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Some quantitative studies of organometallic compounds

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SOME QUANTITATIVE STUDIES OF ORGANOMETALLIC COMPOUNDS

by

32
30

Erwin A. Zoellner

A Thesis Submitted to the Graduate Faculty
for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject: Organic Chemistry

Approved

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1933

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SOME QUANTITATIVE STUDIES OF ORGANOMETALLIC COMPOUNDS

GENERAL INTRODUCTION

There are two phases of the Grignard reagent which have, as yet, not received adequate treatment either in the current literature or in the currently available books¹ on this reagent. One is the comparative utility of the RMgCl, RMgBr and RMgI compounds and the other is the preparation of the Grignard reagent itself under general or special conditions. The phase on the comparative utility of the compounds mentioned above is taken up first, since it is primarily a summary of the data in the literature on this subject. The phase on the preparation of the Grignard reagent under general or special conditions, which forms the substance of this thesis, is taken up in connection with the experimental data.

All the available literature on the comparative study^{utility} of the RMgCl, RMgBr and RMgI compounds has been investigated from the time of the discovery of the Grignard reagent up to the present time. The data so obtained are briefly summarized in a more or less chronological order.

As early as 1904, Meyer and Bertheim² found that alkylmagnesium chlorides were best suited for the preparation of dialkylthallium halides from thallic chloride ($TlCl_3$). The

1. (a) Wren, "Organometallic Compounds of Zinc and Magnesium", London, 1913; (b) Courtot, "Le magnésium en chimie organique", Nancy, 1926; (c) Runge, "Organo-metallverbindungen I. Organomagnesiumverbindungen", Stuttgart, 1932.
2. Meyer and Bertheim, Ber., 37, 2051 (1904)

yields were good and the products were found to be very pure. The alkylmagnesium bromides also gave good yields but a mixture of dialkylthallium chlorides and bromides was obtained. The dialkylthallium bromides, however, were found to be practically insoluble in ether. The alkylmagnesium iodides, were not well suited because the greater part of the thallic chloride was reduced to thallose iodide. Goddard³ found that the action of iso-butyl- and iso-amylmagnesium iodide on the thallic chloride caused a quantitative reduction of the latter to thallose iodide. Krause and Grosse⁴ found, in the preparation of dialkylthallium halides by the action of alkylmagnesium bromides on thallic chloride, that reduction to thallose bromide occurred to the extent of 16%; but with the corresponding alkylmagnesium chlorides, the reduction was only 3-10%. They also found that in the preparation of iso-, propyl- and sec-butylthallium chlorides, it was possible to obtain satisfactory yields only when the alkylmagnesium chlorides were used.

Houben⁵, in a study on the acetylation of alcohols and phenols by the action of acid anhydrides and acid chlorides on the corresponding halogenmagnesium alcoholates, found that the alkyl and arylmagnesium bromides and iodides were suited only for saturated alcohols (and perhaps phenols). For the acetylation of sensitive and unsaturated alcohols and phenols, the alkylmag-

3. Goddard, J. Chem. Soc., 121, 36 (1922)

4. Krause and Grosse, Ber., 58, 1933 (1925)

5. Houben, Ber., 39, 1736 (1906)

nesium chlorides were best suited, giving good yields and pure products. With the alkylmagnesium bromides or iodides, the yields were less and the products were impure, being contaminated with bromine and iodine.

A rather thorough study of the coupling action of alkylmagnesium halides with alkyl halides has been made by Spath⁶. His results show that when the most reactive RMgX compounds were used, the yields of the hydrocarbons were very good. In general, the alkylmagnesium chlorides and bromides gave yields that were approximately 50% higher than those obtained from the alkylmagnesium iodides.

In the preparation of hydrocarbons by the action of organomagnesium halides on diethyl sulfate, Gilman and Hoyle⁷ found that with benzylmagnesium chloride, the yield of n-propylbenzene was practically quantitative. Furthermore, their results show that when the RMgBr compounds were presumably reactive, good yields of hydrocarbons were obtained. Their work suggests that good results should be obtained with alkylmagnesium chlorides. These authors also make the statement: "For reasons, yet unknown, it appears that ethylmagnesium bromide is much better suited than such compounds as methyl- and ethylmagnesium iodide for replacing the acid hydrogen in acetylenic compounds by MgX groups". It is very probable that the alkylmagnesium

6. Spath, Monatsh., 34, 1975 (1915)

7. Gilman and Hoyle, J. Am. Chem. Soc., 44, 2621 (1922)

chlorides may be even better suited for this kind of work, according to the opinion of the writer.) Smith

In a patent by Schmalfluss⁸, in which directions are given for the preparation of methylmagnesium chloride on a commercial scale, a statement is made that not only is methylmagnesium chloride cheaper than the methylmagnesium iodide but compounds can be synthesized by means of the former which are not possible with the latter. As an example, he mentions trans-dimethyl-(2,5)-hexene (3)-diol-(2,5). This compound was made from the action of methylmagnesium chloride on diethyl fumarate. In a study of the enolizing action of Grignard reagents on camphor, Bredt-Savelsberg⁹ reports that the action of methylmagnesium halides increases as the negativity of the halogen in the RMgX compound increases. Under comparable conditions, the enolization of camphor was enhanced by the RMgCl compound to 28.2%, by the RMgBr compound, 24.0%, and by the RMgI compound, 14.8%. Furthermore, a statement is made that the methylmagnesium iodide forms with greater ease than the methylmagnesium chloride, but the latter is far more reactive when once made than the former.

Coleman and Hauser¹⁰ recently initiated a study on the preparation of amines by the action of Grignard reagents on monochloroamine. The first paper of the series reports the results from the use of alkyl- and arylmagnesium halides.

8. Schmalfluss. Ger. pat., 376,368 [Chem. Zentr., IV, 721 (1923)]
9. Bredt-Savelsberg, J. prakt. chem., 107, 65 (1924)
10. Coleman and Hauser, J. Am. Chem. Soc., 50, 1193 (1928)

The yields of the amines with the RMgCl compounds are approximately 50% better than with the RMgBr compounds; and the superiority of the RMgBr over the RMgI compounds is approximately of the same order. In the next study on this subject by Coleman and Yager¹¹ using the iso-, sec-, and tert-alkylmagnesium halides the comparative utility of the RMgX compounds practically duplicates the results of the first paper. In the most recent study of the series, Coleman, Sarcoos and Yager¹² report the results of the action of n-, sec-, tert- and substituted-alkylmagnesium halides on monobromoamines. Again the same order of comparative utility of the RMgCl, RMgBr and RMgI was noted.

In a note to their classical study on the free methyl radical, Paneth and Hofeditz¹³ state that the tetramethyl-lead prepared by means of methylmagnesium iodide was contaminated with organic compounds of iodine. To remove this contaminant, the tetramethyl-lead had to be shaken with silver oxide for several days. This note caused Krause¹⁴ to publish a notice on the comparative value of the alkylmagnesium chlorides, bromides and iodides in the preparation of organometallic compounds. He states that better results were obtained with the alkylmagnesium chlorides and bromides than with the corresponding RMgI compounds, due to the fact that the former Grignard reagents are more

11. Coleman and Yager, J. Am. Chem. Soc., 51, 567 (1929)
12. Coleman, Sarcoos and Yager, ibid., 55, 2075 (1933)
13. Paneth and Hofeditz, Ber., 62, 1335 (1929)
14. Krause, Ber., 62, 1877 (1929)

reactive than the latter. Of the alkylmagnesium chlorides and bromides, he advises the use of the former because the alkyl chlorides are usually less expensive than the alkyl bromides. According to his opinion, the use of the alkylmagnesium chlorides has been retarded, due to the fact that the alkyl chlorides are less reactive towards magnesium than the corresponding alkyl bromides and iodides. To overcome this difficulty, he advises the use of fine magnesium "according to Grignard". As to the preparation of tetramethyl-lead, he states that this compound can be prepared in a pure state by the use of methylmagnesium chloride according to the procedure of Grüttner and Krause¹⁵.

Recently, a study¹⁶ was made of the rates of reaction of n-butylmagnesium chloride, bromide and iodide with valeronitrile. It was found that the time of reaction of these Grignard reagents was one hour and twenty-four minutes, two hours and twelve minutes and thirty two hours, respectively. With phenylmagnesium bromide and iodide and valeronitrile there was, however, no difference in the rates of reaction. In another study¹⁷ of the rates of reaction of n-butylmagnesium chloride, bromide and iodide with azobenzene, the time was fifteen minutes, one hour and thirty minutes, and two hours and thirty minutes, respectively. The yields of benzidine sulfate were 60, 46 and 35%, respectively.

The preparation of cyclohexylmagnesium chloride and bromide

15. Grüttner and Krause, Ber., 49, 1420 (1916)

16. Edith St. John, M. S. Thesis, Iowa State College, (1929)

17. Gilman, Heck and St. John, Rec. trav. chim., 49, 212 (1930)

was generally not without difficulties up to 1931. It was for this reason that a study¹⁸ was made of these Grignard reagents. It was found that under proper conditions, these compounds could be prepared without difficulties and in good yields. Under standard conditions^{19a} the yields of these compounds were 91 and 80%, respectively. When the halides were added rapidly^{19b}, the yields were 90 and 84%, respectively. This signifies that there should be no difficulty in the preparation of the RMgCl compound provided the reagents are dry and pure; however, the yields from the RMgBr compounds could be erratic if the halide is not added slowly. Derivatives were prepared of these compounds by carbonation. The yield of the acid derivative of the RMgCl compound based on the Grignard reagent present was 92%, based on the halide used, 84%; and with the RMgBr compound, the yields were 83% and 66%, respectively.

At the suggestion of the writer, the preparations of di-methylethyl acetic acid^{20a}, *n*-valeric acid^{20a} and cyclohexylcarbinol^{20b} were investigated using the RMgCl instead of the RMgBr compounds. As a result, the yield of di-methylethyl-acetic acid was increased from 66-67% to 76-86%^{20c}, of *n*-valeric acid from 64-65% to 72-75%^{20c} and of cyclohexylcarbinol from 61-65% to 64-69%^{20d}.

18. Gilman and Koellner, J. Am. Chem. Soc., 53, 1945 (1931)
19. (a) Gilman, Koellner and Dickey, ibid., 51, 1576 (1929); (b) ibid., 51, 1583 (1929)
20. (a) "Organic Syntheses" Vol. V. (1932) p. 75; (b) ibid., Vol. VI, (1936) p. 22; (c) ibid., Collective, Vol. I (1932) p. 385; (d) ibid., Collective Vol. I (1932) p. 132.

So far, it has been found that the comparative utility of the RMgCl, RMgBr and RMgI compounds decrease in the order in which they are named. There is little doubt that this is true in general. Gilman and Mayhue²¹, however, found a case where the order of the comparative utility given above is reversed. They made a study of the preparation of benzophenone from the action of phenylmagnesium chloride, bromide and iodide on benzoyl chloride. The yields of the benzophenone from these reactions were 48.0, 55.0 and 68.5%, respectively.

Since 1923, much work has been done on the preparation of organomagnesium halides under general and special conditions. This was made possible by the procedure developed by Gilman and his co-workers²², involving the analysis of the Grignard reagent by the acid titration method. Recently, the procedure has been successfully applied to quantitative studies on the preparation of organolithium compounds²³.

In the continuation of this work, a series of quantitative studies on the preparation of organomagnesium halides and organolithium compounds have been made by the author. The results of these studies are now presented in detail.

21. Gilman and Mayhue, Rec. trav. chim., 51, 47 (1932)

22. (a) Gilman, Wilkinson, Fishel and Meyers, J. Am. Chem. Soc., 45, 150 (1923); (b) Gilman and Meyers, ibid., 45, 159 (1923); (c) Gilman and McCracken, ibid., 45, 2462 (1923); (d) Gilman and Meyers, Rec. trav. chim., 45, 314 (1926); (e) See also Ref. 19.

23. (a) Gilman, Zoellner and Selby, J. Am. Chem. Soc., 54, 1957 (1932); (b) ibid., 55, 1252 (1933)

PART I. QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM CHLORIDES

INTRODUCTION

Only a few studies have appeared in the literature on the preparation of organomagnesium chlorides. For this reason, studies have been made on the preparation of several alkylmagnesium chlorides under general and special conditions. The results of these studies are now given in detail. An effort has been made to correlate with these details the results of some studies already published by the writer and others, in order to facilitate a summary of the data on this phase of the Grignard reagent.

