1972

Lead-Tetraacetate Oxidations of Stereoisomeric 2-Methyl-3-Phenylbutyric Acids.

Alice Theine

Louisiana State University and Agricultural & Mechanical College

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2-METHYL-3-PHENYL BUTYRIC ACIDS.

The Louisiana State University and Agricultural
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LEAD TETRAACETATE OXIDATIONS OF
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A Dissertation
Submitted to the Graduate Faculty of the
Louisiana State University and
Agricultural and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy
in
The Department of Chemistry

by
Sister Alice Theine
B.A., Alverno College, 1959
M.S., Marquette University, 1965
December, 1972
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To my parents

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to the School Sisters of St. Francis
ACKNOWLEDGMENT

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ABSTRACT

Previous studies with stereoisomeric $4\text{-}E$-butylcyclohexane-carboxylic acids have demonstrated that the products derived from the cyclohexyl radical by halodecarboxylation and those derived from the cation by oxidative decarboxylation with lead tetraacetate are independent of the configuration of the starting acids. Similar results have been obtained from the oxidative decarboxylation of the isomeric bornane-2-carboxylic acids and norbornane-2-carboxylic acids. The present study has been concerned with stereoisomeric acids from which substituted 2-phenylethyl cations might be generated.

Halodecarboxylations of the isomeric 2-methyl-3-phenylbutyric acids produce the same 1:1.4 erythro/threo ratio of 2-chloro-3-phenylbutanes. Both the substitution and elimination products from oxidative decarboxylation of these same acids show identical distributions (4.6:1 $Z:E$ 2-phenyl-2-butenes and 1.7:1 erythro/threo 1-methyl-2-phenyl-1-propyl acetates). Apparently a common radical is being generated which is further oxidized to a single cationic species. This one cation then gives rise to both substitution and elimination products independently of the configuration of the starting acids. Different ratios of erythro/threo substitution products are formed from the radical and cationic intermediates, due to differing combinations of steric and other energy factors involved in the two processes.

Solvolytic and deamination reactions in acetic acid solutions and decarboxylation reactions with lead tetraacetate all yield acetate substitution products from 1-methyl-2-phenyl-1-propyl reactants. Solvolysis of the tosylate or brosylate and the deamination reaction give
rise to rearrangement products. In solvolysis only phenyl and hydrogen migration occur, but in deamination phenyl, hydrogen, and methyl migrations are observed. In the decarboxylation, no migration was observed (phenyl migration could not be detected, however, since racemic mixtures of the acids were used for the study). The cationic intermediate in the decarboxylation is apparently an open, classical cation which, however, does not yield rearrangement products.

The elimination products from the decarboxylation are unique when compared to similar products from other reactions of the same system, in that the distribution of cis and trans olefins is independent of the configuration of the starting acid. The major isomer formed is the thermodynamically less stable Z-isomer. No olefins from a rearranged cation were found from the oxidation. The distribution of olefins found does not correspond with that obtained by a concerted cis elimination (as in xanthate decomposition and amine oxide pyrolysis) or by a stereospecific trans elimination (lithium aluminum hydride reduction). This difference in product distribution points to an open cation which is influenced by some other factors, possibly the same ones involved in the formation of substitution products.

The isomer distributions of acetate and olefin products exclude phenyl participation as a significant factor in the generation or subsequent reactions of the cationic intermediate.
I. INTRODUCTION

A. General Comments

This Dissertation is concerned with the properties of the carbocations generated by the lead tetraacetate oxidative decarboxylation of some carboxylic acids. Carbon cations, generated by various methods, have been shown to possess a range of energetic properties. Nitrous acid deaminations are thought to generate highly energetic, unsolvated cationic intermediates.\(^1\) Solvolysis reactions, on the other hand, involve cationic species rather extensively stabilized by solvation.\(^2\)

In a study of the stereochemistry of product formation from the cyclohexyl cation generated in a series of reactions, the stereochemistry of the product formation was independent of the stereochemistry of the parent compound only in the lead tetraacetate oxidative decarboxylation of \(4-t\)-butylcyclohexanecarboxylic acid and in chlorinolysis of the corresponding \(2,4\)-dinitrobenzenesulfenate in acetic acid in the presence of lithium perchlorate.\(^3\) It was concluded from this study that the same free cation was formed from either the cis- or trans-\(4-t\)-butylcyclohexanecarboxylic acid since the same product mixture is formed from either isomeric acid. Nitrous acid deamination reactions of the same system yield predominantly equatorial alcohol from either isomeric amine, but in different percentages.\(^4\) Hydrolysis of the isomeric tosylates\(^*\) yields the corresponding inverted alcohol.\(^3\)

---

\(^*\)Tosylate is the common name for \(p\)-toluenesulfonate. Due to its widespread use, the common name will be used in this Dissertation.
Lead tetraacetate is a common oxidizing agent and has been used as such for a long time. The reaction of lead tetraacetate with carboxylic acids results in loss of carbon dioxide and formation of a mixture of olefin and esters, in proportions dependent on the structure of the parent carboxylic acid. Acetates are the principal esters formed if the reaction is carried out in refluxing benzene in the presence of pyridine.\(^5\)

\[\text{RCOOH} + \text{Pb(OAc)}_4 \xrightarrow{\text{Py}_2\text{C}_6\text{H}_5} \text{CO}_2 + \text{Pb(OAc)}_2 + \text{R-OAc} + \text{HOAc} \quad (1)\]

The reaction is inhibited by oxygen which suggests a radical intermediate.\(^6\) The formation of acetates, in particular of rearranged acetates, results from cationic intermediates however. It is thought that the cation intermediate is formed from a radical precursor in an oxidation step.\(^6\)

The asymmetry of the central carbon atoms in the 1-methyl-2-phenyl-1-propyl (often improperly but conveniently called 3-phenyl-2-butyl) system allows the stereochemistry of reactions of this system to be easily observed. The stereochemistry of product formation of this system has been determined for nitrous acid deamination and solvolysis reactions, as well as for concerted and other cationic reactions, but not for decarboxylation reactions.

This Dissertation extends the study of the lead tetraacetate oxidative decarboxylation to other carboxylic acids, particularly the isomeric 2-methyl-3-phenylbutyric acids. Comparison of the stereochemistry of product formation from this oxidative decarboxylation with those of other reactions of this system enables an assessment of the nature of the intermediate cation involved. A more exact knowledge of
the mechanism of the decarboxylation reaction is possible from a comparison of the product distributions resulting from different carboxylic acids.

B. Oxidative Decarboxylations with Lead Tetraacetate

1. Selected Examples of Previous Work

Corey and Casanova studied the optically active norbornyl system. They found predominant exo-norbornyl acetate formation from either exo or endo carboxylic acid. The net retention of optical purity was somewhat solvent dependent, 43% in benzene and 33% in acetonitrile. The partial racemization (due to rearrangement during the reaction) was regarded as evidence of a cationic intermediate, in particular, a classical cation. The smaller amount of rearrangement of the cation produced in this decarboxylation reaction compared with that produced by nitrous acid deamination was attributed to the greater extent of ion-pair formation in the less polar benzene solvent.

Gream and Wege suggested that the oxidation products of exo- and endo-2-bornanecarboxylic acid are also formed by way of cationic intermediates. The reaction was pyridine-catalyzed in benzene with an excess of lead tetraacetate. Either starting configuration resulted in the product distribution shown below. High optical purity of camphene (A) was observed from reaction of optically active carboxylic acid.
The formation of the acetate of camphene hydrate (C) led to the conclusion that at least some non-classical cations are involved in the reaction.

Studies of 3,3,3-triarylpropionic acid in benzene, chlorobenzene, and acetonitrile revealed migration and cyclization products along with the decarboxylation products, indicating a cationic intermediate. The migratory aptitudes found for phenyl, p-methoxyphenyl and p-nitrophenyl were 1.0, 1.3, and 0.10, respectively. A $\rho$-value of -1.33 was found for a Hammett plot using $\sigma^+$ constants. The products formed by decarboxylation differed from those obtained by thermal decomposition of the corresponding tert-butyl perester. The author interpreted this difference as evidence against the intermediacy of the acyloxy radical in the decarboxylation by lead tetraacetate.

Kochi found the reaction to be sensitive to oxygen inhibition and to catalysis by pyridine or copper(II) salts. The presence of

---

*a* Secondary products from camphene
excess carboxylic acid or catalyst increases the homogeneity of the system whereas the uncomplexed lead tetraacetate is essentially insoluble in benzene. Pyridine was without effect on the nature of the products of the reaction; the introduction of catalytic amounts of copper(II) salts led almost exclusively to olefin formation at the expense of acetate formation. Kochi attributed the olefin formation to the greater ease of the copper(II) ion to oxidize the initially formed alkyl radical. Likewise, addition of other anions, such as cyanide and chloride, in the presence of excess carboxylic acid proved to be a suitable preparative method for the corresponding derivative. 

Davies also presented evidence of a radical intermediate in the oxidation of phenyl-substituted acetic and propionic acids. Biphenyl and diphenylmethane were minor products in the oxidation of phenylacetic acid carried out in benzene solvent with excess carboxylic acid. Similarly, bibenzyl was the major product in the oxidation of 3-phenylpropionic acid in benzene. The major product of the oxidation of phenylacetic acid, however, was benzyl phenylacetate; a small amount of benzyl acetate was also formed.

2. Mechanisms Proposed for Decarboxylations with Lead Tetraacetate

The mechanism generally accepted for the decomposition of carboxylic acids in the presence of lead tetraacetate involves a free radical chain process. A preliminary anion exchange of the carboxylate group for acetate has been proposed (equation 2). Kharasch postulated

\[
\text{RCOOH} + \text{Pb(OAc)}_4 \rightarrow \text{HOAc} + \text{RCOO-Pb(OAc)}_3
\] 

(2)

lead(III) acetate radical formation as the initiation step for the chain process. The course of the propagation and termination steps is
dependent on the nature of the carboxylic acid. For the decomposition of lead tetraacetate itself in acetic acid, Kharasch proposed the formation of \( \text{CH}_3\text{COO}^- \), \( \text{CH}_3^- \), and \( \cdot\text{CH}_2\text{COOH} \) radicals from the lead(III) radical together with a disproportionation to lead(II) acetate and lead(IV) acetate.\(^{13}\)

Mosher and Kehr presented arguments in favor of an ionic mechanism based on experimental evidence from the decompositions of a number of carboxylic acids.\(^{14}\) The absence of both dimerization and disproportionation products from the reaction of trimethylacetic acid speaks against radical intermediates. Likewise, formation of rearrangement products from the decomposition of isobutyric and isovaleric acids led Mosher and Kehr to a mechanistic scheme involving a two electron transfer to form the carbon cation directly, as shown in Scheme I below.\(^{14}\)

**Scheme I**

Mechanism Involving a Direct 2-Electron Oxidation

\[
Pb(\text{OAc})_4 + 4\text{RC-OH} \rightleftharpoons Pb(\text{O-CR})_4 + 4\text{HOAc} \tag{3}\]

\[
Pb(\text{O-CR})_4 \rightleftharpoons Pb(\text{O-CR})_2 + RC^- + RC^+ \tag{4}\]

\[
\begin{array}{c}
\text{RC}^- \\
\text{R}^+ + \text{CO}_2
\end{array}
\]

Kochi, however, found the reaction to be sensitive to oxygen, a factor not usually observed since the reactions had been carried out in refluxing solvent.\(^6\) Kinetic studies indicated inhibition of the reaction as soon as oxygen was admitted into the system and recurrence of reaction when the system was purged of the oxygen. Catalysis of the
reaction by pyridine, acyl peroxides and copper(II) salts provided further evidence of radical intermediates in the chain process. Catalysis by copper(II) salts drastically alters the product distribution in favor of olefin formation. Kochi proposed the following mechanism (equations 5-7) for reactions involving the copper(II) catalyst in the oxidation of primary and secondary carboxylic acids. Olefin formation is thought to occur almost exclusively because of the great ease of oxidation of primary and secondary alkyl radicals (equation 6). No difference in product distribution was observed whether the reaction was performed thermally (80°) or photochemically (30°).

\[
\text{RCO}_3\text{Pb}^{\text{III}} \rightarrow R^* + \text{CO}_2 + \text{Pb}^{\text{II}} \quad (5)
\]
\[
R^* + \text{Cu}^{\text{II}} \rightarrow R(-\text{H}) + \text{H}^+ + \text{Cu}^{\text{I}} \quad (6)
\]
\[
\text{Cu}^{\text{I}} + \text{RCO}_3\text{Pb}^{\text{IV}} \rightarrow \text{Cu}^{\text{II}} + \text{RCO}_3\text{Pb}^{\text{III}} \quad (7)
\]

Catalysis by pyridine, acetate ion, or acyl peroxide was found to have no effect on the products formed from the decomposition compared to the uncatalyzed reaction. Kochi suggested that pyridine might act similarly. The complex formed between the Pb(IV) salt and the base (equation 9) is thought to be more labile than the uncomplexed compound. The mechanistic scheme (Scheme II) presented by Kochi indicates the probable role of the pyridine as a catalyst. Kochi found the reaction to be catalyzed by other nucleophiles and demonstrated the synthetic capabilities of the halodecarboxylation reaction using lithium halide salts. The halodecarboxylation reaction was found to proceed completely by way of a radical pathway. The reaction is sensitive to oxygen, and no rearrangement is observed. The mechanism
Scheme II

Chain Reaction Mechanism for Oxidative Decarboxylation

\[ \text{Pb}^{IV} = \text{Pb} (\text{OAc})_{4-n} (\text{O}_2\text{CR})_n \text{ or Pb} (\text{OAc})_{4-n} (\text{O}_2\text{CR})_n \text{Py}_m \]

\[ \text{Pb}^{III} = \text{Pb} (\text{OAc})_{4-n} (\text{O}_2\text{CR})_{n-1} \text{ or Pb} (\text{OAc})_{4-n} (\text{O}_2\text{CR})_{n-1} \text{Py}_m \]

\[ \text{Pb}^{II} = \text{Pb} (\text{OAc})_{4-n} (\text{O}_2\text{CR})_{n-2} \text{ or Pb} (\text{OAc})_{4-n} (\text{O}_2\text{CR})_{n-2} \text{Py}_m \]

\( \text{HS} = \text{solvent}: \text{Py} = \text{pyridine}; \ n = 1,2,3,4 \)

Pre-equilibration:

\[ \text{Pb} (\text{OAc})_{4} + n\text{RCO}_2\text{H} \rightleftharpoons \text{Pb} (\text{OAc})_{4-n} (\text{O}_2\text{CR})_n + n\text{HOAc} \quad (8) \]

\[ \text{Pb} (\text{OAc})_{n-n} (\text{O}_2\text{CR})_n + m\text{Py} \rightleftharpoons \text{Pb} (\text{OAc})_{n-n} (\text{O}_2\text{CR})_n \text{Py}_m \quad (9) \]

Initiation:

\[ \text{Pb}^{IV} \rightarrow \text{Pb}^{III} + R^* + \text{CO}_2 \quad (10) \]

Propagation:

\[ \text{Pb}^{III} \rightarrow \text{Pb}^{II} + R^* + \text{CO}_2 \quad (11) \]

\[ R^* + \text{Pb}^{IV} \rightarrow R^+ + \text{Pb}^{III} \quad (12) \]

\[ \downarrow \]

(alkene, ester)

Termination:

\[ R^* + \text{Pb}^{III} \rightarrow R^+ + \text{Pb}^{II} \quad (13) \]

\[ \downarrow \]

(alkene, ester)

\[ R^* \xrightarrow{\text{HS}} R^- + S^* \quad (14) \]

\[ \downarrow \]

(disproportionation and/or recombination products)
proposed (Scheme III) is parallel to that for the pyridine-catalyzed, oxidative reaction mentioned previously. The difference between the two mechanisms lies in the mode of the oxidation. In the halodecarboxylation reaction, the oxidation step is thought to be a ligand-transfer process (equations 18 and 22). In the oxidative decarboxylation reaction involving either pyridine or copper(II) catalysts, an electron-transfer reaction (equations 12, 13, 5, 6, and 7) is postulated as the oxidation step.

To explain the formation of benzyl phenylacetate and benzyl acetate from the decarboxylation of phenylacetic acid, Davies however
suggested an intramolecular ionic interchange between the phenylacetic acid and lead tetraacetate. The 2:1 mole ratio of carboxylic acid to lead tetraacetate used for the reaction could explain the formation of more benzyl phenylacetate than benzyl acetate due to the greater availability for anion exchange of carboxylate than of acetate. A similar mechanism was invoked to explain the formation of 3-phenylphthalide by the oxidation of α-benzylbenzoic acid.

C. Previous Studies on the 1-Methyl-2-phenyl-1-propyl System

1. General Comments

The 1-methyl-2-phenyl-1-propyl cation has been the subject of much investigation over the past twenty-three years. Investigations on
reactions involving cationic intermediates, such as solvolyses,\textsuperscript{15} deamination reactions,\textsuperscript{16} and chlorosulfite decompositions,\textsuperscript{17} have been executed. Concerted reactions such as the Chugaev\textsuperscript{18} and Cope\textsuperscript{19} reactions and lithium aluminum hydride reduction\textsuperscript{20} have also been investigated for this system. It was hoped that a comparison of products from the ionic and concerted reactions would afford evidence about the nature of the intermediate cation when it is indeed present.

The selection of the 1-methyl-2-phenyl-1-propyl system was based on its several unique characteristics. Carbon atoms 2 and 3 are each asymmetric. Therefore, both the threo and erythro isomers can be obtained in optically active form. Product studies were carried out simply, by polarimetry, ir spectroscopy, or measurement of the refractive index, without tedious separation of products. Since this system is particularly susceptible to Wagner-Meerwein rearrangements in nonconcerted reactions, the stereochemistry of both the migration origin and terminus can also be determined from optical rotatory measurements.

