it still would not affect seriously our conclusions in view of the experiment (described above) on benzylmagnesium chloride, *p*-chlorotoluene and carbon dioxide. The tests with the several benzoic acids are sufficiently important to warrant further study, and we are collecting samples of benzoic acid which (as well as we can determine) are free of any hereditary and acquired taint of halogen.

Benzylmagnesium Chloride and Cupric Chloride.—From the reaction carried out in the customary manner[14] between 0.3 mole of benzylmagnesium chloride and 0.3 mole of cupric chloride there was obtained a 70% yield of pure dibenzyl and a trace of di-*p*-tolyl. The 4.6 g. of non-steam distillable tar gave only benzoic acid on oxidation.

Benzylmagnesium Chloride and Azobenzene.—From one mole of benzylmagnesium chloride and 0.44 mole of azobenzene there was obtained 52.3% of benzidine and 37% of dibenzyl.

Benzylmagnesium Chloride and Formaldehyde.—Formaldehyde was led over the surface of 0.4 mole of benzylmagnesium chloride until a negative color test[21] was obtained showing that all of the Grignard reagent had been used up. In addition to a 26.9% yield of *o*-tolylcarbinol there was obtained about 0.3 g. of di-*p*-tolyl.

The authors gratefully acknowledge helpful suggestions from Dr. N. J. Beaber and Dr. H. T. Clarke.

Summary

Di-*p*-tolyl is formed in very small quantities incidental to the preparation of benzylmagnesium chloride. The presence of this coupling product is advanced as additional evidence for the preliminary formation of free radicals in the preparation of Grignard reagents.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

THE YIELDS OF SOME GRIGNARD REAGENTS. ALTERNATING PROPERTIES OF NORMAL ALKYL BROMIDES

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RECEIVED JANUARY 21, 1929 PUBLISHED MAY 6, 1929

Introduction

In connection with studies on the relative reactivities of alkyl and aryl halides toward magnesium in ether,[1] it was necessary to determine the yields of some Grignard reagents. These yields were determined under optimal conditions. They differ in several instances from the yields previously determined in this Laboratory.[2] In general, because of an improved mode of preparation and refinements in analytical procedure, the yields are

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[21] Gilman and Schulze, THIS JOURNAL, 47, 2002 (1925), and *Bull. soc. chim.*, 41, 1479 (1927).

[1] A preliminary account of these studies has been reported by Gilman and Zoellner, THIS JOURNAL, 50, 2520 (1928).

[2] (a) Gilman and Meyers, *ibid.*, 45, 159 (1923); (b) Gilman and McCracken, *ibid.*, 45, 2462 (1923); (c) Gilman and McCracken, *Rec. trav. chim.*, 46, 463 (1927). Marvel, Blomquist and Vaughn, THIS JOURNAL, 50, 2810 (1928), have determined the yields of some Grignard reagents prepared in di-*n*-butyl ether.

somewhat higher than those reported earlier. Where the same compounds have been analyzed, the present results are to be preferred. Also, determinations have been made of the yields of a number of compounds not previously studied by us.

An examination of the yields under these standard conditions reveals an apparent alternation with the first members of the *normal* alkyl bromide series. A consideration of this phenomenon together with some general conclusions are given in the Discussion of Results.

Experimental Part

Method of Analysis.—The general analytical procedure was one of the five methods investigated by Gilman, Wilkinson, Fishel and Meyers[3] for the quantitative estimation of Grignard reagents, namely, the acid titration method. Two variations were made.

First, phenolphthalein was used throughout as the indicator. Methyl orange is an unsatisfactory indicator because of individual differences on what constitutes a true end-point, and because of general difficulties in observing color changes when arylmagnesium halides are titrated. A comparative study was made of three indicators: phenolphthalein, methyl red and methyl orange. Three pairs of aliquots from a given preparation of phenylmagnesium bromide were titrated with phenolphthalein, methyl red and methyl orange, and the average titration values with these three indicators were 94, 95.9 and 97.1%, respectively. Also, two pairs of aliquots from a preparation of *n*-butyl chloride when titrated with phenolphthalein and methyl red as indicators showed the titration value with methyl red as the indicator to be about 1.5% higher than that with phenolphthalein.

These differences, selected from several comparative titrations with the different indicators, might have been predicted, in part. Variations of about the same order were noted when magnesium sulfate (of about the quantity and concentration present in a typical Grignard analysis) was titrated with standard alkali, using the three indicators specified.

