An investigation into synthetic routes to optically active trityl systems.

Joseph M. Prokipcak

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AN INVESTIGATION INTO SYNTHETIC ROUTES TO
OPTICALLY ACTIVE TRITYL SYSTEMS

BY

JOSEPH M. PROKIPCAK

A Thesis
Submitted to the Faculty of Graduate Studies through the
Department of Chemistry in Partial Fulfillment
of the Requirements for the Degree of
Doctor of Philosophy at the
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Windsor, Ontario
1964
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ABSTRACT

Two synthetic routes to optically active trityl systems have been found. Both routes involve carboxylic acid intermediates which were formed by the reaction of trityl chloride with either glycolic acid or β-hydroxypropionic acid. In the first reaction sequence, the final intermediate β-triphenylmethoxyethyl chloride was reacted with magnesium to effect elimination and give the starting trityl alcohol. In the second sequence, the methyl ester of the β-triphenylmethoxypropionic acid was degraded in a reverse Michael manner under the influence of triphenylmethyl sodium to yield the original trityl alcohol.

During the course of this study, a general method for the identification of tertiary alcohols was found. Hydrogen phthalate esters of these tertiary alcohols were prepared by the reaction of sodium alkoxides (formed utilizing triphenylmethyl sodium) with phthalic anhydride. These derivatives were readily characterized by their melting points and neutralization equivalents. The hydrogen phthalate esters of the tertiary alcohols pyrolyzed at low temperatures to eliminate phthalic acid and form a mixture of olefins. The pyrolysis temperature occurred at the melting point in the case of tertiary alcohols containing one or two phenyl groups.

Finally, five aliphatic trityl ethers have been prepared by the reaction of the trityl alcohol with the aliphatic alcohol in the presence of iodine.
ACKNOWLEDGEMENTS

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He also wishes to acknowledge support from the National Research Council of Canada in the form of a Research Studentship No. 1-13-19-P-358, during which tenure most of this research was performed. Finally, thanks to Dr. R. J. Thibert for his assistance in these studies.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>ii</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>iii</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vi</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>vii</td>
</tr>
<tr>
<td>Chapter</td>
<td></td>
</tr>
<tr>
<td>I. THEORETICAL CONSIDERATIONS</td>
<td></td>
</tr>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>Optical Isomerism</td>
<td>2</td>
</tr>
<tr>
<td>Racemic Modifications</td>
<td></td>
</tr>
<tr>
<td>1. Formation of Racemic Modifications</td>
<td>4</td>
</tr>
<tr>
<td>2. Properties of Racemic Modifications</td>
<td>8</td>
</tr>
<tr>
<td>3. Methods of Distinguishing the Three Racemic Forms</td>
<td>12</td>
</tr>
<tr>
<td>4. Resolution of Racemic Modifications</td>
<td>13</td>
</tr>
<tr>
<td>Measurement of Optical Activity</td>
<td>18</td>
</tr>
<tr>
<td>Resolution of Alcohols</td>
<td>19</td>
</tr>
<tr>
<td>General Discussion of Solvolysis Reactions</td>
<td>21</td>
</tr>
<tr>
<td>II. TRIPHENYLMETHYL SYSTEM</td>
<td></td>
</tr>
<tr>
<td>Discussion of Previous Work</td>
<td>34</td>
</tr>
<tr>
<td>Hydrogen Phthalate Ester Derivative</td>
<td></td>
</tr>
<tr>
<td>1. Previous Work</td>
<td>42</td>
</tr>
<tr>
<td>Chapter</td>
<td>Page</td>
</tr>
<tr>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>2. Discussion of Experimental Results</td>
<td>45</td>
</tr>
<tr>
<td>Glycolic Acid Derivative</td>
<td></td>
</tr>
<tr>
<td>1. Theoretical Considerations</td>
<td>50</td>
</tr>
<tr>
<td>2. Discussion of Experimental Results</td>
<td>51</td>
</tr>
<tr>
<td>Hydracrylic Acid Derivative</td>
<td></td>
</tr>
<tr>
<td>1. Theoretical Considerations</td>
<td>65</td>
</tr>
<tr>
<td>2. Discussion of Experimental Results</td>
<td>67</td>
</tr>
<tr>
<td>Resume and Conclusions</td>
<td>72</td>
</tr>
<tr>
<td>III. EXPERIMENTAL PROCEDURES</td>
<td>73</td>
</tr>
<tr>
<td>BIBLIOGRAPHY</td>
<td>117</td>
</tr>
<tr>
<td>VITA AUCTORIS</td>
<td>122</td>
</tr>
<tr>
<td>Table</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>I.</td>
<td>Hydrogen Phthalate Ester Derivatives of Tertiary Alcohols</td>
</tr>
<tr>
<td>II.</td>
<td>Ethers Formed Using Iodine</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Enantiomeric Lactic Acids</td>
<td>3</td>
</tr>
<tr>
<td>2.</td>
<td>Melting Point and Solubility Curves for Racemic Mixtures</td>
<td>10</td>
</tr>
<tr>
<td>3.</td>
<td>Melting Point and Solubility Curves for Racemic Compounds</td>
<td>11</td>
</tr>
<tr>
<td>4.</td>
<td>Melting Point and Solubility Curves for Racemic Solid Solutions</td>
<td>12</td>
</tr>
<tr>
<td>5.</td>
<td>Solvolysis of Alkyl Halides</td>
<td>24</td>
</tr>
<tr>
<td>6.</td>
<td>Preparation and Use of Diazomethane</td>
<td>99</td>
</tr>
</tbody>
</table>
CHAPTER I

THEORETICAL CONSIDERATIONS

Introduction

Solvolysis reactions of organic compounds which contain potentially an anionic species (alkyl halides, tosylates, alcohols, etc.) have long been known. The literature is numerous in the number and character of the solvolysis reactions studies. Prior to 1932 simple compounds such as methyl chloride were known to undergo solvolysis reactions with certain protolytic reagents such as water, alcohols, mercaptans, etc., to yield the particular methyl substituted compound. Early workers in the field did not concern themselves with the reaction path but only with the final products. Later, with the development of the transition state theory, interest in the mechanisms of organic reactions developed and the transition state theory proved to be a workable tool in the explanation and prediction of many organic chemical reactions. Basically the classic mechanistic organic chemists divided solvolytic displacement reactions into the following classes:

(1) Ionic

(2) Concerted displacement (Walden Inversion$^{1,2}$)

---

1 P. Walden, *Ber.*, 29, 133 (1896).
The ionic displacement involves prior ionization and demands first order kinetics. The concerted displacement reaction involves simultaneous bond making and bond breaking with coincident Walden inversion about the carbon atom undergoing displacement.

In both the case of the ionic and concerted mechanisms, the use of optical isomerism coupled with kinetic results is of paramount importance in determining the reaction path. In any ionic system where a carbonium ion such as $RR_1R_2C^+$ exists there is $sp^2$ hybridization and the ion is planar and incapable of forming just one enantiomer, when it combines with a solvolytic reagent. Thus any reaction of an optically active compound such as $RR_1R_2C-X$ which would proceed via a carbonium ion mechanism, the carbonium ion $RR_1R_2C^+$ would necessarily lead to a racemic mixture. However, if the reaction of the optically active system $RR_1R_2C-X$ occurred in a concerted manner, optical activity would be retained. This activity can occur with retention or inversion of configuration about the central carbon atom.

**Optical Isomerism**

There is one condition that must be satisfied if a molecule is to show optical activity. This prime condition is that the molecule in question not be superimposable with its mirror image. There are many ways to obtain this condition but the simplest source of dissymmetry in an organic molecule is a carbon atom to which four different atoms or groups are attached. This principle of non-superimposability can be demonstrated using one of the oldest examples of such a system, lactic acid, $HOCH(CH_2)COOH$. 

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The asymmetric carbon atom is at the centre of the tetrahedron. If the four groups are placed at each corner of the tetrahedron and then the mirror image is drawn, one can see that the two mirror images are not superimposable.

There are many other examples where two of the four groups attached to the carbon atom are alkyl groups such as carbinols (2-butanol), amino acids (alanine), halides (2-bromo-octane), etc. Compounds can also be optically active due to asymmetry produced by isotopic substitution as in the case of RCHD\textsuperscript{3} where the isotopic

substituent is attached to the asymmetric carbon atom. An example of this is pure ethyl-benzene-α-D. However, there are cases where the asymmetry is caused by isotopic substitution remote from the asymmetric carbon such as CH₂CHOHCD₂.⁴ There are many other examples of asymmetric compounds but the one of prime importance in this work is of the general form RR₁R₂C-X.

Racemic Modifications

In general, synthesized bulk substances are optically inactive even though the molecules that make up the substance are optically active. This is because the bulk substance is made up of approximately equal numbers of dextrorotatory (+) and levorotatory (-) molecules so that the average rotation is zero. Such an assembly where half of the molecules present are the mirror images of the other half is called a racemic mixture or racemic modification and is denoted by (‡).

1. Formation of Racemic Modifications

(a) By mixing. - This method simply involves the thorough mixing of equal amounts of the (+) and (-) forms of the optical isomers. This method of forming a racemic mixture is used mainly if comparison of the compound is to be made to either the pure (+) or (-) isomer.

(b) By synthesis. - Whenever a reaction takes place between a symmetric molecule or a racemic modification and a non-optically active reagent (no asymmetric physical influence), a racemic

modification always results. A good example of this is the addition of a Grignard reagent $R_2\text{MgX}$ to a carbonyl group.

\[ \text{HO} \quad \text{C} \quad \text{R}_2 \quad \text{R}_2\text{MgX} \quad \text{R}_1 \]

Here the $R_2\text{MgX}$ can approach from either side of the carbonyl group so that equal numbers of both the (+) and (-) forms of the alcohols can form to give a racemic mixture.

(c) By racemization. This involves the production of a racemic modification starting with one of the pure enantiomers. Racemization of the pure enantiomer may occur in several ways:

i. Thermally: In some compounds, one of the bonds to the asymmetric carbon atom can be temporarily broken by thermal energy. When this happens, the separated group exchanges places with one of the remaining groups and racemization occurs.

ii. By Anion Formation: Here when one of the bonds to the asymmetric carbon atom is broken the pair of electrons stay with the central carbon atom. The carbanion has a $\text{sp}^3$ (tetrahedron) configuration and should be capable of optical isomers. However, there is a molecular vibration in a carbanion which rapidly converts one form of the carbanion into its mirror image.
Thus a reaction proceeding via a carbonion intermediate produces complete racemization. The group which leaves without its electrons is usually a proton and the removal is brought about in most cases by bases such as methoxide or ethoxide ions, e.g.,

\[
\begin{align*}
&\text{O Et} \quad \text{O CH}_3 \\
&C_6H_5-C-C-CH_3 \rightarrow C_6H_5-C-C-Et \leftarrow C_6H_5-C=C-CH_3
\end{align*}
\]

iii. By Cation Formation: Here the leaving group leaves with its pair of electrons resulting in the formation of a carbonium ion. Since the tetrahedral carbonium ion (sp\(^3\)) is less stable than the planar carbonium ion (sp\(^2\)), the carbonium ion planarized. When any nucleophilic reagent \(\text{A}^\ominus\) attacks the planar carbonium ion, the attack can occur from both sides of the planar molecule and the final

products are mirror images resulting in the formation of a racemic mixture, e.g.,

\[ \text{CH}_3 - \text{C} - \text{Cl} \xrightarrow{\text{AlCl}_3} \]

optically active

planar carbonium ion

racemic mixture

iv. By Reversible Formation of Stable Inactive Intermediate:

This is where the optically active compound is in equilibrium with an inactive intermediate and because of this equilibrium, the optically active compound loses its optical activity. A good example of this is the dehydrohalogenation-hydrohalogenation of α-phenethyl chloride, e.g.,

\[ \text{C}_6\text{H}_5 - \text{C} - \text{Cl} \xrightarrow{-\text{HCl}} \text{C}_6\text{H}_5\text{CH} = \text{CH}_2 \]

\[ \text{C}_6\text{H}_5 - \text{C} - \text{Cl} \xrightarrow{+\text{HCl}} \text{C}_6\text{H}_5\text{CH} = \text{CH}_2 \]

(d) **By chemical transformation.** - In this case there are no bonds broken at the asymmetric carbon centre, e.g.,

\[
\text{CH}_3 \quad \text{aqueous acetone} \quad \text{CH}_3
\]

In the racemization of 2-cyclohexenyl acid phthalate\(^7\) the racemization is due to the rearrangement of the phthalate group. When the ester group changes position, it gives rise to the formation of products which are mirror images. This results in the total racemization of the initial optically active acid phthalate.

(e) **Epimerization, Mutarotation, and Asymmetric Transformation.**

2. **Properties of Racemic Modifications**

With only a few exceptions,\(^8\) most racemic modifications in the gaseous or liquid state contain nearly an ideal mixture of enantiomeric molecules. Because these racemic modifications are nearly ideal, the mixture and the separate enantiomers have similar properties\(^9\) such as

---


boiling points, index of refraction, density, and have similar infrared spectra. When the mixtures are in the crystalline state there are normally deviations\textsuperscript{10} from ideal behaviour since the molecules in a crystal lattice are more sensitive to geometric changes than are the molecules in a gas or liquid. Crystalline racemic modifications are classified into three main types:

(a) racemic mixtures
(b) racemic compounds
(c) racemic solid solutions

(a) \textbf{Racemic Mixtures}: Here each enantiomer has a greater affinity for molecules of the same kind than for molecules of the other enantiomer. This property allows fractional crystallization of one of the enantiomers which is accomplished by seeding the solution with one of the enantiomers. This results in the crystal growth of the seeding enantiomer leaving the other in solution.

A racemic mixture is a mixture in all respects. The melting point of the racemic mixture is lower than that of either of the pure components and its solubility is higher. The racemic mixture occurs at the eutectic point which in this particular case occurs at a 50-50 composition.

\textit{---}

(b) **Racemic Compounds**: In a racemic compound, one enantiomer has a greater affinity for an enantiomer of the opposite optical activity than for its own kind. If a macroscopic crystal of a racemic compound were broken down, one would get alternatively one enantiomer and then the other so that in complete breakdown, there would be equal numbers of both enantiomers.

---

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The racemic compound is a true compound and differs from the pure enantiomers in most of its physical properties such as melting point, solubility, X-ray powder diagrams, and infrared spectrum in the solid state. The melting point and solubility of the compound may be higher or lower than that of the pure enantiomers.

(c) Racemic Solid Solutions: Here there is little difference in affinity between molecules of like or opposite configuration. This results in the random arrangement of the molecules in any crystal. Because of the affinity of the two enantiomers, these solid solutions behave as ideal gaseous or liquid solutions in that they have identical (or only slightly different) physical properties as do either of the pure enantiomers.
3. Methods of Distinguishing the Three Racemic Forms

In order to determine which racemic form is present, one or more of its physical properties must be compared to that of the pure enantiomers.

(a) Infrared Spectrum. The infrared spectrum can be used for comparison since the only time there is a definite difference between the racemic modification and the pure enantiomers is in the case of a racemic compound. This is apparently due to intermolecular action in the racemic compound which gives rise to a different spectrum than that for either pure enantiomer.

---

(b) Solubility or Melting Point Diagram.\(^{12}\) Essentially this procedure involves tracing out one of the diagrams already mentioned. If the pure enantiomers are mixed together in different proportions and the solubility or melting point of the resultant racemic mixture is checked, we can get a characteristic solubility or melting point curve. These curves allow classification of the racemic modification.

(c) X-Ray Crystallography.\(^{13}\) This method of distinguishing the racemic form is possible because of the differences between a unit cell of a compound as compared to that of a mixture or a solid solution. In a compound, a unit cell has equal numbers of both enantiomers, whereas in the mixture or solid solution it contains only molecules of one or the other enantiomer but not both.

4. Resolution of Racemic Modification

When a racemic modification is resolved, the mixture is separated into its two composite enantiomers. The separation is seldom quantitative. There are several methods that can be used to separate a racemic modification.

(a) Resolution by Mechanical Separation of Crystals.

In some instances\(^{14}\) the two enantiomers may be so

different and so large that one can pick them apart by means of tweezers. The method is rarely applicable and can be used only for situations where the enantiomers have crystal structures visually distinct.

This method has been modified to allow for more extensive use. If a supersaturated solution containing both of the enantiomers is seeded by a pure crystal of one of the enantiomers, (sometimes foreign particles with similar crystal structure may serve the purpose) this seed crystal will grow at the expense of one of the enantiomers in the solution. In this way an appreciable amount of one of the enantiomers may separate giving partial resolution of the mixture.

(b) Formation of Diastereoisomers.

This method is the most useful and general of all methods. Here the racemic modification is allowed to interact with an optically active material (resolving agent) to give two diastereoisomers which have different physical properties. These differences allow the diastereoisomers to be separated by normal means such as distillation,\textsuperscript{15} chromatography,\textsuperscript{16} fractional crystallization, etc. The most effective method is fractional crystallization.


