THE REACTION OF ISOBUTYLENE OXIDE WITH SOME ALKYLMAGNESIUM BROMIDE SOLUTIONS

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THE REACTION OF ISOBUTYLENE OXIDE
WITH
SOME ALKYLMAGNESIUM BROMIDE SOLUTIONS

By

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TABLE OF CONTENTS

INTRODUCTION

Work in this laboratory has revealed that the reaction between Grignard reagents and epoxy compounds is not a simple general reaction as is usually indicated. Henry (1) has shown that in the reaction between isobutylene oxide and methylmagnesium bromide the product formed is that product which would be formed if isobutylene oxide rearranges to isobutyraldehyde and methylmagnesium bromide then adds to it. Norton and Hass (2), on the other hand, have shown that when diethylmagnesium solution is allowed to react with isobutylene oxide the expected product, dimethyl propyl carbinol, is formed. When isobutylene oxide was made available to us, we decided to investigate these reactions.

HISTORICAL

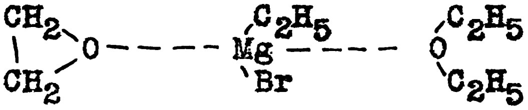
In 1907 Henry (1) reported that when isobutylene oxide is allowed to react with methylmagnesium bromide, 3-methyl-2-butanol is the principal product formed. This is the product which would be formed if the isobutylene oxide isomerizes to isobutyraldehyde and then reacts by the regular addition with methylmagnesium bromide. Henry suggested that this isomerism is influenced by the presence of magnesium.

In 1936 Norton and Hass (2) reported that when isobutylene oxide is allowed to react with diethylmagnesium, the product is 2-methyl-2-pentanol. This is the product which would be formed by breaking the bond between the oxygen and the primary carbon as in the reaction of ethylene oxide with Grignard reagents.

In 1902 Blaise (3) allowed ethylene oxide to react with ethylmagnesium bromide. The principle product after hydrolysis was ethylene bromohydrin.

Grignard (4) studied this reaction and found that when the reaction mixture was heated by distilling off some of the ether, a violent reaction took place. After this "second phase" good yields of n-butyl alcohol were obtained.

Meisenheimer (5) in 1920 analyzed the precipitate which is formed when ethylmagnesium bromide and ethylene oxide are allowed to react at -21°C. This analysis corresponded to the molecular addition of the Grignard reagent to the ethylene oxide. He assigned the following formula to this product:

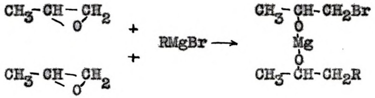


$$\begin{array}{l} CH_2 \\ | \\ CH_2 \end{array} > O \text{- - - - -} Mg \begin{array}{l} C_2H_5 \\ Br \end{array} \text{- - - -} O \begin{array}{l} C_2H_5 \\ C_2H_5 \end{array}$$

Huston and Agett (6) have shown that ethylene bromohydrin is the product formed by hydrolysis of the intermediate formed in the reaction between ethylene oxide and an alkylmagnesium halide. They showed that when dialkylmagnesium is added to the magnesium alcoholate of ethylene bromohydrin, a primary alcohol is formed.

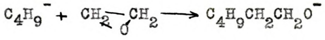
Huston and Bostwick (7) have shown that the predominating product in the reaction between one mole of propylene oxide and one mole of alkylmagnesium bromide is the magnesium alcoholate of propylene bromohydrin. With equal molecular quantities of these reagents the addition product is quite stable, giving small yields of the alcohols. When two moles of epoxide were used however, much better yields of the alcohols were obtained.

They were able to show analytical evidence for the presence of a product similar to the addition product shown below:



In his studies of the reaction of cyclohexene oxide with Grignard reagents which gives alkyl cyclopentane carbinols, Bedos (8) has shown that cyclopentane aldehyde can be isolated in good yields and is probably an intermediate in the reaction.

Cottle and Hollyday (9) suggest that the primary alcohols usually formed in the reaction between Grignard reagents and ethylene oxide can be explained by the nucleophylic attack by the carbanion of the Grignard reagent upon one of the epoxide carbon atoms:


$$C_4H_9^- + \underset{O}{CH_2\text{—}CH_2} \longrightarrow C_4H_9CH_2CH_2O^-$$

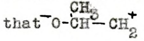
or by the neucleophylic attack of the carbanion upon the bromohydrin:

$$C_4H_9^- + BrCH_2CH_2O^- \longrightarrow C_4H_9CH_2CH_2O^- + Br^-$$

However, neither of these reactions explain the formation of 2-hexanol which is also formed in the reaction.

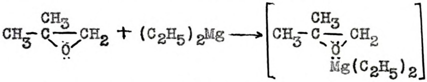
When Cottle and Hollyday heated a mixture of ethylene oxide and magnesium bromide, a violent reaction took place and an acetaldehyde resin was formed. They reason that since a higher yield of 2-hexanol

is obtained when the reaction mixture is heated, acetaldehyde is the intermediate which makes the formation of this alcohol possible.

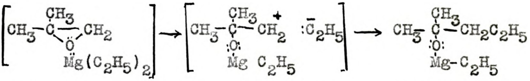
Huston and Bostwick (7) refluxed a mixture of propylene oxide and various alkylmagnesium bromide etherate solutions with benzene. These reagents, which give the expected secondary alcohols at room temperatures, gave large amounts of tertiary alcohols when heated. These are the alcohols which would be formed if propylene oxide rearranged to acetone and the Grignard acted on it. Even when this reaction was run at room temperature and none of the tertiary alcohol was recovered, acetone and polymers of acetone were identified among the reaction products. Huston and Bostwick have proposed that  $^{-}\mathrm{O}\text{-}\overset{\mathrm{CH_3}}{\mathrm{CH}}{-}\mathrm{CH_2^{+}}$ is the intermediate which rearranges to acetone through an intermediate protonized double bond.

