THE REACTION OF PROPYLENE OXIDE WITH ORGANOMAGNESIUM BROMIDES

by

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C. O. Bostwick

CONTENTS

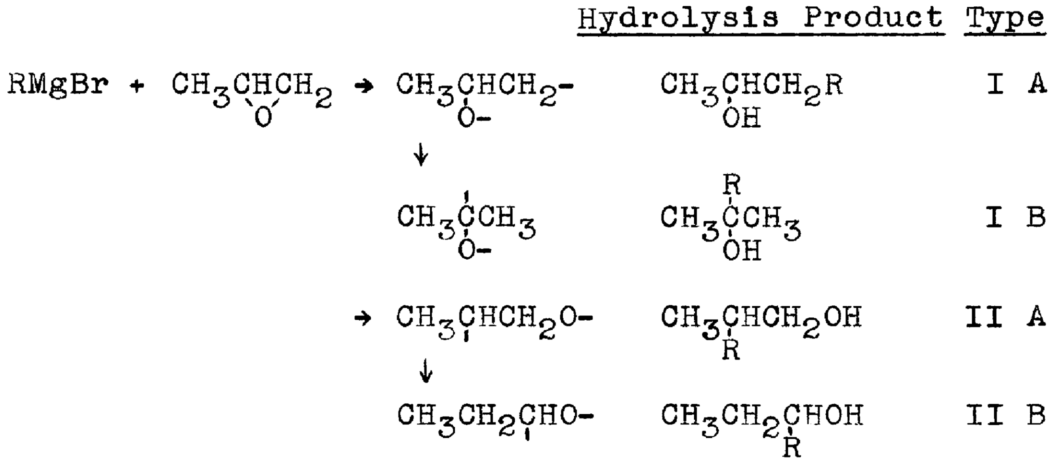
INTRODUCTION

In 1907, Louis Henry reported his studies on the reaction of propylene oxide and ethylmagnesium bromide. Since that date, little has been published on studies of the reaction itself although the method has been used occasionally to prepare the alcohol products.

The purpose of this investigation was to study the reaction of propylene oxide with several organomagnesium bromides. This was done by varying the conditions of reaction and amounts of reagents, investigating intermediate compounds present before hydrolysis, and carrying out other reactions that would throw light on the reaction between propylene oxide and Grignard reagents.

HISTORICAL

In 1907 Louis Henry (1) pointed out that several different alcohols were possible as products when propylene oxide reacted with ethylmagnesium bromide. It depended on how the epoxide split and whether or not rearrangement occured before the product was obtained.



$$\begin{array}{llllc}
 & & & \underline{\text{Hydrolysis Product}} & \underline{\text{Type}} \\
RMgBr + CH_3\underset{\diagdown O \diagup}{CHCH_2} & \rightarrow & CH_3\underset{O-}{CH}CH_2- & CH_3\underset{OH}{CH}CH_2R & \text{I A} \\
 & & \downarrow & & \\
 & & CH_3\underset{O-}{\overset{|}{C}}CH_3 & CH_3\underset{OH}{\overset{R}{C}}CH_3 & \text{I B} \\
 & \rightarrow & CH_3\underset{|}{C}HCH_2O- & CH_3\underset{R}{C}HCH_2OH & \text{II A} \\
 & & \downarrow & & \\
 & & CH_3CH_2\underset{|}{C}HO- & CH_3CH_2\underset{R}{C}HOH & \text{II B}
\end{array}$$

With ethylmagnesium bromide, Henry obtained 60% 2-pentanol (Type I A reaction) on hydrolysis.

Later, Levene and Walti (2) obtained Type I A optically active alcohols with no Walden inversion when optically active propylene oxide was reacted with n-propyl, iso-propyl, and phenyl magnesium bromides.

The action of propylene oxide on ethylmagnesium bromide was studied again in 1936 by Norton and Hass (3). Although they obtained about

11% alcohol (using 1 mole of epoxide to 1 mole of Grignard reagent and then heating), it appeared to be mainly 3-pentanol (compared to commercial 3-pentanol) indicating a Type II B reaction. With diethylmagnesium, however, they obtained 23% 2-pentanol (Type I A reaction).

1-Phenyl-2-propanol was prepared by Newman (4) in 1940 in a 60% yield by refluxing, for 20 hours, a slight molar excess of propylene oxide with phenylmagnesium bromide.

A survey of the literature showed that the majority of aliphatic monosubstituted ethylene oxides appear to give alcohols resulting from Type I A reaction (5). Occasional conflicts of data may be due to different conditions of reaction and subsequent treatment. Styrene oxide exhibits both Type II A and B reactions (6).

In their Grignard reactions with 2,3-epoxybutane, Cottle and Powell (7) found, besides Type I A alcohol, some of the alcohol formed by the addition of the Grignard reagent to methyl ethyl ketone (Type I B alcohol). Upon further investigation, they found that they could obtain this ketone in large yields from the magnesium alcoholate of 3-bromo-2-butanol when it was allowed to warm to room temperature. Decomposition and rearrangement of bromohydrin intermediates were previously noted by Godchot and Cauquil (8) and Bedos (9).

Ketones and aldehydes formed by decomposition and rearrangement of the magnesium alcoholates of the halohydrins account for the alcohols found when the Grignard reactions appear to go by Type I B or II B addition. This explanation appears reasonable since all the reported reactions of epoxides with dialkylmagnesium compounds indicate only Type I A or II A addition even when the reaction mixture is refluxed (3)(6)(10)(11).