Of prime importance in using this method to resolve a racemic modification is the selection of a suitable resolving agent. There are several conditions that must be fulfilled by a resolving agent. First, there must be a semi-permanent linkage between the resolving agent and the two enantiomers to be resolved. This step must be as convenient and as quantitative as possible to make the resolution practical. The linkage formed between the resolving agent and the enantiomers must be stable enough so that no cleavage can result during the recrystallization and yet weak enough to allow it to be broken in the final step without leading to any damage to the desired active compound. This condition is generally met by salts which are formed by reacting the organic acid and base in a suitable solvent. After resolution has been completed, the salt can be decomposed by treatment of the salt with mineral acid. It is thus easiest to resolve organic acids (carboxylic or sulphonic) and bases (amines) since these compounds form salts readily. Other compounds often times must first be converted to these acids or bases in order to be resolved. A second important requirement of a good resolving agent is that the diastereoisomer formed must be crystalline. Also there must be an appreciable difference in the solubilities of the two diastereoisomers. Whether the two diastereoisomers are crystalline with sufficient differences in solubility depends on the nature of the solvent and on the nature of the two enantiomers. There is no method that can be used to predict beforehand whether the resolving agent and the enantiomers will combine to give a crystalline product. The choice of resolving agent and solvent is in general a matter of trial.
and error. A third condition for a good resolving agent is that it be cheap or readily prepared. Also the resolving agent should be available in the optically pure form.

Some basic resolving agents that have been used are the naturally occurring alkaloids such as brucine, strychnine, ephedrine, quinone, quinidine, cinchomine, etc., and some synthetic bases such as α-phenethylamine, menthylamine, and amphetamine. Acidic resolving agents include the camphor derivatives and naturally occurring active forms of tartaric acid and malic acid.

The solvent that can be used to recrystallize any pair of diastereoisomers depends of course on the nature of the resolving agent and the enantiomers themselves. The salts of carboxylic acids are usually formed by adding one equivalent of the base (resolving agent) in the powdered form to the acid which is dissolved in acetone, pure or aqueous methanol, ethanol, or ethyl acetate. Water is not a good solvent since often times the salts are easily hydrolyzed. If the mixture is warmed, solution takes place which on cooling deposits most of the less soluble diastereoisomer. Usually only the least soluble of the two salts can be effectively purified from a particular solvent. When the second salt is desired in the pure form, a new resolving agent and solvent combination is sought such that the second salt is now the least soluble.

After resolution has been completed, the active acid is set free from the salt by cleavage with mineral acids. Usually the salts are dissolved in a suitable solvent such as acetone or ethanol and then the solution is added to a dilute solution of
hydrochloric acid. The active acid precipitates from the solution and the base (resolving agent) is left in the dilute acid solution.

(c) Resolution by Kinetic Asymmetric Transformation.

Because of the different configurations present in stereoisomers, the rates with which these isomers will combine with other reagents may vary appreciably. This can be made use of in the resolution of certain stereoisomers. The asymmetric transformation can occur in several ways:

(i) The two enantiomers may be formed or may react with a reagent at different rates. (Kinetic Method of Resolution)

(ii) The two enantiomers may be destroyed at unequal rates by an asymmetric agent. (Asymmetric Destruction)

(iii) The reaction causes a new asymmetric centre to be formed. (Asymmetric Synthesis)

(d) Biochemical Asymmetric Transformation.

Here the optically active compound is produced either by the interaction of a living organism or by an enzyme. The organism or enzyme usually consumes or combines with one of the enantiomers leaving the other enantiomer behind.

There are other methods that can be used to resolve racemic modifications, but methods (b) and (d) are the most common with (b) i.e., resolution by formation of diastereoisomers being the one of interest in the present work.
Measurement of Optical Activity

Once an enantiomer has been obtained in an optically pure form by one of the methods already mentioned, it will impart rotation to the plane of polarized light when put into solution. This rotation is measured using a polarimeter (a sodium lamp is used as a light source, \( \lambda = 589\text{nm} \)). There are several factors which affect the magnitude of the optical rotation. In addition to the actual nature of the sample, they are:

1. sample thickness
2. sample concentration
3. solvent
4. temperature
5. wavelength of the light source

The optical rotation \( \alpha \) has a linear dependence on the cell length \( l \) and concentration \( c \). When \( l \) is in decimetres and \( c \) is in gms./ml. \( [\alpha] \) is called the specific rotation.

\[
[\alpha] = \frac{\text{observed rotation}}{l(\text{dm.}) \times c(\text{gm./ml.})}
\]

The dependence on wavelength and temperature is usually indicated by subscripts and superscripts respectively. For example, \( [\alpha]_D^{25} \) means the specific rotation of a substance at 25°C measured at the wavelength of the sodium D line. Additional information is denoted as follows: \( [\alpha]_D^{25} -76.3^\circ +0.3 \) (c=5.77 gm./100 ml. ethanol). The changes of specific rotation due to solvent, temperature, and concentration changes are related to some degree to changes in intermolecular...
hydrogen bonding and/or the degree of association and dissociation between the molecules.

Since optical rotatory power is a property of molecules, comparison of molecules of different molecular weights can be made. These comparisons are based on molecular rotations $\rho_D$, calculated as follows:

$$\rho_D = \frac{[a]_M \times \text{Molecular Weight}}{100}$$

The value 100 is arbitrarily chosen to keep the molecular rotations manageably small. These $\rho_D$ values are numbers, not degrees.

Resolution of Alcohols

It was found that there are two main methods for the resolution of alcohols and phenols. One resolution is effected by prior conversion to their hydrogen phthalate esters or succinate esters, formed by treating the alcohol with phthalic or succinic anhydride and pyridine. The esters must be chosen so as to yield solid derivatives which can be separated or resolved as typical acids, e.g., by forming salts with the alkaloids such as brucine or strychnine. After repeated recrystallizations one of the pure diastereoisomers is usually

obtained in the pure form. The salt is decomposed in the usual manner using mineral acids. The acid ester is either saponified with hot aqueous sodium hydroxide or reduced with lithium aluminium hydride (if there is any danger of racemization of the alcohol with base) to yield the optically pure alcohol. The chemistry of this process is as follows:

\[
(\dagger) \text{R-OH} + \text{Brucine} \xrightarrow{\text{pyridine}} (-) \text{Brucine}^* + \text{CO}_2\text{H} \]

\[
\text{CO}_2^* \text{H Brucine} \xrightarrow{\text{HCl}} \text{CO}_2\text{R}^* + \text{Brucine} \cdot \text{HCl}
\]

resolution

active

\[
\text{NaOH} \xrightarrow{\Delta} \text{LiAlH}_4
\]

active

active

active

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Another method of resolving alcohols and phenols involves treating the racemic modification with an optically active acid. Because relatively few esters are satisfactorily crystalline, this method is very limited. Tartranilic acid, menthyl isocyanate, and menthoxyacetyl chloride are among the reagents that have been used to resolve alcohols. There are other methods that have been used to resolve alcohols but the two already mentioned have been used for more than 90% of all recorded resolutions of alcohols.

General Discussion of Solvolysis Reactions

The solvolysis of simple organic compounds of the type -C-G, where G is any convenient leaving group such as halogen, ester, phthalate, benzenesulphonate, p-toluenesulphonate, p-bromobenzene-sulphonate, etc., has been studied in detail both stereochemically and kinetically over a period of approximately forty-five years. Difficulty arises from the interpretation of the data obtained. In general most solvolysis reactions fall into two main classes of cleavage of the C-G bond.

Unimolecular (SN$_1$). This involves prior ionization of $-\text{C-G}$. Here the driving force is the pull of some electrophilic solvent which forms a hydrogen bond or solvates the leaving group G by means of electrostatic forces. This ionization is followed by recombination of the resultant organic cation with the solvent species according to the following sequence:

\[ \text{C} -\text{G} \xrightarrow{\text{ionization}} \text{C}^+ + \text{G}^- \]

\[ \text{C}^+ + \text{ROH} \xrightarrow{} \text{C-O-R} + \text{H}^+ \]

Bimolecular (SN$_2$). This involves simultaneous bond breaking and bond making according to the sequence on the following page. This cleavage can occur with inversion (as shown on page 23) or retention of original configuration.
Hughes, Ingold, and Patel\textsuperscript{23} discussed these nucleophilic substitution mechanisms, $\text{SN}_1$ and $\text{SN}_2$, on a theoretical basis. They predicted (no kinetic evidence) that in the series $R-X$ such as MeX, EtX, i-propyl X, and t-butyl X in which $R$ increases in its power of electron release, the $\text{SN}_2$ reaction should prevail up to a certain point and then the $\text{SN}_1$ reaction should become operative. In 1935 Cleave, Hughes, and Ingold\textsuperscript{24} performed experiments on the solvolysis of alkyl halides and found that there was a transition point in the type of mechanism that was involved. The reaction studied and the data obtained are shown on the following page.


The transition point between the two mechanisms occurred between the ethyl chloride and the isopropyl chloride. Before this transition point the substitution exhibited second order kinetics and the absolute rate decreased with progression through the series. After this point, the kinetics became first order and the overall rate increased. Hughes and coworkers\textsuperscript{25} investigated the reactions of alkyl chlorides with OH\textsuperscript{−} and Br\textsuperscript{−}, and found that here again the mechanism changed from the \( \text{SN}_2 \) to the \( \text{SN}_1 \) type. The main problem at the time

was the interpretation of the first order kinetics data obtained in the solvolytic reactions of tertiary alkyl halides. Cleave and co-workers\textsuperscript{26} in their work supposed that these reactions proceeded via an ionic mechanism.

\[
\begin{align*}
R - X & \quad \text{slow} \quad \rightarrow \quad R^+ + X^- \\
R^+ + R_1 - OH & \quad \text{fast} \quad \rightarrow \quad R - O - R_1 + H^+
\end{align*}
\]

Here the carbonium ion $R^+$ reacts immediately with solvent molecules. Hughes\textsuperscript{27} investigated the hydrolysis of t-butyl chloride in aqueous ethanol as solvent. He found that the reaction was first order with respect to the halide and independent of the concentration of hydroxide ion. It was found that water increased the specific rate constant. Hughes and Ingold\textsuperscript{28} concluded that here again the rate depended on the prior ionization of the halide and that water acted as "solvent alone" where the superior ionizing properties (solvating power) of water over alcohol explained the increase in reaction rate. Hammett and coworkers\textsuperscript{29,30} in their work with optically active $\alpha$-phenylethyl chloride found that the solvolysis reaction followed first order kinetics. However, their results showed that the reaction

\textsuperscript{26} J. L. Cleave, E. D. Hughes, and C. K. Ingold, loc. cit.
proceeded with inversion of configuration. This led them to conclude that the reactions of alkyl halides in water, alcohol, and acetic acid were polymolecular involving several molecules of the solvent, and that the driving force was derived largely from the energy of solvation of the halide ion. Olson and Halford\textsuperscript{31} studied the solvolysis of t-butyl chloride in aqueous alcohol solvents and found that under the reaction conditions both alcoholysis and solvolysis were occurring and that both the hydrolysis and alcoholysis rates were bimolecular. Thus they claimed that under the reaction conditions there was no primary breaking of the carbon-halogen bond i.e., no carbonium ion formation. This mechanism was supported by Taylor.\textsuperscript{32} In his work on the solvolysis of t-butyl bromide, he reported that the bimolecular mechanism best explained the kinetic data obtained.

Winstein\textsuperscript{33} discussed the solvolysis reaction from the standpoint of stereochemical results obtained using optically active halides. In consideration of the ionic mechanism in the hydrolysis of an alkyl halide he proposed the following reaction sequence:

\begin{align*}
\text{CH}_3\text{C} &\rightarrow \text{CH}_3\text{C}^+ + \text{Br}^- \\
\text{CH}_3\text{C}^+ &\rightarrow \text{C} + \text{Br}^- \\
\end{align*}


\textsuperscript{33} S. Winstein, \textit{J. Am. Chem. Soc.}, 61, 1635 (1935).
Reaction (1) represents the ionization process and reaction (2) the process of planarization of the cation. This planarization allows the formation of the two enantiomeric products as shown by reactions (3) and (4). If the half life of the carbonium ion formed is appreciable one would certainly expect to get a racemic mixture of the alcohol from an optically active halide. Ingold and coworkers\textsuperscript{34} however, claimed that the $S_{N}$ process may involve inversion, racemization, or retention of configuration depending on the reaction conditions. In the solvolysis of alkyl halides\textsuperscript{35,36} they obtained predominantly inversion of configuration with more or less racemization. They claimed that the halogen atom X will shield the carbon atom from any frontal attack so that the hydroxyl group attacks from the side away from the halogen atom resulting in inversion of configuration. They postulated that the zwitterion is stabilized by

\begin{equation}
\text{C}^{\ominus} + \text{H}_2\text{O} \rightarrow \text{C} - \text{OH} + \text{H}^{\oplus} \quad (3)
\end{equation}

\begin{equation}
\text{H}_2\text{O} + \text{C}^{\oplus} \rightarrow \text{HO} - \text{C}^{\ominus} + \text{H}^{\oplus} \quad (4)
\end{equation}


the pyramid form so that there is no planar intermediate carbonium ion to allow extensive racemization. Their postulated intermediate is shown below:

\[
\begin{align*}
\text{HO}^+ & \quad \rightarrow \\
& \quad \text{de} \quad \text{de} \quad \text{X}
\end{align*}
\]

Winstein disagreed with Ingold's interpretation of the results. He argued that in order to classify a reaction as unimolecular, the implication is that ionization must be complete thus allowing the carbonium ion to be free from any close shielding effects. This would lead to a racemic product when the carbonium ion reacts with solvent molecules. Again, he proposed that if solvolysis reactions were investigated considering solvent molecules as reactants, one could get a true picture of the mechanism involved. In any ordinary bimolecular substitution or RO⁻ for Cl⁻ inversion occurs and the transition state could be drawn as follows:

\[
\begin{align*}
\text{R} & \quad \text{R} \quad \text{R}_{1} \\
\text{R'} & \quad \text{Cl} \quad \text{Cl}
\end{align*}
\]

37 S. Winstein, loc. cit.
In solvolytic reactions where the solvent molecules may act as reactants, we can get a transition state as shown below:

Here inversion occurs if solvent molecule (1) becomes bonded to the central carbon atom and solvent molecule (2) leaves as part of the solvation sphere of the chloride, or with inversion of solvent molecule (2) becomes bonded to the central carbon atom. Here the reaction would be polymolecular as Hammett and coworkers\textsuperscript{38,39} claimed. Winstein also claimed that if the solvolytic reaction were carried out in an inert solvent containing small concentrations of the hydrolytic reagent, a bimolecular mechanism should prevail in which there were two possible transition states as shown below:

\textsuperscript{38} J. S. Steigman and L. P. Hammett, \textit{loc. cit.}

\textsuperscript{39} N. T. Farinacci and L. P. Hammett, \textit{loc. cit.}
If transition state I existed, there would be inversion of configuration whereas transition state II would result in retention of configuration.

Through recent years there have been many more examples of solvolysis reactions studied. Despite different results and interpretation of data, it is still the consensus of modern day organic chemists that all solvolysis reactions fall into two main types, i.e., the $S_N_1$ and $S_N_2$ processes. By means of experimental data furnished by authors in the field it has been found that there are several factors that play a large role in determining which of the two mechanisms will occur in a given solvolysis reaction. A brief discussion of these factors will illustrate how these different factors might favour a particular mechanism.

1. Solvent Effects.\(^{40,41}\) A particular solvent may stabilize the reactants, the transition state, or the products of a given reaction. In the $S_N_1$ process where there is a separation of charges, polar solvents such as water would be expected to favour the process. Indeed, marked solvent effects have been noted. When the reaction proceeds via a $S_N_2$ mechanism, the solvent usually performs the role of fixing the geometry of the transition state and here non-polar solvents are used for the $S_N_2$ processes.

\(^{40}\) E. D. Hughes, *loc. cit.*

\(^{41}\) E. D. Hughes and C. K. Ingold, *loc. cit.*
2. Nature of the Entering and Leaving Groups.\textsuperscript{42,43,44} - The nature of the attacking group does not influence the rate of the unimolecular process since here the rate depends only on the prior ionization of the original compound. On the other hand, the nature of the attacking nucleophile can have a large effect on the rate of a bimolecular process. It has been shown that ions containing sulfur atoms such as $S^\ominus$, $\text{CH}_2S^\ominus$, $\text{SH}^\ominus$, etc., have high nucleophilic activity. For example, $\text{SH}^\ominus$ is twice as strong a nucleophilic attacking agent as $OAc^\ominus$.

Attacking ions with high nucleophilic activity will tend to react via the $\text{SN}_2$ process while those of low nucleophilic activity will favour the $\text{SN}_1$ process.

The nature of the leaving group has a great effect on both the $\text{SN}_1$ and $\text{SN}_2$ processes, with the most effective leaving groups being those bound to the central carbon atom by relatively weak bonds. The approximate order of ease of removal is:

\[ p\text{-CH}_2\text{C}_6\text{H}_4\text{SO}_2\text{O}(\text{CH}_3\text{SO}_2\text{O})^\ominus > I^\ominus > \text{Br}^\ominus > \text{Cl}^\ominus > \text{Ac}^\ominus > \text{R}_3\text{N}^\ominus \]

3. Nature of the Groups Around the Central Carbon Atom. - The effects here can be classified into the following types:


(a) **Inductive or polar effects.**\(^45,46,47\) This is the tendency of a substituent to release electrons to the central atom through the carbon-carbon bonds and also through space. This electron releasing tendency increases as the number of carbon atoms in the substituent increases.

(b) **Hyperconjugative effect.**\(^48\) This can be considered as a low-order resonance effect. This is where an unsaturated centre (carbonium ion) is stabilized by the conjugation of an electron pair of an adjacent C-H bond. The more C-H bonds there are adjacent to the unsaturated centre, the more stable is the ion formed. For example, \((\text{CH}_3)_2\text{C}^\ominus\) is more stable than \(\text{CH}_2\text{CH}_2^\ominus\) because there are nine C-H bonds at the alpha position in the former while in the latter there are only three.

