Grignard reagent is an extremely strong base, it reacted with starting material as quickly as it was formed. In support of this contention 1-chloro-1-methyl-4-tert-butyl-1-cyclohexane system has been shown to eliminate HCl readily.[29]



(25)

all hydrogens shown as "H"
above are acidic and labile
to the Grignard reagent

It was also reported that the Grignard reagent derived from 1-chloro-1-methylcyclohexane was extremely unstable, and yielded elimination products.[30]

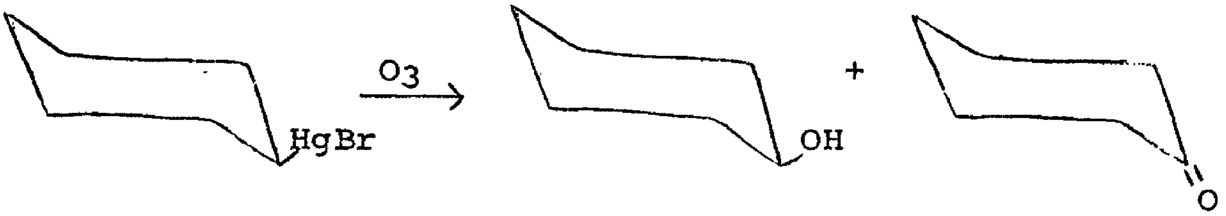


(26)

(decomposition at room temperature)

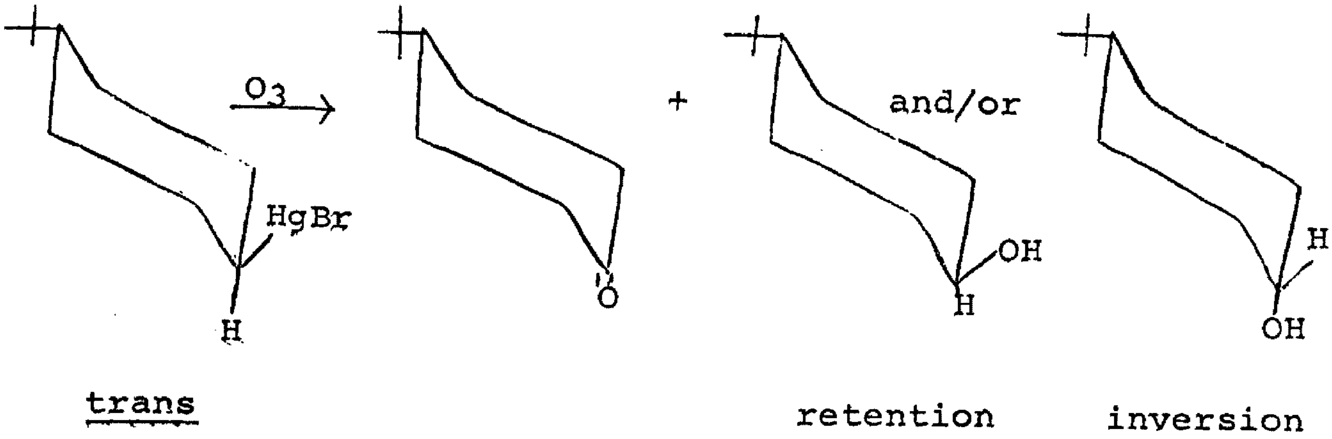
This approach was consequently abandoned.

Since both cis and trans-1-bromomercuri-4-tert-butylcyclohexane had been characterized in the literature[25,26] and since the resulting compounds would show the stereochemical pathway of the reaction, this approach appeared to be the most desirable. To insure that the above compound would give the proper results, bromomercuricyclohexane was ozonized as a test reaction. The desired alcohol was obtained in sufficient yield to perform quantitative work.

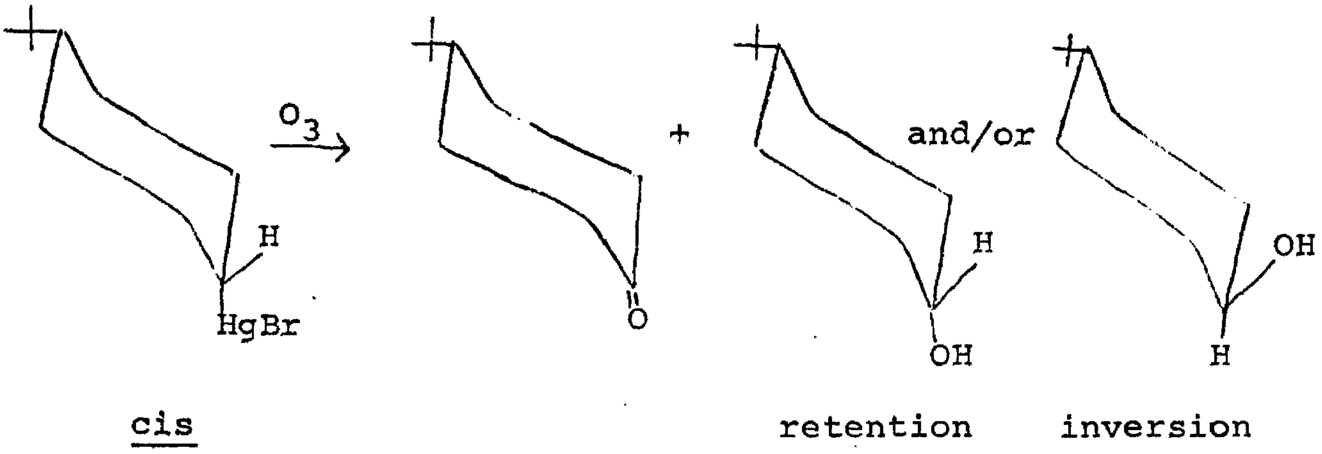


(27)

Therefore, it was concluded that the following results could be anticipated from the ozonolysis of 1-bromomercuri-4-tert-butylcyclohexane.

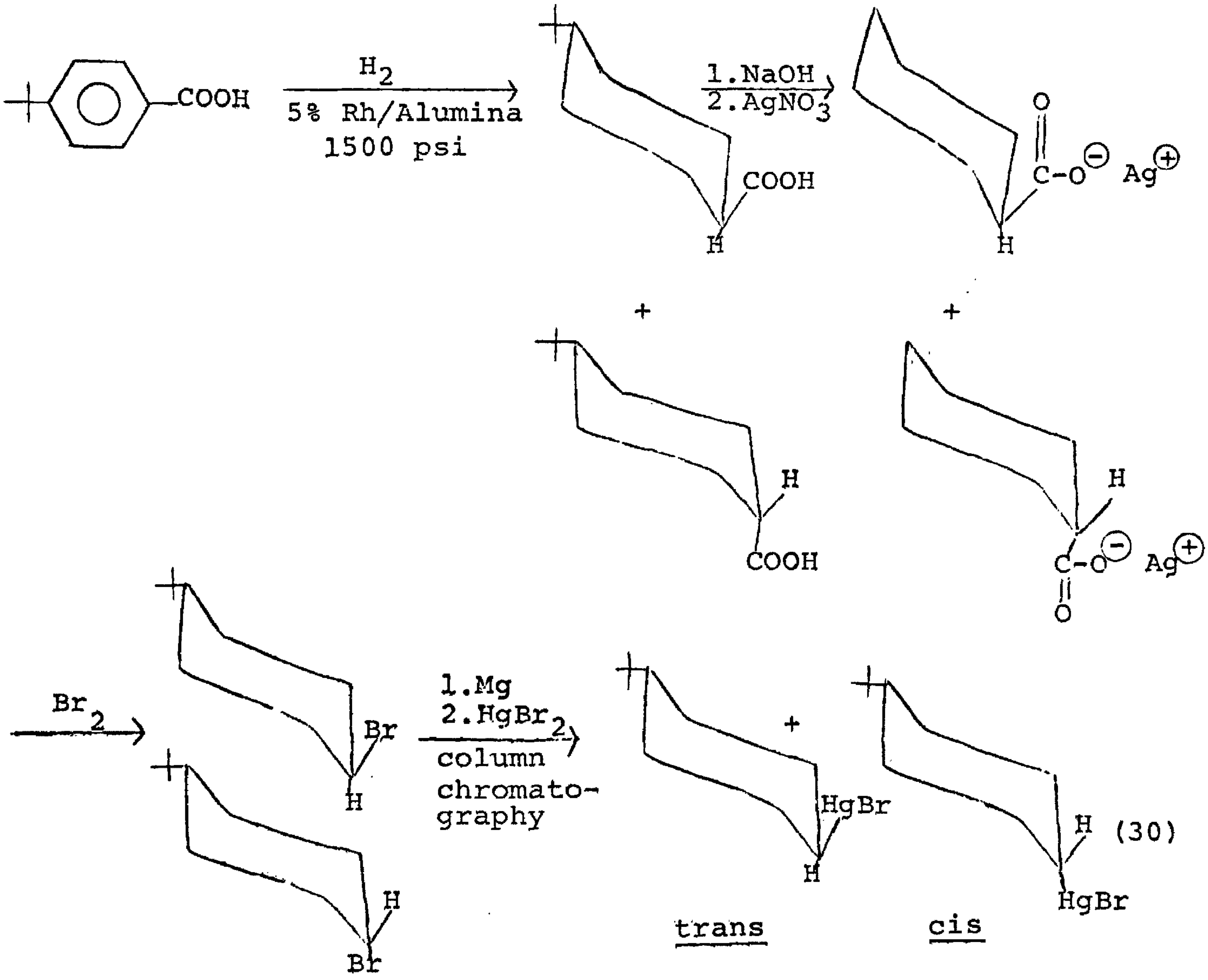


(28)



(29)

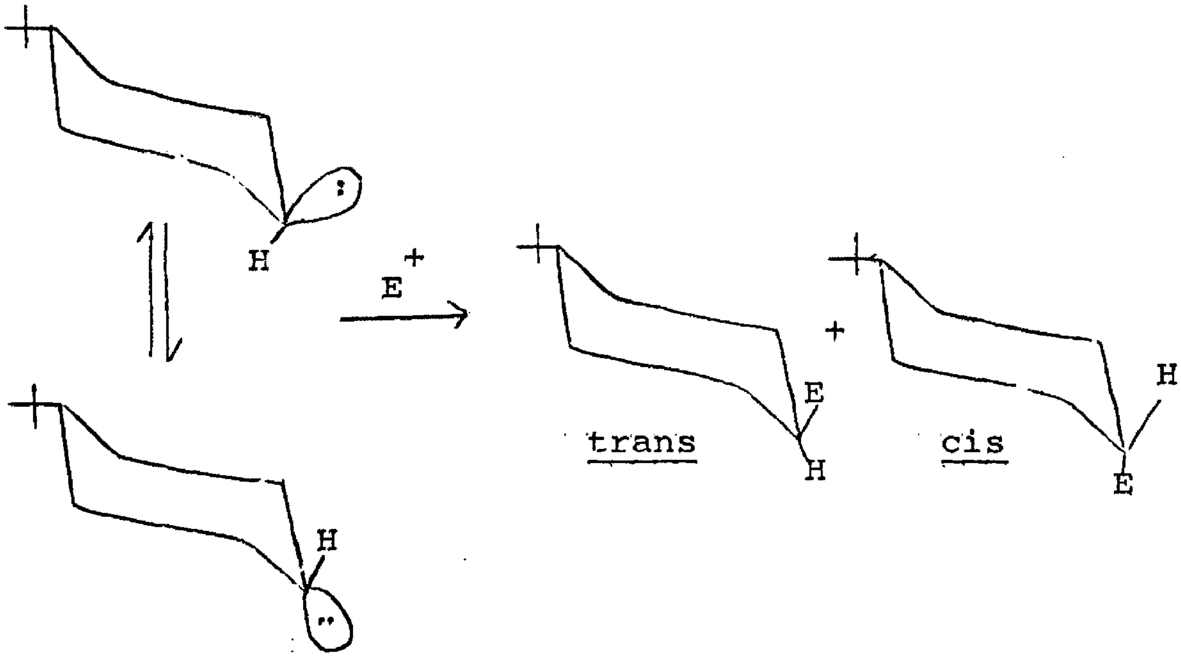
The 1-bromomercuri-4-tert-butylcyclohexane was synthesized by the following route:



(30)

Stereochemical and mechanistic implications. As shown earlier, the $S_E1$ and the $S_Ei$ reactions involve the intermediate formation of a carbanion. A free carbanion would lead to a product mixture of stereoisomers. However, one stereoisomer may predominate over another if electrophilic approach from one side is easier than another. Also, if one carbanion is of higher energy than another, the lower energy carbanion will be in greater quantity (assuming an inversion equilibrium) and, therefore, more available for reaction. The product distribution can also depend on how easily bond formation between the carbanion and the electrophile occurs.

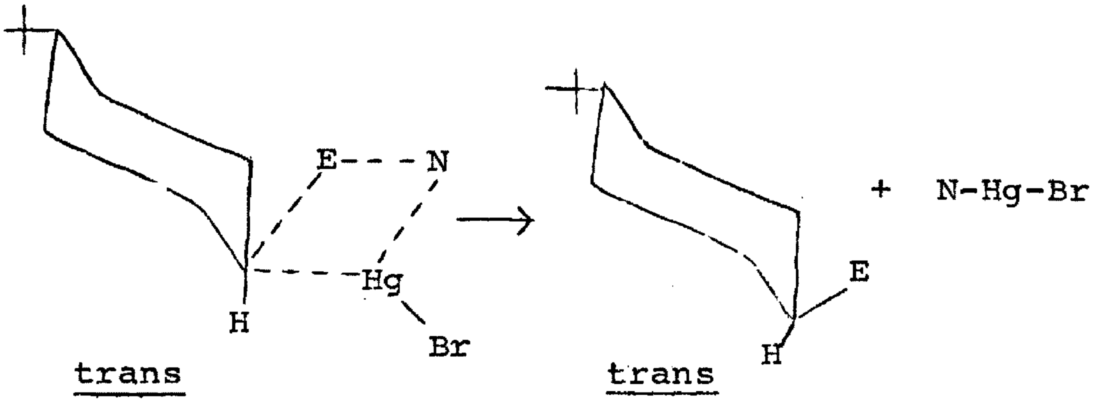
$S_E1$ or $S_Ei$



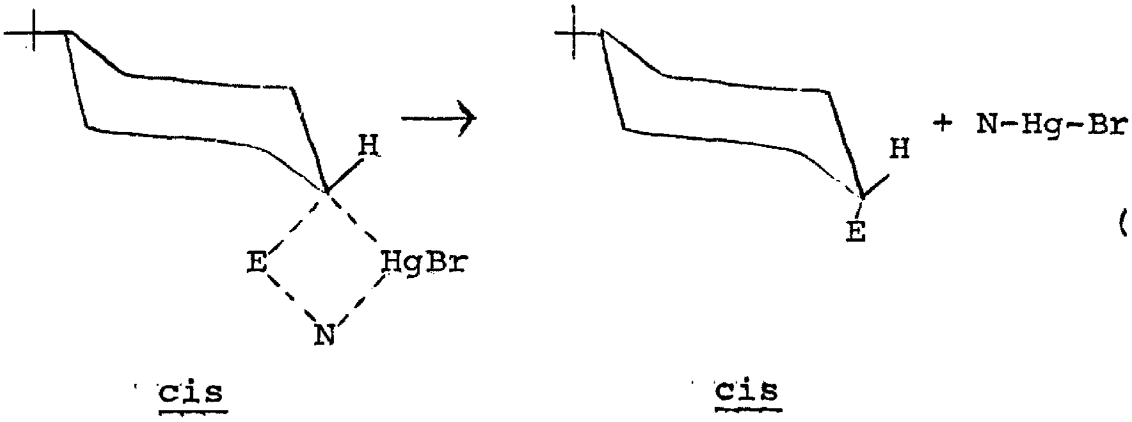
(31)

The four center and the $S_E2$ reactions should give products of retained stereochemistry since no free carbanion is formed.

