

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]
**A STUDY OF THE OPTIMUM CONDITION FOR THE PREPARATION
OF ETHYLMAGNESIUM IODIDE**

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Introduction

Despite the manifold uses of the so-called Grignard reagent, no thorough study has been made of the optimum condition for its formation. Scattered through the comprehensive literature on this subject are a few generally meager and detached accounts of methods of manipulation which are helpful in the preparation of the reagent with improved yields, particularly for specific compounds whose synthesis presents unusual difficulties. Undoubtedly, an important reason for this lack of information is the need of some method or methods for the quantitative estimation of the reagent. Partly with this in view there have been devised two satisfactory methods of analysis which are discussed in the preceding paper.

The experiments described here are in the nature of a preliminary investigation. Ethylmagnesium iodide has been selected as a typical RMgX compound, and it is hoped in subsequent work to make mention of some favorable factors in the preparation of other RMgX compounds of no less importance. A study has been made of the yields of this reagent under a rather wide, yet not necessarily complete, variety of conditions. Without doubt most of the results obtained here can be extended to other reagents. The fact that distinctly appreciable variations are observed under some conditions in the preparation of ethylmagnesium iodide may come as a surprise to many, for, as a rule, the preparation of this reagent is marked by its smoothness and simplicity.

Materials and Apparatus

The reagents used were the same as those described in the preceding paper, and the methods of analysis involving gas analysis and titration with acids were selected for this work. The latter method was used in all determinations, being supplemented in some runs, however, by the more exact gas analysis.

Fig. 1 is a sketch of the apparatus used and from which aliquot portions were directly taken. Flask F, specially constructed for this work, had a content of 100 cc. to the

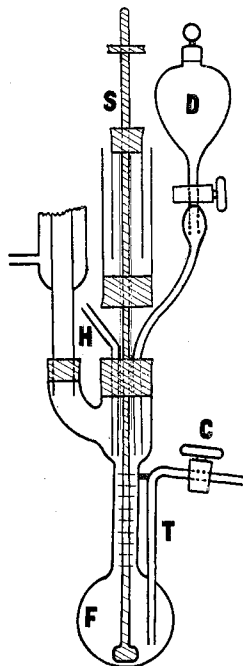


Fig. 1.

¹ This paper is an abstract of a thesis presented by C. H. Meyers in partial fulfillment of the requirements for the degree of Master of Science in Chemistry at Iowa State College.

middle of the graduated neck. The graduations were of 0.2 cc. accuracy, and gave a direct reading of total volume when Stopcock C was open. A side-tube T provided with Stopcock C was sealed into the flask, and through this were forced the samples for analysis. The main upper part of the flask had a 3-hole 25mm. rubber stopper which held a glass stirrer S with a mercury seal, a tube H for admitting hydrogen, surrounded by a water jacket, and a 60cc. dropping funnel D. Attached to the elbow of the upper part was an all-glass condenser, the top of which held a drying tube containing calcium chloride and soda-lime.

All analyses were made in duplicate and at the same time, and a pulley arrangement, therefore, made it possible to stir the contents of 2 similar flasks at the same rate. The hydrogen admitted through Tube H was made in separate generators, and for purification and drying was successively passed through wash bottles containing solutions of silver nitrate, potassium permanganate, sodium hydroxide and finally conc. sulfuric acid.

Procedure

In each run, excepting when a study was made of the effect of an excess of metal, 1.6 g. of magnesium turnings was used. This is about 0.1 g. in excess of that theoretically required for the 9.5 g. of ethyl iodide generally used. After introducing the magnesium, a stream of dry and purified hydrogen was passed through the flask. While the air was thus being swept out, the ethyl iodide was weighed in a 60cc. Erlenmeyer flask provided with a ground-glass stopper. The hydrogen was then turned off, the stopcock of the side-tube of the flask closed, and 25 cc. of ether run in through the dropping funnel. When the ethyl iodide in the weighing flask had been cooled in an ice-bath, about 15 cc. of ether was added, and the solution then transferred to the dropping funnel. The weighing flask was then washed out with two 5cc. portions of ether and the washings transferred to the dropping funnel. All transfers were made rapidly.