These results are of decided importance with reference to the *actual* quantity of Grignard reagent present. Gilman, Wilkinson, Fishel and

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[3] Gilman, Wilkinson, Fishel and Meyers, THIS JOURNAL, **45**, 150 (1923). See also Gilman and Meyers, *Rec. trav. chim.*, **45**, 314 (1926), for a confirmation of our analytical procedure and a criticism of another method. The acid titration method has been extensively employed in a variety of studies in this Laboratory. (See refs. 1 and 2 in this paper and other studies from this Laboratory on organomagnesium halides.) It has also been used by others. More recent references to its application by others are to be found in studies by Marvel, Blomquist and Vaughn, THIS JOURNAL, **50**, 2810 (1928), and Meisenheimer and co-workers, *Ber.*, **61**, 708, 720, 2079 (1928), who also used phenolphthalein as an indicator incidental to an acid titration that was combined with an analysis for halogen by the Volhard method. They (Meisenheimer and co-workers) recommend methyl red when no analysis is to be made for halogen.

Meyers[3] and Gilman and Meyers[2] showed that the quantity of Grignard reagent as determined by the acid titration method is generally about 4% too high, when reference is made to the more exact gas analysis method also studied by them.[2] This is so because the acid titration method, unlike the gas method,[4] is a measure of the Grignard reagent *originally* present, but not all of which is now available because of partial decomposition by traces of moisture, etc., to give basic compounds of the type formed from undecomposed Grignard reagent in the acid titration method of analysis. Accordingly, the use of phenolphthalein as an indicator removes almost entirely the sole serious objection to the acid titration method. This is so because with phenolphthalein the yield of a given aliquot is about 3% *less* than that determined when methyl orange is used as the indicator, and it was with methyl orange as an indicator that the earlier[2] quantitative studies showed the acid titration to give values about 4% *higher* than the gas method. Therefore, with phenolphthalein the results are only about 1% higher than those determined by the gas method.

A second variation in the acid titration procedure was in the heating with an excess of standard sulfuric acid prior to the back titration with standard alkali. In the earlier studies[2] it was recommended that the basic magnesium compounds be heated with the standard acid not over 60° in order to avoid any oxidation of hydriodic acid that might be present when alkyl or aryl iodides were used. It was shown, in the present study, that there is no difference (within experimental error) when aliquots are heated to 60° or boiled for fifteen minutes. This was demonstrated with *n*-butylmagnesium iodide and phenylmagnesium bromide.

Chemicals.—All of the halides, originally of the highest commercial purity, were carefully dried and distilled prior to use. The commercial magnesium turnings were crushed in a dry porcelain mortar and separated from the fine particles. The magnesium so obtained ($^1/_{12}$ to $^3/_8$-inch mesh) was essentially of uniform size. The commercial anhydrous ether was further dried by standing over sodium wire.

The following quantities of materials were used in each experiment: 0.05 mole of alkyl or aryl halide; 0.054 atom of magnesium; 30 cc. or about 6 molecular equivalents of ether and a crystal of iodine which weighed about 0.04 g.

Apparatus.—The special reaction flask used in previous[2,3] studies was simplified. The external delivery tube and stopcock, through which was forced (by gas pressure) the sample for analysis, was removed. These accessory parts for obtaining aliquots are not only unnecessary but also somewhat troublesome because of the need of freeing the open end of products formed by atmospheric decomposition of the Grignard reagent. Aliquots were quickly removed by means of clean 10-cc. pipets. With an ordinary refined technique there is very little opportunity for atmospheric decomposition.

The new simpler reaction flasks have a wider bore (15 mm. instead of 12 mm.) in the graduated necks. This did not decrease essentially the accuracy of a reading, but it did make it possible to use a more efficient stirrer.

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[4] See Gilman and Fothergill, This Journal, **50**, 3334 (1928), for additional comments (p. 3339) on the gas method of analysis.

Procedure.—Inasmuch as this standard procedure will be referred to in several subsequent reports, it is given completely at this time.

The weighed magnesium turnings were placed in the clean reaction flask which had just previously been removed from an electric drying oven heated at about 110°.[5] The flask was then attached to an apparatus consisting of a mercury-sealed stirrer, a Hopkins condenser provided at its upper end with a drying tube filled with calcium chloride and a 100-cc. dropping funnel. After cooling the flask, 6.5 cc. of ether and the crystal of iodine were added. Then the halide, previously weighed out in a 50-cc. glass-stoppered Erlenmeyer flask, was added to the dropping funnel, and 20 drops (about 0.2 cc.) of the undiluted halide was added to the flask. This mixture was refluxed, without stirring,[6] by means of a water-bath kept at 45°.[7] The remaining 23.5 cc. of ether was used to rinse the halide from the Erlenmeyer flask, in which it was weighed, to the dropping funnel. The stirrer was then started and allowed to continue at about 750 r. p. m.