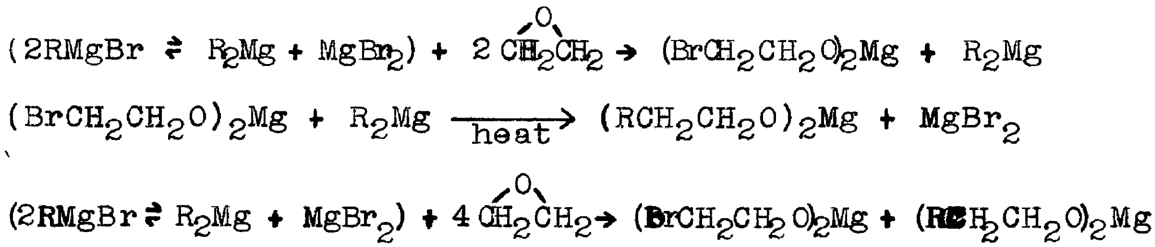
Most of the published data seems to indicate greater reactivity of epoxides with the bromo-magnesium bond than with the alkyl-magnesium bond if the temperature is kept low during addition of the epoxide and the reaction mixture is not heated before hydrolysis. This greater reactivity is indicated by large yields of bromohydrin and small yields of alcohol when the ratio of reactants is 1:1 (12).

The aryl-magnesium bond reacts with greater rapidity and the yield of alcohol may even be greater than the bromohydrin yield with a 1:1 ratio of reactants.

The magnesium alcoholate of ethylene bromohydrin reacts with dialkylmagnesium to give the primary alcoholate formed by replacement of the bromine by the alkyl (11). If any rearrangement of the bromohydrin intermediate to acetaldehyde occurs, it occurs at a much slower rate than the formation of the primary alcohol intermediate. With many of the substituted ethylene oxides, rearrangement of the magnesium alcoholate of the bromohydrin to the aldehyde or ketone followed by other reactions, such as addition of the alkyl-magnesium bond, seems to occur more easily than replacement of the bromine by alkyl on the bromohydrin intermediate (7)(6).

THEORETICAL

Blaise (12), Ribas and Tapia (13), and Huston and Agett (11) successively developed the theoretical aspects of the reaction of ethylene oxide with organomagnesium bromides.



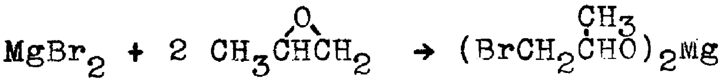
$$(2RMgBr \rightleftharpoons R_2Mg + MgBr_2) + 2\,\overset{O}{CH_2CH_2} \rightarrow (BrCH_2CH_2O)_2Mg + R_2Mg$$

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

$$(2RMgBr \rightleftharpoons R_2Mg + MgBr_2) + 4\,\overset{O}{CH_2CH_2} \rightarrow (BrCH_2CH_2O)_2Mg + (RCH_2CH_2O)_2Mg$$

On hydrolysis, the first reaction yields mainly bromohydrin, the second (after refluxing with benzene) mainly alcohol, and the third large amounts of bromohydrin and alcohol. Analysis of the precipitated intermediate indicated formation of $(BrCH_2CH_2O)_2Mg$ (11). While the oxonium type intermediates, as proposed by Grignard (14) and supported by Meisenheimer (15), may play some part in the reaction, they probably exist but for a brief instant.

For the reaction of propylene oxide with magnesium bromide etherate, an intermediate similar to that formed with ethylene oxide, has been found to exist.



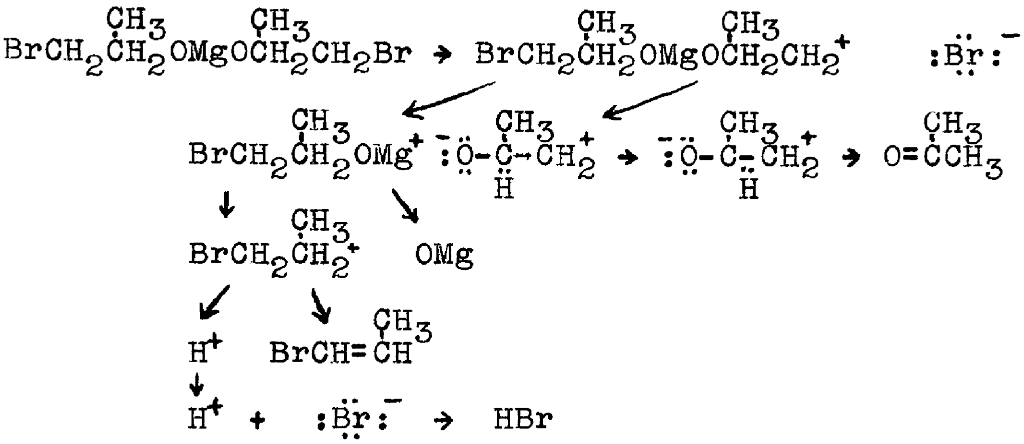
$$MgBr_2 + 2\,CH_3\overset{O}{CHCH_2} \rightarrow (BrCH_2\overset{CH_3}{CHO})_2Mg$$

The magnesium alcoholate of the bromohydrin seemed to be rather soluble in the presence of excess magnesium bromide as evidenced by the necessity of having to add over half of the theoretical amount of propylene oxide to the magnesium bromide before precipitation occured. With all of the organomagnesium bromides, no precipitation took place when the ratio of reactants was 1:1. When the bromohydrin intermediate was prepared by adding one or two moles of propylene bromohydrin to one mole of diethylmagnesium in ether and benzene, precipitation occured immediately.

