SINTHESIS OF ETHER-FREE ORGANOMAGNESIUM COMPOUNDS

APPROVED:

[Signatures]

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SYNTHESIS OF ETHER-FREE ORGANOMAGNESIUM COMPOUNDS

THESIS

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By

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CHAPTER I

HISTORICAL SURVEY OF ORGANOMAGNESIUM COMPOUNDS

In 1898, Phillippo Barbier attempted the synthesis of 2, 6-dimethyl-2-hepten-6-ol from natural 2-methyl-2-hepten-6-one via the Wagner-Saytzeff reaction (64), which is the action of zinc metal and methyl iodide on an ether solution of a ketone. This particular reaction did not work. Barbier decided to substitute magnesium for zinc. The desired reaction proceeded nicely, and Barbier reported his results in 1899 (7). In his article Barbier stated that the substitution of magnesium for zinc in the Wagner-Saytzeff reaction was new, that the modification of the reaction enabled him to perform several new syntheses, and that he reserved the right to further develop his method. Barbier, however, did not publish further work in the area.

When Victor Grignard requested a thesis topic, Barbier suggested that he study the use of magnesium in the synthesis of new organic compounds (42). Because he encountered erratic reactions and poor yields with the Barbier synthesis, Grignard decided to attempt to isolate the organomagnesium compound, which was the assumed reaction intermediate, and then react it with some substrate such as a ketone. Grignard proved with a series of test-tube reactions that alkyl halides readily react with magnesium turnings in the presence of dry
ether to form an organomagnesium compound, which is ether soluble and which reacts with carbonyl compounds to give results, in most cases, than does the Barbier synthesis (34). Grignard published his results in a paper entitled "Sur quelques nouvelles combinaisons organométalliques du magnésium et leur application à des synthèses d' alcoëls et hydrocarbures" in 1900 (29).

The Grignard reaction gained immediate acceptance. By the end of 1905, the chemical literature contained 200 publications dealing with the Grignard reaction, and by the end of 1912, more than 700 publications (42, pp. 481-482).

Grignard proposed that the structure of his reagent in ether solution is RMgX, where R is an alkyl or aryl group and X is chloride, bromide, or iodide (27, 28, 29). Blaise reported that ether is tightly held by the Grignard reagent in spite of heating (10). Baeyer and Villiger proposed an oxonium structure, where the oxygen of the ether is quadrivalent, for the Grignard reagent (6). Several authors (9, 25, 26, 51, 52, 53) accepted the oxonium theory until the report by Thorp and Kamm (56), which showed that the theory is unnecessary for explaining the decomposition products of the Grignard reagent in ethers.

Meisenheimer and Casper (37) viewed the Grignard reagent in ether as a complex compound in which the magnesium atom is central and has a coordination number of four. Two molecules of ether are coordinated, through the oxygen, to the
Magnesium atom. According to this view, when a carbonyl compound reacts with a Grignard reagent, it must first displace one of the coordinated ether molecules on the magnesium before reaction can occur. This view is essentially the modern one of the structure of the Grignard reagent in diethyl ether in concentrations below 0.4 molar (62) and in tetrahydrofuran (3).

Jolibois, based on the fact that the compound \( \text{MgI}_2\cdot2\text{Et}_2\text{O} \), where \( \text{Et} \) is an ethyl group, is known, on the fact that diethylmagnesium, although practically insoluble in ether, readily dissolves in an ether solution of \( \text{MgI}_2\cdot2\text{Et}_2\text{O} \) to give a solution which has many of the properties of the Grignard reagent, on the fact that both the ethyl Grignard reagent and diethylmagnesium decompose in the absence of air at 175° C. to form ethylene and magnesium hydride, proposed the structure \( \text{Et}_2\text{Mg}_x\text{MgX}_2 \) (32, 33).

Terentiev (55) reported that methylmagnesium iodide in diethyl ether is a dimer based on the formula \( \text{Mg}_x\text{MgX} \). Heisenheimer and Schlichenmaier (38) repeated and broadened Terentiev's work and found that the molecular weight of the species in diethyl ether solution varies with concentration.