THEORETICAL

In the reaction between isobutylene oxide and diethylmagnesium an addition product is formed which hydrolyzes to 2-methyl-2-pentanol. This addition product could be formed by going through an intermediate addition compound by the electrophylic attack of the magnesium on the epoxide oxygen:



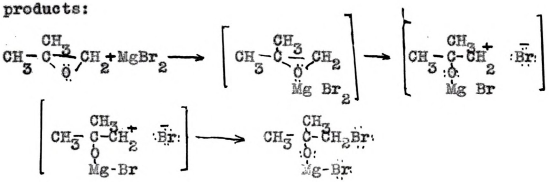
As a result of this electrophylic attack on the oxygen atom, one of the carbon-oxygen bonds is so weakened that the nucleophylic carbanion which is formed is able to add to the electrophylic, primary carbon atom:



This is a slow reaction taking six days or longer to be completed.

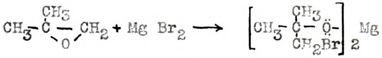
It is suggested that the reaction of isobutylene oxide with magnesium bromide to form an addition product which can be hydrolyzed to isobutylene bromo-

hydrin takes place through the same type of intermediate products:

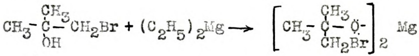


This reaction is very rapid, giving best results if the reaction is kept cooled with salt and ice and hydrolyzed after two hours. The difference in reactivity could be due to the fact that the magnesium-bromine bond ionizes more easily than the alkyl-magnesium bond.

The magnesium alcoholate was prepared by two different methods. Isobutylene oxide was allowed to react with magnesium bromide:



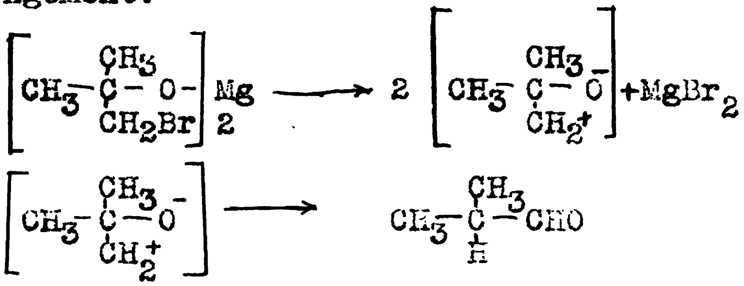
It was also prepared by dropping dimethylmagnesium into isobutylene bromohydrin:



$$CH_3-\underset{OH}{\overset{CH_3}{C}}-CH_2Br + (C_2H_5)_2Mg \longrightarrow \left[CH_3-\underset{CH_2Br}{\overset{CH_3}{C}}-\ddot{O}-\right]_2 Mg$$

The precipitate formed in each case was analyzed, and the halogen content was low indicating that the

addition products were not pure. Each of these products gave isobutylene bromohydrin as the main product when hydrolyzed. However, isobutyraldehyde and isobutyl alcohol are also found in the hydrolysis mixture. These products indicate that the addition compound is unstable and undergoes rearrangement:

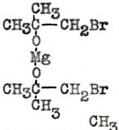


$$\left[CH_3-\overset{CH_3}{\underset{CH_2Br}{C}}-O^-\right]_2 Mg \longrightarrow 2\left[CH_3-\overset{CH_3}{\underset{CH_2^+}{C}}-O^-\right]+MgBr_2$$

$$\left[CH_3-\overset{CH_3}{\underset{CH_2^+}{C}}-O^-\right] \longrightarrow CH_3-\overset{CH_3}{\underset{H}{C}}-CHO$$

This is similar to the transformation of $\overset{-}{O}-\overset{CH_3}{CH}-\overset{+}{CH_2}$ to $CH_3-\overset{O}{C}-CH_3$ which Huston and Bostwick (7) show as one of the intermediates in the decomposition of a similar magnesium dibromohydrin alcoholate. They propose that this transformation requires the intermediate formation of a protonized double bond. It should be noted, however that the ion $(CH_3)_2\underset{CH_2^+}{C}-O^-$ must undergo a preliminary rearrangement to $CH_3-\overset{CH_3}{\underset{\underset{H}{HCO^-}}{C^+}}$ before the hydrogen can shift to its position on the branched carbon.

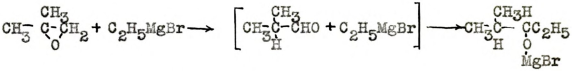
The addition of isobutylene bromohydrin to diethylmagnesium gives, on hydrolysis, 2-methyl-3-pentanol. This alcohol is also formed if diethylmagnesium is allowed to react with isobutyraldehyde. It appears reasonable to conclude, therefore, that the intermediate



$$\begin{array}{c} CH_3\overset{CH_3}{C}-CH_2Br \\ O \\ Mg \\ O \\ CH_3\underset{CH_3}{C}-CH_2Br \end{array}$$

will dissociate to form $CH_3-\overset{CH_3}{\underset{O-}{C}}-\overset{+}{C}H_2$ in the absence of added C_2H_5MgBr of $MgBr_2$.

The reaction between one mole of ethylmagnesium bromide and either one-half or one mole of isobutylene oxide produces an addition product which on hydrolysis gives 2-methyl-3-pentanol.



