The ozonolysis of phenyl Grignard reagent

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THE OZONOLYSIS OF PHENYL GRIGNARD REAGENT

By

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CHAPTER I

INTRODUCTION

Objective of the Research

The objective of this research was to investigate the reaction of ozone with phenylmagnesium bromide. The products of this reaction were to be identified and the corresponding yields determined. This investigation was to be carried out with different methods of addition of ozone and with the use of different ether solvents.

The long range objective of this research was the possible synthetic utility for the ozonation of aromatic Grignard reagents in the production of phenols.

Literature Background

Although the reaction of Grignard reagents with oxygen has been discussed in the literature over the past fifty years, an introduction was made to the ozonation of Grignard reagents only one year ago by Paul E. Pike.\textsuperscript{1} Additional studies of the reaction of ozone with organomagnesium compounds have been conducted since that time by P. Kevin Sysak.\textsuperscript{2}

Reaction of Phenylmagnesium Halide with Oxygen. According to Porter and Steel,\textsuperscript{3} the reaction of phenylmagnesium bromide with oxygen forms phenoxy magnesium bromide which yields phenol upon addi-
tion of water. This may be illustrated by the following equations:

\[
\text{MgBr} + \text{O}_2 \rightarrow \text{OOMgBr}
\]  
(1)

\[
\text{OOMgBr} + \text{MgBr} \rightarrow 2 \text{OOMgBr}
\]  
(2)

\[
\text{OOMgBr} + \text{H}_2\text{O} \rightarrow \text{OH} + \text{MgBrOH}
\]  
(3)

This mechanism was verified by Walling and Buckler by isolation of alkylhydroperoxides. These were produced upon hydrolysis of the alkylperoxymagnesium bromide formed during the oxygenation of aliphatic Grignard reagents. Although the peroxide intermediate was not isolated in the case of the aromatic Grignard reagents, evidence was reported to indicate its existence as an intermediate.

Porter and Steel reported that other products formed, and included \( p \)-dihydroxy-diphenyl and diphenyl ether which were produced as the result of a side reaction between the products of the first two equations above. This is shown by the following equations:

\[
\text{OOMgBr} + \text{OOMgBr} \rightarrow \text{OO} + (\text{MgBr})_2\text{O}
\]  
(4)

\[
\text{OO} \rightarrow \text{OH}
\]  
(5)
The atomic oxygen formed in the last equation above then was said to react with diphenyl peroxide to form quinone. The production of \( p \)-diphenyl benzene was also observed for the reaction of oxygen with phenylmagnesium bromide.

Gilman and Wood\(^7\) reported that biphenyl was found as a by-product of the oxygenation of phenylmagnesium bromide. Another product of the oxygenation reaction was phenylmethyl carbinol. The formation of this product will be discussed in more detail in the next section.

The maximum yield of phenol observed by Gilman and Wood was 29\(\%\), with the optimum temperature near 0\(^\circ\)C.\(^8\) Cooling the reaction to -60\(^\circ\)C did not increase the yield of phenol. On the other hand, Walling and Buckler\(^9\) obtained 43 to 46\% yields of phenol by addition of phenylmagnesium bromide and chloride to a solution containing oxygen.

Kharasch and Reynolds\(^10\) reported that aromatic Grignard reagents produced poor yields of phenols upon reaction with oxygen because the disproportionation reaction between the Grignard reagent and the arylperoxymagnesium halide (equation 2) was slow relative to the initial reaction involving the production of the arylperoxymagnesium halide.
(equation 1).

**Formation of Phenylmethyl Carbinol.** Phenylmethyl carbinol is a by-product formed in the reaction of oxygen with phenylmagnesium bromide. Gilman and Wood\(^\text{11}\) reported that oxygen reacts with diethyl ether to form \(\alpha\)-ethoxyethyl hydroperoxide. This then reacts with phenylmagnesium bromide to form 1-phenylethoxymagnesium bromide which yields phenylmethyl carbinol upon hydrolysis.

\[
\ce{CH_3CH_2OCH_2CH_3 + O2 -> CH_3CH_2OCHCH_3O2H} \tag{7}
\]

\[
\ce{CH_3CH_2OCHCH_3 + \ce{O-MgBr} -> \ce{O-MgBr} + \ce{CH_3CH(OMgBr)CH3}} \tag{8}
\]

