THE REACTION OF ETHYLENE OXIDE WITH VARIOUS GRIGNARD REAGENTS

by

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A THESIS

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To Dr. R. C. Huston I wish to express my gratitude for the many suggestions and the helpful understanding that have made possible this work.

A. H. Agett

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INTRODUCTION

The author noted when tertiary butyl magnesium bromide reacted with ethylene oxide that the expected alcohol was not obtained. The main product of the reaction was ethylene bromohydrin. The results were the same whether the mixture was refluxed in benzene or hydrolyzed immediately.

This anomalous Grignard reaction promoted the investigation.

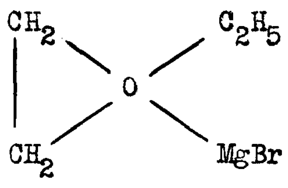
HISTORICAL

In the year 1902 Blaisse (1) reacted ethylene oxide with ethyl magnesium bromide. He obtained as the principle product ethylene bromohydrin. The following scheme was formulated by him to interpret the results:

(I)

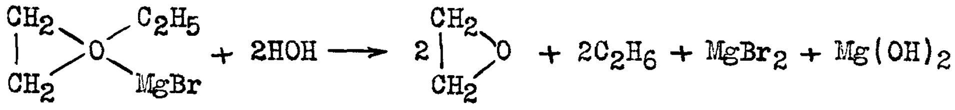
The product (I) would give ethylene bromohydrin upon hydrolysis. But according to this the Grignard reagent is broken between the magnesium and the bromine. All previous cases were explained by the separation of the alkyl group from the magnesium halide.

In 1903 Grignard (2) published an article in which he expressed his views on the manner of the reaction. He explained the formation of the bromohydrin obtained by Blaisse through a secondary reaction in which ethylene oxide formed an addition compound with the following formula:

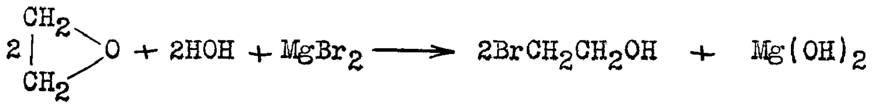


(II)

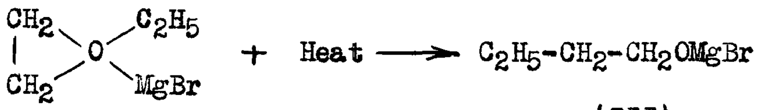
This addition compound was called an oxonium salt by Grignard. It would give upon hydrolysis the following:



The ethylene oxide in the presence of magnesium bromide and water would give ethylene bromohydrin according to the known reaction of Wurtz (3).



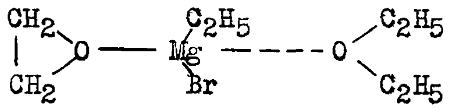
Consequently, the formation of the ethylene bromohydrin was a secondary reaction. Therefore, after the ethylene oxide was added to the ethyl magnesium bromide, Grignard distilled off the ether on a water bath in order to heat the mixture. After a large amount of the ether had been removed a second reaction took place. The mixture began to bubble and swell. If it was not controlled very carefully an explosion took place with the evolution of a great deal of heat. This reaction was called the second phase by Grignard. Upon hydrolysis the mixture then yielded 82% of normal butyl alcohol. This second phase of the reaction could also be produced by distilling off some of the ether and replacing it with benzene or toluene. The new mixture was refluxed for several hours and then hydrolyzed as before. According to Grignard the mechanism of the reaction was the rupture of the oxonium salt by heat as shown below:



(III)

The product (III) upon hydrolysis would yield normal butyl alcohol. The mechanism of the above reaction has been generalized by Grignard, (2) L. Henry (4), Delby (5), and others using ethylene oxide and different Grignard reagents.

Meisenheimer (6) contributed analytical data in confirmation of Grignard's ideas. He analyzed the product which was precipitated when ethylene oxide was reacted at -21° with ethyl magnesium bromide. The results corresponded to the molecular addition between the Grignard reagent and ethylene oxide. Meisenheimer assigned the following formula to this product:



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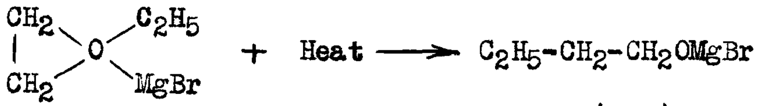

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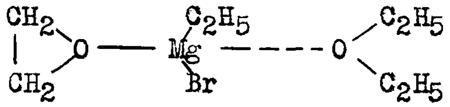


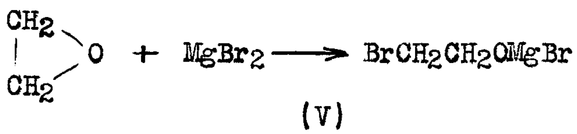
(IV)

This was more in accordance with the ideas of former workers than the first formula assigned by Grignard (3). This product (IV) was kept for several weeks in a vaccum desiccator. At the end of this period it was found to be unchanged. When heated on a water bath it decomposed. Meisenheimer also analyzed the compound formed in the second phase. The analysis corresponded to the formula $C_2H_5-CH_2-CH_2-O-MgBr$. This upon hydrolysis gave the expected normal butyl alcohol.

In 1930 I. Ribas and E. Tapia (7) reacted the ether solution of magnesium bromide with epichlorohydrin and the following compound was formed:

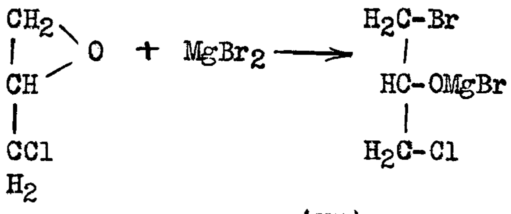
$$BrCH_2-CH_2(OMgBr)CH_2Cl$$

Upon hydrolysis the bromochlorohydrin of the glyceride was formed. In 1931 Ribas and Tapia (8) reacted ethylene oxide, epichlorohydrin, and methoxyepoxypropene with one mole of magnesium bromide. Products were obtained according to the equations:



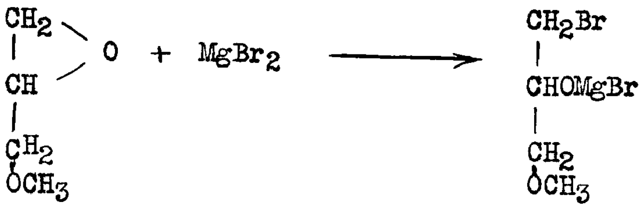
$$\text{CH}_2\text{-CH}_2\text{>O} + MgBr_2 \longrightarrow BrCH_2CH_2OMgBr$$

(V)



$$\text{CH}_2\text{-CH-CH}_2\text{Cl (>O)} + MgBr_2 \longrightarrow H_2C(Br)-HC(OMgBr)-H_2C(Cl)$$

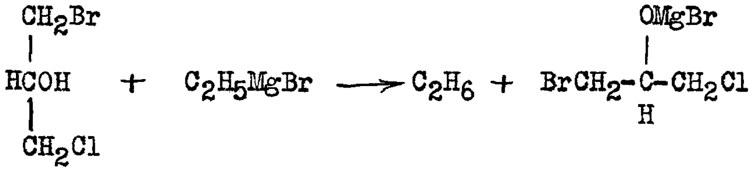
(VI)



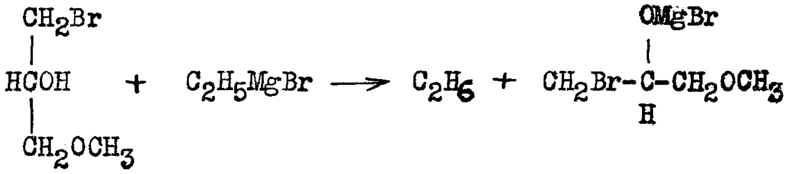
(VII)

These were analyzed and compared to the compounds that were obtained by the following reactions as described by Grignard (9):

$BrCH_2-CH_2OH + C_2H_5MgBr \longrightarrow C_2H_6 + BrCH_2CH_2OMgBr$



$$\underset{CH_2Cl}{\overset{CH_2Br}{HCOH}} + C_2H_5MgBr \longrightarrow C_2H_6 + BrCH_2-\underset{H}{\overset{OMgBr}{C}}-CH_2Cl$$

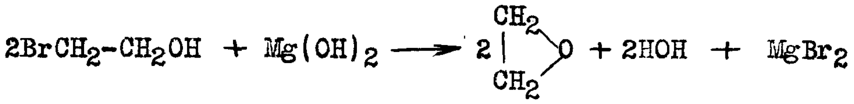


$$\underset{CH_2OCH_3}{\overset{CH_2Br}{HCOH}} + C_2H_5MgBr \longrightarrow C_2H_6 + CH_2Br-\underset{H}{\overset{OMgBr}{C}}-CH_2OCH_3$$

Much trouble was experienced in the analysis of the compounds due to the ease of hydrolysis and to the difficulty encountered in purifying them. Determination of the bromide ion of the precipitates showed that the compounds could not be considered as molecular addition products between the ethylene oxide and magnesium bromide as described by Grignard and Meisenheimer. If the compounds were molecular addition products they would have had all their bromine in the form of the bromide ion, whereas it was found to contain one half of the bromine in the ionic form.