2. Solvolysis Studies

Interest in the 1-methyl-2-phenyl-1-propyl system for solvolysis studies originated with the work of Cram and continues to the present time. Cram's original purpose was to "unequivocally demonstrate for the first time the existence of a discrete molecular species",\textsuperscript{21} the phenonium ion, in a Wagner-Meerwein rearrangement in an acyclic system. Previously, rearrangement studies had been limited to cyclic systems.
Optically pure tosylates were prepared and subjected to solvolysis under a variety of conditions. A summary of the products obtained in these studies\(^{21}\) is presented in Table I. It was found that erythro tosylate led almost completely to erythro acetate. Solvolysis of optically active erythro tosylate resulted in racemic erythro acetate. Polarimetric rate studies showed, however, that racemization was \(94\%\) complete in the first solvolytic half-life, and some erythro brosylate was formed when acetolysis of erythro tosylate was carried out in the presence of brosylate anion.

Four separate reactions were proposed to account for the above observations: solvolysis, racemization, exchange and simple replacement. The role of each of these in accounting for the product distributions is shown in the mechanistic scheme presented by Cram to account for the acetate products obtained from the acetolysis of optically active \textit{erythro-1-methyl-2-phenyl-1-propyl} tosylate.\(^{15}\)

The same mechanistic scheme for the threo tosylate offers a reasonable explanation for the resulting optically active threo acetate from optically active threo tosylate. The phenonium ion intermediate was invoked to explain the high degree of stereospecificity observed throughout the reaction, even with the simultaneous occurrence of racemization and exchange reactions. Brown proposed rapidly equilibrating classical cations to account for the same phenomenon.\(^{22}\)

Hydrogen migration, evidenced by formation of 1-methyl-1-phenyl-1-propyl acetate, was noted when solvolysis of the brosylate was carried out at \(30^\circ\) rather than at \(75^\circ.\)\(^{15}\) The tertiary acetate decomposed to olefin in acetic acid at the higher temperature.\(^{23}\) The product distribution obtained from the solvolysis\(^{15}\) at \(30^\circ\) is given in
<table>
<thead>
<tr>
<th>Starting Configuration</th>
<th>Solvent</th>
<th>Temperature °C</th>
<th>Composition, ester</th>
</tr>
</thead>
<tbody>
<tr>
<td>threo- (+)-</td>
<td>HOAc</td>
<td>75</td>
<td>threo 96, erythro 4</td>
</tr>
<tr>
<td>threo- (-)-</td>
<td>HOAc</td>
<td>75</td>
<td>threo 96, erythro 4</td>
</tr>
<tr>
<td>erythro- (+)-</td>
<td>HOAc</td>
<td>75</td>
<td>threo 5, erythro 94</td>
</tr>
<tr>
<td>erythro- (-)-</td>
<td>HOAc</td>
<td>75</td>
<td>threo 5, erythro 94</td>
</tr>
<tr>
<td>threo- (+)-</td>
<td>HCOOH</td>
<td>25</td>
<td>threo 100, erythro 0</td>
</tr>
<tr>
<td>erythro- (-)-</td>
<td>HCOOH</td>
<td>25</td>
<td>threo 0, erythro 100</td>
</tr>
</tbody>
</table>
Table II. At this lower temperature, the tertiary acetate is neither decomposed to olefin nor racemized. The relative importance of hydrogen and phenyl migrations for the two diastereomers was explained on the basis of steric factors in the bridged ion. Phenyl migration offers the less hindered transition state for the erythro isomer. The smaller hydrogen atom was thought to compete more successfully with the phenyl groups for migration in the threo isomer, since both have cis-oriented bulky groups in the transition state.

<table>
<thead>
<tr>
<th>Olefin</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-2-phenyl-2-butene</td>
<td>52</td>
</tr>
<tr>
<td>Z-2-phenyl-2-butene</td>
<td>2</td>
</tr>
<tr>
<td>2-phenyl-1-butene</td>
<td>46</td>
</tr>
<tr>
<td>3-phenyl-1-butene</td>
<td>0</td>
</tr>
</tbody>
</table>

Decomposition Products of Tertiary Acetate
<table>
<thead>
<tr>
<th>Configuration of Starting Material</th>
<th>% Yield</th>
<th>% Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acetates</td>
<td>Olefins</td>
</tr>
<tr>
<td>threo- (+)</td>
<td>70</td>
<td>12</td>
</tr>
<tr>
<td>erythro- (-)</td>
<td>74</td>
<td>6</td>
</tr>
</tbody>
</table>

a. I = \[\text{Ph}\; \xrightarrow{X} \; \text{Ph}\] ; II = \[\text{Ph}\; \xrightarrow{X} \; X\]

b. IIIE = \[\text{Ph}\; \xrightarrow{X} \; \text{Ph}\] ; IIIZ = \[\text{Ph}\; \xrightarrow{X} \; X\]

c. III = 2-phenyl-1-butene; IV = 3-phenyl-1-butene.
Stereospecificity was found to be dependent on the nature of the solvent. In ethanol, simple $S_N^2$ substitution products result.\textsuperscript{21} In acetonitrile, the reaction proceeds slowly, giving only olefin products.\textsuperscript{15} Formolysis appears to be a more highly stereospecific process than acetolysis.\textsuperscript{15} Less leakage occurs, and racemization is only 10\% complete after the first solvolytic half-life compared to a similar value of 94\% during acetolysis.

The rates of solvolysis of the unsubstituted\textsuperscript{24} and substituted\textsuperscript{25} 2-phenylethyl systems are slower than that of the simple ethyl tosylate in acetic acid. Only in formic acid is the rate increased by the phenyl group.\textsuperscript{26} Brown concludes that phenyl participation is important only for the reaction in formic acid.\textsuperscript{22,27} Rate studies were carried out on the model system, 2-phenylcyclopentyl tosylate. \textit{trans}-2-Phenylcyclopentyl tosylate yields principally the corresponding trans acetate, presumably with the aid of phenyl-bridging.\textsuperscript{26} The cis tosylate, on the other hand, yields mainly olefin; both 1- and 2-deuterium substituted cis tosylates give the same olefin distribution.\textsuperscript{28} Brown proposes hydride shift, following initial cation formation, to give the tertiary cation, for which he admits the possibility of solvent participation. Phenyl participation is ruled out on the basis of the absence of an observed rate enhancement.\textsuperscript{29}

Winstein describes the acetolysis of the substituted 2-phenyl-ethyl system as borderline.\textsuperscript{25,30} The rate enhancement is small even in formic acid, but the order of rates is as anticipated for the para-substituted aryl esters:

\[ p-\text{CH}_3O-\text{C}_6\text{H}_4^- > p-\text{H}-\text{C}_6\text{H}_4^- > p-\text{NO}_2-\text{C}_6\text{H}_4^- \textsuperscript{30,31} \]
Phenyl participation is enhanced with the para-methoxy substituent. Solvent participation is depressed, and a higher percentage of acetate of retained configuration is obtained. When the substituent is para-nitro, phenyl participation decreases, solvent participation competes more successfully, and inverted substitution products predominate.\textsuperscript{31} Comparison of the rate constants for ionization of neophyl (2,2-dimethyl-2-phenyl-1-ethyl) tosylates (a process for which aryl participation is recognized) and of the phenyl-assisted path for the p-substituted 2-phenylethyl tosylates however shows an excellent correlation.\textsuperscript{32}

Studies on the 2-aryl-1-methylethyl system,\textsuperscript{33} on simple alkyl systems,\textsuperscript{34} and on the unsymmetrical 1-aryl-2-arylethyl system\textsuperscript{35} likewise demonstrate that large observable rate enhancements do not necessarily accompany participation from a neighboring group. Studies on the p-substituted 1-methyl-2-phenyl-1-propyl system indicate a considerable increase in the rate of phenyl-assisted pathway (leading to ester of retained configuration) relative to the rate of unassisted pathway (leading to ester of inverted configuration).\textsuperscript{36,37} These two separate pathways for the solvolysis reaction are thought to be in competition with each other, with little, if any, cross-over between them.\textsuperscript{36-38}

3. Chugaev Reaction

The Chugaev reaction consists of a pyrolytic cis elimination of a methyl xanthate (RO-C-SCH\textsubscript{3}) containing a beta-hydrogen to give an olefin, a thiol, and carbon oxysulfide as products.\textsuperscript{39}

Decompositions of optically active erythro- and threo-1-methyl-2-phenyl-1-propyl xanthates led to mixtures of the three olefins:
E- and Z-2-phenyl-2-butene and 3-phenyl-1-butene (capable of optical activity). The products observed from the decompositions are shown in Table III.

The concerted mechanism presented by Cram for the decomposition of the threo isomer, presented in Scheme V, is in agreement with that presented by Bader and Burns who employed S\(^{34}\) and C\(^{13}\) isotope studies to verify the mechanism. The non-conjugated olefin is probably formed by the same mechanism as that by which the conjugated olefin is formed, there being fewer steric interactions involved in the reaction.
### TABLE III

**XANTHATE DECOMPOSITION PRODUCTS**

<table>
<thead>
<tr>
<th>Configuration of Starting Material</th>
<th>% Optical Purity of Starting Material</th>
<th>% Yield Olefin</th>
<th>% Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>threeo</td>
<td>60</td>
<td>76</td>
<td>36 12 38</td>
</tr>
<tr>
<td>erythro</td>
<td>44</td>
<td>91</td>
<td>5 50 38</td>
</tr>
</tbody>
</table>

a. IE = \[\text{Ph} \quad \text{Ph}\], IZ = \[\text{Ph} \quad \text{Ph}\].

b. II = 2-phenyl-1-butene.
The products of a trans elimination, trans olefin from the threo xanthate and cis olefin from the erythro xanthate, were attributed to an intermolecular process.\textsuperscript{18}

4. Chlorosulfite Decomposition

3-Phenyl-2-butanol reacts with excess thionyl chloride to give the corresponding chloride in high yield.\textsuperscript{17} The reaction proceeds stereospecifically through an intermediate chlorosulfite which then decomposes to give the chloride. An $S_{N1}$ (internal nucleophilic substitution) mechanism has been proposed for the decomposition of the chlorosulfite.\textsuperscript{17}

The products obtained\textsuperscript{17} from reaction of the optically active alcohols are given in Table IV. Based on the racemization of the threo isomer and the stability of the product chlorides to the reaction conditions, a mechanism was proposed by Cram for the $S_{N1}$ decomposition of the chlorosulfite.\textsuperscript{17} That mechanism, similar to the one involved in the solvolysis reactions, is shown in Scheme VI. Collapse of the simple,

\begin{center}
\textbf{Scheme VI}
\end{center}

\textit{Mechanism for $S_{N1}$ Decomposition of an Alkyl Chlorosulfite}
<table>
<thead>
<tr>
<th>Starting Material</th>
<th>Temperature °C</th>
<th>% Yield Chloride</th>
<th>% Racemization</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-(-)-threo-alcohol</td>
<td>25</td>
<td>95</td>
<td>97</td>
</tr>
<tr>
<td>L-(+)-threo-alcohol</td>
<td>0</td>
<td>95</td>
<td>97</td>
</tr>
<tr>
<td>D-(-)-erythro-alcohol</td>
<td>25</td>
<td>90</td>
<td>1</td>
</tr>
</tbody>
</table>
bridged ion-pair results in racemic product formation from the starting threo alcohol and in optically active product from the starting erythro alcohol, just as was the case in the solvolysis reactions.

The effects of solvent on the stereospecificity are similar to those exhibited in solvolysis: that is, greater stereospecificity in the more ionizing and less nucleophilic solvent. When the reaction of D-(−)-threo-alcohol was carried out in formic acid the yield of chloride dropped to 7%. Formation of ester predominated (50% yield, 20% racemic), probably by exchange of formate anion for the chloride anion before collapse of the ion-pair.

The possibility of open ion-pairs cannot be ruled out, particularly in the more ionizing solvents. The mechanism presented below for this possibility suggests that the only differences between the SN1 and SN2 reactions are the complexity of the leaving group and the relative rates of internal decomposition of the anion and attack of anion at the rear of the carbon atom undergoing substitution.

Scheme VII
Mechanism for SN1 Decomposition of an Alkyl Chlorosulfite

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5. Lithium Aluminum Hydride Reduction

Upon treatment with an ethyl ether solution of lithium aluminum hydride (LAH), l-methyl-2-phenyl-1-propyl tosylates yield mixtures of 2-phenyl-2-butene and 2-phenylbutane. The yields and stereochemistry of the starting materials and of the products as determined by Cram are shown in Table V. Cram attributed the olefin formation to an E2 reaction of the LAH base by way of a trans elimination. When the same tosylates were treated with sodium ethoxide, trans elimination also occurred, giving olefin products similar to those formed during reaction with lithium aluminum hydride, along with some optically active olefin assumed to be 3-phenyl-1-butene.

The alkane formed by LAH reduction appears to be primarily the result of attack of the hydride on the α-carbon in an $S_N^2$ substitution. The decrease in optical activity in the reduction product from the parent threo tosylate is attributed to a second pathway involving a phenonium sulfonate ion-pair. This second pathway would lead to racemic product from the threo tosylate but to optically active product from the erythro isomer. The LAH reduction therefore represents an intermediate situation, producing some olefin product due to the attack by base ($\text{AlH}_4^-$) on the β-carbon, optically active alkylbenzene by $S_N^2$ attack of the hydride on the α-carbon, and some alkylbenzene formed through phenonium ion intermediates.

6. Deaminative Acetolysis

Deaminative acetolysis of the four optically active 1-methyl-2-phenyl-1-propylamines yielded product distributions indicative of a reaction mechanism different from that of the solvolysis reactions mentioned earlier. The products of the deamination of the threo amine
TABLE V
PRODUCTS OF LAH REDUCTION

<table>
<thead>
<tr>
<th>Configuration of Parent Tosylate</th>
<th>Products, % Yield</th>
<th>Rotation of Alkane&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>II-E&lt;sup&gt;a&lt;/sup&gt;</td>
<td>II-Z&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>L-(+)-threo</td>
<td>-</td>
<td>21</td>
</tr>
<tr>
<td>L-(+)-erythro</td>
<td>22</td>
<td>-</td>
</tr>
</tbody>
</table>

a. II-E = \( \text{Ph} \)

b. I = \( \text{Ph} \)

c. Rotation of optically pure alkane was reported as +23.6°, 40° and -24.3° 41
include products of phenyl, hydrogen, and methyl migration, and of simple solvolysis. On the other hand, deamination of the erythro amine yields products of phenyl and hydrogen migration, and of simple solvolysis, but only minor amounts due to methyl migration. A summary of the product distribution is given in Table VI.

Due to the stability of the nitrogen molecule, it is thought that the cation is stabilized by participation of the neighboring group after departure of the nitrogen molecule, but prior to rotation of the sp$^2$-hybridized carbon atom. In this case, the product distribution is a reflection of the conformational distribution of the initial diazonium ions since the driving force of the reaction is the formation of the nitrogen molecule. The expected importance of these conformations, based on their thermodynamic stabilities, for the two diastereomeric diazonium ions is:

threo: \[ \begin{array}{c}
\text{H} \quad \text{Ph} \\
\text{CH}_3 \quad \text{H} \\
\text{H} \quad \text{CH}_3
\end{array} \quad > \quad \begin{array}{c}
\text{CH}_3 \quad \text{N}_2^+ \\
\text{H} \quad \text{H} \\
\text{H} \quad \text{CH}_3
\end{array} \quad > \quad \begin{array}{c}
\text{Ph} \quad \text{N}_2^+ \\
\text{H} \quad \text{H} \\
\text{H} \quad \text{CH}_3
\end{array} \]

erythro: \[ \begin{array}{c}
\text{CH}_3 \quad \text{N}_2^+ \\
\text{H} \quad \text{Ph} \\
\text{H} \quad \text{CH}_3
\end{array} \quad > \quad \begin{array}{c}
\text{Ph} \quad \text{N}_2^+ \\
\text{H} \quad \text{CH}_3 \\
\text{H} \quad \text{CH}_3
\end{array} \quad > \quad \begin{array}{c}
\text{H} \quad \text{N}_2^+ \\
\text{Ph} \quad \text{CH}_3 \\
\text{H} \quad \text{CH}_3
\end{array} \]

The percentages of products resulting from migration bear out the importance of the conformation of the starting ion, as shown in Table VII.

The optically active 1-methyl-2-phenyl-1-propyl products are attributed to simple solvolysis; the racemic products from the three
### TABLE VI
PRODUCT DISTRIBUTION FROM DEAMINATION

<table>
<thead>
<tr>
<th>Configuration of Parent Amine</th>
<th>% Yield</th>
<th>Distribution of Alcohols</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Olefin Alcohol</td>
<td>I-t&lt;sup&gt;b&lt;/sup&gt; act&lt;sup&gt;c&lt;/sup&gt; rac&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>L-(+)-threo</td>
<td>11 50</td>
<td>6 19 14 5 5 27 24</td>
</tr>
<tr>
<td>L-(-)-erythro</td>
<td>4 50</td>
<td>6 0 68 0 0.2 6 20</td>
</tr>
</tbody>
</table>

a. 3-Phenyl-1-butene; conjugated olefins were destroyed by nitrous acid.

b. I = \( \text{Ph} \) \( \text{X} \); I-t = threo; I-e = erythro.

c. rac = racemic
act = active.

d. II = \( \text{Ph} \) \( \text{HO} \).

e. III = \( \text{Ph} \) \( \text{OH} \).

