THE SYNTHESIS

OF

A HEMI-TERPENE ALCOHOL

by

Mayer B. Goren

Submitted in Partial Fulfillment
of the Requirements for the
Degree of Master of Arts

The Rice Institute
1943
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>Historical Survey</td>
<td>4</td>
</tr>
<tr>
<td>Experimental</td>
<td>7</td>
</tr>
<tr>
<td>Bromination Study on Isoamyl Acetate</td>
<td>7</td>
</tr>
<tr>
<td>Bromination Study on 1° Isoamyl Bromide</td>
<td>20</td>
</tr>
<tr>
<td>Synthesis and Bromination</td>
<td>21-27</td>
</tr>
<tr>
<td>Identification of Dibromide</td>
<td>27</td>
</tr>
<tr>
<td>Dehalogenation of Dibromide</td>
<td>40</td>
</tr>
<tr>
<td>Dehalogenation of Polybromide</td>
<td>47</td>
</tr>
<tr>
<td>2,4 Dihydroxy 2-methyl butane</td>
<td>52</td>
</tr>
<tr>
<td>Modification in Hydrolysis of Dibromide</td>
<td>61</td>
</tr>
<tr>
<td>Synthesis and saponification of Prenyl Acetate</td>
<td>66</td>
</tr>
<tr>
<td>Complete Hydrolysis of Dibromide</td>
<td>66</td>
</tr>
<tr>
<td>Isolation of Glycol</td>
<td>69</td>
</tr>
<tr>
<td>Acetic Anhydride Dehydration</td>
<td>70</td>
</tr>
<tr>
<td>Saponification of Unsaturated Ester</td>
<td>76</td>
</tr>
<tr>
<td>Preparations of Derivatives</td>
<td>76</td>
</tr>
<tr>
<td>Summary</td>
<td>81</td>
</tr>
<tr>
<td>Acknowledgement</td>
<td>84</td>
</tr>
<tr>
<td>Bibliography</td>
<td>85</td>
</tr>
</tbody>
</table>
INTRODUCTION
INTRODUCTION

The chemistry of the terpenes deals with those natural products which may be considered as being comprised of one or more isoprene units, condensed in various manners, and modified in general by the presence of hydroxyl, carbonyl, or carboxyl groups, whose presence is believed due to the addition of water onto the condensed system, followed by oxidation or reduction. The numerous products that are included in this category have, for the sake of convenience in classification, been separated into several groups, based upon the number of isoprene units contained in the parent structure. Thus, compounds containing one isoprene unit are designated as hemiterpenes; two units—terpenes; three units—sesquiterpenes; etc.

The simplest of these products structurally, and the basic constituent of all of them is isoprene, or hemiterpene. A convenient laboratory method for preparing isoprene takes advantage of the fact that the higher terpenes may be thermally broken down into this basic unit by passing the liquid or vapor over an electrically heated coil of iron wire. Thus, turpentine, limonene, and other products may be used as a convenient source for the small-scale production of isoprene (1).
A large variety of the naturally occurring terpenes and their derivatives, such as various esters of the terpene alcohols, etc., have been found to possess highly aromatic qualities, which make desirable their use in the manufacture of perfumes, soaps, and cosmetics. This study was undertaken in order to investigate various properties of one of the simple terpene alcohols, \( \gamma \gamma \)-dimethyl allyl alcohol, which has been described but scantily to date. It was hoped that a simple method might be devised for the synthesis of this alcohol, in order that an extensive investigation of its derivatives might be pursued. However, it must be admitted at the outset, that this simple method was not found, although only a few possibilities were investigated. Several isomeric modifications of this alcohol, as well as their derivatives were obtained in the study. Since very few solid derivatives of these products have been prepared previously, elucidation of their structure has depended upon physical data, supplemented by rupture of the double bond and identification of the resulting carbonyl compounds. However, several solid derivatives of these alcohols were prepared in the course of the investigation, so that these may be used as an aid in their identification. In addition, liquid esters of the primary alcohol have been prepared in order to study their aromatic qualities with a view toward their possible future use as substitutes for essential oils. In general, these liquid esters were found to possess highly pleasing odors which
were dissociated from the "fusel oil" tang that is generally found in the corresponding isoamyl derivatives with which they were compared.
HISTORICAL SURVEY
**HISTORICAL SURVEY**

Dimethyl allyl alcohol was first reported by Courtot (2), who obtained this compound by heating $\delta$-bromo-$\alpha$-dimethyl butyrolactone with 2-molar aqueous potassium carbonate. In addition, he obtained $\delta$-hydroxy,$\alpha$-dimethyl butyrolactone. The unsaturated alcohol boiled at $140^\circ$ at atmospheric pressure, and the position of the double bond was determined by rupture with potassium permanganate and identification of the acetone produced as the semicarbazone (m.p. $185^\circ$). Furthermore, oxalic acid was isolated as the second product of the oxidation, which was identified by means of its calcium salt.

Courtot prepared several derivatives of the alcohol: the acetate, boiling point $152^\circ$; the phenylurethane, recrystallized from petroleum ether and ether, melting at $65^\circ$; and the dibromide, prepared by addition of 1 equivalent of bromine to the double bond. The latter was recrystallized from petroleum ether, and found to melt at $37-38^\circ$.

Ipatieff (3) reported the formation of the ethyl ether of dimethyl allyl alcohol (b.p. $120.5-121.5$) as the primary side product in the debromination of isoprene bishydrobromide, $\text{C}_3\text{H}_5\text{C}^\prime\text{H}_2\text{C}^\prime\text{H}_2\text{Br}$, with alcoholic KOH. In addition, isoprene was obtained as the primary reaction product. Claisen (4) prepared this ether directly from isoprene monohydrobromide, $\text{C}_3\text{H}_5\text{C}^\prime\text{H}_2\text{C}^\prime\text{H}_2\text{Br}$, and
sodium ethylate. The boiling point reported by the latter was 125°, and reduction of the product yielded ethyl isomyl ether.

Of academic, as well as of practical importance are two isomeric modifications of this unsaturated alcohol; viz., 2-methyl 1-butene-4, \( CH_3 - CH_2 - CH = CH - 2 \), and dimethyl allyl alcohol, or isoprene alcohol, \( CH_3 - CH = CH - CH_3 \).

The latter is obtained commercially by condensing acetylene with acetone in the presence of alkali to yield the tertiary acetylenic alcohol (5), which is then electrolytically reduced to the ethylenic configuration (6). Thus,

\[
CH_3 - CH = CH - CH_3 + CH_3 = CH_3 \xrightarrow{k^+} CH_3 = CH = CH_3 \xrightarrow{H_2} CH_3 - CH = CH = CH_3
\]

This tertiary alcohol is useful in the semi-industrial preparation of isoprene, by dehydration over various catalysts (7).

A recent investigation by Faworkii (8) has shown that simple hydrogenation of the tertiary acetylenic alcohol in dilute \( H_2SO_4 \) yields a higher boiling fraction, l-isobutenyl carbinol. Faworkii and Lebedeva (9) have further shown that treatment of the dimethyl vinyl carbinol with 20% sulfuric acid for a few days at room temperature yields a complex mixture, among which were found unaltered tertiary alcohol, isoprene, dimethyl allyl alcohol (b.p. 134-136°; (compare Cournot's value) phenyl urethane: m.p. 63.5-64°; reduction yielded isoamy alcohol), linalool, and traces
of geraniol in addition to other higher boiling terpenic bodies.

These results have led the authors to conclude that an equilibrium isomerism exists between these two substances: dimethyl vinyl carbinol and dimethyl allyl alcohol, in terms of which the existence of the more complex products obtained can be explained.

The other isomeric alcohol, 2 methyl 1-butanol-4, has been reported only once, and admittedly, the constitution of the product was doubtful (10). The substance described was conceded to be possibly a mixture of $$\text{C}_2\text{H}_5$$ and $$\text{CH}_3\cdot\text{C}(-\cdot\text{CH}_2\cdot\text{CH}-\cdot\text{OH})$$, obtained by the dehydration of 2 methyl 1, 4 dihydroxy butane, $$\text{CH}_3\cdot\text{C}(-\cdot\text{CH}_2\cdot\text{CH}-\cdot\text{CH}_2\cdot\text{OH})$$. The mixture resulting from the dehydration was separated into two fractions: (1) 70-100°, and (2) 115-130°. The latter was believed to contain the alcohol in question. The acetate prepared from this fraction was an oily liquid of pleasant odor, boiling between 120-130°. No other mention of this alcohol has been found in the literature to date.

More recently, Spath and Bruck (11) have proposed the name "Prenol" for dimethyl allyl alcohol, and have suggested the designation of the radical $$\text{C}_2\text{H}_5$$ as the "Prenyl" radical in order to emphasize the relationship of this group to isoprene. It is the author's intention to use this system of nomenclature in the subsequent portions of this thesis in order to avoid confusing this alcohol with the closely-related isomers previously mentioned.
EXPERIMENTAL
Section I: Bromination Study on Isoamyl Acetate:

Several varied approaches to the synthesis of prenol were considered carefully before one was selected. Among the more obvious syntheses, the reduction of the unsaturated aldehyde to the alcohol appeared at first as the best approach. Fischer (12) has recently synthesized this aldehyde, 2 methyl butene-2 aldehyde by a series of interesting reactions, using isoamyl alcohol as the starting material. The synthesis may be summarized by the following equations,

\[
\begin{align*}
\text{CH}_3\text{-CH-CH}_2\text{-CH}_2\text{-CH}_3 + \text{H}_2\text{O} & \xrightarrow{\text{B}^+} \text{CH}_3\text{-CH-CH}_2\text{-CHO} + \text{H}_2\text{O} \\
\text{CH}_3\text{-CH-CH}_2\text{-CH}_2\text{-CH}_3 & \xrightarrow{\text{H}^+} \text{CH}_3\text{-CH-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_3
\end{align*}
\]

Because the aldehyde configuration is in the conjugated position with respect to the ethylene linkage, this aldehyde is extremely unstable toward oxidation. This factor alone was most significant in eliminating this approach to the problem.

The acid which may be derived from the alcohol, dimethaeryllic acid, can be synthesized in several elementary ways. However, it appeared improbable that the reduction of the acid to the alcohol could be satisfactorily accomplished.

A third method, and the first one selected, was based on some bromination studies that have recently been carried out in this laboratory. Schiller (13) studied the photochemical and catalytic bromination of several hydrocarbons,
and carried out some preliminary studies on the direct bromination of alcohols, which were supplemented by Marsh (14). The hydrocarbon study indicated that photohalogenation of branched-chain hydrocarbons such as iso-hexane proceeded with almost explosive violence, the tertiary hydrogen undergoing rapid substitution. Further bromination revealed that the carbon atom adjacent to the one containing the bromine was the next one attacked. Thus,

\[
\text{CH}_3 - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \xrightarrow{\text{Light}} \text{CH}_3 - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \rightarrow \text{CH}_3 - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH}_3
\]

Bromination of primary straight chain alcohols, on the other hand, resulted in a variety of products, including the alkyl bromide, acids, esters, and brominated esters.

On the basis of these findings, it was decided to attempt the photobromination of \(1^o\) isoamyl acetate, in which, it would be predicted, the bromine should substitute the tertiary hydrogen of the alkyl group. It was felt that this bromo ester, upon dehalogenation with suitable reagents such as alcoholic KOH or pyridine would yield the acetate of the desired unsaturated alcohol, which would be expected to undergo saponification in the normal manner to yield prenol. The proposed reactions may be summarized in the following manner:

\[
\text{CH}_3 - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \xrightarrow{\text{light}} \text{CH}_3 - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \rightarrow \text{CH}_3 - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{CH}_3
\]

\[
\text{CH}_3 - \text{C} = \text{CH} - \text{CH}_2 - \text{O} - \text{CH}_2 - \text{OH} \xrightarrow{\text{KOH}} \text{CH}_3 - \text{C} = \text{CH} - \text{CH}_2 - \text{OH}
\]
For the preparation of isoamyl acetate, 75 grams of c.p. isoamyl alcohol (b.p. 126-131°) were mixed with 90 grams of acetic anhydride (5% excess) in a 500-ml. flask with attached reflux condenser. To this mixture were added three drops of concentrated H$_2$SO$_4$, and the mixture well shaken. After an induction period of ten minutes, during which no heat was applied, sensible evolution of heat from the mixture was detectable, with a subsequent rapid rise in temperature to such an extent that external cooling had to be applied. Thereupon the mixture was refluxed for two hours and cooled. Purification followed in the normal manner, and the dried product was distilled and collected over the range 140-145°. Yield, 89.5 g., equivalent to 82% (Subsequent preparations gave slightly higher yields).

Preliminary Brominations: Three one-ml. portions of isoamyl acetate were mixed with a few drops of bromine in test tubes and exposed to light of strong intensity from a "Photo-flood" lamp #2. Powdered iron was added to one, and powdered copper to another. Neither of these samples gave evidence of evolution of HBr (breath test). Heating the samples in the absence of strong light produced no reaction. However, heating of the ester-bromine mixture alone while exposed to the flood lamp resulted in evolution of HBr.

Therefore, bromination of the ester on a larger scale
was attempted. 87.5 grams of isomyl acetate was placed in a 500 ml. flask attached with reflux condenser, HBr trap, and dropping funnel. The flask was placed just above the photoflood lamp, which was cooled by ice water from the condenser running through a conical metal jacket surrounding the lamp. By means of the dropping funnel, 115 grams of c.p. bromine were added over a period of about three hours, while the mixture was heated by playing a micro burner over the bottom of the flask so that the liquid was kept in gentle ebullition. After all the bromine had been added, the mixture was refluxed for an hour (Omitted in subsequent brominations as causing undue decomposition). The mixture at this stage was highly discolored due to decomposition products from the corks used.

The brominated product was washed with saturated bisulfite, then successively with water, dilute NaOH, and again with water. The mixture was then steam distilled in order to remove unreacted ester, and the residue was separated without further purification. This product was still discolored, and was not weighed, but was directly subjected to dehalogenation with alcoholic KOH. It is interesting to note that this product was highly lachrymatory, and all subsequent preparations of it exhibited this property.

Dehalogenation of Brominated Ester: Twenty grams of the brominated product were added slowly to 60 ml. of alcoholic KOH (13 g. KOH), contained in a three-necked flask attached
with reflux condenser, dropping funnel, and mercury-seal stirrer. The reaction proceeded rapidly, with evolution of much heat, so that the solution was kept at the boiling point and required external cooling. The reaction was further accompanied by the separation of a white crystalline precipitate (KBr). After all of the brominated ester had been added, the mixture was refluxed for two hours to allow the ester linkage to hydrolyze.