The following equations show how an increase in bromide ion could be expected upon standing. This was true if the magnesium hydroxide did not react rapidly in the nitric acid used to neutralize it.

$$2BrCH_2\text{-}CH_2\text{-}OMgBr + 2HOH \longrightarrow 2BrCH_2CH_2OH + MgBr_2 + Mg(OH)_2$$



$$2BrCH_2\text{-}CH_2OH + Mg(OH)_2 \longrightarrow 2\,\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!\!>O + 2HOH + MgBr_2$$

It could be seen that one mole of magnesium bromide could react with two moles of the oxide to form the following compound:

$$BrCH_2\text{-}CH_2\text{-}O\text{-}Mg\text{-}O\text{-}CH_2\text{-}CH_2Br$$

The product obtained from the reaction of ethyl magnesium bromide with an equal molar quantity of ethylene bromohydrin was analyzed:

	Obtained	Theoretical
Bromide ion	28.0%	27.4%
Magnesium	8.2%	8.3%
Total Bromine	55.6%	55.0%

The theoretical calculations were based upon $BrCH_2\text{-}CH_2\text{-}O\text{-}MgBr$ .86 moles of diethyl ether. The molecular weight equals 292.

The analysis of the product obtained by the reaction of one mole of ethylene oxide with another of magnesium bromide was given as follows:

	Obtained	Theoretical
Bromide ion	27.8%	27.0%
Magnesium	7.8%	8.2%
Total bromine	54.9%	54.3%

The theoretical amount was based upon $BrCH_2-CH_2-O-MgBr$ .91 moles of diethyl ether. Molecular weight equals 295.

The above results proved the identity of the products obtained.

In the same article Ribas and Tapia tried to isolate the addition compound that had been described by Meisenheimer (10). They reacted ethyl magnesium bromide with ethylene oxide at a temperature of -20° C. The reaction mixture was allowed to stand for two hours at the above temperature. The product was filtered and carefully dried between filter papers. The analysis of the product resulted in the following:

Time in hours before titration	Percent Bromine Ion
immediately	14.9, 14.6
12	14.1, 17.0
24	16.8, 16.0
36	18.7, 20.0

In 1932 Ribas and Tapia (11) published another article in which they studied the nature of the precipitates when ethyl magnesium bromide was treated with variable quantities of ethylene oxide. They concluded that the precipitate was a mixture of these two compounds:

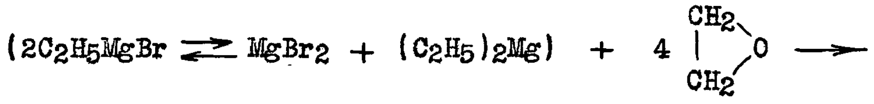
$$BrCH_2-CH_2-O-Mg-O-CH_2-CH_2Br$$

and

$$BrCH_2-CH_2-O-MgBr$$

A study was made of the ether solution from the reaction of one mole of ethyl magnesium bromide and one mole of magnesium bromide. This solution was reacted separately with ethylene oxide and benzophenone. Normal butyl alcohol and diphenyl ethyl carbinol were obtained respectively.

The principle reaction was formulated by them in the following equations:

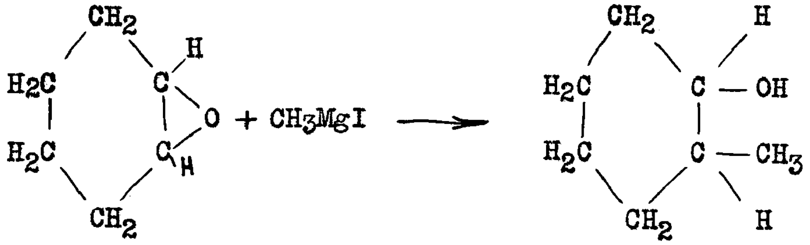


$$(2C_2H_5MgBr \rightleftharpoons MgBr_2 + (C_2H_5)_2Mg) + 4 \begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix} \!\!> O \longrightarrow$$

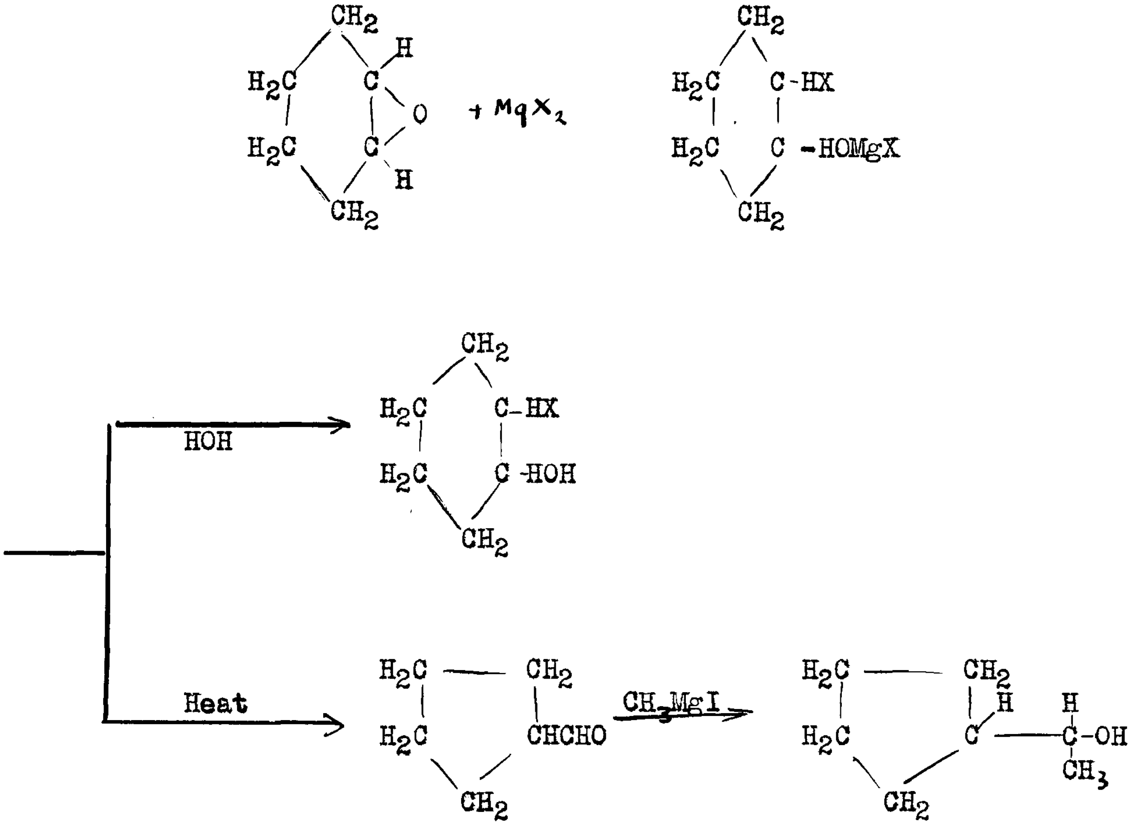
$$(BrCH_2-CH_2-O)_2Mg + (C_2H_5-CH_2-CH_2-O)_2Mg + 4\ HOH \longrightarrow$$

$$2Mg(OH)_2 + 2BrCH_2-CH_2-OH + 2C_2H_5CH_2CH_2OH$$

In 1928 Godchot and Cauquil (12) showed that the reaction of cyclohexene oxide and methyl magnesium bromide was an abnormal one. Formerly the reaction was thought to have gone as:



The product was thought to be cis-2-methylcyclohexanol until it was shown to be unlike the two isomeric 2-cyclo-hexanols prepared from the reduction of o-cresol. It was found that the supposed cis-2 methylcyclohexanol was in reality methyl cyclopentylcarbinol, which resulted from the following series of reactions:



The primary product of reaction between a Grignard reagent and cyclohexene oxide was the halohydrin derivative, which gave the smaller ring when heated. When cyclohexene oxide was heated with magnesium bromide the cyclopentane aldehyde was obtained (13).

Consequently when the dimethyl magnesium was reacted with the cyclohexene oxide the product was 2-methylcyclohexanol, the expected compound.

It has been observed in this laboratory that when tertiary butyl magnesium bromide reacts with ethylene oxide that the expected alcohol was not obtained. The main product of this reaction was ethylene bromohydrin. This had been observed by Whitmore (14) when he reacted tertiary butyl magnesium chloride with ethylene oxide and obtained ethylene chlorohydrin as the main product.