Both heat and excess magnesium bromide (in ether - benzene solutions) caused decomposition of the magnesium alcoholate of the bromohydrin (Table I).

Hydrolysis of the dry precipitate, by acid and strong and weak bases, was also studied and compared with pure distilled bromohydrin (Tables II and III). When the dried bromohydrin magnesium alcoholate was heated in a dry nitrogen atmosphere, it first melted and then acetone, HBr, and what appeared to be $CH_3CH=CHBr$ (from its boiling point and refractive index), distilled from the flask. Some tar was also formed. Heating to 500°C in air gave pure MgO. The following mechanism is proposed for the decomposition of the propylene bromohydrin magnesium alcoholate on heating.

Polymerization of the intermediate carbonium ions may occur.



$BrCH_2\overset{CH_3}{C}H_2OMgO\overset{CH_3}{C}H_2CH_2Br \rightarrow BrCH_2\overset{CH_3}{C}H_2OMgO\overset{CH_3}{C}H_2CH_2^+ \quad :\ddot{Br}:^-$

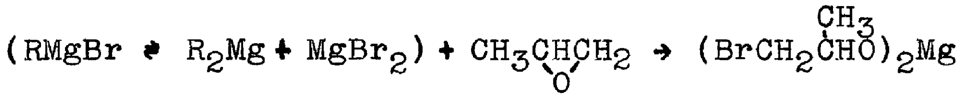
$BrCH_2\overset{CH_3}{C}H_2OMg^+ \; :\ddot{O}^- - \underset{H}{\overset{CH_3}{C}} - CH_2^+ \rightarrow :\ddot{O}^- - \underset{H}{\overset{CH_3}{C}} - CH_2^+ \rightarrow O{=}\overset{CH_3}{C}CH_3$

$BrCH_2\overset{CH_3}{C}H_2^+ \quad OMg$

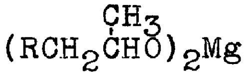
$H^+ \quad BrCH{=}\overset{CH_3}{C}H$

$H^+ + :\ddot{Br}:^- \rightarrow HBr$

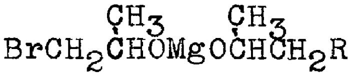
The mechanism proposed for the reaction of propylene oxide with organomagnesium bromides follows. It is felt that a large shift in the Schlenk equilibrium is not necessary.



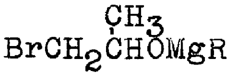
$(RMgBr \rightleftharpoons R_2Mg + MgBr_2) + CH_3\underset{O}{CHCH_2} \rightarrow (BrCH_2\overset{CH_3}{C}HO)_2Mg$ (1)



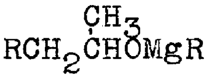
$(RCH_2\overset{CH_3}{C}HO)_2Mg$ (2)



$BrCH_2\overset{CH_3}{C}HOMgO\overset{CH_3}{C}HCH_2R$ (3)



$BrCH_2\overset{CH_3}{C}HOMgR$ (4)



$RCH_2\overset{CH_3}{C}HOMgR$ (5)

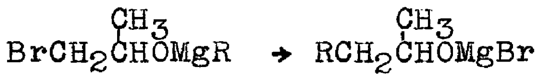
$RMgBr$ (6)

R_2Mg (7)

$MgBr_2$ (8)

When the ratio of reactants is 1:1, for alkylmagnesium bromides, the first, fourth, and seventh intermediates are present in large amounts. The unreacted magnesium bromide present is equivalent to the amount of alkyl which reacted. When the ratio is 1:2 for the more reactive alkylmagnesium bromides, the first three intermediates are present in relatively large amounts.

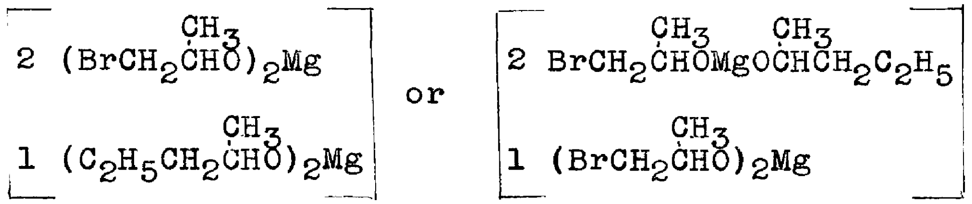
Upon standing for a length of time, the intermediates, present in the 1:1 ratio Grignard reaction mixture, tend to rearrange and produce more secondary alcohol at the expense of the bromohydrin. It may be due to reaction of the dialkylmagnesium and the bromohydrin magnesium alcoholate or more likely, the rearrangement of one of the other intermediates such as the following.



$$\mathrm{BrCH_2\overset{CH_3}{C}HOMgR} \rightarrow \mathrm{RCH_2\overset{CH_3}{C}HOMgBr}$$

Evidence of this was found in the reaction of one mole of propylene bromohydrin with one mole of diethylmagnesium over a period of four days to give some 2-pentanol on hydrolysis. A slight increase in secondary alcohol yield, at the expense of bromohydrin yield, was noticable when the 1:1 reaction mixture of ethylmagnesium bromide and propylene oxide was allowed to stand 2 days at room temperature as compared to 5½ hours cooled in ice (Table IV).