The ethyl alcohol was then distilled out of the mixture from a water bath, and the residue taken up in water; however, very little separation of layers was noted, even after standing overnight. The aqueous mixture was therefore steam-distilled, whereupon an oily layer settled out, whose density, however, was greater than 1. This was indicative of polybromide formation in the bromination procedure. The aqueous portion of the steam distillate and the oily layer both reduced neutral permanganate rapidly; the ethyl alcohol distillate, too, was unsaturated. However, distillation through a packed column equivalent to about six plates effected no separation of components in the alcohol distillate. The equilibrium temperature under total reflux was 74°, increasing to 78° after the first few drops had distilled over. The temperature then remained constant throughout the distillation until only a few ml. of residue remained in the flask. Yet, all fractions collected reduced permanganate rapidly!

A consideration of the solubility of isoamyl alcohol
in water indicated that the aqueous layer of the steam distillate might contain appreciable amounts of the unsaturated alcohol, if it were present. It was therefore saturated with anhydrous $\text{K}_2\text{CO}_3$, and the oily layer which separated was extracted from the water layer with two 25-ml. portions of ether. After drying, the ether was distilled off through the six plate column until the volume of the residue approached ca. ten ml. This was then distilled from a small distilling flask in order to determine its boiling range.

Boiling began at $130^\circ$, and the temperature rose steadily to $210^\circ$. The distillate was collected in two portions; $130-140^\circ$; and $140-210^\circ$. This second portion was highly discolored and gave evidence of much decomposition. Both fractions were unsaturated.

A portion of the $130-140^\circ$ fraction was treated with freshly-prepared 3,5 dinitro benzoyl chloride, whereupon a vigorous reaction resulted. After heating gently for a minute, the mixture was poured into ten ml. of cold water and stirred. The solid which separated was purified and recrystallized twice from alcohol. After drying, the melting point was determined and found to be $91-93^\circ$. Ethyl, 3,5-dinitro benzoate has melting point $92^\circ$; a mixed melting point showed no depression. Therefore, it may be concluded that the alcohol present in this cut was ethyl alcohol, which had been salted out of the steam distillate. The elevation in boiling point is not unusual, since the succeeding portion of distillate
was so high boiling. At any rate, this procedure did not apparently yield the desired unsaturated alcohol.

Several repetitions of the foregoing bromination-debromination-hydrolysis procedure were carried out, all of which yielded similar results. The debromination procedure was modified in that a KOH-methyl alcohol mixture was used instead of ethyl alcohol, in order to increase the difference in boiling points between the final products and solvent. In general, the steam distillate from the dehalogenation contained an oily layer whose density was greater than 1. This oily layer always gave a positive Beilstein test. Furthermore, the permanganate test was always positive. Several times, distillation of the dried debrominated product indicated a small flat near 97-100°. The product boiling at this temperature was unsaturated, slightly soluble in water, and had density less than 1. It reacted readily with acetyl chloride, yielding a product of density greater than 1, and which was still unsaturated. This behavior with acetyl chloride is typical of tertiary alcohols, and these reactions have led to the conclusion that the product was \( \text{CH}_3 - \text{CH} = \text{CH}_2 \) (b.p. 98°). An explanation for its occurrence is offered in a later portion of the thesis (see page 19).

Reflection on the procedures involved, however, revealed several limitations that had not been considered previously.

In the first place, the presence of bromide in this
product which theoretically should have been completely dehalogenated, indicated that the bromination product was evidently a mixture. Recovery of unconverted isoamyl acetate equivalent to ca. 50% of the starting material, as well as the fact that one equivalent of bromine had been taken up, seemed to bear out this conclusion.

Secondly, the procedure employed in the preliminary purification of the brominated ester, on consideration, appeared highly at fault. Michael (15) pointed out that tertiary alkyl halides were very easily hydrolyzed; tertiary amyl bromide being quantitatively hydrolyzed in thirty minutes by simply shaking with water. It is also well known that tertiary butyl chloride is very rapidly hydrolyzed by shaking with water for a short time, as evidenced by the surprisingly high boiling point of the "c.p. butyl chloride" prepared by the average student in the elementary organic laboratory. Therefore, assuming that some tertiary bromide was present in the brominated ester, subjecting it to washing with dilute alkali and steam distillation would present ample opportunity for this halide to undergo hydrolysis, so that the desired product would be lost.

A consideration of these factors led to the decision that no purification of the kind discussed should be attempted on the brominated product, but that it should be subjected to some sort of fractional distillation. Preliminary investigation revealed that the boiling point of
isoamyl acetate was 46-47° under 34 mm. Under the circumstances, the purification of the brominated product was carried out in the following manner:

Immediately after the bromination, the product was transferred to a Gläsern flask and distilled under vacuum. At first, the pressure was reduced gradually, in order to flash off the HBr and any unreacted bromine. Thereupon, the pressure was reduced to 34 mm. by means of a water pump, and the isoamyl acetate distilled from the mixture. The following data represents some mean values from several investigations.

In general, boiling began at ca. 45°, and was followed by a gradual temperature rise as the ester distilled. The per-cent of isoamyl acetate recovered varied appreciably over a series of several runs from as low as 40% unreacted ester to as much as 70-75%, depending upon the equivalents of bromine that had been added in the bromination. As a rule, a flat was observed in the distillations near temperatures of 80-90°, at ca. 30 mm., the product condensing generally showing signs of decomposition, as evidenced by a dark purple color that it would take on as the distillation progressed, and the slow evolution of HBr. This product, designated as "monobromide", generally occurred in very small amounts in comparison to the residual "polybromides" which could not be distilled at 30 mm. without extensive decomposition.

Dehalogenation of the monobromide cut with alcoholic
KOH gave results very similar to those obtained previously in the dehalogenation of the total bromides. Acidification of the aqueous residue remaining in the flask after steam distillation of the unsaturated products, yielded the typical odor of acetic acid, which was identified as the anilide and melted at 111-112° (given: 113°). This then indicated that in the monobromide the halogen entered the R-group, and not the acid residue.

Furthermore, the alcohol distillates from these debrominations were always found to be highly unsaturated, and to contain a low boiling constituent which apparently formed an azeotropic mixture with the alcohol, for fractional distillation through the packed column always yielded products whose boiling points were very close to that of the alcohol used in the dehalogenation, yet were highly unsaturated. Addition of water to these distilled fractions always produced turbidity in these cuts, which theoretically should have been "pure" alcohol. This unsaturated product, it was felt, was probably isoprene, whose presence can be explained on the basis of some trustworthy data which was obtained later in the course of the investigation. Furthermore, the presence of the tertiary unsaturated alcohol mentioned previously may also be explained in the light of these findings. (See p. 19 for discussion).

The "polybromides", on the other hand, yielded some very interesting results. Dehalogenation with alcoholic
KOH yielded the expected unsaturateds of density greater than 1. A search for acetic acid in the acidified residue, however, was unsuccessful. A small portion of the acidified residue was boiled with 25% sulfuric acid, and the distillate was tested with Schiff's reagent. A permanent purple color was produced, which could not be destroyed upon acidification with dilute sulfuric acid; this is a typical reaction of formaldehyde, and indicates that the acid residue in the polybromide is bromo-acetic acid, which on hydrolysis would yield glycolic acid. The latter is oxidized by sulfuric acid to yield formaldehyde, which reacts irreversibly with the fuchsin reagent.

Further examination of the polybromides indicated that they reacted vigorously with the Gladstone-Tribe copper-zinc couple in 95% alcohol (16). A portion of these bromides was then debrominated in this manner, and among the products resulting, the following were identified:

(a). Isoprene: boiling point (impure) 33-40°; unsaturated; reacted with permanganate readily, and decolorized bromine in CCl₄ without liberation of HBr. The isoprene was identified by means of the Diels-Alder addition to maleic anhydride in benzene. The crystals that formed were dried in vacuo over paraffin and found to melt sharply at 63°. (Reported m.p. for this product, 63°).

(b). An unsaturated monobromide (probably) boiling between 120-126°. Reduced permanganate readily, and reacted with aqueous AgNO₃ to give a yellow curdy precipitate.
Sodium fusion confirmed the presence of bromine. This product was believed to be prenyl bromide, for which various boiling points are reported. However, this product was not successfully identified.

An explanation for these observations may lie in the fact that halogen acids can split esters to the alcohol and corresponding acid, the halogen acid thereupon reacting with the alcohol to give the alkyl halide (17). Subsequent studies in this laboratory on the photohalogenation of isoamyl bromide indicated that a mixture of bromides resulted, ranging from dibromides to higher substituted products, probably tetrabromides. Thus,

\[
\begin{align*}
\text{CH}_3\cdot \overset{\text{C}}{\text{C}}\cdot \text{N} - \text{C}_6\cdot \overset{\text{O}}{\text{C}}\cdot \overset{\text{C}}{\text{N}}_3 & \xrightarrow{\text{HBr}} \text{CH}_3\cdot \text{C}_6\cdot \overset{\text{C}}{\text{C}}\cdot \text{C}_6\cdot \overset{\text{C}}{\text{C}}\cdot \overset{\text{O}}{\text{C}}\cdot \overset{\text{C}}{\text{N}}_3 \\
\text{CH}_3\cdot \overset{\text{C}}{\text{C}}\cdot \text{C}_6\cdot \overset{\text{C}}{\text{C}}\cdot \overset{\text{O}}{\text{C}}\cdot \overset{\text{C}}{\text{N}}_3 & \xrightarrow{\text{HBr}} \text{CH}_3\cdot \overset{\text{C}}{\text{C}}\cdot \text{C}_6\cdot \overset{\text{C}}{\text{C}}\cdot \overset{\text{O}}{\text{C}}\cdot \overset{\text{C}}{\text{N}}_3
\end{align*}
\]

The production of isoprene in the zinc-debromination of the polybromides (above) may readily be explained as having been formed from the tetrabromide, and the occurrence of the latter and the tribromides is not difficult to postulate in consideration of the fact that as much as 70% of the isoamyl acetate subjected to bromination with one equivalent of bromine was recovered unreacted. For example, of 161 g. isoamyl acetate brominated with 198 g. of bromine, 120 grams of the ester were recovered, whereas the brominated product weighed 128 grams.

The presence of isoprene in the products obtained by the alcoholic-KOH dehalogenation of the "monobromide" is
readily explained by the fact that 2,4-dibromo 2-methyl butane, one of the products of the brominated isoamyl bromide (b.p. ca. 85° at 30 mm.) is dehalogenated to yield isoprene (3). The "monobromide" must evidently be considered as a mixture of this substance and monobrominated ester (since the acetic acid could be isolated from the hydrolyzed product).

Furthermore, the occurrence of the tertiary unsaturated alcohol, \( CH_3-C=C-C_6H_5 = CH_2 \), may also be explained on this basis. Thus,

\[
\begin{align*}
\text{CH}_3-C = C-C_6H_5-B_2H_3 & \xrightarrow{H_2O} \text{CH}_3-C=CH_2 = CH_2 \\
\end{align*}
\]

Evidence for reaction (1) has been found by Claisen (4), while reaction (2) may be readily predicted.

The failure of the search for the acetic acid residue in the polybromides, and the positive indication of the presence of glycolic acid in the hydrolyzed product led the investigator to search for a similar ester to brominate wherein bromination of the acid residue might be reduced to a minimum. Therefore, a bromination-debromination-hydrolysis series was carried out on isoamyl \( p \)-nitrobenzoate.

To summarize in brief, the bromination was carried out in a benzene solution, the benzene steam distilled from the mixture, and the bromide ester extracted with boiling chloroform, which was flashed off under reduced pressure, leaving
a rather dark, but fairly clean liquid residue.

The debromination was attempted this time with pyr-idine, by refluxing the bromide with this reagent for three hours in an atmosphere of methane. The mixture was then poured into dilute HCl, the organic layer separated, and refluxed for five hours with 20% NaOH. Steam distillation yielded an organic layer, which was salted out with anhydrous K_2CO_3. Distillation of this dried product revealed its boiling point to be that of isoamyl alcohol, 132°. Further this substance had the typical fusel-oil odor of isoamyl alcohol, and did not reduce permanganate.

Acidification of the alkaline residue from the sapon-ification, precipitated a gelatinous mass of yellow platelets, which after drying, did not melt at any temperature up to 250°. The product burned with a smoky flame in an explosive fashion, leaving no residue, was practically insoluble in the ordinary organic solvents, and contained bromine, as indicated by sodium fusion.

On the basis of these findings, it was decided to dis-continue the bromination study of isoamyl esters in the at-tempt to synthesize prenol by a new method.

Section II. Bromination Study on 1° Isoamyl Bromide

It was as a result of these studies on the bromination of isoamyl bromide that many of the problems associated with the first investigations were solved; at least, a logical explanation for the existence of so many products was of-fered.
It was predicted that photocatalysis of isoamyl bromide would yield 2,4 dibromo 2 methyl butane \((\text{CH}_3\text{-}\text{C}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{Br})\) isoprene bishydrobromide. It was felt that the difference in reactivity of the two bromine atoms might allow selective dehalogenation of the tertiary bromine by treatment with one mole of alcoholic KOH per mole of dibromides.

Thus,

\[
\text{C}/\text{H}_3\text{-}\text{C}\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{Br} \xrightarrow{\text{Alc. KOH, 1 Mole}} \text{C}/\text{H}_3\text{-}\text{C} = \text{CH} = \text{CH}_2 = \text{Br}
\]

It was planned then either to hydrolyze the product, or else prepare esters of prenol by refluxing the unsaturated bromide with an excess of the potassium salt of the acid desired. (It has been demonstrated, however, that the bromide undergoes hydrolysis to yield the tertiary unsaturated alcohol (4) (See page 19)).

Preliminary investigation on a small portion of research preparation isoamyl bromide (b.p. 119-123°) revealed that bromination proceeded slowly in the cold in the presence of light from the photoflood lamp, while heating caused the bromine to substitute rapidly, with vigorous evolution of HBr.

**Synthesis of Isoamyl Bromide:** 88 grams of c.p. isoamyl alcohol (1 mol) was mixed in a flask with 200 ml of water containing 153 grams of technical NaBr. Through the attached condenser, 140 ml of conc. H\(_2\)SO\(_4\) were added in ten ml portions, followed by vigorous shaking. After the acid
had been added, the mixture was refluxed for two hours, and
the organic layer distilled over.

The crude bromide was washed with water, then with
cold conc. H₂SO₄ to remove unconverted alcohol. This was
followed by washing with saturated sodium bicarbonate, and
again with water. The product, dried over CaCl₂ was dis-
tilled, and the portion boiling from 119-125° was collect-
ed. Yield, 90 grams, equivalent to 60%. (Subsequent prep-
arrations gave yields up to 83%).