(c) **Steric effects.**\(^49,50\) This is sometimes called the compression factor and causes crowding of the groups around the central carbon atom. The larger the groups, the more crowded they are around the carbon atom.

---


The three effects mentioned above are to some extent inter-related and do in fact lead to the same final result. Since both the inductive and hyperconjugative effects contribute to the stabilization of an ion, they would enhance the ionization of a compound and so favour the unimolecular reaction. On the other hand, the formation of a nucleophilic centre which is necessary for a bimolecular process is retarded by both the polar and hyperconjugative effects. The unimolecular process is enhanced by large substituents because of a crowding effect which favours the formation of a planar carbonium ion. Bimolecular processes on the other hand would have to proceed through a crowded transition state if the substituents are large and hence would be expected to show substantial steric retardation.

In general, it can be said that alkyl or aryl substituents on the central carbon atom would favour the unimolecular process and retard the bimolecular process.

A rather unique case presents itself with the triphenylmethyl system since no one has been able to correlate stereochemical and kinetic data. It is with this goal in mind that the present research was started.
CHAPTER II

TRIPHENYL METHYL SYSTEM

Discussion of Previous Work

Interest in this laboratory in the solvolysis of the triphenylmethyl system resulted from work published by the two leading authors in the field, Sir Christopher K. Ingold and C. Gardner Swain. In 1935¹ Hughes and Ingold investigated the solvolysis of several organic halides. From the results of their kinetic studies they concluded that the solvolysis of tertiary systems and especially the triphenylmethyl system proceeded via the unimolecular mechanism. This means the rate of solvolysis of tertiary systems is proportional only to the concentration of the given tertiary halide which demands the ionization as the rate-determining step followed by a rapid recombination with the solvent. The sequence is as follows:

\[
\begin{align*}
R_1^+ & \quad R_2^+ \quad X^- \\
\text{slow} & \quad \rightarrow & \quad R_1^+ & \quad R_2^- \\
R_1^- & \quad C^+ \quad R_2^- \\
\text{fast} & \quad \rightarrow & \quad R_1^- & \quad C^- \quad OR + H^+
\end{align*}
\]


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Swain claimed that Ingold and coworkers ignored the possibility that the solvent could act as something more than merely an ionizing medium. He pointed out that Ingold's work was carried out in protolytic reagents which were present in such large excess that concentration changes could not be measured and thus pseudo order kinetics were actually observed. Swain studied the kinetics of the solvolysis of triphenylmethyl chloride and used the reagents in low concentrations and determined the kinetic order with respect to all the nucleophilic and electrophilic species present. The nucleophilic and electrophilic reagents which included tertiary amines, phenol, and methanol were examined separately and in various combinations and the concentration of each reagent was independently varied. Swain's results yielded third order kinetics which were interpreted as a simultaneous attack on the central carbon atom and on the halogen atom of the triphenylmethyl chloride by the given reagent. In the case of the reaction with methanol, he postulated the transition state as follows in accordance with the rate equation:

\[
\text{Rate} = [\text{Halide}] \left[\text{CH}_3\text{OH}\right]^2
\]

---

As can be observed from the transition state shown below, one solvent molecule acts as a nucleophilic attacking agent on the central carbon atom and another solvent molecule as an electrophilic species which forms a hydrogen bond with the halogen atom. This work led Swain to conclude that nucleophilic displacements of potentially anionic species from saturated carbon atoms are concerted, requiring two types of driving forces:

1. A pulling effect of the solvent proton on the leaving group.
2. A pushing effect of a solvent molecule on the central carbon atom.

This would make the displacement reaction at least termolecular, (push-pull mechanism). He felt that this mechanism was applicable to all solvolytic displacement reactions including those of the triphenylmethyl system which were previously thought to react only by the carbonium ion mechanism. 4

Ingold and coworkers\textsuperscript{5-10} repeated the above experiments with triphenylmethyl chloride under slightly different conditions. They found that in all the reactions they carried out (reactions of triphenylmethyl chloride with (1) tetra-n-butylammonium radiochloride, (2) methanol, and (3) benzyl alcohol) first order kinetics were obtained. This reaffirmed their suggestion of prior ionization as the rate controlling step. They thus claimed that the "push-pull" mechanism of Swain did not agree with their experimental results. In a later paper, Swain\textsuperscript{11} suggested that this lack of agreement was due to "serious experimental errors" in the work of the Ingold school. Failure to utilize a tertiary amine to bind the hydrogen chloride formed in the reaction and contaminating traces of moisture in the reagents were said to cause other reactions to occur which would render the kinetic data invalid.


\textsuperscript{6} E. D. Hughes, C. K. Ingold, S. F. Mok, S. Patai, and Y. Pocker, \textit{ibid.}, 1220 (1957).

\textsuperscript{7} E. D. Hughes, C. K. Ingold, S. Patai, and Y. Pocker, \textit{ibid.}, 1230 (1957).

\textsuperscript{8} E. D. Hughes, C. K. Ingold, S. F. Mok, and Y. Pocker, \textit{ibid.}, 1238 (1957).

\textsuperscript{9} E. D. Hughes, C. K. Ingold, S. Patai, and Y. Pocker, \textit{ibid.}, 1256 (1957).

\textsuperscript{10} E. D. Hughes, C. K. Ingold, S. F. Mok, S. Patai, and Y. Pocker, \textit{ibid.}, 1256 (1957).

In 1958 Winstein\textsuperscript{12} postulated that the triphenylmethyl chloride could exist in three different kinds of charged species.

\[
\begin{align*}
\text{carbonium ion pair} & \\
\text{solvated carbonium ion pair} & \quad \text{dissociated ions}
\end{align*}
\]

One of the three carbonium ions would predominate in any one given solvent depending on the dielectric constant of the particular solvent. In a non-polar solvent such as benzene the triphenylmethyl chloride would exist as a carbonium ion pair whereas in a polar solvent such as aqueous alcohol solutions, the dissociated ions would be present. Swain made use of Winstein's suggestion of the existence of a carbonium ion pair in his explanation for the results obtained in the acetolysis\textsuperscript{13} and methanolysis\textsuperscript{14} of triphenylmethyl chloride.


\textsuperscript{13} C. G. Swain and A. MacLachlan, \textit{J. Am. Chem. Soc.}, 82, 6101 (1960).

\textsuperscript{14} C. G. Swain and E. E. Paques, \textit{loc. cit.}
He claimed that the results\(^{15}\) on the solvolysis of triphenylmethyl chloride in solvents such as methanol, ethanol, acetone-water mixtures and acetic acid were best explained by the existence of the triphenylmethyl chloride carbonium ion pair. Experimentally, Swain found that the total kinetic order decreased from third order to second order as the amount of solvent was decreased. In the methanolysis of triphenylmethyl chloride using a non-polar solvent such as benzene, the reaction sequence could be written as follows:

\[ \text{C}_6\text{H}_5\text{Cl} \xrightleftharpoons[k_1]{k_2} \text{CH}_3\text{OH} \]

\[ \text{C}_6\text{H}_5\text{C}_6\text{H}_5 \xrightarrow{k_3} \text{C}_6\text{H}_5\text{H}_2\text{O} \]

The rate determining step is indicated by \( k_3 \). Hence in a benzene solution, triphenylmethyl chloride forms an ion pair which reacts with methanol. In this case, the ion pair would not be expected to ionize into formal ions because of the low dielectric constant of the medium. As can be observed from the above reaction sequence, the rate equation can be written as:

\[
\text{Rate} = k_3 \left[ (\text{C}_6\text{H}_5)_3\text{C}-\text{Cl} \right] \left[ \text{Methanol} \right]^2
\]

The rate dependence on the solvent methanol is due to the dual purpose it serves in the reaction. One molecule of solvent methanol acts as an electrophilic agent which forms a hydrogen bond with the halogen atom and the second molecule of methanol as a nucleophilic attacking agent which combines with the central carbon atom. Thus the rate of methanolysis of triphenylmethyl chloride in benzene as solvent is determined by the reaction of the triphenylmethyl chloride carbonium ion with the methanol. This mechanism was used to explain the acetolysis, ethanolysis, and hydrolysis (in acetone) of triphenylmethyl chloride.

From the previous discussion one can see that there are two main views regarding the mechanism of the solvolysis of triphenylmethyl halides, each being supported by experimental evidence. Ingold claimed that the reaction proceeds via a carbonium ion mechanism while Swain argued that the reaction involves a concerted "push-pull" mechanism. It is the present author's opinion that kinetic data alone will not solve this mechanistic problem. Some additional data is needed.
to allow a complete picture to be drawn as regards to the transition state of the reaction. It is the belief of this author that stereochemical data on the solvolysis of triphenylmethyl chlorides or similar trityl systems would provide the necessary proof as to the existence or non-existence of a classical carbonium ion. If the reaction involves the carbonium ion mechanism as proposed by Ingold, a planar cation would probably exist in the transition state and if the initial triphenylmethyl halide were optically active, racemization would occur in the planar transition state so that all optical activity in the final products would be lost. On the other hand, if the reaction proceeded via a concerted mechanism as proposed by Swain, the solvolysis product would retain optical activity. Thus the stereochemical data would indicate whether the solvolysis reaction involved a carbonium ion mechanism or a concerted "push-pull" mechanism. This latter mechanism could lead either to retention or inversion of configuration.

Neither author reported any stereochemical studies with optically active triphenylmethyl systems. It has been accepted in the field of organic chemistry that an optically active system would be very difficult to attain by virtue of a lack of a good reaction sequence which would lead to such a system.
Hydrogen Phthalate Ester Derivative

1. Previous Work

A logical approach to the synthesis of an optically active triphenylmethyl system involves the reaction of the alcohol with phthalic anhydride according to the following sequence:

\[
R-\text{OH} + \text{C}_6\text{H}_4(\text{CO}_2)\text{O} \rightarrow \text{C}_6\text{H}_4(\text{CO}_2)\text{R}
\]

This method has been used to characterize primary and secondary alcohols as early as 1904 and have been used many times since. The hydrogen phthalate esters lend themselves readily to resolution since they offer an acid functional group. Satisfactory methods have been reported for the resolution of all types of aliphatic and mixed aliphatic-aromatic secondary alcohols using these derivatives.\(^\text{16-21}\)

\[\text{References}\]

17 R. H. Pickard and J. Kenyon, \textit{ibid.}, 99, 58 (1911).

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The use of these half phthalates to characterize tertiary alcohols was not accomplished until 1936 when Fessler and Shriner\textsuperscript{24} reported the preparation of half phthalate derivatives of simple trialkyl carbinols. The yields ranged from 36\% to 66\%. The method involved the treatment of the alcohols with ethyl magnesium iodide to obtain the alkoxy magnesium halide which was then treated with tetrachlorophthalic anhydride. The reactions used are shown below:

\[
R_1 - C - OH + \text{EtMgBr} \rightarrow R_1 - C - O\text{MgBr}
\]

\[
\text{Tetrachlorophthalic Anhydride} \rightarrow R_1 - C - O\text{C}-\text{Cl}
\]

\[
H^+, H_2O \rightarrow R_1 - C - O\text{C}-\text{CO}_2\text{H}
\]

No mixed aliphatic-aromatic alcohols were characterized and under no conditions was the half phthalate of triphenylcarbinol prepared.

Doering and Zeiss\textsuperscript{25} in 1950 reported the preparation of the hydrogen phthalate derivative of 2,4-dimethylhexan-4-ol. The method involved obtaining the potassium salt of the alcohol by boiling the alcohol with potassium metal and then adding phthalic anhydride to the potassium alkoxide. Later, in 1951, Zeiss\textsuperscript{26} used the same method to prepare the hydrogen phthalate of 2-phenyl-2-butanol. However, vigorous reaction conditions, lengthy reaction time, and poor yields make this method unsuitable as a general laboratory procedure.

More recently Thaker and Dave\textsuperscript{27} reported the preparation of the hydrogen phthalate of ethylphenyl p-tolyl methanol and \( \alpha \)-naphthylphenyl p-tolyl methanol under much milder conditions. Their procedure involved the reaction of the alcohol with phthalic anhydride in the presence of triethylamine at 90-96\(^\circ\)C for a period of sixteen to eighteen hours. Their method of preparing the hydrogen phthalate derivatives was contrary to the claims made by Balfe and Kenyon.\textsuperscript{28} They reported that they could not make the hydrogen phthalate of triphenylcarbinol using the reaction of the alcohol with phthalic anhydride in the


presence of triethylamine. Indeed, attempts in this laboratory to repeat the work of Thaker have failed to give the reported results.

2. Discussion of Experimental Results

In our research, we have found a convenient procedure for the preparation of hydrogen phthalate ester derivatives of aliphatic, mixed aliphatic-aromatic, and aromatic tertiary alcohols.\textsuperscript{29} The procedure involves the use of the strong base triphenylmethyl sodium to remove the proton from the alcohol at room temperature. This step is very convenient since the triphenylmethyl sodium which has a blood red colour in ether can be titrated rapidly into the colourless ethereal alcohol solution until a persistent red colour occurs. This indicates the complete removal of the proton from the alcohol. To this solution the phthalic anhydride is added and after a short period of stirring (1-2 hours) the solid derivative is obtained. The yields of these derivatives were good with the exception of triphenylcarbinol, and the whole procedure is relatively fast. The solid hydrogen phthalate esters can be identified by their melting points and neutralization equivalents. The reaction sequence used is indicated on the following page.

During the preparation of the hydrogen phthalates of twelve different tertiary alcohols a very interesting phenomenon was observed. It was found that, with the exception of the hydrogen phthalate of triphenylcarbinol, all the half phthalates decomposed on heating.

\[ R_1 - \text{C-H} + (\text{C}_6\text{H}_5)_2\text{C}^\ominus \text{Na}^\oplus \rightarrow R_1 - \text{C-O}^\ominus \text{Na}^\oplus \]

Phthalic Anhydride

\[
\begin{align*}
\text{C} - \text{O} - \text{C} - R_1 \\
\text{R}_2
\end{align*}
\]

\[ \text{CO}_2^\ominus \text{Na}^\oplus \]

\[ \text{H}^\ominus , \text{H}_2\text{O} \]

\[
\begin{align*}
\text{C} - \text{O} - \text{C} - R_1 \\
\text{R}_2
\end{align*}
\]

\[ \text{CO}_2\text{H} \]
The following table gives the starting alcohols, the melting points, and the decomposition points of the corresponding hydrogen phthalate ester derivatives.

**TABLE I**

<table>
<thead>
<tr>
<th>Starting Alcohol</th>
<th>Melting Point$^a$</th>
<th>Decomposition Point$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>t-Butyl alcohol</td>
<td>87-88</td>
<td>151-155</td>
</tr>
<tr>
<td>t-Amyl alcohol</td>
<td>62-63</td>
<td>144-146</td>
</tr>
<tr>
<td>3-Methyl-3-pentanol</td>
<td>80-81</td>
<td>136-138</td>
</tr>
<tr>
<td>3-Ethyl-3-pentanol</td>
<td>77-78</td>
<td>132-133</td>
</tr>
<tr>
<td>2,3-Dimethyl-2-butanol</td>
<td>95-96</td>
<td>137-140</td>
</tr>
<tr>
<td>2,3-Dimethyl-2-pentanol</td>
<td>113-120</td>
<td>132-135</td>
</tr>
<tr>
<td>2-Phenyl-2-propanol</td>
<td>109-110</td>
<td>109-110</td>
</tr>
<tr>
<td>2-Phenyl-2-butanol</td>
<td>114-115</td>
<td>114-115</td>
</tr>
<tr>
<td>2-Phenyl-2-pentanol</td>
<td>105-106</td>
<td>105-106</td>
</tr>
<tr>
<td>3-Phenyl-3-pentanol</td>
<td>114-115</td>
<td>114-115</td>
</tr>
<tr>
<td>1,1-Diphenyl-1-ethanol</td>
<td>110</td>
<td>110</td>
</tr>
<tr>
<td>Triphenylcarbinol</td>
<td>251-253</td>
<td>no decomposition</td>
</tr>
</tbody>
</table>

*a.* All melting points and decomposition points were taken on the Fisher-Johns melting point apparatus.
The hydrogen phthalate esters of the aliphatic tertiary alcohols had decomposition points above their melting points. When one or two of the aliphatic groups were replaced with aromatic groups, the decomposition points of the half phthalates were lowered substantially and here the melting point and decomposition point occurred simultaneously. The half phthalate derivative of triphenylcarbinol did not decompose even at 300°. In all cases of decomposition, phthalic acid was obtained as the only solid derivative and olefin mixtures were the remaining products. The nature of these olefinic mixtures, their mode of formation, and their yield were studied under another research problem.

These hydrogen phthalate esters present a potential means to resolve any tertiary system. However, before this method could be used to resolve the optically active trityl system, it was necessary to find out whether the alcohol could be recovered after the resolution had been completed.

