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Part I. The reaction of some benzhydryl hydrogen phthalate esters with thionyl chloride. Part II. A study of the pyrolysis of the hydrogen and methyl phthalate esters of the cis- and trans-1-phenyl-2-methylcyclohexanols in N,N-dimethylformamide.

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PART I

THE REACTION OF SOME BENZHYDRYL HYDROGEN PHTHALATE ESTERS WITH THIONYL CHLORIDE

PART II

A STUDY OF THE PYROLYSIS OF THE HYDROGEN AND METHYL PHTHALATE ESTERS OF THE CIS- AND TRANS-1-PHENYL-2-METHYLCYCLOHEXANOLS IN N,N-DIMETHYLFORMAMIDE

BY

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A DISSERTATION

Submitted to the Faculty of Graduate Studies through the
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Windsor, Ontario
1971

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363763

To my understanding and inspiring wife

ABSTRACT

PART I

A product study and a stereochemical investigation of the reaction of 4-nitrobenzhydryl hydrogen phthalate with thionyl chloride are reported. The only isolable reaction products are phthalic anhydride and 4-nitrobenzhydryl chloride and the reaction appears to proceed stereospecifically with retention of configuration. An intramolecular mechanism similar to the S_Ni mechanism for the reaction of a secondary alcohol with thionyl chloride in an inert solvent is postulated.

The results of the product study of the reaction of the hydrogen phthalate esters of benzhydrol, 4-methylbenzhydrol and 4-methoxybenzhydrol with thionyl chloride are presented. Phthalic anhydride, the respective benzhydryl chloride and phthalic acid are the only isolable products of each reaction. The formation of the latter compound is suggestive of the operation of a different mechanism for these ester reactions.

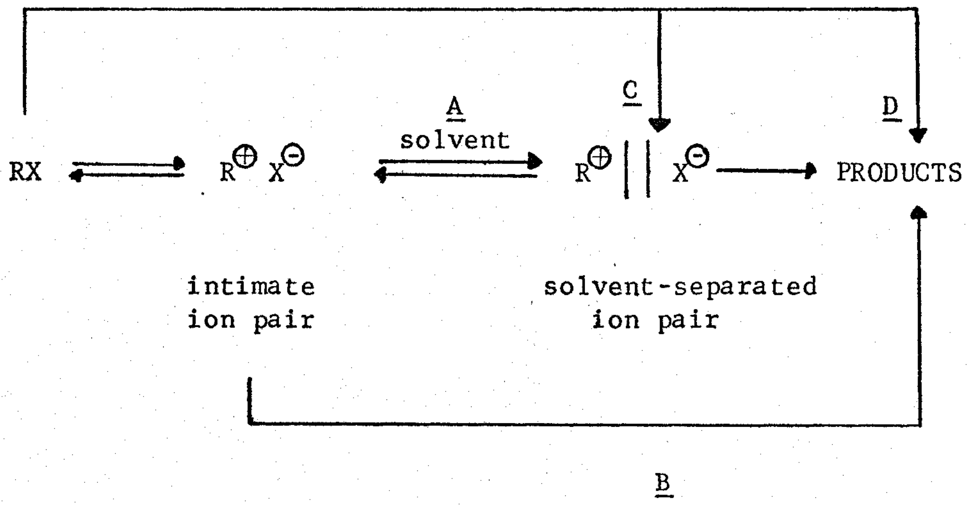
The potential synthetic utility of this reaction is discussed in view of the 4-nitrobenzhydryl hydrogen phthalate-thionyl chloride reaction.

PART II

Kinetic and product distribution studies were carried out on the pyrolysis of the *cis*- and *trans*-1-phenyl-2-methylcyclohexyl methyl phthalate esters in N,N-dimethylformamide and the results are reported. The *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalates pyrolyze 86 and 118 times faster, respectively, than their corresponding methyl phthalate esters. These data are suggestive of *ortho*-carboxyl proton participation during the decomposition of the hydrogen phthalate esters. The product distributions for the methyl phthalate diester pyrolyses are similar and display a strong predominance of Hofmann olefin, 1-phenyl-6-methylcyclohexene, which may be explained by a *cis* (eclipsing) effect.

An isotope study and a stereochemical investigation were conducted on the pyrolysis of *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O in N,N-dimethylformamide. The results are in agreement with those expected for the involvement of reversibly formed intimate and solvent-separated ion pairs during the decomposition of these esters. The proposed intimate ion pair for the *cis*-ester decomposition would appear to be looser and/or more ionic than the corresponding intermediate for the *trans*-ester pyrolysis.

The kinetic, product distribution, isotope exchange and geometrical isomerization data for the pyrolysis of the *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate esters in N,N-dimethylformamide are discussed in view of the following general scheme proposed for ester pyrolysis.



Pyrolysis of the cis-hydrogen phthalate essentially via path A, involving rate-determining formation of an intimate ion pair and product formation from a solvent-separated ion pair, is consistent with the experimental data. Decomposition also may occur by path B but the amount of involvement of this reaction route would seem to be small.

Thermal decomposition of the trans-hydrogen phthalate primarily via path A is in agreement with the experimental results. The rate-determining step seems to be solvent-separated ion pair formation. This ionic intermediate appears to be the species from which products are derived and it seems to be similar in character to the solvent-separated ion pair involved in the cis-ester pyrolysis. Decomposition of the trans-ester may proceed also via path C but the extent to which this pathway is followed is probably small.

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PART I

THE REACTION OF SOME BENZHYDRYL HYDROGEN PHTHALATE ESTERS WITH THIONYL CHLORIDE

CHAPTER I

INTRODUCTION

Various procedures for the formation of optically active secondary alkyl chlorides have been devised.[1] Resolving agents have been used with limited success for the synthesis of these compounds. Reagents such as hydrogen chloride, phosphorus trichloride, chlorodiphenylphosphine, o-phenylene chlorophosphite and triphenylphosphite with anhydrous hydrogen chloride have been used to convert optically active secondary alcohols to the corresponding optically active secondary alkyl chlorides.

These latter compounds modify the hydroxyl group of the alcohol either by protonation or ester formation such that a better leaving group results. Nucleophilic displacement by chloride ion then occurs. For the synthesis of optically pure secondary alkyl chlorides in which the chlorine atom is attached directly to the asymmetric carbon atom, it is essential for the mechanism of displacement of the modified hydroxyl group of the alcohol by the chloride ion to be 100 percent S_N2 in character. However, in these synthetic procedures, the problem of racemization resulting from the intervention of a carbonium ion intermediate in the displacement reaction lowers the optical purity of the alkyl chloride. The intrusion of this carbonium ion character in the displacement reaction also may cause rearrangement. The addition of hydrogen chloride to olefinic side products may contribute to the loss of chemical and optical purity of the alkyl chlorides when this latter reagent is used or is generated in situ.

The reagent thionyl chloride is used often for the conversion of optically active secondary alcohols to alkyl chlorides. The stereochemical outcome of this reaction seems to be dependent to a certain extent on the nature of the solvent medium.[1,2] Reaction conditions are used that reduce the amount of olefinic side products and that eliminate the small amount of rearrangement that may accompany the process. The initially formed alkyl chlorosulfite is usually somewhat unstable and it decomposes to yield alkyl chloride and sulfur dioxide.

The mechanism of the reaction of thionyl chloride with secondary alcohols has been investigated deeply as the alkyl chlorosulfite intermediate usually can be isolated. The postulated pathway for the conversion of a secondary alcohol to the corresponding alkyl chloride using thionyl chloride is shown in Figure 1.[3]

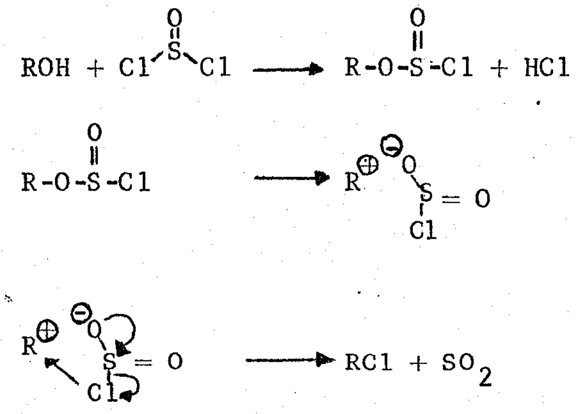


Figure 1 - Mechanism for the Reaction of a Secondary Alcohol with Thionyl Chloride

The first step of this reaction pathway involves the formation of an alkyl chlorosulfite ester that can be isolated. This ester decomposes into an intimate ion pair and in the final step of this mechanistic sequence, part of the leaving group attacks the central carbon atom from the front only since it cannot position itself for a backside approach. The last two steps of this reaction pathway constitute the most outstanding example of the S_Ni mechanism (substitution nucleophilic internal) to date. It should be noted that this mechanism requires that there must be a part of the leaving group that can attack the substrate, detaching itself from the rest of the leaving group in the process and this necessity is satisfied in the thionyl chloride-alcohol reaction. No neighbouring group participation is involved in this mechanism and the stereochemistry of the reaction is determined only in the decomposition stage.

There is appreciable experimental evidence in support of this proposed mechanism. The reaction between a secondary alcohol and thionyl chloride is second-order but the decomposition of the alkyl chlorosulfite is first-order.[4] These two reaction orders are predicted by this mechanism.

Originally, it was thought that the decomposition of an alkyl chlorosulfite was a one-step, intramolecular, concerted process involving a cyclic transition state[4] (Figure 2). However, this was disproved later for the case of secondary alcohols by a product study of the decomposition of 3-methyl-2-butyl chlorosulfite[5] and by a ^{14}C isotope investigation of the 2-butyl chlorosulfite degradation.[6] The results of these studies indicated the presence of an ion pair in the decomposition of each inorganic ester, as there was no other way to explain the rearrangement and the shift of ^{14}C isotope.

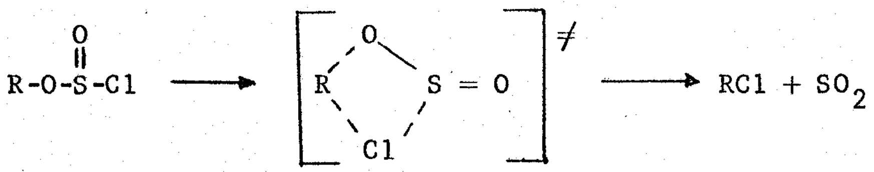


Figure 2 - Concerted Decomposition of an Alkyl Chlorosulfite Ester

It was demonstrated that, in inert solvents, aryl substituents increased the amount of retained stereochemistry in the alkyl chloride.[7] This could be explained by the increased stabilization of the cation of the ion pair of the S_Ni mechanism, which would make this pathway more attractive for chlorosulfite ester decomposition.

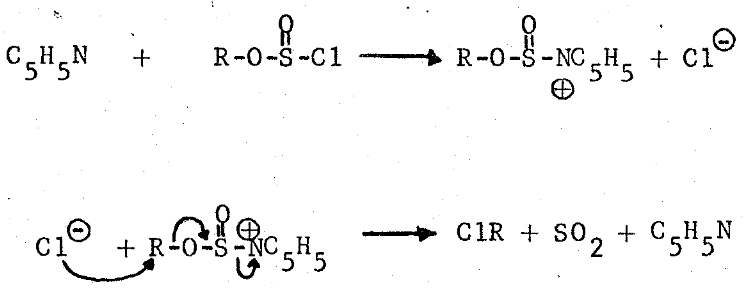
The reaction of thionyl chloride with apocamphyl alcohol, a bridgehead compound, generated the alkyl chlorosulfite.[8] However, this ester did not decompose to the corresponding chloride. This would seem to indicate the need for a planar configuration at the reaction centre for chlorosulfite decomposition.

A primary alcohol, 1-butanol-1-d_1, was chlorinated with thionyl chloride with inversion of configuration.[9] Apparently, chloride ion attacked the central carbon atom of the chlorosulfite ester in an S_N2 manner by default, as unimolecular decomposition to an ion pair involving ionization of the alkyl-oxygen bond would have yielded an unstable, primary carbonium ion. Also, it would appear that even for primary systems the decomposition of the alkyl chlorosulfite *via* a four-membered cyclic transition state is unfavourable (Figure 2).

B-Deuterium kinetic isotope studies were conducted on the reaction of thionyl chloride with a secondary alcohol.[2,4] They indicated ionization of the alkyl chlorosulfite intermediate during decomposition to an ion pair involving B-hydrogen stabilization of the cation's positive charge as in unimolecular solvolytic reactions in which the formation of an ionic aggregate precedes the attack of solvent on the substrate.

As a whole, the preceding data strongly indicate that the reaction of a secondary alcohol with thionyl chloride in an inert solvent initially yields the corresponding alkyl chlorosulfite followed by the decomposition of this ester *via* the S_Ni mechanism involving an ion pair which results in the formation of the alkyl chloride with retained stereochemistry.

The alkyl chloride having predominantly inverted stereochemistry can be obtained by the addition of pyridine to the alcohol-thionyl chloride mixture.[3,10] Inversion of configuration seems to be the result of the reaction of pyridine with the alkyl chlorosulfite intermediate. This occurs before the decomposition of the inorganic ester has an opportunity to take place and the generated chloride ion attacks the pyridinium ion in a backside fashion (Figure 3).



$$C_5H_5N + R\text{-}O\text{-}\overset{O}{\overset{\|}{S}}\text{-}Cl \longrightarrow R\text{-}O\text{-}\overset{O}{\overset{\|}{S}}\text{-}\overset{\oplus}{N}C_5H_5 + Cl^{\ominus}$$

$$Cl^{\ominus} + R\text{-}O\text{-}\overset{O}{\overset{\|}{S}}\text{-}\overset{\oplus}{N}C_5H_5 \longrightarrow ClR + SO_2 + C_5H_5N$$

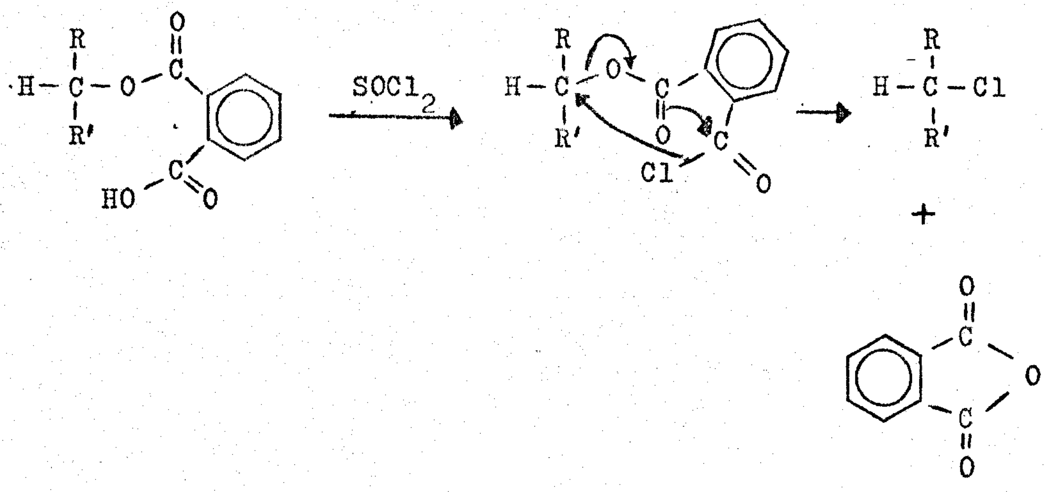
Figure 3- Mechanism for the Reaction of a Secondary Alcohol with Thionyl Chloride in the Presence of Pyridine

In the preparation of aryl-substituted secondary alkyl chlorides from the corresponding alcohols using the phosphorus-containing reagents and hydrogen chloride, the readiness with which alkyl groups carrying α-aryl substituents form carbonium ions makes it virtually impossible to synthesize optically active halides without some racemization.[1] However, for the thionyl chloride reaction with aryl-substituted secondary alcohols, the amount of retained stereochemistry increases in inert solvents.[7]

It was of interest in this laboratory to examine the effect of electron-withdrawing aryl substituents on the stereochemistry of the secondary alcohol-thionyl chloride reaction in an inert solvent.

Thionyl chloride is used as a chlorinating agent not only for the conversion of alcohols to alkyl chlorides but also for the formation of acid chlorides from carboxylic acids.[11] Mechanistically, very little is known about this latter reaction although it might seem quite likely that an acyl chlorosulfite intermediate is involved.

It was observed previously in this laboratory that the treatment of 4-bromo-4'-nitrobenzhydryl hydrogen phthalate with thionyl chloride did not yield the corresponding acid chloride as the reaction product.[12] Instead, 4-bromo-4'-nitrobenzhydryl chloride and phthalic anhydride were formed. An intramolecular, cyclic, concerted mechanism was postulated to account for the reaction products (Figure 4).



R- = 4-Br-C_6H_4-

R'- = 4-NO_2-C_6H_4-

Figure 4- Proposed Mechanism for the Reaction of 4-Bromo-4'-Nitrobenzhydryl Hydrogen Phthalate with Thionyl Chloride

It was decided to determine the outcome of the reaction of thionyl chloride with other benzhydryl hydrogen phthalates and it seemed in order to conduct a stereochemical study as a test of the postulated mechanism.

It should be noted that this reaction would be synthetically useful if its steric course is as indicated, as it would provide a one-step method for the preparation of an optically active substituted benzhydryl chloride from the corresponding optically active hydrogen phthalate ester. This would eliminate the need for the conventional two-step process for optically active benzhydryl chloride formation that involves saponification or hydride reduction of the optically active ester followed by treatment of the optically active alcohol with thionyl chloride.

CHAPTER II

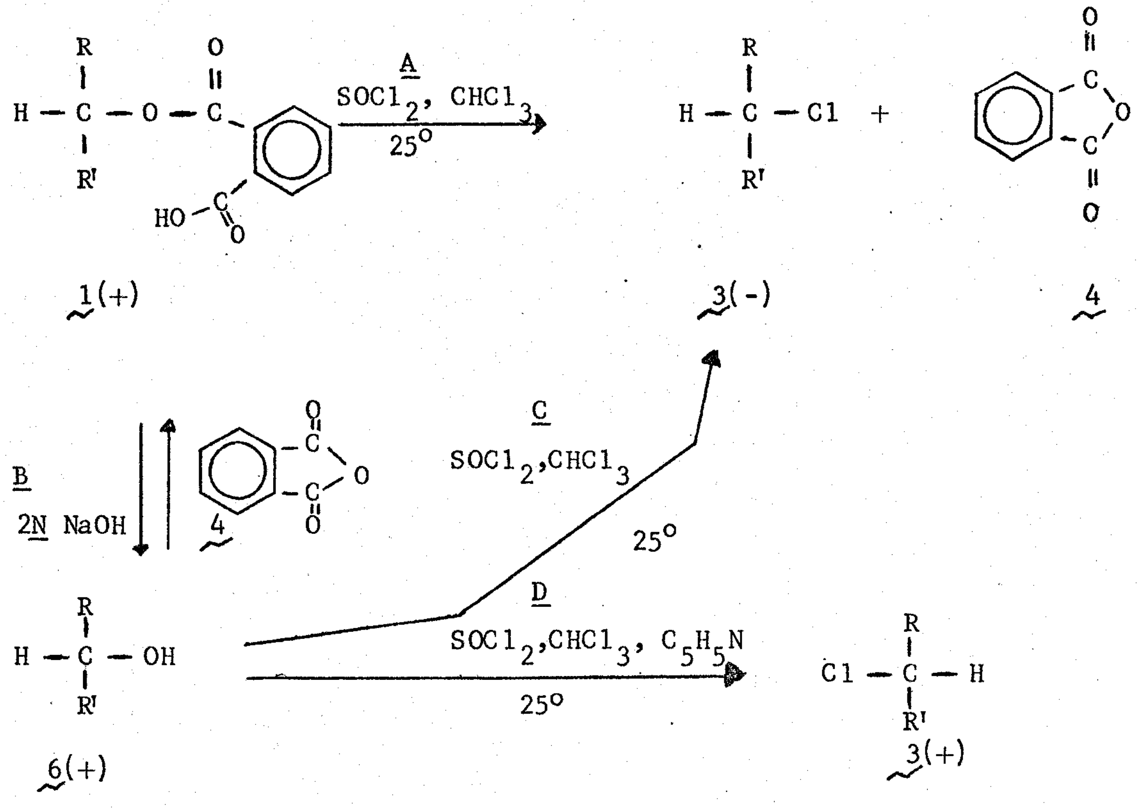
RESULTS AND DISCUSSION

Product and Stereochemical Studies of the Reaction of 4-Nitrobenzhydryl Hydrogen Phthalate with Thionyl Chloride

The reaction of thionyl chloride with 4-nitrobenzhydryl hydrogen phthalate (1) was studied initially to evaluate the generality of the reaction that occurred with 4-bromo-4'-nitrobenzhydryl hydrogen phthalate and the only isolable products were 4-nitrobenzhydryl chloride (3) and phthalic anhydride (4), which were formed in yields of 47 and 62 percent, respectively. Neither the acid chloride (2) nor the acyl chlorosulfite (5) of 4-nitrobenzhydryl hydrogen phthalate could be isolated or detected. Although the inability to isolate 5 is not surprising, the absence of 2 as the desired product of a conventional reaction is intriguing as is the isolation of 3 in reasonable yield.