Four Center

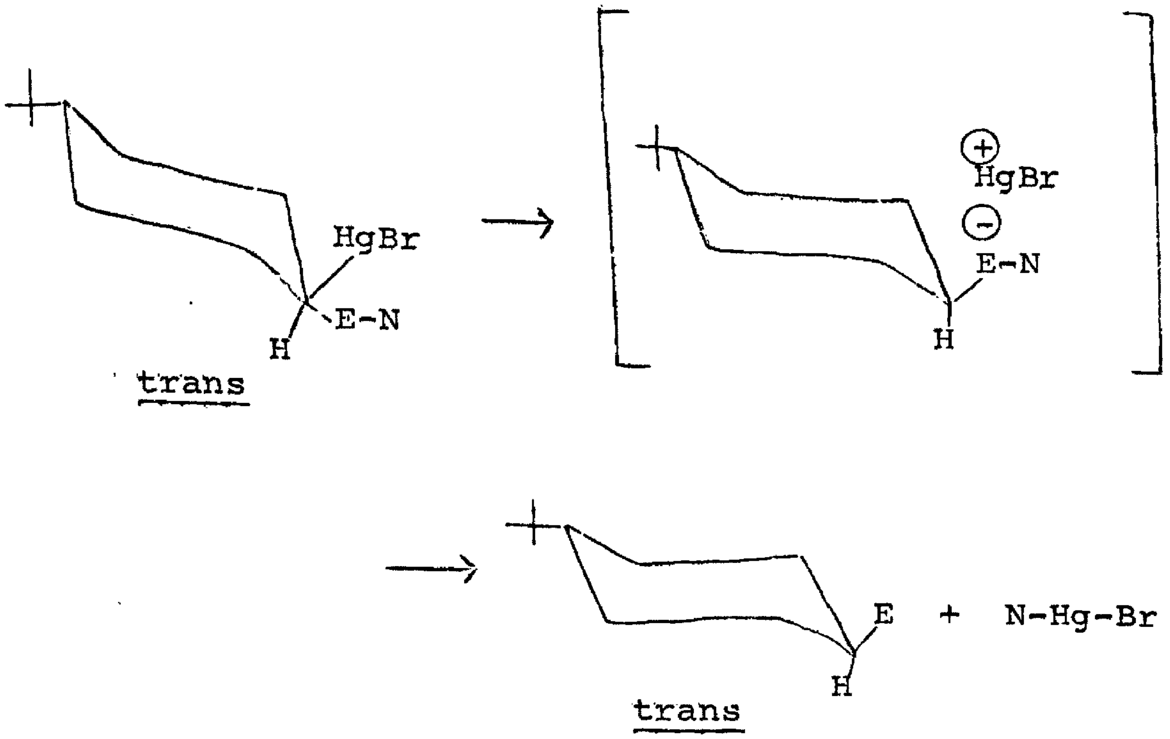


(32)

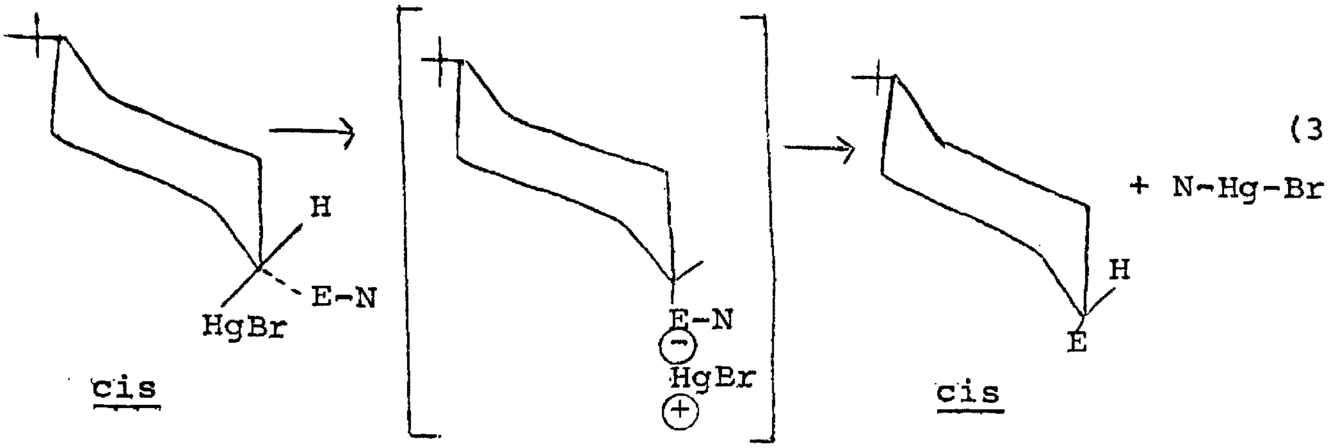


(33)

$S_E2$


HgBr
E-N
H
trans
⊕
HgBr
⊖
E-N
H
E
H
+ N-Hg-Br
trans

(34)


H
E-N
HgBr
cis
E-N
⊖
HgBr
⊕
H
E
cis
+ N-Hg-Br

(35)

# CHAPTER II

# EXPERIMENTAL

## Instrumentation

Product identification was performed by either nuclear magnetic resonance with a Varian Associates Model HA-60 Analytical NMR Spectrometer or with the aid of a Varian Aerograph Series 1700 Gas Chromatograph employing a thermal conductivity detector. Hereafter these instruments will be referred to as the "NMR" or "GC" instruments. Unless stated otherwise all NMR determinations were performed at 33-37°C and employed chloroform as the solvent as well as the lock signal. Those yields determined by GC analysis were acquired with the aid of the internal standard, nitromethane. The column used for the quantitative measurement of alcohols, ketones, as well as products formed from organomercurial ozonolysis was a 10' x 1/4", 10% FFAP on Chromosorb W, hereafter referred to as the "FFAP" column. All GC products were identified by coinjection with compounds of known retention times. An increase in peak height was taken to mean that a compound had been correctly identified.

The program used for all the GC analyses was as follows: the oven temperature was stabilized at 60°C, the injectors were usually heated to 215°C, and the detector temperature was 225°C. Helium gas was passed through the column at a rate of 100 ml/minute. After injecting a sample, the column was held at constant temperature for seven and one half minutes. A linear temperature program was employed which raised the oven temperature 20° per minute until a temperature of 160°C was reached. At this new temperature, the compounds of interest were separated enough to make quantitative determinations.

All melting points were determined with a Meltemp melting point apparatus. The melting points were not corrected.

Use of the Internal Standards. When each sample was injected into the GC, there were generally four peaks of interest. The increase or decrease of a compound was calculated by comparing its increase or decrease of peak area with respect to a nitromethane internal standard. Since the nitromethane was inert to ozone, the actual concentration changes of the compounds could easily be determined. If the original concentration was known, this ratio times a factor gave the actual changes in concentration.

### Experimental Apparatus

The ozone was produced by a Welsbach T-408 electric discharge ozonator. A methylene chloride solution containing the compound of interest was placed in a cylindrical reaction vessel and was cooled to 0°C. The ozone was bubbled into the reaction solution by means of a dipersion tube. The reaction vessel had an upper and lower trap which contained acetone and dry ice. These cold traps prevented any volatile compounds from escaping from the reaction flask. The upper trap was connected to a final ozone trap which was merely another reaction vessel containing potassium iodide in water. Any unreacted ozone was destroyed in the trap via reduction to oxygen and hydroxide ion.

The reaction vessel was considered saturated with ozone when the exit gas caused the solution of potassium iodide to turn yellow. Oxygen was passed through the ozonator at a rate of 350 ml/minute. A power setting of 90 volts was used for the primary of the transformer which controlled the electric discharge plates. The ozonation apparatus is diagramed in Figure 1.

## Chemicals

The methylene chloride, chloroform and carbon tetrachloride used in the experiments were J. T. Baker reagent grade. The methylene chloride and carbon tetrachloride were not purified further. However, purification of the chloroform was necessary to remove the 1% ethanol added to maintain stability. This was done to eliminate the appearance of any multiplets due to ethanol in the NMR. The purification was accomplished following the procedure

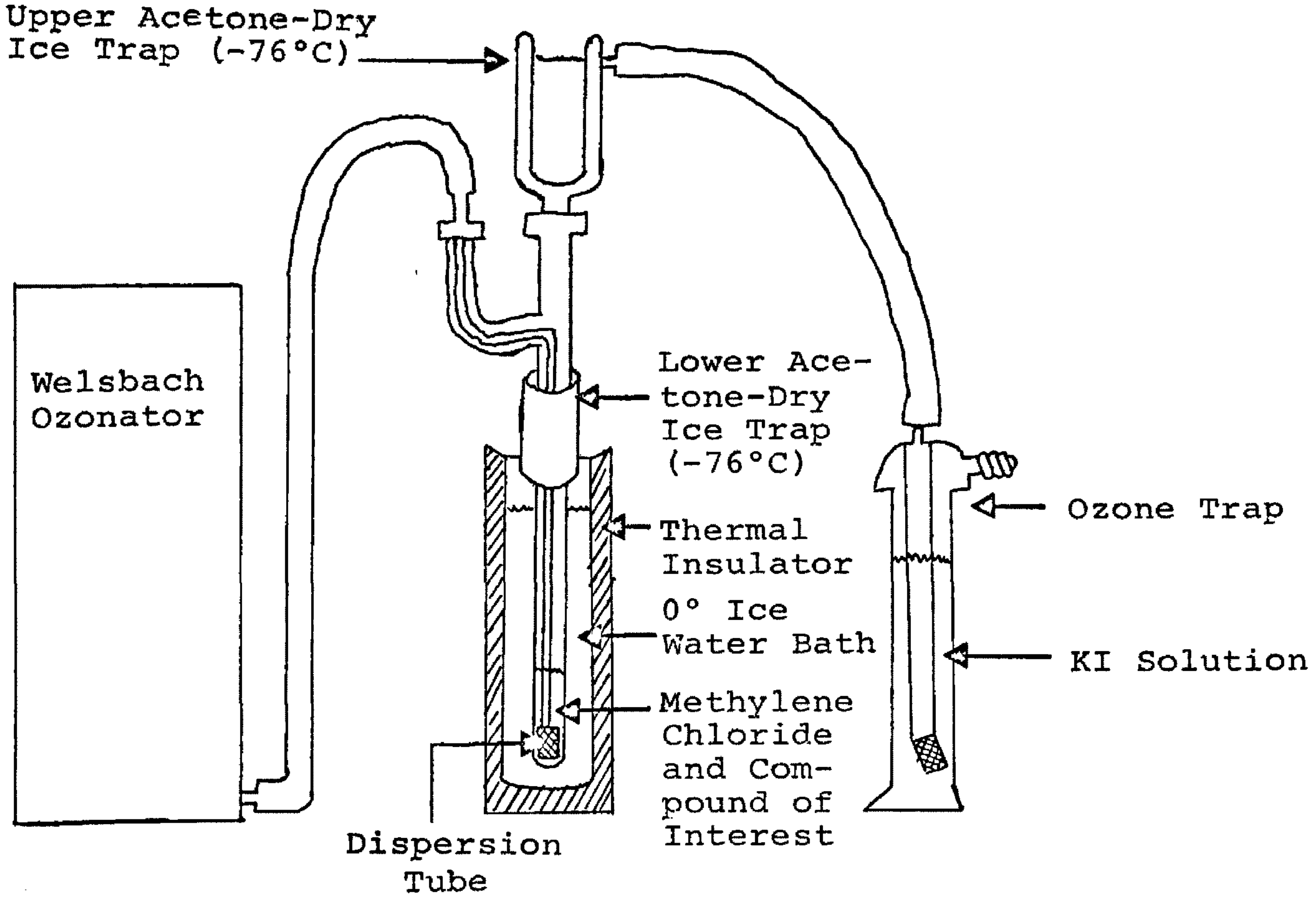

Upper Acetone-Dry Ice Trap (-76°C)
Welsbach Ozonator
Lower Acetone-Dry Ice Trap (-76°C)
Thermal Insulator
0° Ice Water Bath
Methylene Chloride and Compound of Interest
Dispersion Tube
Ozone Trap
KI Solution

Figure 1

outlined in Purification of Laboratory Chemicals.[31] The chloroform was extracted three times with portions of water to remove the ethanol, followed by one washing with a saturated sodium bicarbonate solution. The chloroform was then dried over calcium chloride and distilled from phosphorous pentoxide. To retard decomposition, nitrogen gas was passed through the chloroform for several minutes, and the solution was subsequently stored below 0°C until needed.

The diethyl ether used to prepare the Grignard reagents was anhydrous Baker Analytical Reagent and was stored over sodium wire without further purification. The magnesium chips used for the Grignard reagents were J. T. Baker purified magnesium chips. The mercuric bromide was from Alfa Inorganics and the mercuric chloride was J. T. Baker brand. These mercuric salts were used without further purification.

The nitromethane used as an internal standard for GC work was J. T. Baker technical grade. The nitromethane was judged to be pure by GC on the FFAP column.

The magnesium sulfate used was Anhydrous Baker Analyzed Reagent and the pentane used in column chromatography was J. T. Baker practical grade.

## Preparation of Starting Materials

4-tert-butylcyclohexanol. This reaction was performed in two ways to allow one product to predominate.

Method 1: According to the method of Bernstein,[32] 20 g. (0.130 mole) of 4-tert-butylcyclohexanone was added to a solution of 150 ml of 10 N sodium borohydride in aqueous sodium hydroxide. This solution was made by first dissolving 30 g. (0.75 mole) sodium hydroxide in 150 ml water and then adding 56.7 g. (1.5 mole) sodium borohydride. Eighty milliliters of tetrahydrofuran was added to completely dissolve the ketone in the mixture. This solution was refluxed for two hours (until effervescence had ceased). The solution was cooled, extracted with ether, dried over anhydrous magnesium sulfate, filtered, and the solvent evaporated to yield 20 g. (98%) of 4-tert-butylcyclohexanol.

This crude mixture was injected into the GC instrument and two peaks of very long retention time resulted. The first peak which comprised 9% of the mixture was assumed to be the cis isomer, and the second peak which comprised 92% of the mixture was assumed to be the trans isomer. This identification was made by noting that lithium aluminum hydride reduction proceeds by a similar mechanism,[33] and the fact that similar ratios of alcohol products were also observed with lithium aluminum hydride reductions.[34]

Method 2: This reaction was carried out by Mr. Anthony Rollin. A 20 g. (0.130 mole) sample of 4-tert-butylcycloheanone was dissolved in ethanol and hydrogenated with 2 g. of Raney nickel catalyst at 1800 psi for four hours at 100°C to yield quantitatively 4-tert-butylcyclohexanol.

GC analysis showed that the cis isomer predominated over the trans by a ratio of 3/2.