In general there are two types of fission possible in the reactions of carboxylic esters, alkyl-oxygen and acyl-oxygen:

\[
\begin{align*}
\text{alkyl-oxygen} & : R - C - O + R' \\
\text{acyl-oxygen} & : R - C + O - R'
\end{align*}
\]

Normally the hydrolysis of carboxylic esters in the presence of acids or bases proceed with fission at the acyl-oxygen bond. However, Day and Ingold\textsuperscript{31} pointed out that alkyl-oxygen bonds could be cleaved if the \(\alpha\)-alkyl carbon atom could obtain electrons from the rest of the system. The alkyl-oxygen cleavage had been shown to occur in the hydrolysis of esters by Kenyon and coworkers\textsuperscript{32} and later by Balfe.\textsuperscript{33,34}

In the cases studied, the alcohol portion \(R^1\) was optically pure and when the esters were hydrolyzed, racemization of the \(R^1\) group occurred. This indicated the presence of a planar carbonium ion as an intermediate. Similar results were obtained in the solvolysis of trialkyl esters\textsuperscript{35} the hydrolysis of triphenylmethyl acetate,\textsuperscript{36} and in the hydrolysis of triphenylmethyl benzoate.\textsuperscript{37} For this reason it was felt that base hydrolysis would not be applicable to any potentially optically active system.


In the resolution of 2-phenyl-2-butanol, Zeiss\textsuperscript{38} reported that the reductive cleavage of the optically pure hydrogen phthalate with lithium aluminium hydride occurred smoothly to give the dextro and levro rotatory carbinols in excellent yields. When reductive cleavage of the half phthalate of triphenylcarbinol was tried with lithium aluminium hydride, a compound was obtained whose infrared spectrum indicated both hydroxyl and carbonyl absorption bands. This was believed to be a result of the partial reduction of the half phthalate, i.e., only the free acid group was reduced leaving the ester carbonyl group in its normal state. The failure to reduce the ester group was interpreted as being the result of large steric hinderance of the triphenylmethyl system which prevented the reduction of the carbonyl group. Since no method was found to obtain the starting alcohol from the half phthalate in a manner which would allow retention of optical activity, resolution of an optically active triphenylmethyl system using this method was abandoned.

\textbf{Glycolic Acid Derivative}

\textbf{1. Theoretical Considerations}

Another approach to the problem of resolving an optically active trityl system was based on the inability of a $\beta$-halo ether to form an organometallic complex. It is well established that when one of the more electropositive metals such as sodium, magnesium, or zinc acts on a $\beta$-halo ether, the ether undergoes fission to produce a molecule of

\textsuperscript{38} H. H. Zeiss, \textit{loc. cit.}
metal alkoxide and a molecule of olefin. A mechanism for the process was proposed by Amstatz:\(^39\)

\[
R-O-\text{CH}_2-\text{CH}_2-X + \text{Mg} \rightarrow R-O-\text{CH}_2-\text{CH}_2. \\
R-O-\text{CH}_2-\text{CH}_2. + \cdot\text{MgBr} \rightarrow R-O-\text{CH}_2-\text{CH}_2^\oplus\text{MgBr} \\
R-O-\text{CH}_2-\text{CH}_2^\oplus\text{MgBr} \rightarrow R-O^\ominus + \text{CH}_2=\text{CH}_2 + \text{MgBr}
\]

Grignard\(^40\) made use of this reaction to cause cleavage of \(\beta\)-phenoxyethyl bromide. Wohl and Berthold\(^41\) achieved similar results with sodium while Boord\(^42,43\) made use of zinc in his well known Boord olefin synthesis.

2. Discussion of Experimental Results

It was important that a derivative be made of triphenylcarbinol such that a \(\beta\)-halo ether could be obtained as the final intermediate in the reaction. It was hoped that this \(\beta\)-halo ether could then be

\(^{40}\) M. V. Grignard, Compt. rendu., 138, 1048 (1904).
\(^{41}\) A. Wohl and E. Berthold, Ber., 42, 2175 (1910).
reacted with zinc, magnesium, or sodium to effect elimination and give the starting alcohol. The simplest β-halo ether that could be made was β-triphenylmethoxyethyl chloride. However, the resolution of the alcohol derivative could be accomplished most readily if an acid or base functional group were present. For that reason the glycolic acid derivative was the most practical acid derivative. Once the resolution had been completed by means of this acid derivative, then reduction of the acid to the corresponding alcohol and conversion to the chloride would yield the desired β-halo ether. The reaction sequence that was followed is shown below:
In all preliminary experiments the triphenylmethanol system was used because of its availability. It was felt that any reaction that was successful with the non-optically active system would be equally successful with a substituted potentially optically active trityl system. Once a possible route for the resolution has been found, the
procedure would be repeated with the potentially optically active system.

**Allyl Triphenylmethyl Ether**

In a preliminary experiment the sodium salt of the triphenylcarbinol was reacted with allyl chloride. The sodium salt of triphenylcarbinol was obtained by the action of the base triphenylmethyl sodium on the alcohol. The complete removal of the proton was indicated by the persistent red colour imparted to the solution by a slight excess of the base. The allyl chloride was then added and the mixture was stirred at room temperature for seven hours. The entire reaction mixture was poured on cracked ice and the resultant solid was recovered by filtration. The isolation of triphenylcarbinol as the final product indicated no ether formation using this method.

Next, the preparation of the allyl ether was tried using the method outlined by Helferich and coworkers.\(^4\) A mixture of triphenylmethyl chloride, pyridine, and allyl alcohol were stirred for a period of three hours at room temperature. The reaction mixture was handled in the same way as in the previous experiment and final analysis of the product showed that the desired allyl triphenylmethyl ether had been obtained.

**Glycerin-α-Triphenylmethyl Ether**

The next step in the sequence was the formation of the glycol of

the corresponding allyl triphenylmethyl ether. Helferich\textsuperscript{45} reported
the preparation of glycerin-\(\alpha\)-triphenylmethyl ether from the reaction
of glycerol and triphenylmethyl chloride in the presence of pyridine.
Attempts were made in this laboratory to obtain the glycol by the
oxidation of the double bond of the allyl triphenylmethyl ether. When
the permanganate oxidation of the double bond was carried out, the
reaction proceeded smoothly to give the pure glycol in good yields.

\textbf{Attempted Oxidation of Glycerin-\(\alpha\)-Triphenylmethyl Ether}

The oxidation of the glycol was tried using periodic acid.
However, in the experiments conducted, the final results showed that
no reaction occurred or else the glycol was cleaved in such a manner
that the starting triphenylcarbinol was obtained. The reaction
conditions necessary to cause cleavage at the glycol linkage could
not be found.

\textbf{Triphenylmethoxyacetic Acid}

Attempts to prepare triphenylmethoxyacetic acid directly using
the reaction of triphenylmethyl chloride and glycolic acid proved to
be quite successful. Wallis\textsuperscript{46,47,48} used a similar procedure to

\textsuperscript{45} B. F. Helferich, P. E. Speidel, and W. Toeldte, \textit{op. cit.},
p. 769.

\textsuperscript{46} E. S. Wallis, \textit{J. Am. Chem. Soc.}, 54, 1695 (1932).


\textsuperscript{48} E. S. Wallis and F. H. Adams, \textit{J. Am. Chem. Soc.}, 55, 3838
(1933).
prepare the d,l-phenylbiphenyl-a-napthylmethylthioglycolic acid using phenylbiphenyl-a-napthylmethyl chloride and thioglycolic acid. The method in this laboratory involved heating a mixture of triphenylmethyl chloride, glycolic acid, and pyridine for a period of twelve to fifteen hours. From this reaction mixture the triphenylmethoxyacetic acid was obtained in good purity and fair (60%) yields. The identification of the acid derivative was made by means of infrared spectrum, neutralization equivalent, and elemental analysis of the acid for carbon and hydrogen.

Reduction of Triphenylmethoxyacetic Acid

The reduction of the triphenylmethoxyacetic acid was accomplished using lithium aluminium hydride. The reduction proceeded smoothly to give ethanediol triphenylmethyl monoether.

It is well known that halohydrins undergo epoxide formation readily under the influence of strong alkali solutions. Should an analogous reaction be found to occur in the β-hydroxy ethers, the resolution of the trityl system could be greatly simplified. The desired reaction can be shown as follows:

\[
\text{R-O-CH}_2\text{-CH}_2\text{-OH} + \text{Na}^\circ \rightarrow \text{R-O-CH}_2\text{-CH}_2\text{-OH} \quad \text{R-O-CH}_2\text{-CH}_2\text{-OH} + \text{CH}_2\text{-CH}_2
\]
The alcohol was reacted with sodium in an anhydrous ether medium and the mixture was heated at reflux temperature. However, under the reaction conditions, no elimination occurred. The use of a higher boiling solvent such as dioxane did not alter the results.

2-Triphenylmethoxy-1-Chloroethane

The conversion of the hydroxy ether to the corresponding halo ether was accomplished using thionyl chloride. Care was taken to minimize ether cleavage by keeping the reaction mixture cold and by adding pyridine to the reaction solution to combine with the hydrochloric acid formed in the reaction. Using these precautions, no difficulty was encountered in the preparation of the β-halo ether.

Once the β-halo ether had been obtained, there were several metals which could be used to effect elimination. Magnesium was tried first and it was found that the elimination occurred to give the starting triphenylcarbinol. However, this elimination reaction occurred only at room temperature. If the reaction mixture was heated, the Grignard complex \((\text{C}_6\text{H}_5)_3\text{O}-\text{CH}_2-\text{CH}_2\text{MgX}\) formed rapidly as evidenced by the appearance of a deep red colouration in the ethereal solution. However, apparently this Grignard complex coupled to give the butane 1,4 diol triphenylmethyl diether before elimination can occur. The formation of the diether is supported by the infrared spectrum which showed no hydroxyl or chlorine absorption bands. When the same reaction was carried out at room temperature, the reaction proceeded much more slowly but after three days, a white precipitate of \((\text{C}_6\text{H}_5)_3\text{CO}^\circ\text{MgCl}\) had formed. Decomposition of this Grignard complex
gave the desired starting carbinol indicating that the elimination had occurred. Experimental conditions necessary for an analogous elimination to occur using zinc or sodium could not be found. In both cases, either the carbanion formed failed to eliminate or else a coupling product resulted.

Should it be possible to extend the above reaction sequence to an optically active triphenylmethyl system, it would provide a route for the resolution of the optically active carbinol. The triphenylmethyl system chosen was the p-chlorophenyl-p-bromophenylphenylcarbinol. It was prepared from the reaction of phenyl magnesium bromide with p-bromo-p'-chlorobenzophenone. Difficulty was encountered in obtaining the carbinol in a crystalline form. However, once some seed crystals of the pure carbinol were obtained, further crystallizations were greatly simplified. The melting point of the pure alcohol was higher than that previously recorded, but elemental analysis of the alcohol for carbon and hydrogen was well within the limits of experimental error.

p-Chlorophenyl-p-Bromophenylphenylmethoxyacetic Acid

The preparation of the glycolic acid derivative was accomplished in a similar manner to that used for the model system. The only difficulty encountered in the procedure involved the poor solubility of the sodium salt of the acid. On attempting to extract the reaction mixture with sodium carbonate, it was found that the sodium salt of the acid was not soluble in the carbonate layer to any appreciable
degree. When the basic layer was separated and acidified, only a very small amount of the acid was recovered. When the ether layer was washed with water and the water layer was poured on a mixture of cracked ice and concentrated hydrochloric acid, the glycolic acid derivative was obtained in fair yields (60%).

**Reduction of p-Chlorophenyl-p-Bromophenylphenylmethoxyacetic Acid**

Reduction of the acid with lithium aluminium hydride gave the desired alcohol in very poor yields (10%). The poor yield was believed to be a direct result of the formation of an insoluble lithium salt of the acid which prevented the reaction from proceeding to any appreciable degree.

**Methyl p-Chlorophenyl-p-Bromophenylphenylmethoxyacetate and Reduction**

The methyl ester of the acid was prepared to permit a more complete reduction with lithium aluminium hydride. The methyl ester was prepared by the action of diazomethane on the acid. The general procedure used was outlined in "Organic Reactions". The diazomethane was obtained by the reaction of concentrated potassium hydroxide on N-nitrosomethylurea. Once the methyl ester was formed, the reduction of the ester proceeded very smoothly to give the corresponding alcohol. Although the final product was not obtained in a crystalline form, an infrared spectrum showed no carbonyl absorption band and a very strong hydroxyl absorption band. This indicated that the desired product had been obtained.
Conversion of the alcohol to the corresponding chloride was carried out in the same manner as for the model system. Once again the product failed to crystallize but the infrared spectrum indicated that the reaction was successful and the chloride had been obtained.

Once familiarity with the reaction conditions had been achieved, the resolution of the optically active system was undertaken.

Resolution and Subsequent Reactions for Obtaining the Optically Pure Carbinol

Since choice of resolving agent and solvent for a particular system cannot be predicted, it was decided to try the most common and most available resolving agent, namely brucine. Equimolar amounts of anhydrous brucine and acid were dissolved in acetone and the racemic mixture of the diastereoisomeric salts crystallized from the solution. The specific rotation of this racemic mixture taken in chloroform was $-11.45^\circ$. After several recrystallizations from dilute acetone solutions, the optical rotation of the less soluble salt reached a constant value of $-15.1^\circ$. The elemental analysis of the brucine salt for carbon, hydrogen, and nitrogen corresponded with those calculated for $\text{C}_{14}\text{H}_{22}\text{BrClN}_2\text{O}_7$.

The optically pure glycolic acid derivative was recovered in the normal manner and showed a specific rotation of $-0.37^\circ$. Because of this low specific rotation several other solvents were used to confirm that complete resolution of the acid had been obtained and that the
optically pure salt was not in reality a composite of the two diastereoisomers in a definite percentage. When the recrystallizations were repeated using ethanol and ethyl acetate as solvents, the same constant maximum specific rotation of $-15.1^\circ$ was obtained. This value was taken to be the maximum rotation attainable for the brucine salt.

The optically pure 2-((p-chlorophenyl-p-bromophenylphenylmethoxy)-1-chloroethane was obtained in the manner already discussed. The ester, the alcohol, and the final chloride showed no appreciable optical rotation. Treatment of the chloride with magnesium gave only small amounts of the starting trityl carbinol even when the reaction mixture was stirred for thirty days. This lengthy reaction time made the procedure unattractive for the attainment of the optically pure alcohol from the β-halo ether.

In order to increase the rate of the elimination reaction and also to inhibit any possible reaction of the magnesium with the halogen atoms already on the aromatic rings, the author decided to convert the chloride to the iodide. It was then hoped that the magnesium would react with the iodide to effect the elimination reaction at a faster rate with no undesirable side effects. The preparation of the iodide was attempted using the reaction of the corresponding chloride with potassium iodide. When the chloride and potassium iodide were placed in acetone, a red colouration appeared at once. After a short period of standing at room temperature the acetone solution was very dark brown due to the presence of free iodine. Analysis of the final product showed it to be a hydroxy compound.
Investigation of the nature of this reaction of the β-halo ether with iodine was carried out using the model system since all the intermediates and the starting alcohol were readily attainable in the solid form. When the β-triphenylmethoxyethyl chloride was reacted with potassium iodide in acetone, the product which was isolated was shown to be triphenylcarbinol. A possible mechanism for the liberation of the iodine and the formation of the triphenylcarbinol is illustrated as follows:

\[
\begin{align*}
R - O - CH_2CH_2Cl & \xrightarrow{KI} R - O - CH_2CH_2I \\
R - O^+CH_2CH_2I & \xrightarrow{I^+} R - O^+CH_2 + CH_2=CH_2 + I_2
\end{align*}
\]

It was necessary to insure that the alkyl-oxygen bond at the asymmetric centre would not be broken during the reaction if the above elimination reaction was to be used in the resolution of the potentially active system. To ascertain that the reaction did not involve a
carbonium ion, the reaction was run in a methanol-acetone solution. Heterolysis of the carbon-oxygen bond would give a carbonium ion and would result in the formation of the ether, methyl triphenylmethyl ether. When the reaction was carried out, the methyl triphenylmethyl ether was obtained indicating the presence of the carbonium ion in the reaction.

Further investigations were carried out to determine whether the free carbonium ion was formed during the reaction or whether it was formed after the initial elimination had taken place. Triphenylcarbinol was allowed to stand in methanol-acetone solutions in the presence of potassium iodide, and iodine alone and in combinations. It was found that ether formation resulted only when iodine was present. Thus it was established that the carbonium ion formed due to the action of the iodine liberated in the reaction on the triphenylcarbinol formed. Attempts to remove the iodine liberated by adding sodium thiosulphate to the reaction mixture failed to prevent the formation of the ether. This was probably due to the insolubility of the sodium thiosulphate in the reaction medium.

Since the iodine apparently caused the formation of the triphenylmethyl carbonium ion, it was of interest to see if the triphenylmethyl carbonium ion could be combined with other alcohols other than methanol. The table on the following page shows five ethers which have been formed using iodine.
### TABLE II

<table>
<thead>
<tr>
<th>Starting Alcohols</th>
<th>Ether Formed</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triphenylcarbinol and methanol</td>
<td>Methyl triphenylmethyl ether</td>
<td>91%</td>
</tr>
<tr>
<td>Triphenylcarbinol and ethanol</td>
<td>Ethyl triphenylmethyl ether</td>
<td>78%</td>
</tr>
<tr>
<td>Triphenylcarbinol and n-propyl alcohol</td>
<td>Propyl triphenylmethyl ether</td>
<td>78%</td>
</tr>
<tr>
<td>Triphenylcarbinol and isopropyl alcohol</td>
<td>Isopropyl triphenylmethyl ether</td>
<td>45%</td>
</tr>
<tr>
<td>Triphenylcarbinol and benzyl alcohol</td>
<td>Benzyl triphenylmethyl ether</td>
<td>50%</td>
</tr>
</tbody>
</table>

Further extension of this preparative method is under investigation in this laboratory. It was of interest to see if iodine could be used to form other ethers using systems capable of forming stable carbonium ions such as the benzyl systems and the benzylhydryl systems.

