THE REACTION OF ETHYLENE OXIDE WITH
SOME ALKYLMAGNESIUM IODIDES

By

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TABLE OF CONTENTS

INTRODUCTION

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Ever since the original reaction of Grignard involving magnesium, these organo-magnesium reactions have been used for a variety of organic synthesis.

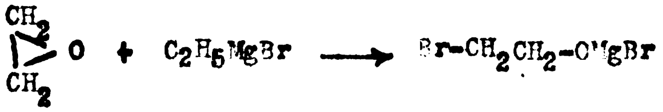
Blaise in 1902 (1) studied the reaction of ethylene oxide with ethyl magnesium bromide. In 1941 Huston and Agett (2) continued this study establishing the mechanism of the reaction. Huston and Langham in 1943 (3) studied a similar reaction using alkylmagnesium chloride solutions with ethylene oxide.

This work was undertaken to compare the reactions of ethylene oxide and alkyl magnesium iodide solutions with those previously studied by Huston and co-workers, and to further substantiate the early work of Meisenheimer (6) by analyzing the precipitate formed when one-half mole of ethylene oxide reacts with one mole of ethyl magnesium iodide.

HISTORICAL

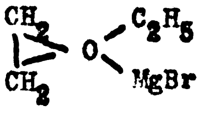
HISTORICAL

The first application in synthetic organic chemistry with the use of magnesium was carried out by Barbier in 1899 (4) using methyl iodide and magnesium in ether with methylheptenone and obtained dimethylheptenol. Blaise (1) applying this principle in 1902 treated ethyl magnesium bromide with ethylene oxide, the principal product obtained was ethylene bromohydrin. He interpreted the results by the following scheme:

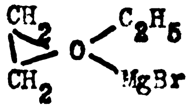


The product of the above reaction upon hydrolysis would give ethylene bromohydrin.

Grignard (5) in 1903 studying the work of Blaise (1) in which ethyl magnesium bromide reacted with ethylene oxide found that after the initial reaction had taken place heating of the addition product, followed by hydrolysis would give n-butanol. He explained the formation of the ethylene bromohydrin through a secondary reaction in which an addition compound was formed as shown by the following formula:

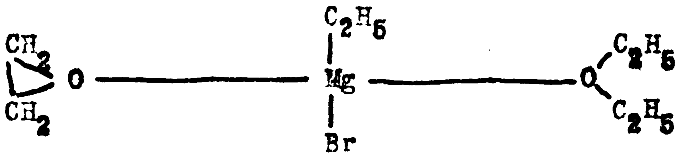


According to Grignard it was the rupturing of this "oxonium salt" by heat with subsequence hydrolysis that produced the n-butanol, as outlined in the next two reactions.

I.  $+ \text{heat} \longrightarrow C_2H_5CH_2CH_2OMgBr$

II. $C_2H_5CH_2CH_2OMgBr + HOH \longrightarrow n\text{-}C_4H_9OH$

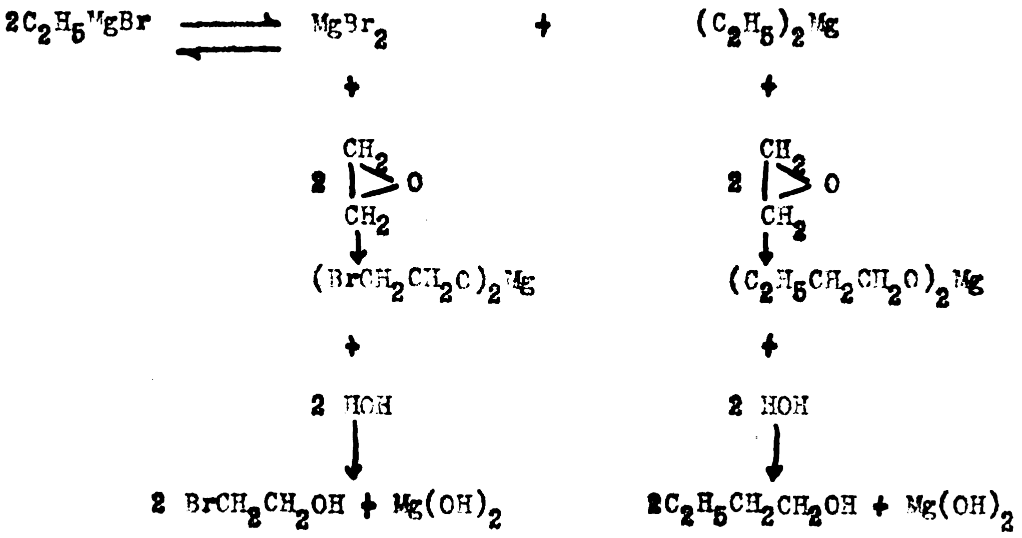
The first analytical data in confirmation of the Grignard explanation of the reaction was given by Meisenheimer (6). He obtained a precipitate from the reaction of ethylene oxide and ethyl magnesium bromide at -21° C. Analyzing the addition product the results correspond to the following assigned formula:



This addition product was kept for several weeks in a vacuum desiccator, at the end of which time it was found not to have changed. When heated on a water bath it decomposed. Analysis showed the compound to have a composition corresponding to the formula, $C_2H_5CH_2CH_2O\text{-}MgBr$ formed as indicated in equation I. This substance when hydrolyzed gave the n-butanol (Equation II).

In 1932 Ribas and Tapia (8) treated ethyl-magnesium bromide with ethylene oxide at -20° C. From their experiments and analysis of the addition product they concluded that it consisted of a mixture of $BrCH_2CH_2OMgBr$ and $(Br\ CH_2CH_2O)_2Mg$.