Separation of cis and trans 4-tert-butylcyclohexanol. The mixtures of alcohols were separated according to the method of Winstein.[35] Five grams (0.035 mole) of the alcoholic mixture was added to a column of 200 g. of aluminum oxide. The column was eluted with 1 liter of 5% ether in pentane. The column was then eluted with 10% ether in pentane until no more residue from the cis isomer appeared in the collection flask. The column was finally eluted with pure ether, and the trans alcohol collected.

4-tert-Butylcyclohexane carboxylic acid. Recrystallized p-tert butylbenzoic acid was reduced according to the method of Jensen.[36] Sixty five grams (0.365 mole) of recrystallized p-tert-butylbenzoic acid was dissolved in 100 ml of hot (60°C) acetic acid. Seventy milliliters of the above solution was added to 0.7 g. of 5% rhodium on alumina and hydrogenated at a pressure of 1500 psi at 70°C until the pressure ceased to drop. Three runs were made and combined, 800 ml of distilled water added, and the resulting solid collected. The solid was recrystallized from ethanol to yield 59.5 g. (89%) of cis and trans-4-tert-butylcyclohexane carboxylic acid. The NMR revealed that the aromatic doublet of doublets between 2 and 3 $\tau$ had disappeared. It was therefore concluded that the reaction had proceeded smoothly.

4-tert-Butylcyclohexyl bromide. Preparation of this compound was performed by three different methods in order to optimize yields.

Method 1: According to the method of Keslow and Marsh,[37] in a minimum of methylene chloride was dissolved 11.5 g. (0.0866 mole) cis and trans 4-tert-butylcyclohexanol. A 23.4 g. (0.0866 mole) sample of distilled phosphorous tribromide in 150 ml of methylene chloride was cooled to 0°C in an ice bath. To this solution was then added 13.8 g. (0.0866 mole) of reagent grade bromine, and the solution was then allowed to cool to 0°C. The yellow precipitate of phosphorous pentabromide was observed. The solution containing the alcoholic mixture was slowly added with stirring to the phosphorous pentabromide solution while maintaining the temperature between 0°C and 5°C. The mixture was allowed to stir for an additional half hour, at which time 500 g. ice water was added, and the organic layer was extracted, washed with water, with a saturated sodium bicarbonate solution and with a saturated sodium chloride solution and dried over magnesium sulfate. The solvent was then evaporated on a rotary evaporator. Purification was achieved by washing the crude liquid through a column of silica gel with pure pentane or by distillation b.p. 84-87°C/2.4 mm (lit. b.p. 73-74°C/2.5 mm,[25] b.p. 70°C/2 mm,[38] b.p. 64-65°C/1 mm[27]). The NMR spectrum of the product matched that of the reported compound.[39]

Method 2: This reaction was performed according to the method of Cason and Correia.[40] To 300 ml of pyridine in a 1,000 ml round bottom flask was added 40.5 g. (0.259 mole) of *cis* and *trans* 4-tert-butylcyclohexanol.

The solution was cooled to 0°C. 101 g. (0.574 mole) of *p*-toluene sulfonyl chloride was added while holding the solution temperature below 5°C. The mixture was allowed to stir for four hours in an ice bath. The reaction vessel was then filled with 300 g. of ice water and the crystals were collected. Upon drying, the theoretical yield of the *p*-toluene sulfonate ester was obtained. NMR analysis confirmed the products structure by showing the same peaks as the starting material and an aromatic doublet of doublets at 2.2-2.8 $\tau$ corresponding to para substitution on an aromatic ring. It also showed a singlet at 7.6 $\tau$ corresponding to methyl substitution on an aromatic ring.

The mixture was then added to a solution of 26.7 g. (0.259 mole) of sodium bromide in 473.2 ml. of anhydrous N,N dimethyl formamide, and allowed to stir for five days at room temperature. Five hundred milliliters of distilled water was then added and the mixture was extracted with three 250 ml. portions of ether. The ether layer was then washed with a solution of dilute HCl and finally with 250 ml distilled water. The ether layer was then dried over magnesium sulfate and the solvent evaporated on a rotary evaporator. NMR analysis revealed only starting material.

The conversion of the p-toluene sulfonate ester to the bromide was then repeated except that 44.8 g. (0.518 mole) of lithium bromide was used in place of the sodium bromide. The reaction was worked up in a similar fashion, but only starting material was recovered. This method was then abandoned.

Method 3: The third synthesis provided optimal results and employed the Hunsdiecker reaction. A 49.5 g. (0.278 mole) sample of cis and trans 4-tert-butylcyclohexane carboxylic acid was slowly added to a hot solution of 12 g. (0.30 mole) of sodium hydroxide in 125 ml. of distilled water. The solution was heated until the acid was completely dissolved. The hot solution was filtered and nitric acid was slowly added until a faint turbidity persisted. A sodium hydroxide solution was slowly added dropwise until the turbidity disappeared. To this solution was slowly added a solution of 47.5 g. (0.275 mole) of silver nitrate in 75 ml. of water, causing a grayish material to precipitate. The wet mass was collected and dried in a covered vacuum dessicator over phosphorous pentoxide for two days. The dried silver salt of the acid was added to 300 ml. of carbon tetrachloride. To another 60 ml. of carbon tetrachloride was added 33 g. (0.206 mole) of bromine. The bromine solution was added to the suspension of the silver salt over a 15 minute period at room temperature.

The mixture was heated until effervescence commenced, and then allowed to stir at room temperature for an hour. The carbon tetrachloride layer was filtered, washed with sodium thiosulfate, and evaporated on a rotary evaporator. The crude oil was distilled and had the same physical and spectral properties as the purified bromide obtained from method 1. The yield was 12.15 g. (20%).

The organomercuric halides were prepared using the Grignard method described by Marvel, Guarke, and Hill.[41]

*cis and trans 1-Bromomercuri-4-tert-butylcyclohexane.* To 10 ml of dry ether was added 15 g. (0.0684 mole) of *cis* and *trans*-4-tert-butylcyclohexylbromide. The solution was slowly added under nitrogen to 4 g. (0.165 mole) of dry magnesium chips in 75 ml of ether. The magnesium had been previously activated by a few drops of 1,2-dibromoethylene. The reaction was stirred an additional two hours. Fifty milliliters of distilled water was added to the reaction vessel. The ether layer was collected and dried over magnesium sulfate, and the ether evaporated on a rotary evaporator. A crude mixture of *cis* and *trans*-1-bromomercuri-4-tert-butylcyclohexane was isolated. The yield was 10.2 g. (41%).

*Separation of cis and trans 1-bromomercuri-4-tert-butylcyclohexane.* Following the method of Jensen,[42] the crude mixture was subjected to column chromatography on

250 g. of neutral alumina. The column was eluted with pure pentane, and every 250 ml fraction was checked by NMR until an extra peak began to appear. The fractions were then divided into two groups: the first one primarily containing a rapidly eluting compound, and the second containing mostly a slowly eluting compound.

Group one was recombined and rechromatographed and fractions collected until they were judged to contain only one compound by NMR spectroscopy. The melting point of the compound collected from group one was 144-146°C and this was judged to be the *cis* mercurial (lit., m.p. 140-142°C pentane,[26] m.p. 149.2-149.6 EtOH).[27] The NMR spectrum revealed a small multiplet at 6.63 π corresponding to carbon-hydrogen next to mercury, multiplets from 7.6-9.1 π corresponding to ring protons, and a large singlet at 9.08 π corresponding to the tertiary butyl peak.

In like fashion, group two was recombined and rechromatographed, and fractions collected and analyzed as above. The melting point of the compound collected from group two indicated that it was the *trans* isomer and had a m.p.of 234-236°C (lit., m.p. 216°C,[26] m.p. 230-231°C).[27] The NMR spectrum revealed a small multiplet at 6.63 π corresponding to carbon-hydrogen next to mercury, multiplets from 7.4-9.1 π corresponding to ring protons, and a large singlet at 9.12 π.

Since the tertiary butyl groups of the cis and trans isomers had different chemical shifts, it was hoped that addition of pyridine to the NMR probe would cause the downfield multiplets to separate. However, even in neat solution of pyridine, this did not occur.

Bromomercuricyclohexane. This compound was prepared by Mr. P. E. Pike and its synthesis, physical properties, and spectral parameters are fully described in his thesis.[43]

## Preparation of Compounds Subsequently Not Used in This Thesis

Attempted hydroxymercuration of tetramethylethylene. To a stirred solution of 100 ml of 25% acetone in water was added 1 g. (0.0119 mole) of tetramethylethylene. A 3.78 g. (0.0119 mole) sample of recrystallized mercuric acetate was then added. The solution turned perceptably yellow, instantly. After overnight, stirring the solution was gray. It was assumed that mercury had precipitated. Two more attempts were made varying the amount of stir time. One reaction was stopped after it just began to yellow, and the other was stopped after 10 minutes. No organomercurials could be detected by NMR analysis.

Cis and trans-4-tert-butyl-1-methylcyclohexanol. According to the method of Houlihan,[44] eighty milliliters of 3.27 M (0.26 mole) methylmagnesium chloride in tetrahydrofuran was added under nitrogen to a large round-bottom flask. The solution was then cooled in an ice bath. Twenty grams (0.13 mole) 4-tert-butylcyclohexanone in 60 ml dry diethyl ether was added under nitrogen at a rate such that the mixture temperature did not rise above 5°C. After the addition was complete, the mixture was allowed to stir at room temperature for an additional two hours. A saturated solution of ammonium chloride was slowly added until the solution turned blue litmus paper red. The aqueous layer was then extracted three times with ether. The ether layer was dried over magnesium sulfate, and the ether evaporated on a rotary evaporator to yield 20.5 g. (94%) of a mixture of the _cis_ and _trans_ alcohols.

The compounds were subjected to GC analysis on the FFAP column and two peaks were noted. The compounds were collected from the column and the first was found to have a m.p. 69-71°C. This compound was thought to be the _trans_ isomer (lit., m.p. 71°C,[44] 66-67°C).[45] The second compound was thought to be the _cis_ isomer and was found to have a m.p. 91-94°C (lit., m.p. 98°C,[44] 89-90°C).[46]

_Cis and trans-4-tert-butyl-1-chloro-1-methylcyclohexane_. According to the method of Kirk,[47] fifteen grams (0.083 mole) of _cis_ and _trans_-4-tert-butyl-1-methylcyclohexanol was dissolved in chloroform and the solution was saturated with dry hydrochloric acid at 0°C for four hours. Anhydrous sodium sulfate was then added to absorb the water formed during the reaction. The solution was filtered and the chloroform removed by rotary evaporation. The crude product was distilled. Unfortunately, starting material was sublimed into the distillate, so the distilled mixture was subjected to column chromatography. Using silica gel and pentane, a mixture of the *cis* and *trans* chlorides was obtained free from other impurities as analyzed by GC with the FFAP column. The combined yield was 9.02 g. (54%) of the *cis* and *trans* chlorides.

*Attempted synthesis of cis and trans-1-bromomercuri-4-tert-butyl-1-methylcyclohexane.* According to the method of Robson and Wright,[48] 0.5 g. (0.0013 mole) of *cis* and *trans* 4-tert-butyl-1-chloro-1-methylcyclohexane was added to 5 ml. of diethyl ether.

This solution was slowly added under nitrogen to 0.350 g. (0.0144 mole) magnesium chips. The mixture was stirred until it became cloudy. Then an additional 2 g. (0.0052 mole) of the chloride was slowly added over a period of 3 hours. It was noted that the magnesium chips became dark brown, so 0.350 g. (0.0144 mole) of new chips were added every 3 hours for 12 hours. The solution was transferred under nitrogen to another flask, and 1.63 g. (0.006 mole) of mercury bichloride was slowly added. The mixture was stirred for two hours, water added, and the solution was extracted with 70 ml. of chloroform. Concentration of the solution and a subsequent check by NMR revealed no products with peaks attributable to the desired organomercuric halide. A flame test of the isolated crystals showed them to be entirely inorganic.

The Grignard reaction was repeated using the entrailment method described by Pearson, Cowan, and Beckler.[49] This trial also proved to be ineffective.

To discover which stage of the reaction was not proceeding properly, the Grignard reaction was repeated a third time using the entrainment method and the product mixture was hydrolyzed. The product analysis showed that while only 4% of the starting material remained, the _cis_ and _trans_ 4-tert-butyl-1-methylcyclohexane products were accompanied by equal yields of 4-tert-butyl-1-methylcyclohexa-2-ene and 4-tert-butyl-1-methylenecyclohexane. A trace amount of the alcohol also appeared. It was concluded therefore, that the Grignard reagent reacted with starting material as quickly as it was formed.

_Cis and trans-4-tert-butyl-1-methylcyclohexane_. A 20 g. (0.135 mole) sample of _p_-tert-butyltoluene was reduced under 1800 psi of Hydrogen gas in a hydrogenation bomb. The Raney Nickel catalyst used had been dissolved in cyclohexane and the water had been removed by refluxing the catalyst in cyclohexane with a Dean Stark trap.

## Ozonolysis of Compounds

General Method. A small sample of compound was usually dissolved in a few milliliters of methylene chloride. A small amount of internal standard was then added. The reaction vessel was cooled to 0°C for a few minutes, then ozone gas was allowed to pass through the reaction chamber. After the ozone trap began to yellow, samples of 0.1 ml. were withdrawn from the methylene chloride solution every 3-5 minutes and these samples were placed in a test tube with a gram of a 50/50 mixture by weight of sodium thiosulfate and potassium iodide. This mixture was then stirred thoroughly with a small spatula. When the color in the test tube disappeared, the test tube was placed in the refrigerator. This process was repeated until enough samples had been taken to insure the necessary data points. The samples were injected into the GC instrument fresh from the refrigerator within at least 10 hours after collection.

Ozonolysis of bromomercuricyclohexane. A 0.635 g. (0.00175 mole) sample of bromomercuricyclohexane was dissolved in 35 ml. of methylene chloride. To this solution was added 0.045 g. (0.0012 mole) of nitromethane as an internal standard. This solution was then introduced into the reaction vessel and ozonized at 0°C for 30 minutes. A 50 μl sample of the methylene chloride solution was then injected into the GC instrument using the FFAP column. Cyclohexanol and cyclohexanone were found to be present by coinjection of known samples of these compounds.

Ozonolysis of *cis*-4-tert-butylcyclohexanol. A 0.60 g. (0.0038 mole) sample of *cis*-4-tert-butylcyclohexanol and 1.2 g. (0.027 mole) of nitromethane was dissolved in 10 ml. of methylene chloride. The solution was then introduced into the reaction vessel and ozonized at 0°C. Samples were taken at 6 and 10 minutes. GC analysis revealed that only 10% starting material was present after 10 minutes. A fresh sample was prepared and ozonized and samples were taken at 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, and 10 minutes. This proved unsatisfactory because products were lost and an apparent increase of starting material was obtained. In other runs, the upper trap was removed, a sample was withdrawn, and the trap was secured again. However, in this case the upper trap was removed during the duration of sampling. It was assumed that the nitromethane was slowly escaping.

Ozonolysis of *trans*-4-tert-butylcyclohexanol. The above reaction was repeated using the *trans* isomer of the alcohol and using 0.60 g. (0.014 mole) of nitromethane. Samples were taken at 6 and 10 minutes. Only slightly more unreacted alcohol was present than observed above.