In 1929, Schlenk and Schlenk (45) found that when dioxane is added to an ether solution of Grignard reagent, practically all of the halogen is precipitated as the magnesium salt. They interpreted these data as meaning that the Grignard reagent in diethyl ether solutions exists as an equilibrium
of either

(a) \[ 2\text{R} \text{MgX} \rightleftharpoons \text{R}_2\text{Mg} + \text{MgX}_2 \]

or

(b) \[ \text{R}_2\text{Mg}\cdot\text{MgX}_2 \rightleftharpoons \text{R}_2\text{Mg} + \text{MgX}_2. \]

Equilibrium (a) should be independent of concentration, they stated, while equilibrium (b) should vary with concentration. Since they found no apparent change in equilibrium for an eightfold dilution of a Grignard solution, they concluded the structure is best described by (a).

Recently, two groups of workers, Smelik and Zeiser (43) and Dassy and Jokes (18), reported the results of electrical methods of analysis. Both groups showed that the conductivity of a mixture of diethylmagnesium and magnesium bromide is higher than would be expected, based on the conductivities of each component alone. These data were interpreted to mean that the two components form a complex which ionizes more readily than does either individual component. Both groups reported that the conductance of a Grignard solution prepared in the ordinary fashion is lower than the conductance of an equimolar solution made by mixing diethylmagnesium and magnesium bromide, although the dielectric constants of these two solutions are identical.

Dassy and co-workers (14, 15, 16, 17, 18, 19, 20, 21, 66) have published a series of papers which tried to establish that the Grignard reagent in diethyl ether exists as the equilibria,

\[ 2\text{R} \text{MgX} \rightleftharpoons \text{R}_2\text{Mg} + \text{MgX}_2 \rightleftharpoons \text{R}_2\text{Mg}\cdot\text{MgX}_2, \]
to which the species R\textsuperscript{1}M\textsubscript{g}X makes a negligible contribution.

The basis for all of Dessy's work on the structure of Grignard reagents is the assumption that the Grignard reagent made by the reaction of an alkyl or aryl halide with magnesium in dry diethyl ether is exactly equivalent to an equimolar mixture of dialkyl- or diarylmagnesium and magnesium halide in diethyl ether. If Dessy's assumption be true and if the equilibrium stated above actually describes the species in solution, then the existence of the entity R\textsuperscript{2}M\textsubscript{g}X offers a pathway for the exchange of R groups or a pathway for the exchange of magnesium. If R\textsuperscript{1}M\textsubscript{g}X is not present in the solution, two chemically different kinds of magnesium are present, one bound to halogen and one bound to alkyl or aryl groups. In this discussion the molecules of ether coordinated to the magnesium atoms have been omitted for clarity. Dessy (21, 66) established that equimolar mixtures of diethylmagnesium and magnesium bromide result in a solution whose kinetics and relative rate of reaction with 1-hexyne are the same as those of the normal ethylmagnesium bromide. Dessy and co-workers then tried to prove by dioxane precipitation (16, 17) and electrical studies (18) that there were two chemically different kinds of magnesium which have no pathway for exchange. Using Mg\textsuperscript{28}Br\textsubscript{2}, Dessy (17) found 6 to 10 per cent exchange. With Mg\textsuperscript{20}Br\textsubscript{2}, however, Dessy and Handler (16) noted complete exchange, a situation they attributed to an impurity in the magnesium, an impurity which acts as a catalyst for the exchange. Here
the word "catalyst" is not used in the normal sense but is used to mean a substance which alters the actual course or mechanism of the reaction. Since he did not find exchange with Grignard grade magnesium, Dessy concluded that the exchange found with Mg²⁵ is not important to the structure of an ethereal Grignard reagent. He stated that the Grignard reagent is best described by the following equilibrium:

\[ R_2\text{Mg} + \text{MgX}_2 \rightleftharpoons R_2\text{Mg}	ext{MgX}_2. \]