The principal reaction in this group of experiments was formulated by the following equations:



Huston and Agett (2) in a more comprehensive study of the work of Ribas and Tapia and of Schlenk (6) on the equilibrium:

$$\text{(III)}\quad 2C_2H_5MgBr \rightleftharpoons (C_2H_5)_2Mg + MgBr_2$$

found that if one mole of ethylene oxide was added to one mole of ethylmagnesium bromide, the main reaction was with magnesium bromide:

$$\text{(IV)}\quad MgBr_2 + 2(CH_2)_2O \longrightarrow (BrCH_2CH_2O)_2Mg$$

Hydrolysis of the addition product, without heating, gave 60 to 70 percent yield of ethylene bromohydrin indicating that the reaction had proceeded by equation (IV).

Huston and Agett (2) obtained excellent yields of n-butanol either by heating the reaction mixture:

$$\text{(V)}\quad (C_2H_5)_2Mg + (BrCH_2CH_2O)_2Mg \longrightarrow (C_4H_9O)_2Mg + MgBr_2$$

or by the addition of a second mole of ethylene oxide:

$$(VI)\quad (C_2H_5)_2Mg + 2(CH_2)_2O \longrightarrow (C_4H_9O)_2Mg$$

Hydrolysis of the addition product obtained by (VI) gave a mixture of n-butyl alcohol and ethylene bromohydrin.

Huston and Agett (2) as well as Huston and Langham (3) have shown that the ethylene halohydrin is the product, when the ethylene oxide attacks the magnesium-halide bond. The alcohol is formed when the ethylene oxide attacks the alkyl-magnesium bond. Huston and Langham (3) also showed that when dialkylmagnesium is added to the magnesium alcoholate of the ethylene halohydrin, a primary alcohol is formed.

THEORETICAL

THEORETICAL

The work of Agett (2) and Langham (3) in this laboratory has shown a fundamental difference between bromide and chloride Grignard reagents with ethylene oxide. Using a similar technique developed by the above authors, the writer was able with care to obtain good yields of iodohydrin and n-butyl alcohol.

When using a mole to mole ratio, without heating, the reactions followed are similar to that of the chlorides:

$$\text{(I)} \quad (C_2H_5)_2Mg + 2(CH_2)_2O \longrightarrow (C_4H_9O)_2Mg$$

or

$$\text{(II)} \quad C_2H_5MgI + (CH_2)_2O \longrightarrow C_4H_9OMgI$$

If the reaction follows reaction (II), it would necessitate a subsequent rearrangement:

$$\text{(III)} \quad 2C_4H_9OMgI \longrightarrow (C_4H_9O)_2Mg + MgI_2$$

The hydrolysis of $(C_4H_9O)_2Mg$ would yield the desired n-butyl alcohol.

Ethylene iodohydrin is formed by the reaction of ethylene oxide with the alkyl magnesium iodide reagents:

$$\text{(IV)} \quad MgI_2 + 2(CH_2)_2O \longrightarrow (ICH_2CH_2O)_2Mg$$

$$\text{(V)} \quad (ICH_2CH_2O)_2Mg + 2HOH \longrightarrow 2ICH_2CH_2OH + Mg(OH)_2$$

It has been reported (2) that a good yield of the alcohol may be obtained by treatment of an alkylmagnesium bromide with one mole of ethylene oxide and heating the reaction mixture:

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

Upon hydrolysis of the addition product formed with the bromides and chlorides good yields of the alcohol were obtained. However, the yields were small in the case of the iodides. It was also observed upon standing rapid decomposition of the addition product with the iodides.

The following scheme of reactions might lead one to expect an increase in the yield of alcohol when a reaction mixture of equal moles of ethyl magnesium iodide and ethylene oxide were heated (2).

$$\text{(VII)}\quad 2C_2H_5I + 2Mg \longrightarrow 2C_2H_5MgI \rightleftharpoons (C_2H_5)_2Mg + MgI_2$$

$$\text{(VIII)}\quad MgI_2 + 2(CH_2)_2O \longrightarrow (ICH_2CH_2O)_2Mg$$

$$\text{(IX)}\quad (C_2H_5)_2Mg + (ICH_2CH_2O)_2Mg \longrightarrow (C_4H_9O)_2Mg + MgI_2$$

$$\text{(X)}\quad (ICH_2CH_2O)_2Mg + 2H_2O \longrightarrow 2ICH_2CH_2OH(13.5\%) + Mg(OH)_2$$

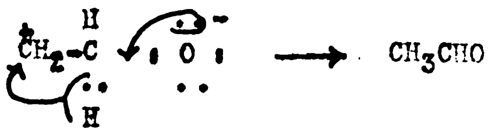
$$\text{(XI)}\quad (C_4H_9O)_2Mg + 2H_2O \longrightarrow 2C_4H_9OH(40\%) + Mg(OH)_2$$

Experiments described here give no evidence of such an increase. One explanation was that the $(ICH_2CH_2O)_2Mg$ might decompose under the influence of heat into MgI_2 and ethylene oxide.

If the addition product $(ICH_2CH_2O)_2Mg$ was allowed to stand for a week or longer, decomposition takes place, and the resulting gas was caught in a container surrounded by dry ice. On analysis the product was identified as acetaldehyde. A possible explanation for the decomposition reaction may be indicated as follows:

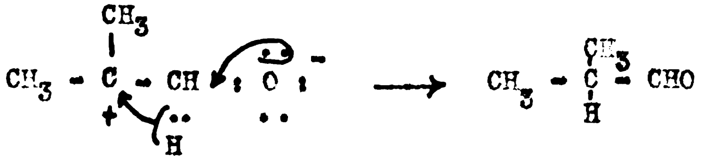
$$\text{(XII)}\quad (ICH_2CH_2O)_2Mg \longrightarrow 2\left[\overset{+}{C}H_2{-}CH_2O^-\right] + MgI_2$$

(XIII)



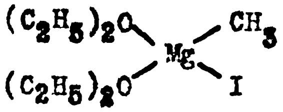
A similar type of transformation for the magnesium dihalohydrin alcoholates was shown by Huston and Bostwick (10), and by Huston and Brault (11).