The above reaction is similar to the reaction of acetaldehyde with phenylmagnesium bromide to give phenylmethyl carbinol upon hydrolysis. Acetaldehyde is one of the decomposition products of \(\alpha\)-ethoxyethyl hydroperoxide.\(^\text{12}\)

**Reaction of Grignard Reagents with Protic Acids.** The reaction of Grignard reagents with protic acids yields hydrocarbons.\(^\text{13}\) It was reported by Gilman and Wood\(^\text{14}\) that large quantities of benzene were formed by reaction of the acidic hydrogen of \(\alpha\)-ethoxyethyl hydroperoxide or many of its decomposition products with phenylmagnesium bromide.

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Reaction of Grignard Reagents with Halogens. Grignard reagents react with halogens to give alkyl or aryl halides. The mechanism for this reaction may be ionic or in the case of Br$_2$ it may sometimes involve a free radical mechanism.\textsuperscript{15}

$$RMgX + X'_2 \rightarrow RX' \quad (\text{where } X'_2 \text{ may be I}_2, \text{ Br}_2, \text{ or } Cl_2)$$

\textbf{Ozonation of Alkylmagnesium Compounds.} Pike\textsuperscript{16} reported that reactions of ozone with cyclohexylmagnesium bromide at -76$^\circ$C produced 50% cyclohexanone and 50% cyclohexanol. No differences were detected when the carrier gas used for ozonation of cyclohexylmagnesium bromide was changed from oxygen to nitrogen.\textsuperscript{17}

Sysak\textsuperscript{18} reported that reactions involving dropwise addition of di-n-hexylmagnesium in cyclopentane to a solution of ozone in cyclopentane at -90$^\circ$C produced a precipitate which yielded hexanol and hexyl hydroperoxide upon hydrolysis. Two possible mechanisms were shown for the formation of the intermediate product that produced hexanol and hexyl hydroperoxide in equal quantities.

$$R-Mg \underset{O_3}{\rightarrow} Mg-R \rightarrow R-Mg MgOOOR \rightarrow R_2Mg + ROMgOOOR \quad (11)$$
\[ \text{R}_2\text{Mg} \xrightarrow{0,3} \text{ROOMgR} \rightarrow \text{ROOMgOR} \]
CHAPTER II

EXPERIMENTAL

Instrumentation

All vapor-phase chromatography was performed on a Varian Aerograph Series 1700 Gas Chromatograph employing a thermal conductivity detector. A Beckman recorder with disc integrator was used to measure constituents quantitatively. Those yields found by vapor-phase chromatography were acquired with the aid of an internal standard. Columns used for quantitative measurements were a 9' x 1/4", 10% SE-30 on Chromasorb W and a 10' x 1/4", 10% FFAP on Chromasorb W. Hereafter in this thesis they will be referred to as the "SE-30" or the "FFAP" column. Columns used for purification of the products obtained in the reactions were a 20' x 3/8", 20% SE-30 on Chromasorb W. Hereafter in this thesis they will be referred to as the "SE-30 Prep" or the "FFAP Prep" column. All products which were identified by vapor-phase chromatography were identified by GC coinjection (see page 23).

All infrared spectra (IR) were recorded on a Beckman IR-33 Spectrometer.

Experimental Apparatus

The ozone was produced by a Welsbach T-408 electric discharge
ozonator. Two types of addition of ozone were investigated. The first type of addition involved dissolving ozone in n-heptane or n-pentane at \(-78^\circ C\) by passing ozone through the solvent (fig. 1). The concentration of ozone was measured by pipetting 5.0 ml. aliquots into an aqueous solution of potassium iodide. The solution was subsequently acidified and then titrated with a 0.01 M solution of thiosulfate.