Dessy's formulation was widely accepted (5). Recently Vreugdenhil and Blomberg (60, 61, 62, 63), Ashby and co-workers (1, 2, 3, 5), and Rundle and co-workers (30, 54) have published papers about the structure of the ethereal Grignard reagent which refute Dessy's conclusions. Ashby and Becker (3) reported that for concentration up to two molar, ethylmagnesium bromide and chloride are monomeric in tetrahydrofuran and have the structure RMgX. Ashby also presented positive evidence for alkyl exchange in tetrahydrofuran and possible evidence for exchange in diethyl ether. He points out that one should expect differences between tetrahydrofuran and diethyl ether to be of degree rather than kind (2, 5); thus one should expect the existence of RMgX in diethyl ether. Rundle and co-workers (30, 54) reported that in the solid state, X-ray diffraction shows that both phenyl- and ethylmagnesium bromide dietherate have the structure RMgX·2Et₂O. One cannot say that structure in the solid
state is the structure of a species in solution. Vreugdenhil and Blomberg (62), working in an oxygen- and moisture-free, sealed glass system which has no ground joints or stopcocks, conclusively proved that for concentrations below 0.14 molar, a diethyl ether solution of ethylmagnesium bromide is not equivalent to a solution of a mixture of diethylmagnesium and magnesium bromide; above concentrations of 0.4 molar, the two solutions are essentially identical. Dessy, Green, and Salinger (15) repeated their work with $\text{Mg}^{2+}$ (17) and found that there is statistical exchange with some but not all grades of magnesium. Ashby (1) has shown that the initial species formed in the reaction of ethyl bromide and magnesium is ethylmagnesium bromide, $\text{RMgX}$. Further, when a diethyl ether solution of ethylmagnesium bromide is added to a large excess of triethylamine, $\text{EtMgBr.N(Et)}_3$ is isolated in 90 percent yield. Ashby concludes that this is proof for the existence of the species $\text{RMgX}$ in diethyl ether solution, as probably the symmetrical dimer

$$\text{R-Mg} \overset{X}{\text{Mg-R}}.$$  

In summary, most chemists now believe that the Grignard reagent in diethyl ether solution exists as either the monomer or symmetrical dimer of $\text{RMgX}$. The unsymmetrical dimer proposed by Dessy,

$$\text{R-Kg} \overset{X}{\text{Kg}}.$$
which is the logical species formed by the mixing of $R_2Mg$
and $MgX_2$, may be a fairly stable species which is slow to
convert to the $MgX$ species or its symmetrical dimer in the
absence of a catalyst. Ashby (1) proposes the following
as a pathway for exchange:

\[
\begin{align*}
R-Mg + Mg-X & \rightleftharpoons 2R-MgX \\
R-Mg + Mg-X & \rightleftharpoons R_2Mg + MgX_2
\end{align*}
\]

Recently Weiss (65) reports that X-ray diffraction studies
of the solid remaining after diethyl ether is removed under
vacuum at 100 to 120 degrees centigrade from methylmag-
nesium chloride and bromide and ethylmagnesium chloride
and bromide indicate that the solid is a mixture of $R_2Mg$
and $MgX_2$. Under these conditions, Kharasch and Reinmuth
state there is still some coordinated ether. Apparently
the major factors are known; however, there are still some
experimental details to be resolved in the study of the
structure of the Grignard.

When an alkyl or aryl halide reacts with magnesium
either in the absence of a solvent or in the presence of a
hydrocarbon solvent, the organomagnesium product is not
identical to the corresponding Grignard reagent (11, 24).
Grignard (28) reported that there is no reaction between alkyl halides and magnesium in benzene or ligroin. Malagren (35) found no reaction between alpha-camphoryl bromide and magnesium in boiling benzene, but reaction occurred in boiling toluene or xylene. Tschelinzeff (53) found no reaction of magnesium with an unspecified series of iodides in boiling benzene after 48 hours. Tschelinzeff used both thiophene-free and thiophene-contaminated benzene. In xylene, however, he found that ethyl, n-propyl, n-butyl, and n-aryl iodides reacted with magnesium without a catalyst.

The reaction of alkyl and aryl halides and magnesium without a solvent was reported by Spencer and Stokes (50) and later Spencer and Crawdson (49). They found that aryl chlorides and the lower alkyl halides, up to n-butyl, form organomagnesium products only in sealed tubes heated to 270 degrees centigrade. Aryl bromides and iodides and the higher alkyl halides form organomagnesium products in yields of 40 to 90 per cent.

