136
035
THS

THE REACTION OF PROPYLENE OXIDE WITH VARIOUS ALKYLMAGNESIUM CHLORIDES

Thesis for the Degree of Ph. D.
MICHIGAN STATE COLLEGE
Harlan E. Tiefenthal
1950

[redacted]

T547.3
T561

This is to certify that the

thesis entitled

"The Reaction of Propylene Oxide with Various Alkylmagnesium Chlorides".

presented by

Harlan E. Tiefenthal

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in Chemistry

Ralph C. Huston
Major professor

Date August 25, 1950

O-169

no dup.

XI no. 2

Chemistry

THESIS ABSTRACT

THE REACTION OF PROPYLENE OXIDE WITH VARIOUS ALKYLMAGNESIUM CHLORIDES

By

Harlan E. Tiefenthal

This investigation has extended the studies that have been conducted on the reactions of various alkylmagnesium halides with ethylene oxide, propylene oxide and isobutylene oxide. It involved the preparation of several Grignard reagents and corresponding dialkylmagnesium compounds, together with their subsequent reactions with propylene oxide using various proportions and conditions.

Grignard reagents were prepared using ethyl-, n-propyl-, sec-propyl-, n-butyl-, sec-butyl-, iso-butyl, and tert-butyl chlorides. Yields were determined by the Gilman [Gilman, H., Wilkinson, P. D., Fishel, W. P. & Meyers, C. H., J. Am. Chem. Soc., <u>45</u>, 150 (1923)] titration.

Each Grignard reagent was treated in four ways:

1. One mole of Grignard reagent was reacted with one mole of propylene oxide without heating.
2. One mole of Grignard reagent was reacted with one mole of propylene oxide and then refluxed with benzene.
3. One mole of Grignard reagent was reacted with two moles of propylene oxide without heating.
4. The dialkylmagnesium compound was made from the Grignard reagent and was reacted with two moles of propylene oxide without heating.

Reactions 1 and 2 were allowed to stand over night before hydrolysis. Reactions 3 and 4 were allowed to stand until they gave a 54 negative Michler's ketone test [Gilman, H. and Schulze, F., J. Am. Chem. Soc., 47, 2002 (1925)]. The ether solutions of the products of reactions 1, 2, and 3 were refluxed with sodium hydroxide to decompose any 1-chloro-2-propanol present. Analysis for chloride ion concentration was made by the Volhard method. The ether layers from all reactions were dried over potassium carbonate and fractionated through a helices packed, Fenske type column.

The physical constants of the alcohols were determined and the 3,5-dinitrobenzoate derivatives prepared.

PERCENT YIELDS OF ALCOHOLS AND 1-CHLORO-2-PROPANOL

Grignard reagent prepared from	RMgCl+ $CH_3\underbrace{CHCH_2}_{O}$		RMgCl+ $CH_3\underbrace{CHCH_2}_{O}$		RMgCl+ $2CH_3\underbrace{CHCH_2}_{O}$		R_2Mg+ $2CH_3\underbrace{CHCH_2}_{O}$
	without heat		with heat		without heat		without heat
	Percent 1-chloro-2-propanol	Percent Alcohol	Percent 1-chloro-2-propanol	Percent Alcohol	Percent 1-chloro-2-propanol	Percent Alcohol	Percent Alcohol
1-chloroethane	35	37	40	42	73	56	60
1-chloropropane	50	28	35	31	64	62	19
2-chloropropane	55	23	53	30	81	46	34
1-chlorobutane	52	41	28	58	77	59	26
2-chlorobutane	54	10	24	16	69	30	9
1-chloro-2-methyl-propane	58	19	19	40	73	62	33
2-chloro-2-methyl-propane	65	0	3	25	61	15	0

Harlan E. Tiefenthal

A comparison of the results of this investigation with those obtained from the reaction of propylene oxide with alkylmagnesium bromides [Huston, R. C. and Bostwick, C. O., J. Org. Chem., 13, 331 (1948)] showed that:

1. In the 1:1 mole ratio reactions:
    a. when heat was not used, the chlorine activated the alkyl-magnesium bond to give higher yields of alcohol and,
    b. when a benzene reflux was used, the chlorides gave improved yields of the secondary alcohols.
2. In the 1:2 mole ratio reactions:
    a. the yields of the alcohols and 1-halo-2-propanols were increased in both cases and,
    b. these yields were essentially the same for the corresponding alkyl group.

Ralph C. Huston

LIBRARY
Michigan State
University

PLACE IN RETURN BOX to remove this checkout from your record.
TO AVOID FINES return on or before date due.
MAY BE RECALLED with earlier due date if requested.

DATE DUE	DATE DUE	DATE DUE

6/01 c:/CIRC/DateDue.p65-p.15

CHEMISTRY

T547.3
T561

THE REACTION OF PROPYLENE OXIDE WITH VARIOUS ALKYLMAGNESIUM CHLORIDES

By

Harlan E. Tiefenthal

A THESIS

Submitted to the School of Graduate Studies of Michigan
State College of Agriculture and Applied Science
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1950

4-10-52

ACKNOWLEDGMENT

With sincere appreciation and gratitude acknowledgment is made to Dr. Ralph Chase Huston for his understanding guidance throughout the course of this study.

--Harlan E. Tiefenthal

273695

TABLE OF CONTENTS

TABLE OF CONTENTS

INTRODUCTION

INTRODUCTION

As with many other chemical reactions, chemists have made many generalizations concerning the Grignard reagent and its reactions. While it is true that its reaction with propylene oxide gives secondary alcohols, these alcohols are not always the main product of the reaction.

This study was initiated to investigate the reactions of various alkylmagnesium chlorides with propylene oxide and to compare these reactions with those of the corresponding alkylmagnesium bromides with propylene oxide.