These investigators, propose the intermediate formation of a protonized double bond. Huston and Brault (11) found that the 2-methylpropanal could be formed only from the magnesium-bromine bond. For such a reaction it was necessary for that ion formed to undergo a preliminary rearrangement to

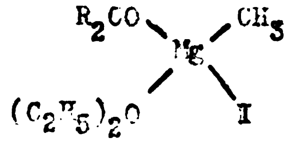


The positive part of the molecule being electrophilic attracts a pair of electrons away from the oxygenated carbon atom. The shifting of the electrons thus results in a shifting of a proton to the new negative carbon with the resultant formation of the methyl group. In turn a pair of electrons from the oxygen shifts to form a carbonyl linkage. The resulting product was an aldehyde. It follows therefore that the percentage of alcohol and iodohydrin would decrease as the yield of aldehydes increases.

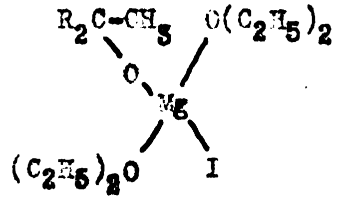
The present work also substantiated the results of Meisenheimer and Casper (6) who state that "The Grignard reactions can be very easily understood if the organic magnesium compounds are regarded as complexes with magnesium functioning as the central atom with a coördination number of four forming,



the alkyl and halogen being bound to the magnesium by principal, the two ether molecules by subsidiary valences. If such a compound is treated with a ketone, aldehyde, etc., the latter possessing far more reaction energy than the ether, replaces one of the ether molecules forming,

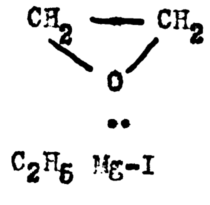


within which there now occurs a shifting of unions, the secondary valence union between the carbonyl oxygen and the magnesium becoming a principal valence union and the alkyl group, displaced from its union with the magnesium by the oxygen, being bound by the principal valence set free at the carbonyl carbon atom, while the coördination position



opened on the magnesium is occupied by ether formation." The formation of this addition product is supported by the observations of Ahrens and Stapler (7).

This verification was brought about by observing the addition of one-half mole of ethylene oxide to one-mole of the Grignard reagent. This reaction resulted in a precipitate formation and analysis showed the composition to correspond to the following formula.



It can be assumed that the ethylene oxide was attached to the magnesium by a weak "subsidiary valence". Upon gentle heating between ninety-two and ninety-four per cent of the ethylene oxide was recovered. Addition of the ethylene oxide up to one-mole, results in the disappearance of the precipitate indicating an increase in the solubility of the addition product. Heating of the solution thus obtained did not give any ethylene oxide showing that the bonding had become complete. This type of behavior is in accordance with the work of Meisenheimer and Casper.

It was further found that the addition of two moles of ethylene oxide to one mole of an alkylmagnesium iodide increased the yield of both the alcohol and iodohydrin. Assuming according to Huston and co-workers (2) and (3) that dialkylmagnesium leads to the formation of the alcohol, the reactions may be represented by the following equations:

(XIII) $R_2Mg + MgI_2 + 4(CH_2)_2O \longrightarrow (RCH_2CH_2O)_2Mg + (ICH_2CH_2O)_2Mg$

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

(XV) $(ICH_2CH_2O)_2Mg + 2H_2O \longrightarrow 2ICH_2CH_2OH + Mg(OH)_2$

However, since the percentage yield of alcohol and iodohydrin are not large enough to indicate the course of the above reactions, it must follow that the treating of the alkylmagnesium iodide with excess ethylene oxide must of necessity attack both the alkylmagnesium bond and the magnesium iodide bond.

(XVI) $C_2H_5MgI + 2(CH_2)_2O \longrightarrow C_2H_5CH_2CH_2OMgOCH_2CH_2I$

(XVII) $C_4H_9OMgOC_2H_4I + 2H_2O \longrightarrow C_4H_9OH + IC_2H_4OH + Mg(OH)_2$

EXPERIMENTAL

EXPERIMENTAL

I. Materials

The following alkyl iodides were prepared by the methods in Organic Syntheses (12):

ethyl iodide
propyl iodide
normal butyl iodide

The methyl iodide, iso-propyl iodide, sec-butyl iodide, and iso-butyl iodide were obtained from the Columbia Organic Chemical Company.

Ethylene oxide was obtained from Dow Chemical Company and dried only for a short period over soda lime. The ethylene oxide was kept in the refrigerator at 5° C.

The magnesium turnings (free from iron) were obtained from the Dow Chemical Company and dried in a desiccator over anhydrous calcium chloride.

Anhydrous ether was dried over sodium ribbon for a period of one week (or until all water was reacted). It was then distilled leaving some of the residue which contained any peroxides. The distillate was also tested at intervals for the presence of peroxides.

The alkyl iodides were fractionated before using for a condensation through a twelve inch Fenske-type column. The alkyl iodides were dried over anhydrous calcium chloride and stored in a dark bottle, in the presence of a few drops of clean mercury (13).

The Grignard reagents prepared and studied were;

methyl magnesium iodide
ethyl magnesium iodide
normal propyl magnesium iodide
iso-propyl magnesium iodide
normal butyl magnesium iodide
sec-butyl magnesium iodide
iso-butyl magnesium iodide

II. Preparation of Grignard Reagents.

A. Preparation of Ethylmagnesium Iodide.

One mole of magnesium turnings was placed in a dry one-liter, three-necked, round-bottom flask.[1] A large reflux condenser and a Hershberg dropping funnel were connected to the side necks of the flask.[2] The center neck was fitted with a mercury-sealed stirrer and an inlet tube for dry nitrogen.[3] The system was flushed out with dry nitrogen and then four-hundred milliliters of anhydrous ethyl ether was admitted through the separatory funnel. To the separatory funnel was added one mole of ethyl iodide and one hundred milliliters of anhydrous ethyl ether. The magnesium-ether mixture was stirred at a moderate rate and the ethyl iodide-ether mixture was added cautiously. The reaction starts at once and was cooled (2° C.) in an ice bath to maintain a moderate rate of reaction. After

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[1] The flask was placed in a drying oven for twenty-four hours. It was stoppered before removing, to eliminate moisture and carbon dioxide.