EXPERIMENTAL PART

The apparatus and technique were essentially the same as those described previously¹⁹. (The ether used was first dried over sodium (eighteen to twenty hours), distilled and then dried over sodium again. This was necessary for, during the time this work was done, the ether from the storeroom was not of the best grade.) All the halides were dried over phosphorous pentoxide²⁰ and then distilled, unless otherwise mentioned. (The solid halides were recrystallized.) All the halides used were obtained from the Eastman Kodak Co., unless otherwise mentioned. The Mallinckrodt brand (1929-1933) of magnesium was used. It was composed of turnings in the form of concentric coils. The dimensions of these coils when unwound were 0.45 mm. in thickness, 4 mm. in breadth and 10-50 mm. in length. (This magnesium was, however, not quite as efficient, in general, as the brand (from Special

Chemical Co.) used in the former work.) The fine magnesium (50-80 mesh) was prepared from magnesium sticks obtained from the American Magnesium Corporation. The metal was designated as 99.8% pure.

The results given in Table I are those obtained under three sets of conditions, namely, "A-conditions", "B-conditions" and "special conditions".

The "A-conditions" are sometimes referred to as general or standard conditions. Under these conditions 1.34 g. (0.058 atom) of magnesium turnings was placed in the reaction flask and covered with 7.5 cc. of ether, to which was added 55 drops of halide. After adding 0.04-0.05 g. of powdered iodine, the mixture was gently refluxed (without stirring) by means of a micro burner under a wire gauze, until the iodine color disappeared which usually took from four to eight minutes. // It was found, by experience, that when the iodine color had completely disappeared, the reaction had started. (An experiment was made in which only the iodine was added to the magnesium in ether. The iodine color failed to disappear after refluxing the mixture for two hours. Now some halide was added. The iodine color disappeared within a few minutes. Furthermore, it has been found that as long as the iodine color remains the solution does not boil smoothly but bumps.)

As soon as the reaction had started, another 7.5 cc. of ether was added by momentarily lifting the condenser. The mixture was again warmed by external heat and refluxed another three

to four minutes. (It was often noted that the addition of this second portion of ether seemingly increased the rate of the reaction.) The rest of the 0.05 mole of halide was mixed with 15 cc. of ether and added uniformly over a period of thirty to thirty-five minutes. The addition of this main portion of halide was started with the application of external heat and stirring. As soon as the reaction caused vigorous refluxing, the external heat was removed, allowing the reaction to proceed under its own heat and with good stirring. The rate of stirring was such that the particles of magnesium were well distributed throughout the solvent without splashing the reaction mixture over the internal parts of the apparatus.

When all the halide had been added, the dropping funnel was rinsed with 5 cc. of ether, adding the washing to the reaction mixture. Stirring was now continued and the time was noted when the reaction apparently ceased after all the halide had been added. After the reaction had apparently ceased, the reaction mixture was stirred and refluxed one hour longer. This time of concluding the reaction was found necessary for n-butylmagnesium chloride and was subsequently adopted for all alkylmagnesium chlorides. In the preparation of organomagnesium bromides and iodides, the reaction is generally concluded with a fifteen minute period of refluxing.

As soon as the reaction had been concluded, the reaction flask was detached from the apparatus and allowed to stand four

or five minutes to allow the magnesium particles to settle before two 5 cc. aliquots were removed for analysis¹⁹. If the solution was allowed to stand longer, it reacted with the oxygen of the air to such an extent that there was doubt of obtaining homogenous samples. Longer standing under inert atmosphere did not affect the yields.

The "B-conditions", or sometimes referred to as "drop-conditions", differed from the "A-conditions" in that the remainder of the halide in 15 cc. of ether was added all at once after the reaction had been started in the two portions of 7.5 g. mentioned above. Again the time was noted when the reaction apparently ceased after all the halide had been added. The reaction was then concluded as given under the "A-conditions".

The time of apparent reaction after all the halide had been added under "A-" and "B-conditions", shows the comparative rates of reaction of the various organic halides with magnesium in a qualitative manner (see Tables I, II and III).

The "B-conditions" are an outgrowth of some work^{19b} on the rates of reaction of organic halides with magnesium in ether. The Grignard reagents that show no drop in yield under these conditions, can be prepared with little attention as to the rate of adding the halides. It is even possible that such Grignard reagents can be prepared without the use of a stirring apparatus (see "sec-Butylmagnesium Chloride" page 26 of this thesis).

The "special conditions" can not be described in general

for these conditions vary with the type of Grignard reagent. These conditions are fully described under the various headings of the RMgCl compounds with which such conditions were used. The runs with the various equivalents of fine magnesium were made under "A-conditions". *in general*

In general, the yields given in Tables I, II and III are the average of two or more runs; the yields of these several runs usually checked within less than 2.0%.

The results of these studies are summarized in Table I and are more fully discussed under the headings of the various Grignard reagents. *in notes*

TABLE I.

SUMMARY OF THE QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM CHLORIDES.

Chloride	% Yields of RMgX Under A- ^a , B-Conditions ^b		Drop of Yield Under ^a B-Conditions	Time of Apparent ^c Reaction Under A-, B-Conditions		% Yields of RMgX Under Special Conditions
	A	B		A	B	
Methyl	----	----	----	----	----	84.0
Ethyl	----	----	----	----	----	90.3
n-Propyl	87.6	----	----	13 min	----	88.2
iso-propyl	80.0	----	----	5	----	88.8
n-Butyl	91.9	91.7	0.2	23	43 min.	----
iso-Butyl	84.0	77.2	6.8	5	30	88.6
sec-Butyl	90.1	88.4	1.7	5	18	88.7
tert-Butyl	45.0	40.0	5.0	5	13	58-90
n-Amyl	87.1	86.1	1.0	28	53	89.9
tert-Amyl	----	----	----	----	----	54.0-73.6
α -sec-Hexyl	89.2	83.6	5.6	5	20	----
β -sec-Hexyl	102.0	96.7	5.3	5	20	----
Cyclohexyl	91.0	90.0	1.0	13	35	94.4-96.6
Phenyl	----	----	----	----	----	68-85
Benzyl	93.2	92.9	0.3	5	13	----
Benzohydryl	----	----	----	----	----	50-71
Triphenyl-methyl	----	----	----	----	----	96.0
β -Phenylethyl	88.9	87.9	1.0	13	30	----

RMgX
P37
RMgX
P58

TABLE I. CONT'D.

SUMMARY OF THE QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM CHLORIDES

<u>Chloride</u>	% Yields of RMgX Under A- ^a , B-Conditions ^b		Drop of Yield ^a Under B-Conditions	Time of Apparent ^c Reaction Under A-, B-Conditions		% Yields of RMgA Under Special Conditions
	A	B		A	B	
γ -Phenyl-propyl	87.2	85.3	1.9	35	45	98
γ -Tetrahydrofurylpropyl	----	----	----	----	----	91.6
Allyl	----	----	----	----	----	89-90
Cinnamyl	----	----	----	----	----	83

For explanation of notes: ^aSee p. 10; ^{b, c}see p. 11;

^dsee p. 12.

Methylmagnesium Chloride

In the literature only two references were found in which directions are given for the preparation of methylmagnesium chloride,--one by Houben⁵ and the other by Schmalfuss⁸.

Houben⁵ prepared this Grignard reagent as described under "Methylmagnesium Chloride" below, except that the reaction mixture was cooled by means of an ice-salt bath. In this manner, he made a 0.5 mole run in twenty-four hours but he does not state how much halide it took to use all the magnesium.

Schmalfuss⁸ made this Grignard reagent practically in the same manner as is given below. His system, was however, open and the reaction was carried out on a water bath. He started the reaction with a little ethyl bromine and iodine. After the reaction had started, the gas was led into the reaction mixture at such a rate that it was absorbed almost quantitatively. In runs using approximately 0.4 atom of magnesium, three hours were required to use up nearly all the magnesium, but he does not state how much halide was required.

An attempt was now made to carry out the preparation of this Grignard reagent in an apparatus similar to that used by Schmalfuss⁸, but in a closed system under a possible positive pressure of 50 mm., in order to avoid the loss of much halide. A three-holed one-liter flask was provided with a mercury sealed stirrer at the large hole containing enough mercury to make possible a positive pressure of 60-65 mm. within the system.

One of the side holes was provided with a Hopkins condenser, with a mercury trap attached at its exit to the atmosphere. The trap consisted of a U-tube containing enough mercury to make possible a positive pressure of 50 mm. within the system. The other side hole was provided with a tube made from a short air condenser (extending just below the surface of the ether) for the addition of the halide and the main portion of the ether after the reaction had been started. The upper end (the wide-mouthed part) of this tube was provided with a two-holed rubber stopper holding a 200 cc. dropping funnel (properly connected with the system for equalization of pressure) and a small bent tube to admit the gaseous halide. From time to time, as the volume of the reaction mixture increased, the large tube (with the dropping funnel and small tube) had to be raised through the rubber stopper with which it was attached to the reaction flask so that the mouth of the tube just extended beneath the surface of the reaction mixture. The addition of the halide beneath the surface of the reaction mixture may, however, not be a necessity when the halide is taken from a bomb, since the rate of the flow of the gaseous halide can, undoubtedly, be controlled better by the valve attached to the bomb. This would add to the convenience of the procedure, for adding the halide beneath the surface of the reaction mixture required much attention when the rate of the flow of the halide was not uniform. When the rate of the addition of the the halide was very slow, some of the reaction mixture was drawn

up into the wide tube. To check this movement of the reaction mixture into the wide tube, provision had to be made whereby the pressure in this tube was equalized with that of the system. This was done by connecting the upper part of the wide tube with the system by means of rubber tubing. The opening and closing of the connection was, however, found to be quite troublesome.

After a few preliminary experiments, the reaction was carried out as described below. In these preliminary experiments, it was found that the fundamental technique of this procedure was a proper adjustment between the rate of adding the halide and the cooling of the reaction mixture, so as to attain two aims: namely, to prevent the loss of halide due to momentary overflows, and to cool the reaction mixture to such a degree that the rate of the reaction allowed the completion of the preparation in a reasonable time.

The system was first swept out with dry nitrogen, since it has been found that alkylmagnesium chlorides are quite active towards the oxygen of the air. Now 12.3 g. (0.5 atom) of magnesium turnings was placed in the reaction flask and covered with 50 cc. of ether. Just before the addition of the halide was started, the flask was warmed to the boiling temperature of the ether. The 50 mm. pressure trap was now attached, a crystal of iodine was added and the addition of the halide was started without stirring. As the gaseous halide entered the flask, the external heat was slowly withdrawn (but not entirely removed) so as to attain a max-

imum concentration of the halide in the ether. With this careful adjustment and maintenance of the temperature between the boiling temperature of the ether and the temperature of the room, the reaction was started in less than five minutes. If the presence of methylmagnesium iodide is not objectionable⁴ a little methyl iodide should be used for the starting of the reaction as the above technique is a very delicate one.

The halide used was obtained from Schering-Kahlbaum A. G., in sealed glass tubes. The tube of methyl chloride was weighed and then cooled in a Dewar flask (containing a suspension of carbon dioxide in 95% ethyl alcohol) to such a degree that there was no decrease of volume. If this is not done the halide will boil with such violence that much of it is lost when the tube is opened. After the tube of halide had been properly cooled, it was opened and an ordinary melting point tube was dropped into it to prevent bumping as the halide boiled. The tube of halide was connected with a purification train²⁴ (previously saturated with the halide) by means of rubber tubing. The rate of the flow of the halide was controlled by raising or lowering the tube of

24. This purification train consisted of a U-tube of soda-lime and calcium chloride (one half of the tube was filled with soda-lime and the other half with calcium chloride) and a bottle of concentrated sulfuric acid provided with a reversible bubbler. This reversible bubbler was merely a tube with a wide-mouthed end dipping just beneath the surface of the acid solution. This reversible bubbler made it possible to reverse the flow of the halide when the pressure within the flask exceeded 50 mm. by merely lowering the tube of halide into its cooling bath.

halide in its cooling bath. This means of control was, however, not sensitive enough to prevent occasional overflows. In order to prevent this loss of halide, the 50 mm. trap was connected with a small Schlenk tube immersed in a cooling bath similar to that used for the tube of halide. In this manner the 3-4% of halide that overflowed was captured and finally added to the reaction mixture.