HISTORICAL

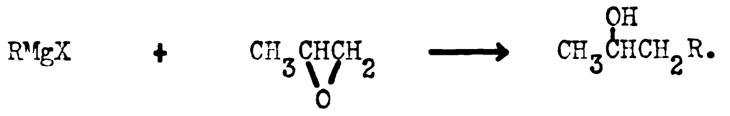
HISTORICAL

Louis Henry (1) was the first to study the reaction of propylene oxide with alkylmagnesium halides. He postulated that it is theoretically possible to obtain several different alcohols when ethylmagnesium bromide is allowed to react with propylene oxide. The product obtained, according to Henry, depends upon how the oxygen-carbon bond splits and upon whether or not rearrangement occurs before the propylene oxide reacts with the ethylmagnesium bromide. If the carbon-oxygen bond splits and addition occurs before isomerization takes place, the product would be $CH_3CHOHCH_2CH_2CH_3$ or $CH_3CH_2CH(CH_3)CH_2OH$. If addition of the ethylmagnesium bromide takes place after isomerization occurs, the product would be $(CH_3)_2CCHCH_2CH_3$ or $CH_3CH_2CHOHCH_2CH_3$. The latter depends on whether isomerization gives the ketone CH_3COCH_3 or the aldehyde CH_3CH_2CHO. In carrying out the reaction of propylene oxide with ethylmagnesium bromide, Henry obtained a 60% yield of 2-pentanol.

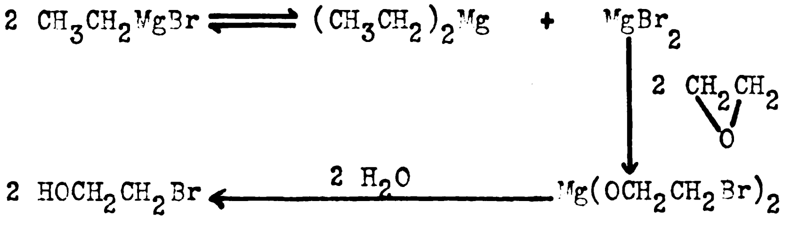
Hess (2) found similar results using α-pyrridyl-magnesium bromide and propylene oxide. Levene and Walti (3) condensed optically active propylene oxide with methyl-, ethyl-, and propylmagnesium bromides. They found that similar alcohols were produced and that Walden inversion did not occur. Further evidence for this type of addition is given by Newman (4) and Sharefkin and Ritter (5). Newman prepared 1-phenyl-2-propanol by using phenylmagnesium bromide and propylene oxide. Sharefkin and Ritter prepared 4-(4-methylphenyl)-2-butanol using xylylmagnesium chloride with propylene oxide.

However, when Norton and Hass (6), carried out the reaction by adding an equimolecular amount of propylene oxide to ethylmagnesium bromide and then heating, they obtained an 11% yield of 3-pentanol. This product indicates an addition which is the reverse of that reported by Henry.

It appears that the products formed during the reaction of Grignard reagents with epoxides have been formed by carbanion attack at the least substituted carbon atom,



The reaction is not a simple one, however, as Huston and Agett (7) have shown that dialkylmagnesium is probably an essential reactant. They found that the addition of one mole of ethylmagnesium bromide to one mole of ethylene oxide gave an addition complex which was the same as that obtained by passing ethylene oxide into an ethereal solution of magnesium bromide. The first mole of ethylene oxide appeared to react almost exclusively with the magnesium bromide, in equilibrium with the Grignard reagent and diethylmagnesium, and formed an addition complex. Hydrolysis at this point gave 60% 1-bromo-2-ethanol and very little 1-butanol.

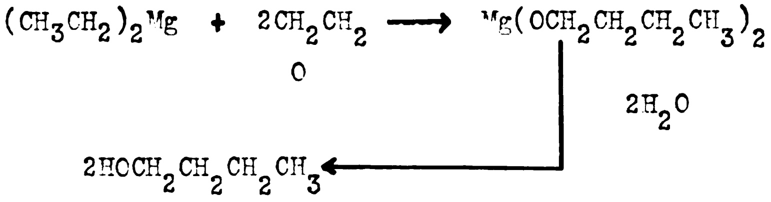


Grignard (8) proposed oxonium type intermediates for this reaction. While his views were supported by Meisenheimer and Casper (9) these oxonium salts probably do not exist for any great length of time.

In order to obtain 1-butanol, the mixture must be heated or a second mole of ethylene oxide added:

$$\begin{tikzcd} (CH_3CH_2)_2Mg + Mg(OCH_2CH_2Br)_2 \arrow[r] & Mg(OCH_2CH_2CH_2CH_3)_2 + MgBr_2 \arrow[dl, "2H_2O"] \\ 2HOCH_2CH_2CH_2CH_3 & \end{tikzcd}$$

or

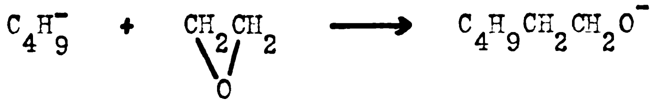


$$\begin{tikzcd} (CH_3CH_2)_2Mg + 2\underset{O}{CH_2CH_2} \arrow[r] & Mg(OCH_2CH_2CH_2CH_3)_2 \arrow[dl, "2H_2O"] \\ 2HOCH_2CH_2CH_2CH_3 & \end{tikzcd}$$

Huston and Langham (10) have shown that when ethylene oxide is reacted with ethylmagnesium chloride the intermediate compound leading to 1-butanol (in 55% yield) is $(C_4H_9O)_2Mg$ from $(C_2H_5)_2Mg$ or C_4H_9OMgCl from C_2H_5MgCl.

While studying the reaction of n-butylmagnesium bromide with ethylene oxide, Cottle and Hollyday (11) obtained a mixture of 1-hexanol and 2-hexanol. They attempted to explain these products by proposing a mechanism involving the nucleophilic attack of the carbanion of the Grignard reagent upon one of the carbon atoms of

ethylene oxide

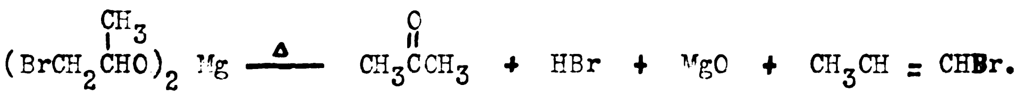


$$C_4H_9^- + \underset{O}{CH_2CH_2} \longrightarrow C_4H_9CH_2CH_2O^-$$

or on the $BrCH_2CH_2O^-$ particle from the magnesium di-(1-bromo-2-ethoxide)