The ether–halide mixture was then added, at room temperature, over a thirty to thirty-five-minute period, by a carefully regulated rate of addition of about 15 drops per ten seconds. When all of the ether–halide had been added, the reaction continued of itself for about three to ten minutes with the alkyl halides and for about ten to forty-five minutes with the aryl halides. Stirring was continued during these additional periods as long as there was any evidence of reaction (as noted by bubbling on the surface of the reaction mixture when stirring was transitorily interrupted). When there was no further evidence of reaction, the mixture (while still being stirred) was refluxed by means of a hot-plate. The time of such refluxing was, in general, five and ten minutes for alkyl halides and fifteen and thirty minutes for aryl halides.[8]

The flask was then cooled in a bath of tap water (12–15°) and during the addition of the diluent (ether or benzene) to bring the contents up to about the 100 cc. mark, the rate of stirring was increased to about 2500 r. p. m. and kept there for two minutes to assure intimate mixing. The flask was then disconnected, stoppered and allowed to stand for five minutes[9] in the tap-water bath in order to permit settling of the magnesium particles. The volume was then read and two 10-cc. aliquots were pipetted off

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[5] In this manner we were assured that the reaction flask was dry. The water condenser was also dry, because when not attached to the reaction flask the lower end was closed by a tight-fitting cork. The upper end was always provided with a drying tube filled with calcium chloride. Moisture has an anti-catalytic effect which must be considered in studies of relative rates of formation of Grignard reagents.

[6] See Gilman, Peterson and Schulze, *Rec. trav. chim.*, **47**, 19 (1928).

[7] In this manner all reactions were permitted to start before adding the main portion of halide. This preliminary procedure also removes any incidental traces of moisture and contributes to a more uniform activation of the magnesium.

[8] By these times we mean that in one run of a given RX compound the period of refluxing was five minutes, for example, and in another run of the same halide the period of refluxing was ten minutes. In this manner it was possible to learn whether the mixture had been sufficiently refluxed so that additional refluxing would not increase the yield. In general, it was found that refluxing at the end of the reaction increased the yield 2–5%.

[9] A longer time of standing (up to one-half hour) showed no difference within the experimental error of two aliquots. The experimental error in titration of two aliquots of a given run is 0.1 to 0.2 cc. of the standard acid. If the variation were greater than 0.25 cc. of acid with the two aliquots, another aliquot was removed from the flask, which was kept in the tap-water bath for such rare variations. These variations are equivalent to 0.7–1.5% in the final yield of the Grignard reagent.

and added to 500-cc. Erlenmeyer flasks containing 150 cc. of distilled water. Sufficient standard acid (about 0.2 *N*) was added so that about 10 cc. of standard base was required in the back-titration with standard sodium hydroxide (about 0.2 *N*). Phenolphthalein was used as the indicator and the pipets, of course, were carefully rinsed with the acid solution and with water. Prior to the back-titration, the acid solution was heated at about 70–80° and the titration was carried out with this hot solution.

Number of Determinations and Accuracy of Method.—The yield of each alkyl halide was determined 3 times, and from each determination at least 2 aliquots were taken for analysis. The analyses checked in a surprisingly satisfactory manner when one considers the nature of the reaction. For example, in 3 separate experiments with ethylmagnesium bromide the average yields (based on at least 2 aliquots from a given experiment) were 93.4, 92.9 and 92.9%; with *n*-butylmagnesium bromide they were 94.0, 94.1 and 93.8%; and, with *n*-hexylmagnesium bromide 91.8, 91.6 and 92.7%. A concordance of this high order indicates that 2 instead of 3 independent analyses of a given halide should have sufficed. However, for some reason as yet unknown, there was a greater variation with the *sec.*-butyl- and *sec.*-amylmagnesium bromides. For example, 4 runs of *sec.*-butylmagnesium bromide gave the following results: 78.4, 75.9, 79.7 and 75.5%.

Only two runs were made with each *aryl*magnesium bromide and the yields agreed within 1%.

The yields given in Table I are the averages of 2 or 3 or 4 separate runs, from each of which at least 2 aliquots were removed for analysis.