[2] The condenser and funnel were closed with tubes containing anhydrous calcium chloride.

[3] The nitrogen used was C. P. water-pumped. This must be dry so a Geissler Potash Absorption Bulb was used filled with concentrated sulphuric acid C. P. and a anhydrous calcium chloride tube.

all the alkyl iodide was added, the ice bath was removed, and the reaction mixture stirred until it reached room temperature. The contents in the reaction flask was allowed to stand over night in the presence of a very slow flow of dry nitrogen.

B. Preparation of Other Grignard Reagents.

The equipment was constructed similar to that used in Experiment II A. The reaction flask was cooled with a salt ice bath (-6° C.) in the reaction of methyl iodide. The methyl magnesium iodide reagent becomes very violent (13) in its reaction if allowed to warm up or when the solvent evaporates. The methyl magnesium iodide was not allowed to stand for any period of time but was immediately reacted with the ethylene oxide. The preparations of the sec- and iso-butyl magnesium iodides take a longer time and they were allowed to stand for forty-eight hours for the reaction to be more complete.

The Grignard reagent was treated in three different ways: (A) reaction of one mole of ethylene oxide with one mole of reagent; (B) same as (A) but followed by heating; (C) reaction of two moles of ethylene oxide with one mole of reagent. The three procedures mentioned above will be described and the results may be found in table IV under Tabulated Results.

III. Reaction of Ethylene Oxide and Grignard Reagents.

Analysis of the Grignard reagent:

The Grignard reagent with its solvent was forced through a glass tube, which contained a small glass wool plug, by nitrogen under pressure. The Grignard reagent was collected in a dry nitrogen filled 500 ml. graduate cylinder and measured. Five milliliter samples were pipetted out and analyzed for the organomagnesium content by Gilman's procedure (15). The samples were placed in 250 ml. Erlenmeyer flasks and covered with watch glasses. Complete hydrolysis was carried out by the careful addition of 10 ml. of water. To the hydrolyzed portion a measured excess of 0.1N hydrochloric acid was added and then heated on the steam bath until all of the basic magnesium chloride was dissolved. The excess acid was titrated with 0.1N sodium hydroxide using phenolphthalein as an indicator.

One milliliter was pipetted out and analyzed by the Volhard method for the iodide ion (16).

A. Reaction of One Mole of Ethylene Oxide with One Mole of Grignard Reagent.

The measured Grignard reagent was added to a dry nitrogen filled one liter three neck flask. The three necked flask was fitted with a reflux condenser, mechanical stirrer, a small glass tube for the admittance of dry nitrogen, and a separatory funnel equipped with an outer metal jacket to permit the use of dry ice as a cooling agent. The Grignard reagent was cooled in an ice-salt bath (-6° C.). Fifty milliliters of anhydrous ether was placed in the separatory funnel and surrounded by dry ice. The calculated amount of ethylene oxide for the reaction was weighed out and added to the separatory funnel. The separatory funnel was stoppered by the use of an anhydrous calcium chloride tube. Cautiously, the ethylene oxide ether mixture was added to the Grignard reagent. The addition product that was formed from the ethylene oxide and Grignard reagent was allowed to remain in the reacting flask in the ice-salt bath for five or six hours, then the ice bath was removed and the stirring process continued for an hour. The addition product of the above reaction was hydrolyzed by adding a aqueous solution of ammonium sulphate in chipped ice. After hydrolysis the ether layer was decanted. The pasty residue was extracted three or four times with small portions of ether. If the ether-water extract showed basic properties (litmus), it was neutralized by a small amount of dilute hydrochloric acid and ice, and again extracted with three (100 ml.) portions of ether. The ether extracts were combined and dried over anhydrous sodium sulfate and then fractionated through a short Fenske-type column.

B. Reaction of One Mole of Ethylene Oxide with One Mole of Grignard Reagent Followed by Heating.

The preparation of the Grignard reagent was accomplished as outlined in II A and B. Addition of the calculated amount of ethylene oxide to the Grignard reagent was accomplished as outlined in III A. After completion of the addition reaction the reflux condenser was set for distillation. The flask containing the addition product was placed in a Glas-Col heating mantle

and about three hundred milliliters of ether was distilled off. The alkyl magnesium iodide-ethylene oxide product was allowed to cool and three hundred milliliters of anhydrous benzene was added. The condenser was set for refluxing and a gentle reflux continued for six hours with continuous stirring. The addition product was hydrolyzed with aqueous ammonium sulphate, extracted with ether, separated with the use of a separatory funnel, dried over anhydrous sodium sulfate and then fractionated as described in III A.

C. Reaction of Two Moles of Ethylene Oxide with One Mole of Grignard Reagent.

The procedure was similar to III A with an equivalent calculated amount of two moles of ethylene oxide. In order to have the reaction of two moles of ethylene oxide with one mole of the Grignard Reagent go to completion, it was necessary to add the ethylene oxide very slowly and stir the reacting mixture briskly. The product was hydrolyzed immediately, extracted with ether, dried, and fractionated as described in III A. The results of the various condensations can be found in Table IV.

IV. The Reaction of Ethylene Oxide with Magnesium Iodide.

Iodoethoxymagnesium was prepared by the addition of ethylene oxide to magnesium iodide. Analysis showed some impurities. See Table III.