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

However, neither of these nucleophilic reactions should give rearrangement and therefore would not account for the 2-hexanol produced. They also found that: 1. when the mixture from the reaction between ethylene oxide and n-butylmagnesium bromide was heated in such a manner that a violent reaction took place, more 2-hexanol was formed than in similar experiments when there was no violent reaction; and, 2. an acetaldehyde resin was formed when the ethylene oxide and magnesium bromide reaction product was heated in a bomb. This led them to postulate that the $BrCH_2CH_2O^-$ particle may, upon heating, loose a bromine ion and then rearrange to acetaldehyde. Further proof that the addition complex decomposes on heating to form a carbonyl compound was found by Huston and Bostwick (12).



$$(BrCH_2\overset{CH_3}{CH}O)_2Mg \xrightarrow{\Delta} CH_3\overset{O}{\overset{\|}{C}}CH_3 + HBr + MgO + CH_3CH = CHBr.$$

Huston and Brault (13) have shown that the magnesium di-(1-bromo-2-methyl-2-propoxide) rearranges spontaneously to isobutyraldehyde. Actually, Huston and Bostwick found acetone among all of their reaction products and Huston and Brault found isobutyraldehyde in all of their reactions.

Norton and Hass (6) reported a 23% yield of 2-pentanol when they reacted diethylmagnesium with propylene oxide. Other reported reactions of epoxides with dialkylmagnesium compounds indicate only simple addition products even when the reaction mixture is refluxed (7, 14, 15, 16 and 17.)

EXPERIMENTAL

I. Materials

Propylene Oxide (B.P. 33.4-34.4°C.). Furnished by the Dow Chemical Company. Used without further purification.

Ethyl Chloride. Secured from the Ohio Chemical Company.

Alkyl Chlorides. Secured from the Columbia Chemical Company.

Magnesium. Secured from the Dow Chemical Company special for Grignard reactions. Dried at 50° C. before use.

Anhydrous Diethyl Ether. Dried over sodium wire for at least one week.

Benzene. Thiophene free and anhydrous. Dried over sodium wire for at least one week.

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

Potassium Carbonate. Anhydrous, C. P.

Ammonium Chloride. C. P.

Silver Nitrate solution, approximately 0.1 N. Prepared from Bakers' Analytical Grade $AgNO_3$.

Potassium Thiocyanate solution, approximately 0.1 N. Standardized against the silver nitrate solution.

Sodium Hydroxide solution, approximately 0.2 N. Standardized against sulfamic acid.

Sulfuric Acid solution, approximately 0.15 N. Standardized against the standard sodium hydroxide solution.

II. Preparation of Grignard Reagents

A. Preparation of Ethylmagnesium Chloride

Two and one-quarter moles (54.7 g.) of magnesium turnings were placed in a dry, three-liter, three-necked, round-bottomed flask which was placed in an ice, salt bath. The flask was fitted with a glycerol sealed stirrer, a dry ice condenser (fitted with a calcium chloride:soda-lime tube) and an inlet tube for ethyl chloride. The ethyl chloride inlet tube extended as near the bottom of the flask as the stirrer would allow. Six hundred milliliters of anhydrous ether were added to the flask and the condenser was then filled with a dry ice and acetone bath. Ethyl chloride was bubbled into the flask through a potassium hydroxide pellet tower and then through concentrated sulfuric acid for two hours while the mixture was stirred. The stirrer was then stopped and the mixture allowed to stand for an hour. During this period the reaction usually began but in those cases in which it did not, a charge of ethylmagnesium bromide was added to start the reaction. Stirring was resumed and ethyl chloride added at a rate sufficient to maintain gentle reflux. After most of the magnesium had reacted, addition of the ethyl chloride was discontinued and stirring maintained for one hour. The stirrer was then stopped and the reaction mixture allowed to come to room temperature by standing overnight.

B. Preparation of Other Grignard Reagents

Three and one-quarter moles (79.0 g.) of magnesium turnings were placed in a dry, three-liter, three-necked, round-bottomed flask which was placed in a container so that external cooling was possible when needed. The flask was fitted with a glycerol sealed stirrer, a bulb condenser (fitted with a calcium chloride:soda-lime tube), and a Hershberg dropping funnel. Four hundred milliliters of anhydrous ether and ten to twenty grams of the alkyl chloride were added to the flask. The reaction was started by the addition of a charge of the alkylmagnesium chloride prepared in a test tube. The rest of the three moles of the alkyl chloride was mixed with an equal volume of anhydrous ether and added at a rate sufficient to maintain a gentle reflux. External cooling was used only when necessary. After addition was complete, stirring was continued for an hour and the mixture allowed to stand overnight.

C. Analysis of the Grignard Reagent

The Grignard reagent was poured, under a stream of nitrogen, into a graduated cylinder and the total volume measured. Two milliliter portions were then taken and analyzed by the Gilman procedure (18) using methyl red as the indicator. The solution of the Grignard reagent was then divided into four approximately equal parts and each was treated in a different way. A typical run for each of the four procedures will be described.

III. Reaction of Propylene Oxide with the Grignard Reagents

A. Reaction of one mole of Propylene Oxide with one mole of the Grignard Reagent without heating

Approximately one quarter of the total Grignard solution was placed in a one-liter, three-necked, round-bottomed flask. The flask was fitted with a bulb condenser, a glycerol sealed stirrer and a dropping funnel. The condenser and the funnel were fitted with calcium chloride:soda-lime tubes to protect the solutions from atmospheric moisture and CO_2. The required amount of propylene oxide was weighed out and placed in the dropping funnel along with an equal volume of anhydrous ether. This solution was added dropwise with stirring as fast as possible and still maintain a gentle reflux. After the addition had been completed, the mixture was stirred for an hour and allowed to stand overnight.

The mixture was then hydrolyzed, without external cooling, by adding a saturated solution of ammonium chloride dropwise, with stirring, at a rate sufficient to maintain gentle reflux (19). About one hundred milliliters of this solution were required to reach a point where a clear separation occurred. The ether solution was decanted from the precipitated magnesium salts and the dense precipitate was washed with one or two portions of ether.