Before the reaction mixture of one mole of ethylmagnesium bromide and two moles of propylene oxide could set to a hard solid (after 20 hours), it was separated and dried to a white powdery solid. On analysis it appeared to be composed of either of two mixtures, the latter being favored by the Schlenk equilibrium.



$$\left[\begin{array}{l} 2\ (\mathrm{BrCH_2\overset{CH_3}{C}HO})_2\mathrm{Mg} \\ 1\ (\mathrm{C_2H_5CH_2\overset{CH_3}{C}HO})_2\mathrm{Mg} \end{array}\right] \text{ or } \left[\begin{array}{l} 2\ \mathrm{BrCH_2\overset{CH_3}{C}HOMgO\overset{CH_3}{C}HCH_2C_2H_5} \\ 1\ (\mathrm{BrCH_2\overset{CH_3}{C}HO})_2\mathrm{Mg} \end{array}\right]$$

Analysis of dry precipitate. Calc'd: Br, 39.1, Mg, 9.23
Found : Br, 36.0, Mg,10.07

Analysis of hydrolyzed dry precipitate.

Moles calc'd: Bromohydrin, 4 ; 2-pentanol, 2
Moles found : Bromohydrin, 3.5; 2-pentanol, 2

However, when the reaction of the magnesium bromide alcoholate of 2-pentanol (prepared from the alcohol and ethylmagnesium bromide) with propylene oxide was carried out, no precipitate was obtained, but a stiff gel. On hydrolysis, a 60% yield of bromohydrin was obtained.

Evolution of gases, among which was identified the unsaturated hydrocarbon corresponding to the Grignard reagent used, were noticable with all of the 1:2 ratio reactions and some of the 1:1 reactions. In most cases considerable amounts were still being evolved after 2 days. Cooling with ice stopped the evolution of gases. Where these gases were observed in greatest amounts, the yield of bromohydrin was usually abnormally low. This evidence indicates some unknown reaction between the unreacted organomagnesium and perhaps the bromohydrin magnesium alcoholate. This reaction does not increase the alcohol yield as the organic radical is lost in the gaseous products.

EXPERIMENTAL

Reagents:

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

Organic Bromides. Eastman Kodak Co. and Columbia Chemicals Co. Dried over anhydrous $CaCl_2$ for at least one week and fractionated slowly through a glass helix packed column with a total reflux, partial take-off,head. Purified bromides distilled over a $\frac{1}{2}$ to 1°C range. Stored in glass stoppered amber bottles in the dark.

Magnesium. Dow magnesium turnings for Grignard reactions.

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

Benzene. Thiophene free and anhydrous. Distilled to remove moisture for Grignard reactions.

Bromine. Dried by shaking with concentrated H_2SO_4.

Dioxane. Dried over sodium.

Sodium Sulfate. Anhydrous, C.P.

Ammonium Bromide. C.P.

Silver Nitrate Solution, .1 N. Prepared from Analytical Grade $AgNO_3$.

Potassium Thiocyanate Solution, about .1 N.

Standardized against .1 N. $AgNO_3$.

Hydrochloric Acid Solution, about .2 N.

Standardized against .2 N. NaOH.

Sodium Hydroxide Solution, about .2 N.

Standardized against sulfamic acid.

Apparatus:

For the preparation of Grignard reagents and magnesium bromide etherate, reactions with propylene oxide, and NaOH reaction with the bromohydrin, a 2 liter, three necked, round bottom flask, fitted with a condenser, mercury seal stirrer, and a Hershberg dropping funnel or separatory funnel, was used. A nitrogen gas inlet was provided for all reactions except reaction with NaOH solution. All Grignard reagents and magnesium bromide etherates were protected from atmospheric moisture and CO_2 by $CaCl_2$ and soda-lime tubes.

For all distillations a heated glass helix packed column 12¼ in. long was used. The head was of the total reflux, partial take-off, type. The pot was heated with a Glas-col mantle.

REACTION OF ORGANOMAGNESIUM BROMIDES WITH ONE OR TWO MOLES OF PROPYLENE OXIDE.

Preparation of Grignard reagents:

One mole of redistilled organic bromide was mixed with 150 ml. of anhydrous ether. Twenty-six grams of magnesium and 100 ml. of ether were placed in the reaction flask. Ten to fifteen milliliters of the bromide - ether solution were added and the magnesium stirred until reaction started. The aromatic bromides sometimes required refluxing to start the reaction. Two hundred and twenty-five milliliters of ether were then added to the reaction and the remainder of the bromide - ether solution added dropwise. The Grignard reagent was stirred for over an hour after all of the bromide was in and then allowed to stand under a nitrogen atmosphere over-night.

The aryl and normal alkyl Grignard reagents were prepared by adding the bromide mixture to the uncooled magnesium and ether as fast as the condenser, and ice placed on top of the flask, would allow. The yield of Grignard reagent was over 90%.

Secondary and iso-alkyl Grignard reagents were prepared by adding the ether - bromide mixture more slowly and not allowing the reaction mixture to get above 35°C. The yield of Grignard reagent with iso-propyl, sec-butyl, and iso-butyl bromide was between 85 and 90%.