At this point, work was directed towards finding an alternate method for resolving a potentially optically active trityl system. If this alternate method failed, then attention would be refocused on the glycolic acid derivative to see if the difficulties encountered could be worked out.
Hydracrylic Acid Derivative

1. Theoretical Considerations

The final approach to the problem involved the preparation and breakdown of the hydracrylic acid derivative. It was hoped that once the acid derivative had been prepared and resolved, utilization of a strong base such as triphenylmethyl sodium would effect breakdown of the acid in a manner similar to a reverse Michael reaction.

The Michael condensation[^49] involves the addition of an anion formed by the removal of a proton by a base (usually an alkali metal alkoxide) to a conjugated system such as an $\alpha,\beta$ unsaturated carbonyl compound. Normally any compound which has a hydrogen atom active by the Zerewitinoff test can serve as a donor. The general reaction scheme of the Michael condensation can be written as follows:

\[
\text{R - C} = \text{C - R}_2 + \text{B}^\ominus \rightarrow \text{R} - \text{C} - \text{C} - \text{R}_2 \tag{1}
\]

\[
\text{R} - \text{C} - \text{C} - \text{C} = 0 + \text{B}^\ominus \rightarrow \text{R} - \text{C} - \text{C} - \text{C} = 0 + \text{B}^\ominus
\]


The overall reaction is in effect a 1,4 addition of the donor to the conjugated system.

It is well known that in many cases the alkoxide anions which are frequently used in the Michael condensation act as the electron donors and undergo addition to the conjugated system. This is particularly the case when the conjugated systems are acrylic esters or acrylonitrile. The reaction sequence is shown below:

\[
\begin{align*}
R-O^\ominus + CH_2=CH-C=O-R' & \rightarrow R-O=CH_2=CH-C=O-R' \\
& \quad \text{ROH}
\end{align*}
\]

The Michael condensation has been shown to be a reversible process: i.e. the adduct can be split into the two starting components by the same catalyst that originally effected the condensation. In general, low temperatures\(^5\) and an excess of one of the reactants favour the forward condensation process while elevated temperatures\(^5\) and excess base catalyst favour the reverse process. It was this latter process which was essential for the resolution of the optically active trityl system using the hydraacrylic acid derivative method.


2. Discussion of Experimental Results

The anticipated synthesis and breakdown of the hydracrylic acid derivative is shown below:

\[
\begin{align*}
\text{C}_6\text{H}_5 - \text{C} - \text{Cl} & \quad \text{+} \quad \text{HO-CH}_2\text{-CH}_2\text{-C-OH} \quad \text{→} \quad \text{C}_6\text{H}_5 - \text{C} - \text{O-CH}_2\text{-CH}_2\text{-C-OH} \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3\text{N}_2 & \quad \text{→} \quad \text{C}_6\text{H}_5 - \text{C-O-CH}_2\text{-CH}_2\text{-C-OCH}_3 \\
\left(\text{C}_6\text{H}_5\right)_3\text{C}\oplus & \quad \text{Reverse Michael}
\end{align*}
\]

\[
\begin{align*}
\text{C}_6\text{H}_5 - \text{C} - \text{O-CH}_2\text{-CH}_2\text{-C-OCH}_3 & \quad \text{→} \quad \text{C}_6\text{H}_5 - \text{C} - \text{O} + \text{CH}_2\text{-CH-C-OCH}_3 \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5
\end{align*}
\]

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β-Triphenylmethoxypropionic Acid

The same general method which was successful for the preparation of the triphenylmethoxyacetic acid was tried. Here the chloride was reacted with β-hydroxypropionic acid utilizing pyridine as a solvent. However, after a reflux period of two days, none of the desired product was obtained. In another run the heating period was increased from two to six days. This enabled the isolation of the β-triphenylmethoxypropionic acid in an average yield of twenty-five per cent. Physical constants were in agreement with those reported in the literature.

Once this acid had been prepared, it was of interest to see whether any difficulties would be encountered in the remainder of the reaction sequence previously discussed. The methyl ester of the acid was prepared as described on page 59 for the preparation of methyl triphenylmethoxyacetate. Once the methyl ester had been prepared, it was reacted with triphenylmethyl sodium. On final analysis, it was found that the product formed was triphenylcarbinol. For the present author's work it was of interest to see whether there was a carbonium ion or an alkoxide ion formed in the reaction. The reaction of methyl β-triphenylmethoxypropionate with triphenylmethyl sodium was repeated but after the addition of the base, phthalic anhydride was added. The formation of the half phthalate derivative of triphenylcarbinol showed that in reality the alkoxide ion was formed. The

formation of an alkoxide ion makes this reaction sequence very attractive in that the alkoxide ion can be reacted with various reagents such as anhydrides, sulphonates, etc., to yield the corresponding half esters and sulphonates whose solvolysis rates could be studied.

\textbf{β-Triphenylmethoxypropionitrile and Attempted Hydrolysis}

In order to find a more fruitful method to prepare the β-tri-phenylmethoxypropionic acid, attention was focused on the corresponding nitrile and ester of β-triphenylmethoxypropionic acid. When the triphenylmethyl chloride was reacted with hydraeylonitrile in ether containing a small amount of pyridine, the nitrile was obtained. However, numerous attempts to hydrolyze this nitrile to the acid using various reagents such as potassium hydroxide, sulphuric acid, hydrochloric acid, and trifluoroacetic acid failed to give the desired acid.

\textbf{Methyl β-Triphenylmethoxypropionate and Subsequent Hydrolysis}

Helferich and coworkers\textsuperscript{54} reported the preparation of ethyl β-triphenylmethoxypropionate. This same procedure was used to prepare the methyl ester. The reaction of methyl β-hydroxypropionate with triphenylmethyl chloride using pyridine as a solvent gave the desired methyl β-triphenylmethoxypropionate. The base hydrolysis of the ester was accomplished using a potassium hydroxide solution to give the corresponding acid. The overall yield of the preparation and saponification of the ester was fair (65%).

\textsuperscript{54} E. F. Helferich, L. Moog, and A. Junger, loc. cit.
To avoid unnecessary problems in purifying the ester, the ester was not isolated. Instead, the total crude product obtained in the preparation of the methyl β-triphenylmethoxypropionate was immediately saponified. This enabled the removal of any base insoluble compound and gave the β-triphenylmethoxypropionic acid in the pure form.

**Methyl β-(p-Chlorophenyl-p-Bromophenylphenylmethoxy)-Propionate**

This compound was prepared in the same manner as that used for the model system. By reacting p-chlorophenyl-p-bromophenylphenylmethyl chloride with methyl β-hydroxypropionate using pyridine as a solvent, the potentially optically active propionic acid derivative was obtained. No attempt to check yield was made with this preliminary experiment. Neutralization equivalent and elemental analysis of the acid for carbon and hydrogen were as calculated.

After the work in this laboratory on the hydrylic acid derivative had almost been completed, Murr\(^{55}\) reported the resolution of a triaryl carbinol. His method of resolution also involved a glycolic acid intermediate and the reaction sequence he used is outlined below:

\[
\begin{align*}
R-\text{OH} & \xrightarrow{\text{acetyl chloride}} R\text{Cl} & & \xrightarrow{\text{pyridine-benzene}} R\text{OCH}_2\text{CO}_2\text{CH}_3 \\
& & & & \\
& & & & 
\end{align*}
\]

The system he chose for his work was the phenylbiphenyl-α-naphthyl-methanol.
Resume and Conclusions

Although complete resolution of a potentially optically active trityl system has not been completed, two feasible routes to this end have been found using the model system (triphenylcarbinol). The two methods involving the glycolic acid intermediate and the hydracrylic acid intermediate are shown by the reaction schemes on pages 52 and 67, respectively. Both could prove very useful with the latter particularly good because of its better overall yield.

Two new reactions were found during the course of the research. One reaction was the low temperature pyrolysis of the hydrogen phthalate esters of tertiary alcohols to give a mixture of olefins and phthalic acid. A second reaction involved the formation of trityl ethers. Here the trityl carbinol was combined with a simple alcohol in the presence of iodine to give the corresponding alkyl trityl ether.

Finally, the research in this laboratory has resulted in the development of a general method which can be used to characterize tertiary alcohols. The hydrogen phthalate esters of the tertiary alcohols are readily formed utilizing the base triphenylmethyl sodium. These solid derivatives can be identified by their melting points and neutralization equivalents.
CHAPTER III

EXPERIMENTAL PROCEDURE

Preparation of Tertiary Alcohols

Tertiary butyl alcohol, tertiary amyl alcohol, and triphenyl-methanol were obtained commercially from Fisher Scientific Company. In the preparation of the remaining alcohols the same apparatus was used and the manner in which the Grignard complex was decomposed was also the same. The preparation of 3-methyl-3-pentanol will serve as an example of the general method used. All starting alkyl halides and ketones were certified reagents obtained from Fisher Scientific Company.

3-Methyl-3-Pentanol. - Magnesium turnings (14.4 g., 0.60 mole) and anhydrous ether (300 ml.) were placed in a two-litre, three-necked, round-bottomed flask which was equipped with a mechanical stirrer, dropping funnel and condenser (drying tube attached). A solution of methyl iodide (85.2 g., 0.60 mole) and anhydrous ether (250 ml.) was added dropwise at a rate sufficient to maintain steady reflux. After this solution was added, the reaction mixture was stirred at room temperature for thirty minutes, and then cooled by immersing the flask in crushed ice. An ethereal solution (250 ml.) of reagent grade 3-pentanone (43.1 g., 0.50 mole) was added to the cooled mixture over a period of two hours after which the reaction mixture was stirred for an additional hour. The contents were then poured onto a mixture of cracked ice and concentrated hydrochloric acid in order to decompose.
the Grignard complex. The ether layer was separated and washed successively with water and 5% sodium carbonate. After an additional washing with water the ether solution was dried over anhydrous sodium sulphate. The sodium sulphate was removed by filtration and the ether was removed in vacuo. Fractional distillation of the resultant oil gave 3-methyl-3-pentanol, b.p. 120-122°; n_D^0 1.4115 (reported\(^1\) b.p. 121.1-122.9°; n_D^2 \(1.418\).)

3-Ethyl-3-Pentanol. This compound was prepared according to the method of Baratajev and Saijew.\(^2\) Ethyl iodide (93.6 g., 0.60 mole) was added to magnesium turnings (14.4 g., 0.60 mole) in 300 ml. anhydrous ether to give the ethyl magnesium iodide. To this ethereal Grignard solution was added 3-pentanone (43.1 g., 0.50 mole) which was dissolved in anhydrous ether (250 ml.). After the Grignard complex was decomposed, the ether layer was separated and dried with anhydrous sodium sulphate. The ether solution was removed in vacuo. Fractional distillation of the resultant oil gave 3-ethyl-3-pentanol, b.p. 139-142°; n_D^25 1.4295 (reported\(^3\) b.p. 140-142°; n_D^22 \(1.4226\).)

2,3-Dimethyl-2-Butanol. To methyl magnesium iodide which was prepared from methyl iodide (85.2 g., 0.60 mole) and magnesium turnings (14.4 g., 0.60 mole) was added an ethereal solution of methyl isopropyl ketone

1 Pariselle and Simon, Compt. rendu., 173, 86 (1921).
3 A. Spassow, Ber., 70, 1926 (1937).
(43.0 g., 0.50 mole in 250 ml. anhydrous ether). The Grignard complex was decomposed in the usual manner and the ether layer was separated. After the layer was dried over anhydrous sodium sulphate, the sodium sulphate was removed by filtration and the ether layer was concentrated in vacuo. Fractional distillation of the remaining liquid gave 2,3-dimethyl-2-butanol, b.p. 115-118°; $n_D^{29}$ 1.4112 (reported b.p. 117-118°; $n_D^{25}$ 1.4151).

2,3-Dimethyl-3-Pentanol. - Ethyl magnesium iodide was prepared from the reaction of ethyl iodide (93.6 g., 0.60 mole) and magnesium turnings (14.4 g., 0.60 mole) in 300 ml. anhydrous ether. A solution of methyl isopropyl ketone (43.0 g., 0.50 mole) and 250 ml. anhydrous ether was added slowly. Decomposition of the Grignard complex in the usual manner and fractional distillation of the resultant oil yielded 2,3-dimethyl-3-pentanol, b.p. 138-140°; $n_D^{29}$ 1.4190 (reported b.p. 136°; $n_D^{20}$ 1.4287).

2-Phenyl-2-Propanol. - This compound was prepared according to the method of Tissier and Grignard. An ethereal solution of phenyl magnesium bromide was prepared from magnesium turnings (14.4 g., 0.60 mole) and bromobenzene (94.2 g., 0.60 mole) and to this was added slowly

4 J. Lindner, Monatsh., 32, 419 (1911).
6 Tissier and Grignard, Compt. rendu., 132, 1184 (1901).
acetone (29.0 g., 0.50 mole) dissolved in anhydrous ether (250 ml.). The reaction mixture was handled in the usual manner and fractional distillation of the final liquid yielded 2,3-dimethyl-3-pentanol, b.p. 88-89° (13 mm.); νD 20.5195 (reported7 b.p. 215-220° (760 mm.); νD 19 1.5314).

2-Phenyl-2-Butanol. - An ethereal solution of phenyl magnesium bromide was prepared from magnesium turnings (14.4 g., 0.50 mole) in 250 ml. anhydrous ether. The Grignard complex was decomposed and fractional distillation of the residual liquid after removal of solvent gave 2-phenyl-2-butanol, b.p. 98-99° (12 mm.); νD 28 1.5164 (reported8 b.p. 211-212° (760 mm.); b.p. 102° (14 mm.); νD 22 1.5158).

3-Phenyl-3-Pentanol. - Bromobenzene (94.2 g., 0.60 mole) in ether solution was reacted with magnesium turnings (14.4 g., 0.60 mole) to give phenyl magnesium bromide. 3-Pentanone (43.1 g., 0.50 mole) in anhydrous ether (250 ml.) was added. Breakdown of the Grignard complex and subsequent isolation of the crude product gave on fractional distillation 3-phenyl-3-pentanol, b.p. 101-103°; νD 22 1.5189 (reported9 b.p. 223-224° (762 mm.); b.p. 109° (15 mm.); νD 20 1.5165).

7 A. Klages, Ber., 35, 2637 (1902).
8 Ibid., p. 3507
9 A. Klages, Ber., 36, 3692 (1903).
2-Phenyl-2-Pentanol. - An ethereal solution of phenyl magnesium bromide was prepared from bromobenzene (94.2 g., 0.60 mole) and magnesium turnings (14.4 g., 0.60 mole). 2-Pentanone (43.1 g., 0.50 mole) which was dissolved in 250 ml. anhydrous ether was added slowly. Decomposition of the Grignard complex in the usual manner gave a clear liquid which on fractional distillation yielded 2-phenyl-2-pentanol, b.p. 107-109° (12 mm.); \( n_D^\text{11} \) 1.5095 (reported b.p. 216° (760 mm.); b.p. 112-114° (14 mm.).

1,1-Diphenyl-1-Ethanol. - This alcohol was prepared according to the method of Tiffeneau.\(^\text{11}\) An ethereal solution of phenyl magnesium bromide was prepared using bromobenzene (94.2 g., 0.60 mole) and magnesium turnings (14.4 g., 0.60 mole). Acetophenone (60.1 g., 0.50 mole) which was dissolved in anhydrous ether (250 ml.) was added dropwise. The Grignard complex was decomposed in the usual manner. The ether layer was separated and dried over anhydrous sodium sulphate. After removal of the sodium sulphate the ether solution was concentrated in vacuo whereupon a precipitate formed. Recrystallization of the product from a chloroform-petroleum ether (b.p. 30-60°) solvent pair yielded white crystals of pure 1,1-diphenyl-1-ethanol, m.p. 78-80° (reported m.p. 80-81°).

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Sodium Amalgam (3%). - In a porcelain crucible one-third filled with mineral oil was placed freshly cut sodium (34.5 g., 1.5 g.-atom). The crucible was heated with a free flame until the sodium had melted and mercury (1150 g., approx. 84 ml.) was added slowly. The solution was then allowed to cool whereupon the amalgam became hard. The amalgam was washed with toluene to remove the mineral oil and then it was pulverized into small pieces in an iron mortar.

Triphenylmethyl Sodium. - This compound was prepared according to the method of Renfrow and Hauser.\textsuperscript{13} A solution of triphenylmethyl chloride (200 g., 0.72 mole) and anhydrous ether (1.75 litres) was placed in a two-litre bottle. To this was added sodium amalgam (3\%) and the bottle was fitted with a rubber stopper which was wired tightly in place. The bottle was placed in a mechanical shaker for a period of eight hours during which time the ethereal solution slowly became deep blood-red in colour. The bottle was refrigerated for one hour and the solids (sodium chloride and mercury) formed in the reaction were allowed to settle.

The ethereal solution of triphenylmethyl sodium was separated from the sodium chloride and free mercury in the following manner: A two-holed stopper was fitted with a straight glass tube and a glass U-tube and then placed in the mouth of the reaction bottle. One end of the U-tube reached well down into the ethereal solution of

the base (but just above the solid residues) while the other end extended into a previously dried bottle. Nitrogen was blown through the straight tube and the ethereal solution was forced through the U-tube into the dried container. In this way the solution was separated cleanly from the residual sodium chloride and mercury without exposition of the base to the moisture in the atmosphere.