The combined ether solution was then placed over 40 grams of sodium hydroxide pellets and 150 milliliters of water were added slowly, with stirring. This mixture was then refluxed, with stirring, for seven hours to convert the 1-chloro-2-propanol to propylene oxide and sodium chloride. It was then allowed to stand overnight and come to room temperature. The layers were separated and the water layer extracted with ether. The combined ether solutions were placed over anhydrous potassium carbonate to dry and the water layer, containing the sodium chloride, was diluted to one liter for analysis. Two milliliter portions were titrated for chloride ion by the Volhard method to give an accurate measure of the yield of 1-chloro-2-propanol.

The dried ether solution of the products was distilled at atmospheric pressure through either a 9.0 inch or a 16.5 inch Fenske-type column packed with 3/32 inch glass helices and fitted with a total reflux, partial take-off type head. Heat was supplied by a Glas-col mantle. All like runs were combined after one fractionation and a refractionation made before physical constants were determined and derivatives made.

B. Reaction of one mole of Propylene Oxide with one mole of the Grignard Reagent followed by refluxing with Benzene

Approximately one quarter of the total Grignard solution was placed in a one-liter, three-necked, round-bottomed flask fitted as described in III A. The addition of the propylene oxide was carried out as described in III A. and allowed to stand overnight. The flask was then placed in a Glas-col mantle, the condenser set for distillation and a thermometer fitted so that the bulb was immersed in the liquid. Approximately one-half of the ether was removed by distillation and then twice this amount of anhydrous benzene was added to the distillation flask. This solution was then distilled until the temperature of the liquid reached 75° C. The condenser was then reset for reflux and the mixture refluxed with stirring for seven hours and allowed to stand overnight. The mixture was hydrolyzed, extracted, dried and fractionated as described in III A. The analysis for chloride ion concentration was also carried out as in III A.

C. Reaction of two moles of Propylene Oxide with one mole of Grignard Reagent

The ether solution of propylene oxide was added to the Grignard reagent as in III A. The reaction mixture was stirred for an hour after addition was completed and then allowed to stand until the test with Michler's ketone was faint or negative (20). By this time the reaction mixture had set-up like a gel but was easily hydrolyzed, extracted, dried and fractionated as in III A. The analysis for chloride ion concentration was also carried out as in III A.

D. Preparation of Dialkylmagnesium reagents and their reaction with two moles of Propylene Oxide

Approximately one quarter of the total Grignard solution was placed in a one-liter, three-necked, round-bottomed flask fitted as described in III A. Slightly more than an equal molar amount of dioxane was mixed with two hundred milliliters of anhydrous ether and added dropwise, with stirring, so that a gentle reflux was maintained. When addition was completed, the stirring was continued for an hour and the mixture allowed to stand overnight. The solution and precipitate were then poured into centrifuge bottles under a stream of nitrogen and stoppered tightly. They were then centrifuged at 1500 r.p.m. for 15 minutes, the ether solution decanted into a graduated cylinder under a stream of nitrogen and the total volume of the solution measured. Two milliliter portions were taken and analyzed by the Gilman procedure using methyl red as the indicator.

This solution was then poured under a stream of nitrogen into a one-liter, three-necked, round-bottomed flask fitted as in III a. The calculated amount of propylene oxide mixed with an equal volume of anhydrous ether was added dropwise, with stirring. The stirring was continued for an hour and the mixture allowed to stand until the test with Michler's ketone was faint or negative.

Hydrolysis was carried out as described in III A. In some of these reactions there was a quantity of solid material in the bottom of the flask which did not hydrolyze. It was found to contain magnesium and chlorine. The chlorine might have come from the ammonium chloride used for hydrolysis. Analysis showed that this solid contained 20.0 percent magnesium.

The ether solution of the products was placed over anhydrous potassium carbonate to dry. The dried solution was then fractionated as described in III A.

IV. Reaction of one mole of Propylene Oxide with one mole of Ethylmagnesium Chloride followed by violent decomposition

The ethylmagnesium chloride was prepared and the proplene oxide added as in the regular 1:1 reaction. After the mixture had stood overnight the apparatus was arranged for distillation and thermometers were placed in each of the three necks of the flask (one was immersed in the liquid, one was near the goose-neck leading to the condenser and the third one registered the temperature of the vapors in the flask.) The distillation was started and the ether began to come off when the temperature of the solution had reached 37° C. Most of the ether had been distilled by the time the temperature of the liquid had reached 60° C. but it was necessary to increase the temperature of the liquid to 84° C. before the following violent decomposition occurred. At this point the black, tarry looking mass swelled rapidly (almost violently) to a puffy white solid with the evolution of a dense white gas that carried over into the receiver. The hottest temperature recorded was near the bottom of the flask where it reached 280° C. At the same time the temperature near the goose-neck reached 120° C. The reaction flask was then set up for refluxing and a volume of dry benzene equal to the amount of ether which had been removed, was added. The resulting mixture was refluxed for seven hours with stirring and allowed to stand overnight. The benzene solution of products was hydrolyzed, extracted, dried and fractionated as in III A. Analysis for chloride ion concentration was made by the Volhard method. The results of magnesium analyses on the white puffy solid, and the yields of 1-chloro-2-propanol and 2-pentanol may be seen in Table I.

V. Preparation of the 3,5-Dinitrobenzoates of the alcohols (21)

Two grams of the alcohol were placed in a large test tube containing five grams of 3,5-dinitrobenzoyl chloride. A large excess of anhydrous pyridine was added. The test tube was fitted with a calcium chloride tube to protect the contents from moisture. The mixture was then placed on the steam bath and allowed to heat for an hour with occasional shaking, following which, it was poured into water to hydrolyze any remaining 3,5-dinitrobenzoyl chloride. The water mixture was extracted with ether and the water layer discarded. The ether layer was then washed successively with 5 percent sulfuric acid, 10 percent sodium carbonate and finally, water. The ether was evaporated on the steam bath and the residue taken up in hexane. This solution was boiled with Norite to decolorize the solution which was then filtered. Where possible, the 3,5-dinitrobenzoate was allowed to crystallize at room temperature. Otherwise, the solution was placed in the refrigerator. The esters were recrystallized from hexane in a similar manner.

As each alkylmagnesium chloride was treated in four different ways, a total of four esters of the same alcohol were prepared in most cases. These were made using the alcohol fraction obtained from the combined fractionations of all like runs.