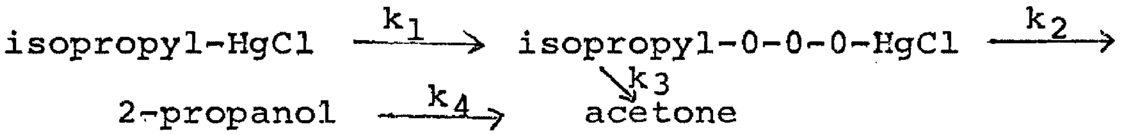
Ozonolysis of cis and trans-4-tert-butylcyclohexanol. A 50/50 mixture of the alcohols weighing 0.75 g. (0.048 mole) was ozonized while using 0.200 g. (0.045 mole) of nitromethane as an internal standard. Samples were withdrawn at 0, 3, 5, 8, 10, 16, and 20 minutes. GC analysis revealed that all starting material had disappeared after 5 minutes, and that the cis isomer was disappearing more rapidly than the trans.

Ozonolysis of cis-4-tert-butylcyclohexanol and bromomercuricyclohexane. To a 0.060 g. (0.00038 mole) sample of cis-4-tert-butylcyclohexanol, was added 0.206 g. (0.00059 mole) of bromomercuricyclohexane and 0.025 g. (0.0055 mole) of nitromethane in 10 ml. methylene chloride. Samples were collected at 0, 3, and 5 minutes at 0°C, and subjected to GC analysis.

Ozonolysis of trans-1-bromomercuri-4-tert-butylcyclohexane. In 10 ml. of methylene chloride were dissolved 250 mg. (0.00597 mole) of trans-1-bromomercuri-4-tert-butylcyclohexane and 0.025 g. (0.00556 mole) of nitromethane. Ozone was bubbled through the reaction at 0°C and aliquots were collected at 5, 10, 20, and 30 minutes. The samples were worked up in the usual way and subjected to GC analysis.

Ozonolysis of cis-1-bromomercuri-4-tert-butylcyclohexane. A 0.150 g. (0.000358 mole) sample of cis-1-bromomercuri-4-tert-butylcyclohexane and 0.015 g. (0.0033 mole) of nitromethane were dissolved in 6 ml. methylene chloride. Ozone was bubbled through the reaction at 0°C and aliquots were withdrawn and quenched at 5, 10, 15, and 20 minutes. The samples were worked up in the usual way and subjected to GC analysis.

<u>Calculation of rate of formation of 2-propanol and acetone from data of Rivera.</u>[17] Assuming the following equation:



$$\begin{tikzcd} \text{isopropyl-HgCl} \arrow[r, "k_1"] & \text{isopropyl-0-0-0-HgCl} \arrow[dl, "k_2"] \arrow[d, "k_3"] \\ \text{2-propanol} \arrow[r, "k_4"] & \text{acetone} \end{tikzcd} \qquad (36)$$

where $k_2 = k_3$ and both are extremely fast; a program was devised by Mr. George Wolfe to determine if the theoretical concentrations of 2-propanol and acetone would fit the concentrations found. Assuming the pathway involving $k_3$ did not exist, the following equations were solved with the aid of a Wang Model 600 Programmable Calculator:

$$[\text{2-propanol}] = \frac{k_1[\text{isopropyl-HgCl}]_o}{(k_4 - k_1)} [e^{-k_1 t} - e^{k_4 t}] \qquad (37)$$

$$[\text{acetone}] = [\text{isopropyl-HgCl}]_o \left[ 1 + \frac{1}{k_1 - k_4} \left( k_4 e^{-k_1 t} - k_1 e^{-k_4 t} \right) \right] . \qquad (38)$$

If any of the acetone was being formed directly from the isopropyl mercuric chloride, the calculated concentrations of isopropanol and acetone would not agree with the actual concentrations found.

Upon failure to give the observed concentrations, a pathway involving $k_3$ is necessary. Assuming a disproportionation reaction of Isopropyl-0-0-0-HgCl to acetone and 2-propanol via $k_3$ and $k_2$, the following equations were solved with the aid of the Wang 600 Programmable Calculator:

$$[\text{2-propanol}] = \frac{k_1[\text{isopropyl-HgCl}]_o}{2(k_4-k_1)}[e^{-k_1t}-e^{k_4t}] \qquad (39)$$

$$[\text{acetone}] = [\text{isopropyl-HgCl}]_o - [(\text{isopropyl-HgCl}) + (\text{2-propanol}) + (\text{fragmentary products})] \qquad (40)$$

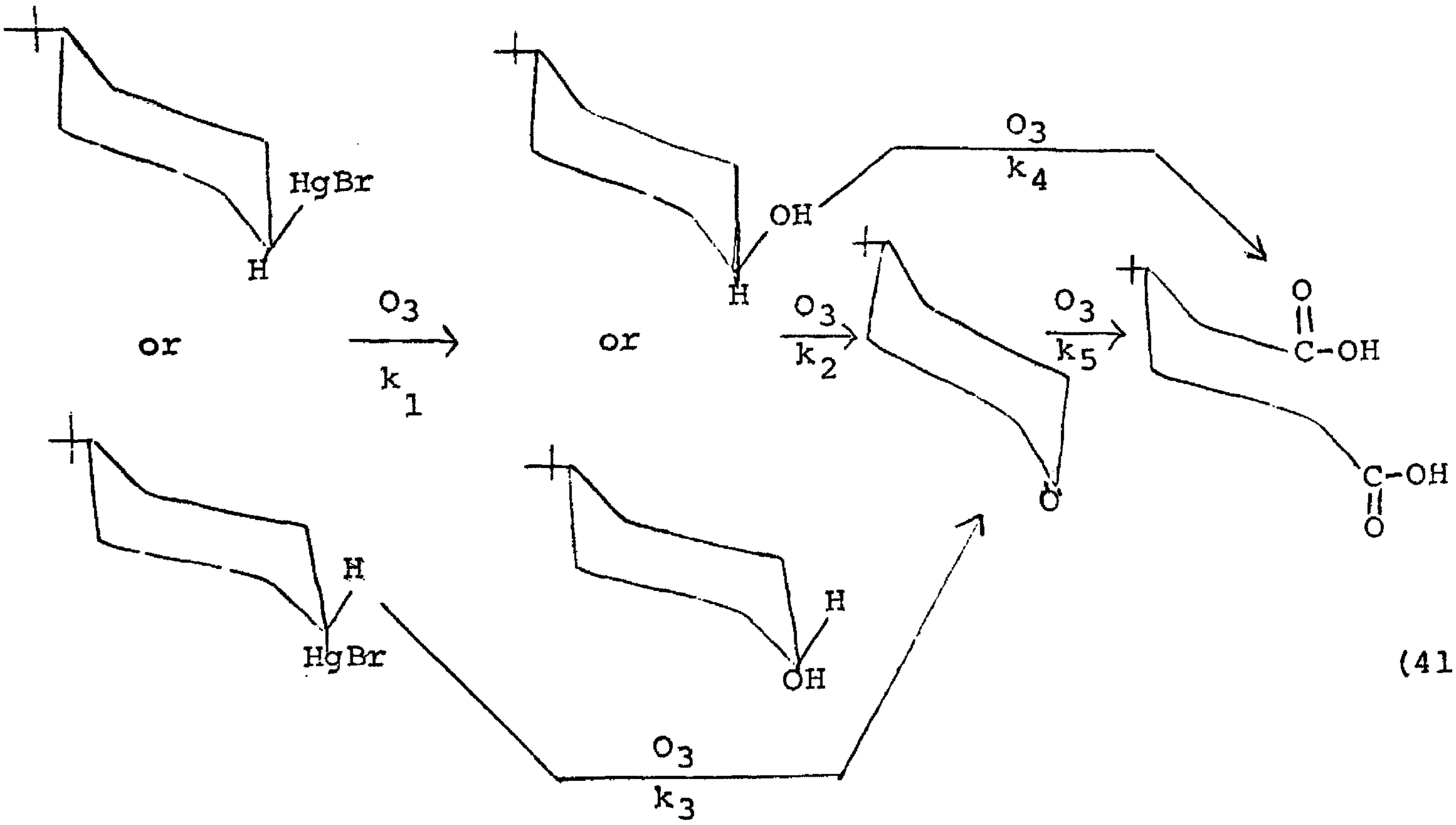
The amount of fragmentary products such as acetic acid and carbon dioxide were calculated by adding the actual amount of acetone and 2-propanol found in the reaction and subtracting this amount from the initial amount of isopropyl mercuric chloride present. This number was assumed to be the amount of organomercurial that should have been present. The difference between this number and the actual amount of organomercurial found in the reaction was taken to be the amount of fragmentary products.

# CHAPTER III

# RESULTS

## Products of Ozonolysis

All the organomercurials were oxidized to alcohols or to ketones by reaction with ozone. After prolonged ozonolysis, the ketones were usually cleaved to fragmentary products which were assumed to be the corresponding diacids. All the alcohol products were oxidized further to ketones, and subsequently to the diacids in the presence of ozone. This sequence is shown below.



(41)

*Ozonolysis of cis-4-tert-butylcyclohexanol.* Ozonolysis of *cis*-4-tert-butylcyclohexanol was complete after 10 minutes at 0°C. Only 4-tert-butylcyclohexanone was detected by GC analysis. The reaction was too fast to obtain the absolute rate constant.

When the reaction was repeated and aliquots were taken every 30 seconds, a lesser amount of 4-tert-butylcyclohexanone than usually observed and a loss of internal standard were detected.

GC analysis of the quenched aliquots showed only product and unreacted starting material.

*Ozonolysis of trans-4-tert-butylcyclohexanol.* In contrast to the *cis* alcohol, *trans*-4-tert-butylcyclohexanol was not completely converted to the ketone after 10 minutes of ozonation under identical ozone flow conditions. This reaction was similar, in that determination of its absolute rate constant was impossible by the techniques described on page 34.

*Ozonolysis of a 50/50 mixture of cis and trans-4-tert-butylcyclohexanol.* Although rate determinations of the above reaction were not feasible by these techniques, a competition reaction between these two alcohols was possible. The rate of disappearance of each alcohol was plotted against time. By dividing the slope of the rate of reaction of the *cis* alcohol by that of the *trans* alcohol, it was found that the *cis* alcohol reacted 3.76 times faster than the *trans* alcohol. Other points were obtained for the *trans* alcohol which fit the line, but do not appear on the graph. (See Figure 2).

*Ozonolysis of cis-4-tert-butylcyclohexanol in the presence of bromomercuricyclohexane*. To make absolutely certain that the alcohols were not epimerizing under all of the reaction conditions, *cis*-4-tert-butylcyclohexanol was ozonized in the presence of bromomercuricyclohexane. Bromomercuricyclohexane was chosen since it was a compound of similar structure, it would give rise to the same type of intermediate, and its oxidation products would be of different retention times than those of 4-tert-butylcyclohexanol and 4-tert-butylcyclohexanone. After 30 minutes of ozonolysis at 0°C, the *cis* alcohol had completely disappeared. The reaction was checked every five minutes by GC analysis, and at no time did any *trans* alcohol appear. Formation of cyclohexanol and cyclohexanone proceeded smoothly.

*Ozonolysis of trans-1-bromomercuri-4-tert-butylcyclohexane*. Ozonolysis of *trans*-1-bromomercuri-4-tert-butylcyclohexane was complete after 20 minutes. 4-Tert-butylcyclohexanone and 4-tert-butylcyclohexanol were the major products. A very small amount of the *cis* alcohol was formed, however, no large build-up occurred. It was also observed that initially the ketone concentration was less than the alcohol, but after 10 minutes the ketone was the major product. (See Figure 3).