**Preparation of Hydrogen Phthalate Esters of Tertiary Alcohols**

All of the hydrogen phthalate esters were prepared by the addition of phthalic anhydride (resublimed) to an ethereal solution of the sodium salt of the corresponding tertiary alcohols. These sodium salts were conveniently prepared by treatment of the tertiary alcohol in ether solution with the solution of triphenylmethyl sodium. Essentially equivalent amounts of all reagents were used. The only variation in the preparation of the half phthalates of the tertiary alcohols was the stirring time of the sodium alkoxides with the phthalic anhydride. This time varied from one to three hours depending upon the steric requirements of the particular alcohol. Thus the stirring time required with the tertiary butyl alcohol and the triphenylcarbinol was one and three hours respectively. The following preparation of the hydrogen phthalate ester of tertiary butyl alcohol will exemplify the general procedure used. For the remaining preparations, only the pertinent data such as quantities of reagents, yields, melting points, decomposition points, and analysis are given.
Hydrogen-2-Methylpropyl-2-Phthalate. - To a solution of tertiary butyl alcohol (5.0 g., 0.068 mole) in anhydrous ether (150 ml.) was added rapidly with stirring an ethereal solution of triphenylmethyl sodium until a persistent red colour indicated a slight excess of base. This procedure was carried out in a one-litre Erlenmeyer flask fitted loosely with a polyethylene stopper. Phthalic anhydride (10.6 g., 0.068 mole) was added in one portion and the mixture was stirred for one-half hour. Water (200 ml.) was added, the layers were separated, and the water layer was poured on a mixture of cracked ice and concentrated hydrochloric acid. The precipitate which formed was recovered by filtration, air-dried, and recrystallized from a chloroform-petroleum ether (b.p. 30-60°) solvent pair. A white powder of hydrogen-2-methylpropyl-2-phthalate was obtained, m.p. 87-88°. The average crude yield of seven runs was 65%. 

Analysis: Calcd. for C_{12}H_{24}O_{4}: C, 64.85; H, 6.90.

Found: C, 64.90; H, 6.38.


Hydrogen-2-Methylbutyl-2-Phthalate. -

Amounts: 5.0 g. (0.057 mole) tertiary amyl alcohol; 150 ml. anhydrous ether, 8.44 g. (0.057 mole) phthalic anhydride.

Yields: 70% (average of nine runs).

Melting Point: 62-63°.

Decomposition Point: 144-146°.
Hydrogen-3-Methylpentyl-3-Phthalate. -

Amounts: 5.0 g. (0.049 mole) 3-methyl-3-pentanol,
150 ml. anhydrous ether, 7.25 g. (0.049 mole)
phthalic anhydride.

Yields: 65% (average of nine runs)

Melting Point: 80-81°.


Analysis: Calcd. for C_{13}H_{16}O_4: C, 66.08; H, 6.83.
Found: C, 66.09; H, 6.88.


Hydrogen-3-Ethylpentyl-3-Phthalate. -

Amounts: 5.0 g. (0.043 mole) 3-ethyl-3-pentanol,
150 ml. anhydrous ether, 6.50 g. (0.043 mole)
phthalic anhydride.

Yields: 85% (average of seven runs)

Melting Point: 77-78°.

Decomposition Point: 132-133°.

Analysis: Calcd. for C_{14}H_{18}O_4: C, 67.18; H, 7.25.
Found: C, 66.79; H, 6.99.

Hydrogen-2,3-Dimethylbutyl-2-Phthalate. -

Amounts: 5.0 g. (0.049 mole) 2,3-dimethyl-2-butanol,
150 ml. anhydrous ether, 7.25 g. (0.049 mole)
phthalic anhydride.

Yields: 80% (average of eight runs)

Melting Point: 95-96°.
Decomposition Point: 137-140°.

Analysis: Calcd. for C_{14}H_{18}O_4: C, 67.18; H, 7.25.
Found: C, 67.17; H, 7.28.

Hydrogen-2,3-Dimethylpentyl-3-Phthalate. -

Amounts: 5.0 g. (0.043 mole) 2,3-dimethyl-3-pentanol,
150 ml. anhydrous ether, 6.50 g. (0.043 mole)
phthalic anhydride.

Yields: 65% (average of seven runs)

Melting Point: 118-120°.
Decomposition Point: 132-135°.

Analysis: Calcd. for C_{15}H_{20}O_4: C, 68.06; H, 7.76.
Found: C, 68.19; H, 7.71.

Hydrogen-2-Phenylpropyl-2-Phthalate. -

Amounts: 10.0 g. (0.073 mole) 2-phenyl-2-propanol,
150 ml. anhydrous ether, 10.8 g. (0.073 mole)
phthalic anhydride.

Yields: 80% (average of five runs)
Melting Point: 109-110°.

Analysis: Calcd. for C₁₇H₁₆O₄: C, 71.82; H, 5.67.
         Found: C, 71.32; H, 5.65.

Hydrogen-2-Phenylbutyl-2-Phthalate.

Amounts: 10.0 g. (0.067 mole) 2-phenyl-2-butanol
         150 ml. anhydrous ether, 9.88 g. (0.067 mole)
         phthalic anhydride.

Yields: 80% (average of three runs)

Melting Point: 114-115°.
Decomposition Point: 114-115°.

Analysis: Calcd. for C₁₈H₁₆O₄: C, 72.47; H, 6.08.
         Found: C, 72.52; H, 6.07.

Hydrogen-3-Phenylpentyl-3-Phthalate.

Amounts: 10.0 g. (0.061 mole) 3-phenyl-3-pentanol,
         150 ml. anhydrous ether, 9.03 g. (0.061 mole)
         phthalic anhydride.

Yields: 85% (average of six runs)

Melting Point: 114-115°.
Decomposition Point: 114-115°.

Analysis: Calcd. for C₁₉H₂₀O₄: C, 73.05; H, 6.45.
         Found: C, 73.08; H, 6.47.
Hydrogen-2-Phenylpentyl-2-Phthalate. -

Amounts: 10.0 g. (0.061 mole) 2-phenyl-2-pentanol,
150 ml. anhydrous ether, 9.03 g. (0.061 mole)
phthalic anhydride.

Yields: 70% (average of six runs)
Melting Point: 105-106°.
Decomposition Point: 105-106°.
Analysis: Calcd. for C_{19}H_{20}O_4: C, 73.05; H, 6.45.
          Found:  C, 73.15; H, 6.47.

Hydrogen-1,1-Diphenyl-1-Phthalate. -

Amounts: 10.0 g. (0.050 mole) 1,1-diphenyl-1-ethanol,
150 ml. anhydrous ether, 7.40 g. (0.050 mole)
phthalic anhydride.

Yields: 80% (average of eight runs)
Melting Point: 110°.
Decomposition Point: 110°.
Analysis: Calcd. for C_{22}H_{18}O_4: C, 76.28; H, 5.24.
          Found:  C, 76.31; H, 5.40.

Hydrogen-Triphenylmethyl Phthalate. -

Amounts: 10.0 g. (0.038 mole) triphenylmethanol,
150 ml. anhydrous ether, 5.63 g. (0.038 mole)
phthalic anhydride.

Yields: 30% (average of eight runs)
Melting Point: 251-253°.
Decomposition Point: no decomposition
Analysis: Calcd. for \( \text{C}_{27}\text{H}_{20}\text{O}_4 \): C, 79.39; H, 4.94.
Found: C, 79.44; H, 5.09.

**Allyl Triphenylmethyl Ether (3-Triphenylmethoxy-1-Propene).** - The preparation of allyl triphenylmethyl ether was accomplished using the method of Helferich and coworkers.\(^{14}\) Triphenylchloromethane (100 g., 0.36 mole) was dissolved in anhydrous ether (200 ml.) to which was added pyridine (80 ml.). Allyl alcohol (27.2 ml., 0.40 mole) was added dropwise with stirring. This operation was carried out in a 500-ml., three-necked, round-bottomed flask which was provided with a mechanical stirrer and a condenser (drying tube attached).

The reaction mixture was stirred at reflux temperature for three hours after which time a white solid (pyridine hydrochloride) formed in the flask. The reaction mixture was poured on a mixture of cracked ice and concentrated hydrochloric acid. The ether layer was separated, washed twice with 5% sodium carbonate, twice with distilled water, and finally dried over anhydrous sodium sulphate. The sodium sulphate was removed by filtration and the ether was concentrated in vacuo. The precipitate which formed was recovered by filtration, m.p. 70-71°. Recrystallization from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave white crystals of pure allyl triphenylmethyl ether, m.p. 77-78° (recorded\(^{14}\) m.p. 76°).

Glycerin-α-Triphenylmethyl Ether (1,2-Dihydroxy-3-Triphenylmethoxy-Propane).- Allyl triphenylmethyl ether (10.0 g., 0.03 mole) was dissolved in reagent grade acetone (200 ml.). To this was added an aqueous solution (200 ml.) which contained an equivalent amount (5.26 g.,) of potassium permanganate. Although the permanaganate was decolourized rapidly, the reaction mixture was stirred for an additional hour at room temperature. A few crystals of sodium sulfite were then added to remove any unreacted potassium permanganate. The insoluble precipitate (manganese dioxide) was removed by filtration and then the solution was partially concentrated by directing a jet of air on the surface. The precipitate which formed was recovered by filtration. Recrystallization of the crude product from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave pure glycerin-α-triphenylmethyl ether, m.p. 93-94°. This melting point corresponded with that previously reported. The average yield of seven runs was 70%.

Attempted Oxidation of Glycerin-α-Triphenylmethyl Ether. - The oxidative cleavage of glycerin-α-triphenylmethyl ether was attempted using periodic acid. The glycol (3.0 g., 0.01 mole) was placed in a 500-ml., single-necked, round-bottomed flask which was equipped with a magnetic stirrer. An aqueous solution (200 ml.) containing acetic acid (100 ml.) and periodic acid (8.00 g.) was added in one portion. The

temperature of the solution was raised to 55-60° and stirred at this temperature for three hours. The reaction mixture was then poured onto cracked ice and the precipitate which formed was recovered by filtration, m.p. 164-166°. The compound had an infrared spectrum identical with that of triphenylcarbinol and a mixture melting point with an authentic sample of triphenylcarbinol was not depressed.

The above reaction was repeated but this time the solution was not heated. The reaction mixture was handled in the same manner, and a precipitate was obtained, m.p. 75-83°. The infrared spectrum indicated that the compound which was recovered was a vinyl ether. However, further investigations regarding its formation and exact identification were delayed to a future date.

**Triphenylmethoxyacetic Acid.** - Triphenylchloromethane (100.0 g., 0.36 mole) was dissolved in pyridine (500 ml.). Glycolic acid (30.0 g., 0.40 mole) was added and the reaction mixture was stirred at reflux temperature for twelve to fifteen hours. This operation was carried out in a one-litre, three-necked, round-bottomed flask equipped with a mechanical stirrer and a reflux condenser (drying tube attached). On cooling the flask, large needle crystals of pyridine hydrochloride formed. The reaction mixture was poured onto a mixture of cracked ice and concentrated hydrochloric acid. The resultant oil was extracted with three portions of ether (200 ml. each) and the ether extracts were combined. The ether was removed in vacuo until the total volume was about 200 ml., the solution was then made basic by adding sodium carbonate solution. The aqueous layer was poured on a mixture of cracked ice and concentrated hydrochloric acid. The precipitate which
formed did not represent a good yield of the desired product. Water (200 ml.) was added to the ether layer and this aqueous layer was poured onto a mixture of cracked ice and hydrochloric acid. The precipitate which formed was recovered by filtration, m.p. 150-153°. Recrystallization of the product from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave a white powder, which, after drying in vacuo over phosphorous pentoxide for two hours at room temperature, showed m.p. 152-154°.

Analysis: Calcd. for C₁₂H₁₈O₃: C, 79.22; H, 5.70.
Found: C, 79.44; H, 5.78.

Ethanediol Triphenylmethyl Monoether. - The ethanediol triphenylmethyl monoether was obtained by the reduction of the triphenylmethoxyacetic acid with lithium aluminium hydride (Metal Hydrides Company) using the general procedure outlined in Organic Reactions.17 Solid lithium aluminium hydride and anhydrous ether (400 ml.) were placed in a one-litre, three-necked, round-bottomed flask which was equipped with a mechanical stirrer, a reflux condenser (drying tube attached), and a dropping funnel. A solution of triphenylmethoxyacetic acid (100 g., 0.36 mole) and anhydrous ether (100 ml.) was added dropwise at a rate sufficient to maintain steady reflux in the reaction flask. After the acid solution had been added, the reaction mixture was stirred at

reflux temperature for two hours. The excess lithium aluminium hydride was reacted with ethyl acetate. Then dilute hydrochloric acid solution was added to dissolve the aluminium salts which had formed during the reaction. The ether layer was separated and washed successively with five per cent sodium carbonate solution and water. After the ether layer was dried with anhydrous sodium sulphate and the sodium sulphate removed by filtration, the ether was removed in vacuo whereupon white crystals formed. The crystals were recovered by filtration, m.p. 93-98°. Recrystallization of the crude product from a chloroform-petroleum ether (30-60°) solvent pair gave pure ethandiol triphenylmethyl monoether, m.p. 104-105°. This melting point corresponded with that previously recorded. The average yield of four runs was 75%. The infrared spectrum gave all the absorption bands for the desired compound.

Reaction of Ethandiol Triphenylmethyl Monoether with Sodium. - Freshly cut sodium (2.09 g.), anhydrous ether (50 ml.), and ethandiol triphenylmethyl monoether (3.04 g., 0.01 mole) were placed in a 250-ml., single-necked, round-bottomed flask (drying tube attached) which was equipped with a magnetic stirrer and a reflux condenser. The reaction mixture was stirred at reflux temperature for four hours after which a white precipitate formed. The excess sodium was destroyed by adding ethanol and the contents were then poured onto cracked ice. The ether

layer was separated, washed successively with five per cent sodium carbonate solution and distilled water. After the ether layer was dried with anhydrous sodium sulphate and the sodium sulphate removed by filtration, the solution was concentrated in vacuo. On addition of petroleum ether to the oil, a white solid was formed. This solid was recovered by filtration, m.p. 97-101°. A mixture melting point of this solid (m.p. 97-101°) with an authentic sample of ethanediol triphenylmethyl monoether (m.p. 104-105°) was not depressed (m.p. 97-100°). The infrared spectra were also identical.

The experiment was repeated using dioxane as a solvent to allow higher reflux temperature. After the reflux period was over, the excess sodium was again removed by adding ethanol. When this reaction mixture was poured onto cracked ice a precipitate was formed at once. The solid was recovered by filtration and air-dried, m.p. 93-97°. Recrystallization from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave crystals, m.p. 102-103°. Once again these crystals were shown to be ethanediol triphenylmethyl monoether using a mixture melting point and an infrared spectrum.

β-Triphenylmethoxyethyl Chloride (2-Triphenylmethoxy-l-Chloroethane). - This β-halo ether was prepared by the action of thionyl chloride on the corresponding alcohol according to the general procedure of Hurd and Fowler19 who prepared β-ethoxyethyl chloride. Ethanediol triphenylmethyl monoether (50.0 g., 0.16 mole) dissolved in anhydrous chloroform

(50 ml.) and pyridine (15 ml.) was placed in a 500-ml., three-necked, round-bottomed flask which was equipped with a mechanical stirrer, a reflux condenser (drying tube attached) and a dropping funnel. Then thionyl chloride (20 ml.) dissolved in chloroform (125 ml.) was added dropwise with stirring. The flask contents were kept at zero degrees by immersing the flask in an ice bath. After the addition of the thionyl chloride, the reaction solution was stirred at room temperature for an additional two hours. The flask contents were poured onto a mixture of cracked ice and concentrated hydrochloric acid. The chloroform layer was separated, washed successively with dilute sodium sulphate. The sodium sulphate was removed by filtration and the solution was concentrated in vacuo. Petroleum ether (b.p. 30-60°) was added to the resultant oil and the solution was cooled in the refrigerator. A white precipitate, m.p. 104-109° was formed. Recrystallization of this solid from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave pure 2-triphenylmethyl-1-chloroethane, m.p. 109-112°.

Reaction of β-Triphenylmethoxyethyl Chloride with Magnesium. - β-Triphenylmethoxyethyl chloride (5.00 g., 0.016 mole) and anhydrous ether (150 ml.) were placed in a predried 250-ml., single-necked, round-bottomed flask which was equipped with a condenser (drying tube attached) and a magnetic stirrer. Magnesium turnings (2.00 g.) were added and the reaction mixture was stirred at reflux temperature for twenty hours after which a grey precipitate had formed. The flask contents were poured onto a mixture of cracked ice and concentrated hydrochloric acid.
The ether layer was separated, washed successively with dilute sodium carbonate solution and distilled water. After the ether layer was dried over anhydrous sodium sulphate and the drying agent removed by filtration, the ether was removed in vacuo. Addition of petroleum ether (b.p. 30-60°) to the resultant oil yielded a white precipitate, m.p. 92-95°. The product which was recrystallized from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave a solid, m.p. 99-101°. A mixture melting point of this solid (m.p. 99-101°) when mixed with an authentic sample of ethanediol triphenylmethyl monoether (m.p. 103-104°) was not depressed (m.p. 100-102°). Thus starting product was obtained.