The melting points of these derivatives were compared with those given in the literature. Further proof of the identity of these alcohols was obtained by taking mixed melting points of their derivatives with those of corresponding authentic compounds.

VI. Calculation of percentage yields

The percentage yields of the alcohols were based on the titrated Grignard reagents.

The percentage yields of 1-chloro-2-propanol were based on the titrated Grignard reagents.

TABLES

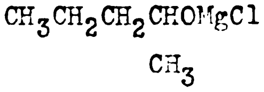
TABLE I

ANALYSIS OF SOLID RESIDUE FROM VIOLENT DECOMPOSITION

Run	Percent 1-Chloro-2-Propanol	Percent Alcohol	Percent Magnesium
1	6.4	37.0	
2	10.9	42.9	
3	0.0	45.5	
4	18.7	41.0	19.5

Analyses for Magnesium	18.9
	20.5
Content	20.1
	20.4
	18.9
Average	19.5

Analyses of Solid Residue	18.9
	16.9
For Magnesium Content after	20.9
	23.9
Extraction with Ether	21.9
	21.8
Average	20.7



Theory for $\underset{CH_3}{CH_3CH_2CH_2CHOMgCl}$ + $MgCl_2$ is 20.1 .

There is definite evidence, however, of the presence of a 1-chloro-2-propanol intermediate.

TABLE II

PERCENT YIELDS OF ALCOHOLS AND 1-CHLORO-2-PROPANOL BASED UPON THE TITRATED GRIGNARD REAGENTS

	RMgCl + $CH_3\underbrace{CHCH_2}_{O}$	RMgCl + $CH_3\underbrace{CHCH_2}_{O}$	RMgCl + $2CH_3\underbrace{CHCH_2}_{O}$	R_2Mg + $2CH_3\underbrace{CHCH_2}_{O}$
	Without heat	With heat	Without heat	Without heat
	Ethylmagnesium chloride			
2-Pentanol	27	42	56	60
1-Chloro-2-propanol	35	40	73	
	n-Propylmagnesium chloride			
2-Hexanol	28	31	62	19
1-Chloro-2-propanol	50	35	64	
	sec-Propylmagnesium chloride			
4-Methyl-2-pentanol	23	30	46	34
1-Chloro-2-propanol	55	53	81	
	n-Butylmagnesium chloride			
2-Heptanol	41	58	59	26
1-Chloro-2-propanol	52	28	77	
	sec-Butylmagnesium chloride			
4-Methyl-2-hexanol	10	16	30	9
1-Chloro-2-propanol	54	24	69	
	iso-Butylmagnesium chloride			
5-Methyl-2-hexanol	19	40	62	33
1-Chloro-2-propanol	58	19	73	
	tert-Butylmagnesium chloride			
4,4-Dimethyl-2-pentanol	0	25	15	0
1-Chloro-2-propanol	65	3	61	

TABLE III

PHYSICAL CONSTANTS OF THE ALCOHOLS

ALCOHOL	n_D^{20}	B.P. °C.	Ref.
2-Pentanol	1.4068	120.1/743 mm.	12, 22, 23
2-Hexanol	1.4140	139.2/743 mm.	12, 23, 24
4-Methyl-2-pentanol	1.4132	131.4/745 mm.	12, 24, 25
2-Heptanol	1.4218	158.8/745 mm.	12, 23
4-Methyl-2-hexanol	1.4236	152.2/744 mm.	12, 26, 27
5-Methyl-2-hexanol	1.4194	150.4/744 mm.	12, 28, 29
4,4-Dimethyl-2-pentanol	1.4241	135.4/742 mm.	12, 30

TABLE IV

3,5-DINITROBENZOATES OF THE ALCOHOLS

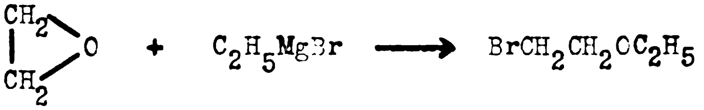
ALCOHOL	M.P. °C.	Ref.
2-Pentanol	60-61	12, 31
2-Hexanol	36-37.5	12, 24
4-Methyl-2-pentanol	60.5-61.5	12, 24
2-Heptanol	47.5-48.5	12, 31
4-Methyl-2-hexanol	50-51	12, 26
5-Methyl-2-hexanol	34.5-35.5	12, 29
4,4-Dimethyl-2-pentanol	93-94	12, 30

THEORETICAL

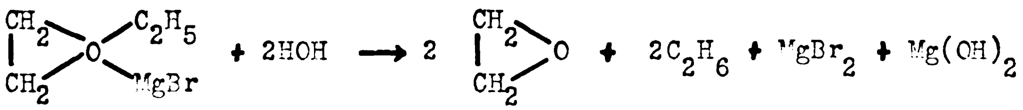
THEORETICAL

Previous work has shown that the reactions of ethylene oxide with alkylmagnesium bromides (7) and ethylene oxide with the corresponding alkylmagnesium chlorides (10) are fundamentally different. It is also true that there are fundamental differences between the reactions of propylene oxide with alkylmagnesium bromides (12) and propylene oxide with the corresponding alkylmagnesium chlorides.

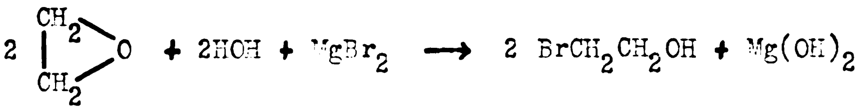
When ethylmagnesium bromide and ethylene oxide are reacted in a mole per mole ratio without heating, the only product reported was 1-bromo-2-ethanol (32). Blaise proposed that the Grignard reagent was broken between the magnesium and bromine bond according to the following scheme:



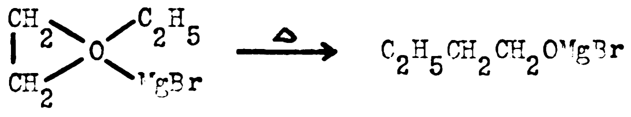
This product would give 1-bromo-2-ethanol on hydrolysis. Grignard (8) proposed that an oxonium salt was formed. This salt would hydrolyze as follows:



A Wurtz type reaction would then follow, giving 1-bromo-2-ethanol.