### TABLE VII
RELATION OF MIGRATION TO STEREOCHEMISTRY OF STARTING MATERIAL IN DEAMINATION REACTION

<table>
<thead>
<tr>
<th>Configuration of Starting Material</th>
<th>% Migration Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Methyl</td>
</tr>
<tr>
<td>threo</td>
<td>32</td>
</tr>
<tr>
<td>erythro</td>
<td>6</td>
</tr>
</tbody>
</table>
isomers are considered to be formed after migration. Simple solvolysis of the optically active threo amine leads to optically active 1-methyl-2-phenyl-1-propyl acetates, and phenyl migration accounts for the corresponding racemic acetates. On the other hand, simple solvolysis accounts for the threo-1-methyl-2-phenyl-1-propyl acetate formed and possibly for some of the erythro-1-methyl-2-phenyl-1-propyl acetate, with most of the erythro isomer arising from phenyl migration.

The mechanism involving methyl migration is shown in Scheme VIII. Similar mechanisms account for the products of phenyl and hydrogen migration. Direct ring opening predominates, but some open ion is necessary to account for the appearance of both racemic threo and erythro acetates from the parent threo amine. Formation of open ions is likely since the phenonium ion in this case is relatively unsolvated and therefore highly reactive.16

7. Pyrolysis of Amine Oxide

The pyrolysis of an amine oxide (Cope reaction) is a cis elimination similar to the pyrolytic elimination reaction of the xanthate which was discussed earlier. The products of the decomposition are olefins and a hydroxylamine. The stereospecificity of the reaction is evidenced by the relative yields of internally conjugated olefins. threo-1-Methyl-2-phenyl-1-propylamine oxide produces only cis olefin, and the erythro isomer leads specifically to the trans olefin.19 The amount of olefin is dependent on the reaction conditions, such as solvent and temperature.19

The products are not the result of an equilibrium-controlled E1 reaction. This conclusion is evident from comparison of the product
Scheme VIII
Mechanism for Methyl Migration

\[
\text{L-}(\pm)-\text{threo-amine} \quad \rightarrow \quad \text{bridged ion} \quad \rightarrow \quad \text{open ion}
\]

\[
\text{L-}(\pm)-\text{erythro-amine} \quad \rightarrow \quad \text{bridged ion} \quad \rightarrow \quad \text{open ion}
\]
distribution of the pyrolysis reaction (Table VIII) with the composition of an equilibrium mixture of the olefins at various temperatures obtained by solvolytic elimination of 1-methyl-2-phenyl-1-propyl compounds (Table IX).

The slight variation in the amount of terminal olefin with solvent change was attributed to the effect of hydrogen-bonding. Only non-hydrogen-bonded molecules are capable of the elimination reaction, a conclusion consistent with the failure of reaction in aqueous formic acid (0.1 M).\textsuperscript{19}
### TABLE VIII

**DISTRIBUTION OF 2-PHENYL BUTENES OBTAINED FROM PYROLYSIS OF AMINE OXIDE**

<table>
<thead>
<tr>
<th>Configuration of Amine Oxide</th>
<th>Solvent</th>
<th>Temp. °C</th>
<th>% Distribution of Olefins</th>
</tr>
</thead>
<tbody>
<tr>
<td>threo</td>
<td>MeOH</td>
<td>75</td>
<td>91</td>
</tr>
<tr>
<td></td>
<td>THF&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>DMSO&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>132</td>
<td>88</td>
</tr>
<tr>
<td>erythro</td>
<td>THF&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>DMSO&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>H&lt;sub&gt;2&lt;/sub&gt;O</td>
<td>138</td>
<td>0</td>
</tr>
</tbody>
</table>

a. Tetrahydrofuran.
b. Dimethyl sulfoxide.
c. II-E = \( \text{Ph} – \text{Ph} \); II-Z = \( \text{Ph} – \text{Ph} \).
d. III = 2-phenyl-1-butene.

### TABLE IX

**EQUILIBRIUM DISTRIBUTION OF 2-PHENYL BUTENES**

<table>
<thead>
<tr>
<th>Temperature °C</th>
<th>Product Composition, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>II-E&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>50</td>
<td>81</td>
</tr>
<tr>
<td>75</td>
<td>79</td>
</tr>
<tr>
<td>100</td>
<td>78</td>
</tr>
</tbody>
</table>

a. 0.90 M toluenesulfonic acid.
b. II-E = \( \text{Ph} – \text{Ph} \); II-Z = \( \text{Ph} – \text{Ph} \); II-E = \( \text{Ph} – \text{Ph} \).
c. III = 2-phenyl-1-butene.
II. RESULTS AND DISCUSSION

A. Synthesis of Isomerically Pure 2-Methyl-3-phenylbutyric Acids

Scheme IX outlines the initially designed plan for obtaining the isomeric 2-methyl-3-phenylbutyric acids ($\alpha$ and $\beta$). Rupe and co-workers, and later Burton and Shoppee briefly recorded the synthesis of the corresponding isomeric unsaturated acids ($\alpha$ and $\beta$) from...
the 3-hydroxy ester (1). Burton and Shoppee specifically reported the formation of only traces of the terminally unsaturated ester, ethyl 2-methyl-3-phenyl-3-butenoate (8), and insignificant fission to acetophenone. Treatment of the dehydration product with refluxing aqueous potassium hydroxide was reported to yield an oil upon acidification. This oil was assumed to be Z-2-methyl-3-phenyl-2-butenopic acid (9).

The crystalline material (mp 112-113°) which slowly separated was presumed to be the corresponding trans (E) acid (4). Evidence for the cis configuration was the formation of 2,3-dimethylindenone (2) upon treatment with concentrated sulfuric acid at 12-15°. The crystalline compound was recovered unchanged from the basic acid washings; this failure to react was taken as further proof of the trans configuration. 43

\[ \text{O} \]
\[ \text{C} \]
\[ \text{C-Me} \]
\[ \text{Me} \]

2

Jackman and Lown, however, found that dehydration of the same hydroxy ester (1) with either potassium bisulfate or thionyl chloride and pyridine yields the terminally unsaturated ester. 44 Nmr analysis of the dehydration product showed absorptions at δ 1.35 (d, -CH₃), 3.65 (d, -C-H), and 5.30 (d, =CH₂), which correspond to the terminally unsaturated ester, ethyl 2-methyl-3-phenyl-3-butenoate (8). After a detailed study of the conditions necessary to achieve the internally conjugated unsaturated acids from the 3-hydroxy ester, they found that only refluxing the ester with iodine in dry benzene for a period of 14
days was successful. The composition of the resulting mixture of methyl esters was estimated from nmr integration to be: Z-2-methyl-3-phenyl-2-butenoate (60%), E-2-methyl-3-phenyl-2-bentenoate (30%), and 2-methyl-3-phenyl-3-butenoate (10%). Separation of the cis and trans unsaturated esters followed by hydrogenation and hydrolysis afforded the isomerically pure acids.

For the present study, the isomerically pure acids were obtained by the method outlined in Scheme X below. Substantially pure

Scheme X

Scheme for the Synthesis of Isomerically Pure 2-Methyl-3-phenylbutyric Acids

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terminally unsaturated ester (8) was obtained from the dehydration of ethyl 3-hydroxy-2-methyl-3-phenylbutyrate (1) with potassium bisulfate, according to the procedure of Burton and Shoppee. Hydrogenation yielded a 4:1 mixture of ethyl erythro- and threo-2-methyl-3-phenylbutyrates (8 and 10) as estimated from the gc chromatogram (8 ft. Carbowax column) and nmr integration of the absorptions at δ 3.76 and 3.99 (−CH₂CH₃). Preferential formation of the erythro isomer can be understood by consideration of the Newman projections of the conformations probably preferred for the molecules involved in the catalytic hydrogenation process. Steric hindrance due to the bulky ethoxy-carbonyl group disfavors adsorption and subsequent addition from the direction that leads to formation of the threo isomer (8).

Spinning band distillation afforded a sufficient amount of the higher boiling, isomerically pure erythro ester (10), which yielded
the corresponding acid (7) upon hydrolysis. The threo acid was ob-
tained by combining the lowest boiling fractions from the spinning
band distillation, which were richest in the threo ester, and hydro-
lyzing these to the acid mixture. The erythro isomer slowly separated
out and was removed by vacuum filtration. Repeated vacuum distilla-
tion of the remaining oil yielded the pure threo acid (6).

B. Results of Halodecarboxylation

Each isomerically pure acid was treated with lead tetraacetate
and lithium chloride, according to the procedure described by Kochi; lead tetraacetate was the limiting reagent. The distribution of the
product chlorides from this halodecarboxylation of the isomeric car-
boxylic acids is given in Table X. The same ratio of erythro:threo
chlorides results from either isomeric reactant. In other words, the
stereochemistry of product formation is independent of the configura-
tion of the starting material. A common radical intermediate is sup-
posedly formed from either starting acid after loss of carbon dioxide.
The ligand transfer step which follows (Equations 18, 21, and 22 in the
Introduction) is then the same for the two isomers and identical product
distributions result. The value of the erythro:threo ratio is deter-
mined by the direction of attack on this one radical intermediate.
TABLE X
PRODUCT DISTRIBUTION OF HALODECARBOXYLATION
OF erythro- AND threo-2-METHYL-3-PHENYLIBUTYRIC ACIDS

<table>
<thead>
<tr>
<th>Configuration of Starting Acid</th>
<th>Time (hr)</th>
<th>Product Distribution</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mole % Ie-Cl&lt;sub&gt;a&lt;/sub&gt;</td>
<td>It-Cl&lt;sub&gt;a&lt;/sub&gt;</td>
</tr>
<tr>
<td>erythro</td>
<td>3</td>
<td>41.5</td>
<td>58.5</td>
</tr>
<tr>
<td>threeo</td>
<td>4</td>
<td>42.2</td>
<td>57.8</td>
</tr>
</tbody>
</table>

Ph

a. I = \(\text{Ph}^X\); It = threo; Ie = erythro.
C. Results of Oxidative Decarboxylation

Oxidative decarboxylation of the same acids was carried out in an excess of lead tetraacetate and pyridine as described by Corey and Casanova.\(^5\) A summary of the products obtained from the isomeric acids is given in Table XI on the following page. \(t\)-Butylbenzene was used as an inert reference standard for monitoring the material balance of the reaction. \(4-t\)-Butylbenzoic acid was recovered quantitatively after treatment with lead tetraacetate and pyridine for a period of 8 hours. Therefore, it was assumed that \(t\)-butylbenzene would be unaffected by the reaction conditions.

The only substitution products formed in the oxidation of either isomeric carboxylic acid are \textit{erythro}- and \textit{threo}-1-methyl-2-phenyl-1-propyl acetates. Those acetates that would result from methyl or hydrogen migration, 1-methyl-1-phenyl-1-propyl acetate and
<table>
<thead>
<tr>
<th>Starting Material (umol)</th>
<th>Recovered Starting Material, Mole %</th>
<th>Product Distribution, Mole %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Acid</td>
<td>t-Butyl-benzene</td>
</tr>
<tr>
<td>3.16</td>
<td>2.52</td>
<td>9</td>
</tr>
<tr>
<td>3.70</td>
<td>2.06</td>
<td>9</td>
</tr>
<tr>
<td>5.03</td>
<td>0.50</td>
<td>30</td>
</tr>
<tr>
<td>3.04</td>
<td>0.32</td>
<td>17</td>
</tr>
<tr>
<td>4.46</td>
<td>0.58</td>
<td>22</td>
</tr>
</tbody>
</table>

avg. = 0.59 ± 0.04

| 12.86                  | 0.37 | 22             | 31        | 68   | -               | 0.2           | -         | 2.4      | 4.6      | 0.52     |
| 5.08                   | 0.18 | 21             | trace     | 55   | 0.2             | 4.5           | 1.0       | 10.0     | 16.8     | 0.60     |
| 2.50                   | 0.33 | 48             | 3         | 69   | 0.2             | 6.0           | 1.4       | 10.7     | 17.4     | 0.61     |

avg. = 0.58 ± 0.04

Ph

a. I = \(-\) ; It = threo; Ie = erythro.

b. II-Z = \(-\) ; II-E = \(-\).

\textsuperscript{a} Ph

\textsuperscript{b} Ph

\textsuperscript{X} X
2-methyl-1-phenyl-1-propyl acetate, respectively, were looked for but not detected in the gc chromatogram of the product mixture. Phenyl migration could not be observed, of course, since the same ester would result from attack of acetate anion on either the rearranged or un­rrearranged cation. Phenyl participation, either in generating the intermediate cation or in subsequent reactions of the cation, must be
at most a minor factor, however, on the basis of the isomer distribution of the acetates. Phenyl participation is expected to favor erythro acetate considerably more substantially (Ity-OAc/Ie-OAc $\sim 0.20$) than is found.*

The formation of identical (within experimental error) erythro:threo ratios of acetates from both isomeric acids indicates the existence of a single cationic intermediate in the oxidation. This is as expected since the halodecarboxylation study demonstrates the formation of a common radical from the isomeric acids. The cation which is generated from this radical in the oxidation (Equations 12 and 13 in the Introduction) must necessarily then be the same for the two acids. The difference in the value of the erythro:threo ratio of acetates from that of the chlorides indicates a different set of energy factors involved in the two types of product formation.

The formation of olefins during the course of the reaction appears somewhat more complex. Rather than a constant ratio of isomers throughout the course of the reaction as was the case with acetate formation, olefin formation appears to occur during the later stages of the reaction. Early in the reaction, no olefin is present. When reaction

*Reasonable models for estimation of the relative energies of the stereo-isomeric bridged intermediate cations are the corresponding 1,2-dimethylcyclopropanes, for which the thermal equilibrium compositions at $380^\circ$ (cis/trans = 0.397) and several higher temperatures (AH = 1.07 Kcal/mol) have been reported$^{45}$ [M. C. Flowers and H. H. Frey, Proc. Roy. Soc. (London), A257, 122 (1960)]. Those data permit the calculation of a cis/trans ratio of $\sim 0.20$ at $80^\circ$. The cis bridged cation would lead to threo acetate, and the trans bridged cation to erythro acetate.
is complete, however, the isomeric olefins, Z- and E-2-phenyl-2-butene, are present. Olefins which could result from rearrangement of the cationic intermediate, namely, 3-phenyl-1-butene and 2-phenyl-1-butene, are absent throughout the course of the reaction.

The olefins anticipated from intermediate cations derived from the isomeric acids, in the absence of rearrangement, rotation, or phenyl-bridged intermediates, are shown below. Instead, the same ratio of Z:E olefins (4.6:1, respectively) is found from oxidation of either isomeric carboxylic acid. Surprisingly, the major isomer found is the trans (Z) olefin. This isomer is the less stable thermodynamically because of the increased steric interaction between the phenyl and methyl groups over that between two methyl groups. A 5.1:1 ratio of E:Z isomers was found in an equilibrium mixture of 2-phenylbutenes. This ratio indicates the greater stability of the E isomer, and represents a
difference in energy of approximately 950 cal/mole. This value differs considerably from the originally calculated value of 520 cal/mole obtained earlier by Cram,\textsuperscript{18} and possibly reflects the difference in accuracy of the analytical methods employed (gc vs. ir).

A small amount of 2-phenylbutane, a radical produce,\textsuperscript{6} is also present in the product mixtures. This hydrocarbon can arise by disproportionation and/or other hydrogen-abstraction reactions. When 2-methylbutyric acid is oxidized by lead tetraacetate at the same temperature used here, the alkane is formed about as extensively as each of three isomeric alkenes and constitutes about 1/4 of the hydrocarbon mixture.

\[ \text{Ph} \text{COOH} \xrightarrow{6 \text{ or } 7} \text{Ph} + \text{Ph} + \text{Ph} \]

\[ \text{2\%} \quad \text{81\%} \quad \text{17\%} \]

\[ \text{Ph COOH} \xrightarrow{} \text{Ph} + \text{Ph} + \text{Ph} + \text{Ph} \]

\[ \text{22\%} \quad \text{33\%} \quad \text{16\%} \quad \text{29\%} \]

The much smaller proportion (2-3% of the hydrocarbon mixtures) of alkane formed from the 3-phenyl substituted acids strongly indicates that the radical mechanism is less important for direct product formation here than it is with the less substituted acids.

Initially during the reaction, a compound of shorter retention time than those of the olefins was found in the gc chromatograms of the
product mixtures from both isomeric acids. Comparison of retention
times on DIDP (diisodecyl phthalate) and Carbowax columns showed that
this peak was not due to ethylbenzene or styrene. Likewise the com-
pound did not correspond to the other phenylbutenes: 3-phenyl-1-butene,
2-phenyl-1-butene, or 2-methyl-1-phenyl-1-propene. This compound is
not present in the product mixture when the reaction is allowed to go
to completion before it is worked up. The possibility of formation of
1-methyl-2-phenylcyclopropane or dimethylbenzocyclobutene was consi-
dered; initial attempts to prepare the cyclopropane separately were
unsuccessful, however. No attempts were made to prepare the cyclobutane.

No general pattern was found for the rate of reaction. Reac-
tions of the erythro carboxylic acid were definitely incomplete after
9 hours. Another reaction run for 30 hours was also incomplete. Two
reactions, 17 and 22 hours in duration, showed no trace of unreacted
acid, however. The disappearance of the initially formed brown precip-
itate and the appearance of a light, cream-colored precipitate in a
yellow solution seem to be good indicators of the completion of reac-
tion. If one uses this criterion, the time of reaction of the erythro
isomer is between 9 and 17 hours. The time for the threo isomer, on
the other hand, is between 21 and 48 hours. The reaction time for 4-t-
butylcyclohexanecarboxylic acid is less than 2 hours by this standard,
and work-up after 5 hours indeed showed complete reaction.

Although the rate of the reaction does not seem to follow any
obvious pattern, the product compositions of the completed reactions
of the two isomeric 2-methyl-3-phenylbutyric acids are in very close
agreement.
Configuration of Starting Acid | % Reaction | % Recovery t-Butylbenzene | I-H | II-Z | II-E | It | Ie | % Yield
---|---|---|---|---|---|---|---|---
erythroid | 100 | 92 | 0.2 | 8.1 | 1.7 | 13.9 | 23.2 |
erythroid | 100 | 67 | 0.2 | 6.4 | 1.6 | 11.1 | 18.9 |
threoo | 97 | 69 | 0.2 | 6.0 | 1.4 | 10.7 | 17.4 |
threoo | 100 | 55 | 0.2 | 4.5 | 1.0 | 10.0 | 16.8 |

a. 2-Phenylbutane.
c. I = erythro, It = threoo, Ie = erythroid.