Since the halide has a boiling point of -23.7° , it was necessary to use a cooling bath of ice and water for the reaction mixture in order to secure a concentration of the halide in the reaction mixture which would make it possible to carry out the reaction in a reasonable period of time. The cooling of the reaction mixture was controlled by means of raising and lowering the ice-water bath. By the combined control of the temperatures of the tube of halide and the reaction mixture as stated above, it was possible to carry out the reaction with fair convenience and in a reasonable time.

After the reaction had been started, as described above, the stirring was begun and the rest of the ether (250 cc.) was added at such a rate that the temperature of the reaction mixture was not greatly affected. In this manner, the ether was added in approximately forty to forty-five minutes.

It took forty-five minutes to add all the halide and sixty-five minutes more for all the halide to react that had dissolved in the reaction mixture. To cause all this dissolved halide to

react, the temperature of the reaction mixture was controlled by the raising and lowering of its cooling bath. As soon as the fluctuation of the pressure ceased, the cooling bath was slowly lowered until the pressure within the system no longer exceeded 40 mm. Now the cooling bath was removed and the reaction allowed to proceed at room temperature until the pressure within the system became equal to the atmospheric pressure. After having stirred and refluxed the reaction mixture ten minutes longer, the 50 mm. trap was removed to expel any unused halide by another ten minute period of refluxing. The reaction mixture was now allowed to cool to room temperature under nitrogen and then a portion was analysed. In this run the tube of halide contained 0.607 mole instead of the usual 0.5 mole. The yield of this Grignard reagent based on the halide used was 84.0%. The yield based on the magnesium, since it was all used up, was 96-98%.

If the halide is taken from a bomb, the above procedure should be quite practical and convenient for the preparation of 0.05-1.0 mole runs of ethylmagnesium chloride in a period of two to three hours.

Ethylmagnesium Chloride

So far, only two references have been found in the literature in which directions are given for the preparation of ethylmagnesium chloride--one by Louben⁶ and the other by Kyriakides²⁵.

25. Kyriakides, J. Am. Chem. Soc., 36, 657 (1914)

Houben's⁵ procedure will be given first. He made a 0.5 mole run by first starting the reaction with old ethylmagnesium chloride (he wished to avoid the use of bromine or iodine, for these halogens contaminated the desired products) and then placed the system (seemingly one without a stirring apparatus) in an ice-water bath. He then added three 20 g. portions of the halide according to the rate the halide was used up. In order to use all the magnesium it took twelve hours and nearly three equivalents of halide to conclude the reaction. Under these conditions, he probably obtained nearly a quantitative yield based on the magnesium and approximately 30-33%, as estimated by the amount used.

Kyriakides²⁵ used a strong walled bottle to carry out the reaction. The reaction was started with 1 cc. of methyl iodide and a crystal of iodine. Seventy-seven g. of magnesium was covered with 1000 cc. of ether. After the reaction had been started, 34 g. of the ethyl chloride was added to the cooled reaction mixture. The flask was now closed tightly and then warmed until the reaction began. The reaction was now allowed to proceed until all the halide had been used up. The rest of the 220 g. of halide was added in 60 g. portions in the same manner. All but 5 g. of the magnesium was used up. In this run, 3.2 atoms of magnesium and 3.3 moles of halide were used. The time of this preparation is not given.

Since both of these procedures are more or less inconvenient,

an attempt was made to improve the preparation of ethylmagnesium chloride in a closed system to prevent the loss of some of the halide which boils at 10.2° . The apparatus used in this experiment was essentially that described above for the preparation of methylmagnesium chloride with the exception that the halide was not added under the surface of the ether. The halide was added by means of a small bent glass tube which entered the system next to the stem of the dropping funnel and was adjusted so that the halide was delivered within 2-3 mm. of the surface of the ether.

The addition of the halide, in the manner described above, was easily controlled. If the rate of the addition of the halide was such that the pressure approached 50 mm., the flow of the halide could not only be stopped by the removal of the external heat from the bottle of halide, but some of the halide could be withdrawn from the system by cooling the bottle of halide. This was made possible by the use of a reversible bubbler in the sulfuric acid bottle of the purification train²⁴.

After the reaction flask was swept out with dry nitrogen, 12.2 g. (0.5 atom) of ordinary magnesium turnings were placed in the flask and covered with 50 cc. of ether. The sealed bottle of ethyl chloride was weighed and then cooled in an ice-water bath. The bottle was then opened and a boiling point tube was dropped into the bottle to prevent bumping; it was now connected with the purification train²⁴ (previously saturated with ethyl chloride) by means of rubber tubing.

After the reaction mixture was warmed to the boiling temperature of the ether by means of a micro burner under a wire gauze, the 50 mm. mercury trap was connected to the exit of the condenser. A crystal of iodine was added to the magnesium in ether. The bottle of halide was now raised from its cooling bath and the halide allowed to enter the reaction flask slowly, until there was approximately a positive pressure of 30 mm. within the system. The flow of the gas was now checked by lowering the bottle of halide into its cooling bath. After the reaction mixture was heated carefully for five minutes without stirring, the reaction started. The gaseous halide was now allowed to pass into the reaction flask at such a rate (controlled by warming or cooling the bottle of halide) that the pressure within the system remained between 30-40 mm.

While the reaction thus proceeded smoothly with stirring and refluxing from its own heat, the rest of the 200 cc. of ether was added by means of a dropping funnel (properly connected with the system for equalization of pressure) at such a rate that refluxing of the reaction mixture from its own heat did not cease. The addition of this main portion of ether took about one hour.

At the end of two hours (from the time of starting the addition of the halide) the pressure began to rise even though the halide was added very slowly, and since the magnesium was very nearly all used up, the addition of the halide was stopped. The bottle of halide was now cooled, sealed and weighed to determine

the amount of halide used and this was found to be 34.0 g. instead of the required 32.3 g. (0.5 mole).

The reaction mixture was now refluxed and stirred for an additional hour (in accordance with the usual procedure in the work on alkylmagnesium Chlorides) and with such intensity that the pressure within the system did not exceed 50 mm. The 50 mm. trap was now removed and the reaction mixture stirred and refluxed ten minutes more to drive off any excess halide.

There was no unused magnesium found in the flask. The yield of the Grignard reagent based on the halide used was 90.5%; based on the magnesium used, the yield was 95.2%.

The above procedure ought to be a convenient one if the halide is taken from bombs.

n-Propylmagnesium Chloride

The b. p. of the halide used was 45-46°. The halide was cooled in an ice-salt bath before it was weighed. Under "A-conditions" the yields were 88.4 and 87.0%. In another run the dropping funnel was cooled by means of a stream of cold air, and cold water (5-10°) was run through the condenser. The yield under these conditions was 88.2%.

Due to the volatility of the halide, no runs were made under "B-conditions".

iso-Propylmagnesium Chloride

The b. p. of the halide used was 35-36°. The halide was weighed as stated under "n-Propylmagnesium Chloride" above.

Under "A-conditions", the yield was 80%. With the cooling conditions as described under "n-Propylmagnesium Chloride", the yield was 88.8%.

Due to the volatility of the halide, no run was made under "B-conditions".

According to Ivanoff and Abdouloff²⁶, the $-MgBr$ radical in iso-propylmagnesium bromide is the most labile in the series of iso-propyl-, ethyl-, n-propyl-, sec-butyl-, n-butylmagnesium bromide, methylmagnesium iodide and iso-butylmagnesium bromide. The lability of the $-MgX$ radicals in the above compounds decreases in the order named. From these results it may be predicted that iso-propyl-, ethyl-, and n-propylmagnesium chlorides ought to be the best suited Grignard reagents for the replacements of active hydrogen, and of these three, the n-propylmagnesium chlorides could be most conveniently prepared.

n-Butylmagnesium Chloride

The b. p. of the halide used was 76-77°. Under "A-conditions", the yields were 91.5 and 92.2% With undistilled halide, the yield was 90.9%. Under "B-conditions", the yield was also 90.9%.

Recently, in connection with the preparation of some di-n-butylmercury, a one mole run of n-butylmagnesium chloride was made. One equivalent of the halide and magnesium was used with five equivalents of ether. The reaction started immedi-

26. Ivanoff and Abdouloff, Compt. rend., 196, 491 (1933)

with 5 cc. of the halide in 100 cc. of ether with a crystal of iodine. The rest of the halide, dissolved in 400 cc. of ether, was added over a period of one hour, without any special attention. The reaction apparently ended thirty-five minutes after all the halide had been added. The reaction was then concluded by one hour of stirring and refluxing. The yield was 95.5%. This run was made and cooled for analysis under nitrogen.

iso-Butylmagnesium Chloride

The b. p. of the halide used was 66-67°. Under "A-conditions" the yields were 83.3 and 85.1%. One run was made in which the reaction was concluded by a two, instead of the usual one hour, period of refluxing. The yield was 88.6%. With three different samples of undistilled halide under "A-conditions", the yields were 74.6, 81.5 and 83.9%, respectively.

Under "B-conditions" the yield was 72.3%.

sec-Butylmagnesium Chloride

The b. p. of the halide used was 68-69°. Under "A-conditions", the yields were 89.6 and 90.5%. With undistilled halide, the yield was 89.8%. One run was made in which the reaction was concluded by a three instead of the usual one hour period of refluxing. The yield was 87.9%. Another run was made under "A-conditions" without stirring at all. The reaction apparently ended in 50 minutes after all the halide had been added and it

was then refluxed one hour without stirring. The yield was 88.7%.

Under "B-conditions", the yield was 88.4%.

tert-Butylmagnesium Chloride

The b. p. of the halide used was 50-51°. The yields under "A-", and "B-conditions" were 45.0 and 40%, respectively. Under special conditions²⁷ it has been possible to obtain this Grignard reagent in yields of 58-70^{27a, b} and 83%^{27c}. Recently, under the same fundamental procedure, the yield has been increased to 85%^{28a} and 90%^{28b}.

Six new tert-alkylmagnesium chlorides of higher molecular weight have recently been prepared by Whitmore and Badertscher²⁹ by the above fundamental procedure in yields of 58-74%. These authors say that according to some preliminary work, they found that the yields of the Grignard reagents from tertiary chlorides were better than from the corresponding bromides and iodides. Before this notice appeared, the writer under special but comparable conditions, found that the yields of tert-butylmagnesium chloride, bromide and iodide were 83.6, 66.6 and 56%, respectively (see page 38 of this thesis). It was also found that in carbonating tert-butylmagnesium chloride, the rate of adding the carbon dioxide did not affect the yield of the acid derivatives.

27. (a) Gilman and Zoellner, J. Am. Chem. Soc., 50, 425 (1928);
(b) Rec. trav. chim., 47, 1058 (1928); (c) J. Am. Chem. Soc.,
53, 1583 (1931)
28. (a) Whitmore and Houk, J. Am. Chem. Soc., 54, 3714 (1932);
(b) Rheinbold, Matt and Malzkus, J. prakt. Chem., 134, 257
(1933)
29. Whitmore and Badertscher, J. Am. Chem. Soc., 55, 1559 (1933)

n-Amylmagnesium Chloride

The b. p. of the halide used was 106-107°. Under "A-conditions" with three different samples of undistilled halide, the yields were 76.9, 77.7 and 82.0%, respectively. With the distilled halide, the yields were 87.1 and 87.1%. A run was made in which the reaction was concluded by a two instead of the usual one hour period of refluxing. The yield was 89.9%.

Under "B-conditions", the yield was 89.9%.

tert-Amylmagnesium Chloride

Under special conditions^{27b} this Grignard reagent has been prepared in a yield of 54% in small sized runs. A large sized run (2.5 moles) was made and then carbonated. The yield of dimethylethylacetic acid was 54.1%. Later Corson, Thomas and Waugh³⁰ following the directions for the preparation of trimethylacetic acid³¹ obtained dimethylethylacetic acid by the carbonation of tert-amylmagnesium chloride in a yield of 60%. Recently Whitmore and Badertscher²⁷, under similar conditions, obtained this Grignard reagent in a yield of 73.6%, in a 5 mole run.

α -sec-Hexylmagnesium Chloride $\left[\text{CH}_3(\text{CH}_2)_3(\text{CHMgBr})\text{CH}_2 \right]$

The halide (b. p. 123.8-124°) was obtained in sealed tubes from Mr. H. E. Buc of the Petroleum Development Co. The yields under "A-conditions" were 89.0 and 89.6%; and under "B-conditions", the yield was 83.6%.