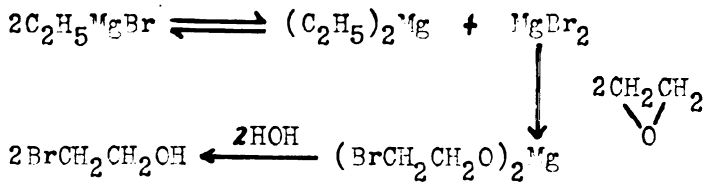


Grignard found that heat produced a "second phase" reaction giving a considerable quantity of the expected 1-butanol. He proposed that the oxonium salt was ruptured as follows:



$$\text{(CH}_2\text{)}_2\text{O(C}_2\text{H}_5\text{)MgBr} \xrightarrow{\Delta} C_2H_5CH_2CH_2OMgBr$$

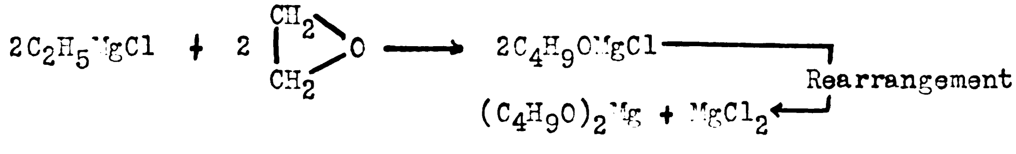
The product would give 1-butanol on hydrolysis. Meisenheimer and Casper (9) presented analytical data supporting Grignard's views. Ribas and Tapia (33) proposed that the addition product consisted of a mixture of $(BrCH_2CH_2O)_2Mg$ and $BrCH_2CH_2OMgBr$. However, their analytical data supports the formula $BrCH_2CH_2OMgBr$. Huston and Agett (7) showed that the intermediate compound is $(BrCH_2CH_2O)_2Mg$, and is formed by the following scheme:



$$2C_2H_5MgBr \rightleftharpoons (C_2H_5)_2Mg + MgBr_2 \xrightarrow{2CH_2CH_2O} (BrCH_2CH_2O)_2Mg \xrightarrow{2HOH} 2BrCH_2CH_2OH$$

When ethylmagnesium chloride and ethylene oxide were reacted in a mole per mole ratio without heating, a 55% yield of 1-butanol was obtained along with 22% 1-chloro-2-ethanol (10). Huston and Langham have shown that the intermediate compound leading to 1-butanol may have consisted largely of either

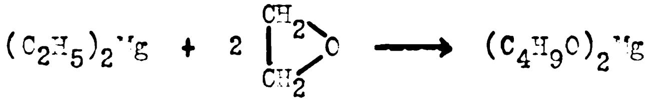
C_4H_9OMgCl produced from



$$2C_2H_5MgCl + 2\,(CH_2)_2O \longrightarrow 2C_4H_9OMgCl \xrightarrow{\text{Rearrangement}} (C_4H_9O)_2Mg + MgCl_2$$

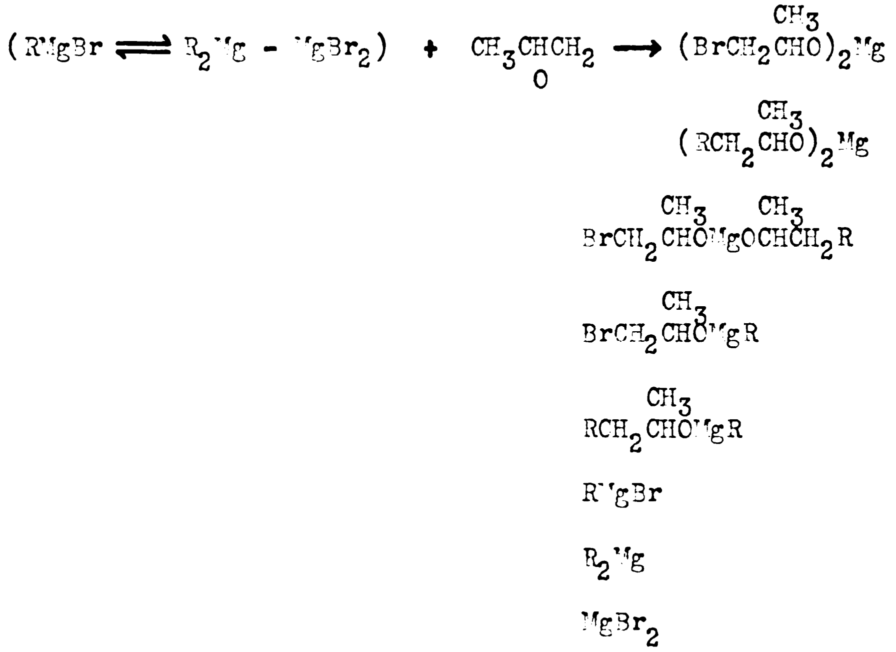
or

$(C_4H_9O)_2Mg$ produced from



Hydrolysis of either intermediate would give 1-butanol. Huston and Langham further showed that $(ClCH_2CH_2O)_2Mg$ was the intermediate precursor leading to 1-chloro-2-ethanol.

When ethylmagnesium bromide was reacted with propylene oxide in a mole per mole ratio without heat, the intermediate reaction products were reported, by Huston and Bostwick (12), to be predominately of the magnesium di-(1-bromo-2-propoxide) type, $(BrCH_2\overset{CH_3}{C}HO)_2\text{-}Mg$. The mechanism proposed for this reaction was:



$$(RMgBr \rightleftharpoons R_2Mg - MgBr_2) + CH_3\underset{O}{CHCH_2} \longrightarrow (BrCH_2\overset{CH_3}{C}HO)_2Mg \qquad (I)$$

$$(RCH_2\overset{CH_3}{C}HO)_2Mg \qquad (II)$$

$$BrCH_2\overset{CH_3}{C}HOMgOCH\overset{CH_3}{C}H_2R \qquad (III)$$

$$BrCH_2\overset{CH_3}{C}HOMgR \qquad (IV)$$

$$RCH_2\overset{CH_3}{C}HOMgR \qquad (V)$$

$$RMgBr \qquad (VI)$$

$$R_2Mg \qquad (VII)$$

$$MgBr_2 \qquad (VIII)$$

When the ratio of reactants was 1:1, the first, fourth and seventh intermediates were present in large amounts.