D. Comparison with Previous Studies

1. Halodecarboxylation

Halodecarboxylation of cis- and trans-4-t-butylcyclohexanecarboxylic acids yields exclusively the corresponding cis- and trans-4-t-butylcyclohexyl chlorides in a 2.04:1 ratio, respectively, from each acid. This single product distribution indicates the existence of a common radical intermediate. The preference for axial attack on this radical
is attributed to the torsional interactions involved in product formation following equatorial attack on the radical.\textsuperscript{46} Equatorial attack on C\textsubscript{1} (structure \textit{a}) requires eclipsing of H\textsubscript{1} with both H\textsubscript{2e} and H\textsubscript{3e} in forming the trans product, whereas axial attack leads directly to the cis product without passing through any such eclipsed conformations. The difference in energy for the two pathways is reflected in the product ratio, which favors the thermodynamically less stable isomer.

The present study with the acyclic, substituted phenylethyl system also gives evidence of the generation of a common radical intermediate. The diastereomeric acids lead to a single distribution of chlorides with a slight preference for threo chloride formation. Threo chloride formation without eclipsing of the C\textsubscript{1} hydrogen with a C\textsubscript{2} substituent similar to that in the cyclohexyl system (Path \textit{b}) requires the
sterically less favored radical intermediate, structure J. If the sterically favored structure, structure G, is involved, then product formation is occurring preferentially by attack along path C which, however, requires the hydrogen to eclipse the phenyl carbon during product formation and which leads to the less stable threo product.

2. Oxidative Decarboxylation

The influence by the stereochemistry of the starting material is apparently lost in the radical stage of the oxidative decarboxylation reaction. Further oxidation leads to a common cation, and the same product distribution from both starting acids must follow. The acetate distributions from the 4-t-butylcyclohexyl system, the norbornyl system, the 2-bornyl system, as well as the 1-methyl-2-phenyl-1-propyl system, all bear this out. A single product distribution is obtained from each diastereomeric pair of acids.

<table>
<thead>
<tr>
<th>Carboxylic Acid</th>
<th>Ratio of Acetate Products</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-t-Butylcyclohexyl</td>
<td>1:1 (axial:equatorial)</td>
<td>3</td>
</tr>
<tr>
<td>2-Norbornyl</td>
<td>4:9:1 (exo:endo)</td>
<td>5</td>
</tr>
<tr>
<td>2-Bornyl</td>
<td>2:1 (exo:endo)</td>
<td>7</td>
</tr>
<tr>
<td>1-Methyl-2-phenyl-1-propyl</td>
<td>0.6:1 (threo:erythro)</td>
<td></td>
</tr>
</tbody>
</table>

The threo:erythro ratio of acetate products from the substituted phenylethyl system follows the same trend as the axial:equatorial ratio of products from the cyclohexyl system; that is, the ratio of less stable product to more stable product is less from reaction of the cation than from the radical.
<table>
<thead>
<tr>
<th>Intermediate</th>
<th>Ratio of Substitution Products</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cyclohexyl (ax:eq)</td>
<td>Phenylethyl (threo:erythro)</td>
<td></td>
</tr>
<tr>
<td>Radical</td>
<td>2.04:1</td>
<td>1.4:1</td>
<td></td>
</tr>
<tr>
<td>Cation</td>
<td>1.1:1</td>
<td>0.6:1</td>
<td></td>
</tr>
</tbody>
</table>

Both the studies on the norbornyl and bornyl acids give evidence that the reaction involves primarily classical cationic intermediates. The retention of optical purity in the norbornyl system and the formation of endo-2-bornyl acetate cannot result from non-classical cationic intermediates. The bridged cationic intermediates in the phenylethyl system, cis and trans phenonium ions, each lead stereospecifically to formation of a single acetate diastereomer, and hence cannot be involved uniquely in the lead tetraacetate oxidative decarboxylation of these phenylethyl carboxylic acids.

Phenyl participation is likewise absent in the oxidation of 3-phenylpropionic acid which gives rise to the unsubstituted phenylethyl radical. Under the same reaction conditions used with the 2-methyl-3-phenylbutyric acids, further oxidation of the radical to the cation occurs to only a minor extent (indicated by a small amount of 2-phenylethyl acetate and styrene, and a trace of 1-phenylethyl acetate). The major product, bibenzyl, results from reaction of the primary radical with the benzene solvent.

Under different reaction conditions even less cationic products are observed. With an excess of the carboxylic acid with respect to lead tetraacetate, bibenzyl is formed exclusively, and indeed, the reaction seems to be a very efficient means of generating 2-phenylethyl radicals.12 In benzene-acetic acid solvent, styrene, ethylbenzene, and 2-phenylethyl acetate are formed, but as minor products.9
$3,3,3$-Triphenylpropionic acid yields a variety of products arising by three separate pathways: carbon-to-oxygen rearrangement ($A$), decarboxylation ($C$), and cyclization ($B$). $^8$ The products are of the same nature as those obtained by decomposition of the related peroxy ester, with indication however, of a greater degree of charge separation in the intermediate radical. $p$-Substituents on a phenyl group exert a definite effect on the rate of the reaction, indicative of some influence by the phenyl group on the rate of the reaction. $^8$ Starnes proposes three separate intermediates for the various pathways:
3. Other Reactions of the Phenylethyl Cation

Comparison of the substitution products from the decarboxylation with the same type of products from other reactions involving 1-methyl-2-phenyl-1-propyl radicals or cations should shed some light on the nature of the radical and cationic intermediates involved in the decarboxylations. A summary of such products from various reactions is given in Table XII on the following page.

Cram attributes the stereospecificity of acetate formation during solvolysis to attack on a phenonium ion intermediate, as discussed in the Introduction. The stability of this non-classical cationic intermediate accounts for the absence of other rearrangement products, 2-methyl-1-phenyl-1-propyl acetate or 1-methyl-1-phenyl-1-propyl acetate. Since the decomposition of the corresponding chlorosulfites follows the same pattern of product stereochemistry, Cram proposes a similar mechanism involving ion-pair intermediates rather than a concerted mechanism.

The more highly energetic cations derived from deamination in acetic acid yield rearranged acetate products in proportion to the distribution of the original amine conformers. The cation is less solvated and attack by acetate is more rapid, occurring before rotation and stabilization as the non-classical phenonium ion. Therefore, the product mixture from the deamination is considered to reflect the distribution of conformers of the original amine. The high percentage of 1-methyl-2-phenyl-1-propyl acetate from the erythro amine reflects the relative stability of the conformer le (page 27 of the Introduction) for which bridging is possible. The conformer of greatest stability for the threo isomer is lt (page 27 of the Introduction). Methyl migration accounts for 32% of the product from this isomer, while phenyl
<table>
<thead>
<tr>
<th>Configuration of Starting Material</th>
<th>Reagent</th>
<th>X</th>
<th>Product Distribution</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ie-X&lt;sup&gt;a&lt;/sup&gt;</td>
<td>It-X&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ie-OTs</td>
<td>HOAc</td>
<td>OAc</td>
<td>94</td>
<td>5</td>
</tr>
<tr>
<td>Ie-OTs</td>
<td>HCOOH</td>
<td>OCHO</td>
<td>100</td>
<td>9</td>
</tr>
<tr>
<td>Ie-OH</td>
<td>SOCl&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Cl</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Ie-NH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>HOAc,HONO</td>
<td>OAc</td>
<td>68</td>
<td>6</td>
</tr>
<tr>
<td>Ie-COOH</td>
<td>Pb(OAc)&lt;sub&gt;4&lt;/sub&gt;,pyr</td>
<td>OAc</td>
<td>63</td>
<td>37</td>
</tr>
<tr>
<td>Ie-COOH</td>
<td>Pb(OAc)&lt;sub&gt;4&lt;/sub&gt;,Cl&lt;sup&gt;−&lt;/sup&gt;</td>
<td>Cl</td>
<td>42</td>
<td>58</td>
</tr>
<tr>
<td>It-OTs</td>
<td>HOAc</td>
<td>OAc</td>
<td>4</td>
<td>96</td>
</tr>
<tr>
<td>It-OTs</td>
<td>HCOOH</td>
<td>OCHO</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>It-OH</td>
<td>SOCl&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Cl</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>It-NH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>HOAc,HONO</td>
<td>OAc</td>
<td>19</td>
<td>25</td>
</tr>
<tr>
<td>It-COOH</td>
<td>Pb(OAc)&lt;sub&gt;4&lt;/sub&gt;,pyr</td>
<td>OAc</td>
<td>63</td>
<td>37</td>
</tr>
<tr>
<td>It-COOH</td>
<td>Pb(OAc)&lt;sub&gt;4&lt;/sub&gt;,Cl&lt;sup&gt;−&lt;/sup&gt;</td>
<td>Cl</td>
<td>42</td>
<td>58</td>
</tr>
</tbody>
</table>

Ph

a. I-X = \( \begin{array}{c} \text{Ph} \\ \text{X} \end{array} \); Ie-X = erythro; It-X = threo.

b. II-X = \( \begin{array}{c} \text{Ph} \\ \text{X} \end{array} \).

c. III-X = \( \begin{array}{c} \text{Ph} \\ \text{X} \end{array} \)
migration accounts for only 24%. This result differs substantially from that obtained by solvolysis, in which phenyl participation is the controlling factor in product formation from both diastereomeric esters.

The intermediate cation generated from the radical in the oxidation by lead tetraacetate is apparently an open cation, in which bridging plays only an insignificant role, if any at all. The decarboxylation takes place in benzene solution, and therefore the availability of the substituting acetate is much lower than in the solvolysis or deamination reactions (both in acetic acid solutions).

The apparent absence of any significant stabilization of one conformation of an intermediate 1-methyl-2-phenyl-1-propyl cation by neighboring phenyl participation causes one to consider seriously an alternative to an alkyl cation intermediate in the processes leading to alkyl acetate products. A ligand-transfer reaction, parallel to that in halodecarboxylation and involving transfer of AcO· to R* is, at first thought, an attractive alternative. However, one must presume that the stereochemical influences for Cl· and AcO· transfer from Pb(IV) species to R* will be quite similar. The reversed ratios of threo:erythro products for the RCl and ROAc mixtures strongly argues for different mechanisms in the two processes.

It is also conceivable that the alkyl acetates are formed by an $S_N^1$-type reaction of an alkyllead intermediate. Again, however,

\[
R^* + \text{Pb(OAc)}_4 \rightarrow R^*\text{Pb(OAc)}_4 \quad (25)
\]

\[
R^* + \text{Pb(OAc)}_3 \rightarrow \text{ROAc} + (\text{AcO})_3\text{Pb}^* \quad (26)
\]
there is no apparent reason for one stereochemical pathway (threo product) being preferred for alkyl chloride formation (ligand transfer from Pb(IV) to R*) and the other (erythro product) for alkyl-lead bond formation (between Pb(IV) and R*) in the intermediate. One would expect the $S_N^i$ reaction, as illustrated above, to occur with retention of configuration at the carbon bound to lead.

Finally, the alkyllead intermediate formed with the same stereochemical preference as is RCl in the ligand-transfer step and pictured above, may undergo $S_N^2$-type displacement by acetate. Although this process would be consistent with the stereochemical results in the present study, it cannot be a general pathway for the formation of alkyl acetates from those systems, such as norbornyl and neopentyl, which yield rearranged products extensively or exclusively, and the composition of the hydrocarbon fraction of the present product mixture appears to require cationic intermediates.

The evidence for the existence of an open, classical cation as an intermediate in the oxidative decarboxylation is supplied by comparison of the elimination products from the 1-methyl-2-phenyl-1-propyl cation. Table XIII gives a summary of the distribution of olefins obtained in the various reactions, together with the equilibrium distribution of the olefins.

Elimination during solvolysis can occur either stereospecifically or non-stereospecifically. Stereospecific elimination results from a phenyl- or hydrogen-bridged cationic species. Where phenyl bridging is less favored for steric reasons, as in the threo isomer, elimination proceeds more extensively. The hydrogen-bridged ions of the threo and erythro isomers lead to the trans and cis olefins,
<table>
<thead>
<tr>
<th>Configuration of Starting Material</th>
<th>Reagent</th>
<th>Temp °C</th>
<th>Yield of Olefin</th>
<th>Product Distribution</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ie-OTsd</td>
<td>HOAc</td>
<td>75</td>
<td>23</td>
<td>56 8 23 13</td>
<td>41</td>
</tr>
<tr>
<td>Ie-OBs e</td>
<td>HOAc</td>
<td>30</td>
<td>6</td>
<td>59 13 13 15</td>
<td>41</td>
</tr>
<tr>
<td>Ie-OTs</td>
<td>CH₃CN</td>
<td>82</td>
<td>50</td>
<td>45 22 12 21</td>
<td>41</td>
</tr>
<tr>
<td>Ie-OC₂CH°</td>
<td></td>
<td>180</td>
<td>50</td>
<td>5 50 38 --</td>
<td>18</td>
</tr>
<tr>
<td>Ie-OTs</td>
<td>LAH f</td>
<td>25</td>
<td>22</td>
<td>22 -- -- --</td>
<td>20</td>
</tr>
<tr>
<td>Ie-NO(CH₃)₂</td>
<td>THF</td>
<td>25</td>
<td>--</td>
<td>0 95 5 --</td>
<td>19</td>
</tr>
<tr>
<td>Ie-COOH</td>
<td>Pb(OAc)₄,pyr</td>
<td>80</td>
<td>9</td>
<td>18 82 -- --</td>
<td></td>
</tr>
<tr>
<td>It-OTsd</td>
<td>HOAc</td>
<td>75</td>
<td>35</td>
<td>42 28 24 6</td>
<td>41</td>
</tr>
<tr>
<td>It-OBs</td>
<td>HOAc</td>
<td>30</td>
<td>12</td>
<td>24 55 13 10</td>
<td>41</td>
</tr>
<tr>
<td>It-OTs</td>
<td>CH₃CN</td>
<td>82</td>
<td>67</td>
<td>34 34 9 23</td>
<td>41</td>
</tr>
<tr>
<td>It-OC₂CH°</td>
<td></td>
<td>180</td>
<td>76</td>
<td>36 12 38 --</td>
<td>18</td>
</tr>
<tr>
<td>It-OTs</td>
<td>LAH f</td>
<td>25</td>
<td>21</td>
<td>-- 21 -- --</td>
<td>20</td>
</tr>
<tr>
<td>It-NO(CH₃)₂</td>
<td>THF</td>
<td>25</td>
<td>80</td>
<td>95 0 5 --</td>
<td>19</td>
</tr>
<tr>
<td>It-COOH</td>
<td>Pb(OAc)₄,pyr</td>
<td>80</td>
<td>6</td>
<td>18 82 -- --</td>
<td></td>
</tr>
<tr>
<td>IV-OAc h</td>
<td>HOAc</td>
<td>75</td>
<td>90</td>
<td>54 3 43 --</td>
<td>41</td>
</tr>
<tr>
<td>IZ, IE or II</td>
<td>HOTs</td>
<td>75</td>
<td>100</td>
<td>79 18 3 --</td>
<td>23</td>
</tr>
</tbody>
</table>

a IZ = Z-2-Phenyl-2-butene; IE = E-2-phenyl-2-butene. b II = 2-Phenyl-1-butene. c III = 3-Phenyl-1-butene. d Ie = erythro; It = threo. e OBs = p-Bromobenzenesulfonate. f LAH = Lithium aluminum hydride. g Yield of olefin was not determined. h IV-OAC = __PhOAc.
respectively (page 16 of the Introduction). These olefins are the principal isomers produced from both reactant tosylates. Non-stereo-specific elimination results from the open 1-methyl-2-phenyl-1-propyl or 1-methyl-1-phenyl-1-propyl cations. The olefins, 2-phenyl-1-butene and 3-phenyl-1-butene, are thought to arise by way of these open cations.\textsuperscript{15}

A concerted cis elimination, such as occurs in the xanthate decomposition,\textsuperscript{18} takes place intramolecularly to give the minor internally conjugated olefin. Removal of the primary hydrogen appears to occur equally well from either diastereomer.\textsuperscript{18} Removal of the secondary hydrogen intramolecularly occurs more predominately from the erythro isomer although leading to the less stable olefin.

Whereas tosylate reduction with lithium aluminum hydride produces olefin in a stereospecific, trans manner,\textsuperscript{20} pyrolysis of the amine oxides yields only products of a concerted intramolecular cis elimination, primarily to the internally conjugated olefin.\textsuperscript{19} Interestingly, Cram postulates a phenonium ion intermediate for the lithium aluminum hydride reduction which appears more stereospecific than the supposedly concerted pyrolysis reaction.\textsuperscript{20}

The distribution of olefins resulting from the oxidative decarboxylation is unique in that the same distribution results from either starting isomeric acid. The olefins formed during the decarboxylation process might, however, arise from that same intermediate which is detected during the earlier stages of the reaction, before any olefin is formed. Whatever the immediate precursor, the olefins do seem to arise from a common intermediate, most likely the same cation from which the acetates derive.
III. CONCLUSION

Results of halodecarboxylation reactions of erythro- and threo-2-methyl-3-phenylbutyric acid show identical ratios of threo: erythro (1.4:1, respectively) chloride substitution products. These results are in agreement with those obtained from reaction of cis- and trans-4-t-butylcyclohexancarboxylic acids. The single product distribution indicates formation of a common radical intermediate.