The reaction was repeated using anhydrous tetrahydrofuran as a solvent to allow a higher reflux temperature. After two hours, a reddish-brown colour appeared. As the stirring was continued, this colour began to disappear until after a heating period (80°) of approximately twenty hours, only a slight brownish colour remained. Once again the reaction mixture was poured onto a mixture of cracked ice and concentrated hydrochloric acid. The oil which formed was extracted with ether (100 ml.). Sodium sulphate was used to dry the ether layer and after removal of the solvent from the dried solution, an oil formed. Several attempts to crystallize the product failed. An infrared spectrum on the oil showed no hydroxyl or chloride absorption bands. However, there was a strong ether absorption band. This would seem to indicate that coupling had occurred and that the oil formed was mainly the 1,4 butanediol triphenylmethyl diether.

A third attempt was made to effect the elimination reaction using magnesium. This time the reaction mixture was stirred at room
temperature for three days after which time a white precipitate had formed. At no time did the solution attain any red colour to indicate the presence of a carbanion. When the flask contents were poured onto a mixture of cracked ice and concentrated hydrochloric acid, a white precipitate formed immediately. The solution was partially concentrated by directing a jet of air on the surface and the solid which formed was recovered by filtration. The crude product which was recrystallized from a chloroform-petroleum ether (b.p. 30-60°) solvent pair, gave 3.50 g. (87%) of a white solid, m.p. 157-159°. A mixture melting point of this sample (m.p. 157-159°) with an authentic sample of triphenylcarbinol (m.p. 162-163°) was not depressed (m.p. 159-160°).

Reaction of β-Triphenylmethoxyethyl Chloride with Sodium. - β-Triphenylmethoxyethyl chloride (3.00 g., 0.009 mole) and anhydrous dioxane (100 ml.) were placed in a 200-ml., single-necked, round-bottomed flask provided with a drying tube. Excess sodium in the form of a sodium dispersion was added and the reaction mixture was stirred at room temperature. After two hours a red colour appeared. Stirring the mixture at room temperature for three days did not alter the colour of the reaction mixture. The excess sodium was removed by the slow addition of ethanol after which the flask contents were poured onto cracked ice. The oil which formed was extracted with 200 ml. petroleum ether (b.p. 30-60°), the ether layer was dried and the ether was removed in vacuo until the volume of the liquid was about 30 ml. The remaining petroleum ether was allowed to evaporate from the flask at room temperature whereupon a white solid formed, m.p. 75-77°. This melting point corresponds
closely to that of ethyl triphenylmethyl ether. The formation of this ether probably resulted from the reaction of the \( \beta \)-triphenylmethoxyethide ion with the ethanol (could have been any protolytic reagent).

The reaction was repeated but this time the reaction mixture was stirred while being heated at 80° for twenty-four hours. The flask contents were handled in the same manner. The isolation of the ethyl triphenylmethyl ether proved that the higher reaction temperature did not alter the final result.

**Reaction of \( \beta \)-Triphenylmethoxyethyl Chloride with Zinc.** - \( \beta \)-Triphenylmethoxyethyl chloride (5.00 g., 0.016 mole), zinc dust (2.00 g.), and \( n \)-propyl alcohol (100 ml.) were placed in a 250-ml., single-necked, round-bottomed flask. The reaction mixture was stirred by means of a magnetic stirrer at room temperature for five days, after which the flask contents were poured onto a mixture of cracked ice and concentrated hydrochloric acid. The oil which formed was extracted with ether (150 ml.). The ether layer was dried over anhydrous sodium sulphate, and the solvent was removed from the dried solution in vacuo. Analysis of the resultant oil using an infrared spectrum showed that the oil contained no hydroxyl band or chloride band.

Repeat of the above experiment at a temperature of 75-80° gave on final analysis a white solid, m.p. 167-170°. A mixture melting point with an authentic sample of triphenylcarbinol (m.p. 162-163°) was depressed (m.p. 133-140°). Once again it was postulated that coupling had occurred before elimination.
p-Bromo-p'-Chlorobenzophenone. - This compound was prepared according to the method of Gomberg and Bailer.\textsuperscript{20} p-Chlorobenzoyl chloride (100.0 g., 0.57 mole) and bromobenzene (89.5 g., 0.57 mole) were placed in a one-litre, three-necked, round-bottomed flask which was equipped with a mechanical stirrer, a condenser (drying tube attached), and a powder-introducing flask. While the reaction flask was cooled in an ice bath, anhydrous aluminium chloride (76.0 g.) was added in 5-10 g. portions. After the addition of the aluminium chloride, the reaction mixture was stirred while being heated on the steam bath until the reaction contents turned solid. The stirrer was removed and the flask was allowed to stand at room temperature for an additional hour. The solid which formed was broken into small pieces and poured onto cracked ice. The precipitate which resulted was recovered by filtration, washed successively with distilled water, 5% sodium carbonate, and again distilled water. The precipitate was dried under suction. The crude product (m.p. 140-145\degree) was obtained in yields of 80-85%. Recrystallization of the crude product from a chloroform-petroleum ether (b.p. 30-60\degree) solvent pair gave flaky white crystals of pure p-bromo-p'-chlorobenzophenone, m.p. 148-149\degree. This melting point corresponds closely with that previously recorded.\textsuperscript{20}

p-Bromophenyl-p-Chlorophenylphenylcarbinol. - Phenyl magnesium bromide was made from the reaction of magnesium turnings and bromobenzene.

Magnesium turnings (25.5 g., 1.11 mole) and anhydrous ether (500 ml.) were placed in a predried two-litre, three-necked, round-bottomed flask provided with a mechanical stirrer, a condenser (drying tube attached), and a dropping funnel. A solution of bromobenzene (172.0 g., 1.10 mole) and anhydrous ether (300 ml.) was added at a rate sufficient to maintain steady reflux. After the addition of this solution, the reaction mixture was stirred at reflux temperature for an additional hour. The reaction contents were cooled to room temperature and bromo-p'-chlorobenzophenone (296 g., 1.0 mole) was added in the solid form by means of the powder-introducing flask. After the addition of the solid the reaction mixture was stirred at reflux temperature for two hours. The Grignard complex was decomposed by pouring the reaction mixture onto a mixture of cracked ice and concentrated hydrochloric acid. The ether layer was separated and washed successively with 5% sodium carbonate solution and distilled water. After the ether layer was dried over anhydrous sodium sulphate, the sodium sulphate was removed by filtration and the ether was removed in vacuo. The resultant oil was dissolved in a chloroform-petroleum ether (b.p. 30-60°) solvent pair. On cooling the crude alcohol was obtained, m.p. 93-96°. When the crude product was re-crystallized from the same solvent pair, pure p-bromophenyl-p'-chlorophenylphenylcarbinol was obtained as a white powder, m.p. 102-103°. This melting point did not correspond to the melting point reported by Stagner\(^{21}\) for the same compound (reported,\(^{21}\) m.p. 91-93°).

An additional crystallization from the chloroform-petroleum ether (b.p. 30-60°) solvent pair gave analytically pure alcohol, which, after drying in vacuo over phosphorous pentoxide for three hours at room temperature, showed m.p. 103-104°.

Analysis: Calcd. for C_{19}H_{14}BrClO: C, 61.07; H, 3.78; Cl, 9.49; Br, 21.39.

Found: C, 60.79; H, 3.88; Cl, 9.20; Br, 21.28.

p-Bromophenyl-p'-Chlorophenylphenylmethyl Chloride. - Pure p-bromophenyl-p-chlorophenylphenylcarbinol (100 g., 0.27 mole) and anhydrous benzene (200 ml.) were placed in a 500-ml., single-necked, round-bottomed flask. The solution was heated to its boiling point and acetyl chloride (20 ml.) was added to the hot solution. The flask was shaken vigorously and more acetyl chloride (25 ml.) was added in 5-ml. portions. The solution was then heated at reflux temperature for two hours.

The solution was then cooled to room temperature and concentrated in vacuo until the total volume was about 50 ml. Petroleum ether (b.p. 30-60°) was added to the resultant oil and the solution was cooled in the refrigerator. The p-bromophenyl-p-chlorophenylphenylmethyl chloride which separates as a white crystalline solid was recovered by filtration, m.p. 76-78°. The average yield of three runs was 70%.

(p-Bromophenyl-p-Chlorophenylphenylmethoxy)-Acetic Acid. - This acid was prepared in an average yield of 60% following the procedure used.
in the preparation of triphenylmethoxyacetic acid on page 87. From p-bromophenyl-p-chlorophenylphenylmethyl chloride (100 g., 0.26 mole) and glycolic acid (22.8 g., 0.30 mole) the crude product, m.p. 150-153° was obtained in an average yield of 50%. Recrystallization of the crude product from a chloroform-petroleum ether (b.p. 30-60°) solvent pair yielded a white powder of analytically pure (p-bromophenyl-p-chlorophenylphenylmethoxy)-acetic acid, which, after drying in vacuo over phosphorous pentoxide for one hour at room temperature showed m.p. 156-158°.

Analysis: Calcd. for C_{21}H_{16}BrClO_{3}: C, 58.41; H, 3.74.
   Found: C, 58.34; H, 3.90.

Reduction of (p-Bromophenyl-p-Chlorophenylphenylmethoxy)-Acetic Acid. -

In an attempt to reduce the acid in the same manner as the triphenylmethoxyacetic acid, the desired alcohol was obtained in very poor yields (5-10%). This was due to the insolubility of the lithium salt of the acid. For this reason it was decided to make the methyl ester of the acid and then reduce the ester to the desired alcohol.

Methyl (p-Chlorophenyl-p-Bromophenylphenylmethoxy)-Acetate. - The ester was prepared using the reaction of diazomethane with the acid. The apparatus used is illustrated on the following page.

1. Potassium hydroxide solution
2. Ether
3. Ether
4. Organic acid

Fig. 6.- Preparation and Use of Diazomethane

p-Bromophenyl-p-chlorophenylphenylmethoxy)-acetic acid (21.6 g., 0.05 mole) and ether (30 ml.) were placed in a 100-ml., round-bottomed flask (B). Potassium hydroxide (50% solution; 8 ml.) and ether (30 ml.) were placed in a 50-ml., round-bottomed flask (A). While the flask (A) was being cooled in an ice bath, N-nitrosomethylurea (3-4 g.) was added. The flask was allowed to stand at room temperature. As the N-nitrosomethylurea decomposed, the diazomethane gas formed dissolved in the ether layer imparting a yellow colour to the solution. This diazomethane was distilled into flask (B) along with the ether by immersing flask (A) in a beaker of warm water.

As the ethereal solution of diazomethane distilled into flask (B) and the diazomethane reacted with the organic acid in the flask, bubbles of nitrogen gas were given off. The procedure was repeated until there was no visible reaction in flask (B), i.e., no nitrogen
bubbles given off. At this point the ether solution in flask (B) had achieved a persistent yellow colour indicating the presence of a slight excess of diazomethane. After all the acid had been converted to the ester, the flask was allowed to stand at room temperature for one hour in the fumehood to allow the excess diazomethane to escape from the ethereal solution and be drawn up into the fumehood. The remaining ether layer was dried over anhydrous sodium sulphate. The ether was then removed in vacuo leaving an oil. Numerous attempts to obtain the product in a crystalline form failed. Although the ester was not obtained in the crystalline form, the infrared spectrum showed no acid hydroxyl band. This indicated the desired product, methyl-(p-bromophenyl-p-chlorophenylphenylmethoxy)-acetate had been obtained.

Ethanediol-(p-Bromophenyl-p-Chlorophenylphenylmethyl)-Monoether. - Lump lithium hydride (4.0 g., 0.1 mole) obtained from Metal Hydrides Company and anhydrous ether (300 ml.) were placed in a one-litre, three-necked, round-bottomed flask which was equipped with a mechanical stirrer, a condenser (drying tube attached), and a dropping funnel. An ethereal solution (250 ml.) containing the ester (44.6 g., 0.10 mole) was added dropwise at such a rate sufficient to maintain steady reflux. A large amount of precipitate formed. After the addition of the ester the reaction mixture was stirred at reflux temperature for an additional two hours. The excess lithium aluminium hydride was removed by the addition of ethyl acetate. The flask contents were then poured onto a mixture of cracked ice and concentrated hydrochloric acid whereupon the aluminium salts formed during the reaction dissolved. The ether layer
was separated and washed successively with 5% sodium carbonate and distilled water. After the ether layer was dried over anhydrous sodium sulphate and the sodium sulphate removed by filtration, the ether was removed in vacuo. The remaining oil was dissolved in a chloroform-petroleum ether (b.p. 30-60°) solvent pair. No crystalline product was obtained. However, the infrared spectrum on the oil showed a very strong hydroxyl band and no evidence of any carbonyl band. This indicated that the reduction of the ester to the alcohol had been successful.

β-(p-Bromophenyl-p-Chlorophenylphenylmethoxy)-Ethyl Chloride. -
Following the procedure used in the preparation of β-triphenylmethoxy-ethyl chloride (page 90) ethanediol (p-bromophenyl-p-chlorophenylphenylmethyl)-monoether (33.0 g., 0.075 mole) was reacted with thionyl chloride (20 ml.) to give the desired chloride. This compound could not be obtained in the crystalline form. Verification of the final product was made by means of an infrared spectrum. The spectrum showed no hydroxyl band.

Resolution of (Z) (p-Bromophenyl-p-Chlorophenylphenylmethoxy)-Acetic Acid. -
In a 500-ml. Erlenmeyer flask were placed 8.64 g. (0.20 mole) of the acid dissolved in 100 ml. acetone and to this was added 7.84 g. (0.20 mole) of anhydrous brucine. The flask was then heated to effect solution. When the solution was cooled the brucine salt crystallized from the solution. The solid was recovered by filtration, yield 16.20 g. This yield of 16.20 g. represented the sum of the two diastereoisomers whose specific rotation was -11.45°. Seven recrystallizations of the racemic
mixture from dilute acetone solutions gave a brucine salt \([\alpha]_{D}^{25} -15.1^\circ\). Further recrystallizations failed to yield any change in the specific rotation of the brucine salt. When ethanol or ethyl acetate were used as solvents for the recrystallizations of the racemic mixture, the same final results were obtained. This value of \(-15.1^\circ\) was taken to represent the specific rotation of the pure diastereoisomer.

Analysis: Calcd. for \(\text{C}_{44}\text{H}_{42}\text{BrClN}_{2}O_{7}\): \(\text{C}, 63.96; \text{H}, 5.12; \text{N}, 3.39\).

Found: \(\text{C}, 63.21; \text{H}, 5.48; \text{N}, 3.20\).

The optically pure organic acid was recovered by cleaving the brucine salt with a mineral acid. The brucine salt was dissolved in acetone and the solution was then poured onto a mixture of cracked ice and concentrated hydrochloric acid. The solution was partially concentrated by directing a jet of air on the surface and the precipitate which formed was recovered by filtration. Recrystallization of this precipitate from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave a white crystalline product, m.p. 158-159°; \([\alpha]_{D}^{25} -0.34^\circ\).

Analysis: Calcd. for \(\text{C}_{21}\text{H}_{16}\text{BrClO}_{3}\): \(\text{C}, 58.14; \text{H}, 3.74\).

Found: \(\text{C}, 58.34; \text{H}, 3.90\).

The remainder of the reaction sequence was performed on the optically active system in the same manner described for the non-optically active system. None of the intermediates nor the final chloride \(\beta-(p\text{-bromophenyl-p-chlorophenylphenylmethoxy})\)-ethyl chloride showed any appreciable optical activity.

Reaction of Optically Pure \(\beta-(p\text{-bromophenyl-p-chlorophenylphenylmethoxy})\)-ethyl Chloride with Magnesium. – \(\beta-(p\text{-bromophenyl-p-chlorophenylphenylmethoxy})\)-ethyl chloride (3.85 g., 0.085 mole) and anhydrous tetrahydrofuran...
(100 ml.) were placed in a 250-ml., round-bottomed flask provided with a ground-glass joint and a water-cooled condenser (drying tube attached). Magnesium powder (0.21 g., 0.085 mole) was added and the reaction mixture was stirred at room temperature for nine days. The reaction contents were then poured onto a mixture of cracked ice and concentrated hydrochloric acid. The oil which formed was extracted with ether (300 ml.) and the ether layer was dried. The ether was removed in vacuo. The resultant oil was analyzed by means of an infrared spectrum which indicated that the final product contained predominately the starting chloride with only a small amount of the desired alcohol.

The reaction was repeated using $\beta$-(p-bromophenyl-p-chlorophenylphenylmethoxy)-ethyl chloride (5.70 g., 0.13 mole), magnesium turnings (0.31 g., 0.013 mole), and anhydrous tetrahydrofuran (100 ml.). The reaction mixture was stirred at room temperature for four weeks after which a white precipitate had formed in the flask. The flask contents were handled in the same way as in the previous experiment. An infrared spectrum of the resultant oil showed a weak hydroxyl absorption band.

$\beta$-(p-Bromophenyl-p-Chlorophenylphenylmethoxy)-Ethyl Iodide. - Ethanediol p-bromophenyl-p-chlorophenylmethyl monoether (3.74 g., 0.01 mole) was dissolved in acetone (100 ml.). Potassium iodide (1.66 g., 0.01 mole) was added and the mixture was allowed to stand at room temperature with occasional shaking for thirty minutes. The solution turned dark red. The reaction mixture was poured onto cracked ice containing a few crystals of sodium thiosulphate. The oil which formed was extracted with ether (100 ml.) and the ether layer was dried over anhydrous
sodium sulphate. The sodium sulphate was removed by filtration and the ether removed in vacuo. Attempts to crystallize the resultant oil failed. The infrared spectrum of the oil showed a strong hydroxyl absorption band and was very similar to that of the starting carbinol p-bromophenyl-p-chlorophenylphenylcarbinol.