A one-liter three-necked round bottom flask was fitted with a mechanical stirrer, reflux condenser, and dropping bottle (17). Five hundred milliliters of anhydrous ether along with one-fifth mole of anhydrous magnesium were placed in the one-liter reaction flask described above. The magnesium ether mixture was cooled in a salt-ice bath. To the mixture was added one-fifth mole of pure iodine. The system was protected from moisture by the use of anhydrous calcium chloride. Nitrogen was continually fed into the system as previously described. After the reaction had gone to completion the iodine dropping bottle was removed and a dropping funnel surrounded by dry ice was attached to the flask. To the funnel was added one hundred milliliters of anhydrous ether with two-fifths mole of ethylene oxide. The ethylene oxide-ether-mixture was added through the separatory funnel to the reaction flask over a period of one hour with continuous stirring. After complete addition of the ethylene oxide the ice-salt bath was removed from around the reaction flask. The stirring was continued until the reaction flask and addition product reached room temperature. The product was hydrolyzed with dilute hydrochloric acid and ice and extracted with three one-hundred milliliter portions of ether. The ether extracts were dried over anhydrous sodium sulfate and fractionally distilled. The ethylene iodohydrin in the aqueous layer was determined by a method described by Gomberg (18). The aqueous portion was distilled until the temperature reached about 60° when there was apparently no ether remaining in the distilling flask. The iodohydrin tends to decompose so a partial vacuum was used until about one-half of the iodohydrin was distilled from the aqueous solution. This aqueous solution of iodohydrin was neutralized with a saturated solution of sodium carbonate. The iodohydrin was separated from the aqueous solution with the use of a separatory funnel, and distilled at 85° (25 mm.). After determining the refractive index of the iodohydrin solution, the amount of ethylene iodohydrin was computed by reference to the curve obtained when plotting index of refraction against percent iodohydrin. The iodohydrin extracted from the ether and water layer gave a yield of 8.3 percent.

V. The Reaction of One-half Mole of Ethylene Oxide with One Mole of Ethyl Magnesium Iodide.

It was noted that a fine precipitate was formed when ethylene oxide was allowed to react with the Grignard Reagent. Cloudiness appears when one-fourth mole of ethylene oxide is added to one mole of the Grignard Reagent. As the amount of ethylene oxide is increased to one-half mole the cloudiness disappears with the formation of a fine precipitate. Finally the precipitate dissolves as the remaining portion of one mole of ethylene oxide was added to the reaction mixture.

The precipitate formed by the reaction of one half mole of ethylene oxide and of one-mole of ethyl magnesium iodide was separated with a high speed centrifuge.

The addition product of one half mole of ethylene oxide and one mole of ethyl magnesium iodide was analyzed for the magnesium and iodide content. The results are recorded in Table II.

A portion of the precipitate was hydrolyzed as described in IIIA. Neither the n-butanol nor iodohydrin were present, indicating that there was not a breaking of the alkylmagnesium or magnesium iodide bond.

A weighed sample of the ethylene oxide ethyl magnesium iodide addition product was placed in a five hundred milliliter round bottom flask with two hundred and fifty milliliters of dry ether. The apparatus was set up as described in the following paragraph.

A five hundred milliliter round bottom flask was placed in a Glas-Col mantle. The round bottom flask was connected to a reflux condenser, which at the top was connected with condensing bulbs surrounded by chipped dry ice in a large thermos bottle. The temperature in the thermos bottle was maintained at -10° to -15° C. The ethylene oxide ethyl magnesium iodide addition product was now heated gently allowing the ether to reflux. The refluxing was continued for two hours, after which time the condenser water was partially shut off to permit the temperature to rise to the boiling point of the ethylene oxide, Ethylene oxide with some ether collected in the condensing bulbs. As the condensing bulbs became full their contents were emptied into an Erlenmeyer flask (500 ml.) kept cool by refrigeration.

Near the end of the refluxing and condensing of the ethylene oxide the water in the reflux condenser was shut off. The balance of the ethylene oxide with some ether was collected in the bulbs. About fifty milliliters of ether and the ethyl magnesium iodide remained in the flask.

The ethylene oxide ether solution was fractionated twice and the percentage of ethylene oxide recovered from the ethylene oxide-ethyl magnesium iodide addition product was calculated as shown in Table II.

VI. Preparation and Analysis of the Intermediate Product from the Reaction of Ethylene Oxide and Grignard Reagent.

The alkyl-magnesium iodide was prepared by the procedure described in II A. With mole to mole ratios of ethylene oxide and the Grignard reagent no precipitation took place. However, when the second mole of ethylene oxide was added a precipitate formed. The reaction mixture, was centrifuged for ten to fifteen minutes at about 2000 r.p.m. to separate the precipitate. After washing with ether and centrifuging again, the precipitate was transferred to a sample bottle and placed in a vacuum desiccator.[1] The ether was completely removed by evaporation with a water pump for three hours, and the oil pump for ten hours. The total iodine was determined by a Parr bomb fusion (19).

In the Parr bomb cup were placed two-tenths grams of the sample, seventy-five hundredths grams of powdered potassium nitrate, four-tenths grams of finely ground sucrose, and

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[1] This procedure should be carried out rapidly as the addition product precipitate hydrolyzed quickly.

fourteen grams of sodium peroxide. The cup was assembled with the top being tightened down and the contents mixed thoroughly by shaking. The sample was ignited over a Meker burner for about two minutes. After allowing the bomb to cool, it was opened and the cap and cup transferred to a covered six hundred milliliter beaker. Two hundred milliliters of distilled water was added cautiously to the beaker and its contents. The excess sodium peroxide was decomposed by boiling after which the cap and cup were rinsed and removed. The resulting solution was cooled and carefully acidified with concentrated nitric acid. The solution was boiled to remove all hydrogen peroxide. After the cooling of the acidified solution, a measured excess of 0.1N silver nitrate was added. The silver nitrate was added in small quantities with vigorous shaking as the silver iodide formed will occlude both the iodide solution and silver nitrate. The solution was heated to complete the formation of silver iodide and the supernatant liquid becomes colorless. The percent of iodine was then determined by the Volhard method for iodine (16).