Cationic oxidative decarboxylation is generally considered to involve oxidation of the radical to a cation which then goes on to product formation. Formation of a common radical intermediate then necessarily implies formation of a single cationic intermediate. The single ratio of substitution products from each of the pairs of the 4-t-butylcyclohexyl-, 2-norbornyl-, and 2-bornyl-carboxylic acids support this hypothesis. The present results with the substituted phenylethyl system lend further support to this consideration; not only the acetate products, but likewise the olefins formed, are independent of the stereochemistry of the reactant acids.

The radical and cationic intermediates must react by different mechanisms since different ratios of isomers are obtained. The increase in the ratio of sterically favorable to unfavorable acetates formed may indicate some influence by product stability from the cationic intermediate.

The product distribution resulting from the cationic intermediate differs from the distributions obtained in other reactions. The present study indicates that the products are formed without significant rearrangement; no products (substitution or elimination) of
methyl or hydrogen migration are found. The cation, therefore, is not like the highly energetic, poorly solvated cation found in the deamination reactions. Formation of a 0.6:1 ratio of threo:erythro acetates speaks against the formation of a non-classical phenonium ion (or the equivalent rapidly equilibrating classical ions), such as that apparently involved in solvolysis reactions.

Concerted product formation from the lead salt (equations 23 and 26) following pre-equilibration of lead acetate and the carboxylic acid (equation 3) has been considered. It is difficult, however, to reconcile the observed product ratios of acetates and/or chlorides by this mechanism.

It appears rather that an alkyl radical immediately precedes chloride formation in the halodecarboxylation reaction. The ratios of acetates and olefins from the oxidative decarboxylation suggests that a cationic intermediate immediately precedes the acetate products. The olefins may arise from that compound which is present early in the reaction but absent from product mixtures of completed reactions; however, the same olefin distribution suggests a single precursor from both diastereomeric acids.
IV. EXPERIMENTAL

A. General Comments

The reagents used in all syntheses were reagent grade commercial chemicals. Unless otherwise indicated, these chemicals were used without further treatment. The solvents used were dried by storage over calcium hydride. Pyridine was stored over potassium hydroxide.

All glass apparatus used for Grignard, Reformatsky, Wittig, and decarboxylation reactions was dried separately in an oven overnight before assembly. After assembly, nitrogen was swept through the system for 15 minutes before the reaction was begun, and a slow stream of nitrogen was passed through the system throughout the reaction. All reaction mixtures were stirred magnetically unless indicated differently.

Infrared (ir) spectra were obtained with a Perkin-Elmer Infra-cord Model 137 infrared spectrometer. Samples of liquid compounds were examined as thin films on sodium chloride plates; samples of solid compounds were examined as solid solutions in potassium bromide discs.

Proton nuclear magnetic resonance (nmr) spectra were obtained with a Varian Associates Model A60A, Varian Associates Model HA100, or a Perkin-Elmer R12B nuclear magnetic resonance spectrometer. Decoupling experiments were done with either the Perkin-Elmer R12B, or with the Varian HA100 instrument with the aid of Dr. Tracy Broussard of the Louisiana State University technical staff. Samples were examined as 10-20% solutions in carbon tetrachloride or deuteriochloroform with tetramethylsilane (TMS) as internal reference. All chemical shifts are recorded relative to TMS in δ units, and all coupling constants are measured in Hz (cycles per second). The following abbreviations are
used to describe the splitting patterns: s - singlet, d - doublet, t - triplet, q - quartet, p - pentet, m - multiplet (unresolved), dq - doublet of quartets, qq - quartet of quartets.

Gas chromatographic (gc) data were obtained with a Hewlett-Packard Model 700 instrument equipped with a hydrogen flame ionization detector and 1/8" aluminum columns.

Element analyses were obtained by Mr. Ralph Seab of the Louisiana State University Chemistry Department technical staff.

Melting points were obtained with a Thomas Hoover melting point apparatus and are uncorrected.

Spinning band distillations were performed on a 24-inch Nester/Faust Annular Teflon Spinning Band Distillation Column.

Refractive indices were obtained with the use of a Bausch and Lomb Abbé refractometer.

B. Syntheses

1. 2-Methyl-3-phenylbutyric Acids

   a. Reformatsky Synthesis

      (1) Ethyl 3-hydroxy-2-methyl-3-phenylbutyrate

      The procedure followed for the Reformatsky reaction was that described by R. L. Shriner.47

      A 1-liter 3-neck flask, reflux condenser, 250-ml addition funnel and nitrogen inlet were assembled. To the flask was added zinc (43.3 g, 0.68 mole) which had been washed consecutively with hydrobromic acid (5% aqueous), water, ethanol, and acetone, and subsequently dried overnight in the oven. The system was swept with nitrogen for 15 minutes, after which a solution of acetophenone (68.4 g, 0.57 mole) and
ethyl 2-bromopropionate (100 g, 0.55 mole) in benzene (125 ml) was added to the flask slowly from the addition funnel to maintain a gentle reflux of the benzene. When addition was complete, heat was applied with a heating mantle to maintain the reflux for an additional hour, during which time the solution turned green. The mixture was cooled to room temperature, ice-cold sulfuric acid (20% aqueous, 125 ml) was added, and the benzene layer was separated. The aqueous layer was extracted with benzene (two 30-ml portions). The combined benzene solution was washed consecutively with cold sulfuric acid (5% aqueous, 30 ml), aqueous sodium carbonate (10%, 15 ml) and water (two 15-ml portions). After drying (magnesium sulfate), benzene was removed under reduced pressure (water aspirator).

Vacuum distillation of the residue yielded 68.6 g (56.2% yield) of a 3:1 mixture of the two racemic diastereomeric hydroxy esters as a colorless oil: bp 109-111° (2.4 mm) [lit47 bp 134-135° (9 mm); 141° (10 mm)43]; ir (neat, liquid film) 3472 (s, OH), 3030-2890 (s, C-H), 1736-1695 (s, C=O), 1449 and 1374 (s, CH₃), 1333 (s, C-OH), 1176 (sb, C-OEt), 1093 and 1078 (s, C-OH), 766 and 702 (sb, C₆H₅) cm⁻¹; nmr (CCl₄) major isomer δ 0.90 (m, 3, OCH₂CH₃), 1.27 (d, 3, J = 7.0 Hz, CH₃CH), 1.36 (s, 3, CH₃COH), 2.91 (q, 1, J = 7.0 Hz, CHCH₃), 3.25 (sb, 1, OH), 3.84 (q, 2, J = 7.0 Hz, OCH₂CH₃), 7.30 (mb, 5, C₆H₅); minor isomer δ 0.90 (m, 3, OCH₂CH₃), 1.20 (d, 3, J = 7.0 Hz, CH₃CH), 1.49 (s, 3, CH₃COH), 2.75 (q, 1, J = 7.0 Hz, CHCH₃), 4.16 (q, 2, J = 7.0 Hz, OCH₂CH₃), 7.30 (mb, 5, C₆H₅). The multiplet at δ 0.90 appears as a five-line pattern in a ratio of 1.4:1:3:1:1.4 with spacings of 3.5 Hz. An absorption consisting of two doublets with coupling constants of 7.0 Hz was anticipated for the methyl groups of the two isomers.
Ethyl 2-methyl-3-phenyl-3-butenoate

The dehydration procedure followed was that of Burton and Shoppee. Ethyl 3-hydroxy-2-methyl-3-phenylbutyrate (68.6 g, 0.31 mole, mixture of diastereomers) and potassium hydrogen sulfate (43.5 g, 0.32 mole) were placed in a 1-neck 200-ml flask equipped with reflux condenser. The mixture was heated at 150°C for 3 hours, after which the product was dissolved in ethyl ether and dried (potassium carbonate). Rotary evaporation removed the ether solvent, and fractional distillation yielded the unsaturated ester as a pale yellow liquid [44.5 g, 71% yield, bp 109-113°C (2.2 mm): ir (neat, liquid film) 1748-1710 (s, C=O), 1445 and 1374 (m, CH3), 1176 (sb, C-0Et), 765 and 702 (sb, C6H5) cm⁻¹; nmr (neat) δ 1.11 (t, 3, J = 7.2 Hz, OCH3CH3), 1.36 (d, 3, J = 7.3 Hz, CH3CH), 3.67 (q, 1, J = 7.1 Hz, CHCOOEt), 4.08 (q, 2, J = 7.2 Hz, OCH2CH3), 5.27 (bs, 1, C=CH cis to C6H5), 5.37 (s, 1, C=CH trans to C6H5), 7.33 (m, 5, C6H5).


The nmr analysis indicated only terminal olefin [lit bp 125-129°C (12 mm)] rather than the internal conjugated olefin [lit bp 128-129°C (10 mm)] reported by the previous workers.

Ethyl 2-methyl-3-phenylbutyrate

A solution of the unsaturated ester (44.5 g, 0.216 mole) in ethanol (aqueous, 95%, 40 ml, previously heated over decolorizing charcoal) was placed in a Paar hydrogenator apparatus, palladium/charcoal (0.3 g, 10%, 50% water wet) was added, the reaction vessel
was swept with nitrogen for 15 minutes, and the mixture was sealed under an initial hydrogen pressure of 40 psig. Reaction was essentially completed in the first 30 minutes, as evidenced by the rate of hydrogen uptake, but the hydrogen pressure was maintained overnight. The rapid uptake of hydrogen indicates the presence of a terminal olefin rather than of a more highly substituted olefin, an $\alpha,\beta$-unsaturated ester.$^{48}$ The reaction mixture was filtered, and the solvent was removed by distillation under reduced pressure (water aspirator). Nmr analysis of the residue (relative intensities of $\delta$ 3.99 and 3.76 absorptions) indicated a 1:4 mixture of the saturated threo and erythro esters [43.7 g, 98.2% yield: bp 101-102$^\circ$ (3.0 mm); lit$^{48}$ bp 128-130$^\circ$ (12 mm)]: nmr (CCl$_4$) major isomer $\delta$ 0.86 (d, 3, $J = 6.6$ Hz, CH$_3$CHC$_6$H$_5$), 1.19 (t, 3, $J = 7.0$ Hz, CH$_3$CH$_2$O), 1.18 (d, 3, $J = 6.5$ Hz, CH$_3$CHCO$_2$), 2.62 (ABX$_3$ pattern for two methine protons: 2 overlapping doublet of quartets); 3.99 (q, 2, $J = 7.0$ Hz, OCH$_2$CH$_3$), 6.93 (s, 5, C$_6$H$_5$); minor isomer $\delta$ 3.76 (q, 2, $J = 7.0$ Hz, OCH$_2$CH$_3$), other peaks overlap with those of the major isomer.

Vacuum distillation on a spinning band column yielded 16.43 g of isomerically pure erythro ester, as shown by gc analysis on a 8 ft Carbowax column at 130$^\circ$. The assignment of configuration was made on the basis of comparison of the properties of the corresponding carboxylic acid with those reported in the literature.$^{44}$

(4) erythro-2-Methyl-3-phenylbutyric acid

Ethyl erythro-2-methyl-3-phenylbutyrate (16.2 g, 78.6 mmoles) was placed in a 100-ml round bottom flask. Sodium hydroxide (82 ml, 1 M, diluted from 3 M aqueous with 95% alcohol) was added, a Friedrich
condenser was attached, and the mixture was heated with stirring for 3 hours. After cooling to room temperature, the solution was diluted with water (150 ml) and acidified with hydrochloric acid (1 M). The resulting white precipitate was vacuum filtered, washed with water, and recrystallized from cyclohexane to yield 9.40 g (67.1% yield) of the isomerically pure erythro carboxylic acid: mp 130-131°C (lit42 mp 130-131°C from ligroin, 132-133°C so); ir (KBr) 3225-2500 (sb, OH), 1672 (s, C=O), 938 (mb, C-OH), 762 and 699 (sb, C6H5) cm⁻¹; nmr (CCl4) δ 0.98 (d, 3, J = 6.4 Hz, CH₃CHCOOH), 1.29 (d, 3, J = 6.6 Hz, CH₂CH₃C₆H₅), 2.7 (m, 2 methine protons), 7.19 (s, 5, C₆H₅), 12.1 (s, 1, COOH), when measured on a 60 MHz spectrometer. The 100 MHz spectrum shows absorptions at δ 0.94 (d, J = 6.9 Hz), 1.29 (d, J = 6.6 Hz), 2.54 (dq, 1, JCH-CH = 6.5 Hz, JCH-CH = 10.0 Hz, CH₂COOH), 2.88 (dq, 1, JCH-CH₃ = 6.5 Hz, JCH-CH = 10.0 Hz, CH₂C₆H₅).

(5) threo-2-Methyl-3-phenylbutyric acid

Fractions 1-5 (6.20 g) from the spinning band distillation of the mixture of esters obtained as described in Sec. a.3., above, were combined and hydrolyzed with sodium hydroxide (45 ml, 1 M, diluted from 3 M aqueous with 95% ethanol) by refluxing, with stirring, for 3 hours. After cooling to room temperature, the solution was diluted with water (75 ml) and neutralized with hydrochloric acid (3 M). The carboxylic acid formed a separate layer and was taken up in cyclohexane. The resultant pale yellow oil that remained after filtration of the crystalline isomer and distillation proved to be the threo acid: bp 109-110°C (0.4 mm); lit44 bp 120-125°C (0.5 mm); ir (neat, liquid film) 3225-2500 (sb, C-OH and C-H), 1710 (s, C=O), 945 (mb, O-H), 765 and 701
\( (s, \text{C}_6\text{H}_5) \text{ cm}^{-1}; \text{nmr} (\text{CCl}_4) \delta 1.08 (d, 3, J = 6.5 \text{ Hz, CH}_2\text{CHOOH}), 1.22 (d, 3, J = 7.2 \text{ Hz, CH}_3\text{CH}_2\text{H}_5), 2.64 (p, 1, J = 6.5 \text{ Hz, CH}_3\text{CH}_2\text{H}_5), 3.15 (p, 1, J = 7.2 \text{ Hz, CH}_3\text{CHOOH}), 7.12 (s, 5, \text{C}_6\text{H}_5), 10.9 (s, 1, \text{COOH}). \) Absorptions in the 100 MHz spectrum are at \( \delta 1.07 (d, J = 7.0 \text{ Hz}), 1.21 (d, J = 7.2 \text{ Hz}), 2.62 (p, J = 7.1 \text{ Hz}) \) and \( 3.12 (p, J = 7.0 \text{ Hz}) \).

Results of decoupling experiments on a 60 MHz spectrometer are summarized below:

<table>
<thead>
<tr>
<th>Position of Irradiation, ( \delta )</th>
<th>Simplified Signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.08</td>
<td>2.65 (d, ( J = 7.2 \text{ Hz} ))</td>
</tr>
<tr>
<td>1.22</td>
<td>3.17 (d, ( J = 7.2 \text{ Hz} ))</td>
</tr>
<tr>
<td>3.15</td>
<td>1.23 (s)</td>
</tr>
<tr>
<td>2.65</td>
<td>1.09 (s)</td>
</tr>
</tbody>
</table>

**Anal.** Calcd. for \( \text{C}_{11}\text{H}_{14}\text{O}_2 \): C, 74.1; H, 7.9. Found: C, 74.2; H, 8.0.

**b. Grignard Synthesis**

(1) \text{3-Phenyl-2-butanol}

A 500-ml 3-neck flask was equipped with a 250-ml addition funnel, nitrogen inlet, and Friedrich condenser with calcium chloride drying tube attached to it. Magnesium (8.5 g, 0.35 g-atom) and ethyl ether (10 ml) were added to the reaction flask. A solution of methyl iodide (42.6 g, 0.30 mole) in ethyl ether (75 ml) was added dropwise to maintain a steady reflux. Refluxing was maintained for an additional 15 minutes after complete addition, heat being applied by a heating mantle. A thermometer was inserted into the reaction flask in place of the nitrogen inlet, and the flask was cooled to -50° in an ice-salt
bath. A solution of 2-phenylpropionaldehyde (33.6 g, 0.25 mole) in ether (25 ml) was added slowly while the temperature was kept below 0°. Saturated ammonium chloride solution was added until the solution became clear and magnesium salts settled to the bottom of the flask, according to the method of Coburn.50 The ether solution was concentrated on a rotary evaporator.

Vacuum distillation yielded the alcohol (31.0 g, 82.7% yield): bp 78-83.0° (2.0 mm) [lit51 bp 77-78° (1.2 mm)]; ir (neat, liquid film) 3390 (s, OH), 2985-2860 (s, C-H), 1447 and 1370 (s, CH₃), 1100-1075 (s, C-OH for a secondary alcohol), 760 and 701 (s, CH₃) cm⁻¹; nmr (CDCl₃) major isomer δ 0.99 (d, 3, J = 6.6 Hz, CH₃C-OH), 1.44 (d, 3, J = 7.1 Hz, CH₃C-C₆H₅), 2.48 (p, 1, J = 7.0 Hz, CH-C₆H₅), 3.79 (p, 1, J = 6.5 Hz, CH-OH), 7.20 (s, 5, C₆H₅); minor isomer δ 1.12 (d, 3, J = 6.4 Hz, CH₃C-OH), 1.21 (d, 3, J = 7.1 Hz, CH₃C-C₆H₅), 2.48 (p, 1, J = 7.1 Hz, CH-C₆H₅), 3.79 (p, 1, J = 6.4 Hz, CH-OH), 7.22 (s, 5, C₆H₅).

The chemical shifts of the corresponding methine protons (HCOH and H-C₆H₅) are the same in the two isomers, but those of the methyl and phenyl protons are not. The absorption for CH₃C-C₆H₅ in the major isomer is downfield by 0.13 ppm from that in the minor isomer, while the absorption for phenyl protons in the major isomer is slightly (0.02 ppm) upfield from the corresponding absorption in the minor isomer. These descriptions permit us to identify the minor isomer as threo and the major one as erythro.