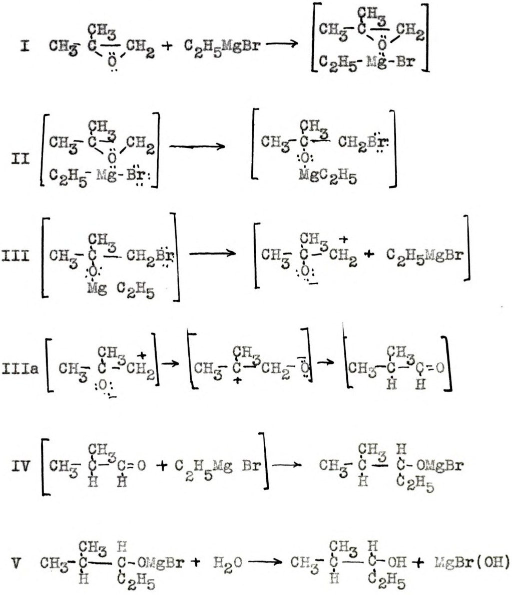
$$CH_3-\overset{CH_3}{C}\underset{O}{-}CH_2 + C_2H_5MgBr \longrightarrow \left[CH_3-\underset{H}{\overset{CH_3}{C}}-CHO + C_2H_5MgBr\right] \longrightarrow CH_3-\underset{H}{\overset{CH_3}{C}}-\overset{H}{\underset{\substack{O\\MgBr}}{C}}C_2H_5$$

This is a comparatively fast reaction, being completed in twelve hours or less.

We have shown above that the magnesium alcoholate of isobutylene bromohydrin rearranges spontaneously to isobutyraldehyde. This rearrangement must take place in the reaction between Grignard reagents and

isobutylene oxide, since isobutyraldehyde was found among the reaction products in every case.

The following series of reactions shows the action of ethylmagnesium bromide on isobutylene oxide to produce 2-methyl-3-pentanol:

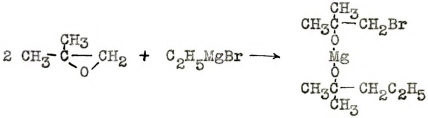


The above reaction takes place any time that isobutylene oxide is allowed to react with an alkylmagnesium bromide solution.

The products formed when one-half mole or one mole of isobutylene oxide is allowed to react with one mole of Grignard reagent are 2-methyl-3-pentanol, isobutylene bromohydrin and isobutyraldehyde.

Besides these three products, when two moles of isobutylene oxide are allowed to react with one mole of Grignard reagent, 2-methyl-2-pentanol and the trimer of isobutyraldehyde are formed. The 2-methyl-2-pentanol is formed because the excess epoxide present allows the reaction shown in the following equation to compete with the normal reaction.

A.



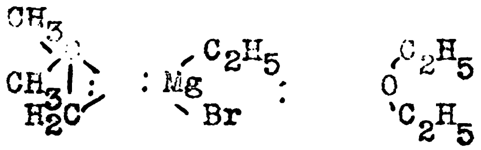
One molecule of the epoxide reacts with the magnesium-bromine bond while a second molecule reacts with the ethylmagnesium bond.

The formation of the trimer of isobutyraldehyde may be attributed to the accumulation of the aldehyde by rearrangement of the ion $(CH_3)_2\text{-}\underset{O_-}{C}\text{-}\overset{+}{CH_2}$ (See reactions

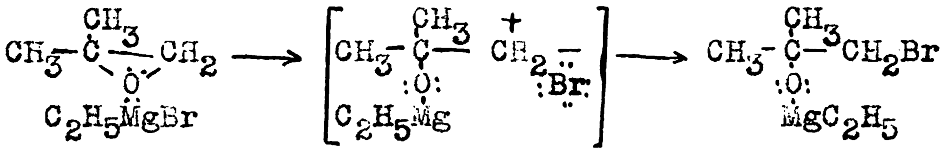
III and IIIa) in the absence of sufficient ethylmagnesium bromide or diethylmagnesium to react with all of the carbonyl.

DISCUSSION

The formation of a coordination compound is generally regarded as the first step in all Grignard reactions (10). For simplicity we have omitted the ether when we show the complex in step I. This complex is undoubtedly the same type as that proposed by Meisenheimer (5) for ethylene oxide which includes ether:



The electrophylic attack of magnesium on the oxygen upsets the electronic equilibrium so that one of the carbon-oxygen bonds is weakened. If an alkylmagnesium bromide is the reagent, the bromide, being partially displaced from the magnesium, attacks the primary carbon nucleophilically.



The magnesium alcoholate of the bromohydrin is thus formed as shown in step III.

If this bromohydrin alcoholate is stable under the conditions of the reaction, as is the case with

the ethylene bromohydrin alcoholate (6) and the propylene bromohydrin alcoholate (7), the bromohydrin is the product formed. Isobutylene bromohydrin alcoholate is not stable even at room temperature. It undergoes rearrangement as shown in steps III and IIIa. This is true whether the reaction is carried out with molar equivalents, or whether an excess of either Grignard reagent or epoxide is present. This is indicated by the alcohols which are formed and by the isobutyraldehyde found in every reaction. It is even true when no Grignard reagent is present as evidenced by the isobutyraldehyde and isobutyl alcohol found when the magnesium alcoholate of isobutylene bromohydrin is hydrolyzed. Considering this evidence we can say that the rearrangement is catalyzed by the magnesium-bromine bond even when this is formed by the decomposition of the magnesium alcoholate.

We obtained the trimer of isobutyraldehyde as the main product when we heated the ether solution of the magnesium alcoholate of isobutylene bromohydrin before hydrolysis. This indicates that heat promotes rearrangement.