EXPERIMENTAL

I.

The following bromides were prepared from the corresponding alcohols (Eastman Technical) by the action of sulfuric acid and hydrobromic acid (15):

Ethyl bromide
N-Propyl bromide
iso-propyl bromide
N-butyl bromide
iso-butyl bromide
sec. butyl bromide
N-amyl bromide
iso-amyl bromide
1 bromo 2 methyl butane
2 bromo pentane
N-hexyl bromide
2 bromo hexane
2 bromo 4 methyl pentane
Tert. butyl bromide
Tert. Amyl bromide

2 bromo 3 methyl butane was prepared from the corresponding carbinol (16) by R. L. Guile.

Bromocyclohexane, phenyl bromide, ethylene chlorohydrin, and benzyl chloride were Eastman Technical. They were fractionated and dried over calcium chloride. The dioxane was Eastman Technical and this was fractionated and dried over sodium.

Ethylene oxide was obtained from Dow Chemical Company and was fractionated and dried by passing it over soda lime.

The ethylene dibromide was obtained from the action of bromine with ethene (17). It was fractionated and dried over calcium chloride.

Ethylene bromohydrin was prepared by the action of magnesium bromide with ethylene oxide in an anhydrous ether solution. It was purified by fractionation.

Magnesium turnings, prepared for Grignard reagents, were used after drying over calcium chloride.

The anhydrous ether was dried over sodium for one week before it was used in the reactions.

Grignard reagents prepared and studied were:

Ethyl magnesium bromide
Propyl magnesium bromide
Iso-propyl magnesium bromide
N-butyl magnesium bromide
Iso-butyl magnesium bromide
Sec. butyl magnesium bromide
Tert. butyl magnesium bromide.
N-amyl magnesium bromide
Iso amyl magnesium bromide
2 methyl 1 bromo-magnesium butane

2 bromo magnesium pentane

3 methyl 2 bromomagnesium butane

N-hexyl magnesium bromide

4 methyl 2 bromomagnesium pentane

2 bromo-magnesium hexane

Phenyl magnesium bromide

Bromo-magnesium cyclohexane

Dibromo-magnesium ethylene

II.

The Grignard reagents were prepared as follows:

In a dry[1] two liter three neck flask, fitted with a glycerine sealed stirrer, efficient reflux condenser and dropping funnel, were placed twenty-four grams (one mole) of magnesium turnings and a crystal of iodine. The flask was heated with a small flame until the iodine vaporized. It was then allowed to cool while one mole of the halide was weighed out. Two mls. of the halide was added to the reaction flask and the remainder was mixed with two hundred mls. of anhydrous ether. After the reaction mixture stood for a few minutes a few mls. of anhydrous ether were added and stirring was started. The reaction began almost immediately and after it had reacted for a few minutes, or if the reaction became too vigorous, fifty mls of anhydrous ether were placed in the flask. The remaining halide ether

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[1] The flask was dried in an oven for twenty-four hours and then rinsed twice with anhydrous ether. The reaction must be protected from carbon dioxide, water vapor and oxygen of the air.

solution was then placed in the dropping funnel. It was added at such a rate that gentle reflux took place. After all the halide ether solution had been added the mixture was stirred for two hours and allowed to stand overnight.

Each Grignard reagent was treated in three different ways. First, the Grignard reagent was reacted with one mole of ethylene oxide and then refluxed with benzene. Second, the Grignard was reacted with two moles of ethylene oxide with no heating. Third, the reagent was treated with dioxane (18) precipitating the halides. The ether soluble dialkyl magnesium compound was then reacted with two moles of ethylene oxide.

A typical run for each of the three reactions will be described.

III A. Reaction of one mole of a Grignard reagent with one mole of ethylene oxide with heating.

The Grignard reagent that has been previously prepared was cooled in an ice salt bath. One hundred mls. of anhydrous ether that had been cooled to zero degrees was placed in a dropping funnel fitted with a tight cork. One mole (44 grams) of ethylene oxide was measured out in a flask previously calibrated and cooled to zero degrees. It was poured immediately into the dropping funnel. The funnel was corked and the contents mixed. Addition of the ethylene oxide ether solution to the Grignard reagent was started cautiously. (If added to fast, a very vigorous reaction takes place.) The ice salt bath was removed as soon as all of the ethylene oxide had been added and the contents were allowed to come to room temperature with vigorous stirring. The reflux condenser was now set for distillation.[1] A water bath kept at fifty degrees[2] was used for the removal of about two hundred and fifty mls. of ether, until the contentns become pasty. Now the condenser was set for reflux and two hundred and fifty mls. of anhydrous benzene were added. The water bath was heated until the benzene solution refluxed gently. Heating was continued with stirring for six hours and the mixture allowed to stand overnight. It was hydrolyzed with one hundred mls. of water. The magnesium hydroxide precipitated as a thick paste and the benzene solution was decanted. The paste of magnesium hydroxide and water was extracted three times with small portions of ether. It was then neutralized with dilute hydrochloric acid and ice. This solution was extracted three times with small amounts of ether. The ether extracts were combined, dried over anhydrous sodium sulfate and fractionally distilled.

III B. Reaction of two moles of ethylene oxide with one mole of Grignard reagent.

The Grignard reagent that was prepared as in II was

[1] All precautions for ether distillation are used.

[2] If the temperature of the contents is raised above fifty degrees a very vigorous reaction takes place with decomposition.

cooled in an ice salt bath. One hundred and fifty mls. of anhydrous ether cooled to zero degrees was poured in the dropping funnel. The funnel was corked and the liquids mixed. Addition of the ethylene oxide solution to the Grignard was quite slow due to the vigorous reaction. The ice salt bath was removed as soon as all of the ethylene oxide was added and the contents were allowed to come to room temperature with stirring. After standing overnight the material was hydrolyzed as described in (A). The combined ether extracts were dried over anhydrous sodium sulfate and fractionated. The alcohols may be freed of any ethylene bromohydrin by extraction them twice with water. This was avoided if possible due to the large loss of alcohol. However, where the boiling point of the alcohol and the ethylene bromohydrin were close together it was essential.

III C. Reaction of two moles of ethylene oxide with one mole of dialkyl magnesium.

Dioxane was added through a dropping funnel to the stirred Grignard reagent at such a rate that gentle reflux took place (18). The addition of dioxane was continued until no more halides were precipitated. This could easily be seen by stopping the stirrer and letting the white precipitate settle. To the clear ether solution one drop of dioxane was added. If a white precipitate was formed it was necessary to add more dioxane.[1]

[1] The yield of the dialkyl magnesium compound was diminished to a large extent if a great excess of dioxane is added.

The mixture was then quickly and carefully poured into dry centrifuge tubes and corked. The white precipitate of the halide was thrown down so that the clear ether solution of the dialkyl magnesium compound could be decanted into a flask fitted as previously described for a Grignard reaction. The total volume of the ether solution was measured. A two ml. aliquoit was removed and hydrolyzed with ten mls. of water. The magnesium hydroxide was titrated with standard .1 N HCl solution using phenolpthalein as an indicator. The best results were obtained if a measured excess of the standard .1 N acid was added and then back titrated with standard .1 N NaOH. From the data obtained one can quickly compute the yield of the dialkyl magnesium compound. It was now possible to add the theoretical amount of ethylene oxide (two moles), which is weighed and added as previously described in III B. The solution was stirred for three hours and allowed to stand overnight. It was then hydrolyzed with enough water so that the magnesium hydroxide becomes a thick paste. The ether solution was decanted and the paste of magnesium hydroxide was extracted three times with small portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate and fractionated.

The following alcohols were prepared by the three methods described:

normal butyl alcohol
normal amyl alcohol
iso amyl alcohol
3,3 dimethyl butanol 1

3 methyl pentanol 1
iso hexyl alcohol
normal hexyl alcohol
normal heptyl alcohol
3 methyl hexanol 1
iso heptyl alcohol
4 methyl hexanol 1
normal octyl alcohol
3,4 dimethyl pentanol 1
3 methyl heptanol 1
benzyl carbinol
2 cyclohexyl ethanol 1
3 phenyl propanol 1

IV. Preparation, analysis and identification of the intermediate compound that was formed in the reaction of ethylene oxide with Grignard reagents

A. Reaction of one mole of ethylene oxide with one mole of ethyl magnesium bromide.

The preparation of the Grignard reagent and the addition of the ethylene oxide was accomplished as previously described in III A. The mixture was stirred for two hours at room temperature and was allowed to stand for one hour. The white precipitate settled out and the ether solution was quickly decanted. The precipitate was washed four times with one hundred ml. portions of anhydrous ether. The washed solid was quickly transferred to a weighing bottle which was immediately placed in a vacuum desiccator.[1] The desiccator was first evacuated with a water pump for three hours and then with an oil vacuum pump at two mm. pressure for twelve hours. All of the ether was removed. The following analysis were made:

Total bromine by Parr bomb (19).