Tert-butylmagnesium bromide was prepared in 50 to 55% yields from the same proportion and quality of reagents. The reaction mixture was cooled in a mixture of salt and ice and the ether - bromide solution added very slowly.

Analysis of the Grignard reagent:

The Grignard reagent was forced through a glass wool plug from the unreacted magnesium by nitrogen pressure. Its volume was measured in a 500 ml. graduated cylinder.

Five milliliters were pipeted out and analyzed for the organomagnesium content by Gilman's procedure (17).

One milliliter was pipeted out and analyzed by the Volhard method for bromide ion (18).

Reaction with propylene oxide:

The Grignard reagent was poured, under a stream of nitrogen, into the reaction flask filled with nitrogen.

When the ratio of reactants was to be 1:1, the amount of propylene oxide was based on the bromide ion titration.

The sum of the number of moles of bromide ion and organic radical was used for calculation of the grams of propylene oxide to be used where the desired ratio was 1:2.

The Grignard reagent was cooled in salt and ice and a mixture of propylene oxide and an equal volume of ether added slowly. The salt and ice bath was allowed to warm up to room temperature and removed the next day.

When the ratio of reactants was 1:1, the reaction was allowed to stand for 2 days. With the 1:2 ratio reactions, the reaction mixture was allowed to stand until the test with Michler's ketone was faint or negative.

Hydrolysis:

The reaction mixture was cooled with ice and then 150-200 ml. of saturated ammonium bromide solution was added dropwise (19). The ether solution was decanted from the precipitated magnesium salts and dried over anhydrous Na_2SO_4. Water was added to the magnesium salts until they were pasty. This paste was extracted with benzene to obtain any remaining product.

Analysis for bromohydrin yield:

The dried hydrolysis products were refluxed with a mixture of 40 g. NaOH (stirred $\frac{1}{4}$ hour) and 150 ml. of water (added slowly) for 1 hour, with vigerous stirring. The mixture was cooled and the layers separated. The water layer was extracted with benzene. The benzene and ether extracts were dried over anhydrous Na_2SO_4. The NaOH layer was heated to boiling to expell excess benzene, cooled, and diluted to 1 liter. A 5 ml. aliquot portion was titrated for bromide ion by the Volhard method.

Analysis for alcohol yield:

The ether - benzene solution of products was distilled at atmospheric pressure until all of the ether and nearly all of the benzene was removed. For most of the alcohols, reduced pressure was used to prevent decomposition.

Calculation of percentage yields:

The bromohydrin yield was found by taking the ratio of the moles of bromide ion found in the analysis of the hydrolyzed reaction mixture to the moles of bromide ion found in the unreacted Grignard reagent.

The alcohol yield was calculated by taking the ratio of the number of moles of alcohol distilled to the number of moles of organic radical present in the unreacted Grignard reagent.

Derivatives:

The 3,5-dinitrobenzoates were made by using pyridine and 3,5-dinitrobenzoyl chloride (20). Another method was developed for any type of alcohol (primary, secondary, tertiary) or phenol which made use of ethylmagnesium bromide. The alcohol must not contain any contaminant that forms other alcoholates with the Grignard reagent. Care must also be exercised not to oxidize the Grignard reagent before reaction with the alcohol. After the slight excess of alcohol had been added to the cooled Grignard reagent (evolution of ethane ceased), ½ to 1 g. of 3,5-dinitrobenzoyl chloride (or other acid chloride) was added. The tube was stoppered with a $CaCl_2$ tube and allowed to stand over-night (or longer - if the alcoholate was slow in reacting).

$$ROH + C_2H_5MgBr \rightarrow ROMgBr + C_2H_6\uparrow$$

$$ROMgBr + R'COCl \rightarrow MgBrCl + R'COOR$$

Water was added to precipitate the magnesium salts and the ether layer filtered off and evaporated. If the derivative was not too soluble in ether, the residue was extracted with some other hot solvent. The ester was then handled in the usual manner.

Alpha-naphthylurethanes were prepared from alpha-naphthyl isocyanate using a drop of trimethylamine - ether solution as catalyst (20).

As further proof, the secondary alcohols were oxidized to ketones with a saturated solution of $KMnO_4$ in 1 to 6 N. H_2SO_4 and filtered. The 2,4-dinitrophenylhydrazones were made by adding this filtrate to 3 ml. of a solution of 2.4 g. of 2,4-dinitrophenylhydrazine in a mixture of 80 ml. of water and 40 ml. of 72% perchloric acid (21). The semicarbazones were made by separating the ketone from the water and using the method for water insoluble ketones (20).

PREPARATION OF PROPYLENE BROMOHYDRIN AND BROMOHYDRIN MAGNESIUM ALCOHOLATE FROM MAGNESIUM BROMIDE ETHERATE.

Preparation of magnesium bromide etherate:

Twenty-nine grams of magnesium were placed in the reaction flask and covered with 500 ml. of ether. One hundred sixty grams (26 ml.) of bromine was added dropwise. After all of the bromine had been added, the reaction mixture was refluxed for an hour and allowed to stand over-night. The magnesium bromide solution was removed from the excess magnesium by nitrogen pressure through a glass wool plug, measured, and titrated for bromide ion by the Volhard method as described under the analysis of the Grignard reagents.