When ethylmagnesium chloride and propylene oxide were reacted in a mole per mole ratio without heating, a 37% yield of the 2-pentanol was obtained along with a 35% yield of 1-chloro-2-propanol. The results of the reaction of alkylmagnesium chlorides with propylene oxide in a mole per mole ratio without heat, indicate that the alkyl-magnesium bond is ruptured more easily when the alkylmagnesium chlorides are used than when the alkylmagnesium bromides are used.

If the mole per mole reaction mixture of ethylmagnesium bromide and ethylene oxide was refluxed with benzene, the yield of 1-butanol was greatly increased at the expense of the 1-bromo-2-ethanol.

$$R_2Mg + (BrCH_2CH_2O)_2Mg \xrightarrow{heat} (RCH_2CH_2O)_2Mg + MgBr_2$$

$$(RCH_2CH_2O)_2Mg + 2H_2O \longrightarrow 2RCH_2CH_2OH + 2Mg(OH)_2$$

There was but slight reaction between R_2Mg and $(ClCH_2CH_2O)_2Mg$ when ethylmagnesium chloride and ethylene oxide were refluxed with benzene.

When propylene oxide and ethylmagnesium bromide in a 1:1 ratio, were refluxed with benzene, there was only a slight increase in the yield of 2-pentanol.

When propylene oxide and ethylmagnesium chlorides in a mole per mole ratio, were refluxed with benzene, the yield of 2-pentanol was increased and the yield of 1-chloro-2-propanol was decreased. (Table II). This increase in alcohol yield was probably due to a slight interaction of the magnesium di-(1-chloro-2-propoxide) with the diethylmagnesium. The rest of the 1-chloro-2-propanol intermediate apparently decomposed to propylene oxide.

Excessive heating of the magnesium di-(1-bromo-2-propoxide) from the propylene oxide and ethylmagnesium bromide reaction mixture caused the formation of acetone along with a complete loss of 1-bromo-2-propanol and only a slight increase in the yield of 2-pentanol.

Excessive heating of the magnesium di-(1-chloro-2-propoxide) from the propylene oxide and ethylmagnesium chloride reaction mixture gave no evidence of acetone formation but there was a great loss in the yield of 1-chloro-2-propanol and only a slight increase in the percent of 2-pentanol formed (Table I). The strong heat generated during this reaction decomposed the 1-chloro-2-propanol intermediate. The product of this decomposition was evidently propylene oxide since no evidence of either acetone or propionaldehyde was found among the products. The slight increase in alcohol yield was probably due to a slight interaction of the magnesium di-(1-chloro-2-propoxide) with the diethylmagnesium. This was also found in the benzene refluxed reactions.

One mole of alkylmagnesium bromide reacted with two moles of ethylene oxide to give increased yields of both 1-bromo-2-ethanol and the 1-butanol:

$$R_2Mg + MgBr_2 + 4(CH_2)_2O \longrightarrow (BrCH_2CH_2O)_2Mg + (RCH_2CH_2O)_2Mg$$

$$(BrCH_2CH_2O)_2Mg + (RCH_2CH_2O)_2Mg + 4H_2O \longrightarrow 2BrCH_2CH_2OH + 2RCH_2CH_2OH + 2Mg(OH)_2$$

The same scheme may be used to represent the reaction of one mole of alkylmagnesium chloride with two moles of ethylene oxide if it is assumed that dialkylmagnesium leads to the formation of the alcohol.

When two moles of propylene oxide were reacted with one mole of alkylmagnesium bromide, the first three intermediates, in the mechanism proposed by Huston and Bostwick, were present in large amounts. This gave increased yields of both 1-bromo-2-propanol and the alcohol.

The reaction of one mole of alkylmagnesium chloride with two moles of propylene oxide also gave greatly increased yields of both the 1-chloro-2-propanol and the alcohol (Table II).

When two moles of ethylene oxide were reacted with one mole of dialkylmagnesium, the expected alcohol was obtained in good yield except when tertiary alkyl groups were involved.

When two moles of propylene oxide were reacted with one mole of dialkylmagnesium, the expected alcohol was obtained, except when tertiary alkyl groups were involved. The yields, however, are much less than when ethylene oxide was used.

DISCUSSION

DISCUSSION

When propylene oxide was reacted with various alkylmagnesium chlorides in a mole per mole ratio, without heating, the principal product in most cases was 1-chloro-2-propanol, (Table II). A comparison of similar reactions of propylene oxide with various alkylmagnesium bromides (12) shows that the yield of 1-chloro-2-propanol was only slightly less than the yield of 1-bromo-2-propanol. It also shows that when the alkylmagnesium chlorides were used the yields of alcohol were considerably greater than when the alkylmagnesium bromides were used. These facts point out that the alkyl-magnesium bond is much more easily broken when the alkylmagnesium chlorides are used than when the alkylmagnesium bromides are used. These facts also show that the ease of rupture of the magnesium-chloride bond is not greatly diminished when the alkylmagnesium chlorides are used.

When the mole per mole reaction mixtures of propylene oxide and alkylmagnesium chlorides were refluxed with benzene, the yields of alcohol were increased in all cases. The increase in alcohol yield was most evident in the iso-butylmagnesium chloride and tertiary-butylmagnesium chloride reactions. In most cases, with the exception of those in which ethylmagnesium chloride and secondary-propylmagnesium chloride were used, the yield of 1-chloro-2-propanol was greatly reduced. The greatest reduction in the yield of 1-chloro-2-propanol occurred when iso-butylmagnesium chloride and tertiary-butylmagnesium chloride were used.

When the ether was completely distilled from the reaction mixture of propylene oxide and ethylmagnesium chloride in a mole per mole ratio and the temperature in the reaction mixture had reached 84° C., a violent reaction took place. The resulting white solid was then refluxed with benzene. This reaction caused almost a complete loss of 1-chloro-2-propanol and a yield of alcohol very similar to that obtained in the benzene refluxed reaction (Table I). No evidences of acetone or propionaldehyde were found in the final reaction mixture or in the material that distilled over during the violent reaction. Therefore, as the yield of 1-chloro-2-propanol was small, it is assumed that the intermediate leading to its formation was decomposed to give propylene oxide.