The magnesium in the Grignard addition product was determined by decomposing a weighed sample into MgO, with the use of a Meker burner. The decomposition was carried out in silica crucibles, which were heated until they were brought to a constant weight. A weighed sample was placed in the crucible, and the crucible and content heated cautiously to prevent ignition and loss by spattering. In a few minutes the temperature was gradually increased until the maximum heat of the burner was attained. The heating was continued for one hour; the crucible was then placed in a desiccator, allowed to cool, and weighed. The crucible and contents were reheated until a constant weight was obtained. The percent of magnesium was calculated from the following equation:

$$\frac{\text{Wt. of MgO} \times 0.6032 \times 100}{\text{Wt. of sample}} = \%\ \text{Mg}$$

VII. Determination of yields of Ethylene Iodohydrin and Alcohol.

The ethylene iodohydrin and alcohol formed by the reaction of alkyl magnesium iodide and ethylene oxide were distilled under reduced pressure. The ethylene iodohydrin and alcohol were collected together, weighed, and placed in a one liter three necked flask. The flask was fitted with a stirrer, and condenser. To the ethylene iodohydrin, alcohol mixture was added forty grams of sodium hydroxide with vigorous stirring for thirty minutes, and then one hundred fifty milliliters of water was added slowly over a period of ninety minutes, with continued stirring. The resulting mixture was allowed to cool, after which it was observed that two layers had separated. The water layer was extracted with anhydrous benzene. The solvents and extracts were combined and dried over anhydrous sodium sulfate. The sodium hydroxide layer was boiled to expel any traces of benzene, cooled, and diluted to one liter. Five milliliters of this aqueous solution was titrated for iodide ion by Volhard's method (18). The iodohydrin yield was found by taking the ratio of the mole of iodide ion found in the analysis of the hydrolyzed reaction mixture to the moles of iodide ion found in the unreacted Grignard reagent.

The ether-benzene solution of the alcohol was distilled at atmospheric pressure. The yield of alcohol was calculated by taking the ratio of the weight of alcohol obtained by distillation to the difference in the weight of the original organic radical present less the unreacted Grignard reagent.

VIII. Identification of the Alcohol.

The alcohols were identified by making the 3,5 dinitrobenzoates (20).

One-half gram of 3,5 dinitrobenzoyl chloride was mixed with one milliliter of the alcohol in a test tube and the mixture boiled gently for five minutes. Ten milliliters of distilled water was added and the solution cooled until the precipitate solidifies. The precipitate was collected on a filter, washed with ten milliliters of two per cent sodium carbonate solution and recrystallized from ten milliliters of a mixture of ethanol and water of such composition that the ester was dissolved in the hot solution but was separated out in small crystals upon cooling. The crystals were removed by vacuum filtration and dried on a porous plate.

The 3,5-dinitrobenzoate of 1-butanol

Melting point of the ester	63.8°
Mixed melting point	63.9°

For a mixed melting point the 3,5 dinitrobenzoate of a known sample of pure 1-butanol was made and its melting point determined. Then equal amounts of the crystals of the known and unknown dinitrobenzoate derivative were thoroughly mixed by crushing in a mortar and the melting point of the mixture was determined.

IX. Identification of Ethylene Iodohydrin.

Ethylene iodohydrin was prepared (21) by a modified method of the preparation of ethylene bromohydrin. The product showed the same properties as the ethylene iodohydrin obtained in the condensations and that reported by Butlerow and Ossokin (21).

The boiling point of ethylene iodohydrin is 176-177°, at this temperature there was a great deal of decomposition. However, if distilled with the use of a vacuum, the distillate was clear at 85°/25 mm. If it was stoppered tightly in a dark bottle it will remain clear for a period of two or three days. Its density at 20° C. is 2.205.

A further test to prove the presence of ethylene iodohydrin was made by using lead hydroxide to see if acetaldehyde was formed, the result was positive.

The formation of acetaldehyde was also shown by preparing the 2,4-dinitrophenylhydrazone for comparison of a sample of the derivative made with a known sample of acetaldehyde. (See VIII)

Melting point of derivative 108.° C.
Mixed melting point 107.5° C.

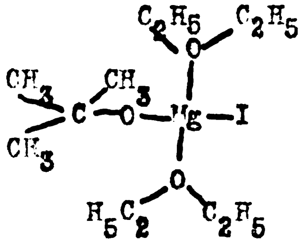
The methyl ether of ethylene iodohydrin was prepared. The methyl-2-iodoethyl ether obtained had a boiling point of 136.9° C. at 750 mm. Butlerow and Ossokin (21) reported the boiling point of methyl-2-iodoethyl ether as 137.8° at 750 mm.

DISCUSSION

DISCUSSION

It is generally accepted that the formation of a coordination compound must be the first step in all Grignard reactions (2), (3), (10), (7), (23). Meisenheimer (6) proposed the ether is held on the Grignard reagent by subsidiary valences

I.



Earlier work by Huston, Agett, and Langham (2), (3), also Schlenk and Schlenk (9), and Ribas and Tapia (8), indicated that the reactions which take place when one mole of ethylene oxide is added to one mole of ethylmagnesium bromide or chloride may be represented by the following equations:

$$\text{II.}\quad 2C_2H_5MgBr \rightleftharpoons (C_2H_5)_2Mg + MgBr_2$$

$$\text{III.}\quad MgBr_2 + 2(CH_2)_2O \longrightarrow (BrCH_2CH_2O)_2Mg$$

If the products of reaction II and III are heated it is found that the amount of n-butyl alcohol is increased.

$$\text{IV.}\quad (C_2H_5)_2Mg + (BrCH_2CH_2O)_2Mg \longrightarrow (C_4H_9O)_2Mg + MgBr_2$$

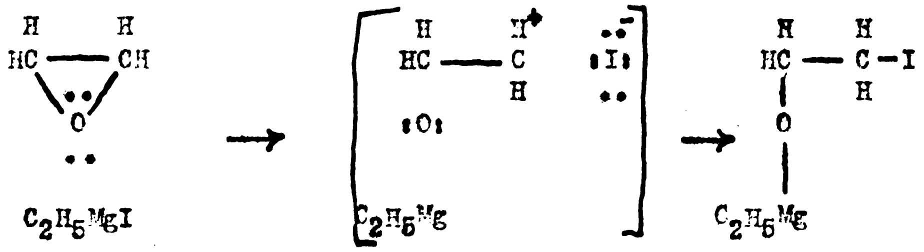
When the coordination compound, $(C_4H_9O)_2Mg$, is hydrolyzed n-butyl alcohol results. The alcohol is also formed when two moles of ethylene oxide react with one mole of ethylmagnesium bromide:

$$(C_2H_5)_2Mg + 2(CH_2)_2O \longrightarrow (C_4H_9O)_2Mg$$

If the addition products of this reaction are hydrolyzed a mixture of

n-butanol and ethylenebromohydrin was obtained. The latter was derived from reaction III.