Bromination of the isoamyl bromide was carried out in
the same manner as the bromination of the acetate, except
that variations were introduced in regard to the amount of
heating applied during the bromination procedure. It was
found that heating the mixture with a micro burner at a
rate such that the bromide was kept in constant ebullition
due to evolution of HBr allowed the bromine to be taken up
very rapidly, an average of about two hours being required
for the addition of 100 ml. of bromine to 300 ml. of the
bromide. On the other hand, allowing the reaction to take
place without heating, but while exposed to the lamp, re-
quired thirty-six hours for comparable quantities. In both
cases the yield of dibromide was about the same: ca. 40%.

After one equivalent of bromine had been added to the
isoamyl bromide, the mixture was allowed to cool, trans fer-
red directly to a Claisen flask, and distilled under reduc-
ed pressure. Preliminary investigation had revealed that
isoamyl bromide boiled at 34-35° under 32-33mm. The pres-
sure was reduced slowly to flash off the remaining HBr. Thereupon, the pressure was reduced to 32 mm., and the mixture distilled. Three cuts were made, which were subsequently redistilled and separated into two fractions:

1. 34-55 at 32 mm. 120-125 at atmospheric pressure; weight 40.4 g. (Recovered isocymyl bromide)

2. 90-110 at 32 mm. weight 54.7 g.; dibromide, undecomposed.


Of the 151 grams of isocymyl bromide used, 40.4 grams were recovered. On the basis of reacted monobromide, 36% was converted to dibromide.

This bromination-distillation procedure was carried out several times until over 100 g. of the product designated as dibromide was obtained. This was then re-distilled several times from the Claisen flask at reduced pressures until a large fraction of these combined portions was obtained which boiled from 85-88° under 29-30 mm. of pressure.

This tedious series of separations involved in this work, as well as a consideration of the variety of products obtained in the halogenation as revealed by subsequent experience, led to the conclusion that the brominated products would require distillation through an efficient fractionating column, under reduced pressure. Several experiments were attempted on the dibromide mentioned above.
However, since the same investigations were subsequently carried out on a much superior and purer product, only the latter are described in the following portions.

A. Preparation and Purification of Isoamyl Bromide:

500 g. of c.p. isoamyl alcohol were treated with the calculated amount of $\text{H}_2\text{SO}_4$-$\text{HBr}$ mixture as described previously. The purification was modified only in that the product was not washed with acid, in order to prevent the possibility of any rearrangements influenced by strong acid. Instead the washed and dried product was fractionally distilled through a Widmer column equipped with a total reflux-partial take-off head adapted for distillation at atmospheric or reduced pressure. The fractionation was carried out at 43 mm., under which, isoamyl alcohol was found to boil at 64°. With a reflux ratio of 6:1, 566 grams of isoamyl bromide, representing a yield of 66%, were collected over a range of 1.2° (38.3-40° at 43 mm.). The residue was unconverted isoamyl alcohol, and only a small amount of fore-run was obtained. From a consideration of the boiling point of isoamyl bromide at various pressures, an empirical expression was obtained by means of an equation derived by Dr. G. H. Richter of The Rice Institute, relating vapor pressure to temperature for this compound:

$$\log p = \frac{-3.651.58}{t+410.83} + 9.75117$$

where $p = \text{pressure in mm. Hg}$

$t = \text{temperature in degrees centigrade}$
This equation was checked several times at various pressures during subsequent fractionations, and the observed temperatures in general found to agree within 0.5° of the calculated value.

The isoamyl bromide was brominated with one equivalent of bromine in the normal manner, and was then immediately transferred to the Widmer column for distillation. The pressure was reduced gradually by means of a water pump until the HBr had been pumped off. Thereupon the pressure was reduced to 75 mm., under which pressure, isoamyl bromide should boil at 52°, according to the vapor pressure-temperature equation above. In support of this calculation, the equilibrium temperature under total reflux was 50° (wet), rising to 52° after the first few drops were bled off. The temperature remained constant until most of the monobromide had been distilled, whereupon the temperature in the still head began dropping rapidly, an indication that the next fraction boiled at a much higher temperature. Of 528 grams monobromide treated in the bromination, 210 g. were recovered. This recovered product was then rebrominated in the usual manner and again fractionated, the residue after removal of unreacted isoamyl bromide (68 g.) being combined with the residue from the first distillation and fractionated together.

In order to diminish thermal decomposition of the dibromides, the residue consisting of dibromides and higher polybromides was distilled at still lower pressures obtained.
by means of a Cenco Hy-Vac pump. Between the pump and the system, were connected in the order listed, two drying towers packed with NaOH pellets; a trap through which all escaping vapors had to pass, immersed in a dry-ice-ether mixture contained in a Dewar flask in order to condense any bromide vapors that might otherwise pass into the pump; and finally, a leak valve, consisting of a long capillary tube which was broken off in small pieces until the desired pressure was obtained. Pressure was indicated by both a differential and an absolute manometer, which were connected into the system between the dry-ice trap and the column, in order that freezing and clogging of the trap would be indicated by a pressure increase in the system.

The dibromide-polybromide mixture was then fractionated, and the following cuts taken:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Pressure</th>
<th>Boiling Point</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 mm.</td>
<td>34-42</td>
<td>isoamyl bromide &amp; lower boiling dibromides</td>
</tr>
<tr>
<td>2</td>
<td>5 mm.</td>
<td>42-45</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4.1 mm.</td>
<td>45</td>
<td>flat</td>
</tr>
<tr>
<td>4</td>
<td>3.8 mm.</td>
<td>45-55</td>
<td>intermediate 5 cc.</td>
</tr>
<tr>
<td>5</td>
<td>Residue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fraction 5 was by far the largest of the distilled fractions (ca. 125-130 ml.) and when it was seen that a flat portion had been reached in the distillation, the pressure was varied several times in order that the boiling points of this dibromide might be observed at various pressures. From
these observations, the following relation relating vapor pressure to temperature for this compound was obtained:

\[
\log p = \frac{-50,340.7}{t - 1,555.1} - 32.723
\]

Of 528 grams of isoamyl bromide subjected to bromination, 68 grams were recovered, and approximately 240 grams of a dibromide boiling over a range of less than 2 degrees was obtained, as well as a residue of higher bromides weighing 321 grams. This represents a yield of slightly over 30% of dibromide as an absolute minimum, since a fair amount of this product was collected with fraction 2 before it became apparent that a flat had been reached.

B. Identification of Dibromide:

The data in the literature that was available on 2,4 dibromo-2 methyl butane was extremely varied. In the past, this product had been obtained by the addition of two equivalents of HBr to isoprene in one case (18), and to dimethyl allene in a second (19). Favorski has reported the occurrence of this dibromide as obtained in thermally-induced rearrangements of trimethylethylene dibromide at 180° (20).

A consideration of the dibromo products that could be expected in the normal course of the bromination of isoamyl bromide, leads to the following possibilities:

1. \( \text{CH}_3 - \text{CH} - \text{CH} - \text{CH} - \text{Br} \) \( \text{Br} \) Isopropyl ethylene dibromide

2. \( \text{CH}_3 - \text{C} - \text{CH} - \text{CH} - \text{CH} - \text{Br} \) \( \text{Br} \) Isoprene bishydrobromide

3. \( \text{CH} - \text{C} - \text{CH} - \text{CH} - \text{CH} - \text{Br} \) \( \text{Br} \) 1,4 dibromo 2 methyl butane
The following table was drawn up to compare the boiling points of these products as reported in the literature both among themselves and, as a whole, with the boiling points for the dibromide obtained in this laboratory as calculated from the equation mentioned previously:

<table>
<thead>
<tr>
<th>Pressure (mm.)</th>
<th>Boiling Point Of (From Literature)</th>
<th>Calc'd B.P.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\text{C}_4\text{H}_6 - \text{C} - \text{C} - \text{CH}_2 - \text{CH}_2 - \text{H}$</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>---</td>
<td>67 (24)</td>
</tr>
<tr>
<td>10</td>
<td>64-66 (21)</td>
<td>61 (20)</td>
</tr>
<tr>
<td>12</td>
<td>61-62 (22)</td>
<td>---</td>
</tr>
<tr>
<td>16</td>
<td>---</td>
<td>74-75 (19)</td>
</tr>
<tr>
<td>20</td>
<td>74-76 (23)</td>
<td>---</td>
</tr>
<tr>
<td>23</td>
<td>---</td>
<td>80-82 (25)</td>
</tr>
</tbody>
</table>

A comparison of the above-listed boiling points shows striking agreement between those for isoprene bishydrobromide and those values observed in this laboratory, although no positive conclusion may be drawn therefrom, since isopropyl ethylene dibromide has comparable values. Notwithstanding this fact, there nevertheless exists a multitude of chemical evidence which supports the conclusion that the dibromide is 2,4 dibromo 2 methyl butane, not the least of which is the rapidity of the reaction between this substance and aqueous AgNO$_3$, which strongly suggested the presence of a tertiary halogen.

The density and refractive index of the dibromide at $20^\circ$ were measured.

air weight dibromide at $20^\circ = 14.9476$ g.  
"       " equal volume H$_2$O = 8.98395 g.
Density at 20° C. : 1.6601

Reported D° : 1.6969 (19)

The refractive index was determined for the Na-D line with a Pulfricht Refractometer at 20°.

Observed angle 36° 53'

\[ \text{n}_d^{20} = 1.50563 \]

\[ [\text{M}]_D^2 : \text{Found, 41.12; Calc'd for C}_5\text{H}_{10}\text{Br}_2, 40.61 \]

More conclusive evidence regarding the nature of this dibromide was obtained by means of several investigations, the results of which were very gratifying in that they bore out the conclusion suggested by the boiling point data listed previously.

The dibromide was analyzed for halogen by the Carius method, and the percent bromine found to agree well with the theoretical.

<table>
<thead>
<tr>
<th>Wt. Sample</th>
<th>Wt. AgBr</th>
<th>% Br (found)</th>
<th>(theory)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2145 g.</td>
<td>0.3467 g.</td>
<td>68.8</td>
<td>69.5</td>
</tr>
<tr>
<td>0.2016 g.</td>
<td>0.3279 g.</td>
<td>69.2</td>
<td></td>
</tr>
</tbody>
</table>

A consideration of the positions of the bromine atoms in the dibromide led to the prediction that debromination of this product by means of the Gladstone-Tribe copper-zinc couple in 95% alcohol should yield dimethyl trimethylene (1,1 dimethyl cyclopropane).

\[
\text{CH}_3 - \text{C} - \text{CH}_2 - \text{CH}_2 \xrightarrow{\text{Zn} \cdot \text{Cu}} \text{CH}_3 \quad \text{CH}_3
\]
Ipatieff, who had prepared this dibromide by the addition of HBr in acetic acid to an acetic acid solution of isoprene (and later, dimethyl allene) at low temperatures, found that the product reacted with zinc in alcohol only upon warming, whereas trimethyl ethylene bromide reacted very vigorously at room temperature. The conclusion that Ipatieff drew therefrom was that the bromines in the former were not in adjacent positions. Furthermore, he too postulated that the hydrocarbon obtained by the zinc debromination was a cyclic ("ein Kohlenwasserstoff mit geschlossener Kette") (19).

The debromination of the dibromide was carried out in the following type of apparatus: A 250-ml. flask was mounted at the base of a short packed fractionating column, the top of which contained a two-hole rubber stopper equipped with a dropping funnel leading into the column, and a reflux condenser connecting at an angle of about 30°. A short piece of glass tubing, which was connected by means of a tightly fitting rubber stopper onto the end of the condenser, led directly into a wash bottle containing 400 ml. of 5% neutral KMnO₄ in order to remove any olefins. The exit tube of the permanganate trap was connected to a drying tube packed with CaCl₂. A glass tube at a right angle then led into a long graduated test tube immersed in a dry-ice-ether mixture contained in a Dewar flask. All rubber connections were coated with a mixture of bees-wax and rosin, so that when a pinch clamp was inserted between the
condenser and the wash bottle, a gas-tight system was obtained.

Thirteen grams of zinc dust were immersed briefly in a dilute solution of copper sulfate, filtered, washed with water, followed by alcohol and ether, then dried briefly in air before using. This metal couple was then placed in the flask at the base of the packed column (ca. six plates) and covered with 40 ml. of 95% ethyl alcohol. Twenty-three grams (0.1 mole) of the pure dibromide were then added slowly to the mixture by means of the dropping funnel at the top of the column. The mixture had to be warmed briefly to initiate the reaction, which then proceeded readily until all the dibromide had been added, with only occasional warming. The alcohol vapors were for the most part held back by the column, whereas the hydrocarbon, which boils at 21° (28), passed to the condenser at the top of the still. The condenser was therefore kept at 22° by a mixture of ice-and-tap-water regulated to that temperature, so that a minimum of alcohol would be carried into the permanganate, whereas all of the low-boiling constituent might pass through and into the Dewar flask.

The permanganate bottle contained 400 ml. of distilled water, to which had been added exactly 20.00 g. of KMnO₄, 100% in excess of the amount necessary to oxidize 0.1 mole of olefin.

After the reaction in the flask had apparently gone to completion, the flask was heated until the alcohol vapors
reached the top of the column and began dropping back from the condenser. The column was then nearly filled with water and 300 cc. of air was passed into the system in order to wash out any remaining hydrocarbon. The condensate in the Dewar flask was then examined and found to have a volume of 5.12 ml, just below the boiling point of the liquid (21.2° at 1 atmosphere).

A systematic literature search brought to attention the results of some additional investigations by Ipatieff into the nature of isoprene bishydrobromide. This investigator at first reported (27) that dehalogenation of this dibromide with zinc in alcohol yielded trimethyl ethylene (b.p. 35-38°) instead of the expected dimethyl cyclopropane. This experiment was repeated a short time later in order to clarify the mechanism of the reaction, whereupon it was discovered that the debromination product was not trimethyl ethylene, but instead, another olefin: isopropyl ethylene (b.p. 21°) (28).

The hydrocarbon obtained in this laboratory and boiling at 21.2°, had, however been passed through a permanganate trap in order to remove olefins, since the article by Ipatieff had not been read before the experiment was carried out. Its nature was therefore of extreme interest. A small portion of it was tested by shaking with dilute permanganate, a similar test being run simultaneously with trimethyl ethylene. The latter decolorized the permanganate so rapidly that a brown gel of MnO₂ was obtained, whereas the
former reacted only very slowly, the permanganate not being completely decolorized after two minutes.