It was decided to conduct a stereochemical study on the 4-nitrobenzhydryl system as the specific rotations of optically pure 4-nitrobenzhydryl hydrogen phthalate (1) and 4-nitrobenzhydrol (6) are known.[13] The results of this investigation are summarized in Figure 5 and Table I.

The optically active ester 1 and alcohol 6 used in the stereochemical investigation were resolved to greater than 98 percent optical purity ($[\alpha]_D^{25} + 36.70^{\circ}$ and $+ 77.11^{\circ}$, respectively) by the method of Puckowski and Ross[13] involving the fractional crystallization of diastereomeric quinine salts. The saponification of optically active ester 1 (path B) yielded optically active alcohol 6 with retained configuration as was shown by the conversion of 6 to 1 ($[\alpha]_D^{25} + 36.50^{\circ}$)



R- = C_6H_5-

R'- = 4-NO_2-C_6H_4-

Figure 5- Stereochemical Study of the Reaction of 4-Nitrobenzhydryl Hydrogen Phthalate with Thionyl Chloride

TABLE I

Specific Rotations of Enantiomeric 4-Nitrobenzhydryl Chloride from Different Reactions

Enantiomer of 4-Nitrobenzhydryl Chloride	Source of 4-Nitrobenzhydryl Chloride	Specific Rotation $[\alpha]^{25}_{D}$
(-)	1(+) + $SOCl_2$	-5.68°
(-)	6(+) + $SOCl_2$	-5.70°
(+)	6(+) + $SOCl_2$ + C_5H_5N	+5.85°

which had virtually the same optical activity as the original ester. The 4-nitrobenzhydryl chloride (**3**) that was obtained from the ester **1** *via* path *A* had the same optical activity as the chloride **3** formed by path *C* from the alcohol **6**, whereas the chloride **3** produced by path *D* had the opposite optical activity. Neither of the enantiomers of **3** lost optical activity when treated with thionyl chloride in chloroform for two days.

The reaction conditions of path *C* for the conversion of **6** to **3** are conducive to reaction *via* the S_Ni mechanism involving retention of configuration about the asymmetric carbon atom.[2] The reaction conditions of path *A* are virtually identical to those of path *C* and the chloride **3** was obtained from the ester **1** with essentially the same optical activity as that of **3** produced from the alcohol **6**. Since the saponification of **1** yielded **6** with retained stereochemistry, it would seem that the thionyl chloride-4-nitrobenzhydryl hydrogen phthalate reaction proceeds with essentially complete retention of configuration.

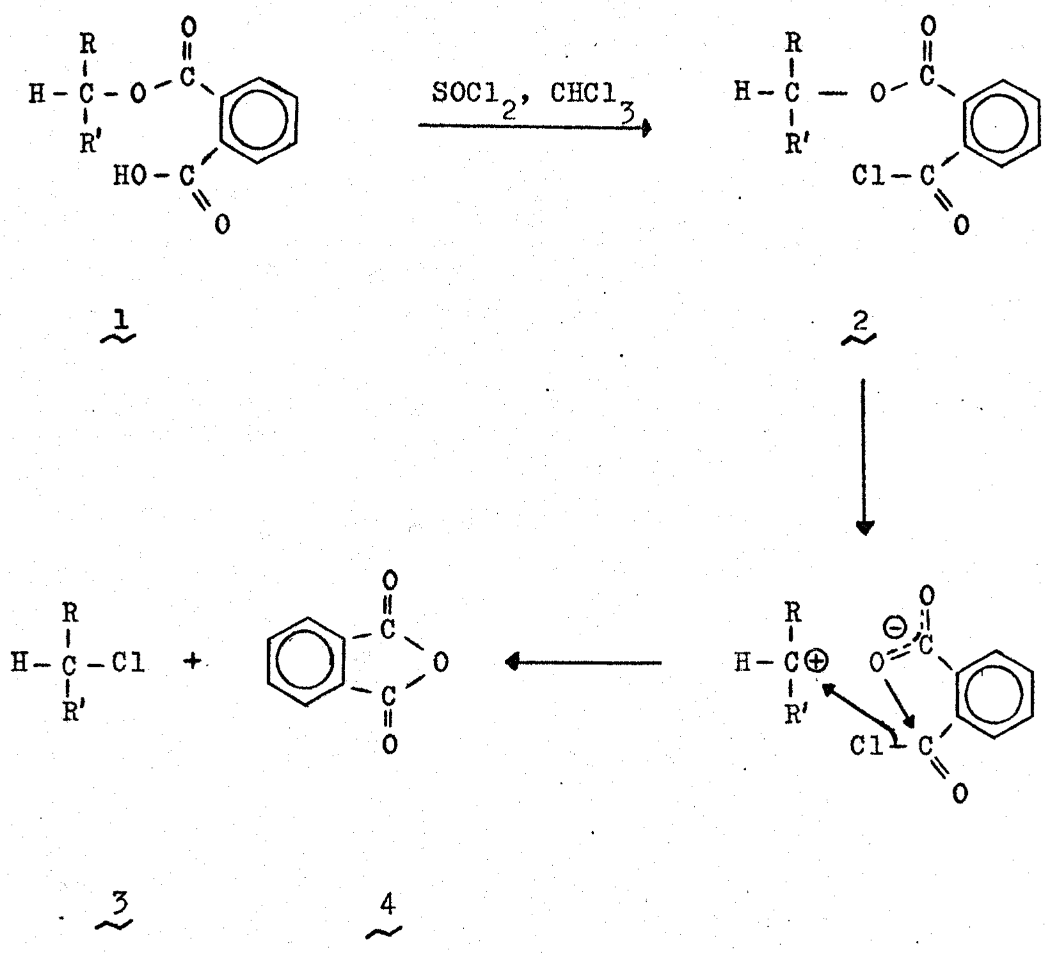
As further evidence for this postulate, the thionyl chloride reaction with the alcohol **6** was conducted in the presence of pyridine. These conditions are very favourable for reaction proceeding by the S_N2 mechanism involving inversion of configuration at the asymmetric carbon atom.[3,10] The chloride **3** produced by path *D* was enantiomeric to the chloride obtained from paths *A* and *C*. This observation adds further support to the proposal that the 4-nitrobenzhydryl hydrogen phthalate-thionyl chloride reaction proceeds stereospecifically with essentially complete retention of configuration.

The stereospecificity of this reaction can be accounted for by an ionic mechanism that involves the formation of an intimate ion pair from an acid chloride intermediate (Figure 6). This reaction pathway is similar to that proposed for the decomposition of an alkyl chlorosulfite (Figure 1). It should be noted that the acid chloride intermediate in the proposed reaction mechanism also could yield products *via* a concerted, intramolecular pathway involving a seven-membered ring transition state, as the nitro substituent of the benzhydryl group would provide little stabilization of positive charge in an ion pair.

Product Study of the Reaction of the Hydrogen Phthalate Esters of Benzhydrol, 4-Methylbenzhydrol and 4-Methoxybenzhydrol with Thionyl Chloride

In order to determine the scope and synthetic utility of this reaction, other substituted benzhydryl hydrogen phthalates were treated with thionyl chloride and a product study was conducted. The results of all thionyl chloride reactions are summarized in Table II.

From this tabulated data, it is noted that both phthalic anhydride and the corresponding benzhydryl chlorides were formed from the reaction of the benzhydryl, 4-methylbenzhydryl and 4-methoxybenzhydryl hydrogen phthalates with thionyl chloride. In addition, phthalic acid was a major product which is indicative of the operation of a different mechanism for these ester reactions. A postulated reaction sequence is shown in Figure 7.



R- = C_6H_5-

R'- = 4-NO_2-C_6H_4-

Figure 6- Proposed Mechanism for the Reaction of 4-Nitrobenzhydryl Hydrogen Phthalate with Thionyl Chloride

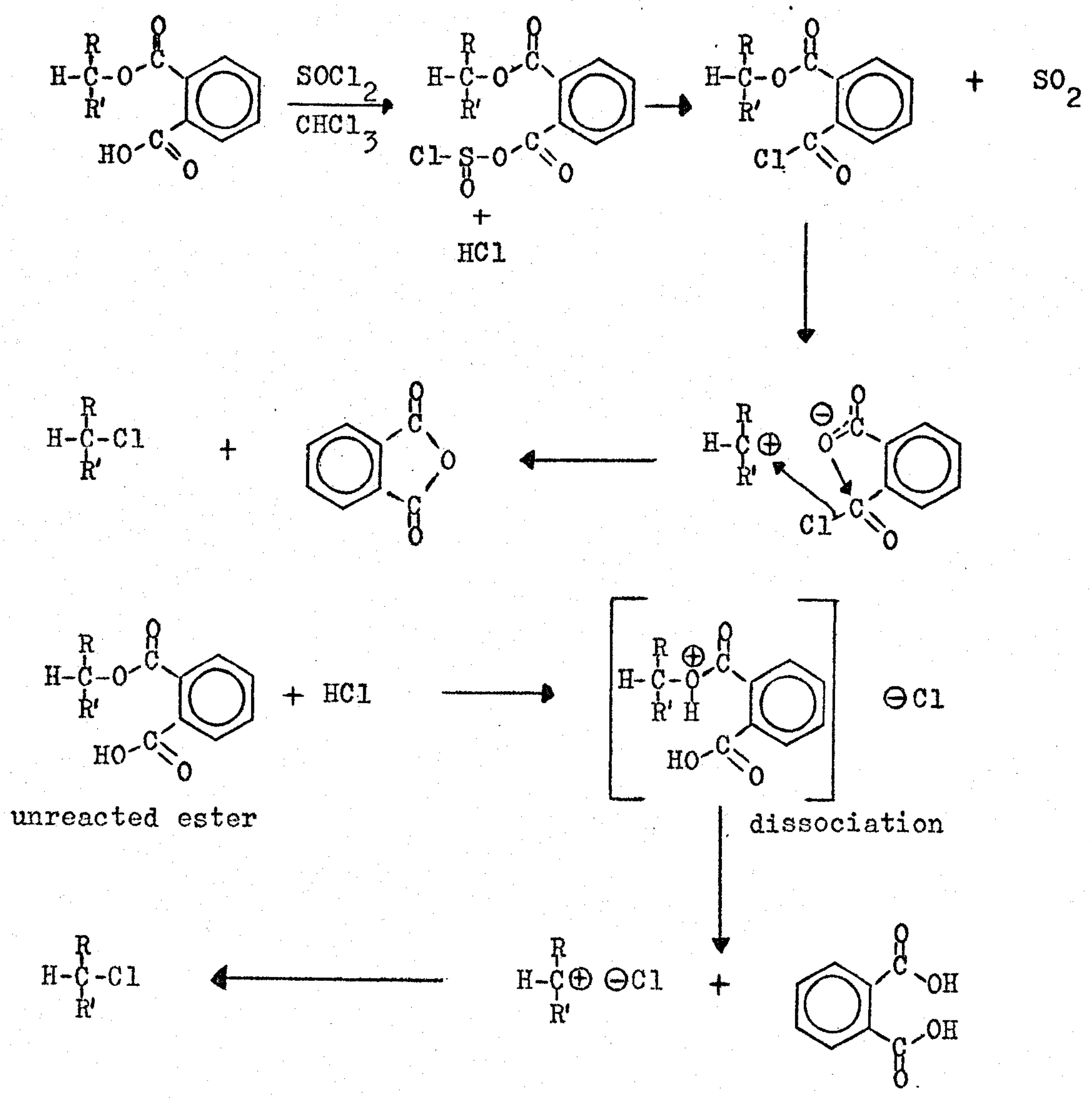
TABLE II

The Reaction of Some Benzhydryl Hydrogen Phthalate Esters with Thionyl Chloride

4-x-4'-y-Benzhydryl Hydrogen Phthalate x,y	Phthalic Anhydride Percent[b]	Phthalic Acid Percent[b]	4-x-4'-y-Benzhydryl Chloride Percent[b]
Br, NO_2	95[a]	0	91[a]
NO_2,H	62	0	47
H,H	8	57	55
CH_3,H	14	68	61
CH_3O,H	17	47	36

a Reference 12.

b The product yields were calculated in the following manner. From z moles of ester, z moles of anhydride and z moles of chloride were formed. For the reactions in which phthalic acid also was produced, the yield of this product was based on an z mole theoretical amount.



R- = C_6H_5-

R'- = 4-x-C_6H_4- (x = H, CH_3 and CH_3O)

Figure 7- Proposed Mechanism for the Reaction of the Hydrogen Phthalate Esters of Benzhydrol, 4-Methylbenzhydrol and 4-Methoxybenzhydrol With Thionyl Chloride

Reaction of thionyl chloride with acid portion of the hydrogen phthalate ester would produce the acid chlorosulfite and hydrogen chloride. This acyl chlorosulfite could decompose to phthalic anhydride and the corresponding benzhydryl chloride through an acid chloride intermediate as previously described. The hydrogen chloride generated _in situ_ could protonate unreacted starting material creating a reasonably good leaving group. Dissociation of the protonated species could occur to yield phthalic acid and an ion pair followed by return of this ionic intermediate to form the benzhydryl chloride. It should be noted that this dissociation process would be enhanced by the presence of an electron-donating substituent in the benzhydryl group.

Summary and Conclusions

It appears that the reaction of thionyl chloride with 4- nitrobenzhydryl hydrogen phthalate in chloroform proceeds stereospecifically with retention of configuration yielding 4-nitrobenzhydryl chloride and phthalic anhydride. At least for the 4-nitrobenzhydryl system, this reaction seems to be synthetically useful for the preparation of an optically active benzhydryl chloride from the corresponding optically active hydrogen phthalate ester in one step. This reaction may be quite general for any benzhydryl system which contains an electron-withdrawing group on one or both of the benzene rings.

The treatment of benzhydryl, 4-methylbenzhydryl and 4-methoxybenzhydryl hydrogen phthalates with thionyl chloride yields the corresponding benzhydryl chlorides along with phthalic acid and phthalic anhydride. Although the degree of stereospecificity of these reactions is unknown, it would appear from a consideration of the product study that the presence of an electron-donating substituent on either or both of the phenyl rings of the benzhydryl group would allow the operation of a mechanism involving two reaction modes which would affect in opposing ways the stereochemical outcome of each reaction. Also, the synthetic utility of the reaction as applied to these benzhydryl systems would seem to be diminished.

CHAPTER III

EXPERIMENTAL

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Optical rotation measurements were determined with a Rudolph Model 80 polarimeter equipped with a sodium lamp (λ589 nm) using 2 dm polarimeter tubes and chloroform as the solvent. The error limits of the specific rotations were not greater than ± 1.0°. The infrared (ir) spectra were obtained using a Beckman IR-10 spectrophotometer equipped with potassium bromide cells. All solutions were weight-weight percent in the solvent specified. Only the significant absorptions are reported (cm^{-1}) and their intensities are expressed as weak (w, 100-75 percent transmission), medium (m, 74-40 percent transmission) or strong (s, 39-0 percent transmission). Microanalyses were determined by Midwest Microlab Inc., Indianapolis, Indiana. The nuclear magnetic resonance (nmr) data were obtained using JEOL C-60 and C-60HL instruments and the chemical shifts are expressed in τ units downfield from internal tetramethylsilane. The splitting pattern of each resonance is reported using the following code: s=singlet, d=doublet, t=triplet, m=multiplet and bm=broad multiplet. These solutions were weight-volume percent in the solvent specified. Analytical thin layer chromatography (tlc) was performed on 0.25-mm fluorescent silica gel plates using benzene as the eluent.

4-Nitrobenzhydrol (6)

This alcohol was prepared according to the procedure of Mamer.[12]

4-Nitrobenzophenone (107.8 g, 475.0 mmole) was dissolved in 1425 ml of tetrahydrofuran in a 2-l. conical flask. To the stirred solution, sodium borohydride (14.3 g, 380.0 mmole) was added in 0.5-g portions each dissolved in 5ml of ice cold water. These aliquots were added at such a rate as to maintain the temperature of the reaction mixture below 35°. After addition was completed, the mixture was stirred for 2.0 hr with the flask loosely stoppered and then poured onto a slurry of 2400 g of ice and 120 ml of 12N hydrochloric acid. The tetrahydrofuran was allowed to evaporate from the hydrolyzed mixture using a stream of nitrogen. The yellow solid that formed was filtered, air dried and recrystallized from chloroform-hexane. This yielded pale yellow crystals of pure 4-nitrobenzhydrol (86.0 g, 78.2 percent) : mp73-75° (lit. [14]mp 73-75.5°); ir ($CHCl_3$, 10 percent) 3600 (m, free OH), 3440 (w, bonded OH), 3010 (m, ArH), 2860 (w, CH), 1600 and 1490 (m, Ar), 1510 and 1340 (s, NO_2), 1020 (m, C-O); nmr ($CDCl_3$, 16 percent) 2.00-2.90 (bm, 9, Ar), 4.35(s, 1, CH), 7.25 (s, 1, OH).

4-Nitrobenzhydryl Hydrogen Phthalate (1)

This ester was prepared according to the procedure of Mamer.[12] A solution of 4-nitrobenzhydrol (19.0 g, 82.0 mmole) and phthalic anhydride (16.4 g, 111.0 mmole) in 100 ml of pyridine was added to a 500-ml conical flask. Sodium hydride (6.0 g of a 50 percent dispersion in mineral oil,125.0 mmole) was added to the rapidly stirred solution maintaining the reaction temperature below 35°. The solution was stirred for 4.0 hr with the flask loosely stoppered, then was poured onto a slurry of 3 kg of ice and 100 ml of 1 N hydrochloric acid and was made acidic to pH 5. The organic material was extracted with 1 l. of chloroform and then was washed with five 100-ml portions of 0.05 N hydrochloric acid followed by washing with a few 100-ml portions of water until the aqueous layer was neutral. The chloroform solution was dried over anhydrous sodium sulfate, filtered and concentrated. The resulting yellow solid was recrystallized from chloroform-hexane yielding pale yellow crystals of pure 4-nitrobenzhydryl hydrogen phthalate (23.3 g, 75.4 percent): mp 157-159° (lit.[13] mp158°); ir ($CHCl_3$, 10 percent) 3500-2400 (s, COOH), 1730 (s, ester C=O), 1700 (s, acid C=O), 1600 and 1490 (m, Ar), 1515 and 1345 (s, NO_2), 1280 and 1250 (s, C-O); nmr ($CDCl_3$, 12 percent) -1.92 (s, 1, COOH), 1.60-2.90 (bm, 14, Ar and CH).

Anal. Calcd for $C_{21}H_{15}NO_6$: C, 66.84; H, 4.01. Found: C, 66.77; H, 4.11.

(+) -4-Nitrobenzhydryl Hydrogen Phthalate (1)

The enantiomeric ester was prepared according to the procedure of Puckowski and Ross.[13] The racemic ester (106.0 g, 281.0 mmole) was dissolved in 1 l. of 99 percent ethanol in a 2-l. conical flask. Quinine (90.4 g, 279.0 mmole) was added in 10-g portions to the warmed and stirred solution. The resulting yellow solution was filtered and stored in a sealed 2-l. flask. The white crystals (68.0 g, mp 124-127°) that formed within ten days were removed by filtration and dissolved in 99 percent ethanol. After one week, a white crystalline solid formed which was collected by filtration (51.0 g, 26.0 percent): mp 126-128°; $[\alpha]_D^{25}$ -61.15° (C 1.00). The quinine salt (28.1 g, 40.0 mmole) was dissolved in 1 l. of 95 percent ethanol and this solution was added to 1120 ml of rapidly stirred, ice cold 0.2 N hydrochloric acid. The solid that formed was collected by filtration, dried and recrystallized from benzene yielding pale yellow crystals of pure (+)- 4- nitrobenzhydryl hydrogen phthalate (8.8 g, 58.3 percent): mp 129-131°; $[\alpha]_D^{25}$ + 36.70° (C2.00) (lit. [13]mp 131-132°, $[\alpha]_D^{20}$ + 37.2° (C 4.0)); ir and nmr spectra were similar to those of the racemic ester.

Anal. Calcd for $C_{21}H_{15}NO_6$: C, 66.84; H, 4.01. Found: C, 67.05; H, 4.15.

(+)-4-Nitrobenzhydrol (6)

A solution of (+)-4-nitrobenzhydryl hydrogen phthalate (4.00 g, 10.7 mmole) in 60 ml of tetrahydrofuran was poured into 1 l. of rapidly stirred, ice cold 2N sodium hydroxide solution. Nitrogen was bubbled through the aqueous solution until no odour of tetrahydrofuran remained. The pale yellow solid that formed was collected by filtration, dried *in vacuo* and recrystallized from benzene yielding pale yellow crystals of pure (+)-4-nitrobenzhydrol (1.37 g, 56.0 percent): mp 79-80.5°; $[\alpha]_D^{25}$ + 77.11° (C 1.99)(lit.[13]mp 80-81°, $[\alpha]_D^{19}$ + 78.2° (C 2.06)); ir and nmr spectra were identical to those of the racemic alcohol.

Anal. Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84. Found: C, 68.22; H, 4.94.

Conversion of (+)-4-Nitrobenzhydrol (6) to (+)-4-Nitrobenzhydryl Hydrogen Phthalate(1)

The procedure described previously for the conversion of racemic 4-nitrobenzhydrol to racemic 4-nitrobenzhydryl hydrogen phthalate was used. (+)-4-Nitrobenzhydrol ($[\alpha]_D^{25}$ + 77.11° (C 1.99)) yielded on reaction with phthalic anhydride pale yellow crystals of (+)-4-nitrobenzhydryl hydrogen phthalate: mp 130-132°; $[\alpha]_D^{25}$ + 36.50° (C 0.85) (lit.[13] mp 131-132°, $[\alpha]_D^{20}$ + 37.2° (C 4.0)); ir and nmr spectral data compared favourably with those of the racemic ester.