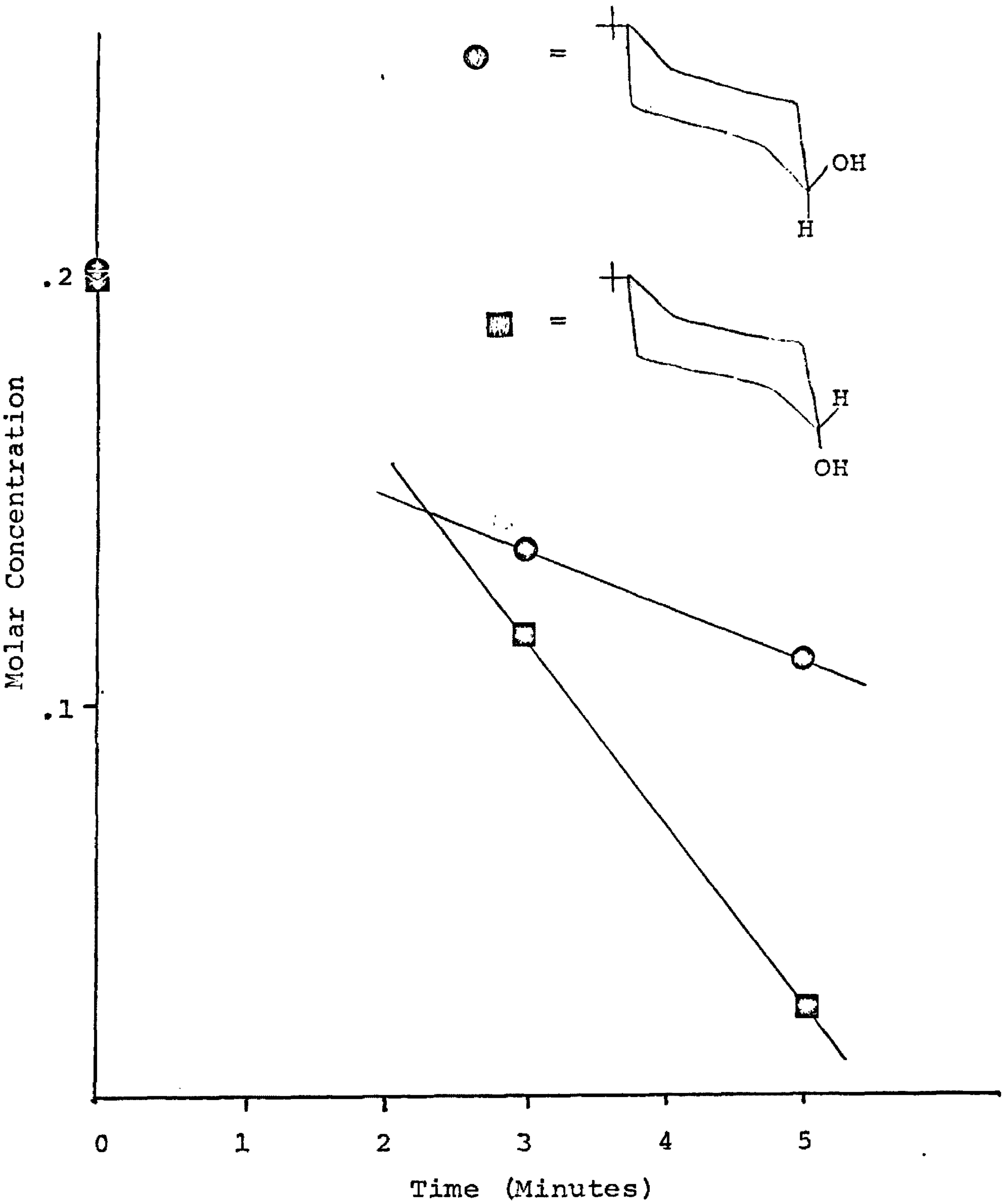


Figure 2

Ozonolysis of trans-4-t-butyl Cyclohexyl Mercuric Bromide

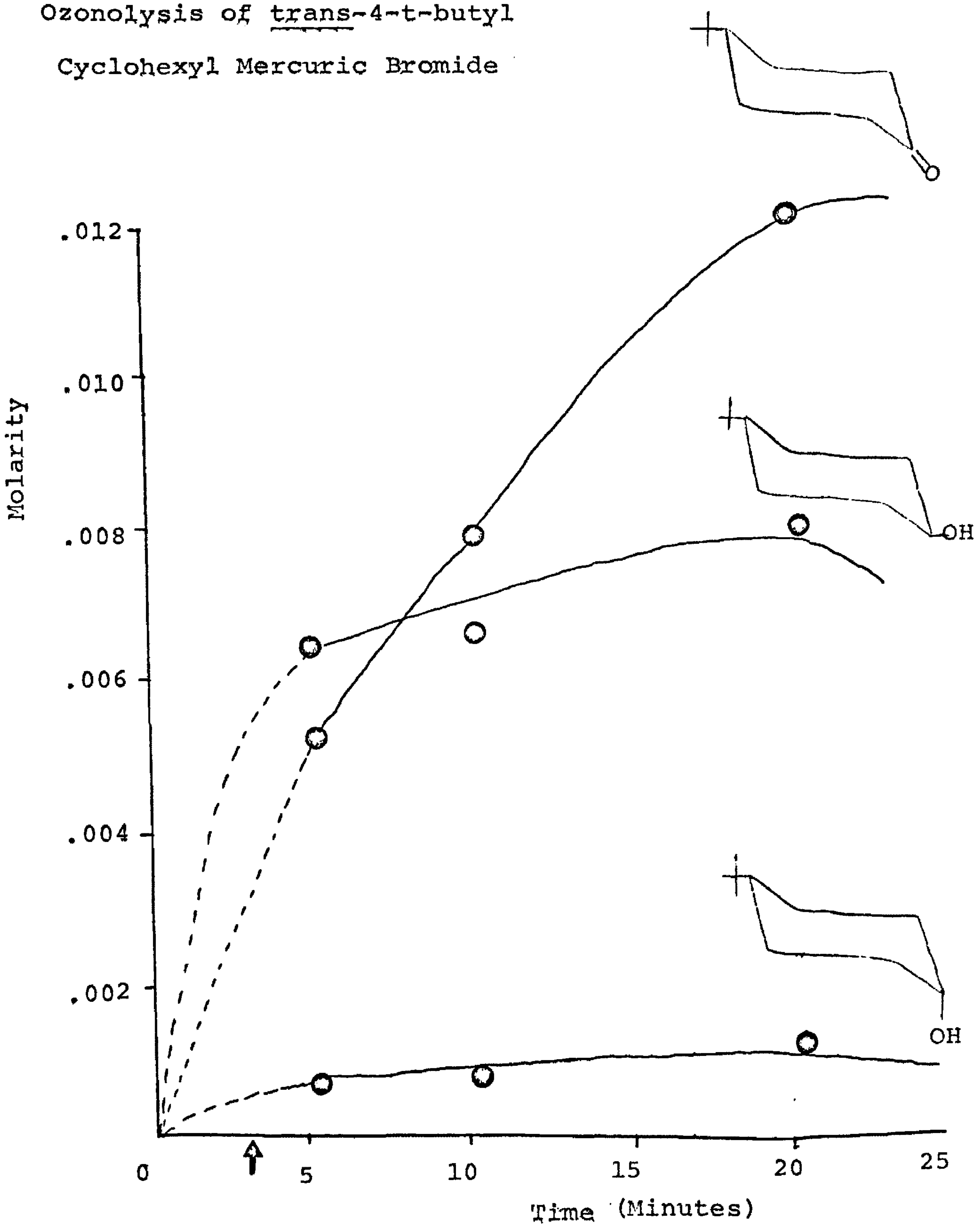


Figure 3

*Ozonolysis of cis-1-bromomercuri-4-tert-butylcyclohexane*. Ozonolysis of *cis*-1-bromomercuri-4-tert-butylcyclohexane was complete after 20 minutes. 4-Tert-butylcyclohexanone and *trans*-4-tert-butylcyclohexanol were the major products. It was noted that the ketone was always present in greater amounts than either alcohol. Initially, the *cis* alcohol was the predominant alochol. However, after the solution became saturated with $O_3$, the *trans* alcohol became the predominant alcohol. (See Figure 4).

*Rate determination of the ozonolysis of secondary alcohols to ketones*. In a program prepared by Mr. George Wolfe, the rate of loss of isopropyl mercuric chloride and the rate of acetone formation were compared. The absolute rate constant for loss of ]-propanol and formation of acetone had been previously reported.[17] By comparing the theoretical amount of acetone which would be formed indirectly from isopropyl mercuric chloride through 2-propanol, it was concluded that the actual formation of acetone occurred not only via the intermediate alcohol, but also directly from the organomercurial. (See Figure 5).

Referring to the sequence on page 37, one must conclude that the intermediate, Isopropyl-0-0-0-HgCl, probably disproportionates to form a mole of ketone and a mole of alcohol. The real amount of acetone and 2-propanol formed is denoted by a solid line in Figure 5, and the calculated

Ozonolysis of cis-4-t-butyl
Cyclohexyl Mercuric Bromide

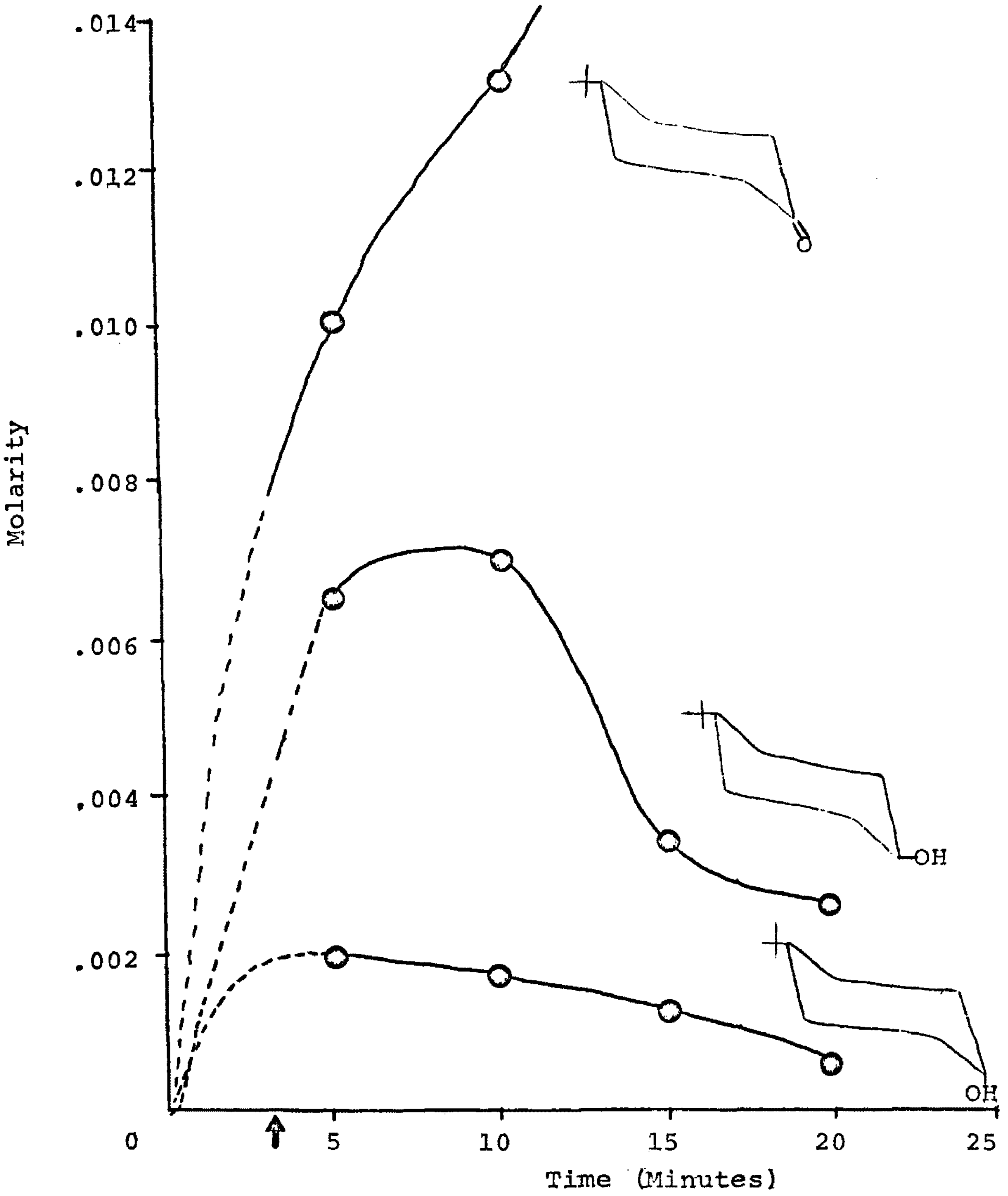


Figure 4

Concentration Build-up for Products from a Non-Disproportionating Intermediate versus the Actual Concentration of Products

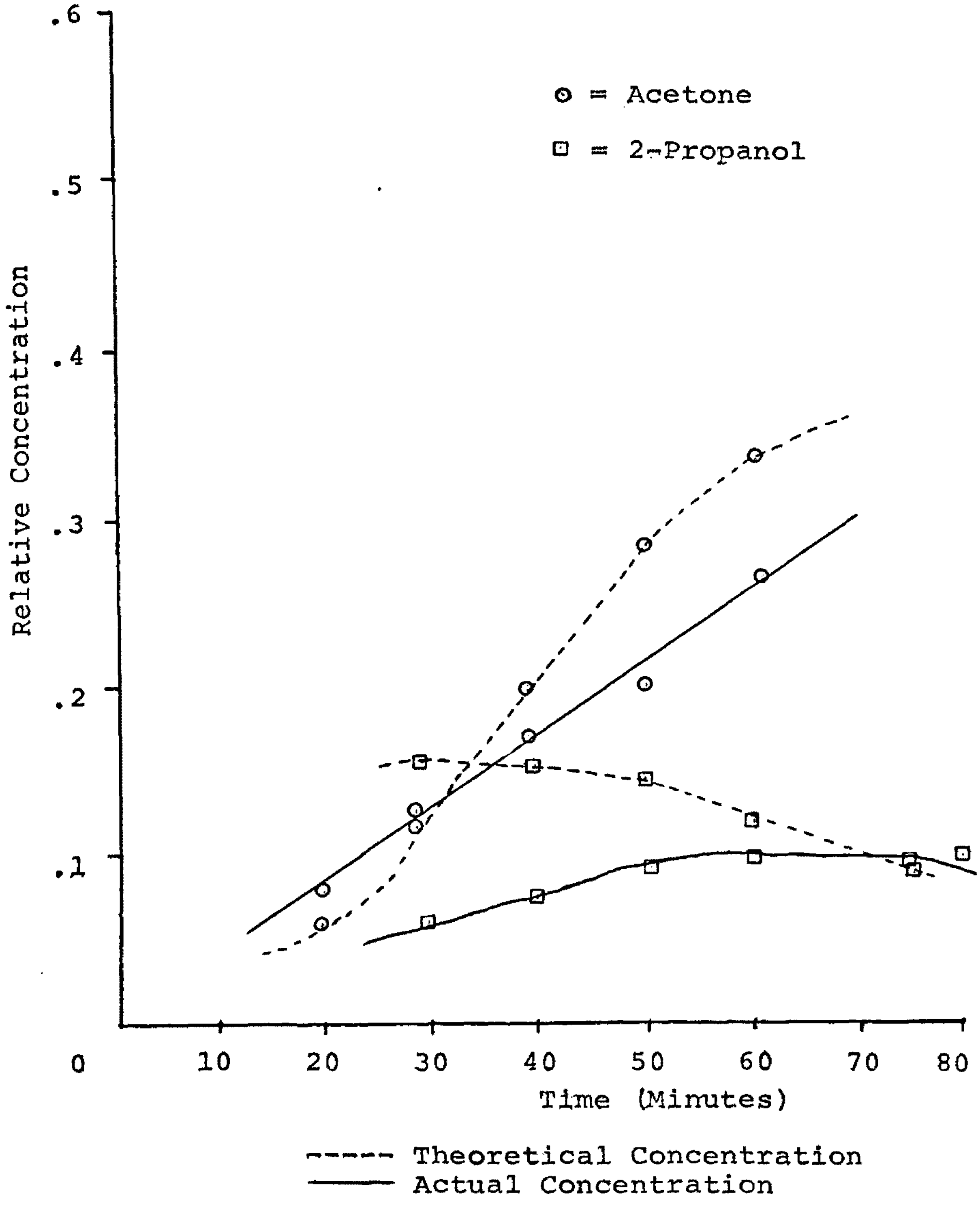


Figure 5

amounts (assuming no disproportionation) are denoted by dotted lines. The curves obviously do not match. Assuming that the intermediate Isopropyl-0-0-0-HgCl did decompose by disproportionation, then the data taken from the computer results from page 38 should match the concentrations found in the reaction. It was found and shown in Figure 6, that the calculated concentrations from page 38 indeed matched the actual concentrations found by Rivera.[17]

Concentration Build-Up for Products from a Actual Concentration Disproportionating Intermediate Versus the Actual Concentration of Products