30. Corson, Thomas and Waugh, *J. Am. Chem. Soc.*, 55, 1559 (1933)
31. "Organic Syntheses", Vol. VII (1928) p. 104

β -sec-Hexylmagnesium Chloride $\left[\text{CH}_3(\text{CH}_2)_2\text{CH}(\text{MgBr})\text{CH}_2\text{CH}_3 \right]$

The halide (b. p. 112.7-113^o) was also obtained from Mr. Buc in a sealed tube. The yields under "A-conditions" were 101.8 and 102.2% and under "B-conditions", 96.7%.

Cyclohexylmagnesium Chloride

A study¹⁸ of this Grignard reagent in connection with cyclohexylmagnesium bromide has been reported. The results of this study are fully discussed on page 6 of this thesis.

Phenylmagnesium Chloride

This Grignard reagent has been prepared³² in a yield of 85% in a bomb tube without a solvent. It has also been prepared³³ in an ordinary apparatus used for the preparation of Grignard reagents by the use of activated copper-magnesium alloy, in yields of 68-80%. This Grignard reagent³⁴ has been recently used for the preparation of β -phenylethyl alcohol in satisfactory yields.

Benzylmagnesium Chloride

The results of this Grignard reagent appearing in Table I were taken from a previous study¹⁹. Since in this study magnesium turnings from the Special Chemical Co. were used and in the work of this thesis magnesium turnings from the Mallinkrodt Chemical Co. were used, a few runs were made with the latter

32. Gilman and Brown, J. Am. Chem. Soc., 52, 3330 (1930)

33. Gilman and St. John, N. B., Rec. trav. chim., 49, 717 (1930)

34. Shorugin and co-workers, Ber., 64, 2584 (1931)

brand of magnesium. In general, the former brand (now no longer on the market) has been found slightly better than the latter, but with this Grignard reagent no difference was, however, detected.

Since the above work has been published, Austin and Johnson³⁵ have obtained benzyl-, 2-chlorobenzyl-, and 2,6-dichlorobenzyl-magnesium chloride in yields of 90, 60-75 and 90%, respectively.

Benzohydrilmagnesium Chloride

This Grignard reagent, up to 1930, had always been prepared in the presence of the reactant for which it was intended. As a result of a recent study³⁶, it has become possible to prepare it in yields of 50-71% under very refined conditions in which an unusual excess of fine magnesium and ether had to be used.

Triphenylmethylmagnesium Chloride

A study³⁷ was made of the preparation of this Grignard reagent due to the fact that the yields reported in the literature were erratic. It was found that under special conditions, using an excess of fine magnesium and 0.25 equivalents of iodine, the Grignard reagent could be prepared consistently in yields of 96%.

Since then, Gomberg and Bachmann³⁸ have found that the corresponding RMgBr compound can be prepared under less refined conditions and in shorter time than the corresponding RMgCl compound in yields of 96-97% (see page 52 of this thesis).

35. Austin and Johnson, J. Am. Chem. Soc., 54, 647 (1932)
36. Gilman and Zoellner, ibid., 52, 3984 (1931)
37. Gilman and Zoellner, ibid., 51, 3493 (1929)
38. Gomberg and Bachmann, ibid., 52, 2455 (1930)

β -Phenylethylmagnesium Chloride

The halide had a b. p. of 78° (11 mm.). The yields of three runs, under "A-conditions", were 87.9, 89.1 and 89.7%, respectively; with undistilled halide, the yield was 84.9%. Under "B-conditions", one run gave a yield of 87.9%.

γ -Phenylpropylmagnesium Chloride

The yields of two runs under "A-conditions" were 87% and 87.4%; under "B-conditions", the yield was 85.3%.

γ -Tetrahydrofurylpropylmagnesium Chloride

This Grignard reagent was prepared by Gilman and Hewlett³⁹ in a yield of 91.6%. A 0.2 mole run was made with one equivalent of 80-200 mesh magnesium powder. The reaction was started with 0.5 g. of the 12.5% activated copper-magnesium alloy. The halide was added over a period of one hour.

Allylmagnesium Chloride

The halide used had a b. p. of $44-45^{\circ}$. This Grignard reagent could not be prepared, at all, with three equivalents of ordinary magnesium turnings. Gilman and McClumphy⁴⁰ prepared allylmagnesium bromide in a yield of 90.3%, using three equivalents of fine magnesium and adding the halide slowly (see page 39 of this thesis). Under these conditions, adding the halide over a period of one hour, a yield of 90.2% of allylmagnesium chloride was obtained from a 0.1 mole run.

39. Gilman and Hewlett, Rec. trav. chim., 51, 93 (1932)

40. Gilman and McClumphy, Bull. Soc. Chim., 43, 1322 (1928)

Every run in the preparation of allylmagnesium chloride was, however, not successful. For reasons, yet unknown, the reaction mixture in some runs became so colloidal that it could no longer be stirred and when this happened nothing could be done with it. The reaction mixture became so viscous that the solution could not be separated from the fine magnesium and consequently no analysis could be made. About 30% of the runs made in the study of this Grignard reagent were lost in this manner. Later Dr. R. E. Towne tried to use this Grignard reagent in the preparation of some allyl compounds of lead. He lost, in the above manner, about 75% of the runs of allylmagnesium chloride. In the preparation of allylmagnesium bromide, this difficulty has, as yet, not been met with.

Cinnamylmagnesium Chloride

This Grignard reagent has been prepared⁴¹ with three equivalents of fine magnesium and the slow addition of the halide in a yield of 83%. Under ordinary conditions of carbonation, the yield of the acid derivative was 38%, but this was, however, improved to 64% by means of an effective spray.

41. Gilman and Harris, Rec. trav. chim., 50, 1052 (1931)

DISCUSSION OF THE STUDIES ON ORGANOMAGNESIUM CHLORIDES

Methyl and ethylmagnesium chloride were prepared in a closed system (provided with a stirring apparatus) under a pressure of 60 mm., since the halides are gaseous at room temperature. The yields were 84.0 and 90.5%, respectively. The technique and apparatus used in the preparation of the above Grignard reagents may possibly be used to prepare other Grignard reagents from gaseous halides, such as vinylmagnesium chloride and bromide. The rest of the alkylmagnesium chlorides could be prepared under ordinary conditions except iso-propylmagnesium chloride. In the preparation of this Grignard reagent, the dropping funnel and condenser had to be kept cold; without this provision the yield was lowered 8.0% due to the loss of the halide.

The yields of n-butyl-, iso-butyl- and n-amylmagnesium chloride were slightly higher than those of the corresponding NEGR compounds¹⁹. The yields of sec-butyl- and tert-butylmagnesium chlorides were appreciably higher than the corresponding NEGR compounds; the yields of α -sec-hexyl- and β -sec-hexylmagnesium chloride were also very good. The yields of β -phenylethyl-, γ -phenylpropylmagnesium chloride and α -phenylethylmagnesium bromide were practically the same.

When the halides were added all at once, the yields of the alkylmagnesium chlorides were only slightly lowered. In general, while the yields of the corresponding NEGR¹⁹ (see

also Table II page 37 of this thesis) and RMgI compounds (see Table III page 56 of this thesis) were appreciably lowered.

In consideration of the data given under "General Introduction" (see pages 1-8 of this thesis) and the data of the "Experimental Part" as summarized above, it is evident that better results can be obtained, in general, with alkylmagnesium chlorides than with the corresponding RMgBr and RMgI compounds.

It was observed, qualitatively, that the alkylmagnesium chlorides were active towards the oxygen of the air. Recently, a quantitative study⁴² has been made of the reaction of oxygen with Grignard reagents. It was found that at low temperatures (0°) where the vapor pressure of ether is not high enough to prevent free access of air to the solution, the oxidation has been found to proceed at a very rapid rate and may become a serious side reaction in the use of the Grignard reagent. It is, therefore, desirable to cool the alkylmagnesium chlorides, used at low temperatures, under an inert atmosphere.

Since benzohydril- and allylmagnesium chloride and bromide can not be prepared independently without the use of fine magnesium, and since triphenylmethyl-, cinnamyl- and tert-alkylmagnesium chlorides can be prepared in excellent yields only with fine magnesium, it would be very desirable if the fine magnesium as prepared in this laboratory could be obtained on the market. This fine magnesium would, undoubtedly, find extensive applications as a "starter" for organomagnesium

42. Goebel and Marvel, J. Am. Chem. Soc., 55, 1693 (1933)

chlorides in connection with ordinary magnesium turnings.

The substance of the work on the preparation of organo-magnesium chlorides (involving the use of the acid titration method of analysis) already published, has been included in Table I and in the experimental details following that Table. This was done to facilitate a comprehensive view of this phase of the Grignard reagent.

PART II. QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM BROMIDES

INTRODUCTION

Studies, on the preparation of a large number of organomagnesium bromides, commonly used, have already been reported¹⁹. In continuation of this work, quantitative studies on the preparation of some organomagnesium bromides, less commonly used, have been made. The results of these studies are now given in detail. An effort has been made to correlate with these details, some studies already published by the writer and others in order to facilitate a summary of the data on this phase of the Grignard reagent.

EXPERIMENTAL PART

The apparatus and technique were essentially the same as those described fully under Part I. The conditions under which the reactions were carried out were also the same, with the exception that the reactions were usually started in two to five minutes with 20 drops of the halide and a crystal of iodine in 7.5 cc. of ether. The reactions were usually concluded by a fifteen minute period of stirring and refluxing after the reaction had apparently ended.

The results of these studies are summarized in Table II and are more fully discussed under the headings of the various Grignard reagent following Table II.

TABLE II

SUMMARY OF THE QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM BROMIDES

Bromide	% Yields of RMgX Under A- ^a , B-Conditions ^b		Drop of Yield Under ^a B-Conditions	Time of Apparent ^c Reaction Under A-, B-Conditions		% Yields of RMgX Under Special Conditions
	A	B		A	B	
<i>b</i> n-Butyl	94.0	79.2	14.8	4 min.	11 min.	93-96
<i>c</i> tert-Butyl	25.1	17.8	7.3	3	8	66.6
<i>d</i> Lauryl	85.3	74.3	11.0	8	13	----
<i>e</i> Cetyl	----	----	----	----	----	72.6-79.6
<i>f</i> Allyl	----	----	----	----	----	90.3
<i>g</i> Buten-3-yl	100.8	----	----	----	----	----
<i>h</i> Cyclohexyl	80.1	54.1	26.1	5	12	81-92
<i>i</i> Benzyl	93.4	88.6	4.8	5	8	----
<i>j</i> p-Methoxybenzyl	---	----	----	----	----	54.0
<i>k</i> β-Phenylethyl	89.3	77.5	11.8	8	13	89-93
<i>l</i> α-Methyl-γ-tetrahydro-2-furylpropyl	----	----	----	----	----	94.0
<i>m</i> 2-Cymyl	87.0	82.7	4.3	8	28	----
<i>n</i> o-Methoxyphenyl	99.2	96.3	3.0	8	28	----
<i>o</i> p-Methoxyphenyl	91.2	82.6	8.6	8	30	97-100
<i>p</i> o-Methoxyphenyl	98.8	98.5	0.3	8	18	----
<i>q</i> p-Ethoxyphenyl	84.5	78.5	6.0	13	43	93-96
<i>r</i> p-Bromophenyl	103.3	99.8	3.5	10	13	113-117

RMgX
10 10
RMgI
P58

TABLE II. CONT'D.

SUMMARY OF THE QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM BROMIDES

<u>Bromide</u>	<u>% Yields of RMgX Under A-^a, B-Conditions</u>		<u>Drop of Yield Under^a B-Conditions</u>	<u>Time of Apparent^c Reaction Under A-, B-Conditions</u>		<u>% Yields of RMgX Under Special Conditions</u>
	<u>A</u>	<u>B</u>	<u>B</u>	<u>A</u>	<u>B</u>	
<i>cu</i> p-Chlorophenyl	95.8	91.2	4.6	18 min	20 min	----
<i>v</i> p-Diphenyl	----	----	----	----	----	75-77
<i>w</i> Mesitylyl	----	80.3	----	----	----	82-82
<i>x</i> β-styryl	50	42	8	12	45	75-90
<i>y</i> Triphenyl-methyl	----	----	----	----	----	96-97

For explanation see pages: ^a page 10; ^b, ^c page 11; ^d page 12 of this thesis.

n-Butylmagnesium Bromide

The yields of 94.0 and 79.2% given under "A-" and "B-conditions" in Table II are taken from a previous study¹⁹.