In a Parr bomb fusion cup were placed fourteen grams (14 g.) of sodium peroxide, seventy-five hundreths grams (.75 g) of powdered potassium nitrate, four-tenths grams (.4 g) of finely powder cane sugar, and two-tenths grams (.2g) of the sample. The Parr bomb was assembled and the contents were carefully mixed by shaking. The sample was ignited by heating two to three minutes with a bunsen burner. The bomb was allowed to cool, opened and the fusion cup placed in a six hundred ml. beaker. The top was thoroughly rinsed off in the beaker with distilled water. A cover glass was then placed on the beaker and two hundred mls. of water were added. As soon as all of the material had dissolved from the fusion cup it was removed and rinsed with distilled water. The solution was boiled until all of the hydrogen peroxide was expelled and all the sodium peroxide decomposed. A measured excess of standard .1 N silver nitrate was added to the hot solution which is then heated for fifteen minutes to insure complete precipitation of the silver bromide. The solution was cooled and carefully acidified with

[1] The white solid hydrolyzed immediately if exposed to the moisture of the air.

concentrated nitric acid. Hydrazine sulfate was added until all reaction ceases and no more nitrogen is given off. The solution was cooled and the bromine determined by the Volhard method for bromine (21).

Total magnesium was determined by decomposing a weighed sample with a Meeker burner. The results compared with the method of converting the magnesium to magnesium sulfate , dried and weighed as such (3). The former method was much faster; ignition capsules were ignited to a constant weight. A weighed sample was placed in each and carefully ignited with a small flame (care must be taken not to heat so fast that the sample catches fire). The temperature was gradually raised until the full heat of the Meeker burner was used. The sample was ignited at this temperature for one hour. They were then allowed to cool to almost room temperature and placed in a desiccator for fifteen minutes. The crucible was weighed and ignited for ten minutes at the highest Meeker burner temperature. It was again allowed to cool as above and weighed. This process was repeated until the crucible attained constant weight. Generally, two ignitions were all that were necessary. From the data it is possible to calculate the percent magnesium in the sample. By this formula the amount of magnesium was obtained:

$$\frac{\text{wt. MgO} \times .6032 \times 100}{\text{wt. of sample}} = \%\ \text{magnesium.}$$

Total carbon and hydrogen was determined by Pregel micro method (20). A low percent of carbon was found due to the formation of magnesium carbonate in burning the sample since it was impossible to heat the combustion tube hot enough to decompose the carbonate that was formed as the sample was burned. The sample was removed from the tube and the carbon dioxide content determined by loss of weigh upon ignition. The total weight of carbon dioxide was obtained from this loss and the increase in weight of the ascarite tube. The percent carbon was calculated from this equation:

$$\frac{\text{Total wt. of carbon dioxide} \times .2727 \times 100}{\text{wt. of sample}} = \%\ C$$

Bromide ion was determined by dissolving a weighed sample (.2 to .4 grams) in thirty ml. of 1:5 nitric acid. The bromine ion liberated was determined by Volhard method (21).

Hydrolysis of the precipitate yielded ethylene bromohydrin.

Analysis

	Found	Theory
C	16.80%	17.62%
H	3.14%	2.94%
Total bromine	56.40%	58.75%
Mg	8.83%	8.93%
Bromide ion	27.30%	29.42%

The theoretical values are based on the formula $(Br-CH_2CH_2-O)_2Mg$.

B. Reaction of one mole of ethyl magnesium bromide with one mole of ethylene bromohydrin.

One mole (125g) of ethylene bromhydrin was added drop by drop to the stirred Grignard reagent that was prepared as previously described. The reaction mixture was stirred for three hours and allowed to stand overnight. The clear ether solution was decanted from the white precipitate which was then washed four times with one hundred ml. portions of anhydrous ether. The precipitate was placed in a weighing bottle and the ether removed by means of a vacuum desiccator as described in IV A.

Analysis

	Found	Theory
Total bromine	64.20%	70.10%
Bromide ion	34.0%	35.0%
Mg	11.72%	10.65%

The theoretical is based upon the formula:

$Br-CH_2CH_2-O-MgBr$

C. Reaction of one mole of normal amyl magnesium bromide with one mole of ethylene oxide.

The procedure was the same as IV A. The white precipitate was analyzed and found:

	Found	Theory
C	17.37%	17.62%
H	3.21%	2.94%
Total bromine	56.23%	58.75%
Mg	9.12%	8.93%
Bromide ion	27.90%	29.37%

The theoretical is based upon the formula:

$(Br-CH_2CH_2-O)_2Mg$

D. Reaction of one mole of magnesium bromide with one mole of ethylene oxide.

One mole of magnesium (24g) and five hundred mls. of anhydrous ether were placed in a three liter three neck round bottom flask fitted with reflux condenser, glycerine sealed stirrer, and dropping funnel. One mole (160 g) of bromine was allowed to drop in the ether magnesium mixture at such a rate that gentle refluxing takes place. After the addition of one half of the bromine, two hundred and fifty mls. of anhydrous ether were poured through the reflux condenser. The reaction was stirred for two hours after all of the bromine had been added. One mole (44g) of ethylene oxide was added to this ether solution cooled to zero degrees, as in IV A. It was stirred an additional two hours and allowed to stand overnight. The ether solution was then decanted from the precipitate which was washed four times with small portions of anhydrous ether. The precipitate was now dried and analyzed as in IV A. The combined ether was solutions and main ether solution were combined and the total bromine contained in them as bromide ion was determined by Volhard method (21).

Analysis

	Found	Theory
Total bromine	56.73%	58.75%
Mg	8.61%	8.93%
Bromide ion	26.84%	29.37%
Total bromine in ether solns.	41.24%	50.00%

Theoretical based on the formula $(BrCH_2CH_2\text{-}O)_2Mg$

E. Reaction of one mole of magnesium bromide with two moles of ethylene oxide.

One mole of magnesium bromide was prepared and two moles (88 g) of ethylene oxide were added to it as in III A. The mixture was stirred for two hours and then refluxed for one hour. It was allowed to stand overnight. The ether solution was decanted from the white precipitate which was washed four times with small portions of anhydrous ether. The precipitate was dried and analyzed as in IV A.

Analysis

	Found	Theory
Total bromine	56.01%	58.75%
Mg	8.68%	8.93%
Bromide ion	28.46%	29.37%
Total bromine in ether solns.	6.92%	00.00%

F. Reaction of one mole of tertiary butyl magnesium bromide with one mole of ethylene oxide.

The white intermediate compound was prepared from one mole of tertiary butyl magnesium bromide to which one mole of ethylene oxide was added as in III A. The ether solution was refluxed for two hours and then decanted from the white precipitate which was washed, dried, and analyzed as in part III A.

Analysis

	Found	Theory
C	17.01%	17.62%
H	2.81%	2.94%
Mg	9.21%	8.93%

Total bromine	55.34%	58.85%
Bromide ion	29.52%	29.41%

The theoretical values are calculated from the formula:

$(Br-CH_2CH_2-O)_2Mg$

G. <u>Reaction of one mole of ethyl magnesium bromide with one mole of ethylene chlorohydrin</u>.

One mole (80.5 g) of ethylene chlorohydrin was added to one mole of ethyl magnesium bromide at such a rate that gentle reflux took place. The mixture was refluxed for two hours after the addition of the ethylene chlorohydrin was completed. The precipitate was washed, dried and analyzed as in IV D. The percent bromide ion that was liberated upon placing a weighed sample in 1:5 nitric acid was determined by Volhard Method (21).

In order to determine the percent bromine and the percent chlorine in the precipitated silver halide from the hydrolysis of the sample in 1:5 nitric acid the following procedure was used. Five grams of the sample were placed in thirty mls. of 1:5 nitric acid. The silver halide was precipitated by the addition of an excess of .1 N silver nitrate. It was filtered, washed with distilled water, acetone, anhydrous ether, and then dried for two hours at one hundred and fifty degrees. A weighed sample was placed in a chlorinating tube and cautiously heated as chlorine gas was passed over it (22). For the first half hour the precipitate was not heated enough to melt it. After, the temperature was raised so that the precipitate melted. The chlorine was replaced with air and the sample allowed to cool. It was placed in a desiccator for fifteen minutes and then weighed. This procedure was continued until the sample attained constant weight. Percent bromine and chlorine contained in the halide was calculated from the following formula:

$$Y = 4.224\ (P-Q)$$

$$X = P-Y$$

P -- wt. of silver chloride and silver bromide
Q -- wt. of silver chloride after conversion.
X -- wt. of silver chloride in original sample
Y -- wt. of silver bromide in original sample.

Total chlorine and total bromine in the sample were found by decomposing a weighed sample by Parr bomb. The halides were precipitated with an excess of silver nitrate and analyzed as described for the determination of bromine and chlorine in the presence of the other.