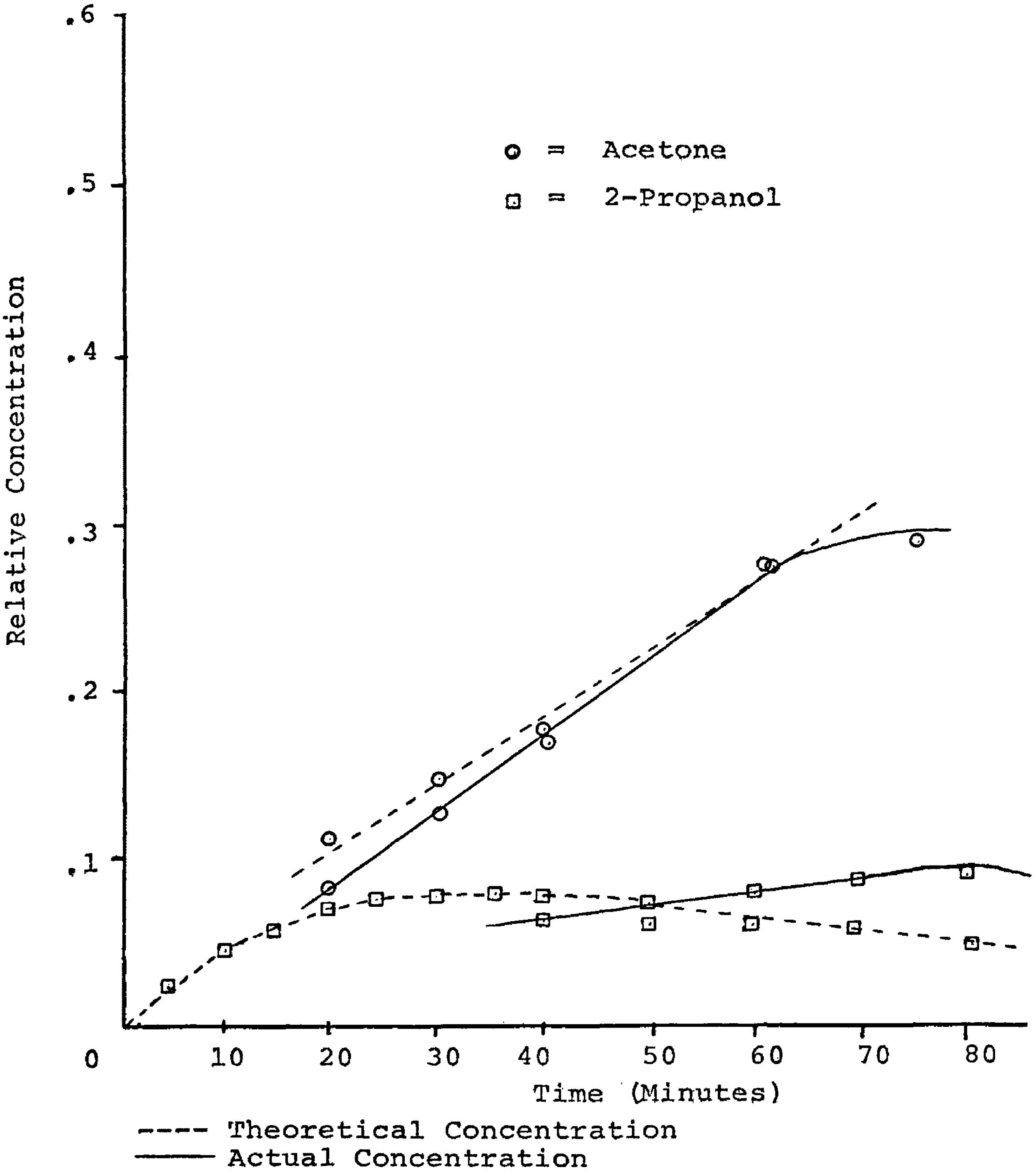


Figure 6

# CHAPTER IV

# DISCUSSION

Stereospecificity of Organomercurial Ozonolysis. It was found that trans-4-tert-butylcyclohexanol predominated over its cis isomer when either cis or trans-1-bromomercuri-4-tert-butylcyclohexane was ozonized. The corresponding ketone, 4-tert-butylcyclohexanone, was also a major product. The disproportionate amount of trans alcohol could have occurred by a more rapid oxidation of the cis alcohol by ozone, by an epimerization of the cis alcohol by ozone, or by a mechanism which allowed the epimerization of an intermediate.

The argument that cis-4-tert-butylcyclohexanol was more rapidly oxidized and therefore, a minor product because it disappeared quickly, does not appear to be borne out for the following reason. It was noted that cis-4-tert-butylcyclohexanol reacted only 3.76 times faster than the trans isomer. It would seem that the cis alcohol would have to disappear much faster to have had the effect that was observed. (See Figure 2). However, further kinetic studies will have to be performed to confirm this, unequivocally.

Epimerization of either alcohol was not observed when each was ozonized alone, or in the presence of other organomercurials. Thus the argument that epimerization of the cis alcohol caused the trans alcohol to predominate, is ruled out.

From the previous arguments it must be assumed that the preponderance of the trans alcohol must occur via an epimerization of some intermediate. Perhaps from stereochemical evidence, the mechanism of this epimerization can be demonstrated.

Mechanisms and Product Distribution in Organomercurial Ozonolysis. As shown earlier, the $S_E1$ and $S_Ei$ mechanism demands that a free carbanion be released as a reactive intermediate. If the $S_E1$ or $S_Ei$ mechanism were in operation, a mixture of cis and trans-4-tert-butylcyclohexanol would be expected from the ozonolysis of either cis or trans-1-bromomercuri-4-tert-butylcyclohexane. The fact that the trans alcohol was a major alcohol component when either cis or trans-1-bromomercuri-4-tert-butylcyclohexane was ozonized might argue for the $S_E1$ or $S_Ei$ mechanisms. The fact that the $S_E1$ or $S_Ei$ mechanism is probably not in operation was demonstrated by Waters.[51] The rate of organomercurial ozonolysis decreased for the series

$$3° > \text{benzyl} > 2° > \text{methyl} > 1° \ .$$

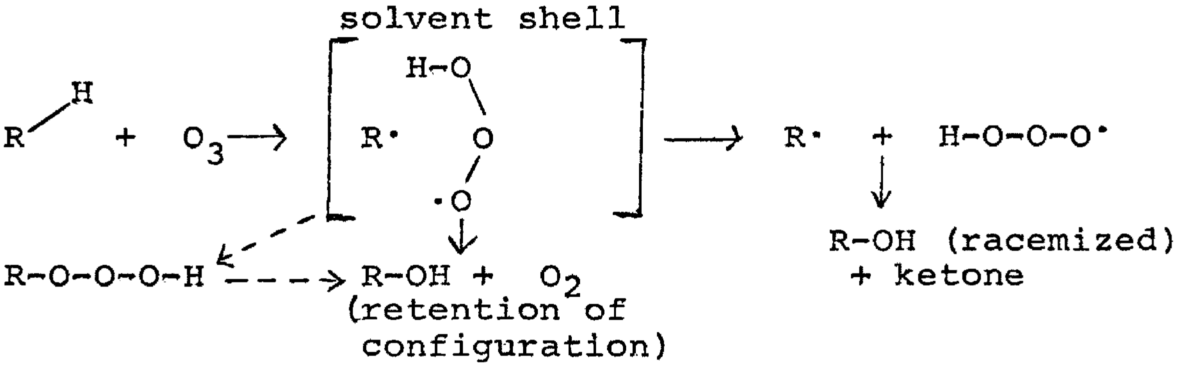
These workers concluded that this series was unlikely for an $S_E1$ or $S_Ei$ mechanism, because the opposite order would have been expected for carbanion intermediates. Also, if the $S_E1$ or $S_Ei$ mechanism were in operation, one would expect the same ratio of alcohol isomers for ozonolysis of both the cis and the trans organomercurials. Each isomer gave a different ratio of cis and trans alcohols.

Unfortunately, invoking a pure four-center or $S_E2$ mechanism does not adequately fit the observed results either. In either case the cis mercurial should have given the cis alcohol and the trans mercurial should have given the trans alcohol, exclusively.

In order to distinguish between the $S_E2$ and four center mechanisms, either the ozone molecule would have to be modified or a solvent study would be necessary. Ozone cannot be modified in order to make one end more polar than the other without changing its character completely. This approach has been used by Charman, Hughes, and Ingold.[52] These workers employed different complexes of Hg(II), and reacted these with optically active organomercuric halides. By changing the solvent polarity, a large rate increase or decrease of ozonolysis would indicate either a polar or non-polar transition state. This would have implied an $S_E2$ mechanism, which exhibits some charge separation in the transition state of the slow step (see page 17). Had there been no correlation between solvent polarity and reaction rate, the four-center mechanism could have been implied.

It is therefore possible that another mechanism entirely different from the $S_E2$ or four center process is taking place.

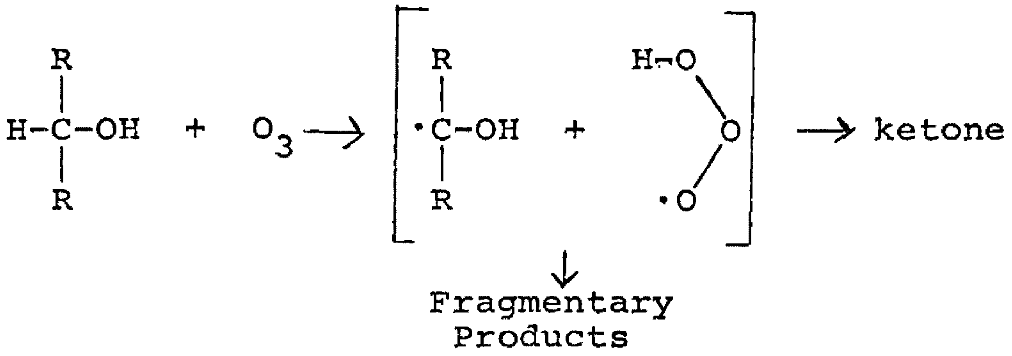
Mechanisms for the Ozonolysis of Alkanes and Alcohols. To help formulate a mechanism for organomercurial ozonolysis, other mechanisms which involve similar attack by ozone or formation of similar products to organomercurial ozonolysis must be discussed. A mechanism postulated by Hamilton,[53] involving attack by ozone on alkanes, invokes the following sequence:



(42)

This mechanism would seem to fit the results found with 1-bromomercuri-4-tert-butylcyclohexane, since both the cis and trans alcohols, as well as the ketone, were produced from each pure isomer. In the case of organomercurials, the ozone would attack the C-Hg bond in the same fashion as ozone attacks the C-H bond shown above in formula 42. The C-Hg bond is a weaker bond that the C-H bond with respect to formation of radicals. The C-Hg bond ranges from 41-51 kcal, whereas the C-Hg bond is on the order of 95 kcal.[54]

The existence of radical pairs as shown in formula 42 was also affirmed by Whitting upon ozonolysis of alcohols.[55] This is shown in formula 43.



(43)

The radical pair formed by the analogous organomercurial could then go on to form an intermediate which could epimerize.

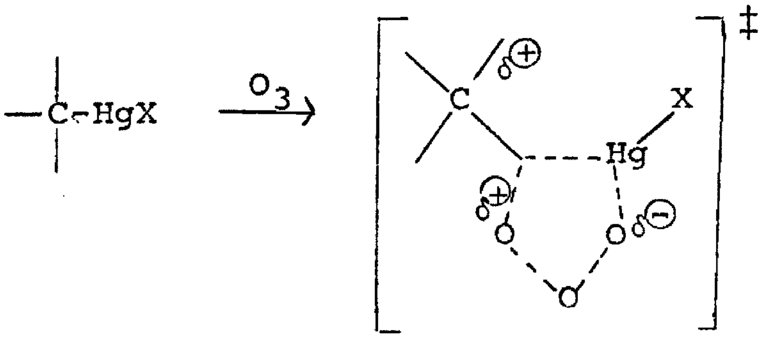
Another possibility would be that the radical could become separated from the solvent and the carbon become $sp^2$ hybridized. In this case the most stable trioxide would result, which would be the trioxide of the trans configuration.

It therefore seems likely that any mechanisms of ozonolysis invoking radical pairs are very reasonable. Moreover, since certain "fragmentary products" such as acids have been isolated from organomercurial ozonolysis,[56] it is likely that they come from this stage. However, if radical pairs exist, one would expect dimers and alkanes.

Since the scope of this project was stereochemical in nature, these products were not looked for. Future studies in this area would be of advantage.

*Transition States and Intermediates in Organomercurial Ozonolysis*. Though the formation of an intermediate involving radical pairs as precursors may be intriguing, other transition states have been suggested for the first step of the reaction.

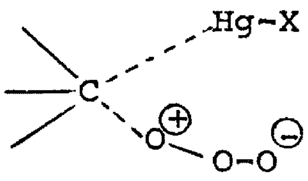
A cyclic four-center-like mechanism where initial attack is on the $sp^3$ orbital of carbon has been suggested by Waters.[14]



(44)

This is similar to the transition state predicted for the bromine or triiodide cleavages of the carbon-mercury bond.[57] The carbon $sp^3$ orbital is depicted as a solid line, while the areas of bond formation are indicated by dotted lines. The charge density on the carbon will be changed by electronic factors rather than by cleavage of the bond.

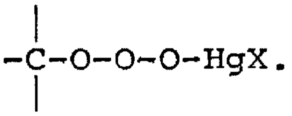
If, however, attack is by an $S_E2$ mechanism, the following transition state seems likely:



(45)

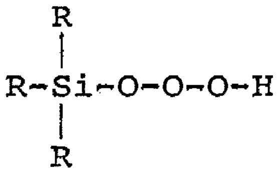
Both the $S_E2$ and four center attack require a front side attack and retained stereochemistry.

Eventually, by either the four center or the $S_E2$ process, the transition state should lead to the trioxide intermediate below:

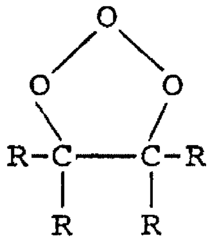


$$-\overset{|}{\underset{|}{C}}-O-O-O-HgX.$$

This intermediate is similar to those postulated for the ozonolysis of organosilanes[58] and olefins[59] as shown below.



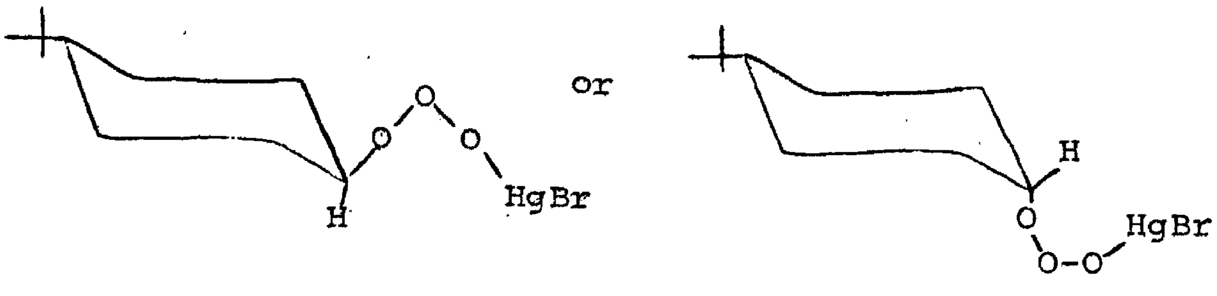
$$R-\overset{R}{\underset{R}{Si}}-O-O-O-H$$



(46)

This type of intermediate is also suggested by the speculation that it could give rise to the products observed.