Recently, in connection with the preparation of some di-n-butylmercury, several one mole runs of n-butylmagnesium bromide were made. In these runs one equivalent of ordinary magnesium turnings, one equivalent of halide and five equivalents of ether were used. The magnesium was covered with 100 cc. of ether and to this was added 3 cc. of halide and a crystal of iodine. With this amount of halide in 100 cc. of ether, the reaction started immediately, and when 5 cc. of halide was used, the reaction started vigorously.

After the reaction had been started, the rest of the halide, in 400 cc. of ether, was added as fast as the condenser would return the ether vapor to the solution. When all the halide had been added, the reaction apparently ended in ten to fifteen minutes. The reaction mixture was then refluxed and stirred fifteen minutes longer.

The yield of one run in which the halide was added over a period of one hour and thirty minutes was 96.0%. In two runs the halide was added over a period of one hour. The yields of these two runs were 93 and 95.6%, respectively

tert-Butylmagnesium Bromide

The yields of 25.1 and 17.8% given under "A-" and "B-conditions" in Table II are taken from a previous study¹⁹.

Since then, a study was made of the comparative yields of tert-butylmagnesium chloride, bromide and iodide with three equivalents of fine magnesium. The halide was added over a period of one hour. The yields of the above Grignard reagents, in the order named, were; 83.6, 66.6 and 56%, respectively.

Laurylmagnesium Bromide (n-C₁₁H₂₃MgBr)

The b. p. of the halide used was 145-147° (12 mm.). The yields under "A-" and "B-conditions" were 85.3 and 74.3%, respectively. The yield previously reported^{22c} was 73.7%.

Cetylmagnesium Bromide (n-C₁₆H₃₃MgBr)

This work was done several years ago. There is no record as to where the halide was obtained. The halide was probably used without distilling it first.

A 0.035 mole run was made with six equivalents of ether. The halide was added over a period of thirty minutes. The yield was 79.6%. Another run of the same size was made in which twelve equivalents of ether were used. The halide was added over a period of forty-five minutes. The yield in this case was 72.6%.

Allylmagnesium Bromide

This Grignard reagent was first prepared by Gilman and McGlumphy⁴⁰ in a yield of 90.3% when 0.5 mole of the halide was added over a period of two hours. Three equivalents of 30 mesh magnesium were used.

Buten-3-yl-magnesium Bromide $\left[\text{CH}_2=\text{CHCH}_2\text{CH}_2\text{MgBr} \right]$

This Grignard reagent was prepared by Dr. E. B. Towne⁴³. A 0.025 mole run was made in which 0.028 atom of ordinary magnesium turnings and twelve instead of the usual six equivalents of ether were used. This increased amount of ether was used so that the reaction mixture could be vigorously stirred. Otherwise, the conditions were essentially those of "A-conditions". The yield was 100.8%

Cyclohexylmagnesium Bromide

The results in Table II, on this Grignard reagent, are taken from a study¹⁹ already reported. This Grignard reagent, in connection with the corresponding RMgCl, is fully discussed on page 6 of this thesis.

Benzylmagnesium Bromide

The b. p. of the halide used was 84-85°. The yields of two runs under "A-conditions" were 93.3 and 93.5%, respectively; and of two runs under "B-conditions", 87.4 and 88.6%, respectively.

p-Methoxybenzylmagnesium Bromide

This Grignard reagent was prepared⁴⁴ in a yield of 54%. A 0.0216 mole run was made, adding the halide over a period of thirty minutes to three equivalents of fine magnesium powder, while the reaction mixture was refluxed and vigorously stirred.

43. E. B. Towne, Ph. D. Thesis, Iowa State College (1932)
44. Gilman and Zoeliner, Bull. soc. chim., 49, 2126 (1931)

With ten to twelve equivalents of the magnesium, the yield could very probably be much increased.

β -Phenylethylmagnesium Bromide

Krause and Schlottig⁴⁵ used this Grignard reagent for the preparation of organolead compounds. In their report, a statement was made that an excess of this Grignard reagent was necessary because its yield was low.

The b. p. of the halide used was 99-100° (15 mm.). Under "A-conditions", the yields of two runs were 88.6 and 90.0%, respectively; with two samples of undistilled halide, the yields were 86.5 and 87.8%. Under "B-conditions", the yield of one run was 77.5%.

With one and one-tenth equivalents of fine magnesium, the yields of two runs were 88.8 and 89.4%, respectively; with two equivalents, 90.3%, and with three equivalents, the yields of two runs were 90.1 and 92.3%, respectively.

α -Methyl- γ -tetrahydro-2-furyl-propylmagnesium Bromide

This Grignard reagent was recently prepared⁴⁶ with fine magnesium in a yield of 94%.

2-Cymylmagnesium Bromide $1,2,4-(\text{CH}_2)\text{-MgBr-}[(\text{CH}_2)_2\text{CH}]_2\text{C}_6\text{H}_3$

The halide used had a b. p. of 115-117° (15 mm.). The yield of a run under "A-conditions" was 86.7%. Another run was made in which the reaction was concluded by a forty-five minute period of refluxing instead of the usual fifteen minute

45. Krause and Schlottig, Ber., 63, 1361 (1930)

46. Gilman and Dickey, J. Am. Chem. Soc., 52, 2144 (1930)

period. The yield was 87.3%. Under "B-conditions," the yield was 82.7%.

o-Methoxyphenylmagnesium Bromide

The halide used had a b. p. of 102° (13 mm.). Under "A-conditions" with undistilled halide, which was slightly colored, the yield was 98.8%. The yields of two runs with distilled halide were 99.2% and 99.4%. Under "B-conditions", the yields of two runs were 96.0 and 96.6%, respectively.

In the above runs 60 cc. of benzene was used as a diluent before removing samples for analysis. Since no two layers formed with 0.05 mole of this Grignard reagent in 35 cc. of ether, a run was made in which 60 cc. of ether was used as a diluent. The yield was 98.3%.

The reaction of this Grignard starts slowly with 20 drops of the halide and a crystal of iodine in 7.5 cc. of ether. It is better to use 40 drops of the halide instead of the usual 20 drops to start the reaction of this Grignard reagent.

p-Methoxyphenylmagnesium Bromide

The m. p. of the halide used was 13°. Under "A-conditions" the yields of two runs with undistilled halide were 88.2 and 88.3%, respectively. With the distilled halide, the yields of three runs were 90.2, 91.2 and 91.2%, respectively. One run was made in which the reaction was concluded by forty-five minute period instead of the usual fifteen minute period of refluxing.

The yield was, however, not improved.

The yield of one run under "B-conditions" was 82.6%.

Since a solution of this Grignard reagent formed two layers, 60 cc. of benzene was used as a diluent before samples were removed for analysis. A run was, however, made in which only ether was used as a diluent. The yield of the Grignard reagent in the upper layer was 53.1%. This shows that this Grignard reagent is soluble in ether to the extent of approximately 0.02 mole per 100 cc.

About 40-50 drops of this halide in 7.5 cc. of ether must be used to start the reaction in the usual time required for organomagnesium bromides (three to five minutes).

The yields of two runs with one and one-tenth equivalents of fine magnesium were 95.7 and 97.4%, respectively; and with two equivalents, the yield of one run was 99.5%.

o-Ethoxyphenylmagnesium Bromide

The halide was prepared by Mr. I. J. Shames. No data of its preparation is given in his report, except that of the b. p. which was 124-126° (29 mm.). The halide was redistilled, b. p. 112° (17 mm.). The yield of one run under "A-conditions" was 98.0% and under "B-conditions" the yield of one run was 98.5%. In these runs 60 cc. of benzene was again used as a diluent. This was evidently not necessary for two layers were not formed with 0.05 mole of this Grignard reagent in 35 cc. of ether. The yield of one run, using ether as a diluent, was 99.5%.

About 40-50 drops of this halide in 7.5 cc. of ether should be used to start this Grignard reagent.

p-Ethoxyphenylmagnesium Bromide

The b. p. of the halide used was 112-113° (13 mm.), and the m. p. was 9-10°. Under "A-conditions", the yield of a run with undistilled halide, slightly colored, was 75%, and the yield of another run with undistilled halide, colorless, was 84.8%. The yields of two runs, with distilled halide, were 84.2 and 84.8%, respectively. Under "B-conditions", the yield of one run was 78.5%.

Since two layers were formed with 0.05 mole of this Grignard reagent in 35 cc. of ether, 60 cc. of benzene was used as a diluent. One run was made in which ether was used as a diluent. The two layers disappeared and the yield was the same as when benzene was used.

About 40-50 drops of the halide in 7.5 cc. of ether should be used to start the reaction of this Grignard reagent.

With one and one-tenth equivalents of fine magnesium, the yield of one run was 93.0%, and with two equivalents, the yield of one run was 96.2%. The yield may be quantitative with three equivalents of fine magnesium.

p-Bromophenylmagnesium Bromide

The halide used was recrystallized from ether. The m. p. then was 87-88°. Four-tenths g. of the halide was used to start the reaction in 7.5 cc. of ether. After the reaction had started, the usual 7.5 cc. of ether was added to fully cover the magnesium.

Twenty-five cc. of ether had to be used with the remainder of the halide, because the 15 cc. usually used did not dissolve the halide. The rest of the procedure was essentially that of the "A-conditions". Since two layers were formed with 0.05 mole of this Grignard reagent, 60 cc. of benzene was used as a diluent before removing samples for analysis. The yield of one run under these conditions was 103.3%; and the yield of one run under "B-conditions" was 99.8%.

A run was made in which 60 cc. of ether was used as a diluent. The yield of the Grignard reagent in the ether layer was 72.2%.

With two and one-tenth equivalents of ordinary magnesium turnings, the yield of one run was 113.5%, and when the time of adding the halide was extended to one hour, the yields of two runs were 115.1 and 115.3%, respectively. Another run was made in which the time of adding the halide was extended to two hours. The yield was 117.3%.

Recently, a study⁴⁷ was made of this Grignard reagent using activated copper-magnesium alloy. This work includes references to earlier studies.

p-Chlorophenylmagnesium Bromide

The halide (m. p. 65-66^o) was not recrystallized since it was evidently very pure. The reaction was started in the same manner as that given for p-bromophenylmagnesium Bromide. The usual 15 cc. of ether used with the main portion of the halide

47. Gilman, Beaber and Jones, Rec. trav. chim., 48, 597 (1929)

was sufficient to dissolve the halide. Under "A-conditions", the yields of two runs were 94.7 and 96.9%; and the yield of one run under "B-conditions" was 91.2%. Two layers did not form with 0.05 mole of this Grignard reagent in 35 cc. of ether.

When this Grignard was exposed to the air, it showed a high degree of luminescence.

p-Diphenylmagnesium Bromide (p-C₆H₅C₆H₅MgBr)

The m. p. of the halide used was 92°, and since it was evidently very pure, it was not recrystallized.

A run was made under "A-conditions". The reaction had seemingly started with 0.68 g. of the 11.68 g. (0.05 mole) used. The remainder of the halide required 35 cc. of ether to dissolve it. Since the reaction mixture did not boil, external heat was applied while the main portion was added in the usual time of thirty to thirty-five minutes. After all the halide had been added, the reaction mixture was stirred and refluxed for forty-five minutes. The reaction mixture now began to turn brown. This was probably the time the reaction had really started. There now was enough heat evolved to keep the reaction mixture boiling but not enough to cause refluxing. The reaction mixture was refluxed and stirred three and one-half hours longer. During this time the color of the reaction mixture changed from brown to a reddish brown and at the same time a grey precipitate began to form. This grey precipitate did not dissolve when 60 cc. of benzene was used as a diluent previous to the analysis. The yield was

67.5% and the amount of unused magnesium qualitatively supports the yield.

The next run was made more or less under "B-conditions". The halide was dissolved in 40 cc. of ether and this solution was placed in the reaction flask with all the other reagents. After adding a crystal of iodine, the reaction mixture was refluxed for fifteen minutes. Since the iodine color had not disappeared, 0.25 g. of the activator prepared by Mr. R. H. Kirby from fine magnesium and iodine in benzene was added. The reaction mixture was now stirred and refluxed for six hours. During this time, the color of the reaction mixture changed to a pale green, then to a brown and finally to a reddish brown. The yield was 75%.