The electrophilic attack on the oxygen by magnesium causes an unbalanced electronic equilibrium so that one of the carbon-oxygen bonds was weakened. The following reaction of ethyl magnesium iodide shows the magnesium attacking the oxygen of the epoxide, thus the iodide was partially separated from the magnesium. The iodide was now in the position to attack the primary carbon of epoxide nucleophilically.



If iodohydrin alcoholate has the greater stability under the conditions of the reaction, then the iodohydrin was the chief product formed upon hydrolysis. This fact has been verified by Huston and Agett (2) and Huston and Langham (3).

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

Huston and Bostwick (10), and Huston and Brault (11), have recorded in their experimentation rearrangement of the addition product.

Acetaldehyde was obtained in very small amounts, the formation of which may be explained by the following mechanism as proposed by Cottle and Hollyday (24). The reaction takes place between ethylene oxide and butyl magnesium bromide:

$$(BrCH_2CH_2O)^- + RO^- \longrightarrow ROH + (BrCH_2CHO)^=$$

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

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

The investigators further suggested that the removal of the second proton from ethylene bromohydrin would only be accomplished under such difficulty that such a mechanism seems most unlikely.

When a 1:1 molar ratio of ethylene oxide and ethylmagnesium iodide was reacted without heating, and then hydrolyzed, the yields were 53.7 percent of n-butanol and 20 per cent of iodohydrin. Considerable ethylene iodohydrin was lost by decomposition. These results were the actual amounts of products recovered in the ether layer.

A precipitate was not formed if equal molecular quantities of ethylene oxide and the alkyl magnesium iodides were reacted. However, from the results shown in Table IV, and observing the amount of decomposition with the alkyl magnesium iodide and ethylene oxide, one can assume the reaction follows the same course as that of the other halogens.

The scheme of reactions are as follows:

$$C_2H_5MgI + (CH_2)_2O \longrightarrow C_2H_5CH_2CH_2OMgI$$

or

$$C_2H_5MgOCH_2CH_2I$$

$$C_2H_5CH_2CH_2OMgI + H_2O \longrightarrow C_2H_5CH_2CH_2OH + MgOHI$$

or

$$C_2H_5MgI + 2(CH_2)_2O \longrightarrow C_2H_5CH_2CH_2OMgOCH_2CH_2I$$

$$C_4H_9OMgOC_2H_4I + 2H_2O \longrightarrow C_4H_9OH + ICH_2CH_2OH + Mg(OH)_2$$

Hydrolysis of the intermediate product would yield the desired n-butanol.

When the molar ratio of ethylene oxide to ethylmagnesium iodide was increased to 2:1, a noted increase in the amount of n-butanol corresponding to 72 percent and 40 percent of the ethylene iodohydrin. By analysis of the precipitate formed and recorded in Table I, it would seem evident that the intermediate for the formation of the alcohol is $(C_4H_9O)_2Mg$. This intermediate could not be isolated in a pure form as it explodes when exposed to air for any period of time.

The intermediate product, C_4H_9OMgI may still be considered and as the solution becomes depleted of magnesium iodide, the decomposition of the above intermediate product occurs according to the equation:

$$2C_4H_9OMgI \longrightarrow (C_4H_9O)_2Mg + MgI_2$$

By this scheme of reaction the n-butanol could be formed either from butoxy magnesium iodide of diethylmagnesium.

According to Schlenk (25), about eighty-five percent dissociation takes place when the ethylmagnesium chloride dissociates into diethylmagnesium and magnesium chloride. The reaction of ethylene oxide with diethylmagnesium appears more probable.

Noller and Castro (26), have given evidence that the $(C_4H_9O)_2Mg$ combines with varying amounts of magnesium chloride. They have suggested that if C_4H_9OMgCl is the product of oxidation, it should have the property of forming a complex with magnesium chloride, probably by virtue of the unshared electrons on the oxygen atom. Thus the two addition products should behave alike. This was further verified by Huston and Langham (3). In experimenting with two moles of ethylene oxide to one mole of ethylmagnesium iodide small quantities of magnesium iodide was isolated and analyzed.

In experimenting with the iodides using one-half mole of ethylene oxide and one mole of ethylmagnesium iodide (Table II) in two experimental condensations the iodide content was found to be 56.5 percent and the magnesium content 9.9 percent. This precipitate (C_4H_9OMgI) if heated as directed in Section V shows a recovery of 23 percent of the epoxide, indicating that neither the alkylmagnesium or magnesium iodide bond have been attacked. (6) To substantiate this belief it was found that when the precipitate was hydrolyzed with dilute ammonium sulphate solution no n-butanol or iodohydrin was present.

There are two possible intermediates for ethylene iodohydrin:

$$\text{I.}\quad MgI_2 + (CH_2)_2O \longrightarrow ICH_2CH_2OMgI$$

or

$$\text{II.}\quad MgI_2 + 2(CH_2)_2O \longrightarrow (ICH_2CH_2O)_2Mg$$

If the reaction follows II one obtains results as shown in Table III. Evidence in Table III shows the intermediate product $(ICH_2CH_2O)_2Mg$ leads to the formation of ethylene iodohydrin.