Conversion of (+)-4-Nitrobenzhydrol (6) to (-)-4-Nitrobenzyhydryl Chloride (3)

(+)-4-Nitrobenzhydrol (0.50 g, 2.2 mmole) was dissolved in 3 ml of chloroform in a 25-ml, round-bottomed flask which was equipped with a condenser and a calcium chloride drying tube. Thionyl chloride (0.39 g, 3.3 mmole) was added dropwise to the solution. The reaction solution was stirred for 24.0 hr at 25° after which tlc analysis (silica gel, benzene) showed only a trace of alcohol. The volatile materials were removed *in vacuo* and the residual oil was distilled yielding (-)-4-nitrobenzhydryl chloride (0.30g, 55.1 percent) as a pale yellow oil that was pure according to tlc analysis (silica gel, benzene): bp 148-149° (30μ); $\underline{n}_D^{20}$ 1.6124 (lit.[15] for racemic chloride bp 168° (2 mm), $\underline{n}_D^{20}$ 1.6171); $[\alpha]_D^{25}$ - 5.70° (C 1.00); ir ($CHCl_3$, 10 percent) 3020 (m, ArH), 2850 (w, CH), 1600 and 1490 (m, Ar), 1520 and 1350 (m, NO_2); nmr ($CDCl_3$, 18 percent) 1.95 - 2.85 (bm, 9, Ar), 4.01 (s, 1, CH). The spectral data were identical to those of racemic 4-nitrobenzhydryl chloride prepared from racemic 4-nitrobenzhydrol.

Anal. Calcd for $C_{13}H_{10}ClNO_2$:C, 63.04; H, 4.07. Found: C, 63.05; H, 4.15.

Conversion of 4-Nitrobenzhydryl Hydrogen Phthalate (1) to 4-Nitrobenzhydryl Chloride (3)

The racemic ester (1.885 g, 5.0 mmole) was dissolved in 15 ml of chloroform. Thionyl chloride (1.070 g, 9.0 mmole) was added to this solution which then was stirred for 108.0 hr at 25° after which tlc analysis (silica gel, benzene) indicated complete reaction. Volatile materials were removed *in vacuo* and the residual yellow gum was dissolved in hot petroleum ether (bp 65-110°). Crystals of pure phthalic anhydride formed (0.460 g, 62.1 percent, mp 129-130°) and were removed by filtration. The filtrate was concentrated and the last traces of phthalic anhydride were removed by sublimation at 40 - 45° (50 μ) for 10.0 hr. The remaining oil was distilled twice yielding racemic 4-nitrobenzhydryl chloride (0.573g, 46.5 percent) as a pale yellow oil that was pure according to tlc analysis (silica gel, benzene): bp 132-134° (35μ); n_D^{20} 1.6160 (lit.[15] for racemic chloride bp 168° (2mm), n_D^{20} 1.6171); ir and nmr spectra were identical to those of 4-nitrobenzhydryl chloride obtained from the reaction of thionyl chloride with the alcohol.

Conversion of (+)-4-Nitrobenzhydryl Hydrogen Phthalate (1) to (-)-4-Nitrobenzhydryl Chloride (3)

The procedure previously described for the conversion of the racemic ester to racemic 4-nitrobenzhydryl chloride was used with the reaction time changed to 52.0 hr. (+)-4-Nitrobenzhydryl hydrogen phthalate (0.210 g, 0.55 mmole) gave (-)-4-nitrobenzhydryl chloride (0.063 g, 46.0 percent) that was unicomponent by tlc analysis (silica gel, benzene): bp 138-140° (20μ); n_D^{20} 1.6147 (lit.[15] for racemic chloride bp 168° (2mm), n_D^{20} 1.6171); $[\alpha]_D^{25}$ - 5.68° (C 1.00); ir and nmr spectra were identical to those of (-)-4-nitrobenzhydryl chloride obtained from (+)-4-nitrobenzhydrol.

Anal. Calcd for $C_{13}H_{10}ClNO_2$:C, 63.04; H, 4.07. Found: C,62.96; H, 4.36.

Conversion of (+)-4-Nitrobenzhydrol (6) to (+)-4-Nitrobenzhydryl Chloride (3)

(+)-4-Nitrobenzhydrol (0.125 g, 0.55 mmole) was dissolved in 2 ml of chloroform. Pyridine (0.043 g, 0.55 mmole) was added to the stirred solution followed by the dropwise addition of thionyl chloride (0.120 g, 1.00 mmole). The solution was stirred for 2.0 hr at 25° after which tlc analysis (silica gel, benzene) showed complete reaction. Volatile materials were removed *in vacuo* and the resulting oil was extracted with petroleum ether (bp 65-110°) leaving a yellow solid residue. The hydrocarbon solution was concentrated and the crude oil was distilled yielding (+)-4-nitrobenzhydryl chloride (0.100 g, 70.0 percent) as a pale yellow oil that was pure according to tlc analysis (silica gel, benzene):bp 154-156° (50μ); n_D^{20} 1.6154 (lit.[15] for racemic chloride bp 168° (2 mm), n_D^{20} 1.6171); $[\alpha]_D^{25}$ + 5.85° (C 1.00); ir and nmr spectra were identical to those of racemic and (-)-4-nitrobenzhydryl chloride.

Anal. Calcd for $C_{13}H_{10}ClNO_2$:C, 63.04; H, 4.07. Found: C, 62.73; H, 4.22.

Treatment of (+)- and (-)-4-Nitrobenzhydryl Chloride (3) with Thionyl Chloride

To a 2-ml chloroform solution of each enantiomer of 4-nitrobenzhydryl chloride (0.130 g, 0.53 mmole), thionyl chloride was added.

Each solution was stirred for 48.0 hr at 25°. Volatile materials were removed *in vacuo* from each solution and the residual oil was dissolved in petroleum ether (bp 65-110°). Each hydrocarbon solution was filtered and concentrated yielding enantiomeric 4-nitrobenzhydryl chloride which physical and spectral properties remained unchanged.

Hydrogen Phthalate Esters of Benzhydrol, 4-Methylbenzhydrol and 4-Methoxybenzhydrol

These esters were prepared in good yields (≥75 percent) according to the procedure described for the synthesis of 4-nitrobenzhydryl hydrogen phthalate. The alcohols used in these preparations were either commercially available or were obtained by the sodium borohydride reduction of the corresponding ketones. The physical and spectral properties of these esters are given below.

Benzhydryl Hydrogen Phthalate: mp 159-159.5° (lit.[16] mp 157-158°); ir ($CHCl_3$, 10 percent) 3500-2400 (m, COOH), 1730 (s, ester C=O), 1705 (s, acid C=O), 1600 and 1490 (m, Ar), 1280 and 1260 (m, C-O); nmr ($CDCl_3$, 12 percent) -2.10 (s, 1, COOH), 2.00-2.85 (bm, 15, Ar and CH).

Anal. Calcd for $C_{21}H_{16}O_4$: C, 75.89; H, 4.85. Found: C, 75.87; H, 4.93.

4-Methylbenzhydryl Hydrogen Phthalate: mp 124-125° (lit.[17] mp 120-122°); ir ($CHCl_3$, 10 percent) 3500-2400 (s, COOH), 1730 (s, ester C=O), 1710 (s, acid C=O), 1600 and 1490 (m, Ar), 1280 and 1255 (s, C-O); nmr ($CDCl_3$, 12 percent) -1.68 (s, 1, COOH), 2.00-3.00 (bm, 14, Ar and CH), 7.78 (s, 3, CH_3).

Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.29; H, 5.24. Found: C, 76.13; H, 5.23.

4-Methoxybenzhydryl Hydrogen Phthalate: mp 101-102° (lit.[16] mp 102-103°); ir ($CHCl_3$, 10 percent) 3500-2400 (s, COOH), 1730 (s, ester C=O), 1705 (s, acid C=O), 1610 and 1510 (m, Ar), 1280 and 1250 (s, C-O); nmr ($CDCl_3$, 12 percent)-1.68 (s, 1, COOH), 2.00-3.40 (bm, 14, Ar and CH), 6.34 (s, 3, CH_3).

Anal. Calcd for $C_{22}H_{18}O_5$: C, 72.92; H, 5.01. Found: C, 73.06; H, 5.22.

Conversion of Benzhydryl Hydrogen Phthalate to Benzhydryl Chloride

The racemic ester (1.660 g, 5.0 mmole) was dissolved in 15 ml of chloroform and to this solution, thionyl chloride (1.070 g, 9.0 mmole) was added. The reaction mixture turned cloudy within two minutes after the thionyl chloride addition and was stirred for an additional 108.0 hr at 25°. The tlc analysis (silica gel, benzene) indicated complete reaction. The white insoluble material (0.470 g, 56.7 percent, mp 195-196.5°) was removed by filtration and identified as phthalic acid. Volatile materials were removed *in vacuo* and the residual yellow gum was dissolved in hot petroleum ether (bp 65-110°). Upon cooling, crystals of phthalic anhydride formed (0.060 g, 8.1 percent, mp 128-130°) and were removed by filtration. The filtrate was concentrated and the last traces of phthalic anhydride were removed by sublimation at 35° (60μ) for several hours. The residual oil was distilled twice yielding benzhydryl chloride (0.553 g, 54.6 percent) as a pale yellow oil: bp 69° (50μ); n_D^{20} 1.5940 (lit.[18] bp 173° (19 mm), n_D^{20} 1.5959); ir ($CHCl_3$, 10 percent) 3010 (m, ArH), 2870 (w, CH), 1600 and 1490 (m, Ar); nmr ($CDCl_3$, 13 percent) 2.73 (m, 10, Ar), 3.93 (s, 1, CH).

According to the above procedure, the 4-methylbenzhydryl and 4-methoxybenzhydryl hydrogen phthalates were converted to their corresponding chlorides. These reactions also yielded phthalic acid in addition to phthalic anhydride and the respective benzhydryl chlorides. The product yields are listed in Table II and the physical and spectral properties of the 4-methylbenzhydryl and 4-methoxybenzhydryl chlorides are recorded below.

4-Methylbenzhydryl Chloride: bp 73.5° (35 μ); $\underline{n}_D^{24}$ 1.5845 (lit.[17] bp 160-164° (7 mm), $\underline{n}_D^{24}$ 1.5865); ir ($CHCl_3$, 10 percent) 3010 (m, ArH), 2920 and 2860 (m, CH_3 and CH), 1600, 1510 and 1490 (m, Ar); nmr ($CDCl_3$, 14 percent) 2.80 (m, 9, Ar), 3.93 (s, 1, CH), 7.70 (s, 3, CH_3).

4-Methoxybenzhydryl Chloride: mp 60-62° (lit.[16] mp 62-63°); ir ($CHCl_3$, 8 percent) 3010 (m, ArH), 2940 and 2840 (m, CH_3 and CH), 1610, 1510 and 1495 (s, Ar), 1245 (s, Ar-O-CH_3); nmr ($CDCl_3$, 14 percent) 2.47-3.36 (bm, 9, Ar), 3.90 (s, 1, CH), 6.25 (s, 3, CH_3).

REFERENCES

1. H.R. Hudson, Synthesis, 112 (1969).
2. C.E. Boozer and E.S. Lewis, J. Amer. Chem. Soc., 75, 3182 (1953).
3. J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure," McGraw-Hill, Inc., New York, N.Y., 1968, pp 268-269.
4. E.S. Lewis and C.E. Boozer, J. Amer. Chem. Soc., 74, 308 (1952).
5. C.C. Lee and A.J. Finlayson, Can. J. Chem., 39, 260 (1961).
6. C.C. Lee, J.W. Clayton, D.G. Lee, and A.J. Finlayson, Tetrahedron, 18, 1395 (1962).
7. W.A. Cowdrey, E.D. Hughes, C.K. Ingold, S. Masterman, and A.D. Scott, J. Chem. Soc., 1252 (1937).
8. P.D. Bartlett and L.H. Knox, J. Amer. Chem. Soc., 61, 3184 (1939).
9. A. Streitwieser, Jr., and W.D. Schaeffer, ibid., 79, 379 (1957).
10. W. Gerrard, J. Chem. Soc., 85 (1944).
11. L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, John Wiley and Sons, Inc., New York, N.Y., 1967, pp 1158-1159.
12. O.A. Mamer, Ph.D. Dissertation, University of Windsor, Windsor, Ontario, 1966.
13. R.T. Puckowski and W.A. Ross, J. Chem. Soc., 3555 (1959).
14. B.B. Smith and J.E. Leffler, J. Amer. Chem. Soc., 77, 2509 (1955).
15. S. Nishida, J. Org. Chem., 32, 2692 (1967).
16. M.P. Balfe, M.A. Doughty, J. Kenyon, and R. Poplett, J. Chem. Soc., 605 (1942).
17. A.G. Davies, J. Kenyon, B.J. Lyons, and T.A. Rohan, ibid., 3474 (1954).
18. R.C. Weast, "Handbook of Chemistry and Physics," 49th ed, The Chemical Rubber Co., Cleveland, Ohio, 1968, p C-404.

PART II

A STUDY OF THE PYROLYSIS OF THE HYDROGEN AND METHYL PHTHALATE ESTERS OF THE CIS- AND TRANS- 1- PHENYL-2-METHYLCYCLOHEXANOLS IN N,N-DIMETHYLFORMAMIDE

CHAPTER I

INTRODUCTION

The pyrolytic elimination reaction involving esters is used often to prepare olefins (Figure 1).[1] This reaction provides a method for the introduction of unsaturation into a system with little or no olefin isomerization. However, high temperatures (300-550°) usually are required for decomposition. As this reaction is known to result in the nearly exclusive removal of a cis-B-hydrogen atom,[1] it occasionally allows the formation of only one olefin, a product which might not be possible to form in a pure state by the use of other elimination reactions.

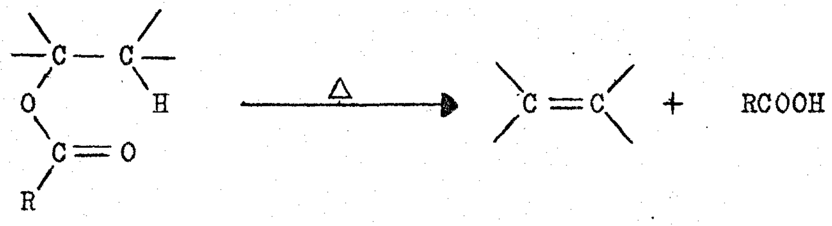


Figure 1 - Thermal Decomposition of Esters

On the basis of the stereochemistry of the reaction, Hurd and Blunck[2] in 1938 proposed a concerted mechanism for the gas phase pyrolysis of esters involving a cyclic, six-membered transition state (Figure 2). This reaction pathway could account for the cis steric course, the first-order kinetics and the negative activation entropy observed for the pyrolysis of esters. However, this postulate was not deemed entirely satisfactory in certain cases since it could not explain the polar effects of substituent groups.

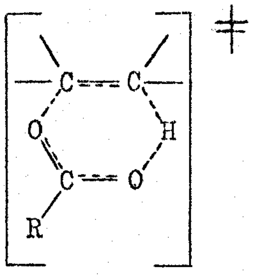
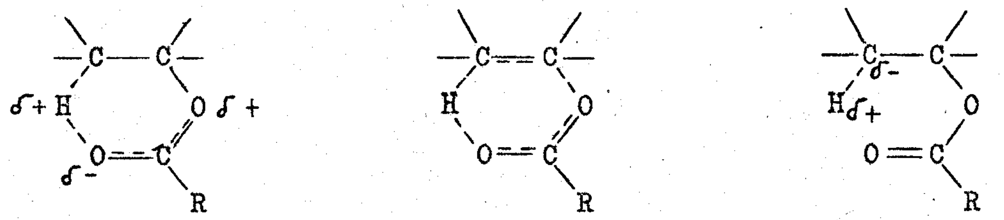


Figure 2 - Cyclic Transition State Proposed by Hurd and Blunck for Ester Pyrolysis

In 1960, DePuy and King[1] extensively reviewed various investigations of the gas phase pyrolysis of the acetate esters of primary, secondary and tertiary alcohols, which included kinetic, stereochemical and product distribution studies. From this survey they proposed that the pyrolytic elimination reaction proceeds via a highly concerted, cyclic mechanism having a six-membered activated complex in which there is a small amount of charge separation and some double bond character between the incipient olefinic carbon atoms. This transition state is able to make some use of polar substituent effects. According to DePuy and King, these effects are not necessary for the pyrolysis to proceed readily and they only slightly affect the reaction rate. In addition, they discussed in detail statistical, steric and thermodynamic effects which seem to be the factors of prime importance in determining the ratios of the olefinic products formed from the pyrolysis of aliphatic esters.

Banthorpe[3] in 1963 proposed a spectrum of transition states for the pyrolysis of aliphatic acetates involving different degrees of bond-breaking and bond-making. The three representations in Figure 3 are special cases that appear to be important in practice and in which particular bonds are broken. However, at that time, Banthorpe believed that the controlling influences of ester pyrolysis were not clear and that more extensive studies were necessary. In effect, he felt that the concerted "homolytic" mechanism had not been proven to be the exclusive pathway for the acetate ester pyrolyses.



E2 - like
"heterolytic"

concerted
"homolytic"

ElcB - like
"heterolytic"

Figure 3 - Transition States Proposed by Banthorpe for the Pyrolysis of Esters

In 1962, Taylor et al.[4] found a ρ value of -0.66 from a Hammett ρ-σ^+ plot for the pyrolysis of several 1-arylethyl acetates. They postulated that the thermal decomposition of these esters occurs *via* a concerted mechanism involving some charge separation which results in the partial formation of carbonium ion character in the transition state of the reaction. However, they were in disagreement with DePuy and King[1] who, in addition to the above factor, placed emphasis on developing double bond character in the transition state for ester pyrolysis.

Scheer et al.[5] in 1963 conducted a detailed study on the gas phase pyrolysis of several alkyl acetates and in Table I the activation parameters for some of these ester decompositions are reported. These researchers stressed the importance of alkyl-oxygen bond heterolysis during decomposition and they suggested a pyrolytic mechanism involving the reversible formation of an ion pair intermediate (Figure 4). They claimed that this mechanism could explain the *B*-deuterium isotope effect reported by De Puy and King[1] for the pyrolysis of acetate esters ($\frac{kH}{kD}$ of *ca.* 2) without the necessity of postulating an intramolecular, concerted mechanism having a large amount of carbon-hydrogen bond cleavage in the transition state of the rate-determining step.

$$\mathrm{RCOOR'} \rightleftarrows [\mathrm{RCOO}]^{\ominus}\,[\mathrm{R'}]^{\oplus} \longrightarrow \mathrm{RCOOH} + \mathrm{OLEFINS}$$

Figure 4- Tentative Mechanism Proposed by Scheer et al. for the Gas Phase Pyrolysis of Alkyl Acetates

In 1965, Maccoll[6] conducted a more recent review of the literature on the gas phase pyrolysis of esters and he postulated the following figure as the probable transition state of the decomposition mechanism which was most in accord with the experimental data (Figure 5).

TABLE I

Activation Parameters for the Pyrolysis of Selected Acetates

Acetate	E exp (kcal/mole)	$\Delta S^{\ddagger}$ (eu)	Temp (°C)
Ethyl	46.5	-7.0	487.8
_n_-Propyl	46.2	-7.6	486.4
iso-Propyl	45.2	-2.9	408.5
_n_-Butyl	44.5	-9.3	481.5
2-Butyl	47.0	+0.6	404.7
tert-Butyl	42.4	+2.6	322.7
_n_-Pentyl	44.9	-8.7	473.3
2-Pentyl	42.3	-5.9	409.3
tert-Amyl	43.1	+5.5	303.9
1-Methylcyclohexyl	44.0	+6.5	313.3

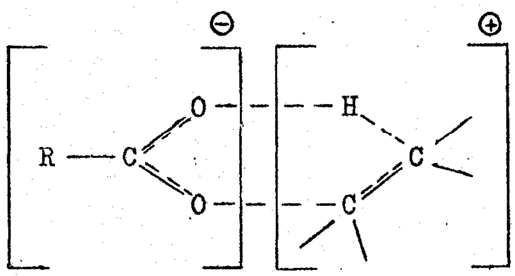


Figure 5 - Transition State Proposed by Maccoll for the Gas Phase Pyrolysis of Esters

Briggs and Djerassi[7] in 1968 investigated the pyrolysis of cis-2-methylcyclohexyl acetate and found the olefinic product to consist of 9 percent 1-methylcyclohexene and 91 percent 3-methylcyclohexene. They put forth the suggestion that the olefin, 1-methylcyclohexene, resulting from an apparent trans elimination could be accounted for by postulating heterolysis of the alkyl-oxygen bond yielding an ion pair followed by direct proton loss or 1,2-hydride shift and subsequent proton loss from the cationic species (Figure 6).