Reaction of magnesium bromide etherate with 2 mole equivalents of propylene oxide:

The magnesium bromide solution was poured into a flask filled with nitrogen and then cooled in a salt and ice bath. A mixture of the propylene oxide and an equal volume of ether was then added slowly.

Analysis of the bromohydrin magnesium alcoholate:

Two hours after addition of all the epoxide, the precipitate was placed in centrifuge bottles, stirred with anhydrous ether, and centrifuged. The ether layer was decanted and the process of washing repeated. The precipitate was dried in a vacuum desiccator over anhydrous $CaCl_2$ for several days at 12 mm. or less. The amount of bromine was determined by the Parr Bomb method (22), and by NaOH reaction and Volhard titration. Ignition of the precipitate in a muffle furnace at 500°C left MgO, from which the percent of magnesium was calculated.

Calc'd for $C_6H_6Br_2MgO_2$: Br, 53.2; Mg, 8.1
Found : Br, 51.7; Mg, 8.5

Hydrolysis of the precipitate and distillation of the bromohydrin:

Two hours after addition of the propylene oxide to the magnesium bromide, the reaction mixture was cooled in ice and 150 to 200 ml. saturated ammonium bromide solution added slowly. The ether - benzene solution was decanted from the precipitated magnesium salts and dried over anhydrous Na_2SO_4. The ether and fractions up to the boiling point of the benzene were removed. The remainder of the benzene was taken off at reduced pressure and the propylene bromohydrin fractionated at 12 to 15 mm.

Proof of structure of the bromohydrin:

Oxidation, with a saturated $KMnO_4$ solution in 6 N. H_2SO_4, gave a derivative which formed a 2,4-dinitrophenylhydrazone.

Conversion of the bromohydrin to acetol, by the method of Levene and Walti (16), proved the structure to be 1-bromo-2-propanol. Acetol derivatives were made and checked the literature values for their melting points.

REACTION PRODUCTS OF DIETHYLMAGNESIUM AND PROPYLENE BROMOHYDRIN.

Preparation of diethylmagnesium:

Two moles of ethylmagnesium bromide were prepared in the usual way. The bromine containing compounds were precipitated by slowly adding 175 ml. dioxane mixed with 200 ml. of benzene to the cooled Grignard reagent (23). The heavy precipitate was separated from the solution of diethylmagnesium by centrifuging. The strength was determined by the Gilman procedure (17).

Reaction of diethylmagnesium with two mole equivalents of bromohydrin:

The calculated amount of bromohydrin was mixed with 200 ml. of benzene, placed in the reaction flask, and cooled with ice. The diethylmagnesium solution was added from the dropping funnel. The resulting white solid (which formed immediately) was washed with ether by centrifuging and dried in a vacuum desiccator under reduced pressure. The analyses for bromine and magnesium were carried out as before.

Calc'd for $C_6H_6Br_2MgO_2$: Br, 53.2; Mg, 8.1
Found : Br, 51.2; Mg, 8.5

Reaction of diethylmagnesium with one mole equivalent of propylene bromohydrin:

The diethylmagnesium solution was placed in the reaction flask and the bromohydrin, mixed with an equal volume of benzene, was added slowly. A white precipitate formed. The reaction mixture was allowed to stand 4 days, refluxed 6 hours, and hydrolyzed. Part of the bromohydrin was recovered along with some alcohol. On oxidation, the alcohol gave 2-pentanone which was checked by a mixed melting point of its 2,4-dinitrophenylhydrazone with a known derivative.

Table I

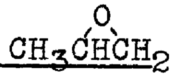
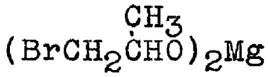
Moles $MgBr_2$	Moles  $CH_3\overset{O}{\widehat{CHCH_2}}$	Temperature	Time	%Bromohydrin
1	$1\frac{1}{2}$	Reflux, C_6H_6	7 hours	24
1	2	Reflux, C_6H_6	7 hours	58
1	2	Reflux, C_6H_6	4 hours	64
1	2	Ice bath	2 hours	80

Table II



Stability of dried $(BrCH_2\overset{CH_3}{C}HO)_2Mg$ towards various bases.

Treatment before titration by Volhard method	%Bromine
Dissolved in HNO_3	8.0
Dissolved in water and HNO_3 added	13.0
Dissolved in NaOH, boiled, cooled, HNO_3 added	51.2
Decomposed by Parr Bomb method	51.1
Theoretical	53.2

Table III

Stability of propylene bromohydrin towards various bases.

Treatment before titration by Volhard method	%Bromine
Dissolved in HNO_3	.6
Dissolved in water, heated, cooled, HNO_3 added	7.0
Dissolved in water and MgO, HNO_3 added	12.0
Dissolved in NaOH, heated, cooled, HNO_3 added	56.8
Theoretical	57.0

Table IV

Reaction of 1 mole of ethylmagnesium bromide and 1 mole of propylene oxide under various conditions.