Several groups of workers (8, 31, 41, 51, 52, 57, 59) have studied the formation of organomagnesium compounds in hydrocarbon solvents in reactions initiated by the addition of a small amount of a basic "catalyst" such as an ether or a tertiary amine. Recently Ashby (4) showed that when a tertiary amine, such as triethylamine, is present in an amount equimolar to the alkyl or aryl halide in a hydrocarbon solvent, the resulting organomagnesium compound is completely soluble and has the structure MgX.
Oddo (39) demonstrated that magnesium does not form organometallic compounds in benzene which is free of all traces of ethers, amines, and thiophene. However, he showed that Barbier-type syntheses could be run in benzene with carbonyl compounds.

Gilman and Brown (22) found that phenyl chloride reacted in 84 per cent yield with magnesium in the absence of solvents in an evacuated, sealed glass tube heated to 150 to 160 degrees centigrade for three hours. Schorin and co-workers (47) obtained a maximum yield of 70 per cent phenylmagnesium chloride in a stirred, iron autoclave heated to 160 to 165 degrees centigrade for three hours with a pressure of two and one half atmospheres. Manske and Levingham (36) used excess phenyl chloride as the solvent for the synthesis of phenylmagnesium chloride. Olah (40) was issued a patent which describes the synthesis of aryl- magnesium halides in an excess of aryl halide. In one example, Olah describes the use of ligroin as a solvent for the synthesis of an alkylmagnesium bromide by using a mixture of a metal hydride and a Friedel-Crafts metal halide catalyst to initiate the reaction. Richards and Holt (43) describe the synthesis of Grignard-type compounds in hydrocarbons which are solids at ordinary room temperatures.

Schlenk (44) reported the reaction of magnesium with a series of alkyl iodides in sealed tubes which were mechanically
shaken for two months. Benzene is the solvent that Schlenk used. Although some of the yields were high, they were rather erratic.

Schorin, Issaguljanz, and Gussewa (46) reported failure in the attempt to react magnesium with n-butyl, i-amyl, or n-octyl chloride at the temperature of the refluxing alkyl halide.

Bryce-Smith and co-workers (11, 12, 13), while studying Friedel-Crafts alkylation with alkyl halides in the presence of small amounts of magnesium, discovered that some organomagnesium compounds can be easily made in hydrocarbon solvents, that in some cases the compounds are made in yields approaching those in ether, that the organomagnesium compounds resulting from the lower alkyl halides, from secondary and tertiary alkyl halides or from benzyl halides, are produced in low yields, and that the solubilities of the compounds in hydrocarbon solvents vary but are usually appreciable. They stated that for high yields in hydrocarbon solvents, extreme attention to experimental conditions, which vary from compound to compound, is required.

Zakharkin and co-workers (67, 68) reported the synthesis of a series of organomagnesium compounds without solvents and in various hydrocarbon solvents. Their reported yields in most cases were almost equivalent to the optimum yields in diethyl ether. Their work is in contrast with the work of
Gilman and McCracken (23), which states that in ether-hydrocarbon mixtures, the yields are about ten per cent lower than the corresponding synthesis in ether.

Recently Glaze and Selman (24) reported that when n-amyl chloride reacts with magnesium in benzene solvent, di-n-amylmagnesium is the species in solution.

At the time this work was begun, there was some confusion about the technique necessary for the successful synthesis of organomagnesium compounds in hydrocarbon solvents and without solvents. It was decided to repeat the work of Bryce-Smith and Zakharin. Thus began the study of the synthesis of organomagnesium compounds without solvents; the study of the reaction products of these organomagnesium compounds in hydrocarbons plus 2-butanone compared to the reaction products of the corresponding ethereal Grignard reagent plus 2-butanone; and a preliminary study of the nature of these organomagnesium compounds in hydrocarbon solvents.
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1. Ashby, E. C., "Proof for the MgX Composition of Grignard Compounds in Diethyl Ether. R_MgX, the Initial Species Formed in the Reaction of RX and Mg," Journal of the American Chemical Society, LXXXVII (June, 1965), 2509-2510.