When one mole of alkylmagnesium chloride was reacted with two moles of propylene oxide without heat, the yield of 1-chloro-2-propanol was at least 60 percent in all cases and the yields of the alcohols were greatly improved. A comparison of these results (Table II) with those obtained when propylene oxide and alkylmagnesium bromides were reacted under similar conditions and in like proportions (6), shows, with the exception of the iso-butylmagnesium halide reactions, that the yields of alcohol and 1-halo-2-propanol for corresponding alkylmagnesium halides are, within experimental error, identical. These facts, when compared with the results of the mole per mole reactions, show that when alkylmagnesium chlorides are used the alkyl-magnesium bond is ruptured much more easily than when the alkylmagnesium bromides are used.

No precipitate was obtained in any of the 1:1 ratio reactions but all of the 1:2 ratio reactions formed a gel-like solid before becoming negative to the Michler's ketone test.

In the reaction of one mole of dialkylmagnesium with two moles of propylene oxide the expected alcohol was obtained in all cases except when di-tertiary-butylmagnesium was used. The yields of the alcohols were considerably less than those obtained when ethylene oxide was used (7). Huston and Agett allowed the reaction mixture to stand only three hours before hydrolysis. The reactions of the dialkylmagnesium compounds with propylene oxide were allowed to stand until a negative Michler's ketone test was obtained. Therefore, a comparison of these results is not entirely valid.

SUMMARY

SUMMARY

1. No evidence of the formation of acetone was discovered in any of the reactions of propylene oxide with the various alkylmagnesium chlorides. No evidence of the alcohol that would have resulted from the reaction of acetone with any of the various alkylmagnesium chlorides was found.

2. Data is presented which shows that the alkyl-magnesium bond of the alkylmagnesium chlorides was ruptured with greater ease than the alkyl-magnesium bond of the alkylmagnesium bromides.

3. The results obtained by refluxing equal molecular quantities of propylene oxide and alkylmagnesium chloride show that increased amounts of the alcohols are obtained by forcing the reactions.

4. The reaction of two moles of propylene oxide with one mole of the various alkylmagnesium chlorides greatly increases the yield of 1-chloro-2-propanol as well as the yield of the alcohol. These results are very similar to those obtained when the corresponding alkylmagnesium bromides are used.

REFERENCES

REFERENCES

1. Henry, L., Compt. rend., 145, 453 (1907).
2. Hess, K., Ber., 46, 3113 (1913).
3. Levene, P. A. and Walti, A., J. Biol. Chem., 90, 81 (1931); 94, 367 (1931).
4. Newman, M. S., J. Am. Chem. Soc., 62, 2295 (1940).
5. Sharefkin, J. G. and Ritter, J. J., J. Am. Chem. Soc., 63, 1478 (1941).
6. Norton, F. H. and Hass, H. B., J. Am. Chem. Soc., 58, 2147 (1936).
7. Huston, R. C. and Aggett, A. H., J. Org. Chem., 6, 123 (1941).
8. Grignard, V., Bull. soc. chim., 29, 944 (1903).
9. Meisenheimer, J. and Casper, J., Ber., 54, 1655 (1921).
10. Huston, R. C. and Langham, C. C., J. Org. Chem., 12, 90 (1947).
11. Cottle, D. L. and Hollyday, W. C., Jr., J. Org. Chem., 12, 510 (1947).
12. Huston, R. C. and Bostwick, C. O. J., Org. Chem., 13, 331 (1948).
13. Huston, R. C. and Brault, R. G., Ph. D. Thesis, Michigan State College, 1948.
14. Columbic, C. and Cottle, D. L., J. Am. Chem. Soc., 61, 996 (1939).
15. Kharasch, M. S. and Clapp, H. G., J. Org. Chem., 3, 355 (1938).
16. Tiffeneau, M. and Fourneau, E., Compt. rend., 146, 697 (1908).
17. Bartlett, P. D. and Berry, C. M., J. Am. Chem. Soc., 56, 2683 (1934).
18. Gilman, H., Wilkinson, P. D., Fishel, W. P. and Meyers, C. H., J. Am. Chem. Soc., 45, 150 (1923).
19. Fieser, L. F., "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., Boston, Mass., 1941, p. 410.
20. Gilman, H. and Schulze, F., J. Am. Chem. Soc., 47, 2002 (1925).

21. Shriner, R. L. and Fuson, R. C., "Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, New York, N. Y., 1948.

22. Sherrill, M. L., Baldwin, C. and Hass, D., J. Am. Chem. Soc., 51, 3036 (1929).

23. Ellis, L. M., Jr. and Reid, E. E., J. Am. Chem. Soc., 54, 1678 (1932).

24. Sutter, P., Helv. Chim. acta, 21, 1269 (1938).

25. Brunel, R. F., J. Am. Chem. Soc., 45, 1337 (1923).

26. Cymerman, J., Heilbron, I. M. and Jones, E. R. H., J. Chem. Soc., 90 (1945).

27. Levene, P. A. and Marker, R. E., J. Biol. Chem., 91, 76 (1931).

28. Rohen, W., Ann., 190, 309 (1878).

29. Tuot, M., Compt. rend., 202, 1339 (1936).

30. Whitmore, F. C. and Homeyer, A. H., J. Am. Chem. Soc., 55, 4194 (1933).

31. Malone, G. B. and Reid, E. E., J. Am. Chem. Soc., 51, 3426 (1929).

32. Blaise, E. E., Compt. rend., 134, 552 (1902).

33. Ribas, I. and Tapia, E., Anales soc. espan. fis. quim., 30, 944 (1932).

JUL 6 - '53

CHEMISTRY LIBRARY 273695
T547.3
T561
Tiefenthal

CHEMISTRY LIBRARY
T547.3 273695
T561
Tiefenthal

The reaction of propylene oxide with various alkylmagnesium chlorides.

JUL 6 - '53

MICHIGAN STATE UNIVERSITY LIBRARIES
3 1293 02363 9945