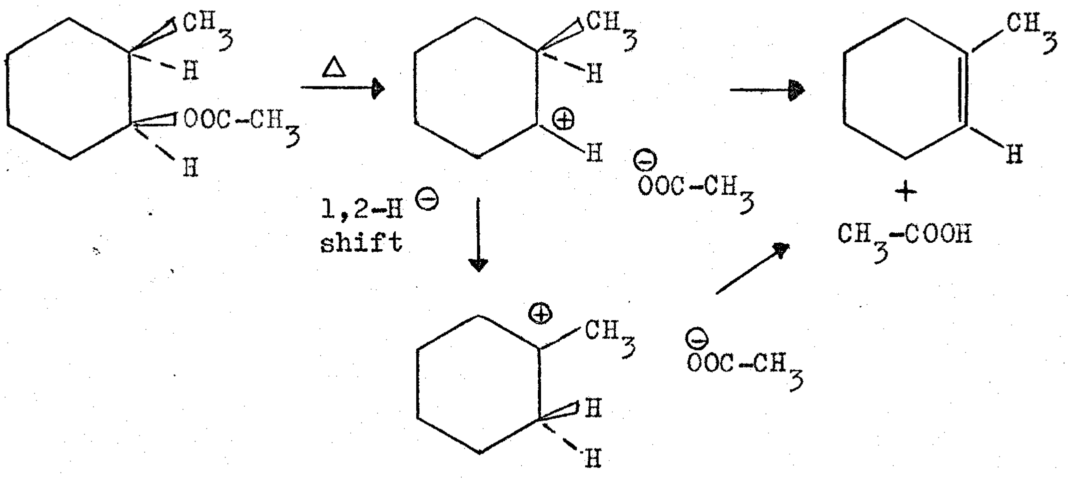


Figure 6- Possible Mechanism for the Formation of 1-Methylcyclohexene from the Pyrolysis of cis-2-Methylcyclohexyl Acetate

In 1951, Zeiss[8] observed that the hydrogen phthalate ester of 2-phenyl-2-butanol decomposed at its melting point (111°). However, no product study was made. In view of this, Rutherford and coworkers[9,10] in 1963 and 1964 prepared and pyrolyzed several tertiary alkyl hydrogen phthalate esters. A study of the decomposition products revealed only phthalic acid and olefins.

It is interesting to note that, whereas primary, secondary and tertiary alkyl acetates decompose to yield acetic acid and olefins, only tertiary alkyl hydrogen phthalates generate alkenes and phthalic acid upon pyrolysis. The hydrogen phthalate esters of primary and secondary alcohols decompose thermally to yield phthalic anhydride and the alcohol used to prepare the ester.[11]

The low decomposition temperatures for tertiary alkyl hydrogen phthalates (135-160°) as compared to those for the corresponding acetates (220-450°) were suggestive of the operation of different pyrolytic mechanisms for the two systems. Hence, Rutherford and Fung[10] in 1964 decided to investigate in detail the products of the pyrolysis of a number of these hydrogen phthalate esters.

The olefinic products obtained from the pyrolysis of <u>trans</u>-1,2-dimethylcyclohexyl hydrogen phthalate were of particular interest in this investigation. It was found that the extreme Saytzeff olefin, 1,2-dimethylcyclohexene, was formed to the extent of 19 percent (Figure 7).[10] Froemsdorf et al.[12] reported that this olefin was not produced in the high temperature (450°), gas phase pyrolysis of <u>trans</u>-1,2-dimethylcyclohexyl acetate. This apparent anomaly indicated that alkyl acetates

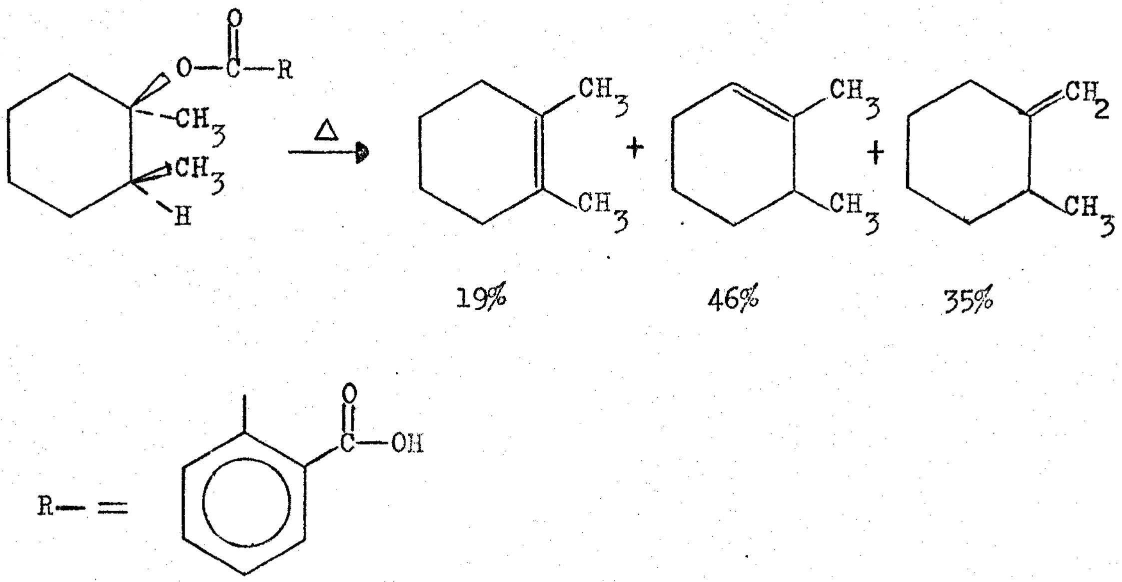
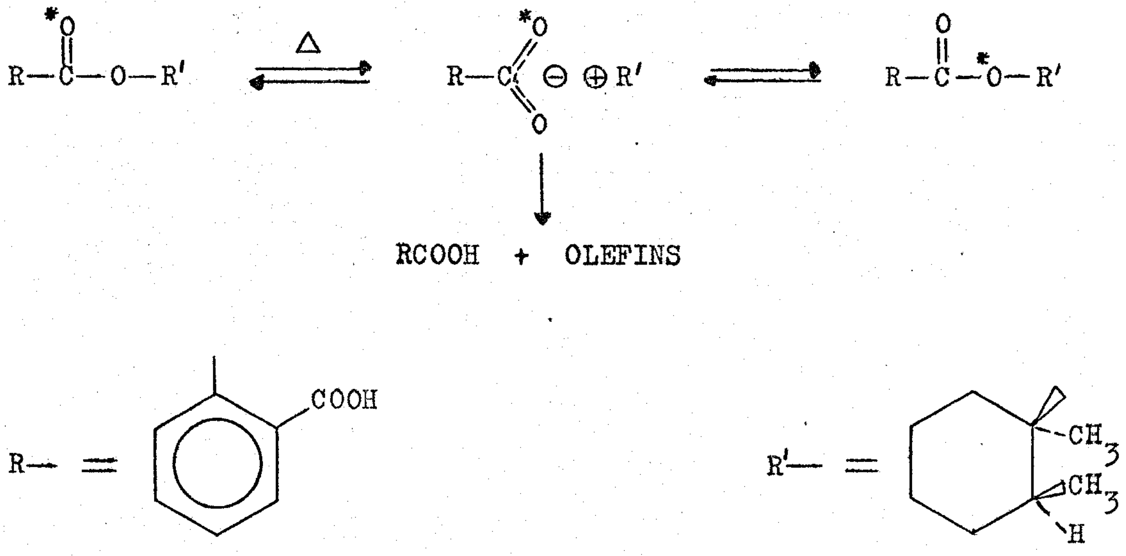


Figure 7 - Olefinic Product Distribution for the Pyrolysis of *trans*-1,2-Dimethylcyclohexyl Hydrogen Phthalate

and alkyl hydrogen phthalates might have different decomposition mechanisms. As no olefin isomerization occurred during pyrolysis of the hydrogen phthalate ester, the formation of 1,2-dimethylcyclohexene seemed to be the result of an apparent *trans* elimination. Hence, Rutherford and Fung[10] postulated the existence of carbonium ion character in the mechanism of this ester pyrolysis and that this elimination is kinetically controlled.

In order to test this proposal, Rutherford and Ottenbrite[13] in 1967 performed an isotope study on the low temperature pyrolysis of *trans*-1,2-dimethylcyclohexyl hydrogen phthalate using ^{18}O enriched ester. The observed increase of ^{18}O isotope in the alcohol portion of the undecomposed ester, representing approximately 17 percent ^{18}O exchange between the alkyl oxygen and carbonyl oxygen atoms, indicated reversible ion pair formation (Figure 8). This supported the earlier proposal of Rutherford and Fung[10] that ionic character is involved in the mechanism for the decomposition of trans-1,2-dimethylcyclohexyl hydrogen phthalate. In addition, it was suggested that this postulate also might apply to the thermal decomposition of other tertiary alkyl hydrogen phthalates which undergo pyrolysis at much lower temperatures than tertiary acetates.



* = ^{18}O enriched oxygen atom

Figure 8- Exchange of ^{18}O between Carbonyl Oxygen and Alkyl Oxygen Atoms in the Pyrolysis of trans-1,2-Dimethylcyclohexyl Hydrogen Phthalate-^{18}O

The activation parameters determined by Scheer et al.[5] for the thermal decomposition of some aliphatic acetates (Table I) indicated a trend, whereby the activation energy seems to decrease as the activation entropy increases on going from primary to tertiary esters. In view of this and the olefinic product distribution and ^{18}O isotope studies conducted on the low temperature pyrolysis of trans-1,2-dimethylcyclohexyl hydrogen phthalate, Rutherford and Wassenaar[14] in 1969 decided to investigate the kinetics of the thermal decomposition of both cis- and trans-1,2-dimethylcyclohexyl hydrogen phthalate in an attempt to elucidate the reaction mechanism.

The cis- and trans-1,2-dimethylcyclohexyl hydrogen phthalate esters were pyrolyzed in the neat and the activation parameters are given in Table II. First-order kinetics and positive activation entropies (10 ± 1 and 6 ± 4 eu for the cis- and trans-esters, respectively) were observed for the cis- and trans-hydrogen phthalate pyrolyses. In addition the olefinic product distributions for these ester pyrolyses were determined (Table III).[14]

In view of these data and the results of the isotope and product distribution studies for the trans-ester pyrolysis, Rutherford and Wassenaar[14] proposed that the cis- and trans- 1,2-dimethylcyclohexyl hydrogen phthalates decompose at low temperatures in a unimolecular manner via an ion pair mechanism. This postulate did not preclude the possibility that these pyrolyses might occur, at least in part, by an irreversible heterolytic or homolytic bond cleavage. The difference between the olefinic product distributions for these ester pyrolyses was explained by an anion proximity effect. Hence, for the decomposition of the cis- and trans-1,2-dimethylcyclohexyl hydrogen phthalates, the breakage of the alkyl-oxygen bond was considered to be the rate-controlling step in the reaction mechanism and

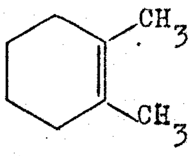
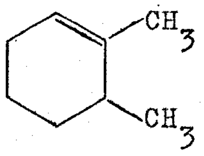
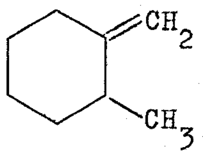
TABLE II

Activation Parameters for the Pyrolysis of *cis*- and *trans*- 1, 2-Dimethylcyclohexyl Hydrogen Phthalate

Compound	Energy of Activation E exp (k cal/mole)	Arrhenius A ($sec^{-1}x10^{-13}$)	Entropy of Activation $\Delta s^{\ddagger}$ (eu)
cis	33.7 ± 0.5	343.8	10 ± 1
trans	32.7 ± 1.6	47.51	6 ± 4

TABLE III

Olefinic Product Distributions for the Pyrolysis of *cis*- and *trans*- 1,2-Dimethylcyclohexyl Hydrogen Phthalate

Compound	Product Distribution Percent		
			
cis	56	20	24
trans	24	46	30

the anion proximity effect and olefin stability appeared to be product-controlling.

In the low temperature pyrolysis of cis- and trans-1,2-dimethylcyclohexyl hydrogen phthalate, it was found that the activation energy for each decomposition was approximately 10 kcal/mole lower than that for various tertiary acetates (Tables I and II). It was proposed by Rutherford and Wassenaar[14] that greater relief of steric strain upon expulsion of the acid phthalate group as compared to that of the acetate group could result in a decrease in the energy of activation. It was also suggested that the formation of a stronger acid in the pyrolysis of a hydrogen phthalate ester could reduce the activation energy since it is known that esters of strong acids decompose faster than those of weaker acids.[15] In addition, they postulated that ortho-carboxyl proton participation, involving the formation of a hydrogen bond between the acid proton and the alkyl oxygen atom of the ester group, conceivably could reduce the activation energy for the pyrolysis of these esters since it would enhance the leaving group ability of the hydrogen phthalate group. This proposed participation is pictured in Figure 9.

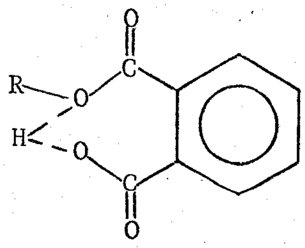


Figure 9- Proposed ortho-Carboxyl Proton Participation in the Pyrolysis of a Tertiary Alkyl Hydrogen Phthalate Ester

Rutherford and Fung[10] noticed that the melting and decomposition temperatures of α-phenyl substituted tertiary alkyl hydrogen phthalates coincided. This suggested added stability of a carbonium ion intermediate in the pyrolysis of such esters as well as increased internal strain of the molecule. These factors could possibly enable ion pair formation to occur at even lower temperatures than for nonaryl substituted hydrogen phthalates. Hence, Rutherford and Wassenaar[14] conducted a kinetic study on the pyrolysis of cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate in order to evaluate, if possible, the effect of the phenyl group.

The cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalates were pyrolyzed in N,N-dimethylformamide (DMF) since the melting and decomposition points of each ester coincide. The activation parameters determined from the kinetic study of these ester pyrolyses are given in Table IV.[14] First-order kinetics were observed for the solution pyrolysis of the cis- and trans- esters and they indicated unimolecular decomposition. A negative activation entropy (-11 ± 4 eu) was observed for the trans-ester pyrolysis and it was explained in terms of a solvent effect since the trans-2,6,6-d_3-hydrogen phthalate showed no appreciable deuterium isotope effect ($\frac{kH}{kD}$ = 1.02). The cis-ester pyrolysis displayed a positive entropy of activation (7 ± 4 eu) which suggested that ionization occurred during decomposition. Rutherford and Wassenaar[14] postulated a unimolecular, ionic mechanism for each ester pyrolysis.

The difference between the positive and negative activation entropies for the cis- and trans- hydrogen phthalate solution pyrolyses,

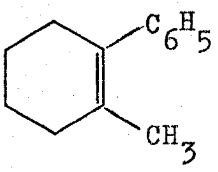
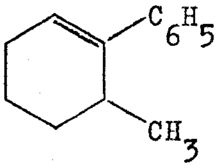
TABLE IV

Activation Parameters for the Pyrolysis of *cis*- and *trans*-1- Phenyl-2-Methylcyclohexyl Hydrogen Phthalate in N,N-Dimethylformamide

Compound	Energy of Activation E exp (kcal/mole)	Arrhenius A (sec^{-1})	Entropy of Activation $\Delta s^{\ddagger}$ (eu)
cis	32.7 ± 1.4	92.04×10^{13}	7 ± 4
trans	26.2 ± 1.6	79.06×10^{11}	-11 ± 4

TABLE V

Olefinic Product Distributions for the Pyrolysis of *cis*- and *trans*-1-Phenyl-2-Methylcyclohexyl Hydrogen Phthalate

Compound	Product Distribution Percent	
		
cis	12	88
trans	8	92
trans-2,6,6-d_3	9	91

respectively, was explained in terms of solvent participation. Rutherford and Wassenaar[14] proposed that the cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate decomposes to an ion pair intermediate which proceeds to the final products too quickly to allow solvation (Figure 10) and that the trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate breaks down into an ion pair that becomes solvated before yielding the reaction products (Figure 11).

In addition, the product distributions for these two ester pyrolyses were determined and were found to be very similar with a strong predominance of the Hofmann olefin, 1-phenyl-6-methylcyclohexene (Table V).[14] A comparison of these product distributions with those for the cis- and trans-1,2-dimethylcyclohexyl hydrogen phthalate decompositions showed that the phenyl group has a definite influence (cis effect) on the ratio of the olefins formed, favouring the Hofmann alkene. An anion effect also was proposed to be operative in these ester pyrolyses, resulting in the preferential removal of those B-hydrogen atoms leading to the Hofmann olefin.

In view of the kinetic and product distribution data for the pyrolysis of cis- and trans-1-phenyl-2-methyl-cyclohexyl hydrogen phthalate in DMF, it seemed to be of interest to conduct an isotope study on these ester decompositions. This investigation should be able to demonstrate the existence or nonexistence of reversibly formed ionic intermediate(s) during these hydrogen phthalate ester decompositions and it might yield further insight into the nature of these species in solution pyrolysis. Also, it was decided to prepare cis- and trans-1-phenyl-2-methylcyclohexyl methyl phthalate and to conduct a preliminary

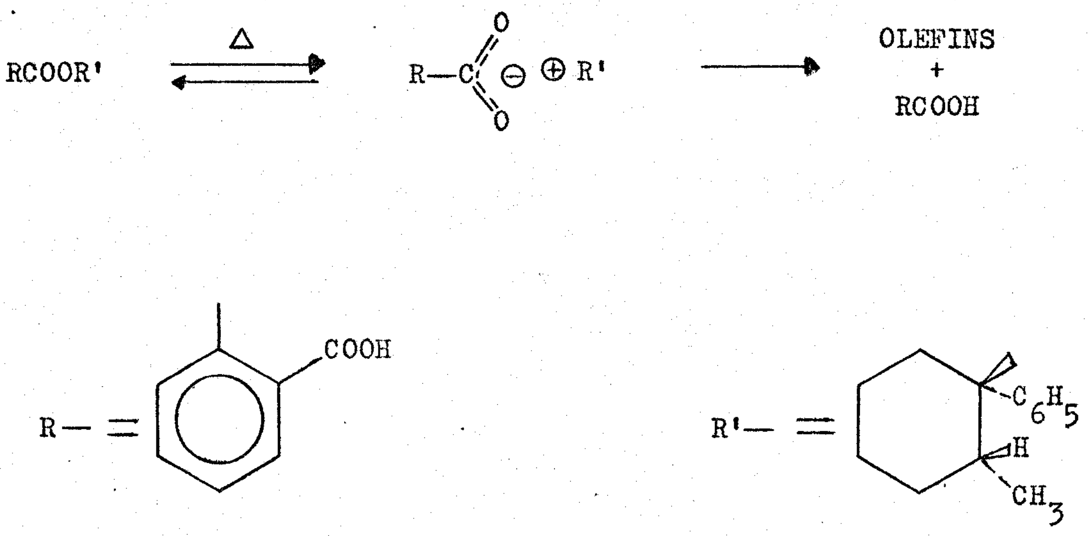


Figure 10- Proposed Scheme for the Pyrolysis of cis-1- Phenyl-2-methylcyclohexyl Hydrogen Phthalate in N,N-Dimethylformamide

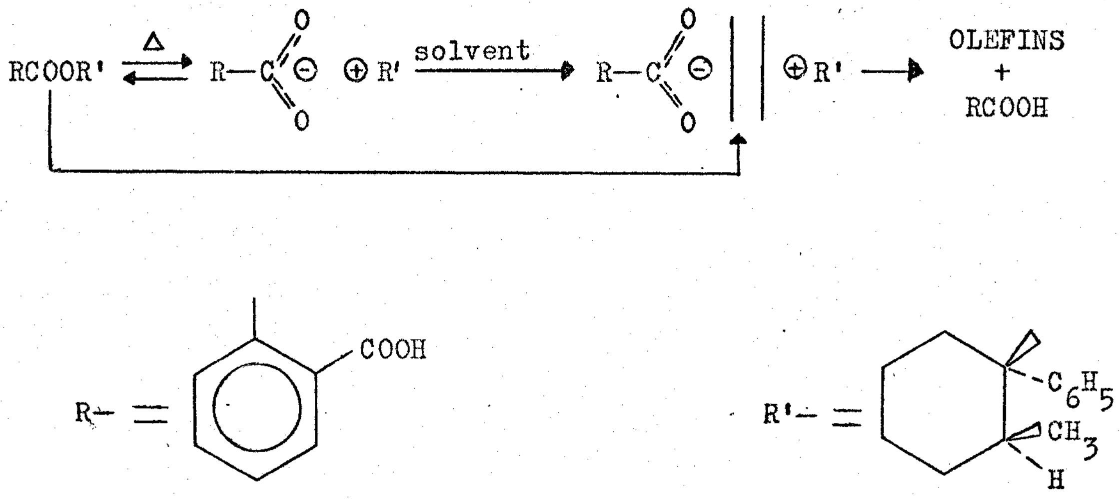


Figure 11- Proposed Scheme for the Pyrolysis of trans-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate in N,N-Dimethylformamide

kinetic study on the solution pyrolysis of these diesters in order to investigate the possibility of ortho- carboxyl proton participation during the thermal decomposition of the corresponding hydrogen phthalate esters in DMF (Figure 9).

CHAPTER II

RESULTS AND DISCUSSION

Stereochemical Elucidation of the Products of the Reaction of Phenyl Magnesium Bromide with 2-Methylcyclohexanone

In order to carry out isotope exchange and geometrical isomerization studies on the pyrolysis of the 1-phenyl-2-methylcyclohexyl hydrogen phthalate system in N,N-dimethylformamide (DMF), it was necessary to elucidate the stereochemistry of the two 1-phenyl-2-methylcyclohexanol isomers.