CHAPTER II

EXPERIMENTAL PROCEDURE

Materials

Three kinds of magnesium are used in this study: an unspecified lot of coarse magnesium turnings described as Grignard-grade from Fisher Scientific Company, an unspecified lot of 70 to 80 mesh magnesium powder from Fisher Scientific Company, and an unspecified lot of purified 150 mesh magnesium powder from Baker and Company.

The benzene and hexane solvents are Phillips Pure Grade hydrocarbons. Both hydrocarbons were dried by distillation from lithium aluminum hydride onto molecular sieve. The diethyl ether purchased from Fisher Scientific Company, is refluxed for twenty-four hours in contact with lithium aluminum hydride and then distilled into a dry flask protected from moisture by calcium hydride.

The alkyl and aryl halides are purchased from Eastman Chemical Company. The organic halides are analyzed by gas chromatography and used without further purification if they are found to be at least 99 per cent pure. Those halides of lower purity are distilled just prior to use.
Preparation and Analysis of Ether-free Organomagnesium Compounds

The solventless organomagnesium compounds are prepared in either one quarter or one half mole quantity. A three neck, one liter, round-bottom flask equipped with 24/40 standard taper ground joints is used. The flask is equipped with a Hirschberg nichrome wire stirrer in an Asco teflon stir gland with a Neoprene o-ring seal, with a 150 milliter dropping funnel with a pressure equalizing line, and with a condenser connected to a nitrogen manifold which maintains about two centimeters of mercury pressure on the system. The Condenser water is chilled with crushed ice. A Glascol heating mantle controlled by a rheostat is used to heat the flask.

The glassware is washed, dried overnight at 125 degrees centigrade, assembled while hot, and cooled under a stream of dry nitrogen. An amount of magnesium equimolar to the organic halide plus a ten weight per cent excess is placed in the flask. The flask is heated to about 150 degrees centigrade. Sometimes at this point a small crystal of iodine is added. The organic halide is added dropwise to the flask in such a way that it falls onto the magnesium rather than the hot walls of the flask. For the higher alkyl halides the reaction is very exothermic, and sometimes the flask must be cooled with an air jet. When most of the organic halide has been added, the contents of the flask
form a thick mud-like mixture. The stirring rate is increased from the initial 30 revolutions per minute. The dropping funnel which contained the organic halide is removed and quickly replaced with another which contains the hydrocarbon solvent. A high nitrogen flow is maintained during the switch to prevent air from coming into contact with the organomagnesium compound. The hydrocarbon is added to the flask and allowed to reflux for about two hours. Then the dropping funnel which contained the hydrocarbon is quickly replaced with one which contains a quantity of 2-butanol, equimolar to the organic halide, dissolved in twice its volume of hydrocarbon. The 2-butanol solution is added dropwise to the flask at such a rate so as to maintain a gentle reflux. Usually the flask is cooled with an air jet.

After all the solution has been added, the flask is heated to maintain gentle reflux for two hours. The reaction complex is hydrolyzed by either pouring the contents of the flask over acidified crushed ice or by carefully adding to the flask of 2.5 normal hydrogen chloride in anhydrous ethanol equimolar to the magnesium present.

The hydrolyzed product is collected and analyzed by gas chromatography. The gas chromatograph is an Aerograph A-350B. Two packed columns are used for analysis: Apiezon L and 26% Carbowax. The conditions for analysis vary for the different compounds. Authentic samples of the tertiary alcohols expected as products are made from the corresponding
ethereal Grignard reagent and 2-butanone. Standard solutions of the purified alcohols are made in hydrocarbon solvents. A series of standard dilutions is used to construct graphs showing the concentration of the alcohol versus the response of the gas chromatograph, which are used to determine the molarity of the alcohol in the reaction product. From the molarity and the total volume, the moles of alcohol are calculated. From the moles of the alcohol and the moles of alkyl halide used, the yield is calculated.

In two cases determination of the yield of ether-free organomagnesium compounds is made by means other than reaction with 2-butanone. "n-Hexylmagnesium bromide" and "phenylmagnesium bromide" were analyzed by hydrolyzing the organometallic compound with acidified ice and determining by gas chromatography the amount of hexane and benzene liberated. Here the quotation marks are used to designate the reaction product of the corresponding organic halide and magnesium in the absence of a solvent; the term inside the quotation marks does not indicate the actual structure of the species.