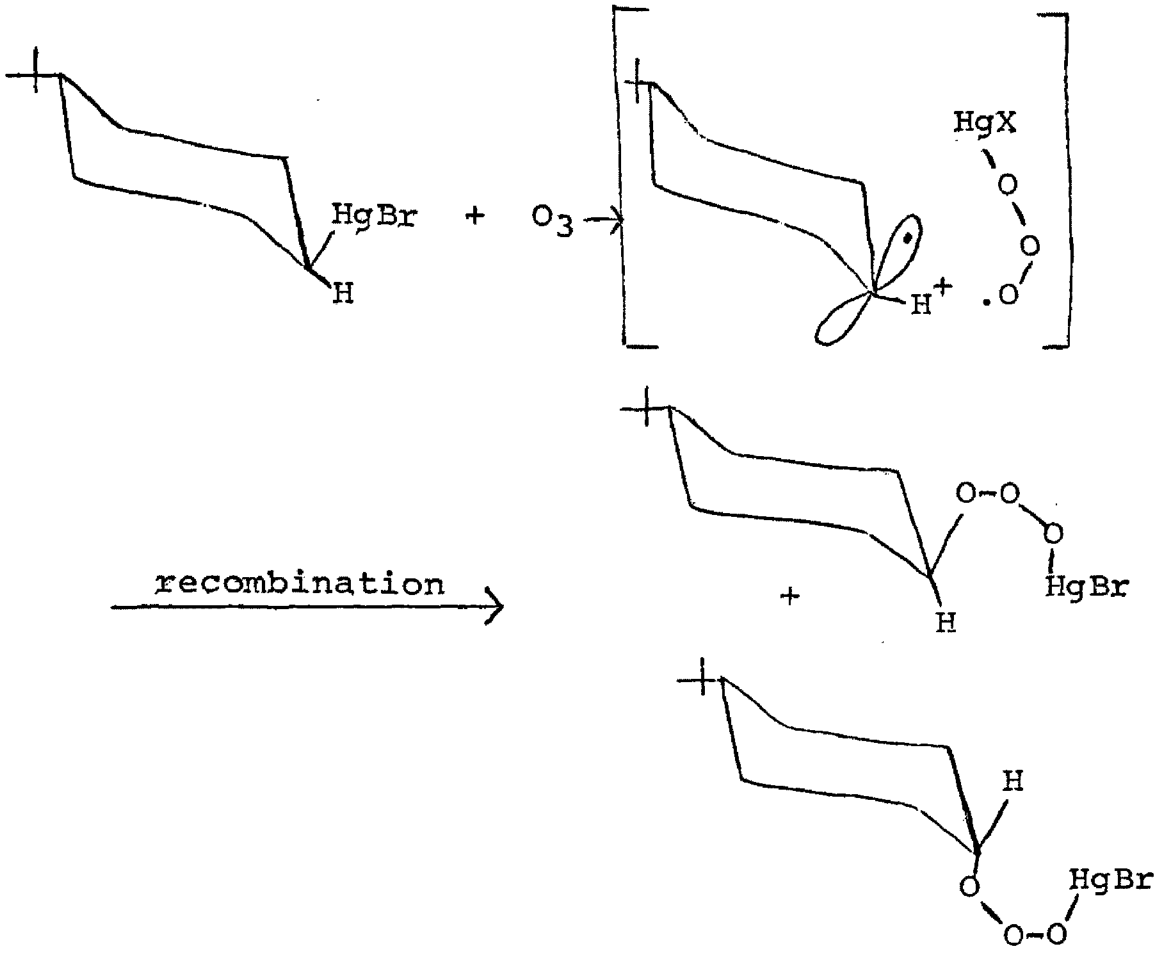
<u>Mechanism of Ozonolysis of *cis* and *trans*-1-Bromomercuri-4-tert-butylcyclohexane.</u> As shown in the previous discussion, the intermediates below



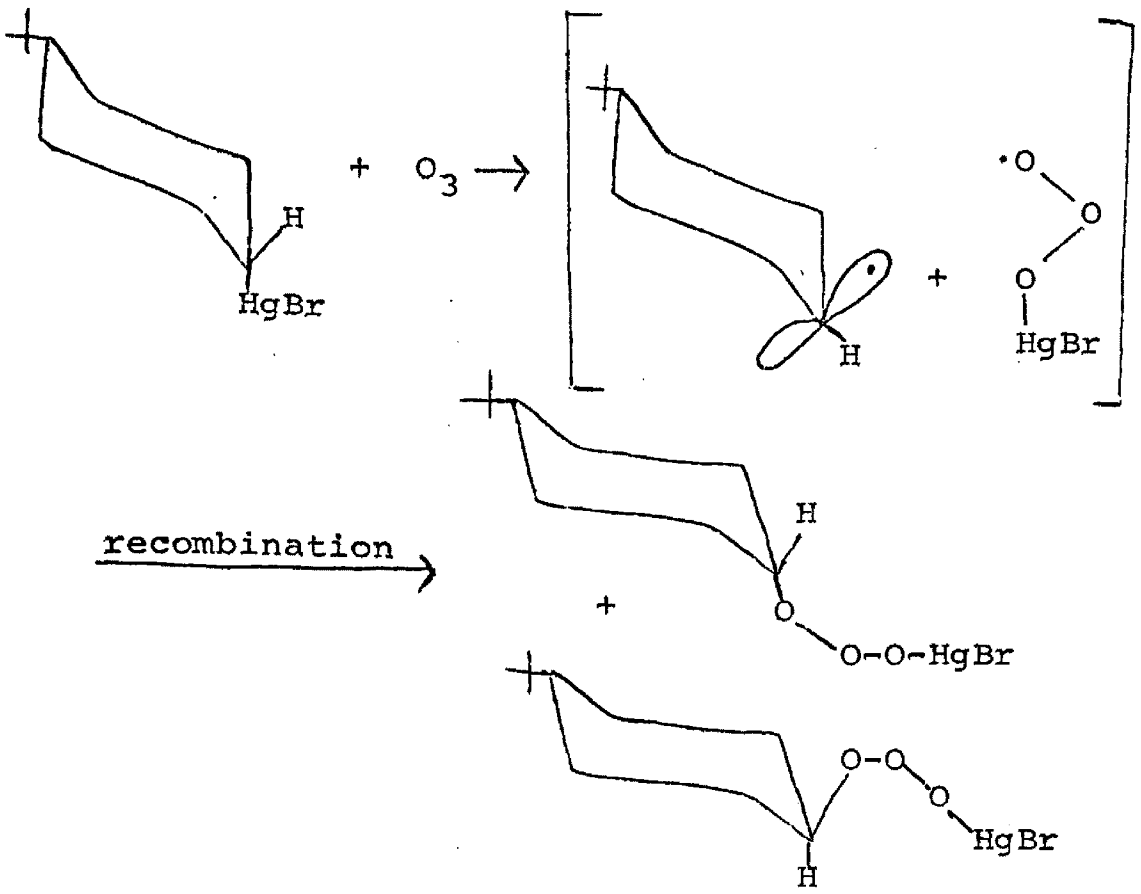
(47)

could form by one of three sequences for each isomer. (Radical intermediates are indicated by a bracket and transition states are indicated by a bracket with a ‡).

Sequence I. Radical Pair

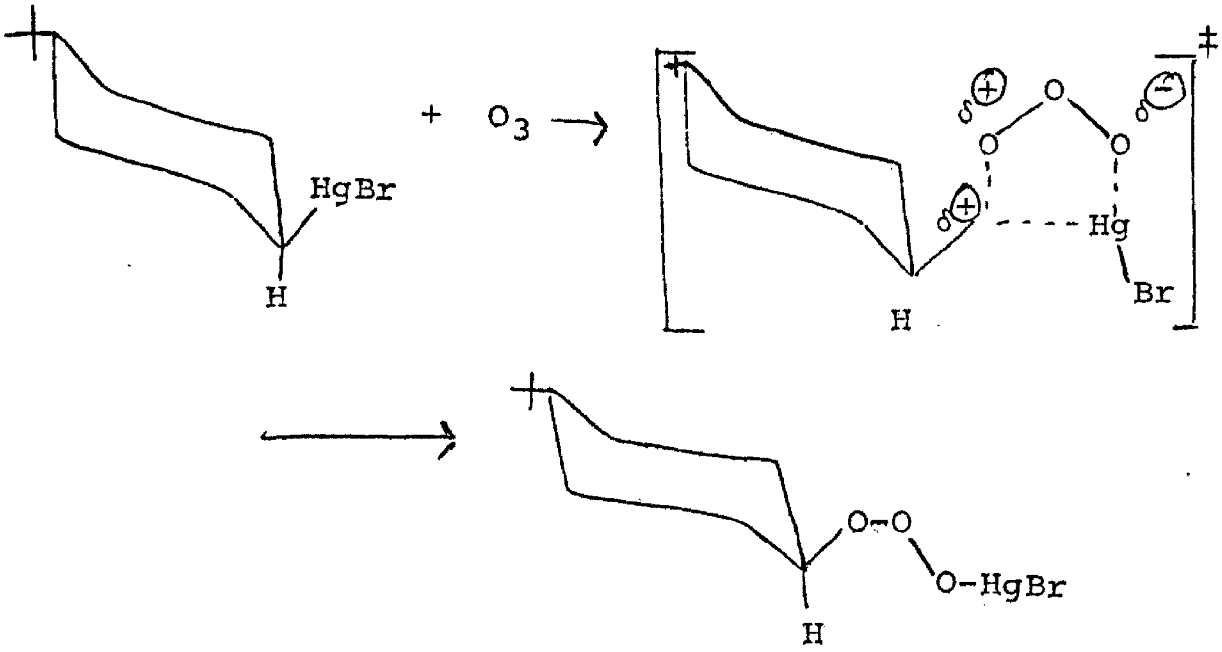


(48)

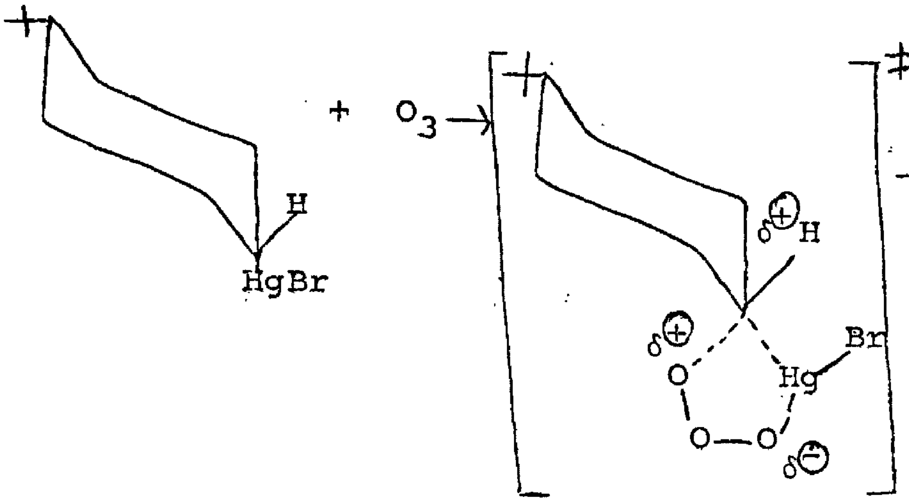


(49)

Sequence II. Four-Center-Like

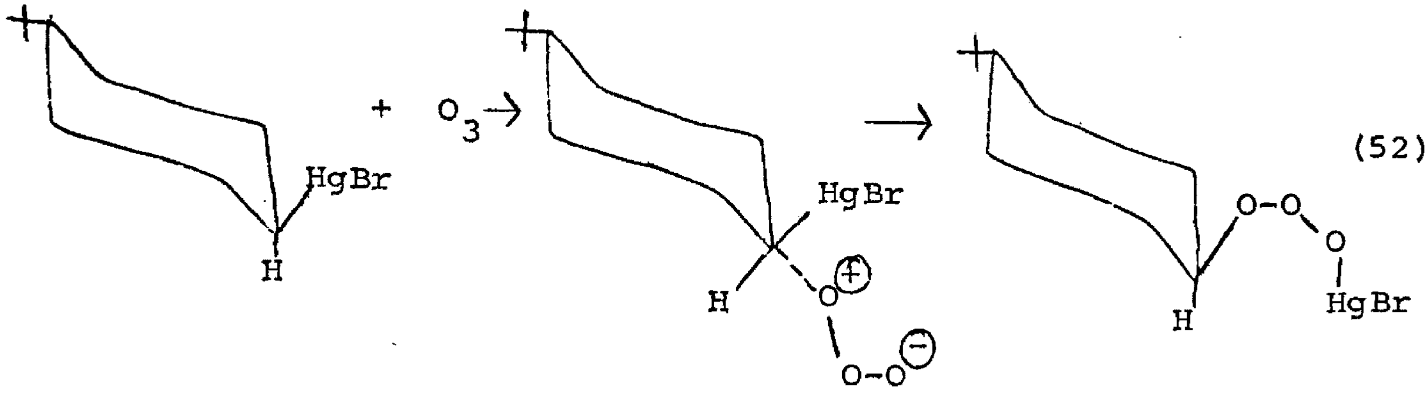


(50)

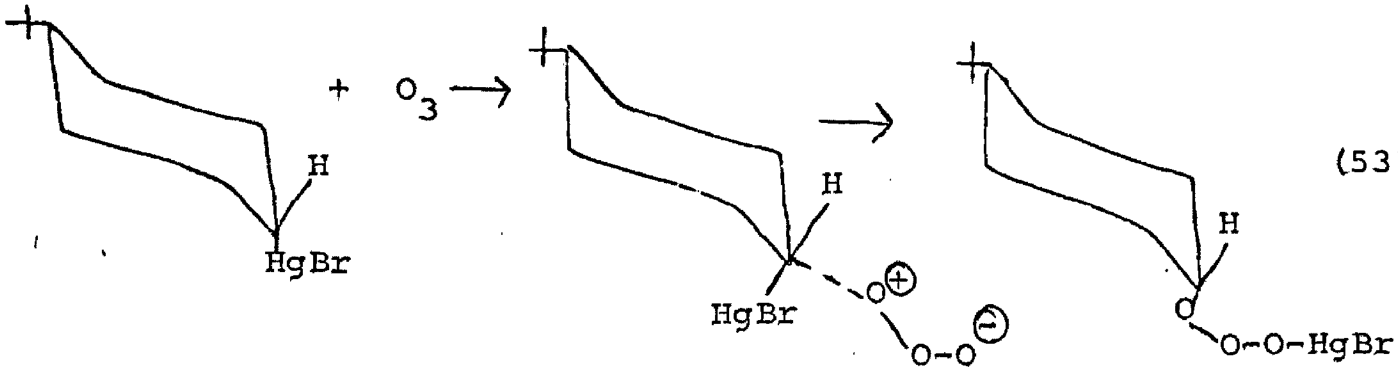


(51)

Sequence III. $S_E2$

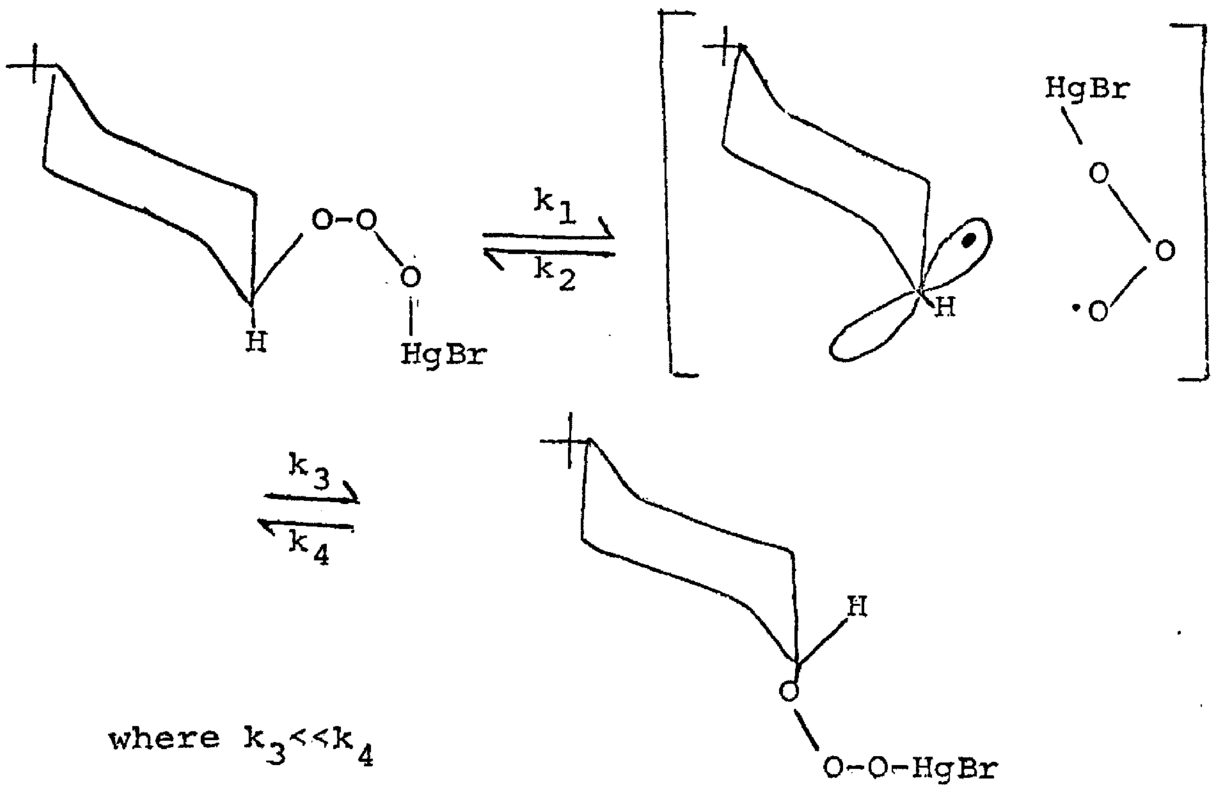


(52)