Cottle and Hollyday (9) have proposed the following mechanism for the aldehyde formation in the

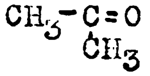
reaction between ethylene oxide and butylmagnesium bromide:

$$(BrCH_2O)^- + RO^- \longrightarrow ROH + (BrCH_2CHO)^=$$

$$(BrCH_2CHO)^= \longrightarrow Br^- + (CH_2CHO)^-$$

$$(CH_2CHO)^- + ROH \longrightarrow CH_3CHO + RO^-$$

After proposing this mechanism, they suggested that the removal of the second proton from ethylene bromohydrin would only be accomplished with such difficulty that such a mechanism seems unlikely. The fact that isobutylene bromohydrin rearranges to an aldehyde also makes this seem unlikely as a general mechanism since there is no hydrogen on the carbon atom to which the oxygen is attached as in ethylene bromohydrin.

The transformation of  $\overset{+}{C}H_2-\underset{CH_3}{C}-O^-$ to  $CH_3-\underset{CH_3}{C}=O$ suggested by Huston and Bostwick (7) can be applied to the transformation of isobutylene oxide to isobutyraldehyde, as we have shown in reaction IIIa.

Step IV is the normal addition of the Grignard reagent to the aldehyde, and step V is the hydrolysis.

Reaction A shows how both 2-methyl-3-pentanol and 2-methyl-2-pentanol can be formed in the reaction between one mole of ethylmagnesium bromide and two moles of isobutylene oxide. If the bromohydrin alc-

oholate rearranges as we have shown before, isobutyraldehyde is formed. Since the reaction between the epoxide and the ethyl magnesium bond is a slow reaction, some is available to react with the aldehyde and form 2-methyl-3-pentanol.

The reactions, when the ethylmagnesium bromide was dropped into the epoxide, show that an addition product like that in reaction A is formed only if excess epoxide is used.

When one mole of the Grignard reagent was dropped into one mole of isobutylene oxide, 2-methyl-3-pentanol and some polymer were formed. When one mole of the Grignard reagent is dropped into two moles of isobutylene oxide, on the other hand, isobutyl alcohol, 2-methyl-2-pentanol and polymer are formed. No 2-methyl-3-pentanol was isolated. The formation of polymer in the former case as contrasted with no polymer in the normal addition indicates that, although the rearrangement is spontaneous and does not need Grignard reagent to catalyze it, if insufficient alkyl group is present, the aldehyde polymerizes. An addition product similar to that in reaction A must be formed when two moles of epoxide were used. This is indicated by the tertiary alcohol formed.

The bromohydrin alcoholate rearranged and polymerized since there was no alkyl group present to react with it.

Isobutyl alcohol was present every time polymer was found. This indicates that if much isobutyraldehyde is present, reduction takes place. Conant and Blatt (12) have shown that reduction is a common reaction between branched aldehydes and Grignard reagents.

The polymer of isobutyraldehyde which is formed in these reactions is of uniform composition, probably the trimer. It distills at the boiling point of the trimer of isobutyraldehyde until the distilling flask is dry. When heated with a drop of sulfuric acid, it decomposes into isobutyraldehyde.

Gaurizchi and Garzino (11) have shown the structure of isobutylene bromohydrin by preparing the sodium sulfate and comparing its melting point with that of $(CH_3)_2C(OH)CH_2SO_3Na$ whose structure was known. We prepared a bromohydrin by the action of methylmagnesium bromide on bromoacetone. The 3,5-dinitrobenzoate of this preparation gave no melting point depression when compared with the same derivative of the bromohydrin prepared by the action of magnesium bromide on isobutylene oxide.

The yields of alcohol are in good agreement with the results expected from consideration of steric effects; the yields are lower as the alkyl groups become more branched. The action of diisopropylmagnesium on the epoxide is the major exception to this rule. This reaction was carried out three times and no 2,4-dimethyl-2-pentanol was detected. When tert-butylmagnesium bromide was allowed to react with the epoxide, some polymer was formed but no alcohol was found. This was the only case that polymer was formed when one-half mole of epoxide was added to one mole of Grignard reagent. The fact that polymer was formed indicates that the alkyl group was not reactive enough to add to the aldehyde before the aldehyde polymerized.

The polymer of isobutyraldehyde is formed only when the magnesium-bromine bond is present to catalyze the rearrangement to isobutyraldehyde, and then only when there is not enough magnesium-alkyl bond to react with the aldehyde. The only exception to this rule is the reaction of tert-butylmagnesium bromide with isobutylene oxide. In this case one must assume that steric considerations slow the addition of the alkylmagnesium to the carbonyl to the extent that none of the expected alcohol is formed.

EXPERIMENTAL

I. MATERIALS:

Isobutylene oxide furnished by the Shell Chemical Company was purified before use by redistillation.

Alkyl bromides were all dried over anhydrous calcium chloride and fractionated before use.

Magnesium turnings were dried overnight in an oven at 110°C.

Bromine was dried by shaking over concentrated sulfuric acid.

Anhydrous diethyl ether was redried over metallic sodium before being used.

Dioxane was purified by refluxing over dilute hydrochloric acid, drying, refluxing over sodium and distilling.

II. APPARATUS:

The apparatus described below was used for all of the reactions. The Grignard reagents and the magnesium bromide etherate solutions were also prepared in it. A one liter three necked, round bottom flask was fitted with a reflux condenser,

a glycerine sealed stirrer, and a Hirshberg dropping-funnel. All of the etherate solutions were protected from atmospheric moisture and carbon dioxide with calcium chloride and soda-lime filled tubes.