Preparation and Analysis of Ethereal Grignard Reagents

The same equipment as described in Preparation and Analysis of Ether-free Organomagnesium Compounds is used for the preparation of ethereal Grignard reagents. A quantity of coarse magnesium turnings, equimolar with respect to the organic halide plus ten weight per cent excess, is placed in
the flask and covered with 500 milliters of diethyl ether freshly distilled from lithium aluminum hydride. Without stirring, a small crystal of iodine and ten to twenty drops of the organic halide are added to the ether in the flask. Reaction usually begins within a few minutes. In some cases the flask is heated so that the ether gently refluxes until the reaction begins. The stirrer is turned on, and the solution of organic halide in twice its volume of ether is added just fast enough to maintain gentle reflux of the ether. After all the organic halide is added, the reaction mixture is refluxed for two hours. The dropping funnel is replaced with one which contains 2-butanone dissolved in twice its volume of ether. The solution is added to the flask dropwise. The flask is cooled with an air jet. The mixture is refluxed for two hours after the addition of all the 2-butanone solution.

The reaction mixture is hydrolyzed by the addition of 2.5 normal hydrogen chloride in anhydrous ethanol. A sample of the hydrolyzed product is analyzed by gas chromatography. The bulk of the ether solvent is removed from the product mixture under vacuum. The product is slowly distilled through a six inch column packed with glass helices. The fraction within two degrees centigrade of the boiling point of the tertiary alcohol is redistilled through a spinning band column with a ten to one reflux to takeoff ratio. The purity of the distilled product is greater than 98.5 per cent.
The tertiary alcohols are identified by their boiling points, indices of refraction, and infrared spectra. (1, 5, 6)

Cryoscopic Molecular Weight Studies

A thermopile is made according to the specifications of Glover and Stanley (2, 3). A telegraph key, a 15,000 volt neon transformer, and two lead pencils are used to weld the junctions. A water and ice mixture is used as the reference point. The sample half of the thermopile is passed through a rubber stopper into a benzene solution of "ethylmagnesium bromide" or "ethylmagnesium iodide" contained in a twelve inch test tube. The organomagnesium product formed by the reaction of methyl iodide, ethyl bromide or iodide and magnesium, which has been in contact with refluxing benzene for at least two hours, is taken into a dry box and filtered through a medium porosity sintered glass frit. The filtrate is placed in a twelve inch test tube with the sample side of the thermopile submerged in the liquid. The test tube is removed from the dry box and placed into a Dewar flask containing crushed ice and water. The reference side of the thermopile is placed into a water and ice mixture. The test tube is shaken by hand. The voltage output of the thermopile is recorded on a 10 millivolt recorder. The test tube is cleaned, filled with pure, dry benzene, and the procedure is repeated. By knowing the concentration of the organomagnesium compound in solution, the difference between the freezing point of the pure solvent and the freezing point of the solu-
tion, the molal freezing point constant of the solvent, and by assuming that the densities of the pure solvent and the solution are the same, one can calculate the apparent molecular weight of the species in solution.

**Infrared Absorption Studies**

Infrared absorption scans were obtained on filtered benzene solutions of the organomagnesium compounds made from methyl iodide, ethyl iodide, and ethyl bromide. The spectra from two to sixteen microns are obtained on a Perkin-Elmer model 237 infrared spectrophotometer, and the spectra from fifteen to thirty-five microns are obtained on a Perkin-Elmer model 21 infrared spectrophotometer equipped with cesium bromide optics. The solutions are loaded inside a dry box into a one millimeter path length cell with cesium bromide windows. Samples of each solution are checked for the presence of the Grignard-type compound by the method of Gilman (4).
CHAPTER BIBLIOGRAPHY


CHAPTER III

RESULTS AND CONCLUSIONS

As mentioned in Chapter I, in spite of a large number of reports in the area of the synthesis of organomagnesium compounds in the absence of solvents and in hydrocarbon solvents, there is much conflicting and ambiguous data in the literature. The problem with which this investigation is concerned is the synthesis of organomagnesium compounds without solvents, the study of the reaction products of these organomagnesium compounds in hydrocarbons plus 2-butanone compared to the reaction products of the corresponding ethereal Grignard reagent plus 2-butanone, and a preliminary study of the nature of these organomagnesium compounds in hydrocarbon solvents.