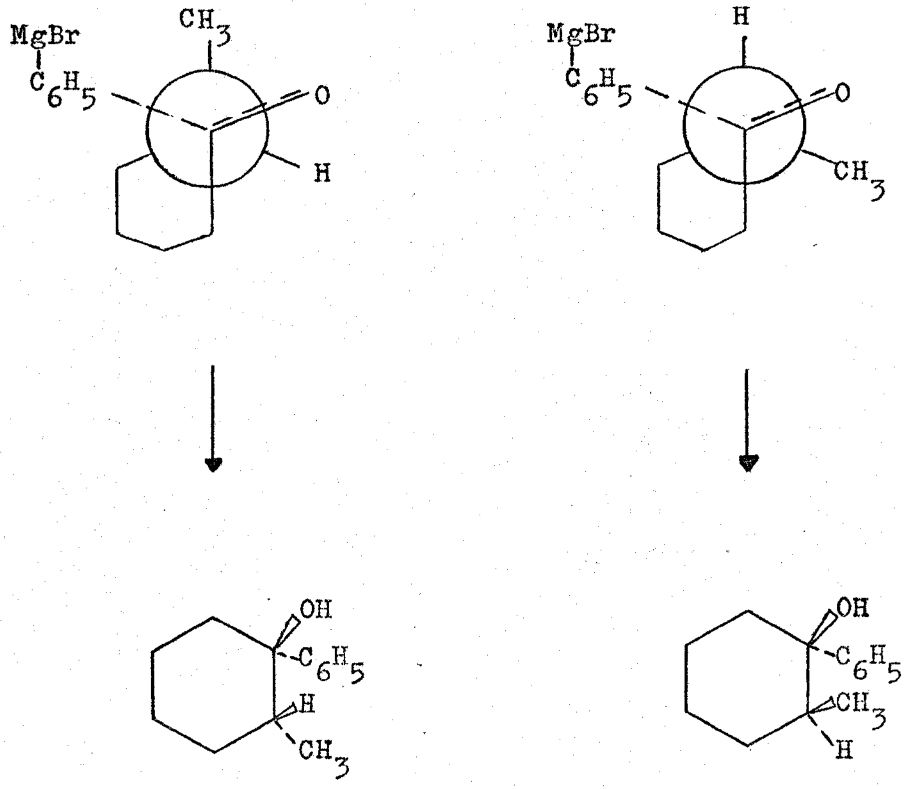
Previously in this laboratory, it was shown by hydroboration that the reaction of methyl magnesium iodide with 2-methylcyclohexanone yielded 83 percent and 17 percent *trans*- and *cis*-1,2-dimethylcyclohexanol, respectively.[14] Hydroboration of purified 1,2-dimethylcyclohexene, obtained from the acid dehydration of an isomeric mixture of 1,2-dimethylcyclohexanol, using oxidizing conditions yielded an alcohol with infrared (ir) and nuclear magnetic resonance (nmr) spectra and gas liquid chromatography (glc) retention time identical to those of the minor product obtained from the Grignard reaction. From this, it was deduced that the minor product was *cis*-1,2-dimethylcyclohexanol and that the major product was the *trans*-alcohol. It should be noted that it would be expected from Cram's rule of ''steric control of asymmetric induction''[16] as applied to an alicyclic system that the major product for this Grignard reaction would be *trans*-1,2-dimethylcyclohexanol.

From this rule, it would seem reasonable that the reaction of

2-methylcyclohexanone with the bulkier phenyl magnesium bromide would result in an even smaller amount of cis-alcohol than in the reaction with methyl magnesium iodide. The former Grignard reaction yielded two isomeric alcohols (92 percent and 8 percent). By hydroboration of pure 1-phenyl-2-methylcyclohexene using oxidizing conditions, an alcohol was obtained having spectral and physical properties identical to those of the 1-phenyl-2-methylcyclohexanol isomer formed in the minor amount from the Grignard reaction. Since the hydroboration reaction results in the overall cis addition of the elements of water to an olefinic double bond producing an alcohol, it is concluded that the product formed in the smaller quantity from the Grignard reaction is cis-1-phenyl-2-methylcyclohexanol and that the major product is trans-1-phenyl-2-methylcyclohexanol. This confirms the prediction made earlier in this laboratory for the reaction of phenyl magnesium bromide with 2-methylcyclohexanone,[14] whereby according to Cram's rule, the cis geometry was assigned to the alcohol isomer formed in the smaller amount as the steric strain in the transition state leading to cis-1-phenyl-2-methylcyclohexanol seems to be greater than that in the activated complex proceeding to trans-1-phenyl-2-methylcyclohexanol (Figure 12).

Kinetic Study on the Pyrolysis of cis- and trans-1-Phenyl-2-methylcyclohexyl Methyl Phthalate in N,N-Dimethylformamide

In order to probe for the existence of ortho-carboxyl proton participation (Figure 9) during the decomposition of the cis- and trans-1- phenyl-2-methylcyclohexyl hydrogen phthalate esters in DMF, the corresponding methyl phthalate diesters were prepared and were pyrolyzed



cis-product

trans-product

Figure 12- Transition States for the Nucleophilic Attack of Phenyl Magnesium Bromide on 2-Methylcyclohexanone leading to *cis*- and *trans*-1-Phenyl-2-methylcyclohexanol

in solution. The results of a preliminary kinetic study are given in Table VI. The kinetic experiments on the cis- and trans-1-phenyl-2-methylcyclohexyl methyl phthalate pyrolyses were performed at the highest temperatures studied for the corresponding hydrogen phthalates due to the slow decomposition rates of the diesters.

The first-order kinetics observed for the methyl phthalate diester pyrolyses indicate unimolecular decomposition. The cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalates were found to decompose 86 and 118 times faster, respectively, than their corresponding methyl phthalate diesters. The difference in steric strain between the hydrogen phthalate esters and the methyl phthalate diesters, as shown by Dreiding models, would not seem to be appreciable enough to account for the relative pyrolysis rates observed. Also, any inductive effect of the methyl group should be of minimal influence in decreasing the ability of the phthalate group to leave.

If ortho-carboxyl proton participation is involved in the pyrolysis of cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate, especially in the rate-determining step of each ester decomposition, one might expect the corresponding methyl phthalate diesters to react slower due to the lack of this proton assistance during decomposition. This prediction is in agreement with the experimental results and indicates that ortho-carboxyl proton participation probably plays an important role in the pyrolysis of the cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate esters in DMF.

This proton involvement could be of the form of hydrogen bonding between the ortho-carboxyl hydrogen atom in the acid phthalate moiety

TABLE VI

Kinetic Study on the Pyrolysis of the Hydrogen and Methyl Phthalate Esters of *cis*- and *trans*-1-Phenyl-2-methylcyclohexanol in N,N-Dimethylformamide

Compound	Temp (°C)	Rate Constant k ($sec^{-1}x10^{+5}$)	Rate Ratio kH/kCH_3	Number of Points	Percentage Completion	Correlation Coefficient
cis-hydrogen phthalate	120.1[a]	56.57±0.72	86	29	62	-0.9978
cis-methyl phthalate	120.1	0.66±0.02		25	31	-0.9930
trans-hydrogen phthalate	135.1[a]	73.15±0.92	118	20	63	-0.9984
trans-methyl phthalate	135.2	0.62±0.02		23	29	-0.9946

[a] These kinetic data were determined by S. Wassenaar, Reference 14.

of the molecule and the alkyl oxygen atom of the ester linkage (Figure 9), which would tend to increase the leaving group ability of the hydrogen phthalate group. This *ortho*-carboxyl proton participation is in agreement with the proposal that the *cis*- and *trans*- hydrogen phthalate esters decompose in an ionic manner.[14]

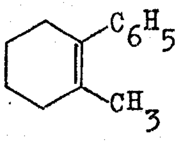
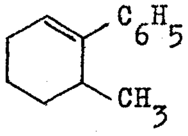
Product Distribution Study on the Pyrolysis of the Hydrogen and Methyl Phthalate Esters of *cis*- and *trans*-1-Phenyl-2-methylcyclohexanol in N,N-Dimethylformamide

The product distributions for the low temperature solution pyrolysis of the *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate esters[17] and their corresponding methyl phthalate diesters were determined by glc analysis of the pyrolysate resulting from each kinetic experiment (Table VII). High temperature pyrolyses were carried out by using the injector port of the gas chromatograph as the decomposition apparatus[14] and the product distributions are given in Table VII.

If the pyrolysis of the *cis*- and *trans*-hydrogen phthalate esters in DMF occurs *via* an ion pair intermediate, then the product distribution for each decomposition, on a statistical basis, would be expected to be 1:2 for 1-phenyl-2-methylcyclohexene and 1-phenyl-6-methylcyclohexene, respectively (Figure 13). As can be seen in Table VII, there is a large predominance of Hofmann product, 1-phenyl-6-methylcyclohexene, for the thermal decomposition of the *cis*- and *trans*-hydrogen phthalates in DMF. However, the statistical product distribution is not obtained for either pyrolysis.

TABLE V11

Pyrolysis of the Hydrogen and Methyl Phthalate Esters of *cis*- and *trans*-1-Phenyl-2-methylcyclohexanol at Different Temperatures

Compound	Temp (°C)	Duration (min)	Product Distribution Percent	
				
cis-hydrogen phthalate[a]	112.6	42	11	89
	120.1	28	10	90
	290	c	25	75
cis-methyl phthalate	120.1	961	13	87
	305	c	22	78
trans-hydrogen phthalate[a]	127.6	35	10	90
	135.1	25	10	90
	290	c	19	81
trans-2,6,6-d_3-hydrogen phthalate[b]	135.1	27	12	88
trans-methyl phthalate	135.2	930	8	92
	305	c	8	92

a These product distributions were determined by S. Wassenaar, References 14 and 17.

b This olefinic product ratio was determined by S. Wassenaar, Reference 17.

c The duration of pyrolysis is not known as the sample was injected directly into the gas chromatograph.

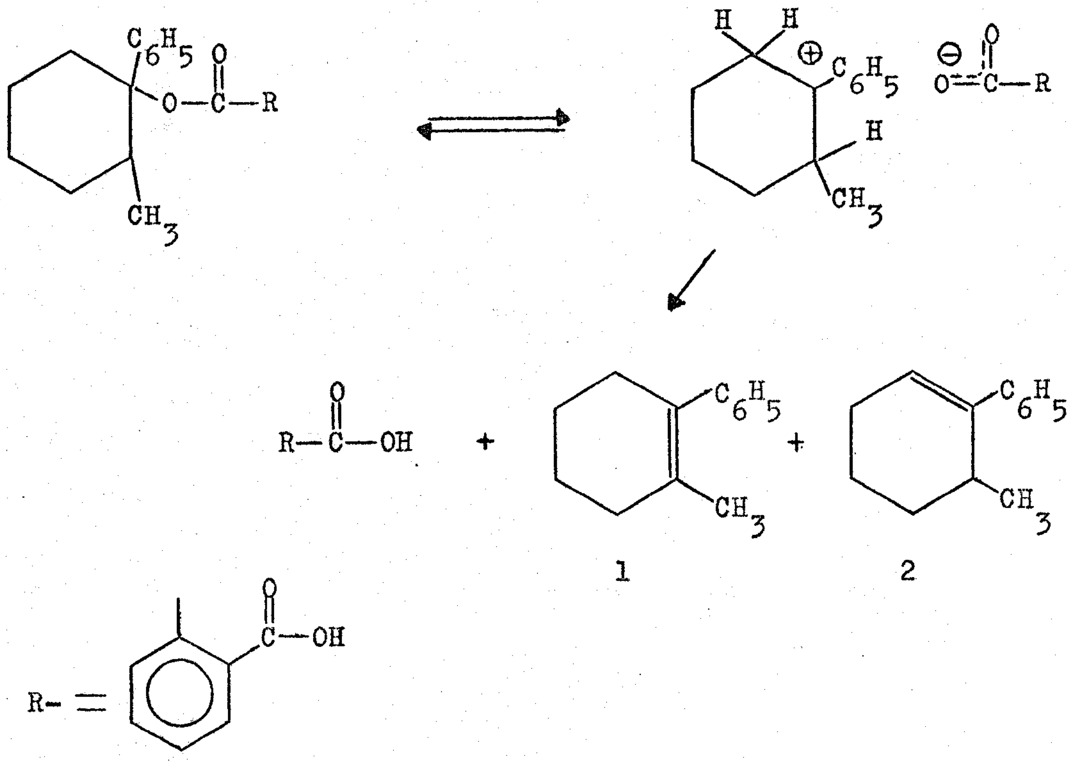


Figure 13- Statistical Product Distribution for the Solution Pyrolysis of 1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate *via* an Ionic Intermediate

As a part of this product distribution study, it was demonstrated that these hydrogen phthalate ester solution pyrolyses are kinetically controlled, that is, there is no olefin isomerization caused by the phthalic acid produced in the thermal decomposition. Hence, the greater than statistical amount of 1-phenyl-6-methylcyclohexene may be caused by a *cis* effect (eclipsing factor) between the phenyl and methyl groups as the olefinic bond of 1-phenyl-2-methylcyclohexene forms, which retards the formation of this latter alkene even though it is more thermodynamically stable. Also, there could be an anion effect operating in which the anion of an ion pair intermediate preferentially removes the proton leading to the Hofmann product, 1-phenyl-6-methylcyclohexene, rather than that giving the Saytzeff olefin, 1-phenyl-2-methylcyclohexene, on account of the cis effect.

If the cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate pyrolyses in DMF yield olefins from an intermediate common to both ester decompositions, very similar product distributions possibly could be obtained. In Table VII, it can be seen that the product distributions for the solution pyrolysis of the cis- and trans-hydrogen phthalates are virtually identical, which agrees with the proposal of a common intermediate from which olefins are formed.

When the product distribution values are considered along with the data obtained from the kinetic study on the pyrolysis of the cis- and trans-hydrogen phthalates in DMF (Table IV), it would seem that this proposed common intermediate is probably not an intimate ion pair which usually precedes solvent-separated ion pair formation. This would appear to be rational since the rate-determining step for the trans-hydrogen phthalate decomposition ($\Delta s^{\ddagger} = -11$ eu) seems to be solvent-separated ion pair formation and it is known that the product-controlling step of a reaction generally does not precede the rate-determining step. This postulated intermediate may be a solvent-separated ion pair. If such is the case, then this common ionic species most likely would be formed after rate-determining production of an intimate ion pair for the pyrolysis of the cis-hydrogen phthalate ($\Delta s^{\ddagger} = 7$ eu). Although kinetically controlled olefin formation directly from an intimate ion pair is not precluded for the cis-ester pyrolysis, it might appear to be fortuitous that the resulting product distribution would be essentially identical to that formed from a solvent-separated ion pair for the trans-ester decomposition.

If an ion pair intermediate is involved in the pyrolysis of the cis- and trans-methyl phthalate diesters in DMF, one might expect again, on a purely statistical basis, the 1:2 ratio of Saytzeff olefin, 1-phenyl-2-methylcyclohexene, to Hofmann alkene, 1-phenyl-6-methylcyclohexene, for the product distribution of each decomposition. As can be seen in Table VII, this is not realized although there is a high predominance of 1-phenyl-6-methylcyclohexene. These product distributions, which were shown to be kinetically controlled, are very similar to those for the corresponding hydrogen phthalate pyrolyses and it seems again that the cis (eclipsing) effect between the methyl and phenyl groups is operative.

In the solution pyrolysis of trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate and its corresponding methyl phthalate diester, the observation that there is formation of 1-phenyl-2-methylcyclohexene is indicative of an apparent trans elimination. This is suggestive of the operation of an ionic mechanism in these ester decompositions.

Pyrolysis of the cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen[14] and methyl phthalate esters also was carried out at higher temperatures. In Table VII, it can be seen that there still exists a predominance of Hofmann olefin, 1-phenyl-6-methylcyclohexene, in the product distribution of each ester decomposition. However, the amount of 1-phenyl-6-methylcyclohexene is reduced except in the case of the trans- methyl phthalate pyrolysis. This decrease in Hofmann olefin may be due to faster decomposition which results in a diminished cis (eclipsing) effect and in less proton selectivity.

Geometrical Isomerization and Isotope Studies on the Pyrolysis of cis- and trans-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O in N,N-Dimethylformamide

In view of the kinetic data for the pyrolysis of cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF, it was decided to conduct these decompositions using esters enriched with 11.0 atom percent ^{18}O in the oxygen atoms of the carboxyl group and of the carbonyl portion of the ester linkage. Then, by means of mass spectrometry, the ^{18}O content of the initially unenriched alkyl oxygen atom of the unpyrolyzed ester could be determined, from which a percent ^{18}O exchange value could be calculated. The data obtained from these experiments should be able to demonstrate the existence or nonexistence of reversibly formed ionic intermediate (s) during the ester pyrolyses. In addition, a deeper understanding of the nature of ion pairs in solution pyrolysis may be realized.

Each ^{18}O enriched hydrogen phthalate ester was pyrolyzed in solution to the extent of 20 percent and 70 percent in two separate experiments using the lowest temperature for which a rate constant of pyrolysis had been determined. The unpyrolyzed ester of each decomposition was recovered and was reduced with lithium aluminum hydride to 1-phenyl-2-methylcyclohexanol, which was analyzed by mass spectrometry to determine the ^{18}O content of the alcohol oxygen atom. Since the hydride reduction does not involve cleavage of the alkyl-oxygen bond of the hydrogen phthalate ester and does not alter the amount of ^{18}O isotope of the 1-phenyl-2-methylcyclohexanol oxygen atom, the ^{18}O content of the alkyl oxygen atom of the unpyrolyzed ester equals that of the alcohol oxygen atom. From this ^{18}O value, the percent ^{18}O exchange between the initially unenriched alkyl oxygen atom of the ester linkage and the ^{18}O labelled oxygen atom(s) can be determined for each thermal decomposition. Similar experimental procedures were used by Goering et al.[18] who demonstrated the involvement of ion pair intermediates in the solvolysis of $\underline{\alpha}$-p-anisylethyl and $\underline{\alpha}$-phenylethyl p-nitrobenzoates in aqueous acetone and by Kice and coworkers[19] who showed ion pair behaviour in the thermal decomposition of aralkyl thiocarbonates.

Before discussing the experimental results, it should be noted that a two-oxygen or a four-oxygen equilibration process or a combination of them may yield scrambling of the ^{18}O enrichment in the undecomposed ester of each partial pyrolysis experiment and this is shown in Figure 14.

Gas chromatographic analysis of the 1-phenyl-2-methylcyclohexanol product obtained by lithium aluminum hydride reduction of the undecomposed hydrogen phthalate ester resulting from each partial pyrolysis experiment also was carried out in order to probe for geometrical isomerization at the $\underline{\alpha}$-carbon atom of the cyclohexyl group.

For 20 percent pyrolysis of each ^{18}O labelled hydrogen phthalate ester, glc analysis of the 1-phenyl-2-methylcyclohexanol resulting from

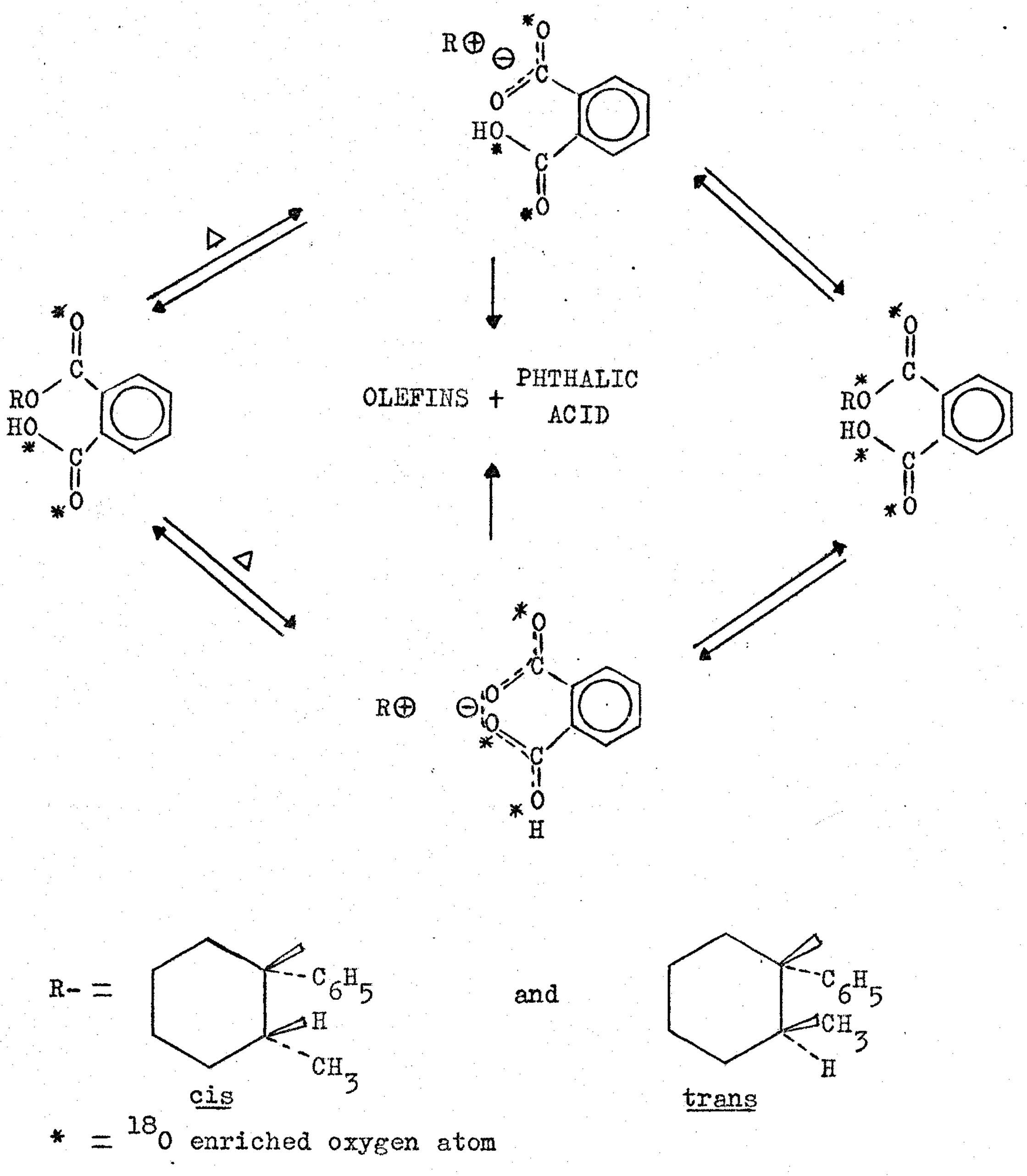


Figure 14- Two-Oxygen and Four-Oxygen Equilibration Processes for Return of an Ion Pair in the Pyrolysis of the *cis*- and *trans*-1-Phenyl-2-methyl-cyclohexyl Hydrogen Phthalate-^{18}O Esters in N,N-Dimethylformamide

the reduction of the unpyrolyzed ester for each thermal decomposition indicated no isomerization of the stereochemistry at the α-carbon atom of the cyclohexyl group (Table VIII). This lack of geometrical isomerization was demonstrated by the observation that cis-1-phenyl-2-methylcyclohexanol was formed exclusively by the reduction of the undecomposed ester from 20 percent pyrolysis of cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O in DMF. Likewise, only trans-1-phenyl-2-methylcyclohexanol was obtained by the reduction of the undecomposed ester resulting from 20 percent pyrolysis of the ^{18}O labelled trans- hydrogen phthalate.