The 20.00 grams of \( \text{KMnO}_4 \) in the washing tower had been only slightly decolorized by the gases which had passed through, so it was decided to determine to what extent it had been reduced. In order to separate the unreduced permanganate from the \( \text{MnO}_2 \) that had formed, the trap contents were filtered through a sintered glass crucible, and the small amount of solid retained, washed several times with water. The solution was then diluted to exactly 1000 ml. and standardized against c.p. oxalic acid dihydrate. Thus, 0.8255 grams of the oxalic acid required 22.18 ml. of the permanganate solution. This represented a minimum of 18.7 grams of permanganate that had not been reduced by the hydrocarbon, and a maximum of 1.3 grams which had been reduced.

Gustavson and Popper (26) found that although dimethyl cyclopropane reacted very slowly with permanganate, it did not completely decolorize the reagent even after 24 hours. These investigators further reported that, in contrast with isopropyl ethylene (29), dimethyl cyclopropane was completely dissolved by 66% sulfuric acid at 0\(^\circ\) in ten minutes. The hydrocarbon obtained in this laboratory, however, was not soluble in 66% sulfuric acid at the end of 30 minutes in a sealed tube immersed in ice water. Instead, when the contents of the tube were investigated after five days in the sealed tube at room
temperature, a product different from the original was obtained, which was steam-distilled out of the acid and dried over potassium carbonate. This product had a pleasant, hydrocarbon-like odor, did not react with acetyl chloride, and did not react at all with permanganate, although it reacted rapidly with bromine in $\text{CCl}_4$, with evolution of HBr. Although $2^\circ$ isoamyl alcohol has never been obtained by the sulfuric acid addition of water to isopropyl ethylene, an iodoform test was made on this product, which, however, was absolutely negative. A micro boiling point taken on the product was inconclusive, indicating that the product was evidently a mixture. The first boiling point observed was 158$^\circ$, but the boiling temperature increased regularly with each determination.

Norris and Joubert (30) have recently made a study on the polymerization of the amylenes by sulfuric acid, in which they reported that isopropyl ethylene is polymerized rapidly at room temperature by conc. sulfuric acid to yield a product boiling mainly between 150-335$^\circ$. On the other hand, ten mols of the hydrocarbon in one mole of 2:1 sulfuric acid is polymerized at the end of seven days to yield mostly a dimer (b.p. 153-158$^\circ$), which decolorized bromine in $\text{CCl}_4$, but was not tested with permanganate.

In order to compare the hydrocarbon obtained in this laboratory with isopropyl ethylene, the latter was prepared from c.p. isoamyl bromide (b.p. 38.8-40$^\circ$ at 43 mm.)
by dehalogenation with alcoholic KOH (29). From 22.6 grams of isoamyl bromide (0.15 moles) and 0.6 moles of KOH in 120 ml. of alcohol, about 1 ml. of condensable hydrocarbon was obtained, the remainder of the bromide being converted into ethyl isoamyl ether (14 ml.). This hydrocarbon boiled at 21°, and reacted with permanganate in exactly the same manner as the hydrocarbon obtained from the dibromide. The odor of the two substances was identical.

These observations suggest that these two hydrocarbons are the same, although a shadow of doubt as to the true structure of the products is cast by the reaction with permanganate. It does not at all appear unlikely that the alcoholic KOH dehalogenation of isoamyl bromide might yield both isopropyl ethylene and dimethyl cyclopropane. In fact, a space model of isoamyl chloride indicates that the halogen is touching the 3° hydrogen in the molecule, and is, in fact much nearer to this hydrogen atom than to the hydrogen on the adjacent carbon atom. The solubility test in 66% sulfuric acid to differentiate dimethyl cyclopropane and isopropyl ethylene is not at all convincing, and there exists much conflicting data in the literature in regard to many unexpected reactions of isopropyl ethylene, as well as of dimethyl cyclopropane (15, 31, 30).

Because this investigation led to rather inconclusive results, several independent methods were employed
to fix more definitely the structure of this dibromide. Michael (15) found that the rate of hydrolysis of $1^0$, $2^0$, and $3^0$ halides was indeed widely different. In general, tertiary butyl halides were completely hydrolyzed at room temperature by shaking for 20 minutes with fifty times their weight of water, whereas the corresponding isoamyl halides required a little longer. The released halogen could then be titrated directly with standard silver nitrate. In contrast $2^0$ halides are not completely hydrolyzed at the end of two hours, while $1^0$ halides are hydrolyzed only upon long standing.

It has further been demonstrated (32) that adjacent dibromides, such as trimethylethylene bromide or isobutylene bromide are hydrolyzed only very slowly, despite the presence of a $3^0$ bromine in the molecule. Moreover, these experiments were carried out in the presence of lead oxide in order to disturb the equilibrium toward the hydrolysis.

In consideration of these facts, it was decided to attempt the direct titration of the $3^0$ halogen in the dibromide obtained, in order to determine the purity of the product. These results were then employed as a basis upon which the purity of subsequent preparations of the dibromide was determined. The procedure followed in each case was simple and yielded excellent result. From 0.4-0.8 grams of sample was weighed out in a small glass bulb and placed in 50 ml. of distilled water containing 0.4 g. of c.p. NaHCO$_3$, contained in a 150-ml. wide mouth bottle with
a tightly-fitting ground glass stopper. The sample bulb was shattered simply by shaking, and the mixture was shaken for forty minutes at room temperature. The bottle was then opened carefully to allow CO₂ to escape, the mixture was filtered through a wet filter paper (to retain the organic material) washed with water, and the filtrate titrated directly with N/10 AgNO₃ by the Mohr method, using 1 ml. of 5% potassium chromate as indicator. Thus, 0.5063 grams of dibromide, after hydrolysis and filtration, required 23.06 ml. of the standard AgNO₃, indicating 1.04 equivalents of tertiary bromine.

In order to exclude the possibility that adjacent dibromides might interfere, a 0.5 g. sample of isobutylene bromide (b.p. 150°) was treated in the same manner. Upon titrating the filtrate, it was found that the end point appeared after the first two or three drops of silver solution had been added. This then apparently excludes the possibility of interference by adjacent dibromides.

On the basis of the preceding experiment, a second series of investigations was begun which led to some additional evidence further supporting the proposed structure for the dibromide. On the assumption that the dibromide hydrolyzed, i.e., substituted a hydroxyl group for the tertiary bromine, whereas the primary bromine did not hydrolyze in forty minutes, the product at the end of that period should be a bromohydrin, \( \text{C}_4\text{H}_9\text{CH} - \text{CN} - \text{CN} - \text{Br} \). This product would be capable of reduction by various rea-
gents, serving to substitute a hydrogen for the bromine, to yield 3\(^0\) amyl alcohol.

To check this proposal, 23 grams of the dibromide was vigorously stirred for half an hour with 100 ml. of 10\% NaHCO\(_3\) in order to hydrolyse the tertiary halogen, whereupon 500 g. of freshly-prepared 2\% sodium amalgam were added to the mixture contained in a three-necked flask equipped with reflux condenser and mercury seal stirrer.

The reduction was allowed to proceed slowly with vigorous stirring; occasionally, the mixture was warmed to about 50\(^0\) with a micro burner. It was found that the evolution of hydrogen progressed satisfactorily if the pH of the mixture were kept just slightly on the acid side; therefore, a few ml. of dilute HCl were added at regular intervals. After three hours, the odor of the mixture had changed markedly, a penetrating camphor odor (resembling 3\(^0\) amyl alcohol) being superimposed on the lesser bromide odor. When the amalgam was completely dissipated (about 15 hours), the mercury was separated, and the mixture was steam distilled. Three portions of steam distillate were collected, the first two of which each contained about two ml. of organic material of density less than 1, and about an equal amount of water. The first of these cuts was saturated with anhydrous K\(_2\)CO\(_3\), the organic layer separated and dried over carbonate. Distillation of the dried material yielded ca. 1.5 ml. of a liquid boiling at 101.5-103.5\(^0\) (3\(^0\) amyl alcohol boils at 102\(^0\)).
The odor of this substance was identical with that of a sample of Eastmann 3° amyl alcohol.

The product boiling at 101.5-103.5° was tested by adding a few drops of the substance to 1 ml. of the Lucas ZnCl₂-HCl reagent, whereupon a cloudy layer was formed immediately. Two drops of 2° butyl alcohol, on the other hand, gave no visible reaction for three minutes. Furthermore, an iodoform test on the product was negative. Both of these tests supported the proposed structure.

A solid derivative was therefore prepared in order to establish conclusively the identity of the alcohol. To 3 ml. of pyridine in a test tube were added 0.1 gram of the alcohol, followed by 0.26 g. of freshly prepared 3,5 dinitro benzoyl chloride. The mixture was well shaken, allowed to stand in a beaker of water maintained at 60° for one hour, then poured into 20 ml. of cold water and stirred vigorously. A feathery solid separated, which was filtered, washed twice with water, then with dilute HCl, and water again. The solid was recrystallized from alcohol to form shiny feathery crystals, which after drying in vacuo were found to melt from 112-115°. The reported melting point for 3° amyl 3,5 dinitro benzoate is 117°. A mixed melting point with this product showed no depression: 113-115°. Therefore, the alcohol obtained by the reduction of the partially hydrolyzed dibromide was 3° amyl alcohol, which definitely fixes the position of the second bromine atom in the photohalogenated isoamyl bromide.
C. Dehalogenation of Dibromide:

Once the identity of the dibromide was satisfactorily established, the immediate problem at hand, then, was the conversion of this substance to prenyl bromide. It appeared logical that this might be brought about if the dibromide were treated with one mole of alcoholic KOH per mole of dibromide, and in such a manner that there would always be an excess of the latter in the mixture; this was to be effected by the slow addition, with vigorous shaking, of the KOH solution to an alcohol solution of the dibromide.

142 grams of dibromide was dissolved in 100 ml. of alcohol, and to the mixture slowly added 40.5 g. of 85% KOH in 125 ml. of alcohol. The mixture was shaken vigorously during the addition, which was accompanied by much evolution of heat and rapid separation of a large amount of KBr. When all of the KOH had been added, the mixture was tested and found to be acid to litmus! (an indication that 2° halogen was still present).

The alcohol and KBr were extracted by washing the mixture several times with water, and the organic layer (light yellow in color) was separated and dried over anhydrous MgSO₄. The dried product (68 ml.) was then distilled through the Widmer column at reduced pressure, and the following fractions taken:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Pressure</th>
<th>B.P. Range</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33.5 mm.</td>
<td>below r.t.-31°</td>
<td>1.7 ml.</td>
</tr>
<tr>
<td>2</td>
<td>&quot;</td>
<td>31-35</td>
<td>3.6 ml.</td>
</tr>
<tr>
<td>3</td>
<td>&quot;</td>
<td>35-40</td>
<td>6.6 ml.</td>
</tr>
<tr>
<td>Fraction</td>
<td>Pressure</td>
<td>B.P. Range</td>
<td>Volume</td>
</tr>
<tr>
<td>---------</td>
<td>------------</td>
<td>------------</td>
<td>--------</td>
</tr>
<tr>
<td>4</td>
<td>33.5 mm.</td>
<td>41-42</td>
<td>14.6 ml.</td>
</tr>
<tr>
<td>5</td>
<td>&quot;</td>
<td>42-42.2</td>
<td>2.6 ml.</td>
</tr>
<tr>
<td>6</td>
<td>&quot;</td>
<td>42.2-82</td>
<td>3.2 ml.</td>
</tr>
<tr>
<td>7</td>
<td>&quot;</td>
<td>82.5-90</td>
<td>20.2 ml.</td>
</tr>
<tr>
<td>8</td>
<td>Residue</td>
<td></td>
<td>8.0 ml.</td>
</tr>
</tbody>
</table>

**Fraction 1 & 2:** On redistillation at atmospheric pressure was found to yield a flat from 96-100°. This substance was at first believed to be the tertiary dimethyl allyl alcohol (B.p. 97-98°); however, no reaction at all could be observed with acetyl chloride, and the product was, furthermore, insoluble in water. Its rapid decolorization of permanganate indicated its unsaturated nature, whereas its density (less than 1), its pleasant odor, and its low boiling point excluded the possibility of its being a bromide (it did not react with alcoholic AgNO₃). This substance was again obtained in a subsequent experiment on the zinc-dehalogenation of the polybromides obtained in the bromination of isoamyl bromide, and is discussed further at that point (see page 48).

**Fraction 2, 3, 4, 5:** Distillation of these cuts at atmospheric pressure indicated that 2 and 3 were intermediate between 1 and 4, tending to split into two definite cuts, the higher-boiling one being 122-124°, which was found to be the boiling point of cuts 4 and 5 (the first apparent flat in the original distillation). Cut 4 was found to boil from 122-123° at 1 atmosphere, was a pleasant-smelling liquid with a biting odor, and was found to reduce neutral permanganate rapidly. It was postulated
that this substance was dimethyl allyl bromide (prenyl bromide), since it reacted readily with aqueous silver nitrate to precipitate AgBr.

In general, there exists wide disagreement in the literature concerning physical properties of this bromide. Its boiling point has been variously reported as 120° at atmospheric pressure by Darzens (33); 26-33° at 12 mm. by Staudinger (34); and 129-133° at 1 atmosphere by Olaisen (4). Staudinger and Claisen separately determined the structure of isoprene monohydrobromide to be not \( \text{CH}_3\cdot\text{C}==\text{CH}==\text{CH}_2\cdot\text{Br} \) as reported by Mokiewski (35), but instead, \( \text{CH}_3\cdot\text{C}==\text{CH}==\text{CH}==\text{CH}_2\cdot\text{Br} \), prenyl bromide, which was found to hydrolyze to the tertiary unsaturated dimethyl allyl alcohol directly, instead of the expected primary alcohol. Furthermore, the primary bromide could be readily prepared from the tertiary alcohol in excellent yield (Claisen).

A Carius determination for halogen on cut 1 immediately indicated that this product was not pure, for the percent bromine was very low. Thus 0.5327 grams of sample yielded 0.4082 grams of AgBr; (° Br found: 32.8%; calc'd: 53.7%). A check run on a second sample yielded similar results. However, a clue to the identity of the second constituent was afforded by the density determination, since the density of the mixture was found to be 1.0403 at 20°, which is very low. On the basis of the Carius determination, it was calculated that the mixture could not contain more than 59.6% of an alkyl bromide corresponding to
prenyl bromide, or an isomer thereof.