Table 1 contains a summary of the data from the syntheses of several organomagnesium compounds in the absence of solvents and the yield of their addition product with 2-butanone. Organomagnesium compounds can be made in the absence of solvents and in some cases can be made in high yields. Bryce-Smith's comment (1) that good yields require extreme attention to experimental details, which vary from compound to compound, is true. There is considerable scatter with the data of the iodomethane, iodoethane, and bromoethane. Apparently the more volatile organic halides are easily lost.
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<td>1.0</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>1-Chlorobutane b</td>
<td>yes</td>
<td>1.0</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>1-Chlorobutane b</td>
<td>yes</td>
<td>1.0</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>1-Chlorobutane c</td>
<td>yes</td>
<td>0.75</td>
<td>82.3  k</td>
<td></td>
</tr>
<tr>
<td>Bromohexane b</td>
<td>no</td>
<td>0.75</td>
<td>59</td>
<td></td>
</tr>
</tbody>
</table>

a Fisher Scientific Company 70-90 mesh magnesium powder.
b Baker purified 150 mesh magnesium powder.
c Fisher Scientific Company Grignard grade magnesium turnings.
d The flask was cool to touch during the halide addition.
e Flask heated to dryness after halide addition before solvent was added.
f Organomagnesium product is spontaneously flammable in air.
g Flask cooled and benzene added as soon as last of halide added.
h 30-50% of alkyl halide found as the coupling product hexane.
i Exothermic reaction.
j Very exothermic reaction.
k Yield determined by hydrolysis and analysis of liberated hydrocarbon.
Neglecting the two runs with iodoethane in which the halide was added to a cool flask and the two runs with iodoethane in which the flask was baked to dryness before the addition of the hydrocarbon solvent, the yields of the addition production of 2-butane with the two halides are 65 and 79 per cent, respectively. The yields of the 1-bromopropene derivative are unique. The presence of large amounts of coupling product in this particular reaction and not in the reaction products of the other alkyl halides has no ready explanation. The only secondary alkyl halide used in this study, 2-bromopropene, formed a product whose yield is much lower than that of the corresponding 1-bromopropene product, a result supported by the data of Bryce-Smith and Cox (1). For the only data reported by Zakharikin and co-workers (5) which is directly comparable to data from this study, the data describing the yields of the organomagnesium compounds derived from the 1-iodo-, 1-bromo-, and 1-chlorobutanes, the Russian work reports yields which average 6.5 per cent higher than the yields found in this work. The paper by Zakharikin and co-workers does not state how the yields of the organomagnesium compounds were determined.

Data in Table I demonstrate that for the 1-haloalkanes above C3, the yield becomes higher as the organic group becomes larger. The addition of iodine to the magnesium metal before the addition of the organic halide has a small but
positive effect upon the yield of the organometallic compound. In the only case when an aryl halide was used, bromobenzene, the reaction conditions were more severe than those used for the alkyl halides.

In some cases some of the organomagnesium compounds splashed high on the walls of the flask where it was unavailable for reaction with the 2-butanone. Higher yields could be gotten if a hydrocarbon solvent is added early in the reaction or if most of the organic halide is added as a hydrocarbon solution.

In most cases the reaction product of the organomagnesium compound and 2-butanone was liberated with 2.5 normal hydrogen chloride in anhydrous ethanol. The reasons for using this rather exotic method are, one, the product, a tertiary alcohol, is fairly soluble in water; two, a gel or two liquid phases result when aqueous hydrochloric acid is used.

Table II contains a comparison of yields of organomagnesium compounds prepared in ether and prepared without solvents. The yields of the organomagnesium compounds prepared in ether in this study compare favorably with the corresponding yields reported in the literature (3). The yields in the literature were determined by acid titration, a method which always gives high results, according to Gilman (2). The solventless organomagnesium compounds can
only be directly compared to the literature report in the cases of the 1-iodo-, 1-bromo-, and the 1-chlorobutane derivatives as mentioned earlier.