Analysis

	Found	Theory
Total bromine	40.21%	43.53%
Total chlorine	18.91%	19.29%
Mg	15.84%	13.23%
% bromine in halide from hydrolysis of sample	98.7%	100.00%

The theoretical values are based on the formula $Cl-CH_2CH_2-O-MgBr$

V. <u>Reaction of one mole of magnesium bromide with one mole of ethylene oxide. The precipitated product of this reaction reacted with one mole of ethyl magnesium bromide.</u>

The product of the reaction of one mole of magnesium bromide with one mole of ethylene oxide was prepared as in part IV D. The white precipitate was washed three times with fifty ml. portions of anhydrous ether and suspended in a two hundred ml. portion of anhydrous ether by stirring. One mole of an ether solution of ethyl magnesium bromide was added at once and stirred for one hour. Three hundred mls. of ether were removed by water bath and replaced with benzene. After refluxing for six hours and standing overnight the mixture was hydrolyzed, extracted, dried, and fractionated as in III A. Fifty-four grams (54 g), a seventy-three percent yield, of normal butyl alcohol was obtained.

VI. Reaction of one mole of ethylene oxide with one mole of propyl magnesium bromide.

(A) The precipitated product of this reaction is placed with the ether solution from the reaction of one mole of ethyle oxide with one mole of normal amyl magnesium bromide.

(B) Also, the ether solution of (A) is reacted with the precipitated product of (B).

Normal propyl magnesium bromide was treated with one mole of ethylene oxide and the precipitate was filtered[1] and washed three times with anhydrous ether. The ether solution was placed in a flask with the precipitate from the reaction of normal amyl magnesium bromide with one mole of ethylene oxide.

[1] Special flasks for these reaction were prepared from two liter three neck round bottom flasks. A stopcock was sealed into the bottom of the flasks in such a manner that glass wool filters were placed in the opening. By use of these flasks it is possible to remove the ether solution from the precipitate without exposing the precipitate or ether solution to the moisture, oxygen, and carbon dioxide of the air.

After removal of ether and replacing with benzene and refluxing for six hours, hydrolysis gave 61% yield of normal amyl alcohol.

Similar ether solution from normal amyl magnesium bromide and one mole of ethylene oxide was added to the precipitate formed from normal propyl magnesium bromide and one mole of ethylene oxide. After removal of ether and refluxing with benzene, hydrolysis gave 46% yield of normal heptyl alcohol.

VII. Hydrolysis of the reaction mixture from the one mole of magnesium bromide with two moles of ethylene oxide.

One mole of magnesium bromide was reacted with two moles (88 g) of ethylene oxide as in section IV D. The reaction mixture was stirred for six hours after the addition of the ethylene oxide and then gently refluxed for one hour and allowed to stand overnight. The reaction mixture was hydrolyzed with fifty mls. of water and the ether solution decanted from magnesium hydroxide solid. The magnesium hydroxide was extracted three times with fifty ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate and fractionally distilled. A 61% yield of ethylene bromohydrin based on two moles of ethylene oxide was obtained.

VIII Reaction of one mole of tertiary butyl magnesium bromide with two moles of ethylene oxide.

The Grignard reagent was prepared and reacted with two moles of ethylene oxide as in IV A. The mixture was allowed to stand overnight and the ether solution was decanted from the white precipitate into a one liter erlenmeyer flask which was stoppered tightly. The flask was allowed to stand for three months in the open. The contents of the flask were then hydrolyzed with fifty mls. of water. The ether water solutions were separated by means of a separatory funnel. The water solution was extracted three times with small portions of ether and the combined ether extracts were dried over anhydrous sodium sulfate for one week. The ether solution was fractionated. Two main fractions were collected:

98° - 104° ---------- 8 grams white solid[1]

140° - 143° --------- 13 grams colorless liquid.

A 3,5 dinitrobenzoate for each fraction was attempted. The solid did not form a benzoate. The liquid formed a 3,5 dinitrobenzoate with a M. P. of 83°.

The alcohol was analyzed for carbon and hydrogen by Richard Jackson (19). The 3,5 dinitrobenzoate was analyzed for nitrogen by Pregel micro method (31).

Analysis

	Found	Theory
C	69.01%	70.59%
H	13.80%	13.72%
Calculated for formula $C_6H_{14}O$		
N	9.54%	9.46%
Calculated for formula $C_{13}H_{16}O_6N_2$		

---

[1] Probably the hydrate of the alcohol 3,3 dimethyl butanol-1

IX Preparation of 3,5 dinitrobenzoates of the alcohols (23)

One half gram of 3,5 dinitrobenzoyl chloride was placed in a test tube with one ml. of the alcohol and the mixture was boiled gently for five minutes. The mixture was cooled and the ester was extracted with a solution made up of one part diethyl ether and five parts of petroleum ether. In this solution the 3,5 dinitrobenzoic acid and 3,5 dinitrobenzoyl chloride were insoluble. The solvent was evaporated and the ester was recrystallized from five to ten mls of ethyl alcohol water mixture of such strength that the ester dissolved in the warm solution but crystallized out upon cooling.

X Preparation of the phenyl and alpha-napthyl urathanes of some of the alcohols (24)

One gram of the anhydrous alcohol was placed in a test tube and five-tenths ml. of phenyl isocyanate or alpha-napthyl isocyanate[1] was added. If a spontaneous reaction did not take place the mixture was warmed on the steam bath for one hour[2]. It was then cooled and dissolved in five mls. of petroleum ether or carbon tetrachloride. The hot solution was filtered and cooled in an ice bath. If the crystals didn't form upon cooling the sides of the beaker may be scratched with a glass rod which promotes crystal formation. The crystals were collected and dried by suction filtration. They were again recrystallized from petroleium ether or carbon tetrachloride, filtered, dried

[1] the isocyanates are powerful lachrymators.

[2] make certain no moisture can enter.

on a porous plate and the melting point determined.

XI Proof of structure for 3,4 dimethyl pentanol-1.

Fifteen grams (15g) of the alcohol 3,4 dimethyl pentanol-1 was mixed with a hundred mls. of water and three grams of sodium carbonate in a three liter three necked flask. A potassium permanganate solution made up of forty grams of potassium permanganate and a liter and a half of water was added with stirring to the flask. The mixture was cooled to four degrees with an ice salt bath and then allowed to come to room temperature. After the mixture had been stirred for twelve hours the manganese dioxide was removed by suction filtering. The solution was evaporated to one hundred mls. on the steam bath. It was cooled, covered with a layer of ether and acidified with dilute sulfuric acid. The acid solution was extracted three times with ether and the combined ether extracts dried over anhydrous sodium sulfate. Upon fractionation three grams of an acid boiling at 210° was made by refluxing one gram of the acid in a small flask with the theoretical amount of thionyl chloride. The mixture was heated gently under a reflux condenser for thirty minutes using a water bath. The cooled residue was treated with approximately two moles of the aniline dissolved in about thirty mls. of benzene, the mixture was refluxed for thirty minutes. Finally, the benzene solution was transferred to a small separatory funnel and washed with two mls. of water, five mls. of dilute hydrochloric acid, five mls. of dilute sodium hydroxide, again with two mls of water, and evaporated to dryness. The anilide was recrystallized from very dilute alcohol. Melting point of the anilide of the acid was 67°.

The corresponding acid was prepared by means of the malonic ester synthesis (27). Two hundred mls. of absolute alcohol were placed in a five hundred ml. three neck round bottomed flask and eleven grams of metallic sodium cut in small pieces were added. Considerable heat was evolved and the flask was placed in cold water. The reaction was completed by refluxing on a water bath for thirty minutes. Through a dropping funnel one half mole (80 g) of malonic ester was added with efficient stirring. The reaction mixture was stirred for one hour and then three fifths of a mole (80.6 g) of 2 bromo 3 methyl butane was added. The solution was heated by means of a water bath (70°-80°). From time to time the solution was tested with litmus and when it became neutral the reaction was considered complete. The alcohol was removed under reduced pressure, the salts dissolved with water, and it was then extracted with three fifty ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate and fractionally distilled. The fraction boiling at 235°-245°, seventeen grams, was collected and saponified with fifty percent potassium hydroxide. The alkaline solution was extracted once with ether and then acidified with dilute sulfuric acid. The acid solution was extracted three times with ten ml. portions of ether. The combined ether extracts were placed in a fractionating column and the ether removed. Carbon dioxide was given off quite rapidly as the temperature was raised to 150°-170°. The decarboxylated acid was fractionated and the fraction boiling at 210°-214° (three grams) was collected. The anilide was made as before (26). Melting point of the anilide 67°. A mixed melting point with the anilide obtained from the oxidation of the alcohol showed no depression.