A check of Ipatieff's results on the complete dehalogenation of 2,4 dibromo-2 methyl butane with alcoholic KOH revealed, as previously mentioned (page 4), that in addition to isoprene, the ethyl ether of prenol was obtained as a side product. The constitution of the product was determined by splitting the ether with HI and identifying the ethyl iodide formed. Claisen prepared this ether directly from isoprene monohydrobromide and sodium ethylate, reporting its boiling point to be 125°, compared with Ipatieff's value of 120.5-121.5°.

It was therefore apparent that cut 4 was probably a mixture of prenyl bromide and ethyl prenyl ether, although the presence of the latter was simply being postulated. Since the two substances boil at approximately the same temperature, physical separation did not appear plausible, and it appeared that the selective dehalogenation of the dibromide was an unsatisfactory approach. Nevertheless, the constitution of the mixture was of extreme interest, since its establishment might prove to be further evidence that the dibromide was the one postulated.

Staudinger (34) had succeeded in alkylating malonic ester with isoprene hydrobromide. The cold hydrolysis of the fractionated, pure, alkylated ester, boiling at 127° under 11 mm. yielded a dicarboxylic acid melting at 95.5-96° after recrystallization from benzene. This product was believed to be dimethyl allyl malonic acid,

\[
\begin{align*}
\text{CH}_3 & - \text{C} = \text{C} - \text{CH}_2 - \text{C} - \text{N} \quad \text{COOH} \\
\text{CH}_3 & - \text{C} = \text{C} - \text{CH}_2 - \text{C} - \text{N} \quad \text{COOH}
\end{align*}
\]
Ipatieff, on the other hand, obtained the same alkylation product as a side reaction in the alkylation of malonic ester with the original dibromide (36). This was explained by the fact that the dibromide underwent an elimination of HBr in the presence of sodium ethylate to give dimethyl allyl bromide, which subsequently alkylated a portion of the ethyl sodio-malonate. This alkylated ester boiled at $140^0$ under 20 mm. (compare Staudinger's value), and was hydrolyzed by heating with alcoholic KOH to yield a dicarboxylic acid, which when recrystallized from benzene, melted from 82.5-83.5°, and which he believed to be dimethyl allyl malonic acid.

The alkylation of malonic ester therefore appeared as a useful procedure whereby the bromide could be separated from the ether, and at the same time, throw some additional light on the structure of the original dibromide.

From the Carius analysis, it appeared that of the 13.6 g. of mixture, 8.12 g. was prenyl bromide, or an isomer thereof. Therefore to 25 ml. of absolute alcohol, freshly dried with magnesium methylate, were added 1.2 g. of sodium followed by 8 ml. of malonic ester. The ether-bromide mixture was then added slowly with shaking, and the mixture was refluxed on a steam bath for six hours, during which a large amount of NaBr separated. The alcohol, and low boiling material was then distilled from the steam bath (25-30 ml. being collected). To the residue was added 30 ml. of cold water containing 1 ml. of HCl,
whereupon a clear red brown organic layer separated, which was washed with water. However, no further purification of this product was attempted.

This mixture of alkylated and non-alkylated malonic ester was dissolved in a mixture containing 25 ml. of water, 12.5 ml. of alcohol, and 12.5 g. of KOH, and allowed to stand for four days at room temperature, with occasional shaking. The alkaline mixture was then extracted with ether in order to remove any remaining unsaturated ether, and the aqueous residue was acidified to Congo red with dilute sulfuric acid. The potassium salt which separated was filtered, and the filtrate and salt both extracted several times with ether. Evaporation of this ether layer left only a large amount of gummy residue which could not be crystallized.

This residue was again taken up in alcohol to which KOH was later added, and the mixture was heated on the steam bath for two hours. Acidification and extraction with ether followed as before. The residue that was left after evaporation of the ether was placed in a desiccator over concentrated sulfuric acid, and the system evacuated to a low pressure. After one day, long needle-like crystals were seen to form in the residue.

These crystals were found to be very soluble in water, ether and alcohol, but only slightly soluble in hexane. Therefore, the entire mass of crystals and gummy residue was recrystallized three times from hexane, during which
the melting point increased from 67-72° to 78-80°. This is in rather close agreement with the value found by Ipatieff, and since his procedure was followed in the hydrolysis (at elevated temperatures), it is not surprising that the agreement is with Ipatieff's value. This therefore establishes the bromide in the mixture to be prenly bromide.

The alcohol distillate from the alkylation procedure (above) was extracted with a large portion of cold water, whereupon an organic layer separated (density less than 1) which was dried over CaCl₂ and distilled. The product distilled from 122.2-128° with superheating toward the last, and was a pleasant-smelling colorless liquid resembling ethyl isooamyl ether in odor. This substance reduced permanganate, did not react with acetyl chloride, and was insoluble in water. It was felt that no more data was needed to prove the identity of this compound, since it would constitute no contribution to the real problem at hand. Nevertheless, it was reassuring to find that the cut investigated (41-42° at 33.5 mm.) turned out to be the mixture that it had been predicted to be, which appears as further proof of the structure of the dibromide.

Fraction 6 & 7: It appeared obvious that 6 was an intermediate few ml. between 4 and 7. A consideration of the boiling point, density, and reaction with AgNO₃ led to the obvious conclusion that fraction 7 was simply the original dibromide, or was partially contaminated with the bromohy-
On the basis of these findings the alcoholic KOH selective dehalogenation of 2,4 dibromo-2 methyl butane was eliminated as an approach to the synthesis of prenol, or its derivatives.

C. Dehalogenation of Polybromides:

The second approach that suggested itself, by which the unsaturated monobromide might be obtained, was a zinc-debromination of the polybromide residues obtained in the bromination of the polybromide residues obtained in the bromination of isononyl bromide. It was believed that treatment of these bromides with one equivalent of zinc would yield two isomeric unsaturated monobromides as the tribromide reaction product, whereas any tetrabromide would be directly converted to isoprene. Thus,

\[
\begin{align*}
\text{CuBr}_3 - & \xrightarrow{Zn} \text{CuBr}_2 + \text{CuBr} - \text{Cu} \xrightarrow{Zn} \text{Cu} = \text{Cu}_2 & \\
\text{CuBr}_3 - & \xrightarrow{Zn} \text{CuBr}_2 + \text{CuBr} - \text{Cu} \xrightarrow{Zn} \text{Cu} = \text{Cu}_2 &
\end{align*}
\]

Since the difference in boiling points between the monobromides is about 30°, a separation could be effected by simple fractionation.

Therefore, 68 g. of previously prepared copper-zinc couple were mixed with 350 ml. of alcohol in a flask, and the polybromide added slowly through a dropping funnel, with vigorous shaking. The reaction proceeded rapidly with much evolution of heat; however, it slowed down appreciably toward the mid-point, so that an excess of 50 g. of zinc...
had to be added. When all the bromide had been added, the mixture was refluxed for half an hour, which initiated appreciable darkening. Thereupon 300 ml. of cold water were added, the mixture steam distilled, and the distillate washed several times with large volumes of water to remove the alcohol. The organic layer was then washed with saturated CaCl₂ and dried over the anhydrous salt overnight. Distillation under various pressures through the Widmer column yielded the following:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Pressure</th>
<th>Boiling Point</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 atm.</td>
<td>31-33</td>
<td>9 ml.</td>
</tr>
<tr>
<td>2</td>
<td>75 mm.</td>
<td>33-34</td>
<td>2.5 ml.</td>
</tr>
<tr>
<td>3</td>
<td>&quot;</td>
<td>34-52</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>38.5 mm.</td>
<td>55-56</td>
<td>22 ml.</td>
</tr>
</tbody>
</table>

Fraction 1, although not identified, was believed to be isoprene as suggested by its boiling point, odor, density, and rapid reduction of permanganate.

Fraction 2, boiling at 98° at atmospheric pressure, was unsaturated, insoluble in water, and had a density less than 1. This product did not react with acetyl chloride, and did not give a reaction with alcoholic AgNO₃. On the basis of boiling point, unsaturation, and density, it was at first believed that the product was the tertiary dimethyl allyl alcohol. However, the failure of the substance to react with acetyl chloride eliminated this possibility.

Reflection on the products obtained in the KOH dehalogenation of the dibromide (page ) revealed that a very similar product was obtained in that experiment (b.p. 31-35°
at 33.5 mm.; 96-100° at 1 atm.). Because of its apparently inert nature (negative tests for alcohol, aldehyde, or ketone), the possibility was considered that this product was an unsaturated ether, possibly an ethyl ether. The low boiling point suggested that the product might be the ethyl ether of the unsaturated tertiary alcohol, since the ethyl ether of 3° amyl alcohol (b.p. 102°) boils at 102-103°, if an analogy may be drawn.

This product was therefore split with anhydrous ZnCl₂ and 2,5 dinitro benzoyl chloride according to the procedure of Underwood et. al. (37). The reaction was accompanied by excessive polymerization, but a solid product was obtained upon pouring the mixture into cold water. Several recrystallizations of this product from alcohol, resulted in the obtaining of a white fluffy crystalline solid, which after drying, melted at 92-93°. (Ethyl 3,5 dinitrobenzoate melts at 93°). Mixed melting point with the synthetic product showed no depression: 92-93°. Therefore, the compound in consideration is apparently an ethyl ether.

No other solid derivative could be obtained from the reaction mixture. This, however, was not unexpected, since tertiary esters are very difficult to prepare, even under the mildest conditions. In consideration of the extreme conditions under which this ether was split, it is not surprising that no tertiary ester was obtained. It therefore appears plausible that this compound, previously unreported, is the ethyl ether of isoprene alcohol, b.p. 41-42° under
Fraction 4 was very similar in color and odor with the fraction 4 obtained in the KOH-dehalogenation of the dibromide (p. 41). However, upon standing for a few days, this product underwent extensive discoloration and polymerization. Although this substance was slightly lachrymatory, unsaturated, and reacted readily with alcoholic AgNO₃, attempts to hydrolyze it with aqueous potassium carbonate were unsuccessful, resulting in further polymerization to yield a rubbery material which was not volatile in steam. Since prenyl bromide hydrolyzes completely on shaking with water for a few minutes (4), this possibility was excluded, and no further attempts to identify this product were made.

The residue remaining from the steam distillation of these volatile fractions, was unsaturated, possessed a distinctly terpene-like odor, but was apparently not volatile in steam. Evidently, this consisted of a mixture of polymers, which it was not attempted to identify.

This series of reactions again led to no useful results, so that, it appears that the polybromides resulting in the bromination of isoamyl bromide must be considered a total loss as regards the immediate problem at hand.

E. Hydrolysis of Dibromide and Dehydration of Product:

The dehydration of tertiary alcohols is a well-known reaction, proceeding smoothly to give, in general, excellent yields of olefins in a very short time. The dehydration of 3° amyl alcohol has been extensively studied, and recent
investigations have indicated that oxalic acid is an excellent reagent serving to bring this reaction about, and capable of being applied in continuous processes (38). A patent held by Kahlbaum describes this process, in which the alcohol is added slowly to oxalic acid (anhydrous or hydrated) at ca. 80°, the amylene distilling over as it is formed (39).

This reaction was tested on commercial 3° amyl alcohol with hydrated oxalic acid, and found to proceed as described.

It was therefore decided to hydrolyze the dibromide with dilute NaHCO₃ to the bromohydrin as previously described, and attempt the dehydration of the product with oxalic acid to yield prenyl bromide. Thus,

\[
\begin{align*}
CH_3 - CH_2 - CH = CH - Br & \xrightarrow{NaHCO_3} CH_3 - CH = CH - CH_2 - Br \\
& \xrightarrow{H,O} CH_3 - CH = CH - CH_2 - Br
\end{align*}
\]

The bromohydrin (0.1 mole), obtained in the normal manner, was heated with 0.2 moles of hydrated oxalic acid for two hours on the steam bath. A sample withdrawn at this point did not test unsaturated. The mixture was therefore heated with a burner, resulting in the evolution of copious volumes of HBr and extensive decomposition, as evidenced by the extreme darkening of the mixture. After cooling, the product was steam distilled to yield about one ml. of volatile material, which after drying, boiled from 110-145°, with a residue remaining in the flask. In consideration of the extensive decomposition occurring and the poor yield of
an apparent mixture, this procedure was cast out.

F. Investigation of 2,4 dihydroxy 2 methyl butane:

2,4 dihydroxy 2 methyl butane has been reported in several instances (19, 20) as having been prepared from the corresponding dihalide (chloride or bromide) by hydrolysis with 10% potassium carbonate. In general, the yields of this product which were obtained were very poor. Thus, Ipatieff (19) reports that from 40 grams of the dibromide, he obtained 4 grams of the glycol, boiling at 202-204°, representing a yield of 22%. It was nevertheless thought interesting to investigate this glycol in order to determine whether it could be selectively dehydrated to yield prenol directly.

Therefore, 23 g. (0.1 mole) of the dibromide was refluxed with a solution of 0.2 moles of K₂CO₃ in 115 ml. of water for 17 hours. At the end of that time, the largest portion of the organic layer had gone into solution, whereas the remaining organic material was now of a density less than 1. The mixture was distilled in order to both drive off the organic volatile matter, as well as to concentrate the solution for isolation of the glycol. The first few ml. of distillate which were condensed contained about 2 ml. of colorless organic material, of very pleasant odor and low density. This product was separated, and the aqueous portion saturated with anhydrous potassium carbonate. Again, a small amount of organic material separated, an indication that the product was in all probability an alco-
Both of these portions tested unsaturated, as evidenced by their rapid reduction of permanganate. Although this product was not identified at this time, a subsequent investigation on a larger scale yielded definite information as to its identity (see page 68).

The aqueous residue from the hydrolysis and distillation was concentrated down until the KBr began to separate, whereupon the mixture was cooled, and saturated with anhydrous K$_2$CO$_3$. Immediately a brown organic layer separated, which was extracted with 95% alcohol. When the alcohol had been evaporated from the glycol, a micro boiling point was taken on this slightly wet product. After several attempts, the boiling temperature became constant at 204-205°, with slight decomposition. The weight of the material thus obtained, and slightly wet, was 4 grams, representing a maximum yield of 38%. At that time, it was strongly suspected that a great deal of the loss was due to dehalogenation instead of straightforward hydrolysis to yield isoprene, since the odor of isoprene was very strong in the laboratory during the course of the reaction.

The first attempt at selective dehydration of the glycol was made on 3.5 g. of the material, using hydrated oxalic acid as the reagent. A preliminary investigation had indicated that whereas 3 amyl alcohol was almost quantitatively dehydrated by oxalic acid at 80-90°, primary isoamyl alcohol was not attacked at all even at reflux temperature (130°). It was therefore felt that perhaps this reagent
might effect the elimination of the tertiary hydroxyl group without altering the corresponding primary group, to yield prenol directly.