The next run was made with one and one-tenth equivalents of fine magnesium. An attempt was made to start the reaction with iodine alone. The reaction could, however, not be started by refluxing for one and one-half hours. The reaction was now started with the above activator. Even with this fine magnesium there was not enough heat evolved to cause the reaction mixture to reflux. As in the last run above, there was only a very slight evidence of boiling. It was refluxed and stirred for six hours. The yield was 76.7%.

The solution luminesces strongly when the benzene is added as a diluent. When exposed to the air, the luminescence is about as strong as that shown by *p*-chlorophenylmagnesium bromide.

More work should be done on this Grignard reagent. Perhaps

an ultimate yield of 75-77% can be obtained between four and six hours time of stirring and refluxing. It may be possible also to increase the yield by a longer period of refluxing and stirring than six hours.

Mesitylylmagnesium Bromide $[2,4,6-(CH_3)_3C_6H_2MgBr]$

In a recent preparation⁴⁸ of isodurene (1,2,3,5-tetramethylbenzene) from mesitylylmagnesium bromide and diethyl sulfate, directions are given for the preparation of this Grignard reagent. In a two mole run, the reaction was started with approximately 25% of the halide used for the run. This was approximately a concentration of 60% of the halide in ether by volume. Even with such a high concentration of the halide in ether, an activator⁴⁹ had to be used to start the reaction. It has been the writer's experience that under the conditions given above, 4-9% of the Grignard reagent may be lost as coupling and disproportionation products. For this reason, a study was made of the preparation of this Grignard reagent, with the hope of starting the reaction in a less drastic manner and, if possible, without the use of the activator.

The halide, having a b. p. of 107-109° (17 mm.), used, was prepared by Mr. Paul R. Van Ess according to the procedure given in Organic Syntheses⁵⁰.

48. "Organic Syntheses" Vol. XI (1931) p. 66.

49. Gilman, Peterson and Schulze, Rec. trav. chim., 47, 19 (1928)

50. "Organic Syntheses" Vol. XI (1931) p. 24

After some preliminary experiments, it was found that the Grignard reagent could be best prepared in 0.05 mole runs as now described. The magnesium was covered with 15 cc. of ether and to this was added all the halide with a crystal of iodine. The reaction was then started in the usual manner. It took eight to ten minutes for the iodine color to disappear. Now 15 cc. more ether was added. The reaction mixture was now stirred without the application of external heat, but since there was no evidence of reaction, external heat was again applied. The reaction mixture was now refluxed and stirred for three hours. The yield was 80.3% under these conditions, and with a two hour period of refluxing, the yield was 75.6%. With longer period of refluxing and stirring than three hours, the yield was not improved beyond 82%. The yield of a run with only four equivalents of ether instead of the usual six equivalents, was 80.0%.

Now several experiments were made with activators for starting the reaction of Grignard reagents, using 12.75% copper-magnesium⁴⁹ alloy (30-80 mesh) and ordinary 30-80 mesh magnesium. The copper-magnesium alloy was obtained from Dr. G. F. Wright who prepared it in benzene and ether according to the directions of Mr. R. H. Kirby. The activator so prepared contained by weight 16.7% iodine, 10.6% copper and 72.7% magnesium. Twenty-five hundredths g. of this activator was reactivated by heating in a test tube by means of a flame

from a Bunsen burner to such an extent that the iodine vapor formed at first was reabsorbed by the metal and all the residual benzene was driven off. While still hot (50-60°) it was added to the starting mixture as described in the run above. The reaction started immediately but slowly in cold ether. It was now refluxed and stirred for three hours so as to make the conditions comparable with the run described above. The yield was 83.2%. In a second run 0.5 g. of the activator was used to ascertain whether or not the yield would be affected by increasing the amount of the activator. The yield was 83.4%. In a third run, 0.25 g. of plain fine magnesium with a crystal of iodine was used to start the reaction. The reaction did, however, not start by itself in thirty minutes. After the application of external heat, the reaction started well in five minutes. It was now refluxed and stirred for three hours. The yield was 81.7%. It is very probable that the use of this fine magnesium may find a general application as a "starter" for Grignard reagents.

One run was made in which only fine magnesium was used. The reaction started immediately with 60 drops of the halide and a crystal of iodine in 10 cc. of ether. Even with this fine magnesium, the reaction was so slow that the ether did not boil. The reaction was refluxed and stirred for three hours as described above. The yield was 82.3%.

✓ In a recent⁵¹ study on the steric hindrance and the

51. Gilman and Heck, Ber., 62, 1379 (1929)

Grignard reaction, a yield of 50% was reported for this Grignard reagent. A 0.1 mole run was made. Activated copper-magnesium alloy was used to start the reaction. It was now allowed to proceed at room temperature for three hours, when the reaction apparently ceased. The yield of the acid derivative was 50%, based on the Grignard reagent used.

3-Styrylmagnesium Bromide ($C_6H_5CH_2=CHMgBr$)

The halide used had a b. p. of 84° (4 mm.) and a m. p. of $2-3^\circ$. Under "A-conditions" the yields of three runs were 49.0, 50.0 and 50.9%, respectively; and under "B-conditions" the yields of two runs were 41.6 and 41.8%, respectively. To start the reaction 40-50 drops of halide with a crystal of iodine in 7.5 cc. of ether had to be used. With gentle refluxing under these conditions, the reaction was started in six to eight minutes.

Under the conditions above, a yield of 47.5% was reported^{22c} for this Grignard reagent. Rupe and Proske⁵² obtained styrene in a yield of 54% by the hydrolysis of this Grignard reagent.

It is well to mention here that a solution of this Grignard reagent is opaque and is very dark colored. In starting the reaction of this Grignard reagent the appearance of this color is a good indication that the reaction has set in.

In 0.1 mole runs with three equivalents of ordinary magnesium turnings and the addition of the halide over a period of

52. Rupe and Proske, Ber., 43, 1231 (1910)

two hours, the yields were 75-85%; when fine magnesium was used under these conditions, the yield was 85-90%. The highest yield of the acid derivative by carbonation under ordinary conditions was 32%. Lately, Dr. S. A. Harris has obtained the acid derivatives under special conditions of carbonation in a yield of over 70%.

So far, seventeen Grignard reagents of the styrene types have been reported in the literature but very few of these have been prepared in satisfactory yields. As a result of the study reported above, this type of Grignard reagent may now be prepared in satisfactory yields.

Triphenylmethylmagnesium Bromide

This Grignard reagent was recently prepared by Gomberg and Bachmann³⁸ without the aid of an activator. Sixteen and two-tenths g. of the halide was reacted with 1.34 g. of magnesium ribbon in a solution of 25 cc. of ether and 50 cc. of benzene in one hour with the application of external heat. The yield was 96-97%.

The triphenylmethylmagnesium bromide can be prepared more conveniently than the corresponding RMgCl ³⁷ compound and in less time. In the preparation of the latter Grignard reagent, an excess of fine magnesium and twenty-five hundredths of iodine is required; and it takes three hours to carry out the reaction.

DISCUSSION OF THE STUDIES ON ORGANOMAGNESIUM BROMIDES

Twenty of the commonly used alkyl- and arylmagnesium bromides have been discussed in a previous study¹⁹. The results of the studies on some organomagnesium bromides less commonly used, as given above in the experimental part, will now be discussed.

It has been shown above that n-butylmagnesium bromide can be prepared in yields of 93.0-95.6% by adding one mole of halide to the magnesium over a period of one hour. Under these conditions, the yield of n-butylmagnesium chloride was 95.5% (see page 25 of this thesis). In these runs, the halide was added as fast as the condenser could return the ether vapor to the reaction mixture. Recently, studies⁵³ have been reported in which it was shown that good yields of n-butylmagnesium bromide may even be obtained by adding the halide at a rate of one mole per twenty to thirty minutes.

Under ordinary conditions, the yield of tert-butylmagnesium bromide is 25.1%. This yield has been increased to 66.6%, by the use of excess fine magnesium and slow addition of the halide.

The yield of laurylmagnesium bromide ($C_{11}H_{13}MgBr$) under standard conditions was 85.3%, and when the halide was added

53. Borgstrom, Wagner and Griffin, J. Am. Chem. Soc., 51, 1861 (1929); Gilman, Edith L. St. John and Nina B. St. John, Rec. trav. chim., 48, 593 (1929)

all at once, the yield was lowered 11.0%. Under corresponding conditions, as reported in a previous study^{19b}, the yields of n-propyl-, n-butyl-, n-amyl-, n-hexyl- and n-octylmagnesium bromide were 91.7, 94.0, 88.6, 92.0 and 88.8%, respectively; and when the halides were added all at once, the yields were lowered, 9.2, 14.8, 15.4, 14.8 and 15.9%, respectively. In consideration of the above data, it is evident that the yields of n-alkylmagnesium bromides decrease only slightly as the length of the alkyl radical is increased. The yield of cetyl-magnesium bromide ($C_{16}H_{33}MgBr$) was 72.6-79.6%, but since this Grignard reagent was not prepared under standard conditions, the results can not be considered in the above discussion.

Allylmagnesium chloride and bromide can now be prepared in yields of 90% with excess of fine magnesium and slow addition of the halide. It is not advised, however, to replace the $RMgBr$ compound with the $RMgCl$ compound, in general laboratory practice, since the latter compound can not always be successfully prepared, due to the fact that its reaction mixture often assumes a colloidal state. When this happens, the reaction can not be completed.

The yield of benzylmagnesium bromide under ordinary conditions and with ordinary magnesium turnings was 93.4%, while with an excess of fine magnesium and slow addition of halide, the yield of p-methoxybenzylmagnesium bromide was only 54%. The corresponding $RMgCl$ compound of the latter can very probably be prepared in a much better yield.

β-Phenylethyl-, 2-cyml-, *o*- and *p*-methoxyphenyl-, *o*- and *p*-ethoxyphenyl-, *p*-bromophenyl-, *p*-chlorophenyl-, *p*-diphenyl-, mesityl- and *β*-styrylmagnesium bromide have been prepared in excellent yields either under ordinary or special conditions. The above compounds contain hydrocarbon radicals that are important in synthetic work of organic chemistry.

Of the above Grignard reagents, more work should be done on the reaction of *p*-dibromobenzene with magnesium. The results of the experimental part on this reaction, above, indicate that a mixture of the mono- and dimagnesium bromide is formed, since the reaction mixture separates in two liquid layers. Under given conditions, it was found that the combined yield was 102.3%, while the yield in the ether layer was only 78.2%.

It is the writer's opinion that probably only the mono-magnesium bromide dissolves in ether and that all the dimagnesium bromide is found in the lower layer, when the reaction mixture is diluted with ether. If this is true, each of the Grignard reagents could be made available for specific purposes by simply separating the two liquid layers. It must be ascertained by experiment whether or not the above suggestion is practical.

Furthermore, it may be possible to increase the yield of the di-Grignard reagent by removing the lower layer as it is formed. It is the opinion of the writer, based on the experience of preparing di-Grignard reagents, that the thick and

viscous lower layer either acts as an anti-catalyst or prevents good contact of the $R(X)MgX$ compound with the magnesium.

The substance of the work on the preparation of organomagnesium bromides (involving the use of the acid titration method of analysis) already published has been included in Table II and in the experimental details following that table. This was done to facilitate a comprehensive view of this phase of the Grignard reagent.

PART III. QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM IODIDES

INTRODUCTION

Since very little work has been done on the preparation of organomagnesium iodides under general and special conditions, studies have been made of some of the typical compounds. The results of these studies are now given in detail. An effort has been made to correlate with these details the results of a few studies reported in the literature in order to facilitate a summary of the data on this phase of the Grignard reagent.

EXPERIMENTAL PART

The apparatus and technique were essentially the same as those described fully under the Experimental Part of Part I. The conditions in general under which the reactions were carried out are those given in the experimental part of part II.

In general, the reactions of the organomagnesium iodides started less readily than the reactions of the organomagnesium bromides but with greater ease than the reactions of the organomagnesium chlorides.

The times of apparent reactions, after all the halides had been added, under "A-" and "B-conditions", for the alkylmagnesium iodides, were approximately those of the corresponding RMgBr compounds¹⁹. The work on the alkylmagnesium iodides was done before the value of such data was realized.