The amide of 3,4 dimethyl pentanoic acid was prepared by the following procedure (28). One gram of the acid was heated under a reflux condenser with five ml. of thionyl chloride for fifteen to thirty minutes. The reaction mixture was poured into fifteen mls. of concentrated ammonia (caution). The precipitated amide was filtered and purified by recrystallization from alcohol or water. Melting point of the amide 95.5°.

The acid was analyzed for carbon and hydrogen (macro method) by Richard Jackson (29).

Analysis

	Found	Theory
Carbon	64.69%	64.61%
Hydrogen	10.80%	10.76%

XII Proof of structure for 3,3 dimethyl butanol-1

Five grams of 3,3 dimethyl butanol-1 were oxidized as in XI, corresponding molar quantities being used. One gram of an acid boiling 177°-184° at 740 mm pressure was obtained. The amide of this acid was prepared by refluxing one gram of the acid with five ml. of thionyl chloride for thirty minutes. The reaction mixture was cooled and poured into fifteen mls. of concentrated ammonium hydroxide. The precipitated amide was filtered and recrystallized from a water alcohol mixture. Melting point of the amide 131°.

Tertiary butyl acetic acid was prepared by the following method (30). Ninety grams of diisobutylene (b.p. about 100° degrees) were combined with a solution of two hundred and seventy grams (270 g) of crude sodium dichromate in three hundred mls (300) of water. To this was added over a two day period a mixture of two hundred sixteen mls. (216) of concentrated sulfuric acid in two hundred and sixty mls. of water. The mixture was stirred and additional eight days, making ten days in all. Finally, the mixture was fractionated and a yield of twenty grams (20 g) of 2,2 dimethyl pentanone-4 was obtained boiling at 122°-126°.

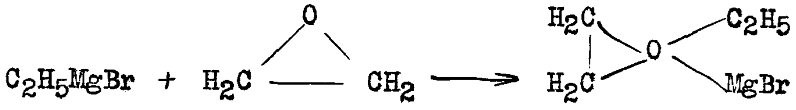
One hundred grams (100 g) of finely crushed ice and a solution of fity-two grams (52 g.) of sodium hydroxide in two hundred mls. of ice cold water were placed in a three neck flask fitted with a glycerine seal stirrer, a dropping funnel, and a thermometer. The flask was surrounded with an ice salt bath. Twenty-four mls of bromine was then added through the dropping funnel over a period of one hour. The sodium hydroxide solution was constantly stirred. After all the bromine had been added seventeen grams (17g) of 2,2 dimethyl pentanone-4 were added in ten minutes through the dropping funnel. The mixture was allowed to come to room temperature with stirring and it was allowed to stand overnight. The thermometer was replaced with a condenser arranged for distillation. The cooling bath was removed and the flask heated with a bunsen burner flame. Stirring was continued throughout the distillation which was stopped when no more oil came over. After the residue in the flask had cooled it was acidified with sixty mls. (60 mls.) of concentrated sulfuric acid. The mixture was then steam distilled until no more oil came over. The oily layer was separated from the water layer, dried and then fractionated. The fraction boiling between 178°-148° at 740 mm was collected. It weighed ten grams (10 g)

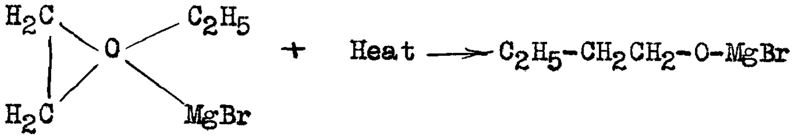
The amide was made as in XII. Melting point 131.5° corresponds to that prepared by Whitmore (14).

A mixed melting point of the amides of the acids prepared was taken and there was no depression.

THEORETICAL

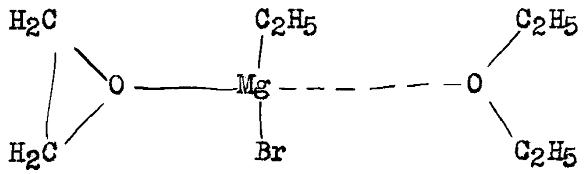
Until very recently the mechanism of the reaction of ethylene oxide with a Grignard reagent was thought to have been through the formation and splitting of an oxonium salt by heat (2):





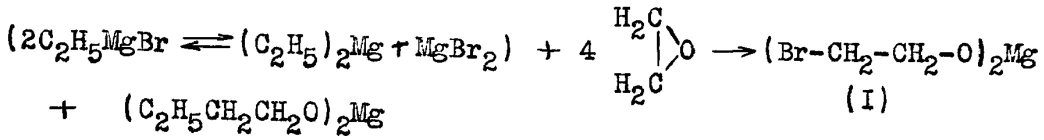
$$C_2H_5-CH_2CH_2-O-MgBr + HOH \rightarrow C_2H_5-CH_2CH_2CH_2OH + MgBrOH$$

The mechanixm was given analytical support by Messenheimer (6). He assigned the following formula to the molecular addition compound:



This idea remained unchanged until Ribas and Tapia (3), (7), (8), (11) published their series of articles. According to them the main portion of the reaction goes as follows:

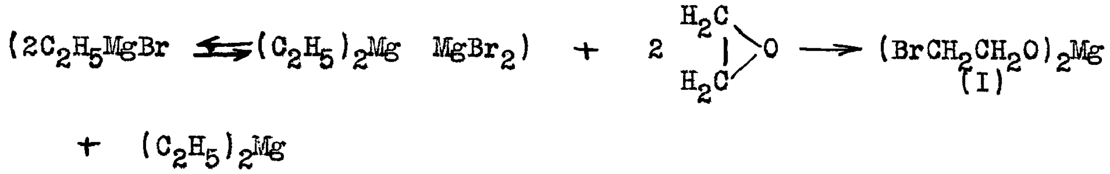
Reaction of two moles of ethylene oxide with ~~one mole of ethyl~~ magnesium bromide.



$$(2C_2H_5MgBr \rightleftharpoons (C_2H_5)_2Mg + MgBr_2) + 4\ \begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!\!>O \rightarrow \underset{(I)}{(Br{-}CH_2{-}CH_2{-}O)_2Mg} + (C_2H_5CH_2CH_2O)_2Mg$$

$$(Br{-}CH_2{-}CH_2{-}O)_2Mg + (C_2H_5CH_2CH_2O)_2Mg + 4\ HOH \rightarrow 2Br{-}CH_2CH_2OH + 2\ C_2H_5CH_2CH_2OH + 2\ Mg(OH)_2$$

Reaction of one mole of ethylene oxide with one mole of ethyl magnesium bromide.



$$(2C_2H_5MgBr \rightleftharpoons (C_2H_5)_2Mg\ \ MgBr_2) + 2\ \begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!\!>O \rightarrow \underset{(I)}{(BrCH_2CH_2O)_2Mg} + (C_2H_5)_2Mg$$

$$(BrCH_2CH_2O)_2Mg + (C_2H_5)_2Mg + \text{Heat} \rightarrow (C_2H_5CH_2CH_2{-}O)_2Mg + MgBr_2$$

$$(C_2H_5CH_2CH_2O)_2Mg + MgBr_2 + 2\ HOH \rightarrow 2\ C_2H_5CH_2CH_2OH + MgBr_2 + Mg(OH)_2$$

(I) was said to be a mixture of $BrCH_2CH_2{-}O{-}MgBr$ and $(BrCH_2CH_2{-}O{-})_2Mg$, although all of their analytical data confirms the formula $BrCH_2CH_2{-}O{-}MgBr$ with fractional parts of ether absorbed.

The following series of reactions are the result of work accomplished in this laboratory. Where R is used it refers to any alkyl or aryl grouping other than a tertiary alkyl[1] or benzyl group

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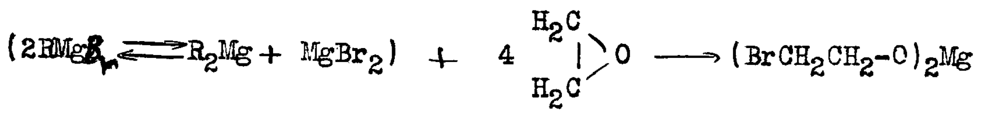
[1] Tertiary butyl group did react under certain conditions as seen in the experimental part to give the expected alcohol.

Two moles of ethylene oxide with one mole of Grignard.