(53)

Since it was observed that trans-4-tert-butylcyclohexanol predominated in both cases, it must be assumed that the trans intermediate is more easily formed or else is more stable and less readily oxidized to other products. Also, since the cis mercurial gave a large amount of the trans alcohol there must be some means for converting the cis intermediate to the trans, if sequence I is not in operation. This can be explained by formation and interconversion of the intermediates of sequence II or III. Once one of these intermediates is formed by perhaps the four-center mechanism (44) an interconversion could occur in the following manner:



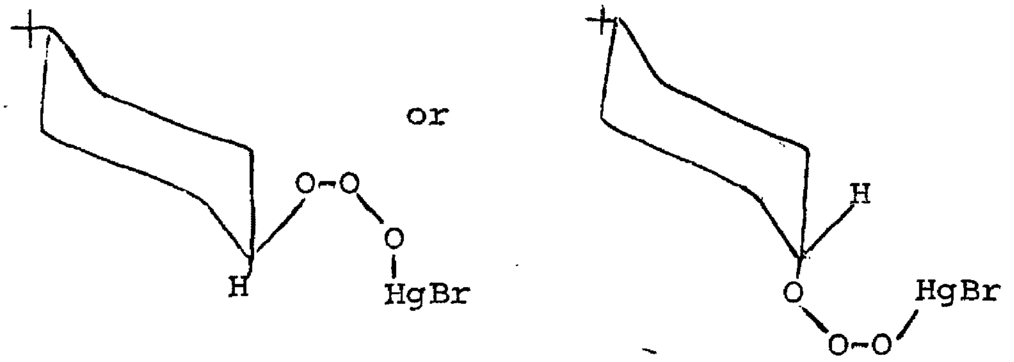
where $k_3 << k_4$

$k_1 << k_2$

and $k_2/k_1 >> k_3/k_4$ (54)

The fact that a conversion of this intermediate would involve breaking the carbon-oxygen bond may appear unusual since cleavage of an oxygen-oxygen bond eventually leads to the products observed and a carbon-oxygen bond is usually thought to be weaker than an oxygen-oxygen bond. However, there is a driving force for the *cis* intermediate to convert to the *trans* since the 1-3 diaxial interactions of oxygen with hydrogen are minimal with the *trans* intermediate. It must also be assumed that the reverse of this conversion is more difficult and that no easier reactions of this type occur.

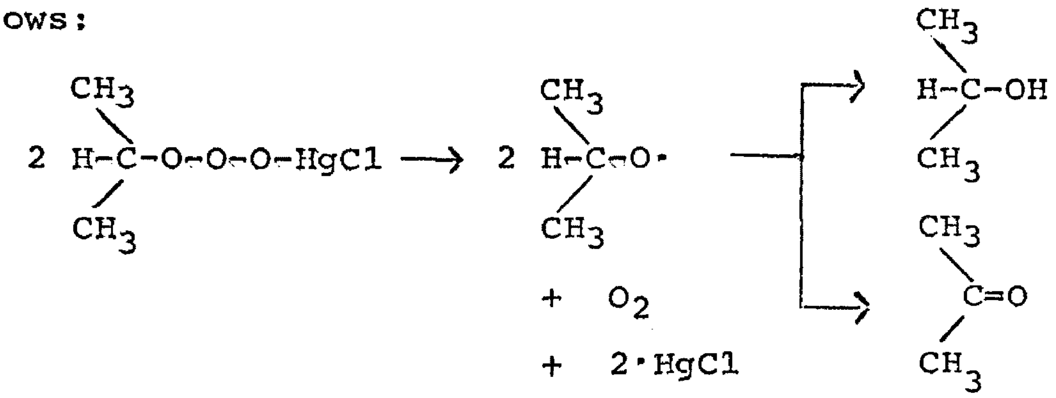
Once the intermediate below



(55)

is formed, it can then decompose to products by disproportionation.

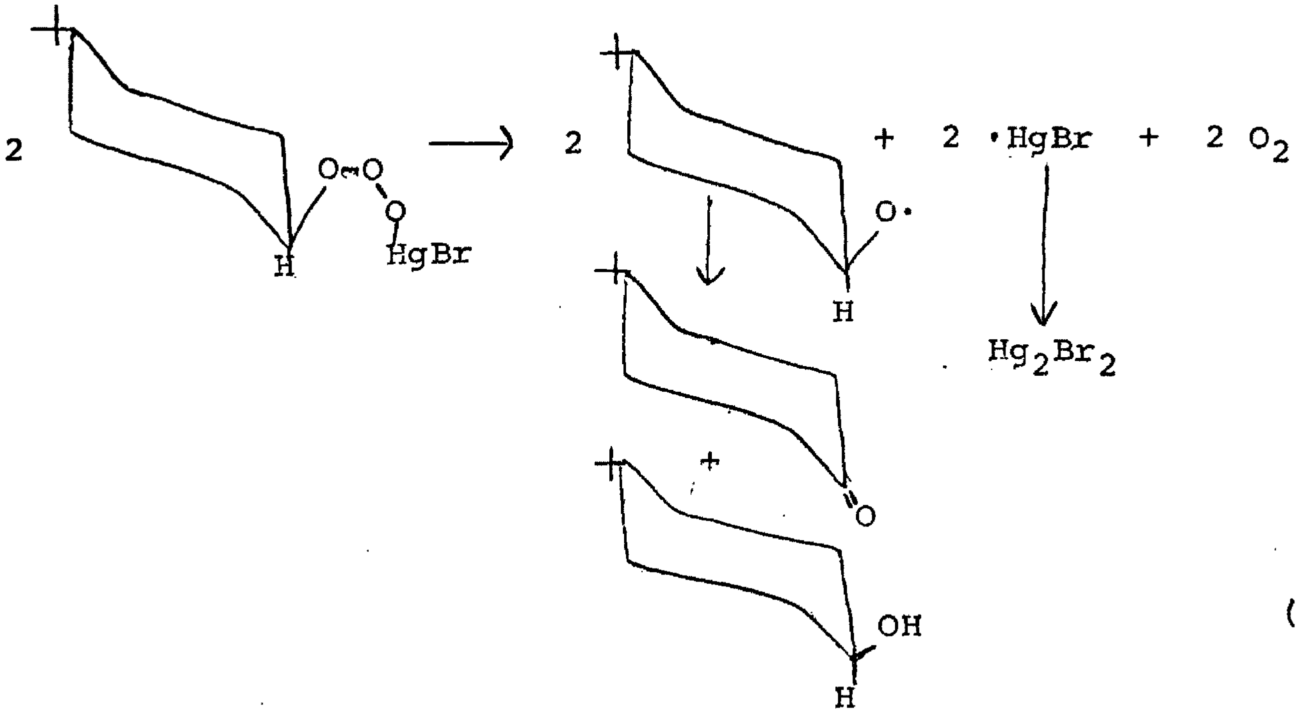
*Intermediate Disproportionation and Product Formation.* Reevaluation of the data of Rivera[17] indicates a mechanism involving a disproportionation reaction. The data in Figure 5 confirms that acetone formation via only oxidation of the intermediate alcohol is not feasible since the calculated concentrations do not fit the observed concentrations for this prediction. However, by modifying the equation such that one considers the intermediate isopropyl-O-O-O-HgCl breaking down to a mole of acetone and a mole of 2-propanol, the observed data fits the calculated data quite well (see Figure 6). The breakdown probably occurs as follows:



$$2\ \mathrm{H{-}C(CH_3)_2{-}O{-}O{-}O{-}HgCl} \longrightarrow 2\ \mathrm{H{-}C(CH_3)_2{-}O\cdot} + \mathrm{O_2} + 2\cdot\mathrm{HgCl} \longrightarrow \mathrm{H{-}C(CH_3)_2{-}OH} + \mathrm{(CH_3)_2C{=}O}$$

(56)

By applying this principal to the 4-tert-butyl system, the following sequence would lead to the observed products.



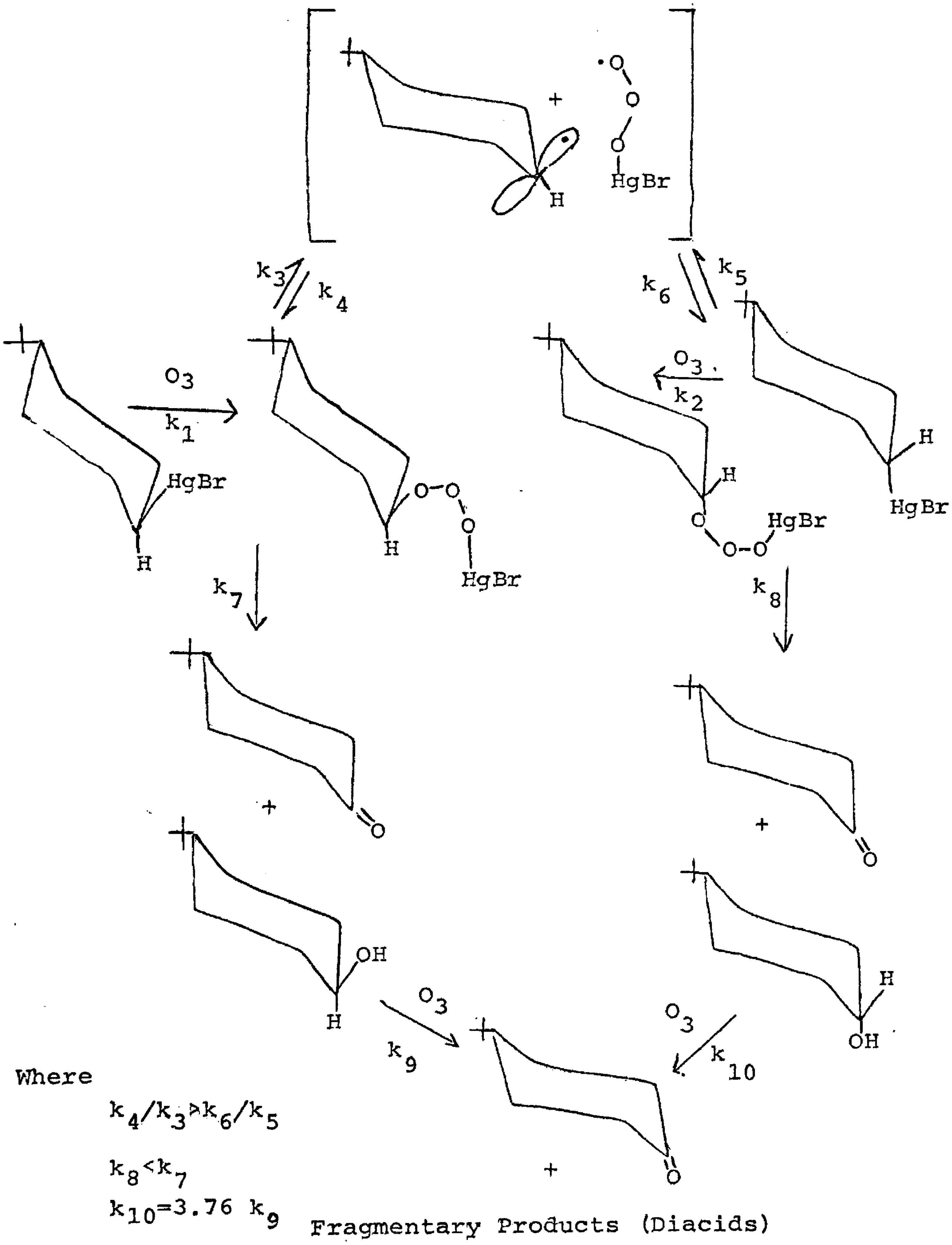
(57)

By the same sequence, the <u>cis</u> compound can lead to similar products. This type of decomposition fits the data nicely since both alcohol and ketone as well as Hg(I) compounds have been found as reaction products.[56] This also explains how the ketone can come directly from the mercurial as well as the alcohol.

According to the results of this study, the total reaction process for the ozonolysis can be shown in Figure 7. Since no elemental mercury was isolated from the reaction vessel, reactions such as

$$2\ {\cdot}\mathrm{HgBr} \longrightarrow \mathrm{HgBr_2} + \mathrm{Hg^o}$$

seem unlikely. Though formation of Hg(II) salts are not explained, in all probability Figure 7 demonstrates the major reaction pathway.



Where

$k_4/k_3 > k_6/k_5$

$k_8 < k_7$

$k_{10} = 3.76\ k_9$

Figure 7

# CHAPTER V

## SUMMARY

In order to elucidate the mechanism of the electrophilic cleavage of organomercurials by ozone, *cis* and *trans*-1-bromomercuri-4-tert-butylcyclohexane were synthesized and ozonized. Upon ozonolysis it was found that both the *cis* and *trans* organomercurials yielded both *cis* and *trans*-4-tert-butylcyclohexanol as well as 4-tert-butylcyclohexanone. The *trans* alcohol was the predominant alcohol in both cases.

In order to test the argument that the *trans* alcohol predominated because the *cis* alcohol was more rapidly oxidized, we ran a competitive rate study on both alcohols. It was found that the *cis* alcohol reacted only 3.76 times faster than the *trans* alcohol. A much larger rate difference would be expected if this were the reason for the low yield of *cis* alcohol relative to the *trans* isomer.

A second possible reason for the *trans* alcohol being the predominant alcohol is that the *cis* alcohol epimerized during the reaction. This idea was disposed by noting that ozonolysis of pure *cis*-4-tert-butylcyclohexanol failed to yield epimerized products. Epimerization of the *cis* alcohol also failed to occur in the presence of bromomercuricyclohexane.

An unequivocal mechanism for the entire reaction could not be arrived at, but results based on previous studies and this work indicate that the intermediate cannot be carbanion-like. However, formation of a trioxide via intermediates similar to those postulated for the ozonolysis of alkanes or alcohols can account for the products observed.

Once the intermediate forms, it can decompose directly to a radical pair, or epimerize and then reform the radical pair. The radical pair can further react to form the alcohols and ketone as well as oxygen and inorganic mercury products.

The fact that the trans organomercurial gave mostly trans alcohol implies that organomercurials can be valuable intermediates in stereo-selective syntheses of alcohols, employing ozone and mercuric salts.

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