III. REACTION OF ISOBUTYLENE OXIDE WITH ONE-HALF, ONE AND TWO MOLES OF ALKYLMAGNESIUM BROMIDE SOLUTIONS

A. Preparation of Grignard reagents.

One and one-tenth moles (26.5 g.) of magnesium turnings were placed in the flask. Approximately ten milliliters of a mixture of one mole of the alkyl halide and an equal volume of anhydrous ether were dropped into the flask and the mixture stirred until the reaction was started. Four hundred milliliters of anhydrous ether were then added to the flask and the remainder of the alkyl halide solution was added dropwise. After the alkyl halide addition was complete, the stirring was continued for two hours.

The primary alkyl Grignard reagents were prepared by adding the alkyl halide at such a rate that a gentle reflux was maintained.

The best yield of isopropylmagnesium bromide was obtained when the isopropyl bromide was added

slowly enough at room temperature that the reaction mixture did not warm up enough to cause the ether to reflux. About twenty-four hours were taken to prepare one mole of isopropylmagnesium bromide.

Tert-butylmagnesium bromide was most successfully prepared when the reaction flask was cooled to -10°C with ice and salt and the tert-butyl bromide was diluted with twice as much ether as usual. The addition of the magnesium-ether slurry was made over a twenty-four hour period.

Methylmagnesium bromide was prepared in essentially the same apparatus. The dropping funnel was replaced by a tube leading from the tank of methyl bromide gas to below the surface of the ether. All of the ether was placed over the magnesium, the stirrer started and the methyl bromide was bubbled into the ether at such a rate that a gentle reflux was maintained.

The Grignard solutions were decanted from the excess magnesium into a graduated cylinder. Two milliliter aliquots were removed and analyzed by Gilman's titration in the following way: The aliquot was hydrolyzed with water, an excess

of standard hydrochloric acid added and back titrated with standard sodium hydroxide solution to a phenolphthalein endpoint.

B. Reaction with isobutylene oxide.

The Grignard reagent which had been prepared and analyzed as described above was placed in a clean dry apparatus. The flask was cooled by surrounding it with crushed ice and salt. The calculated amount of isobutylene oxide was mixed with an equal volume of anyhdrous ether, placed in the dropping funnel and allowed to drop slowly into the cooled Grignard solution. When the addition was complete, the temperature was raised to room temperature.

The mixture was hydrolyzed after standing twenty-four hours. In the case of Grignard solutions, use of Michler's ketone showed that no Grignard reagent was left after twelve hours.

The reaction was hydrolyzed by cooling the mixture with ice and then adding 175 to 225 milliliters of saturated ammonium bromide solution dropwise. The ether solution was decanted from the basic precipitate and dried over anhydrous sodium sulfate.

C. Analysis of the reaction products.

1. Decomposition and analysis of the bromohydrin.

The dried products of hydrolysis were refluxed over a mixture of forty grams of sodium hydroxide and two hundred milliliters of water for two hours with vigorous stirring. The mixture was cooled, the layers were separated, and the aqueous layer was extracted three times with twenty-five milliliters of ether. The ether extracts were re-dried over anhydrous sodium sulfate. The aqueous layer was diluted to one liter. Five milliliter aliquot portions were removed and titrated for bromide ion by the Volhard method.

2. Alcohol distillation.

The dried ether solution containing the alcoholic products was distilled at atmospheric pressure. The results of these distillations are collected in Tables I and II.

3. Alcohol derivatives.

The 3,5-dinitrobenzoates were prepared using 3,5-dinitrobenzoyl chloride and pyridine (13).

Alpha-naphthylurethans and phenylurethans were prepared from the corresponding isocyanates using a drop of 5% trimethylamine-ether solution as catalyst (14).

The acid phthalates were prepared by refluxing the alcohol with phthalic anhydride in pyridine. (15).

Isobutyraldehyde was identified in the fraction boiling between 55 and 65°C. of every reaction. This was shown by preparing the 2,4-dinitrophenylhydrazone and comparing it with the same derivative of pure isobutyraldehyde. M.p. 183°C. (16).

In the reaction between one-half mole of tert-butylmagnesium bromide and one mole of isobutylene oxide no 2,4,4 trimethyl-3-pentanol was found. About eight grams of polymer were recovered. No polymer was found in any of the other reactions between one-half mole of epoxide and one mole of Grignard reagent.

When two moles of isobutylene oxide were allowed to react with one mole of a Grignard reagent, isobutyl alcohol and a polymer were isolated. The isobutyl alcohol was identified by its boiling point, 106-108°C and by preparing

its 3,5-dinitrobenzoate, which gave no depression in melting point when mixed with the same derivative prepared from known isobutyl alcohol. The polymer was found to contain no halogen. When heated with a drop of sulfuric acid, it slowly depolymerized into isobutyraldehyde. Its physical properties, B.p.$_{17mm}$127°C. ; n_D^{20}1.4370 indicate that it is the trimer of isobutyraldehyde. n_D^{17}1.4329 (17); B.p.105-108°C (29)

IV. REACTION OF ISOBUTYLENE OXIDE WITH DIALKYLMAGNESIUM SOLUTIONS.

A. Preparation of Dialkylmagnesium.

One mole of Grignard reagent was prepared in the manner described in IIIA. A mixture of 110 milliliters of dioxane and 100 milliliters of anhydrous ether was slowly added to the Grignard reagent to precipitate the bromine-containing compounds. This mixture was allowed to stand from three to five days before the dioxane precipitate was separated from the dialkylmagnesium by centrifuging. The dialkyl concentration was determined by the Gilman method.

B. Reaction of isobutylene oxide with dialkylmagnesium.

The dialkylmagnesium was cooled and a mixture of the calculated amount of isobutylene oxide in anhydrous ether was slowly dropped into the cooled dialkylmagnesium.