Conditions	Time	%Bromo-hydrin	% Alcohol
1.Grignard reagent mixed with equal volume of mesitylene and cooled in ice and salt during addition.	1½ hour		
Refluxed.	2 hours		
Ether distilled off.	1½ hour		
Temperature rose rapidly from 80 to 150°C. Cooled quickly.		0	23.*
2.Grignard reagent cooled in ice during addition.	2 hours		
Ether distilled off, replaced with benzene and refluxed.	6 hours		
Room temperature.	17 hours	10.	22.*
3.Grignard reagent cooled in ice and salt during addition.	2 hours		
Refluxed with an equal volume of benzene added.	4 hours	59.	9.*
4.Grignard reagent heated to reflux with equal volume of benzene added during addition of epoxide.	2 hours		
Kept warm.	3 hours	56.	14.*
5.Grignard reagent cooled in ice and salt during addition.	1½ hour		
Kept in ice bath.	4 hours	68.	5.
6.Grignard reagent cooled in ice and salt during addition.	2 hours		
Allowed to come slowly to room temperature and remain.	2 days	62.	13.

* Includes tertiary alcohol

Table V

Reaction of 2 moles of propylene oxide with 1 mole of ethylmagnesium bromide under various conditions.

Conditions	Time	%Bromo-hydrin	% Alcohol
1.Grignard reagent cooled in ice and salt during addition.	1½ hour		
Ice removed and mixture allowed to warm up and reflux gently without applied heat.	1½ hour	80.	45.
2.Grignard reagent cooled in ice and salt during addition.	1½ hour		
Kept in ice.	2 hours		
Allowed to warm to room temperature and refluxed gently with applied heat.	4½ hour	74.	55.*
3.Grignard reagent cooled in ice and salt during addition.	1½ hour		
Kept in salt and ice.	2 hours	76.	15.
4.Grignard reagent cooled in ice and salt during addition.	1½ hour		
Cooling bath allowed to thaw and come slowly to room temperature.	1½ days	76.	54.

* Includes some tertiary alcohol.

Table VI

Yields of alcohols formed by the reaction of propylene oxide with organomagnesium bromides.

Grignard reagent prepared from	RMgBr + $CH_3\overset{O}{CHCH_2}$ 2 days		RMgBr + 2 $CH_3\overset{O}{CHCH_2}$		
	% yield Bromohydrin	% yield Alcohol	Time days	% yield Bromohydrin	% yield Alcohol
Ethyl bromide	62	13	2	76	54
n-Propyl bromide	69	4	6	74	51
iso-Propyl bromide	50	7	7	76	38
n-Butyl bromide	67	5	8	70	56
sec-Butyl bromide	62	4	21	62	31
iso-Butyl bromide	64	4	25	28	15
tert-Butyl bromide	62	4	44	52	15
Phenyl bromide	39	47	1	74	67
Mesityl bromide	35	58			

Table VII

Physical constants of the alcohols.

Alcohol	n_D^{20}	B.P. °C		Ref.
1-Bromo-2-propanol	1.4801	49.6	(12mm.)	16, 24
2-Pentanol	1.4068	118.8	(745mm.)	3
2-Hexanol	1.4155	139.5	(740mm.)	25
4-Methyl-2-pentanol	1.4120	68	(52mm.)	26, 27
2-Heptanol	1.4214	77	(24mm.)	27
4-Methyl-2-hexanol	1.4223	85.5	(44mm.)	28
5-Methyl-2-hexanol	1.4227	73	(32mm.)	29
4,4-Dimethyl-2-pentanol	1.4248	65	(40mm.)	30
1-Phenyl-2-propanol	1.5221	95	(7mm.)	4, 6, 27
1-Mesityl-2-propanol	1.5282	137	(9mm.)	

Table VIII

Derivatives of the alcohols and corresponding ketones.

	M.P. °C	Ref.	
1-Bromo-2-propanol			
3,5-dinitrobenzoate	85-87	24	
alpha-naphthylurethane	116-116.5		a
2,4-dinitrophenylhydrazone	128		a
2-Pentanol			
3,5-dinitrobenzoate	59-61	3	
alpha-naphthylurethane	75	27	
2,4-dinitrophenylhydrazone	143-145	27	*
2-Hexanol			
3,5-dinitrobenzoate	36-37	31	
2,4-dinitrophenylhydrazone	106-108	27	*
4-Methyl-2-pentanol			
3,5-dinitrobenzoate	61-62	31	
alpha-naphthylurethane	94-95.5	2	a
2,4-dinitrophenylhydrazone	91-92	27	*
2-Heptanol			
3,5-dinitrobenzoate	47.5-48.5	27	
2,4-dinitrophenylhydrazone	72.5-73.5		*
4-Methyl-2-hexanol			
3,5-dinitrobenzoate	62.5-63.5	28	a
semicarbazone	128-129	28	*
5-Methyl-2-hexanol			
3,5-dinitrobenzoate	34-36		a
2,4-dinitrophenylhydrazone	94-96	27	

	M.P. °C	Ref.
4,4-Dimethyl-2-pentanol		
3,5-dinitrobenzoate	48-50	30
1-Phenyl-2-propanol		
alpha-naphthylurethane	88-89.8	6
semicarbazone	193	27
1-Mesityl-2-propanol		
3,5-dinitrobenzoate	153.8-154.8	a
alpha-naphthylurethane	114.8-115.2	a
semicarbazone	206-206.5	

* Checked by a mixed M.P. with a known derivative.

a Analyzed for nitrogen content (Table IX).

Table IX

Analyses of new derivatives for nitrogen by the Micro Kjeldahl method (32).