Recorded in Table IV are the percentage yields of the various Grignard reagents reacting with ethylene oxide. It shows the general mechanics of the reactions. The branching of the carbon chain in the Grignard reagent tends to decrease the yield of the alcohol. It was not possible to carry out the reaction of tertiary butyl magnesium iodide with the epoxide, due to the decomposition of t-butyl iodide. However, from the experimental data and the work of Huston and Langham (3) and Whitmore (27), the tertiary butyl magnesium iodide would yield only ethylene iodohydrin. When methyl magnesium iodide was used either in the 1:1 or 1:2 mole ratio great care must be used with the addition products. When allowed to become dry, or separated from its solvent by decantation, the addition product will explode with great violence.

SUMMARY

SUMMARY

1. The alkyl magnesium iodides react in a way similar to the alkyl chlorides. One mole of ethylene oxide and one mole of Grignard reagents formed by the treatment of alkyl chlorides with magnesium is between the ethylene oxide and R_2Mg, or $RMgI$.

2. Analytical results from condensation of two moles of ethylene oxide with one mole of magnesium iodide indicates the formation of $(ICH_2CH_2O)_2Mg$.

3. In the condensation of two moles of ethylene oxide and one mole of alkyl magnesium iodide, results point to the formation of $(C_4H_9O)_2Mg$. This addition product is formed in a similar method as the chlorides, from C_2H_5MgI it is C_4H_9OMgI which rearranges giving $(C_4H_9O)_2Mg$ and MgI_2.

4. Analytical results further show that the combined formula of the 2:1 ratio is $(C_4H_9O)_2Mg \cdot 2MgI_2$.

5. The percentage yield of the alcohol and ethylene iodohydrin is increased considerably with the addition of two moles of ethylene oxide and one mole of alkylmagnesium iodide.

6. No precipitate was formed when one mole of the epoxide was used to one mole of the Grignard reagent.

7. The addition products between ethylene oxide and alkylmagnesium iodide are not stable.

8. It was shown that one-half mole of the epoxide does not react fully with one mole of alkylmagnesium iodide, and that Meisenheimer's suggested subsidiary and principal valence can be used in explaining the addition product formed when the epoxide reacts with the Grignard reagent.

TABLES

TABLE I

ANALYSIS OF ADDITION PRODUCT FROM $2(CH_2)_2O$ and C_2H_5MgI

Condensation No.	% Iodine	% Magnesium
1	46.30	9.50
2	47.72	8.65
3	45.92	9.00
4	47.35	8.75
5	46.21	8.87
6	49.53	9.28

Based upon the production of $C_2H_5CH_2CH_2OMgOCH_2CH_2I$

Theoretical Mg 8.95%

I 47.25%

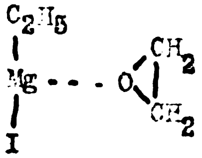
It is significant that a mixture of dibutoxymagnesium $(C_4H_9O)_2Mg$ and di-iododiethoxymagnesium $(ICH_2CH_2O)_2Mg$ in equal parts would have the same percentage composition.

TABLE II

ANALYSIS OF ADDITION PRODUCT FROM $\frac{1}{2}(CH_2)_2O$ AND C_2H_5MgI

Condensation No.	% Iodine	% Magnesium
1	53.8	10.00
2	55.1	9.85
Theoretical	53.7	10.7

Theoretical formula



Recovery of ethylene oxide

1	93%
2	91.4%

TABLE III

ANALYSIS OF ADDITION PRODUCT FROM $2(CH_2)_2O$ AND MgI_2

Condensation No.	% Iodine	% Magnesium
1	69.95	7.82
2	69.90	7.62
3	71.21	6.91
4	68.96	6.42
5	69.51	6.75

Based upon the production of $(ICH_2CH_2O)_2Mg$

Theoretical Mg 6.55%

I 69.30%

TABLE IV

PERCENTAGE YIELDS OF ALCOHOLS AND ETHYLENE IODOHYDRIN BASED UPON THE TITRATED GRIGNARD REAGENTS

	RMgI + $(CH_2)_2O$ No Heat	RMgI + $2(CH_2)_2O$ No Heat	RMgI + $(CH_2)_2O$ Heat
	Methylmagnesium Iodide		
1-Propanol	54%	64%	Exploded
Iodohydrin	30%	29%	
	Ethylmagnesium Iodide		
1-Butanol	53.7%	72%	40%
Iodohydrin	20%	40%	13.5%
	n-Propylmagnesium Iodide		
1-Pentanol	36.3%	61.5%	35%
Iodohydrin	30%	53%	15%
	i-Propylmagnesium Iodide		
3-Methyl-1-butanol	32.6%	49.3%	30%
Iodohydrin	21.5%	51%	18.4%
	n-Butylmagnesium Iodide		
1-Hexanol	35.2%	64.3%	30.9%
Iodohydrin	24.3%	58.1%	23.2%
	s-Butylmagnesium Iodide		
3-Methyl-1-pentanol	18%	35%	
Iodohydrin	20.2%	43%	
	i-Butylmagnesium Iodide		
4-Methyl-1-pentanol	18.5%	30.3%	
Iodohydrin	30.1%	54.3%	

TABLE V

PHYSICAL CONSTANTS OF THE ALCOHOLS

Alcohol	$N_D^{20^\circ}$	B.P.°C.	Ref.
1-Propanol	1.38543	97.19	18
1-Butanol	1.39931	117.7	18
1-Pentanol	1.40963	137.9	18
3-Methyl-1-butanol	1.4084	132.	28
1-Hexanol	1.4161	157.5	19
3-Methyl-1-Pentanol	1.4115	152.4	28
4-Methyl-1-Pentanol	1.4490	152.	28

TABLE VI

DERIVATIVES OF THE ALCOHOLS

	M.P. °C.	Ref.
1-Propanol 3,5-dinitrobenzoate	74	18
1-Butanol 3,5-dinitrobenzoate	64	18
1-Pentanol 3,5-dinitrobenzoate	46.4	18
3-Methyl-1-butanol 3,5-dinitrobenzoate	61	28
1-Hexanol 3,5-dinitrobenzoate	58.4	28
3-Methyl-1-Pentanol 3,5-dinitrobenzoate	38	28
4-Methyl-1-Pentanol 3,5-dinitrobenzoate	72	28

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