Since this was a much slower reaction than those involving the Grignard reagent, these reactions were allowed to stand from one to three weeks before they were hydrolyzed with saturated ammonium bromide solution in the same manner as reaction III B. The ether solution of the products was dried over anhydrous sodium sulfate.

The dried mixture was distilled, and the results are shown in table I.

Ditertiarybutylmagnesium was prepared by using tert-butyl chloride because better yields of tert-butylmagnesium chloride are obtained than of tert-butylmagnesium bromide.

Dimethylmagnesium was found to be so pyrophoric that it was not possible to handle it in the same manner used with all the others. The dimethylmagnesium was separated from the dioxane precipitate by adding an excess of ether, allowing the precipitate to settle and decanting the supernatant ether solution. As this dialkylmagnesium

was not analyzed, no quantitative information is available for the reaction between dimethylmagnesium and isobutylene oxide.

V. REACTIONS OF ISOBUTYLENE BROMOHYDRIN WITH DIETHYLMAGNESIUM.

A. Preparation of isobutylene bromohydrin.

The apparatus for the reaction was the same as that used to prepare the Grignard reagents except that all connections were ground glass joints and a mercury sealed stirrer was used. One and one-tenth moles (26.5 g.) of magnesium turnings were placed in the flask with 500 milliliters of anhydrous ether. One mole (26 ml.) of bromine was slowly dropped into the flask. After the bromine addition was complete , the solution was refluxed for an hour and allowed to stand over night.

The mixture was decanted from the unreacted magnesium into a graduated cylinder and an aliquot was titrated for bromine by the Volhard method.

The ether solution was placed into another clean, dry flask and then cooled in a mixture of salt and ice. The calculated amount of isobutylene oxide in an equal volume of ether was dropped slowly into the magnesium bromide solution.

The solution was kept cool and stirred for two hours after which it was decomposed in ice. The basic salts were dissolved in dilute hydrochloric acid. The ether layer was separated, shaken with five percent sodium bicarbonate solution and then with water and dried over anhydrous sodium sulfate. The ether fraction was removed until the boiling point rose to fifty degrees, after which reduced pressure was used and the isobutylene bromohydrin fractionated at 14 to 16 millimeters. Fifty-six grams were recovered between 58 and 60°C. This represents a 36.6% yield.

A precipitate forms in this reaction, In one case this precipitate was removed and washed with anhydrous ether by centrifuging and dried in a vacuum desiccator. This precipitate was analyzed for bromine and magnesium.

1. Analysis of the precipitate.

Magnesium was determined by decomposition of weighed samples with Meker burners and weighed as MgO. The percentage magnesium was calculated from the formula:

$$\frac{\text{Wt. of MgO} \times 0.6032 \times 100}{\text{Wt of sample}} \quad \text{\% Magnesium}$$

Bromine was determined by the Volhard method. Weighed samples were hydrolyzed in fifteen milliliters of water and enough nitric acid was added to dissolve the precipitate. Seven grams of sodium hydroxide were added and the samples were refluxed for one hour. The samples were then cooled and diluted with one hundred and fifty milliliters of water, made acidic with dilute nitric acid and titrated with one-tenth normal silver nitrate and potassium thiocyanate, using the ferric alum indicator.

Calc'd for $C_8H_{16}O_2MgBr$: Mg, 7.31; Br, 48.78
Found : Mg, 7.67; Br, 42.30

In another experiment the reaction was refluxed over night before hydrolysis. When this reaction was hydrolyzed, dried and distilled as usual, the only product found was the polymer of isobutyraldehyde.

B. Addition of one mole diethylmagnesium to two moles isobutylene bromohydrin.

One-fourth mole of diethylmagnesium was prepared as described in IIIA. It was analyzed and the calculated amount of isobutylene bromohydrin in an equal volume of ether was placed in

a 500 milliliter reaction flask. The diethylmagnesium was placed in the dropping funnel. The flask was cooled with salt and ice and the addition started. A precipitate formed immediately. When the addition was complete, the solution was stirred for two hours. Some of the precipitate was removed and washed with ether by centrifuging. The precipitate was dried in a vacuum desiccator and analyzed for magnesium and for bromine. The solution was hydrolyzed with saturated ammonium bromide solution as usual, separated from the precipitate and dried over anhydrous sodium sulfate.

Calc'd for $C_8H_{16}O_2MgBr_2$: Mg, 7.31; Br, 48.78
Found : Mg, 9.40; Br, 42.91

1. Analysis of the hydrolyzed solution.

The dried solution was fractionated. Isobutyraldehyde, isobutyl alcohol and isobutylene bromohydrin were identrified.

C. <u>Addition of one mole isobutylene bromohydrin to one mole diethylmagnesium</u>.

One-fourth mole of diethylmagnesium was prepared as above, analyzed and placed in the reaction flask. The calculated amount of isobutylene bromohydrin was placed in the dropping funnel and dropped slowly into the cooled diethylmagnesium. A precipitate formed which was separated and analyzed as above.

a 100 milliliter reaction flask. The [illegible]

magnetic bar placed in the [illegible]. The

flask was [illegible]

[illegible]

the [illegible]

[illegible]

Calc'd for $C_{12}H_{26}O_2Mg$: Mg, 10.73
Found : Mg, 9.64; Br, 5.95

VI. PREPARATION OF ISOBUTYLENE BROMOHYDRIN

Isobutylene bromohydrin was prepared by the action of methylmagnesium bromide on bromoacetone.