The stirrer was then started and the ethyl iodide added at a certain rate and under conditions to be mentioned later. When all had been added, the last traces were washed into the flask with two 5cc. portions of ether. At the end of the reaction, sufficient ether was added to bring the volume to about 100 cc. Uniform concentration was insured by stirring for 5 minutes thereafter, and by bubbling hydrogen through the side-tube. To diminish evaporation of ether while the reaction mixture stood for 1 hour, a stopper was placed in the drying tube at the top of the condenser. In this time any sediment settled leaving a clear supernatant solution. The stopper was then removed from the drying tube. Stopcock C was opened to permit the liquid in the tube to come to the same level as that in the flask, and then it was closed.

A reading was thereupon made of the total volume of solution, the correction for the volume of the stirrer being applied later. After the stopper was replaced in the drying tube the hydrogen was turned on in order to force over, through the side-tube, the samples for analysis. The first 10 cc. of solution was discarded, and the portions for the titration

with acid were run into graduated test-tubes. For the gas analysis, the ether solution was run directly into the buret of the gas apparatus, described in the preceding paper.

Minor alterations in procedure were made in several of the runs, and these are discussed in connection with experimental results.

Experimental Results

Duplicate runs were made simultaneously with every set of conditions. From each of these runs 2 aliquot portions were removed for analysis, so

TABLE I
RESULTS

Expt.	C ₂ H ₅ I G.	Total vol. of reaction mixture Cc.	Volume of aliquot Cc.	Acid-base 0.2584 N Cc.	C ₂ H ₅ MgI %	Average C ₂ H ₅ MgI %
1	9.6300	98.6	25.35	51.53	83.90	..
1	21.78	44.64	84.60	..
1a	9.6326	101.3	23.58	47.88	86.08	..
1a	21.00	42.66	86.12	85.2
2	9.4840	99.3	22.68	47.68	88.74	..
2	21.90	46.41	89.45	..
2a	9.4936	99.2	23.34	48.79	88.06	..
2a	21.64	45.59	88.75	88.7
3	9.6004	99.1	21.65	47.88	92.03	..
3	18.90	42.02	92.52	..
3a	9.5918	100.0	23.00	48.44	88.52	..
3a	19.68	41.67	88.99	90.5
4	9.5584	98.85	23.13	51.93	93.60	..
4	20.35	45.99	94.22	..
4a	9.5486	99.1	22.32	49.43	92.66	..
4a	20.10	44.61	92.86	93.3
5	9.4996	100.65	23.30	50.67	92.89	..
5	20.85	45.73	93.68	..
5a	9.4832	100.7	22.70	48.69	91.82	..
5a	21.10	45.29	91.89	92.6
6	9.5378	100.2	22.44	44.42	85.79	..
6	20.75	41.29	84.28	..
6a	9.5320	99.7	23.80	48.07	85.15	..
6a	21.45	43.76	86.02	85.2
7	78.6
8	94.3
9	94.6
10	91.6
11	92.2
12	75.4
13	82.3
14	88.2
15	81.5
16	95.0
17	95.2
18	84.8

that in the determination of a given factor 4 analyses are given. The average of these appears in the last column of the table. Only the averages for experiments after 6 are given.

For purposes of comparison all results have been calculated as percentages of ethylmagnesium iodide, and are based on 100% ethyl iodide.

The particular conditions under which each experiment was carried out are included in preceding Table.

Discussion and Conclusions

Rate of Addition of Ethyl Iodide.—The results in Expts. 1–6, inclusive, compare the effect of adding ethyl iodide in ether to magnesium at various rates. The reaction mixture was refluxed on a water-bath for 15 minutes, either directly after the ethyl iodide had been added as in Expts. 2–5, inclusive, or after an additional period of stirring, as in Expts. 1 and 6. Stirring was continued in all cases during the period of refluxing.

In Expt. 1 the ethyl iodide was added as rapidly as possible ($\frac{1}{2}$ minute). To provide a fairer basis of comparison between this and Expt. 2 the reaction mixture was stirred for 15 minutes before being refluxed.