TABLE I

AVERAGE PERCENTAGE YIELDS OF RMgX COMPOUNDS

Halide used	Yield of RMgX compd., %	Halide used	Yield of RMgX compd., %
Ethyl bromide[a]	93.1	*n*-Heptyl bromide	88.8
n-Propyl bromide	91.7	*n*-Octyl bromide[c]	88.4
*Iso*propyl bromide	84.0	*n*-Butyl chloride[d]	91.2
n-Butyl bromide	94.0	*n*-Butyl iodide[e]	85.6
*Iso*butyl bromide	87.2	Benzyl chloride	93.1
Sec.-butyl bromide	77.7	Bromobenzene[f]	94.7
Tert.-butyl bromide	25.1	*o*-Bromotoluene[g]	92.7
n-Amyl bromide	88.6	*m*-Bromotoluene	88.0
Iso-amyl bromide	88.0	*p*-Bromotoluene	86.9
Sec.-amyl bromide[b]	66.8	α-Bromonaphthalene[h]	94.8
Tert.-amyl bromide	23.7	β-Bromonaphthalene	83.8
n-Hexyl bromide	92.0		

[a] Because of the volatility of ethyl bromide several runs were made with an extra condenser. However, this added precautionary measure did not give any higher results than those obtained with the one condenser used with all other halides.

[b] The 66.8% yield is the average of 4 experiments which in turn averaged 69.5, 69.6, 65.8 and 62.3%.

[c] The original pure commercial sample of *n*-octyl bromide boiled between 197–200.5° (uncorr.). This was distilled before use and the fraction boiling between 198–

200.5° gave yields of 87.4 and 88.5%. On redistillation of the halide a fraction boiling at 200–201° was collected and this gave a yield of 89.2%.

[d] The average yields of 3 runs were 89.8, 92.1 and 91.6%. In the 89.8% yield run there was evidence of a reaction one hour after all of the halide had been added, and in this run the mixture was refluxed for twenty minutes. In the 92.1% yield run there was evidence of reaction after one hour and ten minutes. This mixture was then stirred an additional one and one-half hours and then refluxed for thirty minutes. The 91.6% yield run was like the 92.1% run with the exception of a two-hour (instead of a thirty-minute) period of refluxing.

[e] The 85.6% yield of *n*-butylmagnesium iodide is from freshly distilled iodide. In two other runs where the iodide was distilled one month prior to use the yield was 3–4% lower. Some bromides, like *n*- and *iso*butyl and phenyl, showed essentially no difference in yield whether the commercially pure compounds were distilled or not distilled.

[f] There was evidence of reaction ten minutes after all of the bromobenzene was added. The mixture was then refluxed for ten minutes. With the exception of *n*-butyl chloride, bromobenzene appeared to react for a longer time than any alkyl bromide after all of the halide had been added.

[g] The three bromotoluenes appeared to react thirty-five to fifty minutes after all of the halide was added. They were then refluxed for fifteen and thirty minutes, respectively, in alternate runs in order to assure completeness of reaction (see ref. 8 of this paper).

[h] The bromonaphthalenes appeared to react twenty to thirty minutes after all of the halide was added. They were then refluxed for fifteen and thirty minutes, respectively, in alternate runs. Benzene was used as a diluent in the experiments with the bromonaphthalenes in order to bring the solutions to the 100-cc. mark. Methyl orange is an unsatisfactory indicator under these conditions. The naphthylmagnesium bromides were, of course, prepared in the 30 cc. of ether, but like RMgBr compounds from *p*-bromoanisole and *p*-bromophenetole, they or their etherates are sparingly soluble in ether and more soluble in an ether–benzene mixture.

Discussion of Results

Alternation of Normal Alkyl Bromides.—A glance at the yields of *normal* alkylmagnesium bromides from propyl to heptyl reveals an apparent alternation. The even-numbered halides give yields higher than the *preceding* halides that have an odd number of carbon atoms. This alternation may be accidental. However, we are inclined to doubt that this is the case because the differences are well beyond any experimental error in the method of analysis.

If this alternation is not fortuitous, then methylmagnesium bromide might be expected, under the conditions of our experiments, to give a yield less than that of ethylmagnesium bromide. The difficulty of handling methyl bromide, although not overly serious, might be sufficient to throw some doubt on values obtained with it. Furthermore, results with it might be open to various interpretations because of the known irregularities of first members of homologous series.

Octyl bromide, on the basis of alternation, should give a higher yield of the Grignard reagent than heptyl bromide. The only indication of a higher yield is found in the single experiment described in Footnote (c) of Table I. Possibly, if the phenomenon of alternation is sound, it may become very weak or disappear entirely at the octyl bromide level.

It is interesting to recall that in the earlier studies by Gilman and McCracken[2b] attention was directed to an apparent alternation with normal *iodides*. Here, however, the *odd*-numbered iodide gave a *higher* yield than the preceding iodide having an even number of carbon atoms. This alternation broke down completely, as was mentioned at that time, in the case of propyl iodide, which gave a distinctly lower yield of Grignard reagent than did ethyl iodide.