Bromoacetone was prepared by Levene's procedure (18):

> A three liter, three-necked, round-bottom flask was provided with an efficient mechanical stirrer, a reflux condenser, a thermometer, and a 250 milliliter separatory funnel, the stem of which reached nearly to the bottom of the flask. This apparatus was placed in a water bath. 800 milliliters of water, 250 milliliters of acetone and 166 milliliters of glacial acetic acid were placed in the flask. The stirrer was started and the temperature of the water bath raised to 70-80°C. Then 174 milliliters (3.6 moles) of bromine were carefully added through the separatory funnel. After the bromine addition was completed and the solution was colorless, it was diluted with 400 milliliters of

cold water, cooled to 10°C, made neutral to congo red with solid anhydrous sodium carbonate. The oil which separated was fractionated and the fraction boiling at 40-42°C was taken. Yield 119 grams (25%).

One-half mole of methylmagnesium bromide was prepared and analyzed as described in IIIA.

One-half mole (68.3 g.) of bromoacetone was placed with an equal volume of ether in a three liter, three-necked, round bottom flask and cooled to 0°C with salt and ice. The Grignard reagent was added dropwise from a separatory funnel. The reaction mixture was hydrolyzed immediately after the addition was completed with saturated ammonium bromide solution. The ether solution was dried over anhydrous sodium sulfate and fractionated. Twenty milliliters of isobutylene bromohydrin was obtained. B.p.$_{15mm}$ 47°C.

The dinitrobenzoate of this alcohol was prepared and it was shown by the mixed melting point method to be the same as the bromohydrin obtained by the action of magnesium bromide on isobutylene oxide. M.p. 120°C.

VII. ADDITION OF ETHYLMAGNESIUM BROMIDE TO ISOBUTYLENE OXIDE.

A. Addition of one mole ethylmagnesium bromide to one mole isobutylene oxide.

One mole of ethylmagnesium bromide was prepared and analyzed as in IIIA. A mixture of the calculated amount of isobutylene oxide in an equal volume of anhydrous ether was placed in the flask and cooled with salt and ice. The ethylmagnesium bromide was placed in a separatory funnel and slowly dropped into the flask. After the addition was completed, the reaction was stirred for two hours. It was hydrolyzed and dried as usual.

The bromohydrin was decomposed as in section III and the bromine titrated. Yield: 27.26% bromohydrin.

The dried ether solution was distilled. Yield: 13.7% 2-methyl-3-pentanol; 3 g. polymer.

B. Addition of one mole ethylmagnesium bromide to two moles isobutylene oxide.

One mole of ethylmagnesium bromide was prepared, analyzed and allowed to drop into a mixture of two moles of isobutylene oxide in an equal volume of ether as above.

The reaction products were analyzed similarly.

Results: 63.15% bromohydrin; 5.8% isobutyl alcohol;
8.5% 2-methyl-2-pentanol; 11 g. polymer.
No 2-methyl-3-pentanol could be detected.

SUMMARY

1. Isobutyraldehyde is an intermediate in the formation of isopropyl alkyl carbinol by the action of alkylmagnesium bromide on isobutylene oxide.

2. The magnesium alcoholate of isobutylene bromohydrin undergoes rearrangement to isobutyraldehyde to a slight extent at 0°C and to a greater extent when heated.

3. Isobutylene oxide does not rearrange to isobutyraldehyde when treated with dialkylmagnesium.

4. The magnesium-bromine bond is necessary to catalyze the rearrangement of isobutylene oxide to isobutyraldehyde.

5. The addition of two moles of alkylmagnesium bromide to one mole of isobutylene oxide produces both the alcohol formed by the rearrangement of

isobutylene oxide to isobutyraldehyde and the alcohol formed by the direct addition of an alkylmagnesium to the epoxide.

6. The structure of isobutylene bromohydrin is shown to be $(CH_3)_2C(OH)CH_2Br$ by its preparation by the action of methylmagnesium bromide on bromoacetone.

Table I

Percentage Yields of Alcohols and Isobutylene Bromohydrin

Grignard reagent prepared from	$1\ CH_3\overset{CH_3}{C}\underset{O}{—}CH_2 + 1\ RMgX$		$2\ CH_3\overset{CH_3}{C}\underset{O}{—}CH_2 + 1\ RMgX$				$\frac{1}{2}\ CH_3\overset{CH_3}{C}\underset{O}{—}CH_2 + 1\ RMgX$		$R_2Mg + CH_3\overset{CH_3}{C}\underset{O}{—}CH_2$
	bromo-hydrin	secondary alcohol	bromo-hydrin	sec. alcohol	tert. alcohol	grams polymer	bromo-hydrin	sec. alcohol	tertiary alcohol
Methyl bromide							40.2	40.8	---.-*
Ethyl bromide	28.27	42.4	51.25	13.16	17.9	10	40.4	51.37	35.0
n-Propyl bromide	30.54	39.39	57.2	12.80	15.13	20	23.0	44.5	25.5
iso-Propyl bromide							59.2	21.5	00.0
n-Butyl bromide							40.4	19.7	11.5
tert-Butyl bromide							55.8	00.0	6.0

* Sufficient alcohol was obtained for identification, but no quantitative information is available.