The three staggered conformations for each isomer may be represented by the following formulas.
The electronic environment for the methine protons is identical only in the two conformations, le and lt. The hydroxyl group is expected to shift the vicinal methyl protons downfield in the erythro isomer and the phenyl protons downfield in the threo isomer for the same conformations. If other conformations were important contributing structures for the threo isomer, a decrease in the coupling constant, $^3J$, would be expected due to the shift from a trans to a gauche arrangement of the methine protons. A difference in chemical shift for the methine protons would be expected if other conformations of either isomer were important contributing structures.

Gc analysis on an 8 ft Carbowax column at $138^\circ$ showed a ratio of 1:1.8 threo:erythro isomers, similar to that found previously by Cram, and as predicted by Cram's rule for attack at a carbonyl carbon adjacent to an asymmetric carbon atom. Comparison of retention times
with those of isomerically pure alcohols confirmed the assignment of configuration.

(2) 2-Chloro-3-phenylbutane

Thionyl chloride (65.7 ml, 40.1 g, 0.90 mole) was placed in a 100-ml 3-neck flask equipped with reflux condenser, addition funnel and thermometer. 3-Phenyl-2-butanol (45.9 g, 0.366 mole, 1:1.8 mixture of diastereomers) was added dropwise to the stirred solution to keep the temperature below 30°C. The solution was stirred for an additional 2 hours at room temperature and for 1 hour at reflux temperature. Most of the excess thionyl chloride was distilled off through a short path condenser. The residue was poured over ice, and the chloride was extracted with pentane (three 50-ml portions). The pentane solution was washed consecutively with sodium carbonate solution (10% aqueous) and water, and was dried (potassium carbonate). Removal of pentane by rotary evaporation followed by distillation [69.0-69.5°C (1.9 mm)] yielded the chloride (43 g, 85% yield).

Gc analysis on an 8 ft Carbowax column at 140°C showed a mixture of threo and erythro chlorides in a ratio of 1:1.9, respectively, assuming the same relative retention times as for the isomeric alcohols. In (neat, liquid film) 1447 and 1370 (s, CH₃), 745 (m, C-Cl), 762 and 701 (s, C₆H₅) cm⁻¹; nmr (CCl₄) δ 1.32 (m, 6, methyl protons), 2.83 (m, 1, CH-C₆H₅), 4.1 (m, 1, CH-Cl), 7.16 and 7.18 (singlets for the phenyl protons of the two isomers).

Separation of the isomeric chlorides from a similar mixture was achieved by spinning band distillation at 3.0 mm. The absorptions in the ir spectrum which are stronger for the threo isomer than for the
mixture are found at 1266, 1220, 1080, 1059, 1006, 962, and 855 cm\(^{-1}\).

Absorptions of the mixture which are stronger than those from the threo isomer are at 1109, 1043, 954, 840, and 745 cm\(^{-1}\). The nmr spectrum for the threo isomers shows the absorptions: \((\text{CCl}_4) \delta 1.32 (d, 3, J = 7.2 \text{ Hz}, \text{CH}_3\text{C-C}_6\text{H}_5), 1.44 (d, 3, J = 7.2 \text{ Hz}, \text{CH}_3\text{C-Cl}), 2.87 (dq, 1, ^2J = 7.8 \text{ Hz}, ^3J = 7.2 \text{ Hz}, \text{CH-C}_6\text{H}_5), 4.06 (dq, 1, ^2J = 7.8 \text{ Hz}, ^3J = 7.2 \text{ Hz}, \text{CH-Cl}), 7.18 (s, 5, \text{C}_6\text{H}_5)\). The erythro isomer shows absorptions at: \(\text{nmr (CCl}_4) \delta 1.34 (d, 6, J = 7.2 \text{ Hz}, \text{methyl protons}), 3.01 (dq, 1, ^2J = 5.4 \text{ Hz}, ^3J = 7.2 \text{ Hz}, \text{CH-C}_6\text{H}_5), 4.17 (dq, 1, ^2J = 5.4 \text{ Hz}, ^3J = 7.2 \text{ Hz}, \text{CH-Cl}), 7.16 (s, 5, \text{C}_6\text{H}_5)\).

The absorption pattern for the methyl protons found in the spectrum of the chloride mixture is more easily interpreted after observing the spectra of the purified isomers. The five-line pattern observed for the methyl protons consists of the doublet for the six methyl protons of the erythro isomer (probably an accidental coincidence of the doublets of the two methyl groups) and the three line pattern for the same protons of the threo isomer (two doublets whose center peaks overlap to give a 1:2:1 pattern).

The difference in ^2J values seems to indicate a preference for conformations 1t and 1e below as a first approximation.

threeo:

\[
\begin{align*}
\text{Cl} & \quad \text{H} & \quad \text{Ph} \\
\text{CH}_3 & \quad \text{H} \\
\text{1t} \\
\end{align*}
\]

\[
\begin{align*}
\text{Cl} & \quad \text{H} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{H} \\
\text{2t} \\
\end{align*}
\]

\[
\begin{align*}
\text{Cl} & \quad \text{Ph} & \quad \text{H} \\
\text{CH}_3 & \quad \text{H} \\
\text{3t} \\
\end{align*}
\]
(3) 2-Methyl-3-phenylbutyric acid

A 500-ml 3-neck flask was equipped with a 250-ml addition funnel, nitrogen inlet and Friedrich condenser. A drying tube (calcium chloride) was attached to the condenser. Magnesium (4.13 g, 0.17 g-atom) and ethyl ether (20 ml) were placed in the reaction flask. A solution of the above chloride (25.3 g, 0.15 mole 1:1.9 mixture of diastereomers) in ethyl ether (50 ml) was added slowly from the addition funnel. Several crystals of iodine were added to the reaction flask to initiate the reaction, and after the reaction was definitely initiated, additional ether (150 ml) was added to the reaction flask. Upon completion of addition, the solution was refluxed for 30 minutes, cooled to room temperature, and then poured over an excess of Dry Ice and ether. The flask was swirled to insure complete reaction and allowed to come to room temperature before hydrolysis of the magnesium complex with water and dilute hydrochloric acid. The ether layer was separated; the aqueous layer was extracted with ether (three 50-ml portions). Neutralization of the basic solution gave a mixture of acids which was separated into 7.20 g of white crystals (27.0% yield, mp 127-129° after one recrystallization from cyclohexane) by recrystallization from cyclohexane and 3.78 g (14.4% yield) of a yellow oil left by evaporation of the cyclohexane solvent.
The crystalline material was the same compound as that obtained in pure form by the Reformatsky synthesis above (Sec. 1.a), as indicated by comparison of melting points, nmr and ir data, and therefore was the erythro acid.

The oil, which exhibited ir and nmr spectra identical to those of the acid obtained by the Reformatsky synthesis also, was identified as the threo acid.

2. Reference Compounds for the 1-Methyl-2-phenyl-1-propyl system
   a. Olefins
      (1) 2-Phenyl-2-butanol

      Magnesium turnings (5.3 g, 0.22 g-atom) were added to a 500-ml 3-neck flask equipped with 250-ml addition funnel, nitrogen inlet and Friedrich condenser to which was attached a drying tube (calcium chloride). Reaction was initiated by addition of a solution of bromobenzene (1 ml) in ethyl ether (15 ml), rapid stirring and slight heating supplied by a heating mantle. When reaction was initiated (evidenced by appearance of a dark brown color), a solution of bromobenzene (29 ml, a total of 32.4 g, 0.21 mole) in ethyl ether (150 ml) was added from the addition funnel at a rate sufficient to maintain a moderate reflux. When addition was completed, heat was again applied to maintain the reflux for 30 minutes. A solution of butanone (14.4 g, 17.9 ml, 0.20 mole) in ethyl ether (100 ml) was then added from the addition funnel as rapidly as possible while maintaining a gentle reflux, and then the reaction mixture was allowed to cool to room temperature. Upon addition of the ketone, the solution turned first a bright yellow and then a white precipitate formed.
Ammonium chloride solution (10% aqueous, approximately 40 ml) was added dropwise, with stirring, to form first a greyish-white solution and finally a clear, yellow solution with a dense white precipitate which settled rapidly. The ether layer was decanted, and the precipitate was washed several times with ether. The combined ether solution was dried (magnesium sulfate) and concentrated by rotary evaporation to yield the crude alcohol product.

A second sample was prepared in the same way and distilled under vacuum to give the pure alcohol: bp 78-80° (2.3 mm); $\frac{D}{D}^{20} = 1.5163$ (lit $\frac{D}{D}^{20} = 1.5162$); ir (neat, liquid film) 3425 (s, OH), 3050-2875 (s, C-H), 1445 and 1370 (s, CH$_3$), 763 and 702 (s, C$_6$H$_5$) cm$^{-1}$; nmr (CCl$_4$) δ 0.72 (t, 3, J = 7.2 Hz, CH$_3$CH$_2$), 1.33 (s, 3, CH$_3$COH), 1.74 (a, 2, J = 7.2 Hz, CH$_2$CH$_3$).

(2) E-2-Phenyl-2-butene (2-phenyl-cis-2-butene)

The procedure followed was that described by Garbisch for the preparation of arylalkenes from tertiary aryl alcohols.$^{54}$

The crude product mixture from the first Grignard synthesis of 2-phenyl-2-butanol just described was warmed with a heating mantle. A solution of sulfuric acid (8 ml) in acetic acid (32 ml) was prepared and, while still warm, added to the alcohol. The flask was swirled for 30-45 seconds, until two phases separated. The mixture was then poured into an ethyl ether-water (120 ml-200 ml) mixture. The ether layer was separated, washed with water and sodium bicarbonate solution (10%) consecutively, dried (calcium chloride), and concentrated on a rotary evaporator. Spinning band distillation at reduced pressure yielded 17.5 g of a mixture of olefins and excess bromobenzene [bp 54-90° (22 mm)].
and 12.6 g (48% yield) of pure \( \text{E-2-phenyl-2-butene} \): bp 90.0-93.5\(^\circ\) (22 mm); ir (neat, liquid film) 3030-2810 (s, C-H), 1927, 1855, 1788 and 1727 (w, C\(_6\)H\(_5\)), 1440 and 1375 (s, C\(_3\)H), 752 and 675 (sb, C\(_6\)H\(_5\)) cm\(^{-1}\); nmr (CCl\(_4\)) \( \delta 1.74 \) (dd, 3, \( ^3J = 7.0 \text{ Hz} \), \( ^4J = 1.1 \text{ Hz} \), CH\(_2\)CH), \( 1.95 \) (m, 3, \( ^4J = 1.1 \text{ Hz} \), CH\(_3\)). 5.83 (qq, 1, \( ^3J = 7.0 \text{ Hz} \), \( ^4J = 1.1 \text{ Hz} \), C=CH), 7.25 (m, 5, C\(_6\)H\(_5\)). Purity of the fractions was established by gc analysis.

The original product mixture was shown by nmr integration to consist of bromobenzene (65%), \( \text{E-2-phenyl-2-butene} \) (16%), \( \text{2-phenyl-1-butene} \) (19%), and a trace of \( \text{Z-2-phenyl-2-butene} \). The product distribution presently obtained and that obtained earlier by Kwart\(^{52}\) for the same dehydration are given below.

<table>
<thead>
<tr>
<th>Compound</th>
<th>% Distribution</th>
<th>Present Work</th>
<th>Earlier Work(^{52})</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{E-2-phenyl-2-butene} )</td>
<td>82</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>( \text{Z-2-phenyl-2-butene} )</td>
<td>trace</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>( \text{2-phenyl-1-butene} )</td>
<td>17</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

Cram determined the composition of an equilibrium mixture of the three olefins, as given below.\(^{23}\) Equilibration was achieved by heating the olefin in glacial acetic acid at 50\(^\circ\) in the presence of 0.90 M p-toluenesulfonic acid for 50 hours. Solvolytic elimination of

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l-methyl-2-phenyl-1-propyl acetate in glacial acetic acid with 9 mM
p-toluenesulfonic acid quenched after several minutes yielded the prod-
uct composition: E olefin (53%), Z olefin (2%), and terminal olefin
(15%).

The present reaction conditions definitely do not give an
equilibrium controlled product mixture. Perhaps the temperature and
time of swirling are more critical factors with respect to product dis-
tribution than indicated in the original presentation of the synthetic
procedure.

(3) 2-2-phenyl-2-butene

The trans olefin was prepared by fractional distillation of
the lower-boiling trans olefin from an equilibrating mixture of the
olefins after the method of Cram. 18

A mixture of olefins obtained as above was treated with p-
toluenesulfonic acid and calcium chloride in a 100-ml flask. A frac-
tionating column was fitted to the flask and the trans isomer distilled
over slowly. The lower boiling fraction which contained small amounts
of the cis and terminal olefins was distilled on a spinning band column:
bp 57-60° (10 mm) [lit 18 bp 77-79° (29.5 mm)]; ir (neat, liquid film)
3030-2825 (s, C-H), 1445 and 1370 (m, CH₃) 763 and 700 (s, C₆H₅) cm⁻¹;
nmr (CCl₄) δ 1.56 (dq, 3, 3J = 6.9 Hz, 5J = 1.5 Hz, CH₃CH), 1.99 (m, 3,
4, 5J = 1.5 Hz, CH₃C-C₆H₅), 5.51 (qq, 1, 3J = 6.9 Hz, 4J = 1.5 Hz,
HC-CH₃), 7.17 (m, 5, C₆H₅).

(4) 2-Phenyl-1-butene

Nmr and gc analysis of the higher boiling mixture of olefins
obtained as described above (Sec. 2.a.2) indicated the presence of
2-phenyl-1-butene: nmr (CCl$_4$) $\delta$ 1.04 (t, 3, $^3J = 7.0$ Hz, CH$_2$CH$_3$), 2.45 (m, 2, $^3J = 7.0$ Hz, CH$_2$CH$_3$), 5.01 (m, 1, $^4J = 1.2$ Hz, ethylenic proton trans to phenyl), 5.24 (m, 1, $^4J = 1.2$ Hz, ethylenic proton cis to phenyl), 7.3 (m, 5, C$_6$H$_5$).

(5) 3-Phenyl-1-butene

The procedure followed was that described by Wittig and Schöllkopf.$^{55}$

A 500-ml 3-neck flask was equipped with nitrogen inlet, Friedrich condenser, and mechanical stirrer. A drying tube (calcium chloride) was attached to the condenser. Ethyl ether (200 ml) and a solution of butyllithium in hexane (13.2%, 75 ml, 0.10 mole) were added to the reaction flask. Methyltriphenylphosphonium bromide (35.7 g, 0.10 mole, available in this laboratory) was added slowly to the stirred solution over a 10-minute period. The resultant mixture was stirred for 4 hours at room temperature, during which time the solution turned to a deep orange with formation of a yellow precipitate. Upon dropwise addition of 2-phenylpropionaldehyde (14.5 g, 0.11 mole) to this mixture a white precipitate formed and the solution became pale yellow. The mixture was heated at reflux overnight, cooled to room temperature, and vacuum filtered. The precipitate was washed with ethyl ether (100 ml); the filtrate was washed with water (four 100-ml portions) until neutral to pH paper and dried (calcium chloride). After removal of ethyl ether by atmospheric distillation, vacuum distillation gave 1.75 g (13.3% yield) of 3-phenyl-1-butene; bp 29.1° (1.2 mm); $\eta^2$ D$_{24}$ 1.5108; ir (neat, liquid film) 3050-2850 (s, C-H), 1445 (s, CH$_3$), 913 (s, CH=CH$_2$), 759 and 699 (s, C$_6$H$_5$), 675.
(m, CH=CH₂) cm⁻¹; nmr (CCl₄) δ 1.32 (d, 3, J = 7.0 Hz, CH₃CH), 1.75 (m, 1, \(^1^J = 7.0\) Hz, CH₂OH), 1.87 (m, 1, ethylenic proton cis to alkyl group), 5.09 (m, 1, ethylenic proton trans to alkyl group), 5.99 (dd, 1, \(^4^J = 6.1\) Hz, \(^3^J_{\text{cis}} = 9.3\) Hz, \(^3^J_{\text{trans}} = 17.6\) Hz, C=CH–CCH₃), 7.14 (s, 5, C₆H₅).