For those who would seek an explanation of the observed alternations it is well to remember that the reaction of an RX compound with magnesium in ether is not simple. All that we have measured here is the quantity of Grignard reagent that formed. Several minor side reactions have been considered recently by Gilman and Fothergill.[4]

Decrease in Yield with Ascent of Series.—There is no doubt concerning the general and gradual drop in yield in a given series with the ascent of that series to halides of higher molecular weight. However, this drop is so gradual that it is necessary to revise drastically ideas that are still current concerning the decided drop in yield (to 50% or so) with hexyl or octyl groups.[4,10]

Effect of Branching.—With a given series, the order of *decreasing* yield is *normal, secondary* and *tertiary*. Special conditions are necessary for the preparation of tertiary Grignard reagents in distinctly satisfactory yields. These have been described by Gilman and Zoellner.[11]

Reactivity of Halogen.—With a given R group (the *n*-butyl, for example) the lowest yields are with the iodide and the highest with the bromide. The alkyl chlorides react quite slowly, and if sufficient time is taken it is possible that the chlorides will be found to give higher yields than (or yields at least as high as) the corresponding bromide.

The chlorine in benzyl chloride and the bromine in allyl bromide are decidedly more active than the chlorine in *n*-butyl chloride and yet all three have given yields in excess of 90%. Different types of halides must be handled differently in obtaining optimum yields of the corresponding Grignard reagents. This is strikingly illustrated with benzyl chloride and allyl bromide, each of which has a highly reactive halogen. For example, benzyl chloride can be added at once to magnesium in ether and yet give

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[10] The sustained high yields are strikingly illustrated by the as yet unpublished work of Houben and Bödler, a brief account of which is given in Houben-Weyl, "Die Methoden der Organischen Chemie," **4**, 725, second edition, published in Leipzig in 1924. It is interesting to note (private communication from Professor Houben) that phenolphthalein was used as an indicator in their titrations. See also ref. 4 in the article by Gilman and Meyers, *Rec. trav. chim.*, **45**, 314 (1926).

[11] Gilman and Zoellner, THIS JOURNAL, **50**, 425 (1928); *Rec. trav. chim.*, **47** (1928).

an excellent yield of benzylmagnesium chloride (see following paper); whereas if allyl bromide is added at once to magnesium in ether, very little allylmagnesium bromide results, and most of the allyl bromide couples to form diallyl. However, by the special conditions described recently by Gilman and McGlumphy[12] it is possible to obtain allylmagnesium bromide in greater than 90% yields.

The Naphthylmagnesium Bromides.—The yield of α-naphthylmagnesium bromide reported earlier[2b] is incorrect. This was very probably due to the sparing solubility of this Grignard reagent in ether (see footnote *h* to Table I). The comparatively high yield of β-naphthylmagnesium bromide is both interesting and valuable in view of the discouragingly low yields of this RMgBr compound reported by others.[13]

The authors gratefully acknowledge assistance from R. W. Borgeson and L. L. Heck.

Summary

The yields of a number of typical Grignard reagents have been determined. Where comparisons can be made with earlier determinations these revised yields are higher. Attention is directed to a number of generalizations, particularly the apparent alternation in yields with the *n*-alkyl bromides.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

THE EFFECT OF RAPID ADDITION OF HALIDE ON THE YIELDS OF SOME GRIGNARD REAGENTS

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RECEIVED JANUARY 21, 1929 PUBLISHED MAY 6, 1929

Introduction

In studies on the relative reactivities of alkyl and aryl halides toward magnesium in ether,[1] all of the halide is added at once to the magnesium in ether and the reaction is interrupted at regular intervals to determine the rate of reaction. This makes it necessary to have comparative values showing the yields of Grignard reagent when all of the halide is added at once. Yields under such conditions have been determined and are here reported. The results of such studies have an importance over and above

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[12] Gilman and McGlumphy, *Bull. soc. chim.*, **43**, 1322 (1928).

[13] Loevenich and Loesser, *Ber.*, **60**, 320 (1927), reported a 28.5% yield of β,β'-dinaphthyl and no β-naphthoic acid when their reaction product of β-bromonaphthalene and magnesium was treated with carbon dioxide. Probably the highest yield of a compound from β-naphthylmagnesium bromide is a 50% yield of β-naphthaldehyde reported by Chichibabin, *Ber.*, **44**, 443 (1911).

[1] A preliminary account of these studies has been reported by Gilman and Zoellner, THIS JOURNAL, **50**, 2520 (1928).