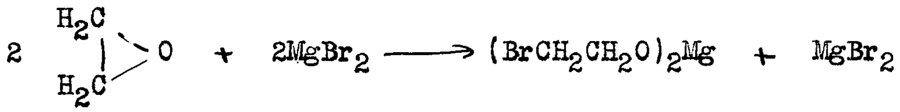
$$(2RMgBr \rightleftharpoons R_2Mg + MgBr_2) + 4\ \begin{array}{c} H_2C \\ | \\ H_2C \end{array}\!\!>O \longrightarrow (BrCH_2CH_2-O)_2Mg$$

$$+ (RCH_2CH_2-O)_2Mg$$

$$(BrCH_2CH_2-O)_2Mg + (RCH_2CH_2-O)_2Mg + 4\ HOH \longrightarrow 2BrCH_2CH_2OH$$

$$+ 2RCH_2CH_2OH + 2\ Mg(OH)_2$$

One mole of ethylene oxide with one mole of magnesium bromide

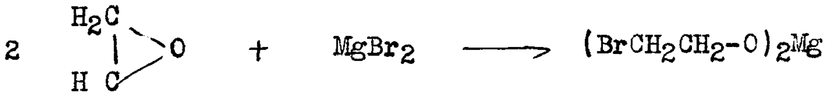


$$2\ \begin{array}{c} H_2C \\ | \\ H_2C \end{array}\!\!>O + 2MgBr_2 \longrightarrow (BrCH_2CH_2O)_2Mg + MgBr_2$$

$$(BrCH_2CH_2O)_2Mg + MgBr_2 + 2\ HOH \longrightarrow 2\ BrCH_2CH_2OH + MgBr_2$$

$$+ Mg(OH)_2$$

Two moles of ethylene oxide with one mole of magnesium bromide.



$$2\ \begin{array}{c} H_2C \\ | \\ H\ C \end{array}\!\!>O + MgBr_2 \longrightarrow (BrCH_2CH_2-O)_2Mg$$

$$(BrCH_2CH_2-O)_2Mg + 2\ HOH \longrightarrow 2BrCH_2CH_2OH + Mg(OH)_2$$

One mole of ethylene bromohydrin with one mole of Grignard

$RMgBr + BrCH_2CH_2OH \longrightarrow RH + BrCH_2CH_2OMgBr$

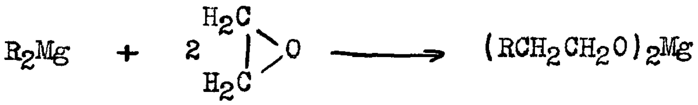
$BrCH_2CH_2OMgBr + 1\ HOH \longrightarrow Br{-}CH_2CH_2{-}OH + MgBrOH + RH$

One mole of ethylene chlorohydrin with one mole of Grignard.

$RMgBr + ClCH_2CH_2OH \longrightarrow RH + ClCH_2CH_2OMgBr$

$ClCH_2CH_2OMgBr + 1\ HOH \longrightarrow ClCH_2CH_2OH + MgBrOH + RH$

Two moles of ethylene oxide with one mole of dialkyl magnesium

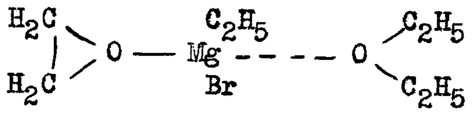


$$R_2Mg + 2\ \begin{matrix} H_2C \\ | \\ H_2C \end{matrix}\!\!>O \longrightarrow (RCH_2CH_2O)_2Mg$$

$(RCH_2CH_2O)_2Mg + 2\ HOH \longrightarrow 2\ RCH_2CH_2OH + Mg(OH)_2$

DISCUSSION

The intermediate compound that is formed in the reaction of a Grignard reagent with one mole of ethylene oxide is $(BrCH_2CH_2O)_2Mg$ and not the oxonium salt,

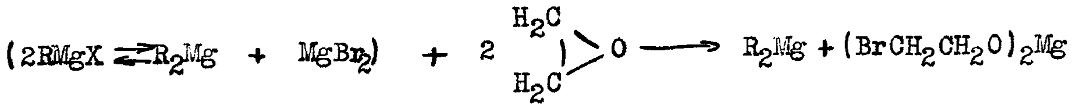


described by Grignard and Meisenheimer (2), (6), This intermediate compound was prepared by two methods. First, by the reaction of one mole of magnesium bromide with one or two moles of ethylene oxide. Second, by the reaction of one mole of various Grignard reagents with one mole of ethylene oxide. Analysis agree with the molecular formula $C_4H_8O_2Br_2Mg$. When two moles of ethylene oxide react with one mole of magnesium bromide the resulting yield of ethylenebromohydrin is sixty percent based on the two moles of ethylene oxide used. Whereas, if the oxonium compound or $BrCH_2CH_2$-OMgBr were formed, fifty percent would be the maximum yield possible. Furthermore when the Grignard reagents are crossed as in the experimental part VI the products could not have been formed from the oxonium salt. If the intermediate compound were the oxonium salt the resulting alcohols in each instance would have been the opposite. This also proves that the dialkyl magnesium compound must have been contained in the ether solution that was crossed with the precipitates. This is in agreement with the equations that are proposed by us in the theoretical part.

Ribas and Tapia (3)submit the following experimental evidence as a basis for their proof that the oxonium salt is not formed. When the intermediate compound is hydrolyzed in 1:5 nitric acid approximately one half of the total bromine is given up in the form of the bromide ion. The oxonium salt, according to the formula assigned to it, would have all of the bromine given up. They therefore claimed that the intermediate compound was $BrCH_2CH_2-O-MgBr$. It can be seen that this compound would yield one half of the total bromine as the bromide ion on hydrolysis with 1:5 nitric acid. The intermediate compound when hydrolyzed in 1:5 nitric acid gives 27% - 30% bromide ion. If the compound is $BrCH_2CH_2-O-MgBr$, one half of the total bromine should be freed as bromide ion. Theoretically this should be 35%. This value has never been attained in any of the experimental results. The percent bromide ion that is obtained, 27% - 30%, is in agreement for the theoretical of $(BrCH_2CH_2-O)_2Mg$ if one half of the total bromine is freed upon hydrolysis (29.3%). We therefore conclude, with the supportof the analytical data, that one molecule of ethylene oxide is attached differently, so that one half of the bromine is liberated as the bromide ion upon hydrolysis.

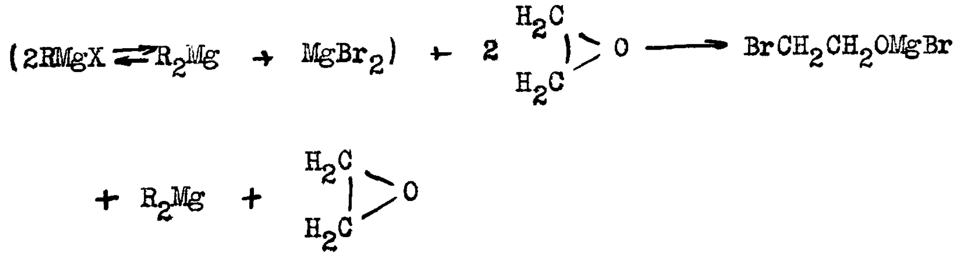
In a later paper Ribas and Tapia (11) stated that they believe that the intermediate compound was a mixture of $BrCH_2CH_2\text{-}O\text{-}MgBr$ and $(BrCH_2CH_2\text{-}O)_2Mg$. However, all of their analytical data was in support of the $BrCH_2CH_2O\text{-}MgBr$

It is a known fact that the reaction of one mole of a bromo Grignard with one mole of ethylene oxide will yield only ethylene bromohydrin unless heat treated or allowed to stand for a long period, (1), (2). It has been shown in this paper that ethylene oxide will react in the cold, without standing, with the dialkyl magnesium compounds. Also, the reaction of two moles of ethylene oxide with one mole of a Grignard reagent yields the expected alcohol without heating. If the intermediate compound is a mixture of the two compounds, $BrCH_2CH_2\text{-}O\text{-}MgBr$ and $(BrCH_2CH_2\text{-}O)_2Mg$ then the following reactions would take place when one mole of ethylene oxide reacts with one mole of a Grignard reagent:



$$(2RMgX \rightleftharpoons R_2Mg + MgBr_2) + 2\begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!\!>O \longrightarrow R_2Mg + (BrCH_2CH_2O)_2Mg$$

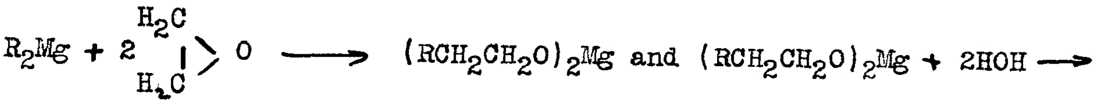
and



$$(2RMgX \rightleftharpoons R_2Mg + MgBr_2) + 2\begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!\!>O \longrightarrow BrCH_2CH_2OMgBr$$

$$+ R_2Mg + \begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!\!>O$$

The dialkyl magnesium compound and the ethylene oxide that are found as products in the second series of reactions would react as follows:



$$R_2Mg + 2\begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!>O \longrightarrow (RCH_2CH_2O)_2Mg \text{ and } (RCH_2CH_2O)_2Mg + 2HOH \longrightarrow$$

$$RCH_2CH_2OH + Mg(OH)_2$$

Therefore one would find measurable amounts of the alcohol. Absence of the alcohol makes it seem very improbable that there could be a very large percent of the single compound present. If the bromine ion produced by hydrolysis (27% - 30%) is due to the single compound then the mixture, as proposed by Ribas and Tapia, would be about eighty percent $BrCH_2CH_2OMgBr$. The unused ethylene oxide would react with the dialkyl magnesium compound to produce the alcohol, contrary to results.