For 70 percent pyrolysis of the ^{18}O enriched cis- and trans-hydrogen phthalates, a mixture of cis- and trans-1-phenyl-2-methylcyclohexanol was obtained from the reduction of the unpyrolyzed ester of each thermal decomposition (Table VIII). The geometrical isomerization at the α-carbon atom of the cyclohexyl ring in each partial pyrolysis must have occurred during pyrolysis since lithium aluminum hydride reduction does not affect the stereochemistry at the α-alkyl carbon atom of the ester. This was demonstrated by reducing the cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O esters individually and by analyzing the resulting 1-phenyl-2-methylcyclohexanol (Table VIII).

The ^{18}O exchange percentages for the cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O ester pyrolyses in DMF, as determined by the mass spectrometric analysis of the 1-phenyl-2-methylcyclohexanol samples, are given in Table IX for both two-oxygen and four-oxygen equilibration processes and on the basis of the ^{18}O content of

TABLE V111

Geometrical Isomerization Study on the Pyrolysis of *cis*- and *trans*-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O in N,N-Dimethylformamide

Compound	Temp (^{o}C)	Duration (min)	Percent Pyrolysis	Percent *cis*-1-Phenyl-2-methyl-cyclohexanol	Percent *trans*-1-Phenyl-2-methyl-cyclohexanol
	-	-	0	100	0
cis-ester	112.6	15.0	20	100	0
	112.6	81.1	70	96.5	3.5
	-	-	0	0	100
trans-ester	127.6	8.8	20	0	100
	127.6	50.6	70	13.2	86.8

TABLE IX

Isotope Study on the Pyrolysis of *cis*- and *trans*-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O in N,N-Dimethylformamide

Compound	Temp (°C)	Duration (min)	Percentage Decomposition	Percentage $\frac{M+2}{M}$	Atom Percentage ^{18}O	1-Phenyl-2-methyl-cyclohexanol analyzed	Percent ^{18}O Exchange Equilibration	
							2-Oxygen	4-Oxygen
cis-hydrogen phthalate-^{18}O	-----	----	0	1.2044	0.248	*cis*	---	---
	112.6	15.0	20	3.4436 ±0.6815	2.428 ±0.642	*cis*	40.4 ±12.0	27.0 ±8.0
	112.6	81.1	70	6.6433 ±0.5311	5.383 ±0.472	*cis*	95.2 ±8.9	63.5 ±5.9
				10.1909 ±1.1739	8.450 ±0.995	*trans*	152.1 ±18.2	101.4 ±12.2
trans-hydrogen phthalate-^{18}O	-----	----	0	1.1771	0.220	*trans*	-----	------
	127.6	8.8	20	1.9994 ±0.2562	1.035 ±0.250	*trans*	15.1 ±4.6	10.0 ±3.1
	127.6	50.6	70	3.4161 ±0.3022	2.398 ±0.285	*trans*	40.3 ±5.3	26.9 ±3.5
				2.1618 ±0.3736	1.192 ±0.367	*cis*	18.0 ±6.5	12.0 ±4.4

the cis- and trans- alcohols where applicable. The presence of more than the initial starting abundance of ^{18}O isotope is observed in the oxygen atom of each 1-phenyl-2-methylcyclohexanol sample. From an analysis of the ^{18}O exchange percentages obtained from the isotope experiments, it would appear that these results are consistent with the operation of an ionic mechanism for the pyrolysis of cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF, involving reversibly formed ionic intermediate(s).

For 20 percent pyrolysis of cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O in DMF, no geometrical isomerization was observed at the α-carbon atom of the alcohol moiety of the undecomposed ester (Table VIII) and 40.4 percent ^{18}O exchange based on the two-oxygen equilibration process (27.0 percent ^{18}O exchange by the four-oxygen equilibration pathway) was found (Table IX). These data are consistent with the operation of an ionic mechanism for the solution pyrolysis of the cis-hydrogen phthalate. This ionic pyrolytic pathway would appear to involve return from a reversibly formed intimate ion pair, in which the anion and the cation are in relatively close proximity to one another such that negligible geometrical isomerization accompanies the scrambling of the ^{18}O enrichment between the labelled and unlabelled oxygen atoms. The research of Goering[18] on the solvolysis of α-phenylethyl p-nitrobenzoate in aqueous acetone supports this proposed intimate ion pair character in which he found no racemization at the asymmetric carbon atom upon return of the intimate ion pair to the ester.

For 70 percent pyrolysis of the ^{18}O labelled cis-hydrogen phthalate, a small amount of geometrical isomerization at the α-carbon atom of the cyclohexyl ring was observed yielding trans-hydrogen phthalate (3.5 percent) in the undecomposed ester. This result would seem to be consistent with a small but definite amount of return to the ester from a solvent-separated ion pair, in which the anion and the cation are separated sufficiently to allow isomerization of the stereochemistry at this α- alkyl carbon atom.

If this is the case, one might expect a large incorporation of ^{18}O isotope into the alkyl oxygen atom of the trans-hydrogen phthalate in the unpyrolyzed ester and possibly the operation of a four-oxygen equilibration process. This would seem rational since the separation of the cation and the anion in the proposed solvent-separated ion pair should be appreciable enough to allow the participation of all four oxygen atoms in the mode of exchange. This prediction is realized in the experimental data (Table IX).

The ^{18}O exchange value of 152.1 percent, based on the two-oxygen equilibration process, for the 3.5 percent trans-hydrogen phthalate in the unpyrolyzed ester resulting from 70 percent pyrolysis of the ^{18}O labelled cis-hydrogen phthalate is not very reasonable on the basis of an ionic mechanism for decomposition. The operation of an exchange pathway having either a four-membered or a seven-membered cyclic transition state, which involves an ^{18}O enriched oxygen atom and the α-carbon atom of the cyclohexyl group, would seem to be required during decomposition to obtain such a high percent ^{18}O exchange. This would seem quite unlikely in view of steric and entropy considerations. On the basis of the four-oxygen process, 101.4 percent ^{18}O

equilibration was observed for the 3.5 percent trans-ester in the unpyrolyzed hydrogen phthalate. Within the limits of experimental error, this value would seem to be consistent with complete ^{18}O equilibration by the four-oxygen process and is in agreement with an ionic pyrolytic mechanism. Hence, it would appear that this minor quantity of trans-hydrogen phthalate (3.5 percent) in the undecomposed ester for 70 percent pyrolysis of cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O could result from a small amount of solvent-separated ion pair return, which would allow ^{18}O exchange to occur via the four-oxygen process. It should be noted that this type of return also may be involved during 20 percent pyrolysis of the ^{18}O labelled cis-hydrogen phthalate but it is not sufficient to detect by glc analysis.

The cis-hydrogen phthalate (96.5 percent) in the unpyrolyzed ester from 70 percent pyrolysis of cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O was found to have an ^{18}O isotope content (5.383 atom percent ^{18}O) in its alkyl oxygen atom which may be the result of either a two-oxygen (95.2 percent exchange) or a four-oxygen (63.5 percent exchange) equilibration process or a combination of them (Table IX). This large amount of cis-hydrogen phthalate in the unpyrolyzed ester and the ^{18}O isotope exchange associated with it are consistent with that which might be expected for return primarily from an intimate ion pair, as discussed previously. It should be noted that some of the ^{18}O exchange in the undecomposed cis-ester from 70 percent pyrolysis of the ^{18}O enriched cis-hydrogen phthalate may be derived from the small amount of solvent-separated ion pair return that seems to yield the 3.5 percent trans-ester in the undecomposed hydrogen phthalate.

As discussed previously, the activation parameters (Table IV) and the product distribution values (Table VII) for the pyrolysis of *cis*-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF are consistent with a mechanism involving rate-determining formation of an intimate ion pair ($\Delta s^{\ddagger} = 7$ eu) and kinetically controlled olefin formation from a solvent-separated ion pair (Figure 15). The geometrical isomerization and ^{18}O exchange data for the thermal decomposition of the *cis*-hydrogen phthalate also seem to be in agreement with this proposed mechanism. It would appear that both intimate and solvent-separated ion pairs are reversibly formed with the latter ionic intermediate contributing very little to the ion pair return process.

$$RX \overset{\Delta}{\rightleftarrows} \underset{\substack{\text{intimate}\\ \text{ion pair}}}{R^{\oplus}X^{\ominus}} \overset{\text{solvent}}{\rightleftarrows} \underset{\substack{\text{solvent-separated}\\ \text{ion pair}}}{R^{\oplus}||X^{\ominus}} \longrightarrow \text{OLEFINS} + \text{PHTHALIC ACID}$$

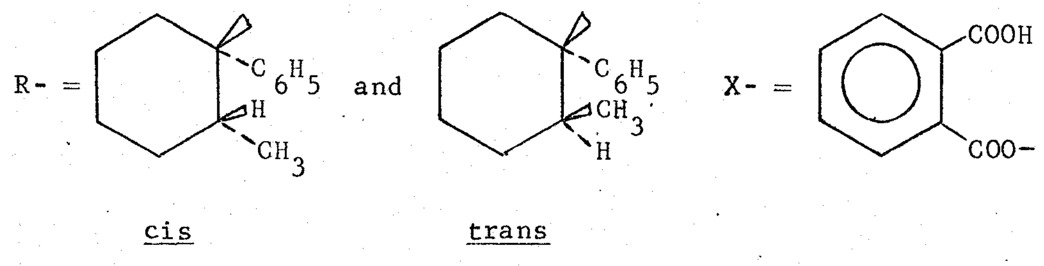


Figure 15- Proposed Scheme for the Pyrolysis of *cis*- and *trans*-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate in N,N-Dimethylformamide

For 20 percent pyrolysis of *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O in DMF, no detectable amount of stereochemical isomerization was found at the α-alkyl carbon atom of the cyclohexyl ring in the unpyrolyzed ester (Table VIII). As can be seen in Table IX, 15.1 percent ^{18}O exchange was detected in the unpyrolyzed *trans*-hydrogen phthalate based on the two-oxygen equilibration process (10.0 percent ^{18}O exchange by the four-oxygen equilibration path). These data are consistent with decomposition of the *trans*-hydrogen phthalate in solution *via* an ionic mechanism involving return to the neutral ester from a reversibly formed intimate ion pair, in which the attractive forces are strong enough to preserve the stereochemistry at the α-alkyl carbon atom. This intimate ion pair intermediate probably would precede solvent-separated ion pair formation, which seems to be rate-controlling for the solution pyrolysis of the *trans*-hydrogen phthalate ($\Delta s^{\ddagger} = -11$eu).

For 70 percent pyrolysis of the ^{18}O enriched *trans*-hydrogen phthalate in solution, there was a slight amount of geometrical isomerization at the α-alkyl carbon atom of the cyclohexyl group, yielding 13.2 percent *cis*-hydrogen phthalate in the unpyrolyzed ester. This observed isomerization is in agreement with that expected for a small amount of return from a reversibly formed solvent-separated ion pair in which the interionic forces are too weak to preserve the stereochemistry at this α-alkyl carbon atom. The ^{18}O isotope exchange associated with this small amount of *cis*-hydrogen phthalate could have resulted from either a two-oxygen (18.0 percent exchange) or a four-oxygen (12.0 percent exchange) equilibration pathway or a combination of them. However, the separation between the cation and the anion of a solvent-separated ion pair would seem to be more suitable for scrambling of the ^{18}O enrichment by the four-oxygen equilibration process during return of this ionic intermediate to the neutral ester. It should be noted that the preceding ^{18}O exchange values seem to be lower than those expected for return from a solvent-separated ion pair. One possible explanation for this anomaly involves the nucleophilic attack of a small amount of water on an ion pair intermediate, yielding cis-1-phenyl-2-methylcyclohexanol with virtually no ^{18}O enrichment. This would reduce the actual ^{18}O content of the cis-alcohol obtained from the reduction of the cis-hydrogen phthalate in the unpyrolyzed ester, thereby having an adverse effect on the percent ^{18}O exchange. This postulate was tested experimentally. Gas chromatographic analysis of the pyrolysate resulting from 70 percent decomposition of the trans- hydrogen phthalate in DMF indicated a small amount of cis-alcohol. However, further research would seem to be necessary to completely resolve this discrepancy.

The trans-hydrogen phthalate (86.8 percent) in the unpyrolyzed ester resulting from 70 percent pyrolysis of trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O was found to have an isotope content of 2.398 atom percent ^{18}O in its alkyl oxygen atom which could have resulted from a two-oxygen (40.3 percent exchange) or a four-oxygen (26.9 percent exchange) equilibration process or a combination of these pathways. This large amount of trans-hydrogen phthalate in the undecomposed ester and the ^{18}O exchange associated with it could be explained primarily by return from a reversibly formed intimate ion pair. Some of the ^{18}O exchange associated with this trans-ester may be the result of a small amount of solvent-separated ion pair return which seems to account for the 13.2 percent cis-hydrogen phthalate in the unpyrolyzed ester.

These isotope exchange and geometrical isomerization values for the pyrolysis of trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF along with the previously discussed kinetic and product distribution data are consistent with the operation of an ionic mechanism involving reversibly formed intimate and solvent-separated ion pairs (Figure 15). This latter ionic intermediate seems to participate only slightly in the ion pair return process. The rate-controlling step seems to be solvent-separated ion pair formation ($\Delta s^{\ddagger} = -11$ eu) and the decomposition products appear to be formed in a kinetically controlled manner from a solvent-separated ionic intermediate.

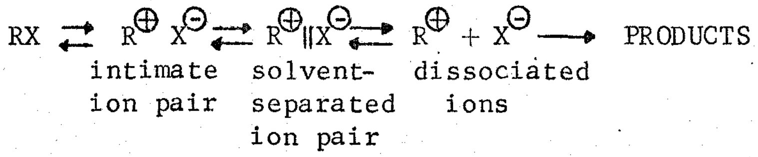
Examination of the ^{18}O exchange data for the 20 percent and 70 percent partial pyrolyses of cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O in DMF reveals a greater amount of isotope equilibration for the cis-ester decompositions than for the corresponding trans-ester pyrolyses. This may be caused by the repetition of a mechanism involving ionization to an ion pair followed by return to the neutral ester with the percent ^{18}O exchange increasing with the number of times that this process is repeated. Alternatively, it may be due to the looseness (charge separation) of an ion pair with the greater the charge separation between the anion and the cation of this ionic aggregate the more randomization of the ^{18}O enrichment upon return to the ester thus yielding a larger percent ^{18}O exchange. It may be the result of the ionic character (charge development) of an ion pair with the greater the charge development the more ^{18}O exchange upon return to the ester.

For the cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O thermal decompositions, ^{18}O exchange was observed in the unpyrolyzed ester (Table IX). There was only a small amount of geometrical isomerization detected at the α-alkyl carbon atom of the undecomposed ester for 70 percent pyrolysis of the ^{18}O labelled cis-hydrogen phthalate (Table VIII) and this is consistent with that expected for only a small amount of involvement of a solvent-separated ion pair in the return process. Hence, it appears that the majority of ^{18}O exchange in the unpyrolyzed ester of these partial decompositions is a result of return from an intimate ion pair which has relatively strong interionic forces. Likewise, return from an intimate ion pair seems to be the source of the majority of the isotope exchange observed in the undecomposed ester of the trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate - ^{18}O pyrolyses.

For the solution pyrolysis of the cis-hydrogen phthalate, there is probably a greater tendency for formation of a solvent-separated ion pair from an intimate ion pair, which is formed in the rate-determining step ($\Delta s^{\ddagger} = 7$ eu), than for internal return to the ester. Whereas for the thermal decomposition of the trans-hydrogen phthalate in DMF, there may be a large amount of repetition of the ionization-return process as a result of the greater preference of an intimate ion pair to return to the ester than to form a solvent-separated ion pair *via* the rate-determining step ($\Delta s^{\ddagger} = -11$ eu). The fact that the ^{18}O exchange percentages for the cis-ester decompositions are larger than those for the *trans*-ester pyrolyses suggests that the amount of charge development and/or the degree of looseness of an intimate ion pair has a greater influence on the magnitude of isotope exchange than does the repetition of the ionization-return process. Hence, it would seem that the proposed intimate ion pair in the pyrolysis of the *cis*-hydrogen phthalate in DMF is looser and/or more ionic in character than the corresponding ionic intermediate in the pyrolysis of the *trans*-ester in DMF.

Summary and Conclusions

Winstein and coworkers[20,21] investigated unimolecular solvolytic reactions over a period of years. From kinetic, stereochemical and rearrangement studies along with common ion and special salt effects, they proposed the following scheme involving intimate and solvent-separated ion pairs and dissociated ions (Figure 16).



$$RX \rightleftarrows R^{\oplus}X^{\ominus} \rightleftarrows R^{\oplus}\|X^{\ominus} \rightleftarrows R^{\oplus} + X^{\ominus} \longrightarrow \text{PRODUCTS}$$

Figure 16- Mechanism Proposed by Winstein for Unimolecular Solvolyses

For unimolecular pyrolytic reactions in solution, the following general scheme is proposed which involves four possible pathways for decomposition (Figure 17).

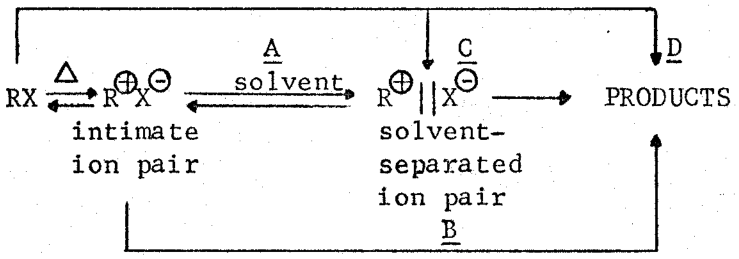


Figure 17- Proposed General Scheme for Solution Pyrolyses

Kinetic, isotope exchange, stereochemical and product distribution studies were conducted on the pyrolysis of cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF. In view of Figure 17, the data obtained from these investigations should be able to elucidate the particular pathway(s) involved in these ester decompositions.

Pyrolysis of the cis-ester in solution is first-order which is indicative of unimolecular decomposition. The entropy of activation for pyrolysis (7 eu) is consistent with rate-determining formation of an intimate ion pair. This hydrogen phthalate ester would appear to decompose by path A and/or B. The involvement of paths C and D seems to be small as these routes would display a negative activation entropy.

The ratio of the rate constants for the cis-hydrogen phthalate and methyl phthalate solution pyrolyses (86) agrees with that expected for ortho-carboxyl proton participation (Figure 9) in the rate-determining step of the hydrogen phthalate decomposition and is in keeping with an ionic mechanism.

The product distribution data for the cis- and trans-hydrogen phthalate solution decompositions (Table VII) are very similar and they show a strong predominance of Hofmann olefin (90 percent), 1-phenyl-6-methylcyclohexene, as compared to Saytzeff alkene (10 percent), 1-phenyl-

2-methylcyclohexene. It is difficult to place a definite interpretation on these data with respect to the mechanism of pyrolysis of the cis- and trans-hydrogen phthalates in DMF. However, the nearly identical product distributions are in agreement with that which might be expected for kinetically controlled olefin formation from an intermediate common to both ester pyrolyses involving a cis (eclipsing) effect that plays an important role in alkene formation.