Table II

Physical Constants of the Alcohols

Alcohol	n_D^{20}	B.P. °C	Ref.
1-Bromo-2-methyl-2-propanol	1.4710	49.5 (16mm)	19
3-Methyl-2-butanol	1.3973	110-112 (745mm)	20
2-Methyl-2-butanol	1.4020	102 (740mm)	21
2-Methyl-3-pentanol	1.4168	127-128 (740mm)	22
2-Methyl-2-pentanol	1.4125	117-118 (740mm)	23
2-Methyl-3-hexanol	1.4178	142-145 (740mm)	24
2-Methyl-2-hexanol	1.4175	139-140 (740mm)	25
2,4-Dimethyl-3-pentanol	1.4250	137-138 (740mm)	22
2-Methyl-3-heptanol	1.4259	165-167 (740mm)	22
2-Methyl-2-heptanol	1.4248	65 (15mm)	26
2,4,4-Trimethyl-2-pentanol	1.4038	55 (15mm)	26

Table III

Derivatives of the Alcohols

	M.P. °C	Ref.
1-Bromo-2-methyl-2-propanol		
3,5-dinitrobenzoate	120	
3-Methyl-2-butanol		
3,5-dinitrobenzoate	163	
2-Methyl-2-butanol		
3,5-dinitrobenzoate	116	28
2-Methyl-3-pentanol		
3,5-dinitrobenzoate	85	28
3-nitrophthalate	150.5	22
2-Methyl-2-pentanol		
3,5-dinitrobenzoate	72	28
benzoate	182-183	23
2-Methyl-3-hexanol		
3,5-dinitrobenzoate	59-60	
acid phthalate	59-60	20
2-Methyl-2-hexanol		
3,5-dinitrobenzoate	141-142	
phenylurethane	44-45	27
2,4-Dimethyl-3-pentanol		
3,5-dinitrobenzoate	75	
phenylurethane	94-94.5	12
2-Methyl-3-heptanol		
3,5-dinitrobenzoate	53-54	
acid phthalate	47-48	20

	B.P. °C.	Ref.
2-Methyl-2-heptanol		
3,5-dinitrobenzoate	43-44	

Table IV

Analyses of New Derivatives for Nitrogen by Semimicro Kjeldahl (30)

Alcohol	% N Calc'd	% N Found
1-Bromo-2-methyl-2-propanol		
3,5-dinitrobenzoate	8.04	8.11
3-Methyl-2-butanol		
3,5-dinitrobenzoate	9.93	10.13
2-Methyl-3-hexanol		
3,5-dinitrobenzoate	9.80	9.60
2-Methyl-2-hexanol		
3,5-dinitrobenzoate	9.03	8.68
2,4-Dimethyl-3-pentanol		
3,5-dinitrobenzoate	9.03	9.27
2-Methyl-3-heptanol		
3,5-dinitrobenzoate	8.64	8.44
2-Methyl-2-heptanol		
3,5-dinitrobenzoate	8.64	8.40

REFERENCES

1. Henry, L., Compt. rend., 145, 21 (1907)

2. Norton, F.H. and Hass, H.B., J. Am. Chem. Soc. 58, 2157 (1936)

3. Blaise, M., Compt. rend., 134, 552 (1902)

4. Grignard, V., Bull. Soc. Chim., [3] 29, 944 (1903)

5. Meisenheimer, J., Ann., 442, 180 (1925)

6. Huston, R.C. and Agett, A.A., J. Org. Chem., 6, 123 (1941)

7. Huston, R.C. and Bostwick, C.O., J. Org. Chem., 13, 331 (1948)

8. Bedos, P. and Ruyer, A., Compt. rend., 188, 962 (1929)
   Bedos, P., Compt. rend., 189, 255 (1929)

9. Cottle, D.L. and Hollyday, W.C., J. Org. Chem. 12, 510 (1947)

10. Gilman, H., "Organic Chemistry, an Advanced Treatise" 2nd. Ed., P.509, John Wiley and Sons, Inc., New York, 1943.

11. Gaurischi, J. and Garzino, L., Ann. Chim. Farmicoligia, 87, 110 (1887)
    Garzino, L., Jahrbrichte uber die Fortschritte der Chemie, 1329 (1889)

12. Conant, J.B. and Blatt, A.H., J. Am. Chem. Soc., 51. 1233 (1929)

13. Cheronis, N. and Entrikin, J.B., "Semimicro Qualitative Organic Analysis", P.223, Thomas Y. Crowell Co., New York, 1947

14. Shriner, R.L. and Fuson, R.C., "Identification of Organic Compounds" 3rd Ed., P.163, John Wiley and Sons, New York, 1948

15. Elving, P.J. and Warshowsky, B.J., Anal. Chem., 19, 1006 (1947)

16. Bryant, W.M.D., J. Am. Chem. Soc., 54, 3758 (1932)

17. Quelet, P. and Sicard, G., Compt. rend., 212, 162(1932)

18. Blatt, A.H., "Organic Synthesis" Collected Volume II, P.88, John Wiley and Sons, Inc., New York, 1943

19. Suter, C.M. and Zook, H.D., J. Am. Chem.Soc., 66, 738 (1944)

20. Pickard, R. H. and Kenyon, J., J. Chem. Soc., 101, 633 (1912)

21. Timmermans, J. and Hennault-Roland, J. Chim. Phys., 29, 529 (1932)

22. Pukirea, A., Chem. Centr., 1942 II, 389

23. Deschamps, A., J. Am. Chem. Soc., 42, 2672 (1920)

24. Henry, L., Compt. rend., 143, 103 (1905)

25. Whitmore, F.C. and Woodburn, H.M., J. Am. Chem. Soc., 55. 361 (1933)

26. Huston, R.C., Guile, R.L., Sculati, J.J., and Wasson, W.N., J. Org. Chem., 6, 252 (1941)

27. Jones, E.R.H. and McCombie, J.T., J. Chem. Soc., 261(1943)

28. Sutter, P., Helv. Chem. Acta., 21, 1266 (1939)

29. Franka, A. and Wozelka, H., Chem. Centr., 1912 II,322

30. Clark, E.P., "Semimicro Quantitative Organic Analysis", P.37, Academic Press, Inc., New York, 1943