The time of addition in Expt. 2 was 15 minutes; in Expt. 3, 30 minutes; in Expt. 4, 45 minutes; and in Expt. 5, 60 minutes. From the results of these experiments it is obvious that *there is a steady increase in the percentage of Grignard reagent formed when the rate of addition of ethyl iodide is progressively decreased*, with no advantage gained by extending the addition over a longer period than 45 minutes.

Expt. 6 was carried out to decide whether the determining factor was the rate of addition or the time of stirring. Assuming the optimum time of addition to be 45 minutes, the ethyl iodide was added as rapidly as possible ($\frac{1}{2}$ minute) and then stirred for 45 minutes before refluxing. The yield was 85.2%, or as low as that when the solution has been stirred as in Expt. 1 for but 15 minutes. From this it may be concluded that the more important factor for improved yields is slow addition.

Stirring.—In Expt. 7 the conditions, with the exception of stirring, were those of Expt. 4 which had given the highest yield in the study of rate of addition. It was found that by completely avoiding the use of a stirrer the reaction was slow to start, did not proceed vigorously when once started, and gave a very low yield of reagent. It is a significant fact that this low yield came between two high-yield runs (5 and 8) when stirring was used, so that probably the decided drop was due primarily to the absence of stirring. As a result of this experiment stirring was used in all other runs.

Refluxing.—In Expt. 8, the conditions observed were those of Expt. 4 with the single exception that the 15-minute period of refluxing following the addition of ethyl iodide was replaced by a like period of stirring without

refluxing. The yield, 94.39%, was 1% higher than that of the best run previously described. For the purposes of the present study this experiment was considered sufficiently conclusive to justify the substitution of a 15-minute period of stirring without refluxing for a like period of stirring with refluxing, and this was accordingly done in all subsequent experiments.

Excess Magnesium.—In Expt. 9, a 25% excess of magnesium was used. A correction was made for this excess magnesium in the total volume of reaction mixture. The very slightly improved yield is within the experimental error, and any considerable excess of magnesium is not to be recommended in the preparation of RMgX compounds. In every preparation of the Grignard reagent an excess of magnesium is present when equal moles of the metal and RX compound are taken, because the Würtz-Fittig reaction, which invariably occurs to some extent, requires but $\frac{1}{2}$ the magnesium per mole of RX compound required in the preparation of the RMgX compound.

Quantity of Ether.—In Expt. 10, the quantity of ether used was $\frac{1}{2}$ that used in all other runs. Instead of covering the magnesium with 25 cc. of ether, the ethyl iodide in 25 cc. of ether was added directly to the metal. The yield, 91.6%, was 2.7% lower than that in Expt. 8 which was followed in detail, with the exception noted. Apparently the yield is adversely affected by so reducing the quantity of ether. However, when larger amounts of reagents are employed it is certain that the quantity of ether can be materially reduced below the low concentrations necessarily used here. Experiments on the replacement of ether by other less costly, less inflammable, and more readily prepared solvents have sufficiently progressed to show that a reasonable part of the ether can be replaced without adversely affecting the yield.

Protection from Air.—In Expt. 11 the conditions were again those of Expt. 8 with the exception that no protection was provided for excluding the moisture and carbon dioxide in the air. The drying tube at the top of the condenser was removed, and in this run unlike all others no atmosphere of dry and purified hydrogen was provided. The yield, 92.2%, was 2.1% lower than that of Expt. 8. This indicates that drying is desirable rather than necessary.

In the presence of moisture, for reasons given in the preceding paper, the method of gas analysis is more reliable than that of titration, and accordingly gas analyses were also made of the products of this run. They confirmed the drop in yield.

Kind of Magnesium.—In all experiments a standard quality of American-made magnesium was used. For Expts. 12–15, inclusive, the magnesium was machine-turned so as to provide 3 grades,—coarse, medium and fine. No one of these grades duplicated the magnesium used in other experiments, so that comparisons are to be restricted to these 3 grades.

Again, the conditions observed were those of Expt. 8. In Expt. 12, coarse turnings were used, some 6 pieces weighing 1.6 g. In Expt. 14, fine turnings were used, and the 1.6 g. nearly filled the bulb of the reaction flask. In Expt. 13, an intermediate grade of turnings was used.