When the product distribution data for the trans-ester solution pyrolysis are considered in conjunction with the entropy of activation for decomposition (-11 eu), it would appear that the olefins possibly are formed from a solvent-separated ion pair. If this ionic intermediate also is involved in olefin formation for the solution pyrolysis of the cis-ester, then it most likely is formed after rate-determining formation of an intimate ion pair. In the case of the cis-ester decomposition, kinetically controlled olefin formation from an intimate ion pair is not precluded. However, it might seem somewhat coincidental that olefin formation predominantly from an intimate ion pair for the cis-ester decomposition and primarily from a solvent-separated ion pair for the trans-ester pyrolysis would yield virtually identical product distributions.

The ^{18}O exchange percentages and the geometrical isomerization values for the cis-hydrogen phthalate partial pyrolyses in DMF (Tables VIII and IX) are consistent with the involvement of reversibly formed intimate and solvent-separated ion pairs during decomposition. However, the amount of solvent-separated ion pair return would seem to be much less than that for internal return of an intimate ion pair to the ester since only 3.5 percent of the trans-ester was found in the unpyrolyzed hydrogen phthalate for the 70 percent decomposition experiment.

Hence, thermal decomposition of cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF primarily via path A would seem to be consistent with the experimental data. Pyrolysis by route B also may be involved, but the extent to which this occurs is probably small.

Thermal decomposition of the trans-hydrogen phthalate in DMF also is first-order and this again is indicative of unimolecular pyrolysis. The entropy of activation (-11 eu) and the B-deuterium isotope effect (kH/kD = 1.02) for the pyrolysis of this ester are in agreement with rate-determining formation of a solvent-separated ion pair and with decomposition proceeding via path A and/or C. The participation of path B would seem small since it would give rise to a positive activation entropy and the involvement of route D appears to be negated by the B-deuterium isotope effect.

The observation that the trans-hydrogen phthalate pyrolyzed 118 times faster in solution than the corresponding methyl phthalate diester is consistent with ortho-carboxyl proton participation (Figure 9) in the rate-determining step of the hydrogen phthalate decomposition and is in agreement with an ionic pyrolytic mechanism.

As discussed previously, the product distribution data for the trans-ester solution pyrolysis in conjunction with the results from the kinetic study are in agreement with the postulate that olefin formation may be occurring from a solvent-separated ion pair similar in character to that proposed for the decomposition of the cis-ester. In addition, it appears that a cis (eclipsing) effect plays an important role in the formation of the olefinic products.

The ^{18}O exchange and stereochemical isomerization data for the trans-hydrogen phthalate-^{18}O partial pyrolyses in DMF (Tables VIII and IX) appear to be consistent with the proposed involvement of reversibly formed intimate and solvent-separated ion pairs during decomposition. Internal return from an intimate ion pair would seem to be the major contributor to the return process from these ionic intermediates. Return from a solvent-separated ion pair appears to be less important since only 13.2 percent of the cis-ester was detected in the unpyrolyzed hydrogen phthalate for the 70 percent pyrolysis experiment. From a close examination of the ^{18}O exchange and kinetic data for the cis-and trans-hydrogen phthalate decompositions, it would seem that the proposed intimate ion pair for the cis-ester pyrolysis is looser and/or more ionic than the corresponding intermediate for the trans-ester decomposition.

From the preceding discussion, it appears that decomposition of trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF essentially via path A is consistent with the experimental data and that any pyrolysis by route C probably would be small.

In conclusion, the behaviour of the cis- and trans- 1-phenyl-2-methylcyclohexyl hydrogen phthalate esters during pyrolysis in DMF is consistent with the operation of an ionic mechanism (path A) and would appear to be similar to that observed for the 1,2-dimethylcyclohexyl system. All experimental data are in agreement with the postulated reaction scheme for pyrolytic eliminations (Figure 17).

CHAPTER III

EXPERIMENTAL

All infrared (ir) spectra were recorded on a Beckman IR 12 spectrophotometer equipped with potassium bromide cells and all solutions were weight-weight percent in the specified solvent. Only the significant absorptions are reported (cm^{-1}) and their intensities are expressed as weak (w, 100-75 percent transmission), medium (m, 74-40 percent transmission) or strong (s, 39-0 percent transmission). The nuclear magnetic resonance (nmr) spectra were measured with a JEOL C-60 HL instrument and all solutions were weight-volume percent in the stipulated solvent. The chemical shifts are reported in τ downfield from internal tetramethylsilane. The splitting pattern of each resonance is reported using the following code: s = singlet, d = doublet, bd = broad doublet, t = triplet, m = multiplet and bm = broad multiplet. The mass spectral analyses were conducted by Dr. O.A. Mamer, Department of Clinical Biochemistry, Royal Victoria Hospital, Montreal, Quebec. Microanalyses were determined by Midwest Microlab, Inc., Indianapolis, Indiana. Melting and decomposition points were determined with a Fisher-Johns melting apparatus and are uncorrected. All gas liquid chromatography (glc) was conducted on a Hewlett Packard 720 instrument and peak areas were determined with a disc integrator. Preparative glc columns were all of the same dimensions (8 ft x 0.5 in.) and were packed with 10 percent Carbowax 20 M or 10 percent LAC-728, on Diatoport W, 60-80 mesh, using steel columns. The following analytical columns were used: 10 ft x 0.25 in. copper column packed with 10 percent LAC-728 on Chromosorb W A/W DMCS, 80-100 mesh and 6 ft x 0.25 in. copper column packed with 10 percent Carbowax 20 M on Chromosorb W NAW, 60 mesh or 10 percent silicone gum rubber SE-30 on Diatoport W, 60-80 mesh. Analytical thin layer chromatography (tlc) was performed on 0.30-mm fluorescent silica gel and alumina plates using the indicated solvents as eluents.

1-Phenyl-2-methylcyclohexene

An isomeric mixture of 1-phenyl-2-methylcyclohexanol (5.0 g, 26.3 mmole) was dehydrated with 15 ml of a 16.5 percent sulfuric acid-acetic acid solution (V/V) according to the method of Garbisch.[22,23] The solution was stirred for 1.0 hr at 25° and poured into 100 ml of 1:1 hexane-water. The organic layer was separated, washed with 5 percent sodium bicarbonate until basic and with water until neutral, dried over anhydrous magnesium sulfate, concentrated and distilled yielding olefin (3.2 g, 72.1 percent) as a colourless liquid which was shown by glc analysis (LAC-728, 130°) to be a mixture of isomers (12.9 percent and 87.1 percent): bp 56-58° (0.15 mm); n_D^{25} 1.5468; ir (CCl_4, 5 percent) 3020 (m), 2930 (s), 2860 (s), 2830 (s), 1600 (m), 1490 (m), 1440 (m). The olefinic isomers were separated by preparative glc (LAC-728, 140°) and the major component with the shorter retention time was 1-phenyl-2-methylcyclohexene which was shown to be 100 percent pure by glc analysis (LAC-728, 130°) and by nmr integration: n_D^{25} 1.5470 (lit.[23] n_D^{25} 1.5452); ir (CCl_4, 5 percent) 3070 (m, C_6H_5), 2940 and 2860 (s, CH_3 and CH_2), 1600 and 1495 (m, C_6H_5), 1445 (s, CH_3 and CH_2); nmr (CCl_4, 18 percent) 2.83 (m, 5, C_6H_5), 7.50-8.40 (bm, 8, $(CH_2)_4$), 8.47 (s, 3, CH_3). The nmr data were in good agreement with those reported by Garbisch[23] for 1-phenyl-2-methylcyclohexene. This olefin was used to prepare cis-1-phenyl-2-methylcyclohexanol by the method of Brown and Zweifel[24] involving hydroboration.

The alkene formed in the minor amount with the longer retention time was 1-phenyl-6-methylcyclohexene. This isomer was separated with 93.2 percent purity and the other component (6.8 percent) was 1-phenyl-2-methylcyclohexene as shown by glc analysis (LAC-728, 130°): $\underline{n}_D^{25}$ 1.5528 (lit.[23] $\underline{n}_D^{25}$ 1.5539); ir ($CDCl_3$, 7 percent) 3030 (w, C_6H_5 and C=C-H), 2935 and 2870 (s, CH_3, CH_2 and CH), 1600 and 1490 (m, C_6H_5), 1445 (m, CH_3 and CH_2); nmr ($CDCl_3$, 7 percent) 2.70 (m, C_6H_5), 4.10 (m, C=C-H), 6.83-8.66 (bm, CH_2 and CH), 9.08 (d, $\underline{J}$=7.0 Hz, CH_3). The nmr data coincided with that found by Garbisch.[23]

cis-1-Phenyl-2-methylcyclohexanol via Hydroboration of 1-Phenyl-2-methylcyclohexene

The olefin (0.800 g, 4.64 mmole) and a solution of sodium borohydride (0.145 g, 3.83 mmole) in 10 ml of freshly distilled tetrahydrofuran were placed in a wide-mouthed, 50-ml flask fitted with a constant addition funnel, thermometer and condenser. The reaction was conducted under nitrogen maintaining the temperature at 20-30° with an ice bath during the addition of freshly distilled boron trifluoride etherate (1.09 g, 7.65 mmole). The solution was stirred for 1.0 hr at 25° followed by the cautious addition of 2 ml of water. When initial reaction ceased, 5.6 ml of 3 $\underline{N}$ sodium hydroxide was added quickly followed by the rapid addition of 5.6 ml of 30 percent hydrogen peroxide. The solution was stirred for 1.0 hr at 25°, after which it was salted out with sodium chloride and extracted with 25 ml of ether. The ethereal layer was washed with five 10-ml portions of ice cold water, dried over anhydrous sodium sulfate and concentrated. The crude product was analyzed by glc (Carbowax 20 M, 180°) and the major component (66.9 percent) was purified by preparative glc (Carbowax 20 M, 200°) and by crystallization from hexane yielding crystals of 1-phenyl-2-methylcyclohexanol (0.296 g, 33.4 percent):

mp 61-63° (lit.[14] mp 59-61°); ir (CCl_4, 5 percent) 3605 (m, free OH), 3480 (w, bonded OH), 3060 (w, C_6H_5), 2940 and 2860 (s, CH_3, CH_2 and CH), 1600 and 1495 (m, C_6H_5), 1445 (m, CH_3 and CH_2); nmr ($(CD_3)_2$ SO, 10 percent) 2.57 (m, 5, C_6H_5), 5.27 (s, 1, OH), 7.50-8.90 (bm, 9, $(CH_2)_4$ and CH), 9.40 (d, 3, $\underline{J}$ = 7.0 Hz, CH_3).

1-Phenyl-2-methylcyclohexanol

A solution of phenyl magnesium bromide was prepared from magnesium turnings (7.3 g, 0.30 mole), bromobenzene (42.0 g, 0.27 mole) and 200 ml of anhydrous ether. Reaction of the Grignard reagent with 2-methylcyclohexanone (28.0 g, 0.25 mole) dissolved in 100 ml of anhydrous ether yielded after distillation an isomeric mixture of 1-phenyl-2-methylcyclohexanol (31.1 g, 65.5 percent) as a colourless oil: bp 93-96° (0.38 mm); $\underline{n}_D^{25}$ 1.5363 (lit.[25] bp 105-106° (1 mm), $\underline{n}_D^{25}$ 1.5359); ir (CCl_4, 10 percent) 3610 (m, free OH), 3060 and 3020 (m, C_6H_5), 2930 and 2850 (s, CH_3, CH_2 and CH), 1600 and 1490 (m, C_6H_5), 1445 (m, CH_3 and CH_2). Analysis by glc (LAC-728, 180°) showed two well defined peaks representing the isomeric alcohols in the amounts of 92.0 percent and 8.0 percent, respectively.

cis- and *trans*-1-Phenyl-2-methylcyclohexanol

The isomers of 1-phenyl-2-methylcyclohexanol were separated by the preparation of the hydrogen phthalate ester of the isomeric mixture of alcohol according to the method of Rutherford et al.[9] followed by the saponification of the isomeric hydrogen phthalate ester mixture using dilute sodium hydroxide solution as described below.

To an isomeric mixture of 1-phenyl-2-methylcyclohexyl hydrogen phthalate (30.0 g, 88.8 mmole), 0.1 $\underline{N}$ sodium hydroxide (932.0 ml, 93.2

mmole) was added. The solution was refluxed for 4.0 hr and cooled to 25° followed by the addition of 100 ml of chloroform through the condenser. The organic layer was separated, dried over magnesium sulfate and concentrated. The yellow oil (15.0 g) was distilled yielding three fractions (13.2 g). Fraction one constituted 25 percent of the distilled product: bp 25-82° (0.5 mm); ir indicated olefin. Fraction two comprised 43 percent of the distilled reaction product: bp 82-93° (0.45 mm); ir indicated alcohol. The third fraction constituted 32 percent of the product and it solidified partially: bp 73-85° (0.05 mm); ir showed alcohol. Fractions two and three were combined and glc analysis (LAC-728, 180°) indicated that the two alcohols were present in the amounts of 43.4 percent and 56.6 percent, respectively. Preparative glc (Carbowax 20 M, 200°) was used to separate the alcohols. The alcohol isomer with the shorter retention time (43.4 percent) was a liquid: $\underline{n}_D^{25}$ 1.5355 (lit.[14] for trans-1-phenyl-2-methylcyclohexanol $\underline{n}_D^{25}$ 1.5334); ir (CS_2, 5 percent) 3610 (m, free OH), 3065 and 3030 (m, C_6H_5), 2935 and 2855 (s, CH_3, CH_2 and CH), 1600 and 1490 (m, C_6H_5), 1445 (m, CH_3 and CH_2); nmr ($(CD_3)_2$ SO, 18 percent) 2.67 (m, 5, C_6H_5), 5.50 (s, 1, OH), 7.83-8.83 (bm, 9, $(CH_2)_4$ and CH), 9.50 (d, 3, $\underline{J}$ = 5.5 Hz, CH_3). The isomer alcohol with the longer retention time (56.6 percent) was recrystallized from hexane yielding a solid: mp 62-64° (lit.[14] for cis-1-phenyl-2-methylcyclohexanol mp 59-61°); ir (CS_2, 5 percent) 3600 (m, free OH), 3470 (w, bonded OH), 3065 (m, C_6H_5), 2945 and 2865 (s, CH_3, CH_2 and CH), 1600 and 1570 (m, C_6H_5), 1450 (m, CH_3, CH_2 and CH); nmr ($(CD_3)_2$ SO, 18 percent) 2.60 (m, 5, C_6H_5), 5.28 (s, 1, OH), 7.58-8.92 (bm, 9, $(CH_2)_4$ and CH), 9.43 (d, 3, $\underline{J}$ = 7.0 Hz, CH_3). These alcohols were similar in their physical and spectral properties to those obtained from the Grignard reaction of phenyl magnesium bromide with 2-methylcyclohexanone. The solid alcohol compared favourably in all respects with cis-1-phenyl-2-methylcyclohexanol, which was obtained by the hydroboration of 1-phenyl-2-methylcyclohexene. Hence, the liquid alcohol is concluded to be trans-1-phenyl-2-methylcyclohexanol and the solid isomer is deduced to be cis-1-phenyl-2-methylcyclohexanol. Analysis by glc (LAC-728, 180°) showed the former alcohol to be 100 percent pure and the latter to be 99+ percent pure.

cis- and trans-1-Phenyl-2-methylcyclohexyl Methyl Phthalate

Diazomethane was used to convert the cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate esters, prepared by the method of Rutherford et al.,[9] to the corresponding methyl phthalate diesters.

An ethereal-alcoholic solution of diazomethane, generated from N-methyl-N-nitroso-p-toluenesulfonamide,[26] was added dropwise to cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate (1.0 g, 2.96 mmole) dissolved in 50 ml of 1:1 chloroform-ether until there was a persistent yellow colour indicating excess reagent. The reaction solution was allowed to stand for 12.0 hr at 25°, filtered and concentrated yielding cis-1-phenyl-2-methylcyclohexyl methyl phthalate (1.0 g, 96.2 percent) as a viscous oil, which was unicomponent by the tlc analysis (alumina, ether): ir ($CDCl_3$, 5 percent) 3080 and 3045 (w, C_6H_5 and C_6H_4), 2950 and 2870 (s, CH_3, CH_2 and CH), 1725 (s, ester C = O), 1600 and 1495 (m, C_6H_5 and C_6H_4), 1450 (s, CH_3 and CH_2), 1300 (s, C-O); nmr ($CDCl_3$, 13 percent) 1.83 - 2.83 (bm, 9, C_6H_5 and C_6H_4), 6.22 (s, 3, $COOCH_3$), 6.73 - 7.23

(bm, 1, CH), 7.33 - 8.83 (bm, 8, $(CH_2)_4$), 9.36 (d, 3, J = 7.0 Hz, CH_3).

Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.94; H, 7.12.

In a similar manner, trans-1-phenyl-2-methyl-cyclohexyl methyl phthalate (1.0 g, 96.2 percent) was obtained as a solid, which was pure by tlc analysis (alumina, ether): mp 73 - 76°; ir ($CDCl_3$, 5 percent) 3070 and 3040 (w, C_6H_5 and C_6H_4), 2940 and 2865 (s, CH_3, CH_2 and CH), 1725 (s, ester C = O), 1600 and 1495 (m, C_6H_5 and C_6H_4) 1450 (s, CH_3 and CH_2), 1295 (s, C-O); nmr ($CDCl_3$, 13 percent) 1.66-2.83 (bm, 9, C_6H_5 and C_6H_4), 6.10 (s, 3, $COOCH_3$), 6.60-7.07 (bm, 1, CH), 7.60-8.76 (bm, 8, $(CH_2)_4$), 9.23 (bd, 3, CH_3).

Anal. Calcd for $C_{22}H_{24}O_4$: C, 74.98; H, 6.86. Found: C, 74.79; H, 6.79.

Kinetic Study on the Pyrolysis of cis- and trans- 1-Phenyl-2-methylcyclohexyl Methyl Phthalate in N,N-Dimethylformamide

The cis- and trans-1-phenyl-2-methylcyclohexyl methyl phthalate pyrolyses were conducted in N,N-dimethylformamide (DMF) in order that a comparison of the rate constants for these diester decompositions could be made with those for the corresponding hydrogen phthalate esters.

The reaction solvent was dried in the following manner.[27] A 1-l. quantity of N,N-dimethylformamide was stirred with 200 g of freshly dried (500°, 3 hr) magnesium sulfate for 18 hr at 25°. The solvent was decanted from the drying agent and was distilled at reduced pressure from 100 g of dried magnesium sulfate. The second fraction of distillate (bp 63° (3.5 cm)) was collected and used in the kinetic runs.

A 35-ml aliquot of DMF was pipetted into a 100-ml, three-necked, round-bottomed flask fitted with a mechanical stirrer, condenser and septum adapter for a hypodermic syringe. A (0.6-0.7)-g sample of the solid trans-methyl phthalate diester was pressed into a pellet. The apparatus was heated in a Haake model NBS high temperature circulating and thermostated oil bath having an R20 controller. When the desired temperature was reached and the system was equilibrated, the septum adapter was removed momentarily and the accurately weighed pellet was added to the solvent. After a two minute waiting period to allow complete dissolution of the pellet, 1.0-ml aliquots were removed at regular intervals using the hypodermic syringe and these samples were placed into 25-ml conical flasks each containing 5 ml of ice cold tetrahydrofuran (THF). These samples were titrated with standardized (0.014-0.015)N sodium hydroxide solution against phenolphthalein indicator. Blank corrections were made for both THF and DMF.

For the cis-methyl phthalate diester kinetic experiment, an accurately weighed sample of the viscous oil was dissolved in 35 ml of DMF and this solution was placed in the pyrolysis apparatus, which was set at the desired temperature. A half hour delay was incorporated to allow the solution to reach temperature equilibrium and then the same procedure was followed as in the trans-methyl phthalate kinetic experiment. The solution pyrolysis of the cis-methyl phthalate was performed on a small scale (0.1 g ester, 5 ml DMF) and it was shown by tlc analysis (alumina, ether) that the decomposition was very slow. Hence, the above method of sample introduction probably resulted in only a small amount of pyrolysis. This, coupled with the fact that the first sample taken represented the aliquot at zero time, appeared to justify the use of this technique.

The solution pyrolyses required a correction factor for the solvent volume, as it was measured at room temperature, but the samples were removed at the decomposition temperature thereby altering the concentrations of reactant and products. The solvent expansion was determined for each pyrolysis by placing in the oil bath a small graduated glass tube containing some DMF and observing the change in volume on heating. This was used to calculate the initial concentration of the methyl ester.

The rate constant for each diester pyrolysis was determined by using the first-order rate equation:

$$\ln E_L = -kt + \ln E_o$$

where: E_L = methyl phthalate diester left at any time t

E_o = methyl phthalate diester at time o.

k = rate constant (sec^{-1})

t = time (sec)

The raw experimental data (sample weight, expanded solvent volume, volume of base for blank titration, base normality, number of samples, aliquot size, times at which samples were taken and experimental titration volumes for the samples) were punched on computer cards, which then were placed in the programme designed to calculate the rate constant for each pyrolysis.

For a print-out of the programme and a description of the calculations involved, see the dissertation of H.H. Holton.[28]

Product Distribution Study on the Pyrolysis of *cis*- and *trans*-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate

The olefinic product ratios for the pyrolysis of *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate in DMF were determined by Wassenaar in the following manner.[17]

The remaining pyrolysis solution from each kinetic experiment, containing unreacted ester, decomposition products and DMF, was extracted with 25 ml of petroleum ether (bp 30-60°). The hydrocarbon layer was washed with 25 ml of water, dried over anhydrous magnesium sulfate and concentrated. A (2-3)-μl sample of a 50 percent ethereal solution of the olefinic mixture was injected into the glc (LAC-728, 100°) and the product distribution was determined with the aid of a disc integrator.