Therefore, 3.5 grams of the glycol were mixed with 3 g. of hydrated oxalic acid in a small flask and heated with a micro burner. When the oxalic acid melted, the mixture became homogeneous, and shortly thereafter began to boil. Within a few minutes, a distinct layer began to separate to the top of the mixture, and after five minutes of additional heating, the reaction was stopped.

Dilute KOH was poured into the mixture, in order to hydrolyze any oxalate esters that might have been formed, and the mixture was steam distilled. Only a very small portion of the organic layer distilled over readily (0.2 ml.), whereas the majority of the liquid, orange-yellow in color, and slightly viscous, was apparently not volatile in steam. This residue was separated and dried over carbonate, and found to have a distinct terpene-like odor, but did not distill below 200°. Both the volatile and non-volatile constituents were insoluble in water, and reduced permanganate readily.

This evident polymerization was not unexpected, since the isomeric unsaturated tertiary alcohol polymerizes readily in dilute acid at room temperature to yield a complex mixture of terpenic bodies. Undoubtedly, dehydration of the glycol was effected by the oxalic acid; however, the corresponding polymerization induced by both the high temperature
and the acid, necessitated the elimination of this procedure.

Although the foregoing reactions had yielded undesirable results, it was felt that this selective dehydration of the glycol might be effected if at the same time the primary hydroxyl group could be "masked" or protected in some manner so that it would not undergo dehydration or some sort of anionotropic shift which would result in extensive rearrangement and polymerization, a mechanism that may be useful in explaining the presence of the high-boiling, insoluble (therefore not the glycol) materials resulting from the oxalic acid dehydration of the glycol.

It is well known that although primary alcohols may be esterified with various reagents such as acyl halides, anhydrides, etc., to yield the corresponding esters, tertiary alcohols under the same conditions generally undergo dehydration to a marked extent. Thus, in Pickard's method for preparing the mono-acid phthalates of alcohols by heating with phthalic anhydride, the conversion of the primary alcohols to the ester proceeds in the normal manner, whereas tertiary alcohols, for the most part, undergo dehydration to the corresponding olefin. Under the circumstances, it was felt that acetic anhydride might serve in the same capacity as a dehydrating agent for tertiary alcohols, especially in the presence of a trace of inorganic acid, such as sulfuric or phosphoric. This proposal was tested in a qualitative manner on 3° amyl alcohol, and it was found that in the presence of a few drops of conc. H₂SO₄,
the conversion of the alcohol to amylene occurred readily at the boiling temperature. Subsequently, when the details of this procedure were worked out, some quantitative data was obtained in a series of more carefully conducted experiments which are reported below.

For the present it was felt sufficient that acetic anhydride was effective in dehydrating the tertiary alcohol. The reaction with primary isoamyl alcohol had been studied previously (p. 9) so it was postulated that the reaction of the glycol with acetic anhydride in the presence of mineral acid might yield prenyl acetate.

\[
\begin{align*}
\text{CH}_3 &= C - \text{CH}_2 - \text{CH}_2 - \text{OH} & \xrightarrow{\text{Ac}_2\text{O}} & \text{C}_6\text{H}_5 - C - \text{CH}_2 - \text{CH}_2 - \text{OH} - \text{CH}_3
\end{align*}
\]

The ester linkage would thereby serve to block the primary hydroxyl group and prevent acid-catalyzed rearrangements from occurring.

Therefore, the remaining glycol (0.75 ml.) was dissolved in a large excess of acetic anhydride (20 ml.) and one drop of conc. sulfuric acid added to the mixture. In the course of a fifteen minute induction period during which no heat was applied, the mixture was found to warm appreciably, as in the case of the isoamyl alcohol alone. The mixture was then refluxed for 45 minutes, during which time some slight darkening occurred. Upon cooling, dilute alkali was added to neutralize the acid, whereupon a small amount of organic material separated. This was steam distilled and
ca. 0.2 ml. of a clear liquid of density less than 1 was obtained, of very pleasant odor, somewhat like isomyl acetate, yet dissociated from the characteristic cough-producing qualities of the latter. The aqueous portion of this steam distillate reduced permanganate rapidly.

Since not enough of this material was available for saponification, etc., it was decided to rupture the ethylenic linkage with permanganate and attempt to isolate acetone from the products. The entire steam distillate was therefore refluxed for 45 minutes with 150 ml. of water containing 4 grams of KMnO₄. After slight cooling, the mixture was distilled, and the first two ml. of condensate were collected and tested for acetone.

To 1 ml. of the product (no odor of acetone detectable) was added 5 ml. of a saturated alcoholic solution of 2,4-dinitro phenyl hydrazine, and the mixture boiled for a minute. Three drops of conc. HCl were then added, the mixture boiled briefly, and then poured into 60 ml. of cold water. A very small amount of yellow precipitate formed; however, not enough was available for a melting point determination.

A similar test was carried out on 1 ml. of a mixture containing two drops of acetone in 10 ml. of water, and a comparable amount of yellow solid material was obtained.

The remaining 1 ml. of distillate from the permanganate oxidation was made slightly alkaline with dilute NaOH, and a few drops of iodine-KI solution were added. A visible yellow precipitate possessing the characteristic odor of
Iodoform was produced, which it was felt was confirmatory for acetone. It was therefore decided to pursue the study of this reaction further on a larger scale, since these results were definitely encouraging.

The foregoing investigations had exhausted the supply of the dibromide prepared previously; so the conversion of isoamyl alcohol to the dibromide was again undertaken. Except for one modification which is discussed immediately below, the general procedure previously described was followed throughout. Thus, 738 grams of isoamyl bromide, boiling primarily between 119-121 were obtained from 520 grams of the alcohol, representing a yield of 83%.

As a matter of interest, the bromination of the isoamyl bromide was attempted on 1 mole of this product and one mole of bromine in direct sunlight without heating. The mixture was placed in a 500 ml. flask with standard taper neck into which was inserted a calcium chloride tube bent in an inverted U, and connected to an inverted funnel over a beaker of dilute NaOH. The reaction began immediately upon exposure to direct sunlight, with sensible evolution of heat, and vigorous evolution of HBr. The time required for the complete disappearance of color was three hours.

Distillation under reduced pressure through the Widmer column at a reflux ratio of 5-6:1, yielded the expected unconverted monobromide. Some slight variations of boiling points (ca. 1-2° higher) for both the mono and dibromides were observed in this as well as in subsequent distillations.
This may have been due to some error in the manometer, or to a leak in the system between the manometer and the still.

The following fractions were obtained:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Pressure</th>
<th>Boiling Point</th>
<th>Weight</th>
<th>Identity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>69 mm.</td>
<td>50-51</td>
<td>50</td>
<td>Isoamyl Bromide</td>
</tr>
<tr>
<td></td>
<td>34 mm.</td>
<td>35.2</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5.7 mm.</td>
<td>40-50</td>
<td>--</td>
<td>Intermediate</td>
</tr>
<tr>
<td>3</td>
<td>9 mm.</td>
<td>58-62</td>
<td>59</td>
<td>Believed to be desired dibromide</td>
</tr>
<tr>
<td></td>
<td>5 mm.</td>
<td>50-51</td>
<td>49.5</td>
<td></td>
</tr>
</tbody>
</table>

The inconsistency of the boiling point of the dibromide in cut 3 was suspicious. A titration for $3^\circ$ halogen was therefore run as described on page 37 in order to make certain of the identity of the product.

0.9531 grams of this cut were therefore hydrolyzed and titrated in the normal manner, the ionizable halogen requiring 25.72 ml. of N/10 AgNO$_3$ to the chromate end point (overrun). Calculations indicated that the product contained only 60% of a dibromide containing a $3^\circ$ halogen. This was repeated again, very carefully, 0.8358 grams of sample requiring 21.47 ml. of the standard silver, or equivalent to 58.8% of a tertiary bromide.

A check on the remainder of the dibromide from the first synthesis indicated that there was no error in the titrations, 0.4031 and 0.4046 grams of sample requiring 18.54 and 19.04 ml. of the silver solution, indicating 1.05 and 1.08 equivalents of the tertiary halogen, respectively. It therefore appeared that sunlight bromination does not yield the same products that are obtained in photoflood illumination com-
bined with heating, although no conclusions were drawn as
to the cause of this difference or to the nature of the prod-
uct obtained in direct sunlight without heating.

Therefore, the old procedure was resorted to in the
synthesis of the dibromide. The bromination was carried
out in several steps, each time the recovered monobromide
being rebrominated in the same manner. Fractional distilla-
tion of the total mixtures obtained yielded the following:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Pressure</th>
<th>Boiling Point</th>
<th>Weight</th>
<th>Identity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>varied</td>
<td></td>
<td>102 g.</td>
<td>Isoamyl bromide</td>
</tr>
<tr>
<td>A</td>
<td>9 mm.</td>
<td>r.t.-37</td>
<td>22.7 g.</td>
<td>bromide</td>
</tr>
<tr>
<td>B-1</td>
<td>9 mm.</td>
<td>37-49.5</td>
<td>33 g.</td>
<td>forerun of</td>
</tr>
<tr>
<td>B-2</td>
<td>7 mm.</td>
<td>43-52</td>
<td>32 g.</td>
<td>dibromides</td>
</tr>
<tr>
<td>B-3</td>
<td>7 mm.</td>
<td>52-54</td>
<td>25 g.</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>6 mm.</td>
<td>52-53</td>
<td>52 g.</td>
<td>Believed</td>
</tr>
<tr>
<td></td>
<td>5 mm.</td>
<td>51.2</td>
<td>49 g.</td>
<td>to be de-</td>
</tr>
<tr>
<td></td>
<td>6 mm.</td>
<td>54</td>
<td>52 g.</td>
<td>sired dibro-</td>
</tr>
<tr>
<td></td>
<td>5 mm.</td>
<td>51.5</td>
<td>49 g.</td>
<td>mide, but</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>303 g.</td>
<td>boiling</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>slightly high.</td>
</tr>
<tr>
<td>C</td>
<td>Trap contents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Residue</td>
<td></td>
<td>355 g.</td>
<td>Hybromides</td>
</tr>
</tbody>
</table>

Cut D was checked for identity by hydrolysis and titra-
tion for tertiary halogen, since the boiling points were
slightly high, as before. However, 0.4901 g. of sample D,
after hydrolysis and filtration in the normal manner, re-
quired 22.49 ml. of standard silver solution, equivalent to
0.002249 mols. of 3° halogen (calc'd: 0.00213). Therefore,
this dibromide was in all probability identical with the
first one obtained in the investigation.

Of 60° grams of isoamyl bromide, 102 grams were recov-
ered, and 303 grams of 2,4 dibromo 2 methyl butane were ob-
tained, representing a yield of 40% on the basis of mono-bromide used up.

G. Modifications in Hydrolysis of Dibromide:

Because of the poor yield of glycol obtained in the hydrolysis of the dibromide, both in this laboratory and as reported by several investigators in the literature (page 52) it was sought to modify this procedure in order that the yield might be increased. A consideration of the mechanism involved in the reaction reveals both limitations and suggestions for modifications.

The reaction of alkyl halides with aqueous alkali can normally proceed in two fashions: (1) the straightforward hydrolysis of the halogen leading to substitution by an hydroxyl group, or (2) elimination of a molecule of halogen acid to yield the olefin.

If the second reaction, i.e., elimination of the halogen acid occurs, then the unsaturated bromide can again undergo two reactions: hydrolysis in the normal way to yield isoprene alcohol, or elimination to yield isoprene. The elimination reaction is apparently favored in both steps at boiling temperatures, since the odor of isoprene was very marked in the laboratory during the course of the "hydrolysis", and a strip of filter paper moistened with dilute
permanganate was immediately discolored when held at the mouth of the reflux condenser. Therefore, the following modifications were attempted in the hydrolysis of the dibromide:

1. 0.3 mols. of K₂CO₃ were dissolved in 125 ml. of water contained in a flask adapted with a dropping funnel and a condenser set downward for distillation. The alkali was heated to boiling, and 23 g. of the dibromide was added slowly and allowed to steam distill over. The steam distillate contained an organic layer that was of greater density than 1, and which reduced permanganate. This distillate was recombined with the residue in the flask and refluxed for six hours. Steam distillation yielded only ca. 1.5 ml. of organic material, density slightly greater than 1. Concentration of the residue from the hydrolysis, and saturation with anhydrous carbonate yielded again about 1.5 ml. of the glycol, much less than in the first investigation where the dibromide and alkali were mixed in the cold and then heated. Obviously, the remainder of the dibromide must have been converted to isoprene, which escaped through the condenser because of its volatility.

2. 0.1 mole of the dibromide was mixed with 200 ml. of water in a 3-necked flask equipped with reflux condenser and mercury-seal stirrer, and stirred vigorously for one hour at room temperature, during the course of which time, 0.05 mols of K₂CO₃ were added at intervals in order to neutralize the HBr formed. After one hour of stirring, 0.15
mols excess of carbonate were added, and the mixture stirred at room temperature for 20 hours. At the end of this time there was still a large amount of organic layer present, so the mixture was heated and kept at 80-90° with stirring for three hours, during which most of the organic material went into solution. At the end of eight hours, only about one ml. of organic layer was present.

The mixture was distilled, and the first 20 ml. of distillate were saturated with potassium carbonate, whereupon ca. two ml. of a colorless organic layer separated, which had an odor strongly resembling that of 3° amyl alcohol, but which was unsaturated. This was undoubtedly the tertiary unsaturated alcohol previously discussed, although no attempt was made to identify it at the time.

The residue in the flask was concentrated to 75 ml. and saturated with carbonate, whereupon 7 grams of glycol separated. This then represented a yield of about 67%, and was satisfactory in that an unreasonable amount of dibromide was not lost in the procedure. Therefore, a careful study of the effects of acetic anhydride and various mineral acids upon 3° amyl alcohol, allyl alcohol, and allyl acetate was undertaken.

(1). Tertiary amyl alcohol:

(a). 0.1 moles of c.p. 3° amyl alcohol was added slowly through a dropping funnel to 0.12 moles of acetic anhydride at 60°, containing five drops of conc. H₂SO₄ contained in a flask equipped with an ice-water condenser set
downward for distillation. Reaction at this temperature was very slow, the vapors of amylene rising slowly and distilling. Increasing the temperature caused a corresponding increase in the reaction rate so that a steady flow of condensate was observed. The temperature of the vapors did not rise above 45° during the entire course of the reaction. When the rate subsided, the flask was heated more strongly until at length the temperature began to drop in the "goose-neck", and heating was discontinued. The volume of amylene collected was 6.2 ml. (60% yield), while hydrolysis and neutralization of the excess reagent in the flask yielded a separate organic layer which was steam distilled, washed and dried. This product was undoubtedly 3° amyl acetate, and had a not pleasant ester odor (volume: 2 ml.).