TABLE III

SUMMARY OF THE QUANTITATIVE STUDIES OF SOME ORGANOMAGNESIUM IODIDES

Iodide	% Yields of RMgX Under A- ^a B-Conditions ^b		Drop of Yi Yield Under ^a B-Conditions	Time of Apparent ^c Reaction Under A-, B-Conditions		% Yields of RMgX Under Special ^d Conditions
	A	B		A	B	
<i>a</i> Methyl ^a	90.3	90.1	0.2	----	----	90.2-91.7
<i>b</i> Ethyl	87.5	78.5	9.0	----	----	90.0-92.4
<i>c</i> <u>n</u> -Propyl	80.7	71.4	9.3	----	----	----
<i>d</i> <u>n</u> -Butyl	80.1	62.0	18.0	----	----	----
<i>e</i> <u>tert</u> -Butyl	----	----	----	----	----	56.0
<i>f</i> <u>n</u> -Amyl	78.2	58.2	20.0	----	----	----
<i>g</i> <u>n</u> -Hexyl	59.5	----	----	----	----	----
<u>n</u> -Heptyl	64.3	----	----	----	----	----
<u>n</u> -Octyl	44.2	----	----	----	----	----
<i>h</i> <u>n</u> -Nonyl	66.2-70.7	--	----	----	----	----
<u>n</u> -Decyl	51.1-58.8	--	----	----	----	----
<u>n</u> -Undecyl	69.5-71.5	--	----	----	----	----
<i>i</i> Cetyl	----	----	----	----	----	69-77
<i>j</i> Phenyl	85.6	72.3	13.3	8 min	13 min	92-94
<i>k</i> 2-Furyl	87.9	86.6	1.3	19	30	93.2-95.0
<i>l</i> 2-Methyl-5-Furyl	89.9	91.3	0.0	5	18	----
<i>m</i> 2-Thienyl	98.6	99.7	0.0	8	15	----

For explanation of notes; ^a see page 10; ^{b, c} see page 11;

^d see page 12.

RMgX
P 37
RMgCl
P 14

Methylmagnesium Iodide

The b. p. of the halide used was 41° . Under "A-conditions" the yield was 90.3% and with undistilled halide, 88.4-90.0%. Under "B-conditions" the yield was 89.8-90.4%.

With one and one-tenth equivalents of fine magnesium, the yield was 90.2-90.5% and with two equivalents, 91.7%.

Ethylmagnesium Iodide

The b. p. of the halide used was 71° . Under "A-conditions" the yields were 85.5, 86.2 and 87.2%. When the halide was added over a period of one hour, the yield was not improved. With undistilled halide the yield was 84.5-87.8%. Under "B-conditions" the yield was 78.3-78.6%.

With one and one-tenth equivalents of fine magnesium the yield was 90.0%. When the halide was added over a period of one hour, the yield was not improved. With two equivalents, the yield was 92.4%.

Yields of 84-96%^{22c} have been reported for this Grignard reagent.

n-Propylmagnesium Iodide

The b. p. of the distilled halide was not recorded. It was probably $100-101^{\circ}$, according to the Eastman Kodak Co. catalogue. Under "A-conditions" the yield was 80.6-80.8%, and under "B-conditions", 71.4%.

A yield of 79.4% has been reported^{22c}.

n-Butylmagnesium Iodide

The b. p. of the halide used was 128.8-130°. Under "A-conditions" the yield was 78.5-80.4%, and with undistilled halide, 79.4-81.4%. Under "B-conditions" the yield was 61.8-62.8%.

Under "A-conditions" yields of 65.2^{22c} and 85.6%¹⁹ of this Grignard reagent have been reported.

tert-Butylmagnesium Iodide

It is doubtful that this Grignard reagent can be prepared with one and one-tenth equivalents of ordinary magnesium turnings. It has, however, been prepared in a yield of 56.0% under special conditions (see page 38 of this thesis).

n-Amylmagnesium Iodide

The halide (b. p. 154-155°) used was obtained from Eastman Kodak Co. in compliance with an order for a fresh and pure sample. The halide so obtained was colorless and was used without redistilling it. The yield of a run under "A-conditions" was 78.2% and under "B-conditions", 58.2%.

With old halide, but redistilled, the yields were 4-8% lower than those given above.

A yield of 75.8%^{22c} has been reported for this Grignard

n-Hexyl-, n-Heptyl-, n-Octylmagnesium Iodide

The yields of these Grignard reagents reported in the order named above were; 59.5^{22c}, 64.3^{22c} and 44.2%^{22c}.

n-Nonyl-, n-Decyl- and n-Undecylmagnesium Iodide

Sixteen g. of each of the halides used were obtained from Frankel and Laudau.

None of the halides was distilled because only two 0.025 mole runs could be made with the above amounts. Of these halides, the decyl iodide was slightly colored but the rest were colorless. The yields of the Grignard reagents from these halides were:

n-Nonylmagnesium Iodide	66.2 and 70.7%
n-Decylmagnesium Iodide	51.1 " 58.8
n-Undecylmagnesium Iodide	69.5 " 71.5

Cetylmagnesium Iodide (n-C₁₆H₃₃MgI)

The halide was not redistilled. There is no record as to where the halide was obtained.

Several 0.025 mole runs were made in which twelve equivalents of ether were used. The halide was added over a period of forty-five minutes. The yields ranged from 69% to 77%.

Phenylmagnesium Iodide

The b. p. of the halide used was 65° (12 mm.). Under "A-conditions" the yield was 85.5-85.7% and under "B-conditions", 71.8-72.8%.

With one and one-tenth equivalents of fine magnesium, the yield was 92% and when the halide was added over a period of one hour, the yield was 94%. With two equivalents (adding the halide in the usual time) the yield was 93.4%.

A yield of 84.6%⁵⁴ has been reported for this Grignard reagent.

The time of apparent reaction, after all the halide had been added under "A-conditions", was eight minutes, and under "B-conditions" the time was thirteen minutes. These periods of apparent reaction, after all the halide had been added, were found to be the same for phenylmagnesium bromide.

2-furylmagnesium iodide

The halide was prepared according to the directions given in a recent study⁵⁴ on 2-furyl iodide and the corresponding Grignard reagent. The b. p. of the halide used was 45-47° (15 mm.). Under "A-conditions", the yields of three runs were 87.4, 88.0 and 88.2%. The reaction was started with 40 drops of halide (instead of the usual 20 drops) in three to five minutes in the usual manner. The reaction was concluded with a forty-five instead of the usual fifteen minute period of stirring and refluxing after the reaction had apparently ceased.

Under "B-conditions", the yield of one run was 86.6%.

With two and three equivalents of ordinary magnesium turnings the yields were 93.2 and 93.3%, respectively. With one and one-tenth equivalents of fine magnesium, the yields of three runs were 74.4, 82.1 and 88.7%, respectively and with two equivalents the yields of four runs were 90.8, 92.0, 94.8 and 95%.

54. Gilman, Mallory and Wright, J. Am. Chem. Soc., 54, 733 (1932)

The residues of this Grignard reagent were found to be inflammable in air. This fact has already been reported by Gilman, Mallory and Wright⁵⁴, who first prepared this Grignard reagent. They obtained this Grignard reagent in a yield of 95% using fine magnesium powder.

The above data are taken from a study with Mr. H. E. Mallory on the comparative yields of phenylmagnesium bromide and iodide, and 2-furylmagnesium iodide.

2-Methyl-5-furylmagnesium Iodide

The halide was prepared by Mr. R. R. Burtner. The b. p. of the halide was 54° (12 mm.). Under "A-conditions", the yield was 89.9% and under "B-conditions", 91.3%. Another run was made under "B-conditions" in which all the halide was placed in a flask with the ether and magnesium. The reaction was started in the usual manner with a crystal of iodine and the application of external heat. After the reaction had started, it became very vigorous and was apparently completed in two or three minutes. The reaction mixture was now stirred and refluxed fifteen minutes longer.

Much white precipitate had formed in this run. There was no precipitate formed in the runs above. An analysis of the ether layer gave a yield of 13.0%. The residue showed a positive test with Michler's ketone⁵⁵. The precipitate was now dissolved in 40 cc. of benzene and 40 cc. of ether. The yield in this

55. Gilman and Schulze, J. Am. Chem. Soc., 47, 2002-2005 (1925)

solution was 20.2%. Since this halide, like 2-iodofuran, is rather unstable, it may be possible that a decomposition of the halide began before the reaction was started. The first two runs of this Grignard reagent were made immediately after the halide had been prepared. The last run was made from the same halide which had been kept in the ice-box for three hours.

The Grignard reagent from the above runs was given to Mr. R. R. Burtner. He has no record as to whether or not the residues of this Grignard reagent were inflammable. According to his memory he believes that the residues were inflammable.

2-Thienylmagnesium Iodide

The halide used was prepared by Dr. E. B. Towne according to the directions in Organic Syntheses⁵⁶. The b. p. of the halide was 182-183° (atm. pressure) and 74-75° (15 mm.).

Under "A-conditions", the yields of three runs were 98.0, 98.4 and 98.8%, respectively, and under "B-conditions", the yield of one run was 99.8%. The reaction was started with 40 drops of the halide in the usual manner in five minutes.

This Grignard reagent has been prepared, apparently, in quantitative yields by Schlenk and Ochs⁵⁷. They obtained the acid derivative in yields of 86-100%.

In the preparation of thiophene derivatives of thallium, silicon, bismuth and tellurium, Krause and Renwanz⁵⁸ found

56. "Organic Syntheses", Vol. 12, (1932) p. 44.

57. Schlenk and Ochs, Ber., 48, 676 (1919)

58. Krause and Renwanz, Ber., 62, 1710 (1929)

that 2-thienylmagnesium iodide could not be used and for this reason they used 2-thienylmagnesium bromide instead. They, however, found that the preparation of 2-thienylmagnesium bromide is more difficult than that of the corresponding 4-yl compound. To complete the reaction of the 4-yl compound, a three hour period of refluxing was required.

DISCUSSION OF THE STUDIES ON ORGANOMAGNESIUM IODIDES

The yields of the alkylmagnesium iodides (see Table III of this thesis, page 58) under ordinary conditions were lower than the corresponding RMgCl and RMgBr compounds¹⁹ (see Tables I and II of this thesis, pages 14 and 37). This was also the case when the halides were added all at once, with the exception of methylmagnesium iodide. The yield of this Grignard reagent was not affected when the halide was added all at once.

The view of the above data and that given under "Discussion of the Studies on Organomagnesium Chlorides" (see page 54 of this thesis), it is desirable, in general, to use the alkylmagnesium chlorides in preference of the alkylmagnesium bromides and iodides, with the exception of methyl- and ethylmagnesium chloride. The preparations of methylmagnesium chloride and bromide and ethylmagnesium chloride are inconvenient because the halides used in the preparation of these Grignard reagents are gases at room temperature. Ethylmagnesium bromide can be prepared under ordinary conditions and should be used in preference to the RMgI compounds in view of the data given under "General Introduction" (see pages 1-8 of this thesis) on the comparative utility of the RMgCl , RMgBr and RMgI compounds.

It is advisable to call attention to the study by Bredt-Savelsberg⁹ on the enolizing action of camphor by methylmagnesium chloride, bromide and iodide. According to the above study

(see page 9 of this thesis) the Chugaev-Zerewitinoff⁵⁹ values for active hydrogen of compounds, which exist in enol and keto forms, will vary with the methylmagnesium halides used.

The yields of 2-furyl-, 2-methyl-5- and 2-thienylmagnesium iodide were higher than that of phenylmagnesium iodide under ordinary conditions. When the halides were added all at once, the yields of the former RMgI compounds were not lowered, while the yield of phenylmagnesium iodide under these conditions was lowered 13.2%. The time of apparent reaction after all the halides had been added in the runs of the above furyl- and thienylmagnesium iodides when compared with the time of apparent reaction of phenylmagnesium iodide and bromide (see Table III, page 58 and also page 61 of this thesis) indicate that the furyl and thienyl halides are less reactive towards magnesium than the corresponding aromatic halides.

Copper-magnesium alloy had to be used to prepare the Grignard reagents of 2-bromofuran⁶⁰ and 2,5-diiodofuran⁶¹. It is known that the corresponding halides of benzene react easily with ordinary magnesium turnings.