(6) 2-Methyl-1-phenyl-1-propanol

A 500-ml 3-neck flask was equipped for a Grignard synthesis (described in Sec. 1.b.1). Freshly distilled 2-bromopropane (1.5 g) was added to magnesium turnings (4.13 g, 0.17 g-atom) in ethyl ether (10 ml) to initiate the reaction. As soon as reaction commenced, a solution of 2-bromopropane (17.0 g, total of 0.15 mole) in ethyl ether (125 ml) was added dropwise from the addition funnel at a rate sufficient to maintain a gentle reflux. Reflux was maintained for 30 minutes after addition was completed. A solution of benzaldehyde (14.9 g, 0.14 mole) in ethyl ether (75 ml) was added, again maintaining a gentle reflux. After the cream-colored reaction mixture had been cooled to room temperature, saturated ammonium chloride solution (30 ml) was added to hydrolyze the magnesium complex. The ether solution was separated, concentrated by rotary evaporation, and distilled under vacuum to yield 9.5 g (45% yield) of the alcohol: bp 72.2-75.8° (1.4 mm); \(\text{n}^2^4_D\) 1.5141 (lit\(^{16}\) \(\text{n}^2^5_D\) 1.5113); ir (neat, liquid film) 3390 (s, OH), 3030-2850 (s, C-H), 1380 and 1364 (m, C-H for isopropyl group), 1020 (sb, C-OH), 752 and 702 (sb, C₆H₅) cm⁻¹; nmr (CCl₄) δ 0.72 (d, 3, J = 6.9 Hz, CH₃CH), 0.89 (d, 3, J = 6.6 Hz, CH₂OH), 1.78 [m, 1, CH(CH₃)₂], 3.24 (bs, 1, CHOH), 4.18 (m, 1, \(^3^J = 6.5\) Hz, CHOH), 7.16 (s, 5, C₆H₅).
(7) 2-Methyl-1-phenyl-1-propene

The procedure described by Garbisch for the preparation of arylalkenes was followed, although the preparation is not recommended for use with secondary alcohols.\textsuperscript{54}

A freshly prepared, warmed solution of sulfuric acid in acetic acid (20\% v/v, 6 ml) was poured into the warm alcohol (4.5 g, 30 mmoles) and swirled for 60 seconds. Two phases separated during this time and the solution became darkly colored. The mixture was poured into an ethyl ether-water mixture (18 ml-30 ml). The ether layer was separated and was washed with water (20 ml) and with aqueous potassium bicarbonate (10\%, 20 ml). After drying (calcium chloride) and removal of the ether solvent by rotary evaporation, the olefin was vacuum distilled and a yield of 0.86 g (26\% yield) was obtained: bp 40.0-42.0° (1.8 mm) [lit\textsuperscript{57} bp 76-77° (18 mm)]; \( n_2^D \) 1.5371 (lit\textsuperscript{57} \( n_2^D \) 1.5368); ir (neat, liquid film) 3075-2820 (s, C-H), 1447 and 1385 (s, CH\textsubscript{3}), 835 (s, C=C-H), 741 and 697 (s, C\textsubscript{6}H\textsubscript{5}) cm\textsuperscript{-1}; nmr (CCl\textsubscript{4} \( \delta \) 1.80 [m, 6, \( \textit{J} = 1.5 \) Hz, (CH\textsubscript{3})\textsubscript{2}C=C], 6.40 (m, 1, \( \textit{J} = 1.5 \) Hz, C=CCH\textsubscript{3}), 7.14 (s, 5, C\textsubscript{6}H\textsubscript{5}).

b. Acetates

(1) 1-Methyl-2-phenyl-1-propyl acetate

Acetic anhydride (13.7 g, 0.134 mole) was added to a solution of 3-phenyl-2-butanol (10.0 g, 0.067 mole) and pyridine (8.0 g, 0.10 mole) in a 100-ml flask. A reflux condenser was added, and the solution was heated at 80° for 2 hours. The mixture was then poured into ice-water (30 ml), and the acetate was extracted with pentane (three 50-ml portions). The combined organic layer was washed with sodium
carbonate solution (10% aqueous, 20 ml) and with water (20 ml) and then dried (potassium carbonate). Vacuum distillation yielded the acetate as a colorless liquid (10.5 g, 81.4% yield): bp 98.0-102.2° (4.2 mm); \( n^D_24 \) 1.4954; ir (neat, liquid film) 1748 (s, C=O), 1250 (s, C-O for acetates), 765 and 702 (s, C<sub>6</sub>H<sub>5</sub>) cm<sup>-1</sup>; nmr (CDCl<sub>3</sub>) δ 0.9-1.2 (m, 6, CHCH<sub>3</sub>), 1.81 (s, O=C-CH<sub>3</sub> for the minor isomer), 1.95 (s, O=C-CH<sub>3</sub> for the major isomer), 2.85 (m, 1, J = 7.0 Hz, CH-C<sub>6</sub>H<sub>5</sub>), 5.0 (m, 1, CH-OAc), 7.17 (s, 5, C<sub>6</sub>H<sub>5</sub>)

Gc analysis and integration of the acetate methyl proton absorptions at δ 1.81 and 1.95 showed the product to consist of two isomers (threo:erythro) in a 1:1.5 ratio. Assignment of configuration was based on comparison of retention times and chemical shifts with those of the pure isomers.

(2) threo-3-Phenyl-2-butanol

The procedure followed was that described by Zweifel and Brown.\textsuperscript{58}

A 50-ml 3-neck flask was equipped with a reflux condenser, addition funnel and thermometer. A drying tube (calcium chloride) was attached to the condenser, and a nitrogen inlet to the addition funnel. Nitrogen was flushed through the system for 15 minutes before addition of E-2-phenyl-2-butene (12.6 g, 0.096 mole, obtained as described in Sec. 2.a.2 above) and tetrahydrofuran (THF; 48 ml). The flask was cooled to 0° in an ice-salt bath. Diborane (48 ml, 1 M solution in THF) was added from the addition funnel at a rate sufficient to maintain the temperature between 0-2°, after which the solution was allowed to stand at room temperature for 30 minutes. Water (9.6 ml) was added

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to decompose the excess diborane; sodium hydroxide (3 M, 23 ml) and hydrogen peroxide (30%, 23 ml) were added consecutively, during which time the temperature was maintained between 30-50° by means of a water bath. The reaction mixture was stirred for 1 hour at room temperature, during which time a white precipitate formed. Potassium carbonate (67.2 g) was added, and the organic layer was separated. The aqueous layer was washed with THF (30 ml), and the THF was removed from the combined organic layers by distillation at atmospheric pressure after diluting the alcohol solution with carbon tetrachloride (10 ml). Vacuum distillation yielded two fractions: the first [1.98 g, bp 54-76° (1.8 mm)] consisted of E-2-phenyl-2-butene, as shown by nmr analysis; the second was similarly shown to be threo-3-phenyl-2-butanol (13.0 g, 90.3% yield): bp 77-79° (1.8 mm) [lit58a bp 95-96° (8 mm), 108° (10 mm)21]; ir (neat, liquid film) 3390 (s, OH), 1110-1087 (sb, C-OH for secondary alcohols), 762 and 702 (s, C₆H₅) cm⁻¹; nmr (CCl₄) δ 1.04 (d, 3, J = 6.1 Hz, C₆H₅OH), 1.18 (d, 3, J = 7.2 CH₃-C₆H₅), 2.65 (p, 1, J = 7.2 Hz, CH-C₆H₅), 3.77 (p, 1, J = 6.1 Hz, CHOH), 7.15 (s, 5, C₆H₅).

(3) threo-1-Methyl-2-phenyl-1-propyl acetate

threo-3-Phenyl-2-butanol (5.0 g, 33 mmoles) was treated with acetic anhydride (6.5 g, 63 mmoles) and pyridine (4.0 g, 50 mmoles) in a 100-ml flask fitted with a reflux condenser to which was attached a drying tube (calcium chloride). The solution was heated at 80° for 2 hours, and then the reaction mixture was poured into ice-water (25 ml). The acetate was extracted with pentane (three 25-ml portions). The pentane solution was washed first with sodium carbonate solution (10%
aqueous, 10 ml) and then with water (25 ml), and was dried (potassium carbonate). The pentane was removed by rotary evaporation. Vacuum distillation yielded the threo acetate (4.5 g, 70% yield): bp 97.5-99.6°C (3.7 mm); $^1$H NMR ($^1$HOD) 1.4877 (lit $^1$H NMR 1.4877); IR (neat, liquid film) 3010 (m, C-H), 1739 (s, C=O), 1242 (s, C-O for acetates), 763 and 702 (s, C$_6$H$_5$) cm$^{-1}$; nmr (CCl$_4$) $\delta$ 1.10 (d, 3, $J$ = 6.0 Hz, CH$_3$C-OAc), 1.19 (d, 3, $J$ = 7.0 Hz, CH$_3$C-C$_6$H$_5$), 1.80 (s, 3, CH$_3$CO$_2$), 2.92 (p, 1, $J$ = 7.0 Hz, CH-C$_6$H$_5$), 5.05 (p, 1, $J$ = 6.0 Hz, CHOAc), 7.17 (s, 5, C$_6$H$_5$).

(4) erythro-3-Phenyl-2-butanol

Z-2-Phenyl-2-butene (4.50 g, 34 mmoles, obtained in pure form by the method described in Sec. 2.a.3) was dissolved in THF (9 ml) and treated with diborane (18 ml, 1 M solution in THF) as described in Sec. 2.b.2 above for the preparation of the corresponding threo alcohol. Vacuum distillation yielded 2.30 g (45% yield) of the erythro alcohol: bp 84-86°C (2.5 mm); IR (neat, liquid film) 3390 (s, OH), 2970-2840 (s, C-H) 762 and 702 (s, C$_6$H$_5$) cm$^{-1}$; nmr (CCl$_4$) $\delta$ 0.98 (d, 3, $J$ = 6.2 Hz, CH$_3$C-OH), 1.28 (d, 3, $J$ = 7.1 Hz, CH$_3$C-C$_6$H$_5$), 2.60 (p, 1, $J$ = 7.1 Hz, CH-C$_6$H$_5$), 3.63 (m, 1, $^3$J = 6.2 Hz, CHO), 7.15 (s, 5, C$_6$H$_5$).

(5) erythro-l-Methyl-2-phenyl-l-propyl acetate

erythro-3-Phenyl-2-butanol (2.0 g, 13 mmoles) was treated with acetic anhydride (2.65 g, 26 mmoles) and pyridine (2.0 g, 25 mmoles) as described in Sec. 2.b.3 above. Vacuum distillation yielded the erythro acetate (1.41 g, 56.4% yield): bp 76-77°C (1.5 mm); IR (neat, liquid film) 3010-2850 (m, C-H), 1730 (s, C=O), 1486 and 1445 (m, CH$_3$), 1242 (s, C-O for acetates), 763 and 702 (s, C$_6$H$_5$) cm$^{-1}$; nmr (CCl$_4$) $\delta$ 0.95 (d, 3, $J$ = 6.3 Hz, CH$_3$C-OAc), 1.24 (d, 3, $J$ = 6.8 Hz,
CH₃C-C₆H₅, 1.87 (s, 3, O=C-CH₃), 2.80 (p, 1, J = 6.8 Hz, CH-C₆H₅),
4.97 (m, 1, 3J = 6.3 Hz, CH-OAc), 7.17 (s, 5, C₆H₅).

(6) 1-Methyl-1-phenyl-1-propyl acetate

The procedure followed for the preparation of the tertiary acetate was that described by Cram. 41

2-Phenyl-2-butanol (7.0 g, 46.7 mmoles) was placed in a 100-ml round bottom flask. Pyridine (10.0 ml, 9.8 g, 123 mmoles) and acetic anhydride (25 ml, 27 g, 264 mmoles) were added; the flask was equipped with a reflux condenser and trying tube (calcium chloride, and the mixture was heated at 90° for 16 hours. The mixture was cooled to room temperature, poured into ice-water, and extracted with pentane (three 10-ml portions). The pentane solution was washed consecutively with sulfuric acid (0.5 M, 10 ml), sodium carbonate solution (10% aqueous, 10 ml), and water (10 ml), and was dried (potassium carbonate). The pentane was removed by distillation at reduced pressure (water aspirator).

Nmr analysis of the residue showed a mixture of alcohol and acetate. A pure sample of the acetate was obtained by chromatographic separation on a 35-cm alumina column prepared in pentane. The column was washed with a pentane-ethyl ether solution (97:3 v/v). Evaporation of the solvent yielded the tertiary acetate: ir (neat, liquid film)
3030-2865 (m, C-H), 1710 (s, C=O), 1245 (sb, C-O for acetates), 768 and 704 (s, C₆H₅); nmr (CDCl₃) δ 0.72 (t, 3, J = 7.0 Hz, CH₃CH₂), 1.76 (s, 3, CH₃C-C₆H₅), 1.94 (s, 3, CH₃-CO₂), 2.0 (m, 2, CH₂CH₃), 7.21 (s, 5, C₆H₅).

The compound proved to be stable to distillation at reduced pressure [bp 61.0-61.4° (0.47 mm)], which yielded 6.0 g (67% yield) of the acetate.
(7) 2-Methyl-1-phenyl-1-propyl acetate

Pyridine (4.0 g, 50 mmoles) and 2-methyl-1-phenyl-1-propanol (prepared as described in Sec. 2.a.6; 4.5 g, 30 mmoles) were placed in a 50-ml flask. Acetic anhydride (6.5 g, 65 mmoles) was added; a reflux condenser with attached drying tube (calcium chloride) was fitted to the flask, and the solution was heated at 80° for 2 hours. The solution was cooled to room temperature and poured into an ice-water mixture (25 ml). The ester was extracted with pentane (three 25-ml portions), and was washed with aqueous sodium carbonate (10%, 10 ml) and water (25 ml) consecutively. The solution was dried (potassium carbonate), concentrated on a rotary evaporator, and vacuum distilled to give 3.46 g (60% yield) of the acetate: bp 68.0-73.0° (0.8 mm); n^2^4^1^.4890 (lit^16^ n^2^0 = 1.4853); ir (neat, liquid film) 3030-2875 (s, C-H), 1742 (s, C=O), 1385 and 1370 (s, isopropyl C-H), 1240 (s, C-O for acetates), 758 and 702 (s, C6H5) cm^{-1}; nmr (CCl4) 6 0.77 (d, 3, J = 6.6 Hz, CHaCHCH3), 0.93 (d, 3, J = 6.6 Hz, CH3CHCH3), 1.93 (s, 3, CHaCO2), 2.02 [m, 1, J = 6.6 Hz, CH(CH3)2], 5.47 (d, 1, J = 7.5 Hz, CH-OAc), 7.22 (s, 5, C6H5).

(8) 2-Benzyl-2-propanol

A 500-ml 3-neck flask was equipped for a Grignard synthesis. Magnesium turnings (4.37 g, 0.18 g-atom) were placed in the flask. Ethyl ether (10 ml) and freshly distilled benzyl chloride (1.5 g) were added to initiate the reaction, after which a solution of benzyl chloride (19.3 g, 0.16 mole total) in ethyl ether (150 ml) was added slowly from the addition funnel so as to maintain a gentle reflux. The mixture was allowed to reflux an additional 30 minutes and then a solution
of acetone (8.72 g, 0.15 mole) in ethyl ether (75 ml) was added, again maintaining a gentle reflux. The mixture was cooled to room temperature; saturated ammonium chloride solution (50 ml) was added to hydrolyze the greyish-white magnesium complex. The ether solution was poured off, concentrated by rotary evaporation, and vacuum distilled to give the alcohol: 18.2 g, (80.9% yield); bp 64° (0.8 mm)-61.0° (0.6 mm) [lit56 bp 103-105° (10 mm); ir (neat, liquid film) 3390 (s, OH), 2975-2915 (s, C-H), 1375 and 1360 (s, C-H for geminal dimethyl group), 1160-1120 (sb, C-OH for tertiary alcohols), 730 and 702 (s, C,H5) cm⁻¹; nmr (CCl₄) δ 1.12 [s, 6, (CH₃)₂C], 2.68 (s, 2, CH₂-C₆H₅), 7.16 (s, 5, C₆H₅).

(9) 1-Benzyl-1-methylethyl acetate

2-Benzyl-2-propanol (9.00 g, 0.060 mole) and pyridine (8.0 g, 0.10 mole) were placed in a 100-ml round bottom flask. Acetic anhydride (13.0 g, 0.13 mole) was added, a reflux condenser fitted with a drying tube (calcium chloride) was attached, and the solution was heated at 90° for 16 hours. After being cooled to room temperature, the solution was poured into ice-water (40 ml), and the ester was extracted with pentane (three 30-ml portions). The combined pentane solution was washed with water (30 ml) and with sodium carbonate solution (10%, 30 ml), dried (potassium carbonate), concentrated by rotary evaporation, and distilled to give 9.16 g of an alcohol-ester mixture [bp 59.0-65.8° (0.6 mm)]. Nmr integration showed a 1:1.5 mole ratio of alcohol:ester, giving 5.5 g (48% yield) of the ester.

A sample of the pure ester was obtained by column chromatography through a 40-cm silica gel column with a pentane-ethyl ether solution (90:10 v/v): \( \frac{n_{\text{D}}}{D} = 1.4911 \) (lit57 \( \frac{n_{\text{D}}}{D} = 1.4912 \)); ir (neat,
liquid film) 3020-2915 (m, C-H), 1730 (s, C=O), 1380 and 1365 (s, C-H for a geminal dimethyl group), 1250 (sb, C-O for acetates), 735 and 703 (s, \( \text{C}_6\text{H}_5 \) cm\(^{-1} \); nmr (CCl\(_4\)) \( \delta \) 1.40 [s, 6, (CH\(_3\))\(_2\)C], 1.88 (s, 3, CH\(_3\)CO\(_2\)), 3.03 (s, 2, CH\(_2\)-C\(_6\)H\(_5\)), 7.17 (s, 5, C\(_6\)H\(_5\)).