These results indicate in a striking way that under a standard set of conditions the finer the grade of turnings the higher the yield, but the factor really most affected is the *rate* of reaction. To verify this conclusion, the same coarse turnings used in Expt. 12 were employed in Expt. 15, but here the time of stirring was extended to 45 minutes, or 30 minutes more than in Expt. 12. The yield under these conditions, 81.5% was 6.1% higher than that in Expt. 12. The *rate* of reaction, therefore, increases with the fineness of the turnings used.

Runs were also made under like conditions with other qualities of magnesium, one of them an imported sample; appreciable variations in yield were observed. It cannot be emphasized too strongly that these variations are probably not due to the quality of the magnesium, for the purity of every sample exceeded 99.6%, and satisfactory yields were obtained with a metal containing but 92% of magnesium. The other constituents of these metals exert, so far as is known, no harmful influence on the course of the Grignard reaction.

A very fine grade of turnings approximating a thin ribbon might appear to be best. However, from experiments it is concluded that thinness is of secondary importance to a surface such as that of more compact turnings which because of its somewhat foliated and striated nature may offer a greater surface.

Catalysts.—In Expts. 16 and 17 a study was made of the effect of catalysts, the conditions otherwise being those of Expt. 8. The catalysts selected were iodine and dimethyl-aniline. A very small quantity of the former was used in Expt. 16. In Expt. 17 a measured small amount of dimethylaniline was used, and as this compound is alkaline to methyl orange a correction was made in the titration with acid.

Temperature.—In Expt. 18, the reaction flask was immersed in an ice-bath during the entire run. The conditions otherwise were those of Expt. 16, in which were incorporated, as far as possible, all the optimum conditions of the preceding experiments. The low yield, 84.8%, might have been expected, in a way, because of the really unnecessary cooling throughout. In a comparable experiment where the reaction flask was cooled only during the addition of ethyl iodide, there was a small increase in yield over that given in Expt. 18.

Summary

1. A study has been made of some of the factors which influence the yield in the preparation of ethylmagnesium iodide and, therefore, to some extent the yield of other Grignard reagents.

2. The conditions investigated were: the rate of addition of ethyl iodide, stirring, refluxing, excess magnesium, quantity of ether, protection from air, kind of magnesium, catalysts and temperature.

3. The quantitative methods used for determining yields were two of those discussed in the preceding paper, titration with acid and gas analysis.

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ADDITION REACTIONS OF PHOSPHORUS HALIDES. VI. THE 1,2 AND 1,4 ADDITION OF DIPHENYL-CHLOROPHOSPHINE

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Introduction

This work was undertaken for several reasons. In the first place no disubstituted derivative of phosphorus trichloride had hitherto been added to saturated or unsaturated aldehydes or ketones; the theoretical interpretation of the addition reactions of trivalent phosphorus halides was, therefore, obviously incomplete.¹ Furthermore, it was hoped that certain β -bromo compounds might be prepared by brominating the product of the reaction between diphenyl-chlorophosphine and an unsaturated ketone. A study of the action of alkali on such bromo compounds promised to be of interest in connection with the peculiar decomposition of many β -bromo acids.² Finally, it was thought probable that the products would be high-melting stable substances and that this reagent might be used, therefore, for investigating the addition reactions of benzoquinone and related substances.

As the results presented in this paper show, diphenyl-chlorophosphine behaves exactly as we had hoped, and experiments with quinone indicate that tractable substances can be obtained; the work with quinone has not yet, however, passed beyond the preliminary stage and will, therefore, be considered in a later paper.

The reaction between diphenyl-chlorophosphine and either benzaldehyde or benzalacetophenone is entirely parallel to the corresponding reaction with the trichloride or phosphenyl chloride.³ As in the previous work in this Laboratory, either acetic acid or acetic anhydride was used in order to cause the reaction to go to completion. The products of the reaction are acetyl chloride and the keto-phosphine oxide which often separates

¹ THIS JOURNAL, 43, 1705 (1921).

² *Ibid.*, 42, 833 (1920); 43, 1667 (1921); 44, 2530 (1922).

³ Compare other papers of this series.