The preparation of the Grignard reagents in ether is straightforward. No problems were encountered except for two unreported reactions in which the contents of the flask boiled out through the condenser because too much organic halide had been added to the flask in attempting to start the reaction.

The molecular weight determinations of three different preparations of each of the organomagnesium derivatives of iodomethane, iodoethane, and bromoethane were all inconclusive. In each case although the benzene solution of the organomagnesium compound gave a positive color test for the presence of a Grignard-type compound, only a single drop of 0.35 normal hydrochloric acid was necessary to titrate five milliters of the benzene solution to a phenolphthalein indicator end point, indicating that the concentration of the organomagnesium compound in the benzene was less than 0.006 normal. Cryoscopically, no differences could be discerned between the benzene solutions and the pure benzene within experimental error. In each case the precipitate remaining from the filtration of the benzene solution of the organomagnesium was stirred with freshly distilled diethyl ether for two hours and then tested for the presence of Grignard-type compounds.
TABLE II

COMPARISON OF YIELDS OF ORGANOMAGNESIUM COMPOUNDS PREPARED IN ETHER AND WITHOUT SOLVENTS

<table>
<thead>
<tr>
<th>Organic Halide</th>
<th>Per Cent Yield</th>
<th>Ether Solvent (Literature)a</th>
<th>Ether Solvent (This Work)b</th>
<th>No Solvent (This Work)b</th>
<th>No Solvent or Hydrocarbons (Literature)c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iodomethane</td>
<td>100</td>
<td>96</td>
<td>44.5</td>
<td>40-50d</td>
<td></td>
</tr>
<tr>
<td>Bromoethane</td>
<td>97</td>
<td>7.5</td>
<td>50d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iodoethane</td>
<td>96.4</td>
<td>95</td>
<td>67</td>
<td>79d</td>
<td></td>
</tr>
<tr>
<td>1-Bromopropane</td>
<td>92.5</td>
<td>89</td>
<td>36.5</td>
<td>84d</td>
<td></td>
</tr>
<tr>
<td>1-Iodobutane</td>
<td>85</td>
<td>71</td>
<td>71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Bromobutane</td>
<td>83.5</td>
<td>62</td>
<td>75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Chlorobutane</td>
<td>98.5</td>
<td>64</td>
<td>70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Bromopentane</td>
<td>88.6</td>
<td>87</td>
<td>78.5</td>
<td>92d</td>
<td></td>
</tr>
<tr>
<td>1-Bromoheptane</td>
<td>86.8</td>
<td>87</td>
<td>82e</td>
<td>93d</td>
<td></td>
</tr>
<tr>
<td>Bromobenzene</td>
<td>94.7</td>
<td>59e</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Kharasch and Reinmuth (3, pp. 19, 32).
b The yield was determined by reaction with 2-butancne.
c Zakharkin and co-workers (2).
d These reactions were run by heating three milliters of the organic halide with magnesium until the halide boiled and then slowly adding the rest of the halide as a hydrocarbon solution.
e The yield was determined by hydrolysis and analysis of the liberated hydrocarbon.
In each case the Gilman color test was positive; however, two drops or less of 0.35 normal hydrochloric acid was required to titrate five milliters of the ether solution to a phenolphthalein end point.

Infrared spectra were obtained on portions of each of the solutions used for the cryoscopic molecular weight studies in an attempt to find the characteristic C-Mg-C absorption. Scans were got on both the ether and the benzene solutions. The solutions were so dilute that no meaningful conclusions could be drawn about the species in solution.

To recapitulate, organomagnesium compounds can be made in the absence of solvents in yields which, in the cases of the higher alkyl primary halides, approach the yields of the corresponding Grignard reagents. The organomagnesium compounds made from alkyl halides higher than propyl and aryl halides show appreciable solubility in hydrocarbons. The methyl and ethyl halide derivatives are practically insoluble. These organomagnesium compounds have chemical properties similar to those of the corresponding Grignard reagents.
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