Krause and Renwanz⁵⁸ found that the reaction of 2-bromothiophene with magnesium was much slower than the 2-iodothiophene. According to the time of apparent reaction, as stated

59. Chugaev, Ber., 35, 3913 (1902); Zerewitinoff, Ber., 40, 2023 (1907)

60. Shephard, Winslow and Johnson, J. Am. Chem. Soc., 52, 2083 (1930)

61. Gilman and Wright, Iowa State Coll. J. Sci., 5, 85 (1931)

above, 2-iodothiophene reacts slower with magnesium than bromo- and iodobenzene.

The data above show that the halides of furan and thiophene are less reactive towards magnesium than the corresponding aromatic halides. According to Gilman and Towne⁶², the lesser reactivity of the above furan halides, as compared with the corresponding aromatic halides, may be designated as a superaromatic property of the above furan compounds.

62. Gilman and Towne, Rec. trav. chim., 51, 1054 (1932)

PART IV. QUANTITATIVE STUDIES OF SOME ORGANOLITHIUM COMPOUNDS

INTRODUCTION

In a recent study^{25a}, it was shown that organolithium compounds, first prepared directly from the halides by Ziegler and Colonius⁶³ in a sealed Schlenk tube, could be prepared conveniently under the condition and in the apparatus generally used for the preparation of Grignard reagents. Since the metal is easily attacked by the oxygen of the air, it was, however, found necessary, in general, to carry out the reactions under dry nitrogen. More recently, a study has been reported^{23b} on the preparation of more than twenty organolithium compounds from alkyl and aryl halides, in good yields. In continuation of this work, studies have been made on the preparation of methyl-lithium from methyl chloride, and n-butyl-lithium from n-butyl iodide.

EXPERIMENTAL PART

The preparation of methyl-lithium from the methyl chloride was carried out in a practical sized run, under the conditions and in the apparatus used for the preparation of methylmagnesium chloride, as described above (see page 15 of this thesis). The reaction of n-butyl iodide with lithium was carried out essentially under the "C-conditions" as described in a previous study^{23b}.

63. Ziegler and Colonius, Ann., 479, 135 (1920)

The Preparation of Methyl-lithium from Methyl Chloride

The preparation of this organolithium compound was carried out in a 0.5 mole run. In accordance with the advice given in a previous study^{23b}, ten instead of the usual six equivalents of ether was used.

After the reaction flask was swept out with dry nitrogen, 150 cc. of ether was placed in the flask. Next 6.9 g. (1.0 atom) of lithium in the form of 225 chips was added, as described previously^{23b}. The halide obtained from Schering-Kahlbaum & Co., in sealed glass tubes, was added in the manner as described in the preparation of methylmagnesium chloride referred to above. Now the 50 mm. mercury trap was attached to the exit of the condenser after having warmed the contents of the flask to 35°. After the stirrer was started, the external heat was slowly withdrawn (but not entirely removed) and at the same time the gaseous halide was allowed to enter the reaction mixture 1-2 mm. beneath the surface of the ether. In this manner, the reaction started immediately. The external heat was now entirely removed and the reaction flask was surrounded with an ice-water bath. The temperature of the reaction mixture was controlled by the raising or lowering of the bath. In this way, the halide was added as fast as it distilled from its container, which had been removed from its cooling bath. While the reaction thus proceeded, a pressure of 30-40 mm. of the halide in the system was maintained by means of controlling the temperature, as stated above.

As soon as the reaction was well started and under control, the rest of the ether, 350 cc., was added by means of the dropping funnel attached to the apparatus. The rate of adding the ether was dependent on the proper control of the temperature and pressure of the reaction mixture by its cooling bath. Under these conditions, the main portion of the halide was added in thirty to thirty-five minutes.

It was not always possible to control the temperature and pressure to such an extent that there was no loss of halide through the 50 mm. mercury trap. Any halide that overflowed through this mercury trap was caught in a Schlenk tube surrounded by a cooling bath similar to that used for the tube containing the halide. In this manner, about 1 cc. of the halide that overflowed was recovered and this was later added to the reaction mixture.

After all the halide had been added, which took one hour, the reaction was allowed to proceed until the pressure of the system became equal to the atmospheric pressure as the cooling bath of the reaction flask was slowly removed. It required thirty minutes for the pressure in the reaction flask to become equal to that of the atmospheric pressure. The reaction mixture was now refluxed and stirred one hour longer in accordance with the directions given in a previous study^{23a}. The 50 mm. mercury trap was next removed and the reaction mixture was refluxed and stirred another ten minutes to remove

any unused halide. The reaction mixture was now cooled under nitrogen and analysed in the usual manner.

The amount of halide used in this run was 25.1 g. (0.509 mole). The yield of methyl-lithium based on the halide, was 88%, and based on the lithium, since it was all used up, the yield was 89%.

The preparation of methyl-lithium from methyl chloride, according to the above procedure, may be accomplished, undoubtedly, with greater convenience if the halide is taken from a bomb.

The preparation of methyl-lithium from methyl chloride has been reported in a patent by Ziegler and Colonius⁶⁴. In this patent it is stated that the reaction is started by means of a little methyl bromide or iodide and then carried out at a low temperature. In this manner, a yield of 70-80% was obtained.

The Attempted Preparation of *n*-Butyl-lithium from *n*-Butyl Iodide

The run of this halide and lithium made under "C-conditions" of a previous study^{23b}, is given in detail. The reason for this is that it may be possible to use *n*-butyl iodide in connection with the acid titration method to determine the exact amount of organolithium compound formed. This will be fully discussed after the details of this run are given.

A 0.05 mole run was made in which the lithium was cut into 150 pieces into 35 cc. of ether. After the reaction was started with the usual 40 drops of halide, the remainder of the halide

64. Ziegler and Colonius, Ger. pat., 512,882. [Chem. Zentr., I 1165 (1931)]

was mixed with 15 cc. of ether and added over a period of thirty-five minutes while the reaction mixture was vigorously stirred. Enough heat was developed to cause gentle refluxing. The reaction apparently ended in less than five minutes after all the halide had been added. The reaction mixture was now stirred and refluxed fifteen minutes longer. After standing for fifteen minutes, it was titrated. The yield was 3.7%, but the color test⁵⁵ with Michler's ketone was negative. The reaction mixture was now allowed to stand over-night and then titrated again. The yield was now 2.6%.

Since the color test⁵⁵ was negative and since approximately one-half of the lithium was used up, the titration values very probably came from the lithium ethylate formed by the splitting of the ether by the n-butyl-lithium before the latter compound had time to undergo the Wurtz reaction with the halide present. Ziegler and Colonius⁶³ were also unable to prepare n-butyl-lithium from n-butyl iodide.

In the preparation of n-butyl-lithium from n-butyl chloride and bromide in ether, Ziegler and Colonius⁶³ found that some of the n-butyl-lithium reacted with the ether to form lithium ethylate. They determined the amount of n-butyl-lithium lost in this way in the following manner. First they determined the total basicity of the solution of n-butyl-lithium by titration with standard acid. Next, another aliquot portion of n-butyl-lithium solution was treated with n-butyl bromide and dibenzylmercury. The dibenzylmercury reacted with the n-butyl-lithium to form

di-n-butylmercury and benzyl-lithium. The benzylplithium immediately reacted with the n-butyl bromide. In this manner, all the n-butyl-lithium was decomposed. The solution was now hydrolysed and then titrated with standard acid to determine the amount of lithium ethylate present in the solution. The value so determined was now subtracted from the value obtained in the first titration. In this way, they obtained the true yield of the n-butyl-lithium. They found that the yields of n-butyl-lithium (in ether) from n-butyl chloride and bromide, based on the total basicities of aliquot portions of the solutions, were 63.5 and 24.0%, respectively. Aliquot portions of the solutions were next treated with n-butyl bromide, dibenzylmercury and standard acid as described above. In this way, it was found that 7.9 and 5%, respectively, had to be deducted from the above yield. Thus, it was found that the true yields of n-butyl-lithium were 56.6 and 19%, respectively.

It is very probable, that the value of 2.6% in the above run of n-butyl iodide with lithium expresses the amount of lithium ethylate formed. A priori, it may be possible to treat an aliquot portion of a solution of organolithium compound with n-butyl iodide to decompose the organolithium compound by the Wurtz reaction. The solution so treated may be hydrolysed and then titrated with standard acid. The value obtained would designate the lithium ethylate formed. Now another aliquot portion may be hydrolysed and titrated with standard acid to obtain the total basicity. After deducting partial basicity,

due to the lithium ethylate, from the total basicity, the true yield of the organolithium compound may be determined.

If this method of determining the true yields of organolithium compounds is found applicable by experiment, it would be a much simpler method than that proposed by Ziegler and Colonius⁶⁵. In a few experiments in this laboratory, the above method was not found convenient in its application. First of all, the preparation of the dibenzylmercury and n-butyl bromide in a pure state and free from the oxygen of the air took much time. Secondly, concordant results could not be obtained in a reasonable period of time.

The determination of the amount of lithium ethylate formed, when organolithium compounds are prepared in ether, is of practical importance. As in the application of the Grignard reagents, it is often essential to know the exact normalities of the organolithium solutions prior to their practical application. Furthermore, a simple method to determine the stability of organolithium compounds in ether would, undoubtedly, find extensive application in future work on the preparation of new compounds.

DISCUSSION OF THE STUDIES ON SOME ORGANOLITHIUM COMPOUNDS

The methyl-lithium was prepared from methyl chloride in the closed system under a pressure of 50 mm. as proposed for the preparation of Grignard reagents from gaseous halides (see page 33 of this thesis). Under these conditions, the methyl-lithium was prepared in a yield of 88-89%. The yield was 9-18% higher than that reported in a recent patent⁶⁴.

Methyl-lithium can, undoubtedly, be prepared from methyl bromide (b. p. 6.4°) in the above manner. It may be possible to dissolve the halide in cold ether first and then add the halide-ether solution from the dropping funnel attached to the closed system as described above (see page 16 of this thesis).

Under the conditions used for the preparation of Grignard reagents, methyl-lithium has been prepared from methyl iodide in yields of 73.6-81.5%^{23b}.

The methyl-lithium can, undoubtedly, be prepared in the least expensive way from methyl chloride, if the halide is taken from a bomb. If no bomb of methyl chloride is on hand, the next best way of preparing the methyl-lithium would, probably, be from methyl bromide as suggested above.

It should be mentioned that methyl-lithium⁶⁵ unlike n-butyl-lithium, is stable in ether for weeks, while n-butyl-lithium can only be kept in ether a few hours.

65. Ziegler and Zeiser, Ann., 485, 174 (1931)

It has been shown that n-butyl-lithium can be prepared in ether from n-butyl chloride in yields of 76.1-77.1%; and from n-butyl bromide, in yields of 59.0-68.8%. These reactions were carried out in an apparatus and practically under the same conditions used for the preparation of Grignard reagents.

It has not been possible to prepare n-butyl-lithium from n-butyl iodide. Evidently the n-butyl-lithium formed, immediately reacts with the unused halide in the solution.

In benzene, n-butyl-lithium has been prepared⁶³ from n-butyl chloride in yields of 80-100%. The reaction was carried out in a Schlenk tube. The reaction mixture was agitated by shaking at a temperature of 50-60° for twenty four hours.

Siegler and Colonius⁶³ determined the amount of lithium ethylate formed when the preparation of organolithium compounds were carried out in ether by the use of n-butyl bromide, dibenzylmercury and standard acid (see page 73 of this thesis). Since the rate of reaction of n-butyl iodide with n-butyl-lithium is seemingly rapid, it has been suggested that n-butyl iodide may be used in the place of n-butyl bromide and dibenzylmercury to determine the amount of lithium formed (see page 74 of this thesis).

SUMMARY

A survey made of the literature on the application of the Grignard reagents shows that the comparative utility of the RMgCl , RMgBr and RMgI compounds decreases in the order the above compounds are named.

Studies have been made on the preparation of a number of organomagnesium chlorides, bromides and iodides under general and special conditions. When the results of these studies are correlated with those already published, it is hoped that a more or less adequate treatment can be made of this phase of the Grignard reagent.

Methyl-lithium has been prepared from methyl chloride under the conditions and in an apparatus used for the preparation of Grignard reagents from gaseous halides. As a result of this study, the methyl-lithium compound can now be prepared from methyl chloride in better yields and in a more convenient manner than that given in a recent patent.

It was not possible to prepare n-butyl-lithium from n-butyl iodide in ether. The results of the attempt may, however, lead to a procedure for the determination of the amount of lithium ethylate formed when organolithium compounds are prepared in ether.