	% N Calc'd	% N Found
1-Bromo-2-propanol		
alpha-naphthylurethane	4.54	4.33
1-Bromo-2-propanone		
2,4-dinitrophenylhydrazone	17.66	17.56
4-Methyl-2-pentanol		
alpha-naphthylurethane	5.16	4.96
4-Methyl-2-hexanol		
3,5-dinitrobenzoate	9.03	9.09
5-Methyl-2-hexanol		
3,5-dinitrobenzoate	9.03	8.97
1-Mesityl-2-propanol		
3,5-dinitrobenzoate	7.42	7.36
alpha-naphthylurethane	3.97	3.84

DISCUSSION

Attempts to bring about the interchange of the organic Grignard radical for the bromine on the bromohydrin intermediate by heating (Table IV), caused only a slight increase in alcohol percent, this increase being largely made up of tertiary alcohol (as evidenced by boiling point and refractive index). Excessive heating caused violent reaction with total loss of bromohydrin and only a slight increase in total alcohol percent (Table IV, reaction 1.). The tertiary alcohol probably resulted from the reaction of the Grignard reagent with the acetone, formed from decomposition of the bromohydrin intermediates.

With a 1:2 ratio of reactants, many of the alkylmagnesium bromides required considerable time for complete reaction at room temperature, as evidenced by a positive Michler's ketone test (17). Tert-butylmagnesium bromide, for example, gave a positive test after standing for a month. On the other hand, phenylmagnesium bromide was completely reacted in 20 hours. In all cases, the 1:2 ratio of reactants gave a very stiff gel or a very hard solid, the time depending on the reactivity of the Grignard reagent.

Some uncertainty in the percent yield of bromohydrin, reported for the various Grignard and magnesium bromide reactions, is indicated in the data of Table II. As shown in the titration of the bromohydrin magnesium alcoholate for bromide ion, after placing it directly into acid, a considerable amount of bromohydrin was lost to the basic magnesium compounds even under the best conditions of acid hydrolysis. The use of a saturated ammonium bromide solution, for hydrolysis of the Grignard and magnesium bromide reactions, prevented a greater loss of bromohydrin.

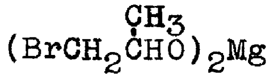
As some doubt may be expressed concerning the addition of ammonium bromide during hydrolysis of the Grignard reaction mixture, it should be pointed out that in the case of the zero percent yield of bromohydrin (Table IV), and the small percent yields of bromohydrin from magnesium bromide under certain conditions (Table I), the analysis was carried out in the same manner without introducing any bromine from this source.

In analyzing the hydrolyzed Grignard for bromohydrin percent, sodium hydroxide reaction, followed by Volhard titration, was used due to the instability of the bromohydrin at elevated distillation temperatures.

In all of the distillations, propylene oxide and acetone were noticable. The former was all attributed to the hydrolysis of the bromohydrin with sodium hydroxide and the latter to the same source and also from the decomposition of the bromohydrin magnesium alcoholate. The acetone was checked by a mixed melting point of its 2,4-dinitrophenylhydrazone. There was also some evidence of some unsaturated bromide. All these, and any water that remained, were removed by low boiling azetropes formed with benzene. Mesityl oxide (identified by the melting point of its 2,4-dinitrophenylhydrazone addition compound) and other unsaturated ketones caused difficulty in separation of some of the alcohols. With several Grignard reactions, a wax-like product was precipitated out of the residue by adding petroleum ether. It had a softening point of 62 - 63°C.

The bromohydrin yield did not vary greatly in the 1:1 ratio reactions of the alkylmagnesium bromides, since they were of nearly the same order of reactivity. The few abnormally low yields of bromohydrin were probably due to higher room temperatures and consequently greater decomposition of bromohydrin intermediate (to acetone and 1-bromopropene?) by the unreacted organomagnesium (which also decomposes). Very little decomposition of this type can occur if the organomagnesium reacts quickly.

SUMMARY

1. Analysis of the precipitate formed from magnesium bromide and propylene oxide or from 1-bromo-2-propanol and diethylmagnesium, indicated formation of  $(BrCH_2\overset{CH_3}{C}HO)_2Mg$.

2. The intermediate reaction products in the reaction of 1 mole of propylene oxide with 1 mole of alkylmagnesium bromide, were predominantly of the bromohydrin-alcoholate type.

3. Heat or time caused no appreciable reaction of bromohydrin magnesium alcoholate with organo-magnesium bond to give substitution of the organic radical for the bromine on the bromohydrin intermediate.

4. Excessive heating of the bromohydrin alcoholate in the presence of Grignard reagent, excess magnesium bromide, or in the dry state, caused formation of acetone. In the dry state, 1-bromo-propene, HBr, and MgO were also formed. When Grignard reagent was present, tertiary alcohol was obtained by reaction with the acetone.

5. All of the alkylmagnesium bromides gave poor (4-15%) yields of methyl alkyl carbinol when the ratio of reactants was 1:1, the major product (50-70%) being 1-bromo-2-propanol. With a 1:2 ratio

of reactants, the normal alkyl Grignard reagents gave methyl alkyl carbinol yields of about 55%, iso-propyl and sec-butyl yields of about 35%, and iso- and tert- butyl yields of about 15%. These reactions also gave large yields of bromohydrin. Arylmagnesium bromides gave carbinol yields of about 50% or more, even with a 1:1 ratio of reactants.

6. Esters of phenols and alcohols of all types (primary, secondary, and tertiary) were made by addition of a slight excess of the alcohol to cold ethylmagnesium bromide, followed by reaction (in the cold) with an acid chloride.

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