The reaction of benzyl magnesium chloride with ethylene oxide is very interesting. When one mole of benzyl magnesium chloride reacts with one mole of ethylene oxide the alcohol is obtained without heating or standing. The amount of ethylene chlorohydrin produced is small. When two moles of ethylene oxide are used and the amount of benzyl magnesium chloride is again one mole, the yield of the alcohol is practically the same as when one mole of ethylene oxide is used and the amount of ethylene chlorohydrin produced is again small. It appears that the benzyl magnesium chloride is the only Grignard reagent studied which reacts faster with ethylene oxide than do the magnesium chloride or the dialkyl magnesium produced from it.

The only product that is obtained when tertiary amyl magnesium bromide, tertiary hexyl magnesium bromide, or the Grignard that is produced when one mole of ethylene dibromide is reacted with two moles of magnesium, is ethylene bromohydrin. From this we conclude that the dialkyl magnesium compounds formed from these Grignard reagents do not react readily, if at all, with ethylene oxide or $(BrCH_2CH_2O)_2Mg$.

A technique for reacting tertiary butyl magnesium bromide with ethylene oxide was devised and small yields of the alcohol 3,3 dimethyl butanol-1 were obtained.

A proof of structure of 3,3 dimethyl butanol-1 and 3,4 dimethyl pentanol-1 was obtained by oxidizing the alcohols with alkaline potassium permanganate to the corresponding acid. Each acid was then synthesized. Derivatives of the acids were made, analyzed, melting points determined, and mixed melting points of the derivatives of the corresponding acids showed no depression.

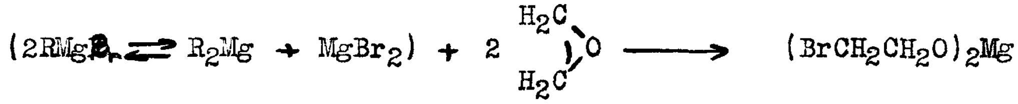
The equations outlined in the theoretical part give very good evidence for the support of the Schlenk equilibrium of a Grignard reagent:

$$2\ RMgX \rightleftarrows MgX_2 + R_2Mg$$

SUMMARY

1. The intermediate compound formed in the reaction of one mole of ethylene oxide with one mole of the Grignard reagent is $(BrCH_2CH_2-O)_2Mg$. All Analytical data support the molecular formula but the structural formula is not definitely established in as much as one half of the bromine is liberated upon hydrolysis.

2. The reaction of one mole of ethylene oxide with one mole of a Grignard reagent takes place in two steps as:



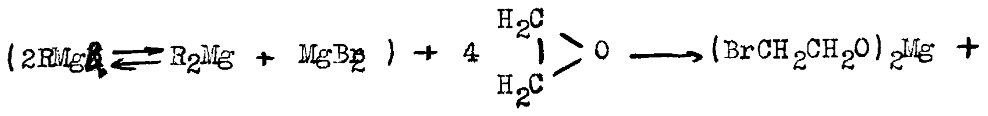
$$(2RMgBr \rightleftharpoons R_2Mg + MgBr_2) + 2\begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!\!>O \longrightarrow (BrCH_2CH_2O)_2Mg$$

$$+ R_2Mg$$

$$(BrCH_2CH_2O)_2Mg + R_2Mg + \text{Heat} \longrightarrow (R-CH_2CH_2O)_2Mg + MgBr_2$$

$$(R-CH_2CH_2O)_2Mg + MgBr_2 + 2HOH \longrightarrow 2RCH_2CH_2OH + Mg(OH)_2 + MgBr_2$$

3. One mole of a Grignard reagent will react with two moles of ethylene oxide at room temperature according to the following equations:



$$(2RMgBr \rightleftharpoons R_2Mg + MgBr_2) + 4\begin{matrix}H_2C\\ |\\ H_2C\end{matrix}\!\!>O \longrightarrow (BrCH_2CH_2O)_2Mg +$$

$$(R-CH_2CH_2O)_2Mg$$

$$(BrCH_2CH_2O)_2Mg + (R-CH_2CH_2O)_2Mg + 4HOH \longrightarrow 2BrCH_2CH_2OH +$$

$$2R-CH_2CH_2OH + 2Mg(OH)_2$$

4. Dialkyl magnesium compounds react with two moles of ethylene oxide at room temperature to form the expected alcohol.

5. Tertiary amyl and tertiary hexyl Grignards and the Grignard formed from the action of ethylene dibromide do not react with ethylene oxide to form the expected alcohol.

6. Tertiary butyl Grignard reagent did react with ethylene oxide to produce the alcohol in small yields.

7. Benzyl magnesium chloride reacts with one mole of ethylene oxide at room temperature to form the alcohol.

8. Additional evidence is given in support of the equilibrium equation ($2RMgX \rightleftharpoons MgX_2 + R_2Mg$) as proposed by Schlenk (32).

9. Proof of structure of two alcohols, 3,3 dimethyl butanol-1 and 3,4 dimethyl pentanol-1 was given and derivatives prepared.

10. A number of primary alcohols were prepared by the reaction of a Grignard reagent with ethylene oxide.

Table I

Alcohol	B.P. at 740 mm.	n^{23}	d^{24°	Derivative
Normal butyl (33)	116°-118°	1.3993	.807	a-naphthyl urathane 71° (35)
Normal amyl (33)	135°-137°	1.4100	.816	a-naphthyl urathane 65.5° (35)
Iso amyl (34)	130°	1.4081	.812	a-naphthyl urathane 67° (35)
Normal hexyl (33)	153°-155°	1.4131	.818	a-naphthyl urathane 59° (36)
3 methyl pentanol-1 (34)	151°-152°	1.4112	.823	a-naphthyl urathane 58° (36)
Iso Hexyl (33)	150°-152°	1.4132	.815	a-naphthyl urathane 60° (36)
3,3 dimethyl butanol-1	141°-143°	1.4160	.814	3,5 dinitrobenzoate 83.5°
Normal heptyl (33)	173°-174°	1.4231	.816	a-naphthyl urathane 62° (36)
3 methyl hexanol-1 (38)	161°-162°	1.4213	.817	a-naphthyl urathane 45°-47° (38)
Iso heptyl (33)	168°-169°	1.4251	.819	3,5 dinitrobenzoate 54.5° (36)
4 methyl hexanol-1 (38)	168°-169°	1.4233	.821	a-naphthyl urathane 50° (38)
Normal Octyl (33)	190°-193°	1.4303	.824	a-naphthyl urathane 66° (36)
3,4 dimethyl Pentanol-1 (39)	160°-162°	1.4261	.819	amide of the acid 95.5° anilide " " " 67°
3 methyl heptanol-1 (40)	101° @ 26 mm	1.4293	.821	
Benzyl carbinol (37)	217°-219°	1.5258	1.027	a-naphthyl urathane 119° (36)
B-cyclohexyl ethyl	88°-90° @ 17 mm	1.4693	.9185	3,5 dinitrobenzoate 70.5°
gamma phenyl propyl (41)	233°-235°	1.5351	1.006	phenyl urathane 47° (36)

Table II

Yields of Alcohols

Halide	$R_2Mg + 2\ H_2C\overset{O}{-}CH_2$	$RMgX + 2H_2C\overset{O}{-}CH_2$ no heat		$RMgX + 2H_2C\overset{O}{-}CH_2$ heat	
	% yield of alcohol	% bromohydrin	% yield alcohol	% bromohydrin	% yield alcohol
Ethyl bromide	88	45	72	11	79
Propyl bromide	90	43	75	6	76
Iso propyl bromide	85	45	70	7	74
N-butyl bromide	82	41	71	5	70
Sec.butyl bromide	70	51	65	9	65
Iso butyl bromide	80	41	69	3	64
Tert. butyl bromide	9	50	none	60	none
N-amyl bromide	75	40	60	10	69
Sec. amyl bromide	60	44	50	5	53
Iso amyl bromide	70	41	56	4	59
1-bromo 2 methyl butane	68	35	53	9	58
Tert. amyl bromide	none	48	none	42	none
Tert. amyl chloride	none	chlorohydrin 35	none	chlorohydrin 39	none
N hexyl bromide	50	30	47	4	49
2 bromo 3 methyl Butane	45	41	46	10	40
2 bromo Pentane	55	47	40	6	43
Tert. Hexyl bromide		42		48	
Phenyl bromide	72	50	55	42	58
Cyclohexyl bromide	60	42	45	8	50
Ethylene dibromide	none	68	none	51	none
Benzyl chloride		5	79	3	73

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