A product distribution study on the high temperature pyrolysis of the *cis*- and *trans*-hydrogen phthalate esters also was carried out by Wassenaar[14] and the procedure is described in his dissertation.

The results of the product distribution study of the solution and high temperature hydrogen phthalate ester pyrolyses are given in Table VII.

Product Distribution Study on the Pyrolysis of *cis*- and *trans*-1-Phenyl-2-methylcyclohexyl Methyl Phthalate

For the pyrolysis of *cis*- and *trans*-1-phenyl-2-methylcyclohexyl methyl phthalate in DMF, the remaining solution from each kinetic experiment, containing unreacted diester and the pyrolysis products, was subjected to trap to trap distillation at 25° for 24.0 hr at reduced pressure (10 μ) using liquid nitrogen as a coolant. The last traces of olefin were distilled by heating the flask at 35° for 5.0 hr. The olefin-DMF distillate was added to 20 ml of water and the resulting solution was extracted with two 25-ml portions of hexane. The hexane solution was dried over anhydrous sodium sulfate, filtered and concentrated. The olefin was analyzed by glc using a 10-μl sample of a 10 percent hexane solution (Carbowax 20 M, 130°).

For the pyrolysis of the *cis*- and *trans*-methyl phthalate diesters at high temperature, a 10-μl sample of a 10 percent hexane solution of each diester was injected directly into the glc and the olefinic product distribution was determined for thermal decomposition in the injector port (Carbowax 20 M, 130°).

The olefinic product distributions obtained from this study are given in Table VII.

Stability of 1-Phenyl-2-methylcyclohexene and 1-Phenyl-6-methylcyclohexene under the Conditions of Pyrolysis in N,N-Dimethylformamide

The stability of a mixture of 1-phenyl-2-methylcyclohexene and 1-phenyl-6-methylcyclohexene under the conditions of the *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate solution pyrolyses and of the corresponding methyl phthalate decompositions was studied in two separate experiments.

A small aliquot of a known olefinic mixture was placed in a DMF solution containing either phthalic acid or methyl hydrogen phthalate. The concentrations of the various components in each solution approximated those existing at the end of a kinetic determination. Each solution was heated to an average pyrolysis temperature and for an average reaction time as determined from the kinetic study.[14] Each test solution was worked up in the same manner used for the determination of the olefinic product distributions and it was found that each olefin ratio varied by only 1-2 percent towards the Saytzeff alkene, 1-phenyl-2-methylcyclohexene.

Likewise, two test solutions containing a known olefinic mixture, DMF and the pyrolysate residue from either a hydrogen phthalate ester pyrolysis or a methyl phthalate diester decomposition were allowed to stand for one month. The product distribution of the olefinic mixture in each solution was determined and a change of 2-3 percent towards Hofmann alkene, 1-phenyl-6-methylcyclohexene, was noted.

Hence, it appears that there is very little olefin isomerization under the conditions of pyrolysis.

Phthalic Anhydride-^{18}O

Phthalic anhydride (13.7 g, 92.6 mmole) was added to 50 ml of freshly distilled, dry tetrahydrofuran. To this solution, 20 atom percent ^{18}O enriched water (4.9 g, 272.2 mmole) was added followed by refluxing for 20.0 hr under nitrogen. The solution was cooled to 25° and anhydrous hydrogen chloride was bubbled through it for 0.5 min with stirring. The acidic solution was refluxed for 12.0 hr and after cooling, dry hydrogen chloride was passed through it for 5.0 min. The solution was stirred at 25° for 12.0 hr yielding a white solid and the reaction mixture was refluxed for another 12.0 hr followed by cooling, dry hydrogen chloride addition for 1.0 min and stirring at 25° for 1.0 hr. The mixture was cooled to 0° and 250 ml of ice cold pentane were added. The white solid was collected by filtration, washed with 200 ml of hot chloroform and dried in vacuo yielding phthalic acid (13.7 g, 89.1 percent). The phthalic acid was dehydrated under reduced pressure (12.5 cm) in a sublimator with an oil bath as an external heat source. With the temperature of the oil bath at approximately 228°, needles of phthalic anhydride formed (10.8 g, 78.8 percent) which were unicomponent by tlc analysis (silica gel, chloroform): mp 131.5 - 133.5° (lit.[29] mp 130.8°); ir ($CHCl_3$, 5 percent) 3040 (m, C_6H_4), 1855 and 1780 (s, anhydride C=O), 1600 and 1470 (m, C_6H_4), 1255 (s, C-O). Mass spectral analysis indicated 11.030 atom percent ^{18}O in the phthalic anhydride. The experimental method and calculations involved in the determination of the atom percent ^{18}O can be found in the section on the mass spectral analysis of 1-phenyl-2-methylcyclohexanol.

cis- and trans-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O

These esters were prepared from cis- and trans-1-phenyl-2-methylcyclohexanol and phthalic anhydride-^{18}O according to the method of Rutherford et al.[9]

The cis-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O ester was formed with a 53.0 percent yield and was unicomponent by tlc analysis (silica gel, ether): mp 116-118° dec (lit.[14] mp 124° dec); ir ($CDCl_3$, 5 percent) 3400-2400 (s, COOH), 1725 (s, ester C=O), 1705 (s, acid C=O), 1600 and 1495 (m, C_6H_5 and C_6H_4), 1295 (s, C-O); nmr ($CDCl_3$, 10 percent) -1.20 (s, 1, COOH), 1.93-3.13 (bm, 9, C_6H_5 and C_6H_4), 6.53-7.30 (bm, 1, CH), 7.37-8.93 (bm, 8, $(CH_2)_4$), 9.37 (d, 3, *J* = 7.0 Hz, CH_3).

The trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O ester was synthesized with a 42.2 percent yield and was pure by tlc analysis (silica gel, ether): mp 141-142^{o} dec (lit.[14]mp 142^{o} dec); ir ($CDCl_3$, 5 percent) 3480-2400 (s, COOH), 1725 (s, ester C=O), 1710 (s, acid C=O), 1600 and 1495 (m, C_6H_5 and C_6H_4), 1295 (s, C-O); nmr ($CDCl_3$, 11 percent) -1.20 (s, 1, COOH), 1.87 - 3.00 (bm, 9, C_6H_5 and C_6H_4), 6.60-7.13 (bm,1, CH), 7.60 - 9.00 (bm, 8, $(CH_2)_4$), 9.27 (bd, 3, CH_3).

Partial Pyrolysis of *cis*- and *trans*-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O in N,N-Dimethylformamide

In four separate experiments, the *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O esters were decomposed to the extent of 20 percent and 70 percent using the following procedure.

A (0.5-0.7)-g sample of ester was pressed into a pellet. After weighing, it was added to 35 ml of freshly distilled DMF in a three-necked, 100-ml, round-bottomed flask fitted with a condenser, mechanical stirrer and glass stopper, all of which had been equilibrated at the desired temperature using a Haake model NBS high temperature circulating and thermostated oil bath having an R20 controller. The reaction solution was stirred for a prescribed time period, as determined from the pyrolysis rate constant, to allow the desired amount of decomposition. The ester pyrolysis was terminated by pouring the reaction solution into an ice cold flask. The decomposition temperatures and reaction times are given in Table IX.

Reduction of the Undecomposed 1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O from each Partial Pyrolysis

The DMF solution from each decomposition was subjected to trap to trap distillation at reduced pressure (10 μ) for 24.0 hr using liquid nitrogen as a coolant. To the undistilled residue 25 ml of ether was added. The resulting cloudy solution was filtered to remove phthalic acid and the ethereal filtrate containing undecomposed hydrogen phthalate ester was placed in a three-necked, 100-ml, round-bottomed flask which was equipped with a condenser and two glass stoppers. Lithium aluminum hydride was added to the solution, which was under a nitrogen atmosphere, until vigorous reaction ceased and the reaction mixture became gray in colour. The reduction mixture was stirred for 1.0 hr at 25° and then was refluxed for 1.0 hr. Excess lithium aluminum hydride was destroyed by the cautious, dropwise addition of ethyl acetate and the lithium and aluminum complexes were decomposed by the addition of n ml of water (n=weight of reducing agent used), n ml of 15 percent sodium hydroxide solution, and 3 n ml of water. A white crystalline solid formed which was collected by filtration and washed with two 10-ml portions of ether. The ethereal filtrate and washings were combined, washed with three 20-ml portions of saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate and concentrated. The organic residue was treated with 25 ml of hexane. The hydrocarbon solution was separated from the insoluble, yellow, viscous oil (ω,ω'-dihydroxy-o-xylene), concentrated and analyzed by glc (LAC-728, 180°; Carbowax 20 M, 180°; SE-30, 130°) from which the relative amounts of *cis*- and *trans*-1-phenyl-2-methyl-cyclohexanol were determined. The glc data for all partial pyrolyses are given in Table VIII.

Mass Spectrometric Analysis of 1-Phenyl-2-methylcyclohexanol and the Calculation of the Percent ^{18}O Exchange in the Undecomposed 1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O from each Partial Pyrolysis

A sample of the reduction product from each partial pyrolysis, containing *cis*- and /or *trans*-1-phenyl-2-methylcyclohexanol, was sent with a glc chromatogram (SE-30, 130°) for mass spectral analysis.

An LKB 9000 combination gas chromatograph-mass spectrometer, equipped with a 6 ft x 0.25 in. glass column packed with 3 percent SE-30 on Chromosorb W HP, was used. The following conditions were maintained for all 1-phenyl-2-methylcyclohexanol analyses: injector temperature, 280°; separator temperature, 280°; ion source temperature, 290°; ionizing energy, 20 or 70 eV at 60 μA; helium flow rate, 20 cc/min; column temperature, 140° + 4°/min; sample size, 1 μl of 2 percent chloroform solution.

The following conditions were used for phthalic anhydride analysis: injector temperature, 250°; separator temperature, 280°; ion source temperature, 290°; ionizing energy, 70 eV at 60 μA; helium flow rate, 35 cc/min; column temperature, 100° + 4°/min and 145°; sample size, 1 μl of 2 percent chloroform solution.

The heights of the M(m/e 190) and M + 2(m/e 192) peaks were measured by ruler and a relative uncertainty for each determination was assigned. These limits were incorporated into the calculation of (M + 2/M) percent to give maximum and minimum values as demonstrated in the following example (20 percent pyrolysis of *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O).

$M = 31.3 \pm 0.2$ mm (low sensitivity scale)

$M + 1 = 4.6 \pm 0.3$ mm, 45.8 ± 0.4 mm (low and middle sensitivity scales respectively)*

$M + 2 = 6.2 \pm 0.3$ mm (middle sensitivity scale)

$$\left(\frac{M+2}{M}\right)\%\text{: maximum value} = \frac{\frac{4.9}{45.4} \times 6.5}{31.1} \times 100 = 2.2556$$

$$\text{minimum value} = \frac{\frac{4.3}{46.2} \times 5.9}{31.5} \times 100 = 1.7432$$

$$\text{average value} = 1.9994 \pm 0.2562$$

For two mass spectral analyses of a sample, the average of the two (M+2/M) percent values was used and for three determinations, the mean value of (M+2/M) percent was used. The error limits of the (M+2/M) percent values for these latter cases were set equal to the square root of the sum of the squares of the deviations for the individual determinations.

Using the following equation, the (M+2/M) percent values corresponding to given atom percent ^{18}O values were determined:

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[*] The M + 1(m/e 191) measurements were used to put the M and M + 2 values on the same sensitivity scale.

$$\frac{M+2}{M} = \frac{Z\,^{18}O}{100-{}^{17}O-{}^{18}O} + \frac{W(W-1)}{2}\left(\frac{C}{100-C}\right)^2 + \frac{X(X-1)}{2}\left(\frac{H}{100-H}\right)^2 +$$

$$\frac{Z(Z-1)}{2}\left(\frac{^{17}O}{100-{}^{17}O-{}^{18}O}\right)^2 + WX\left(\frac{C}{100-C}\right)\left(\frac{H}{100-H}\right) +$$

$$WZ\left(\frac{C}{100-C}\right)\left(\frac{^{17}O}{100-{}^{17}O-{}^{18}O}\right) + XZ\left(\frac{H}{100-H}\right)\left(\frac{^{17}O}{100-{}^{17}O-{}^{18}O}\right)$$

where: $C_WH_XO_Z$ = $C_{13}H_{18}O$; $W = 13$; $X = 18$; $Z = 1$; $^{17}O = 0.039$ percent;
$C = 1.069$ percent; $H = 0.016$ percent; $^{18}O = 0$-50 percent.

This equation was solved by computer for different values of atom percent ^{18}O and a graph of (M+2/M) percent versus atom percent ^{18}O was obtained. From this plot, the atom percent ^{18}O and its uncertainty limits were determined for each (M+2/M) percent value. Hence, an (M+2/M) percent of 1.9994 ± 0.2562 corresponds to an atom percent ^{18}O of 1.035 ± 0.250.

This mathematical equation was also used for the mass spectral analysis of phthalic anhydride-^{18}O and a graphical representation of the M+2/M results, derived from the computer substitution of different values of atom percent ^{18}O (0-19 percent) for $C_8H_4O_3$ in the equation, was obtained. Interpolation of the measured M+2/M percent value (37.5800) on the graph gave an atom percent ^{18}O of 11.030 for phthalic anhydride-^{18}O.

The percent ^{18}O exchange values for the ester pyrolyses were calculated for both two-oxygen and four-oxygen equilibration modes in the following manner.

For *cis*- and *trans*-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O before pyrolysis, the atom percent ^{18}O for each of the ester carbonyl and carboxyl oxygen atoms was 11.030 and that of the ester alkyl oxygen atom was set equal to x. On the basis of the two-oxygen exchange process between the alkyl and carbonyl oxygen atoms of the ester group, the maximum obtainable atom percent ^{18}O in the former oxygen atom for complete equilibration was $\frac{11.030 + x}{2}$. However, there was an abundance of x atom percent ^{18}O in this alkyl oxygen atom before pyrolysis. Hence, the maximum obtainable excess atom percent ^{18}O for complete exchange was $\frac{11.030 - x}{2}$. Likewise, this abundance value (x atom percent ^{18}O) was deducted from the experimentally determined atom percent ^{18}O for the oxygen atom of 1-phenyl-2-methylcyclohexanol, which represented the alkyl oxygen atom of the unpyrolyzed ester. The division of the actual excess atom percent ^{18}O for each sample by the theoretical value for complete equilibration and the multiplication of the quotient by 100 gave the percent ^{18}O exchange between the oxygen atoms of the ester linkage in the unpyrolyzed hydrogen phthalate for each thermal decomposition. For the example being used, the abundance of ^{18}O in the alkyl oxygen atom before pyrolysis was 0.220. Hence, the percent ^{18}O exchange was $\frac{0.815 \mp 0.250}{5.405} \times 100 = 15.1 \pm 4.6$ percent.

For the four-oxygen equilibration process involving all oxygen atoms of the hydrogen phthalate ester, the maximum obtainable atom percent ^{18}O for the alkyl oxygen atom due to complete exchange was $\frac{33.090 + x}{4}$. By taking into account the ^{18}O abundance of this alkyl oxygen atom before pyrolysis, the maximum obtainable excess atom percent ^{18}O for complete exchange was $\frac{33.090-3x}{4}$. By using this theoretical excess atom percent ^{18}O value, the actual excess atom percent ^{18}O for each sample of 1-phenyl-2-methylcyclohexanol and the same mathematical approach utilized for the case of the two-oxygen equilibration process, the percent ^{18}O exchange between all oxygen atoms in the undecomposed ester was calculated for each pyrolysis. For 20 percent pyrolysis of trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O, the percent ^{18}O exchange was $\frac{0.815 \pm 0.250}{8.108}$ x 100 = 10.0 ± 3.1 percent.

In Table IX, the (M+2/M) percent, atom percent ^{18}O and percent ^{18}O exchange values along with their error limits are reported for the different ester pyrolysis experiments.

Reduction of cis- and trans-1-Phenyl-2-methylcyclohexyl Hydrogen Phthalate-^{18}O and Gas Chromatographic and Mass Spectrometric Analyses of cis- and trans-1-Phenyl-2-methylcyclohexanol

In order to determine if any geometrical isomerization and/or ^{18}O exchange occurred during the lithium aluminum hydride reduction of the undecomposed ester from each partial pyrolysis experiment and in the isolation of the corresponding 1-phenyl-2-methylcyclohexanol, the cis- and trans-1-phenyl-2-methylcyclohexyl hydrogen phthalate-^{18}O esters were reduced and the products were isolated as previously described. The 1-phenyl-2-methylcyclohexanol from each hydrogen phthalate reduction was analyzed by glc (Table VIII). Samples of 1-phenyl-2-methylcyclohexanol and ω,ω'-dihydroxy-o-xylene from each ester reduction were sent for mass spectral analysis.

The only alterations in the mass spectrometer conditions were the following:

for 1-phenyl-2-methylcyclohexanol--column temperature, 180°.

for ω,ω'-dihydroxy-o-xylene--column temperature, 120°; ionizing energy, 15eV at 60 μA; flash pyrolysis unit temperature, 280° (for the conversion of ω,ω'-dihydroxy-o-xylene to 1,3-dihydroisobenzofuran).

The atom percent ^{18}O values of the ω,ω'-dihydroxy-o-xylene samples from the cis- and trans-hydrogen phthalate-^{18}O reductions showed no significant deviations from the atom percent ^{18}O of the phthalic anhydride used to synthesize these labelled esters. The atom percent ^{18}O values for the 1-phenyl-2-methylcyclohexanol samples are given in Table IX.

REFERENCES

1. C.H. DePuy and R.W. King, Chem. Rev., 60, 431 (1960).
2. C.D. Hurd and F.H. Blunck, J. Amer. Chem. Soc., 60, 2419 (1938).
3. D.V. Banthorpe, "Elimination Reactions," American Elsevier Publishing Co., Inc., New York, N.Y., 1963, pp 167-195.
4. R. Taylor, G.G. Smith, and W.H. Wetzel, J. Amer. Chem. Soc., 84, 4817 (1962).
5. J.C. Scheer, E.C. Kooyman, and F.L.J. Sixma, Rec. Trav. Chim. Pays-Bas, 82, 1123 (1963).
6. A. Maccoll in "Advances in Physical Organic Chemistry," Vol. 3, V. Gold, Ed., Academic Press Inc., New York, N.Y., 1965, pp 91-122.
7. W.S. Briggs and C. Djerassi, J. Org. Chem., 33, 1625 (1968).
8. H.H. Zeiss, J. Amer. Chem. Soc., 73, 2391 (1951).
9. K.G. Rutherford, J.M. Prokipcak, and D.P.C. Fung, J. Org. Chem., 28, 582 (1963).
10. K.G. Rutherford and D.P.C. Fung, Can. J. Chem., 42, 2657 (1964).
11. G.P. Shulman, J.H. Bennett, and D.G. Botteron, J. Org. Chem., 27, 3923 (1962).
12. D.H. Froemsdorf, C.H. Collins, G.S. Hammond, and C.H. DePuy, J. Amer. Chem. Soc., 81, 643 (1959).
13. K.G. Rutherford and R.M. Ottenbrite, Can. J. Chem., 45, 679 (1967).
14. S. Wassenaar, Ph.D. Dissertation, University of Windsor, Windsor, Ontario, 1969.
15. W.J. Bailey and J.J. Hewitt, J. Org. Chem., 21, 543 (1956).
16. D.J. Cram and F.A. Abd Elhafez, J. Amer. Chem. Soc., 74, 5828 (1952).
17. S. Wassenaar, University of Windsor, Windsor, Ontario, unpublished results, 1969.
18. H.L. Goering, R.G. Briody, and G. Sandrock, J. Amer. Chem. Soc., 92, 7401 (1970).
19. J.L. Kice, R.L. Scriven, E. Koubek, and M. Barnes, J. Amer. Chem. Soc., 92, 5608 (1970).

20. C.D. Nenitzescu in ''Carbonium Ions,'' Vol. 1, G.A. Olah and P.v.R. Schleyer, Ed., Interscience, New York, N.Y., 1968, pp 59-64.

21. E.M. Kosower, ''An Introduction to Physical Organic Chemistry,'' John Wiley and Sons, Inc., New York, N.Y., 1968, pp 359-367.

22. E.W. Garbisch, Jr., J. Org. Chem., 26, 4165 (1961).

23. E.W. Garbisch, Jr., J. Org. Chem., 27, 4243 (1962).

24. H.C. Brown and G.Zweifel, J. Amer. Chem. Soc., 83, 2544 (1961).

25. R.B. Carlin and H.P. Landerl, J. Amer. Chem. Soc., 75, 3969 (1953).

26. L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol.1, John Wiley and Sons, Inc., New York, N.Y., 1967, pp 191-192.

27. A.L. Vogel, ''Elementary Practical Organic Chemistry,'' Longmans, Green and Co., Inc., London, 1958, p 692.

28. H.H. Holton, Ph.D. Dissertation, University of Windsor, Windsor, Ontario, 1971.

29. R.C. Weast, ''Handbook of Chemistry and Physics,'' 49th ed, The Chemical Rubber Co., Cleveland, Ohio, 1968, p C-475.

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