C. Decarboxylations

1. General Procedure for Oxidative Decarboxylation\(^5\)

A 25-ml 3-neck flask was equipped with a nitrogen inlet and reflux condenser. A drying tube (calcium chloride) was attached to the condenser. Nitrogen was passed through the system for fifteen minutes to rid the system of oxygen; benzene (10 ml), pyridine (3.5 mmoles) and the carboxylic acid (3.0 mmoles) were added; the solution was cooled in an ice bath, and lead tetraacetate (4.0 mmoles) was added all at once with stirring. The lead tetraacetate dissolved to give a yellow solution initially. The reaction flask was placed in an oil bath preheated to 82-85\(^\circ\) and heated at reflux for a specified time period. The solution became darkly colored soon after heating was begun. Completion of reaction was evidenced by the formation of a yellow solution and white precipitate. At the end of the reflux period the solution was cooled to room temperature, and the precipitate was removed by simple filtration and washed with benzene. The combined filtrate and benzene wash was then washed sequentially with a dilute perchloric acid-sodium chloride solution (two 10-ml portions), saturated aqueous sodium chloride (10 ml), saturated sodium bicarbonate (10 ml), and saturated sodium chloride (10 ml). After drying (magnesium sulfate), the reaction mixture was analyzed by gc method; internal standards were used for quantitative determination of the mole ratios of the products.
The basic wash was acidified with 3 M hydrochloric acid to recover any unreacted carboxylic acid.

a. erythro-2-Methyl-3-phenylbutyric acid

In a typical run, benzene (10 ml), pyridine (0.261 g, 3.30 mmoles), t-butylbenzene (0.042 g, 0.316 mmole), and erythro-2-methyl-3-phenylbutyric acid (0.540 g, 3.04 mmoles) were placed in the reaction flask and cooled in an ice bath. Lead tetraacetate (1.80 g, 4.06 mmoles) was added, and the solution was heated at reflux for 17 hours. The reaction mixture consisted of a yellow solution with a white precipitate, which settled rapidly when stirring was discontinued. After work-up of the solution, gc analysis showed recovery of 0.291 mmole (92%) of t-butylbenzene and the product distribution shown below.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mmoles</th>
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<tbody>
<tr>
<td>s-butylbenzene</td>
<td>0.0066</td>
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<tr>
<td>Z-2-phenyl-2-butene</td>
<td>0.247</td>
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<tr>
<td>E-2-phenyl-2-butene</td>
<td>0.131</td>
</tr>
<tr>
<td>threo-1-methyl-2-phenyl-1-propyl acetate</td>
<td>0.422</td>
</tr>
<tr>
<td>erythro-1-methyl-2-phenyl-1-propyl acetate</td>
<td>0.706</td>
</tr>
</tbody>
</table>

Several small unidentified peaks were also found. These peaks did not coincide with those of the corresponding alcohols, although the retention times were similar to those of the alcohols synthesized as reference compounds.

b. threo-2-Methyl-3-phenylbutyric acid

In a typical run, benzene (10 ml), pyridine (0.232 g, 2.93 mmoles), t-butylbenzene (0.045 g, 0.33 mmole), and threo-3-methyl-3-phenylbutyric acid (0.445 g, 2.50 mmoles) were placed in the reaction...
flask. Lead tetraacetate (1.47 g, 3.32 mmoles) was added after cooling; the mixture was stirred and heated at reflux for 48 hours. The reaction mixture consisted of a light brown precipitate and a yellow solution. The reaction mixture was worked up as described above. Gc analysis showed recovery of 0.231 mmoles (51%) of t-butylbenzene and the product composition as below.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mmoles</th>
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<tbody>
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<td>s-butylbenzene</td>
<td>0.004</td>
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<tr>
<td>Z-2-phenyl-2-butene</td>
<td>0.145</td>
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<td>E-2-phenyl-2-butene</td>
<td>0.035</td>
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<tr>
<td><em>threo</em>-1-methyl-2-phenyl-1-propyl acetate</td>
<td>0.260</td>
</tr>
<tr>
<td><em>erythro</em>-1-methyl-2-phenyl-1-propyl acetate</td>
<td>0.424</td>
</tr>
</tbody>
</table>

The basic wash was acidified with 3 M hydrochloric acid. The unreacted acid was taken up in carbon tetrachloride. Nmr analysis, using methylene chloride as an external standard for integration, showed 0.07 mmole of unreacted acid.

2. General Procedure for the Kochi Reaction

A 25-ml 3-neck flask was equipped with a reflux condenser and nitrogen inlet. A drying tube (calcium chloride) was attached to the condenser. Benzene (10 ml), carboxylic acid (22.5 mmoles), lead tetraacetate (4.5 mmoles), and lithium chloride (4.5 mmoles) were added consecutively. The pale yellow reaction mixture was heated at reflux for three hours. The resultant white precipitate was filtered and washed with benzene. The combined benzene wash and colorless filtrate was washed with a dilute aqueous perchloric acid-sodium chloride solution.
(10 ml) and aqueous sodium carbonate (two 10-ml portions, 10%), and dried (magnesium sulfate).

The product composition was determined by gc analysis: an internal standard was used to obtain molar ratios. The unreacted acid was recovered by acidification of the basic wash solution.

a. **erythro-2-Methyl-3-phenylbutyric acid**

Benzene (10 ml), **erythro-2-methyl-3-phenylbutyric acid** (4.01 g, 22.5 mmoles), lead tetraacetate (1.99 g, 4.5 mmoles) and lithium chloride (0.19 g, 4.5 mmoles) were placed in the reaction flask and heated at reflux for 5 hours. The reaction was apparently complete in less than 1 hour as evidenced by the formation of the precipitate of lead salts and the cessation of carbon dioxide evolution.

Gc analysis showed formation of **erythro-** and **threo-2-chloro-3-phenylbutane** (0.132 and 0.186 mmoles, respectively) as the only products of the reaction. Acidification of the basic wash solution and filtration of the carboxylic acid yielded 1.36 g of unreacted acid.

b. **threo-2-Methyl-3-phenylbutyric acid**

Benzene (5 ml), **threo-2-methyl-3-phenylbutyric acid** (2.00 g, 11.2 mmoles), lead tetraacetate (1.00 g, 2.2 mmoles) and lithium chloride (0.095 g, 2.2 mmoles) were placed in the reaction flask and heated at reflux for 4 hours.

Gc analysis of the solution after work-up showed 0.464 and 0.655 mmoles of **erythro-** and **threo-2-chloro-3-phenylbutane**, respectively. Nmr integration, using methylene chloride as an external standard, showed 1.02 g of unreacted carboxylic acid.
3. Control Reactions

a. Stability of Acetates

(1) Stability to work-up procedures

A mixture of threo- and erythro-1-methyl-2-phenyl-1-propyl acetates was treated with the dilute perchloric acid-sodium chloride solution and was then washed consecutively with saturated aqueous sodium chloride, 1 M sodium hydroxide, and saturated sodium chloride solutions. The solution was then dried (magnesium sulfate). Comparison of the gc traces of the mixture of esters before and after work-up treatment showed no change in composition of the mixture.

(2) Stability to oxidative decarboxylation conditions

A 25-ml 3-neck flask was equipped with nitrogen inlet and reflux condenser. A drying tube (calcium chloride) was attached to the condenser. Benzene, the acetate, and pyridine were added to the flask. The flask was cooled in an ice-bath, and lead tetraacetate was added. The mixture was then heated at reflux in an oil bath for 8-9 hours. The lead tetraacetate did not go into solution and the mixture remained a dark reddish-brown throughout the entire reaction time. At the end of the reflux period, the mixture was cooled and filtered. The filtrate was washed consecutively with a dilute perchloric acid-sodium chloride solution, saturated aqueous sodium chloride, saturated 1 M sodium hydroxide, and saturated aqueous sodium chloride solution. After drying (magnesium sulfate), the solution was analyzed by gc method.

The mixture of threo- and erythro-1-methyl-2-phenyl-1-propyl acetate, 1-methyl-1-phenyl-1-propyl acetate, and 2-methyl-1-phenyl-1-propyl acetate were separately subjected to the decarboxylation conditions.
as described above. Comparison of the gc traces of solutions of the
esters before and after treatment with lead tetraacetate showed the
acetates to be stable to the decarboxylation and work-up conditions.

b. Stability of Olefins

2-Methyl-1-phenyl-1-propene was treated with lead tetraacetate
in the presence of pyridine as described in Sec. 3.a.2 above for the
acetates. Comparison of the gc traces of the olefin in benzene solution
and of the reaction mixture showed that the olefin was stable to the
reaction conditions.
V. SUMMARY

erythro- and threo-2-Methyl-3-phenylbutyric acids were synthesized and purified. The isomerically pure acids were subjected to both radical halodecarboxylation and cationic oxidative decarboxylation in an effort to study the relation of product stereochemistry to the stereochemistry of the reactant acid. Previous studies with the cyclohexyl system demonstrated that both the radical and cationic reactions yield product mixtures which are independent of the stereochemistry of the reactant acid.

Halodecarboxylation of the diastereomeric butyric acids yielded the same 1.4:1 threo:erythro mixture of 2-chloro-3-phenylbutanes from both carboxylic acids. A common radical intermediate is indicated by the single product distribution.

Formation of the same threo:erythro mixture (0.6:1, respectively) of 1-methyl-2-phenyl-1-propyl acetates by oxidative decarboxylation of the isomeric acids lends support to the hypothesis that such decarboxylation involves initial formation of a radical intermediate followed by further oxidation to a cationic intermediate and then to products. The lack of formation of acetates from cations which have undergone methyl or hydrogen migration indicates that the cation formed in the decarboxylation reaction is not like the high energy, poorly solvated cation found in deamination reactions. Likewise, the formation of erythro and threo acetates in a 1:0.6 ratio suggests that the cationic intermediate is not a non-classical phenonium ion as is found in the solvolysis reactions or chlorosulfite decompositions. The possibility of concerted processes is difficult to support, both on the basis of the
concurrent formation of erythro and threo isomers and of the difference in the erythro:threo ratios of the chlorides and acetates. It appears, therefore, that a cationic intermediate is formed in the oxidative decarboxylation reaction which differs from the cations involved in other reaction types.

The olefin distribution obtained from the oxidative decarboxylation likewise differs from those obtained by other reactions. The major product is the thermodynamically less stable olefin, 2-phenyl-2-butene. Olefins that would result from methyl or hydrogen migration in the cation are absent from the product mixture.
LIST OF REFERENCES


42. H. Rupe, H. Steiger, and F. Fiedler, Ber., 47, 63 (1914).
SELECTED BIBLIOGRAPHY


APPENDIX I
RESPONSE FACTORS FOR GC ANALYSES

The following response factors were obtained on a 10 ft x 1/8 in. DIDP (diisopropyl phthalate) aluminum column. The response factors of the hydrocarbons are relative to m-dichlorobenzene as standard, and those of the acetate and chloride derivatives are relative to 2-phenylethyl acetate.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Standard</th>
<th>Response Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylbenzene</td>
<td>m-Dichlorobenzene</td>
<td>1.50 ± 0.09</td>
</tr>
<tr>
<td>s-Butylbenzene</td>
<td>m-Dichlorobenzene</td>
<td>1.36 ± 0.15</td>
</tr>
<tr>
<td>t-Butylbenzene</td>
<td>m-Dichlorobenzene</td>
<td>1.38 ± 0.16</td>
</tr>
<tr>
<td>2-Methyl-1-phenyl-1-propene</td>
<td>m-Dichlorobenzene</td>
<td>1.40 ± 0.05</td>
</tr>
<tr>
<td>3-Phenyl-1-butene</td>
<td>m-Dichlorobenzene</td>
<td>1.21 ± 0.01</td>
</tr>
<tr>
<td>2-Phenyl-1-butene</td>
<td>m-Dichlorobenzene</td>
<td>2.19 ± 0.18</td>
</tr>
<tr>
<td>E-2-Phenyl-2-butene</td>
<td>m-Dichlorobenzene</td>
<td>1.52 ± 0.06</td>
</tr>
<tr>
<td>Z-2-Phenyl-2-butene</td>
<td>m-Dichlorobenzene</td>
<td>1.54 ± 0.13</td>
</tr>
<tr>
<td>threo-1-Methyl-2-phenyl-1-propyl acetate</td>
<td>2-Phenylethyl acetate</td>
<td>1.37 ± 0.03</td>
</tr>
<tr>
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<td>2-Phenylethyl acetate</td>
<td>1.18 ± 0.01</td>
</tr>
<tr>
<td>1-Methyl-1-phenyl-1-propyl acetate</td>
<td>2-Phenylethyl acetate</td>
<td>1.19 ± 0.06</td>
</tr>
<tr>
<td>2-Methyl-1-phenyl-1-propyl acetate</td>
<td>2-Phenylethyl acetate</td>
<td>1.37 ± 0.02</td>
</tr>
<tr>
<td>1-Benzyl-1-methylethyl acetate</td>
<td>2-Phenylethyl acetate</td>
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</tr>
<tr>
<td>threo-2-Chloro-3-phenylbutane</td>
<td>2-Phenylethyl acetate</td>
<td>1.60 ± 0.01</td>
</tr>
<tr>
<td>erythro-2-Chloro-3-phenylbutane</td>
<td>2-Phenylethyl acetate</td>
<td>1.49 ± 0.02</td>
</tr>
</tbody>
</table>
Table XIV gives a summary of the assignments made and the important data from the spectra obtained.

The following nmr spectra were obtained with a Varian A60A 60 MHz spectrometer. The samples used were 10-20% solutions in carbon tetrachloride, unless indicated otherwise, with TMS (tetramethylsilane) as reference standard.
TABLE XIV
SUMMARY OF NMR DATA

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<thead>
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<th>Compound</th>
<th>Phenyl</th>
<th>1</th>
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<th>-OCH$_2$CH$_3$</th>
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<td>2.75(q,7.0)</td>
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<td>1.20(d,7.0)</td>
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</tr>
<tr>
<td>threo</td>
<td></td>
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<td>3.67(q,7.1)</td>
<td>---</td>
<td>5.27(m)$^a$</td>
<td>1.36(d,7.3)</td>
<td>4.08(q,7.2)</td>
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<tr>
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<td>---</td>
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<td>---</td>
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<td>1.18(d,6.5)</td>
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<tr>
<td>erytho</td>
<td></td>
<td>6.93(s)</td>
<td>---</td>
<td>2.62(m)</td>
<td>---</td>
<td>0.86(d,6.6)</td>
<td>1.18(d,6.5)</td>
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<tr>
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<td></td>
<td>6.93(s)</td>
<td>---</td>
<td>2.62(m)</td>
<td>---</td>
<td>0.86(d,6.6)</td>
<td>1.18(d,6.5)</td>
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<td>Ph Me HO to Cl</td>
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<td>1.32(m)</td>
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<td>1.42(d,7.2)</td>
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<td>4.18(m)</td>
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<td>1.34(d,7.2)</td>
<td>1.42(d,7.2)</td>
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<td>7.16(s)</td>
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$a$ 60 MHz spectrum.

$b$ 100 MHz spectrum.

(Continued)
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<tr>
<td>3 2 1 COOH</td>
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</tr>
<tr>
<td>erythro 7.19(s) 2.7(m)</td>
<td>1.29(d,6.6)</td>
<td>0.98(d,6.4)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
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<td>3 2 1 OH</td>
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<td></td>
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<td>threeo 7.15(s) 3.77(p,6.1) 2.65(p,7.2) 1.18(d,7.2) 1.04(d,6.1)</td>
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<sup>a</sup> 60 MHz spectrum.

<sup>b</sup> 100 MHz spectrum.

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TABLE XIV (Continued)

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**TABLE XIV (Continued)**
Figure 1. Nmr spectrum of racemic ethyl RR- and RS-3-phenyl-3-hydroxy-2-methylbutyrate.
Figure 2. Nmr spectrum of ethyl 2-methyl-3-phenyl-3-butenoate. Absorptions between 3.3, 2 - 1.9 are due to impurities in the sample. The spectrum was obtained on a neat sample.
Figure 3. Nmr spectrum of a 1:1 mixture of ethyl threo- and erythro-2-methyl-3-phenylbutyrate.
Figure 5. NMR spectrum of threo-2-methyl-3-phenylbutyric acid.
Figure 6. NMR spectrum of a 1:2 mixture of threo- and erythro-3-phenyl-2-butanol. The sample was dissolved in deuteriochloroform.
Figure 7. NMR spectrum of a 1:2 mixture of threo- and erythro-2-chloro-3-phenylbutane.
Figure 9. Nmr spectrum of threo-2-chloro-3-phenylbutane.
Figure 10. Nmr spectrum of E-2-phenyl-2-butene.
Figure 11. NMR spectrum of 2,2-phenyl-2-butene.
Figure 12. Nmr spectrum of a mixture of 3-phenyl-1-butene and 2-2-phenyl-2-butene. Absorptions at 5.1, 6.2, and 5.5 are due to the trans olefin.
Figure 13. NMR spectrum of 3-phenyl-1-butene. Absorptions at 6 2.1, 2.4, and 5.3 represent impurity.
Figure 14. Nmr spectrum of 2-methyl-1-phenyl-1-propanol.
Figure 15. Nmr spectrum of 2-methyl-1-phenyl-1-propene.
Figure 16. Nmr spectrum of a 1:2 mixture of threo- and erythro-1-methyl-2-phenyl-1-propyl acetate.
Figure 17. Nmr spectrum of threo-3-phenyl-2-butanol. Small absorptions at δ 1.5, 1.9, and 3.5 represent impurity.
Figure 18. NMR spectrum of threo-1-methyl-2-phenyl-1-propyl acetate.
Figure 19. Nmr spectrum of erythro-3-phenyl-1-2-\(\alpha\)-anol.
Figure 20. NMR spectrum of erythro-1-methyl-2-phenyl-1-propyl acetate.
Figure 21. NMR spectrum of 2-phenyl-2-nutanol.
Figure 22. Nmr spectrum of 1-methyl-1-phenyl-1-propyl acetate.
Figure 23. Nmr spectrum of 2-methyl-1-phenyl-1-propyl acetate.
Figure 24. Nmr spectrum of 2-benzyl-2-propanol.
Figure 25. Nmr spectrum of 1-benzyl-1-methylethyl acetate.
VITA

Alice Theine was born in the Town of Menomonee, Wisconsin, where she received her elementary education. She was graduated from Pius XI High School, Milwaukee, Wisconsin, in June, 1954. She received the B.A. degree from Alverno College, Milwaukee, Wisconsin, in 1959, and the M.S. degree from Marquette University, Milwaukee, Wisconsin, in 1965.

Sister Alice Theine was received into the community of the School Sisters of St. Francis on June 13, 1955, and made her final profession of vows in the community on June 21, 1963.

During the years 1959-1966, Sister Alice taught high school science and mathematics at St. Boniface High School, Westphalia, Iowa, and at St. Joseph High School, Milwaukee, Wisconsin. Sister Alice was a member of the science faculty at Alverno College from 1966 until returning to Louisiana State University for full-time study in 1970. In September, 1972, she returned to her teaching position at Alverno College.

Sister Alice Theine is presently a candidate for the Doctor of Philosophy degree with a major in organic chemistry and minor in physical chemistry from Louisiana State University, Baton Rouge.
EXAMINATION AND THESIS REPORT

Candidate: Sister Alice Theine

Major Field: Chemistry

Title of Thesis: Lead Tetraacetate Oxidations of Stereoisomeric 2-Methyl-3-Phenylbutyric Acids

Approved:

[Signatures]

Date of Examination:

December 4, 1972

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