Konowalow (17) reports that 3° amyl acetate is thermally unstable, decomposing at 150° into amylene and acetic acid (40). Investigation of the dynamics of this reaction revealed that the rate of the decomposition is catalyzed markedly by the presence of acetic acid, and to a lesser extent by other organic acids, whereas the halogen acids decomposed the ester at various rates to yield, in general, the 3° alkyl halide. It would appear therefore that the mechanism involved in the "dehydration" is in effect an esterification followed by elimination of acetic acid. This mechanism was subsequently proved rather conclusively in a dehydration-esterification study on the glycol.

(c). Dehydration of the alcohol was attempted with
33% H₂SO₄, in order to compare with the yields of amylene obtained above. A 70% yield of olefin was obtained, which compared favorably with the yields obtained above.

(2). Allyl alcohol:

11.5 ml. of acetic anhydride and three drops of sulfuric acid were heated nearly to boiling and 6.8 ml. of allyl alcohol added dropwise to the hot solution. The reaction following each addition was rather violent. The mixture was refluxed for ten minutes, steam distilled, and the ester purified. Distillation yielded 8.3 cc. of product boiling at 104.6-106° (literature: 104°) or 78% yield.

In order to determine whether any polymerization or decomposition of this unsaturated ester might result under the conditions of the experiment, one ml. of the ester was refluxed with two ml. of acetic anhydride and one drop of sulfuric acid for one hour. No carbonization or decomposition was observed. Addition of water to the cooled mixture resulted in layer separation, the ester odor being found persistent in the organic layer.

(3). Reaction of Glycol with Acetic Anhydride-H₂SO₄:

Fourteen grams of wet glycol obtained by the complete hydrolysis of the dibromide were added slowly through a dropping funnel to a heated mixture of 38 ml. of acetic anhydride containing four drops of H₂SO₄ in a flask adapted with a condenser set for distillation. The reaction proceeded as the addition continued, and the odor of isoprene became apparent at the condenser mouth, although no condensate could be seen. After complete addition, the mixture
was kept at a near boiling temperature for half an hour, and then cooled. A large amount of water was added, and the mixture steam distilled. The organic layer, 5 ml., was separated, washed with dilute KOH and water and dried over CaCl₂. A portion of this substance was then distilled and found to boil primarily between 148-150°. The reported boiling point of prenyl acetate is 152° (Courtot). It therefore appeared highly probable that this ester was the desired product, although apparently the yield was poor.

III. SYNTHESIS AND SAPONIFICATION OF PRENYL ACETATE
A. Complete Hydrolysis of 2,4 dibromo 2 methyl butane:

In accordance with the procedure described previously, one mole (230 g.) of the dibromide was mixed with 150 ml. of water in a 3-necked flask equipped with reflux condenser and mercury seal stirrer, and stirred vigorously for one hour, during which one mole of anhydrous K₂CO₃ was added in small portions. The mixture was then stirred for 19 hours at room temperature. Titration of a neutralized one-ml. sample of the aqueous layer with N/10 AgNO₃ revealed, however, that only 0.03 mols of the dibromide had undergone hydrolysis. A carbonate-bicarbonate analysis substantiated this result.

Michael (15) has shown that the optimum conditions for the hydrolysis of tertiary alkyl halides required the presence of at least fifty times as much water by weight as halides. However, in the interest of purification and isolation of the glycol, this amount of water appeared prohibitive in the most extreme sense. The optimum conditions for the hy-
drolysis were therefore sought.

The addition of 120 ml. more of water and stirring for three hours, followed by analysis, indicated a bicarbonate-carbonate ratio of 1.63:32.03, or very little hydrolysis. 100 ml. more of water were added, the mixture stirred for 14 hours and the organic layer analyzed for 3° halogen by the procedure previously described. 0.4822 grams after shaking for forty minutes and filtering, required 20.94 ml. of H/10 silver solution, equivalent to .00209 mols of 3° halogen (calculated: .00209).

Although the mechanism whereby the hydrolysis of the bromide was so markedly retarded did not appear clear, it was suspected that the large excess of highly hydrated potassium carbonate might in some measure be responsible. The aqueous layer was therefore gassed with CO₂ until the carbonate had been completely converted to bicarbonate, and the hydrolysis was continued. The aqueous layer (500 ml.) was analyzed at intervals for ionizable halogen with the following results:

<table>
<thead>
<tr>
<th>Time of Stirring</th>
<th>Vol. Sample</th>
<th>Ml. AgNO₃</th>
<th>% Hydrolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 hrs.</td>
<td>1 ml.</td>
<td>9.97</td>
<td>49.8</td>
</tr>
<tr>
<td>48 hrs.</td>
<td>&quot;</td>
<td>15.60</td>
<td>78.0</td>
</tr>
<tr>
<td>72 hrs.</td>
<td>&quot;</td>
<td>19.44</td>
<td>97.2</td>
</tr>
</tbody>
</table>

After 72 hours of stirring with the saturated bicarbonate, the hydrolysis appeared to be nearly complete. A check for tertiary halogen in the organic layer substantiated this conclusion, so it was considered safe to continue the hydrolysis at higher temperatures in order to convert the bromohydrin to the glycol. After three days of heating on the steam bath
and stirring, the hydrolysis was complete, as indicated by analysis for halogen in the aqueous layer.

The mixture at this time tested strongly unsaturated, and the characteristic odor of a tertiary alcohol was persistent. This was not unexpected, since this product had always been obtained in the previous investigations on the hydrolysis of the dibromide. Distillation of the mixture and saturation of the condensate with anhydrous potassium carbonate yielded 17 ml. of a colorless liquid which was separated, dried over two portions of freshly-heated carbonate and distilled.

Distillation of this product yielded two rather definite flats, after the low-boiling constituent (isoprene) had distilled:

1. 95-105° and 2. 130-134°

Both cuts were unsaturated, and reacted with acetyl chloride. The lower-boiling constituent had the characteristic alcohol odor typical of tertiary alcohols, and was undoubtedly isoprene alcohol; whereas the higher boiling constituent was believed to be a primary alcohol isomeric with the former.

Two derivatives of the tertiary alcohol were prepared: the 3,5 dinitro benzoate and the phenyl urethane. The former was prepared by dissolving 0.5 grams of this alcohol (which on redistillation boiled from 95-100°) in 1.5 ml. of pyridine and adding 1.5 g. of the acyl halide. After allowing to stand for three hours at room temperature, the mixture was poured into cold water and purified in the normal
manner. Recrystallization from alcohol yielded shiny, pale-yellow crystals, which after drying in vacuo were found to melt sharply from 108.5-109°. A mixed melting point with synthetically prepared 3-ethyl 3,5-dinitro benzoate (m.p. 115-116°) gave a depression of six degrees; therefore, the alcohol was in all probability isoprene alcohol.

Combustion of this solid derivative yielded supporting evidence.

<table>
<thead>
<tr>
<th>Wt, sample (mg.)</th>
<th>wt, H₂O (mg.)</th>
<th>wt, CO₂ (mg.)</th>
<th>%H found</th>
<th>%H calc.</th>
<th>%C found</th>
<th>%C calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.948</td>
<td>6.214</td>
<td>30.252</td>
<td>4.36</td>
<td>4.32</td>
<td>51.76</td>
<td>51.43</td>
</tr>
</tbody>
</table>

The phenyl urethane was prepared from 0.5 g. of the alcohol and 0.745 g. of phenyl isocyanate in the presence of one drop of anhydrous pyridine. After standing for one day at room temperature, the derivative was separated from the diphenyl urea by extraction with ligroin (b.p. 30-60°) and after recrystallization from the same solvent, yielded shiny white needles that melted from 48-49°. No combustion was made on this product.

The higher boiling alcohol was not identified until after the dehydration-esterification of the glycol, which yielded the same product (page 68).

B. Isolation of Glycol:

The residue from the steam distillation of the volatile constituents, containing the glycol, was saturated with potassium carbonate, whereupon the light amber oil separated. 100 ml. of ether was added to the mixture, resulting in the formation of three layers: ether-glycol; glycol-water, and water-carbonate. The water layer was separated.
filtered to remove precipitated solids, and extracted twice with a total of 150 ml. of ethyl alcohol. This alcohol extract was distilled on the steam bath in a Claisen flask until no more alcohol could be seen distilling, whereupon the pressure was reduced to flash off part of the remaining water. This was accompanied by separation of carbonate, from which the glycol was decanted. The carbonate was washed with 25 ml. of alcohol, the washings combined with the glycol, and the mixture again distilled first at atmospheric, and then at reduced pressure on a steam bath. After four repetitions of this procedure, the glycol was extracted with ether from the remaining carbonate which precipitated. This ether solution was then dried twice over anhydrous K₂CO₃, and then distilled on the steam bath until no more ether could be detected. The residue in the flask, a light amber color, weighed 20 grams.

The ether-glycol, water-glycol mixture obtained in the first extraction which resulted in the formation of the three layers (preceding page) was extracted several times with large volumes of ether until the aqueous layer dwindled to 3-4 ml. The combined ether extracts of about 500 ml. were then dried, and the ether distilled off, leaving the dry glycol as residue, which weighed 43 grams, and was combined with the other portion of the glycol. This product was then used without further purification. Yield: 63 grams, representing 60.5%.  

C. Modification of Acetic Anhydride Dehydration Procedure:
In an attempt to increase the yield of unsaturated ester obtainable in the dehydration of the glycol, several modifications of the procedure were investigated:

1. Substitution of Phosphoric for Sulfuric Acid:

Fifteen ml. of 30° amyl alcohol were mixed with 23 ml. of acetic anhydride and 1 ml. of 85% phosphoric acid in a 200 ml. flask with condenser set for distillation. Upon heating the mixture, the reaction proceeded with almost explosive force, so that a large amount of the material was lost.

The experiment was repeated and modified by the addition of only five drops of the acid. A short fractionating tube packed with glass tubing was mounted above the flask, and connected to the condenser. The mixture was allowed to stand without heating for 30 minutes, with no noticeable evolution of heat, whereupon the contents were heated gently until boiling began, and the flame was removed. This was repeated several times until a constant gentle ebullition resulted. Immediately the amylene began to distill (36°). Gentle heating was continued until the rate of distillation decreased appreciably, whereupon the mixture was heated more strongly until the high boiling vapors began to approach the thermometer in the column, when heating was discontinued. Over 11 ml. of amylene were collected, representing a yield of over 90%, which compares most favorably with the sulfuric acid process (65%).

This experiment was repeated on allyl alcohol, in which
it was necessary to allow a 20-minute induction period, with subsequent cooling, in order to prevent a violent reaction. Refluxing the unsaturated ester prepared in this manner with comparable amounts of acetic anhydride-phosphoric acid resulted in very little darkening.

The conclusions which may be drawn from these experiments indicate that the reaction of acetic anhydride with primary hydroxyl groups proceeds readily at room temperature, whereas the reaction with the tertiary group occurs only upon heating. It may therefore be expected that in the glycol, the primary group would undergo esterification at low temperatures, followed by dehydration of the remaining group at elevated temperatures. It appears reasonably safe, from the study on allyl acetate, to assume that prenyl acetate would not undergo extensive decomposition upon refluxing in the acid medium, although some may be expected.

D. Acetylation and Dehydration of Glycol:

To the entire volume of glycol previously obtained, placed in a 500 ml. standard taper flask with dropping funnel and reflux condenser, was added 100 ml. (of the calculated 253 ml.) of acetic anhydride, containing five drops of phosphoric acid, and the mixture was well shaken. No noticeable heating was detectable upon fifteen minutes standing. Addition of 100 ml. more of the anhydride and ten drops of acid produced slight warming after ten minutes, whereupon the remainder of the anhydride and five drops of acid were added.
During a twenty minute induction period, during which no heat was applied, the temperature of the mixture began to rise, slowly at first, and then more rapidly, until the mixture had to be cooled as it approached the boiling point. After cooling, it was found that the mixture still tended to become hotter, once again approaching the boiling point, so that cooling was again required. After an additional hour of standing, no more evolution of heat could be detected. The mixture was then refluxed vigorously, and in order to follow the rate of dehydration, 1 ml. samples of this mixture were taken at intervals and titrated in acetic acid with a standard solution of bromine in glacial acetic acid, prepared of such strength that absorption of 10 ml. of the standard solution would indicate 100% completion of the reaction.

<table>
<thead>
<tr>
<th>Time of Refluxing (Minutes)</th>
<th>ML. Bromine Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>3.35</td>
</tr>
<tr>
<td>30</td>
<td>4.20</td>
</tr>
<tr>
<td>45</td>
<td>4.61</td>
</tr>
<tr>
<td>60</td>
<td>5.10</td>
</tr>
<tr>
<td>90</td>
<td>5.50</td>
</tr>
<tr>
<td>210</td>
<td>5.80</td>
</tr>
</tbody>
</table>

After 3½ hours of refluxing, the reaction had apparently reached a flat, and it was considered not feasible to continue the heating, in order to incur as little decomposition as possible.

After cooling, the mixture was slowly neutralized over a period of three hours with the calculated amount of KOH in 350 ml. of water, while keeping the flask chilled in ice water. The light yellow organic layer was separated, and
the aqueous portion was extracted with ether, the ether extract being combined with the organic material previously separated. This was dried over anhydrous \( \text{K}_2\text{CO}_3 \) for two days, and then distilled through a Claisen flask modified in that the bent arm had numerous indentations punched into the walls, so that it acted as a small fractionating column. After the ether-isoprene mixture had distilled off, the temperature rose rapidly, to yield a flat at 145-149° of 25 grams, and leaving a residue of 20 grams.

The residue, which was assumed to be the hydroxy ester,

\[
\text{CH}_3 - \overset{\text{O}}{\text{C}} - \text{CH}_2 - \text{CH} = \overset{\text{O}}{\text{C}} - \text{CH}_3
\]

was mixed with 1.5 equivalents of acetic anhydride and 5 drops of phosphoric acid. After fifteen minutes, during which no heat was evolved, the mixture was brought to a vigorous boil. Because of marked darkening, no titration could be run. Therefore, after one hour of heating, the mixture was cooled, neutralized and purified as before. After removal of ether, five grams of unsaturated ester boiling at 146-148° were obtained, which was combined with the 25 grams obtained previously.