β-Triphenylmethoxyethyl Iodide (2-Triphenylmethoxy-l-Iodoethane). - β-Triphenylmethoxyethyl iodide (2.00 g., 0.006 mole) was added to a mixture of potassium iodide (2.00 g., 0.012 mole) and 50 ml. acetone. As the reaction mixture was allowed to stand at room temperature, a reddish-brown colour appeared in the reaction solution due to the liberation of free iodine. Also a large amount of precipitate formed. The reaction mixture was allowed to stand until all the potassium iodide had dissolved after which the flask contents were poured onto cracked ice. The free iodine was removed by adding a few crystals of sodium thiosulphate. The precipitate which formed was recovered by filtration and air-dried, m.p. 155-158°. The crude product was obtained in a yield of 70%. Recrystallization from a chloroform-petroleum ether (b.p. 30-60°) solvent pair yielded a white solid, m.p. 162-163°. A mixture melting point with an authentic sample of triphenylcarbinol (m.p. 162-163°) was not depressed (m.p. 162-163°). Their infrared spectra were also identical.

The reaction was run again but this time the solvent used was a 50% methanol-acetone solution. The reaction mixture was handled in the same manner as above. When the contents were poured onto crushed ice an oil formed. This oil was extracted with ether (100 ml.). The
ether layer was dried over anhydrous sodium sulphate and then the ether was removed in vacuo. A precipitate formed, m.p. 70-74°. The precipitate was recrystallized from petroleum ether (b.p. 30-60°) and gave a white solid, m.p. 75-78°. This melting point corresponds closely with that reported for methyl triphenylmethyl ether, m.p. 82-83°.

The mode of formation of the methyl triphenylmethyl ether was investigated using the following reactions:

(a) 5.2 g. triphenylcarbinol
   5.06 g. iodine
   100 ml. of a 50% acetone-methanol solution

(b) 5.2 g. triphenylcarbinol
   5.06 iodine
   3.32 g. potassium iodide
   100 ml. of a 50% acetone-methanol solution

(c) 5.2 g. triphenylcarbinol
   3.32 g. potassium iodide
   100 ml. of a 50% acetone-methanol solution

(d) 5.2 g. triphenylcarbinol
   0.4 g. iodine
   100 ml. of a 50% acetone-methanol solution

All the reactions were allowed to stand at room temperature for a period of three hours after which each of the reaction mixtures were poured onto cracked ice containing a few crystals of sodium thiosulphate to remove the free iodine. The oil which formed was handled in the
same manner as previously described.

In reactions (a), (b), and (d) the product obtained was the methyl triphenylmethyl ether. However, in the case of (d), the yield was much lower (30%) than in the other two cases (85-90%). In reaction (c) the product obtained was the triphenylcarbinol which was recovered in an almost quantitative yield, indicating no ether formation.

Preparation of Ethers Using Iodine

In the preparation of the following ethers, the same general procedure used has been outlined on page 105. The two alcohols were dissolved in acetone and to this was added the potassium iodide in the solid form. The reaction mixture was then allowed to stand at room temperature with occasional stirring for three hours after which the flask contents were poured onto cracked ice. A few crystals of sodium thiosulphate were then added to remove the free iodine. The oil which formed was extracted with petroleum ether (b.p. 30-60°), the ether layer was dried over anhydrous sodium sulphate, and the sodium sulphate was removed by filtration. Allowing the petroleum ether to evaporate from an open beaker yielded the crude ethers. In the following preparations only the pertinent data such as quantities of reagents, crude yields, and crude melting points will be given.

Methyl Triphenylmethyl Ether. -

5.2 g., (0.02 mole) triphenylcarbinol
5.06 g. (0.02 mole) iodine
100 ml. anhydrous acetone
30 ml. anhydrous methanol
Yield, 90%
Melting point, 73-75°. (reported2 m.p. 80-82°)

**Ethyl Triphenylmethyl Ether.**

5.2 g., (0.02 mole) triphenylcarbinol
5.06 g., (0.02 mole) iodine
100 ml. acetone
30 ml. anhydrous ethanol
Yield, 78%
Melting point, 74-76°. (reported25 m.p. 83°)

**Propyl Triphenylmethyl Ether.**

5.2 g., (0.02 mole) triphenylcarbinol
5.06 g., (0.02 mole) iodine
50 ml. acetone
50 ml. n-propyl alcohol
Yield, 78%
Melting point, 47-50°. (reported26 m.p. 56°)


Isopropyl Triphenylmethyl Ether. -

5.2 g., (0.02 mole) triphenylcarbinol
5.06 g., (0.02 mole) iodine
50 ml. acetone
50 ml. isopropyl alcohol
Yield, 45%
Melting point, 102-105°. (reported 111-113°)

Benzyl Triphenylmethyl Ether. -

5.2 g., (0.02 mole) triphenylcarbinol
5.06 g., (0.02 mole) iodine
100 ml. acetone
30 ml. benzyl alcohol
Yield, 50%
Melting point, 102-104°. (reported 106-107°)

β-Triphenylethoxycpropanic Acid. - β-Hydroxypropionic acid (10.0 g., 0.11 mole), triphenylethyl chloride (33.5 g., 0.12 mole), and pyridine (150 ml.) were placed in a 250-ml., three-necked, round-bottomed flask which was equipped with a reflux condenser and a mechanical stirrer. The reaction mixture was stirred at 80° for two days. When this reaction mixture was poured onto a mixture of cracked ice and concentrated hydrochloric acid an oil formed. The oil was extracted with

28 G. L. Stadnikov, Ber., 57, 6 (1924).
ether (200 ml.) and the ether solution was washed with distilled water. Sodium carbonate was then added to the ether solution and the aqueous layer was poured onto a mixture of cracked ice and concentrated hydrochloric acid. No precipitate formed.

The reaction was repeated but this time the reflux period was extended to four days. The reaction contents were handled in this same way and when the aqueous sodium carbonate layer was poured onto a mixture of cracked ice and concentrated hydrochloric acid a white precipitate formed. The precipitate was recovered by filtration and dried under suction, m.p. 158-162°. The crude product was recrystallized from a chloroform-petroleum ether (b.p. 30-80°) solvent pair to give the pure β-triphenylmethoxypropionic acid, m.p. 164-166°. This melting point corresponds very closely to that previously recorded.\(^{29}\) The average yield of three runs was 25%.

**Methyl β-Triphenylmethoxypropionate.** - This compound was prepared using the method outlined on page 96 in the preparation methyl triphenylmethoxyacetate. The crude ester was obtained, m.p. 110-112°. An additional crystallization from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave analytically pure ester, which, after drying in vacuo at room temperature for an hour, showed m.p. 113-114°.

Analysis: Calcd. for \(\text{C}_{22}\text{H}_{22}\text{O}_3\): C, 79.74; H, 6.40.

Found: C, 79.69; H, 6.39.

Reaction of Methyl β-Triphenylmethoxypropionate with Triphenylmethyl Sodium. - Methyl β-tri phenylmethoxypropionate (2.00 g., 0.006 mole) and anhydrous ether (50 ml.) were placed in a 500-ml. Erlenmeyer flask fitted with a polyethylene stopper. An ethereal solution of triphenylmethyl sodium was added rapidly with stirring until a persistent red colour indicated a slight excess of base. The mixture was stirred for one-half hour. Water (100 ml.) was added, the layers were separated and the ether layer was dried over anhydrous sodium sulphate. The sodium sulphate was removed by filtration and the ether was removed in vacuo. During the removal of the ether, a solid crystallized. A small amount of petroleum ether (b.p. 30-60°) was added and the precipitate which formed was recovered by filtration, m.p. 155-157°. The solid was washed with petroleum ether to remove any triphenylmethane and the insoluble portion was recrystallized from a chloroform-petroleum ether (b.p. 30-60°) solvent pair to give a white powder, m.p. 153-160°. A mixture melting point determination with an authentic sample of triphenylcarbinol (m.p. 162-163°) was not depressed (m.p. 159-161°). The infrared spectra were also identical.

The reaction was repeated using double the above quantities. This time after the addition of the base and the subsequent stirring period, phthalic anhydride (1.78 g., 0.12 mole) was added to the flask in one portion and the reaction mixture was stirred for twenty-four hours. Water (100 ml.) was added, the layers were separated, and the water layer was poured onto a mixture of cracked ice and concentrated hydrochloric acid. The precipitate which formed was recovered by filtration, air-dried, and recrystallized from a chloroform-petroleum ether...
(b.p. 30-60°) solvent pair to give pure hydrogen triphenylmethyl phthalate, m.p. 251-253°. A mixture melting point determination with an authentic sample of hydrogen triphenylmethyl phthalate (m.p. 253-255°) was not depressed (m.p. 251-253°). The infrared spectra were also identical.

**β-Triphenylmethoxypropionitrile.** - The β-hydroxypropionitrile (10.0 g., 0.14 mole) was dissolved in anhydrous ether (100 ml.). To this was added triphenylmethyl chloride (36.0 g., 0.113 mole) and pyridine (15 ml.). This operation was carried out in a 200-ml., three-necked, round-bottomed flask equipped with a mechanical stirrer and a condenser (drying tube attached). The reaction mixture was stirred at reflux temperature for three hours whereupon a white precipitate of pyridine hydrochloride formed. When the reaction mixture was poured onto a mixture of cracked ice and concentrated hydrochloric acid a precipitate formed. The precipitate was recovered by filtration. Recrystallization from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave a white solid, m.p. 167-169°. A mixture melting point determination with a sample of triphenylcarbinol (m.p. 161-162°) was depressed (m.p. 135-140°). An infrared spectrum of the product showed the characteristic nitrile absorption band as well as the ether absorption band.

**Attempted Hydrolysis of β-Triphenylmethoxypropionitrile.** - Several attempts were made to hydrolyze the nitrile using different hydrolyzing agents. All these attempts were carried out using 5.0-g.
samples of the nitrile.

(a) Potassium hydroxide. Hydrolysis was first tried by heating a mixture of the nitrile and 100 ml. of potassium hydroxide (50%) on a steam bath for twenty-four hours. The reaction mixture was poured onto a mixture of cracked ice and concentrated hydrochloric acid and the precipitate which formed was recovered by filtration. Recrystallization from a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave a white solid, m.p. 167-168°, which was shown to be the starting nitrile using a mixture melting point determination and an infrared spectrum.

(b) Sulphuric acid. The nitrile was placed in a 250-ml. Erlenmeyer and 100 ml. of 1:1 sulphuric acid were added. The reaction mixture was stirred at zero degrees for four hours. When the reaction mixture was poured onto cracked ice, a precipitate formed. The precipitate was recovered by filtration and recrystallized from a chloroform-petroleum ether (b.p. 30-60°) solvent pair to give a white crystalline solid, m.p. 167-169°. A mixture melting point determination with an authentic sample of \( \beta \)-triphenylmethoxy propionitrile (m.p. 167-169°) was not depressed (m.p. 166-168°).

The reaction was repeated but this time the reaction mixture was heated on the steam bath for two hours. The recrystallized product was again shown to be triphenylcarbinol.

(c) Hydrochloric acid. The nitrile along with hydrochloric acid (100 ml.) were heated on the steam bath for twenty-four hours. The remaining precipitate was removed by filtration and air-dried. Recrystallization of the crude product from a chloroform-petroleum
ether (b.p. 30-60°) solvent pair gave a white solid, m.p. 155-158°. A mixture melting point determination with an authentic sample of triphenylcarbinol was depressed (m.p. 130-140°), but a mixture melting point determination with an authentic sample of the starting nitrile was not depressed.

(d) Trifluoroacetic acid. In a 200-ml., round-bottomed flask provided with a condenser was placed triphenylmethoxypropionitrile dissolved in 100 ml. trifluoroacetic acid. The solution was heated at 75° while being stirred by means of a magnetic stirrer for a period of six hours. Water was then added, but care was taken to keep the reaction contents homogeneous. The solution was then heated for an additional eighteen hours on the steam bath after which time the reaction solution was poured onto cracked ice. The precipitate which formed was recovered by filtration and air-dried, m.p. 158-160°. The yield was 4.0 g. The product was shown to be triphenylcarbinol by means of an infrared spectrum and a mixture melting point determination.

Methyl $\beta$-Hydroxypropionate. - This compound was prepared according to the method of Greshman and coworkers.$^{30}$ Anhydrous methanol (100 ml., approx. 6 mole) was placed in a one-litre, three-necked, round-bottomed flask provided with a condenser (drying tube attached), a dropping funnel, and a thermometer. Sodium metal (2 g.) was added. While the reaction contents were kept at zero degrees by immersing the flask

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in a dry ice-acetone bath, propiolactone (72.06 g., 1.0 mole) was added dropwise with stirring. Care was taken to keep the flask contents at zero degrees throughout the addition. After the addition of the propiolactone, hydrochloric acid was added to the reaction contents until the solution was just acidic to litmus paper. The sodium chloride which formed was removed by filtration and then the methanol was removed in vacuo. The remaining liquid was distilled under reduced pressure. The fraction distilling at 78-80° at 15 mm. was collected, n\(^{22}_D\) 1.4219. This corresponded to the reported properties of methyl \(\beta\)-hydroxypropionate, b.p. 71° (13 mm.); n\(^{20}_D\) 1.4225. The yield was 50%. 

Preparation and Saponification of Methyl \(\beta\)-Triphenylmethoxypropionate. - The methyl-(\(\beta\)-triphenylmethoxy)-propionate was prepared using a method similar to that of Helferich and coworkers\(^{31}\) who prepared the ethyl \(\beta\)-triphenylmethoxypropionate. Triphenylmethyl chloride (27.8 g., 0.10 mole), methyl \(\beta\)-hydroxypropionate (10.4 g., 0.10 mole), and pyridine (200 ml.) were placed in a 500-ml., single-necked, round-bottomed flask. The reaction contents were stirred by means of a magnetic stirrer at 45-50° for two days after which time a white precipitate (pyridine hydrochloride) formed. The reaction mixture was poured onto a mixture of cracked ice and concentrated hydrochloric acid. The precipitate which formed was recovered by filtration and air-dried, m.p. 105-108°. Recrystallization of the crude product from a chloroform-petroleum

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\(^{31}\) B. F. Helferich, L. Moog, and A. Junger, loc. cit.
ether (b.p. 30-60°) solvent pair gave white crystals of pure methyl 

The crude methyl β-triphenylmethoxypropionate obtained from the 
previous experiment and 25% potassium hydroxide solution (200 ml.) 
were placed in a 250-ml., round-bottomed flask. The reaction mixture 
was heated at 75-80° with stirring for twenty hours. Water (200 ml.) 
was added and the mixture was filtered to remove any base insoluble 
impurities. The clear basic layer was then poured onto a mixture of 
cracked ice and concentrated hydrochloric acid and the precipitate 
which formed was removed by filtration. Air drying the product gave 
a white solid, m.p. 152-157° in a crude yield of 22 g. The yield re-
presented an overall yield (preparation of the ester and subsequent 
saponification) of 65%. Recrystallization of the crude product from 
a chloroform-petroleum ether (b.p. 30-60°) solvent pair gave the pure 
β-triphenylmethoxypropionic acid, m.p. 163-165°.

Preparation and Saponification of Methyl β-(p-Chlorophenyl-p-bromophenyl-
phenylmethoxy)-Propionate. - p-Bromophenyl-p-chlorophenylphenylmethyl 
chloride (40 g., 0.10 mole), methyl β-hydroxypropionate (10.5 g., .11 
mole), and pyridine (200 ml.) were placed in a one-litre, round-bottomed, 
three-necked flask provided with a mechanical stirrer and reflux 
condenser. The reaction mixture was heated for five days with stirring 
at a temperature of 50-60°. After this the flask contents were poured 
onto a mixture of cracked ice and concentrated hydrochloric acid and 
the oil which formed was extracted with ether. The ether layer was 
concentrated in vacuo. No attempt was made to analyze the crude product.
The crude product obtained from the previous experiment was placed in a 500-mL., round-bottomed flask provided with a ground-glass joint and a water-cooled condenser. An ethanol-water solution (150 mL. water and 50 mL. ethanol) was added. Potassium hydroxide (20 g.) was added and the reaction mixture was stirred at room temperature for sixteen hours, after which the contents were poured onto cracked ice. The oil which resulted was extracted with a small portion of ether (100 mL.). The aqueous layer was poured onto a mixture of cracked ice and concentrated hydrochloric acid whereupon very little precipitate formed. Water (300 mL.) was added and the aqueous layer was poured onto cracked ice and concentrated hydrochloric acid yielding an appreciable amount of solid. The precipitate which formed was recovered by filtration and recrystallized from a chloroform-petroleum ether (b.p. 30-60°) solvent pair to give a white powder, m.p. 136-139°. An additional crystallization from the same solvent pair gave analytically pure alkoxy acid, which, after drying in vacuo for one hour at room temperature, showed m.p. 137-139°.

Analysis: Calcd. for C_{22}H_{40}O_2BrCl: C, 59.30; H, 4.07.
Found: C, 60.45; H, 3.74.

All melting points were taken on the Fisher-Johns melting point apparatus. Microanalyses were done by Spang Microanalytical Laboratory, P. O. Box 1111, Ann Arbor, Michigan and Swarzkopf Microanalytical Laboratory, 56-19 37th Avenue, Woodside 77, New York.
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