It was noted during the course of this distillation that when the oil bath temperature reached ca. 200°, distillation continued readily, but the condensate smelled strongly of acetic acid, and was, indeed, acid to litmus. This suggests that the tertiary hydroxyl group is esterified first, followed by elimination of acetic acid at higher temperatures. This is in accord with the results reported by Konowalow on the thermal decomposition of 3° amyl acetate.
A portion of the residue (di-ester) was treated with magnesium turnings to remove acetic acid, and to the resulting liquid was added a few ml. of freshly prepared ethyl magnesium iodide. A solid was formed immediately, but without the characteristic violent evolution of ethane which results upon the addition of the Grignard reagent to an alcohol. This, therefore, confirms the absence of the hydroxyl group in the residue.

In order to remove any acetic acid that might have formed during the distillation of the ester, the product was washed several times and dried over anhydrous K₂CO₃. Distillation of the dried material yielded 24 grams of ester boiling primarily between 146-148°, the temperature rising to 150° as the volume in the flask became very small. Yield (based on 63 gms. of glycol): 31%. The remainder was undoubtedly converted to isoprene, since the ether distillate was strongly unsaturated, and exhibited the characteristic olefin odor.

The density and refractive index of the ester were determined in order to calculate the molecular refraction.

Air Wt. of Ester at 20° : 22.5652 g.
Air Wt. equal to H₂O : 24.860 g.
Density of Ester at 20° : 0.9062

Observed angle on Pulfrich at 20°: 50° 58' 20
nD (calculated) : 1.42332

\[ [\hat{\alpha}]^{20}_D \] (found): 36.02; (Calc.) 35.71
E. Saponification of Unsaturated Ester:

A preliminary investigation with isooamyl acetate indicated that this ester was almost completely saponified by refluxing with 30% KOH for one hour. Therefore, the 24 grams of ester obtained were refluxed with two equivalents of 30% KOH for nearly four hours to insure complete hydrolysis. The typical ester odor had completely disappeared at the end of the first two hours.

After cooling, the mixture was distilled until the condensate was no longer cloudy, the distillate was saturated with K₂CO₃, and the alcohol layer separated and dried over two fresh portions of freshly heated carbonate. Distillation yielded 15.2 grams of an unsaturated alcohol, boiling at 131.5-133°, with a higher boiling portion, due to superheating, of less than one gram (b.p. 133-134.5°). The yield of unsaturated alcohol obtained, boiling at 131.5-133° was 62%.

The density and refractive index of the alcohol were obtained at 20°, and the molecular refraction calculated:

\[ \text{Air wt. of Alcohol at } 20°: 7.6579 \text{ g.} \]
\[ \text{Air wt. equal vol. } H₂O : 8.3721 \]
\[ \text{Density of Alcohol at } 20°: 0.8522 \]
\[ \text{Observed angle on Pulfrich: } 43° 53' 20" \]
\[ nₚ (\text{calc.) : 1.4353g} \]
\[ [\text{M}]^{2b} \text{ (found): 25.39; (calc.) 26.35} \]

F. Preparation of Derivatives:

1. Phenyl Carbamate: The phenyl urethane of the alco-
hol which he designated as γδ-dimethyl allyl alcohol was prepared by Courtot, and upon recrystallization from an other petroleum ether mixture, melted at 65°.

To one gram of the unsaturated alcohol in a small tube was added 1.49 grams of phenyl isocyanate, and one drop of anhydrous pyridine. There was gentle evolution of heat, so the mixture was cooled, and allowed to stand at room temperature for two hours. The mixture was extracted with 10 ml. of ligroin, and the diphenyl urea separated. The filtrate was chilled in ice-HCl in order to precipitate the urethane, which at first came down as an oil, and solidified slowly. The solid was filtered and recrystallized from ligroin, but after drying was found to melt at about room temperature, since touching the dried white crystals with a spatula caused them to melt. It is therefore evident that this solid compound is not the same described by Courtot.

2. α-Naphthyl Carbamate:

2.1 g. of α-naphthyl isocyanate were added to 1 g. of the alcohol and one drop of pyridine. After standing for two days at room temperature, the mixture had solidified completely, whereupon the urethane was separated from the insoluble urea by extraction with hot ligroin.

In order to determine whether more than one derivative was present, the urethane was subjected to a series of careful fractional crystallizations, the results of which indicated the product to be homogeneous. After final recrystallization from ligroin, the melting point of the white
crystalline needles was determined, and found to be 67-67.8°. Combustion yielded the following:

- weight sample : 15,479 mg.
- weight H₂O : 9,238 mg.
- weight CO₂ : 42,646 mg.

% H (found) : 6.68; (calc.) : 6.71
% C (found) : 75.18; (calc.) : 75.27

3. 2,5-dinitro benzoate:

The dinitro benzyol ester was prepared by dissolving 1 g. of the alcohol in three ml. of pyridine and adding slowly, in portions, with shaking and cooling, 3.0 g. of freshly prepared 3,5 dinitro benzyol chloride. After standing at room temperature for three hours, the mixture was poured into 15 ml. of cold water and stirred vigorously in order to induce crystallization. The solid that formed was separated, washed several times with water, dilute alkali, and again with water and subjected to systematic fractional crystallization from 95% alcohol. The product appeared to split into two definite cuts, the larger one (ca. 95% of the product) melting at 57.5-58°, while the remainder melted from 42-44°. Portions of the two were fused together, and upon resolidification found to melt from 56-58°. A second mixture of equal amounts of the two, melted at first from 42-58°, and upon resolidifying was found to melt at 41-43°. The addition of more of the high-melting derivative to this mixture resulted in conversion to the lower melting form. It therefore appeared evident that the products were simply
polymorphic modifications of the same compound. The di-
nitrobenzoate reduced permanganate in acetone, indicative
of unsaturation, and gave a mixed melting point with iso-
amyl dinitro-benzoate (m.p. 61°) of 48-52°, a depression of
c. 9 degrees.

Combustion of the higher melting product yielded the
following:

<table>
<thead>
<tr>
<th>wt. sample</th>
<th>wt. H₂O</th>
<th>wt. CO₂</th>
<th>% Hydrogen</th>
<th>% Carbon</th>
</tr>
</thead>
<tbody>
<tr>
<td>14.622 mg.</td>
<td>5.825 mg.</td>
<td>27.684 mg.</td>
<td>4.45</td>
<td>51.67</td>
</tr>
<tr>
<td>14.793 mg.</td>
<td>5.777 mg.</td>
<td>27.796 mg.</td>
<td>4.27</td>
<td>51.28</td>
</tr>
</tbody>
</table>

4. Salicylate:

1.0 g. of the alcohol was mixed in a test tube with
1.8 g. of salicylic acid, and 1 drop of 85% phosphoric acid.
The test tube was corked and the mixture heated on the steam
bath for 30 hours. The mixture was then neutralized with
dilute KOH, and the excess alcohol extracted with ether.
The ester was then separated from the acid by bubbling
CO₂ through the mixture until the turbidity that resulted
became constant, and the mixture was no longer alkaline to
phenolphthalein. Extraction with ether and evaporation of
the solvent yielded ca. 0.2 ml. of a viscous liquid of very
pleasant odor strongly resembling that of carnations. No
attempt to determine the boiling point was made.

5. Butyrate:

The butyrate was prepared from the alcohol and buty-
ryl chloride in pyridine. The solvent was extracted with
dilute HCl, and the ester was washed several times with water and extracted with ether. The odor was a pleasant, fruity one, not unlike isoamyl butyrate, and with a trace of the cough-producing quality of the latter. The ether extract was dried over CaCl₂, the ether evaporated and an attempt made to distill the ester at atmospheric pressure, resulting in extensive decomposition and charring.

6. Phenyl acetate:

The phenyl acetate was prepared from the alcohol and phenyl acetyl chloride in pyridine, as above. After preliminary purification, the ester was steam distilled. A few tenths of a ml. of oily material were obtained, which steam distilled very slowly. The ester had a very pleasant, sweet odor, and had no trace of the fusel oil "tang" which, in contrast, was found closely associated with the corresponding isoamyl derivative prepared for comparison.

It therefore appears that this alcohol might present definite possibilities in the essential oils industries if a practical method could be developed whereby it might be prepared economically, for it certainly possesses marked desirable qualities over the saturated, isoamyl alcohol.
SUMMARY
The synthesis of an unsaturated primary alcohol, which may be classed as a hemiterpene has been successfully carried out by the following series of reactions:

\[
\begin{align*}
\text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{NH}_2} \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \\
\text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{light}} \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \\
\text{KNCO} & \xrightarrow{\text{H}_2 \text{O}} \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \\
\text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{KCN}} \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 \\
\text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{PON}} \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_3
\end{align*}
\]

It is felt that an equilibrium isomerism exists between these two primary alcohols, although its nature has not been investigated. This isomerism is undoubtedly related to the similar type existing among numerous members of the terpenes: viz., geraniol, which exists in two modifications and nerol, its geometrical isomer which also exists in two forms.

**geraniol:**

\[
\begin{align*}
\text{CH}_3 - \text{CH} & = \text{CH} - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{PON}} & \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_3 \\
\text{CH}_3 - \text{CH} & = \text{CH} - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{PON}} & \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_3
\end{align*}
\]

**nerol:**

\[
\begin{align*}
\text{CH}_3 - \text{CH} & = \text{CH} - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{PON}} & \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_3 \\
\text{CH}_3 - \text{CH} & = \text{CH} - \text{CH}_2 - \text{CH}_3 & \xrightarrow{\text{PON}} & \text{CH}_3 - \text{CH} - \text{CH}_2 - \text{CH}_3
\end{align*}
\]
This isomerism is further observed in the partially reduced derivatives i.e., in which the ethylene linkage \( \equiv \) to the hydroxyl group has been reduced.

The mechanism whereby individual isomers of the hemi-terpene alcohols is obtained is not clear, and that a difference exists between the product obtained in this investigation and the prenol described by Courtot is obvious from a consideration of the physical as well as chemical properties. The deductions that Courtot postulates for the mechanism concerned in obtaining prenol from the butyrolactone by hydrolysis involves the existence in the mixture of isopropyl ethylene bromide which undergoes dehalogenation followed by hydrolysis:

\[
\begin{align*}
\text{CH}_3\text{C} & \rightarrow \text{CH}_3\text{C} \\
\text{CH}_3\text{C} & \rightarrow \text{CH}_3\text{C} \\
\text{CH}_3\text{C} & \rightarrow \text{CH}_3\text{C}
\end{align*}
\]

That this mechanism is doubtful appears from the investigations of Claisen, which were previously mentioned, in which it was found that the intermediate hydrolyzes to yield isoprene alcohol.

Additional evidence of the isomerism proposed appears from a consideration of the properties of several derivatives of prenol. Thus the product obtained by the addition of one equivalent of HBr to isoprene boils at 129-133° (Claisen), whereas the supposedly identical compound prepared from Courtot's alcohol and HBr boils at 120° (Darzens & Levy). The ethyl ether of the alcohol too has comparable differences in physical properties. It must be
pointed out that since these products have never been carefully analyzed by ozonolysis, which is much superior to permanganate rupture, the issue is still in doubt, and merits more careful investigation. Nevertheless, a consideration of these discrepancies lends support to the conclusion, and it is not unusual that the isomerism postulated does exist.

Of unusual interest is the result observed during the course of the investigation, of the dissimilarities of the product obtained in the sunlight bromination of isoamyl bromide in comparison with artificial photohalogenation combined with heating. Thus, whereas the reaction in sunlight proceeds rapidly, with vigorous evolution of HBr and heat, the opposite is true in the latter instance, the halogenation proceeding very slowly unless heat is applied. No doubt the difference in these activational energies accounts for the difference observed in the products obtained.

The structure of the dibromide obtained in the photo-flood halogenation has been proved in several ways, and expressions relating vapor pressure to temperature both for this dibromide and for isoamyl bromide have been derived.

The nature of the by-products resulting from the complete hydrolysis of the dibromide has been investigated, and several new derivatives of the tertiary and the primary alcohol have been prepared. The liquid esters of the latter have further been found to possess aromatic qualities in general superior to those of the corresponding isoamyl derivatives.
ACKNOWLEDGEMENT

To Dr. G. Holmes Richter, whose encouragement, insight, and patience have been a source of inspiration to this student in his introduction to research, this paper is respectfully dedicated.
BIBLIOGRAPHY
BIBLIOGRAPHY

(1) Staudinger & Klever; Berichte 44, 2215
(2) Courcot; Bl. Bl. (3) 35, 660
(3) Ipatieff; J. Pr. (2) 52, 522, 525
(4) Claisen; J. Pr. 105, 69
(5) Russian Patent 31,017; Sept. 30, 1937
(6) Favorskii & Lebedeva; J. Gen. Chem. (U.S.S.R.) 8, 879, 1938
(7) Kyriakees; J. Am. Chem. Soc. 35, 985, 999
(8) Favorskii; Uchenye Zapiski Leningrad. Gosudart Univ.
    2, No. 17, 171-30 (1937)
    8 (70), 879-83
(10) Buler; Berichte 28, 2956
(11) Spath & Bruck; Berichte 71, 2706-11
(12) Fischer; Berichte 64 B, 30-4 (1931)
(13) Schiller; Ph.D. Thesis. The Rice Institute. 1941
(14) Marsh; Ph.D. Thesis. The Rice Institute. 1942
(15) Michael, Annalen 379, 263-287 (1911)
(16) Gladstone & Tribe; J. Chem Soc. 26, 445 (1873)
(17) Konowalow; Zeit. f. Phys. Chemie 2, 6
(18) Ipatieff; J. Pr. (2) 55, 2,8
(19) Ipatieff; J. Pr. (2) 53, 149
(20) Favorskii; Annalen 354, 378
(21) Ipatieff; Centr. 1898, II, 472
(22) Kutscherow; Centr. 1914, I, 754
(23) Braun; Monatsh. 17, 218
(24) Aschan; Centr. 1918, II, 939
(25) Lebedeva; Centr. 1914, I, 1406
(26) Gustavson & Popper; J. Pr. 58, 458
(27) Ipatieff; Centr. 1898, II, 472
(28) Ipatieff; Centr. 1901, I, 1195
(29) Wischnegradsky; Annalen 190, 354
(30) Morris & Joubert; J. Am. Chem Soc. 49, 879 (1927)
(31) Gustavson; J. Pr. (2) 62, 271
(32) Krassuski; Centr. 1902 I, 628
(33) Darzens & Levy; Compt. Rend. 191, 1456
(35) Mokiewski; Centr. 1900 (2) 331
(36) Ipatieff; J. Pr. 59, 544
(37) Underwood et. al.; J. Am. Chem. Soc. 52, 4087
(38) Saytzew; J. Pr. 57, 38
(39) Frdl. III, 980
(40) Menschutkin; Berichte 15, 2512