Since one mole of ozone is used to make one mole of iodine, the following equation was used to determine the quantity of ozone entering into the reaction:

\[
\text{Liters} \times \text{Molarity} \times \left(\frac{1}{2}\right) \times \left(\frac{\text{Volume of solvent}}{\text{Volume of aliquot}}\right) = \text{moles O}_3
\]

\(\text{Liters} = \text{liters of Na}_2\text{S}_2\text{O}_3 \text{ used in the titration.}\)

\(\text{Molarity} = \text{molarity of Na}_2\text{S}_2\text{O}_3.\)

\(\text{Volume of solvent} = \text{ml. of solvent used in the reaction.}\)

\(\text{Volume of aliquot} = \text{ml. of aliquot titrated.}\)

The ozone solution was then added dropwise from a jacketed addition funnel to the Grignard reagent which had been pipetted into the oxygen-free reaction flask. The temperatures of the Grignard reagent solution and the ozone solution were maintained at \(-78^\circ C\) by a dry ice-acetone bath (fig. 2).

For the second type of ozone addition, ozone was separated from oxygen by selective adsorption on silica gel at \(-78^\circ C\). The undeter-
Ozonation Apparatus

Figure 1

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Figure 2

Ozone Solution Addition Apparatus

Ozone Solution

Dry Ice-Acetone Bath
-78°C

Phenylmagnesium Bromide in Ether

Dry Ice-Acetone Bath
-78°C

N₂

Mercury Bubbler

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mined quantity of ozone was removed from the silica gel with a constant flow of nitrogen. The ozone-nitrogen mixture was bubbled through the phenylmagnesium bromide solution in an ozonation tube (fig. 3).

Chemicals

The diethyl ether used to prepare the Grignard reagents was anhydrous Baker Analytical Reagent and was stored over sodium wire without further purification. The magnesium used in the preparation of Grignard reagents was J. T. Baker purified magnesium chips, which were stored in a dessicator containing $\text{P}_2\text{O}_5$. The bromobenzene used in the preparation of Grignard reagents was Mallinckrodt Analytical Reagent. Dimethoxymethane used as a solvent for Grignard reagents was Matheson Coleman and Bell Practical Grade. Purification was accomplished following the procedure outlined in Purification of Laboratory Chemicals. Methanol was removed by treatment with sodium, followed by fractional distillation from sodium. The anhydrous dimethoxymethane was stored over sodium wire.

The n-pentane used as a solvent for ozone was J. T. Baker Practical Grade. Purification was accomplished following the procedure outlined in Purification of Laboratory Chemicals with certain variations. The pentane was shaken with successive quantities of concentrated sulfuric acid. It was then washed with successive solutions of potassium permanganate in $3.0\text{ N}$ sulfuric acid, followed by an
GASEOUS OZONE ADDITION APPARATUS

Figure 3
aqueous solution of sodium bicarbonate. The pentane was then dried with magnesium sulfate and distilled from sodium wire and stored over sodium wire. The n-heptane used as a solvent for ozone was J. T. Baker Practical Grade. Purification was accomplished following the procedure outlined in *Purification of Laboratory Chemicals*.

The heptane was shaken with successive quantities of concentrated sulfuric acid, followed by an aqueous solution of sodium bicarbonate. The heptane was then dried with magnesium sulfate and distilled from sodium wire and stored over sodium wire.

The 1,2,3,4-tetrahydronaphthalene used as an internal standard for G. C. analysis was J. T. Baker Practical Grade. This was used without further purification after inspection of its purity by vapor-phase chromatography.

The oxygen used to react with phenylmagnesium bromide and used to prepare ozone was Union Carbide U. S. P. which was dried by flowing through anhydrous calcium sulfate. The nitrogen used as an inert atmosphere for the Grignard reagent was Industrial Air Products. The nitrogen was dried by flowing through anhydrous calcium chloride.

### Preparation of Phenylmagnesium Bromide

Three concentrations of phenylmagnesium bromide were prepared in diethyl ether for this research. All solutions were prepared in quantities greater than that necessary for a single ozonation.
The first Grignard reagent was prepared by adding 471 g. (3.0 mole) of bromobenzene, diluted with 500 ml. of diethyl ether, to 700 ml. of diethyl ether containing 72.9 g. (3.0 mole) of magnesium chips. The addition took one hour with the system isolated from air by a nitrogen atmosphere. The solution was not filtered from the un-reacted magnesium. The concentration of phenylmagnesium bromide was 2.46 M.

A large amount of unreacted bromobenzene and a high boiling oil that was identified as the lubricant used for the power stirrer was discovered upon G. C. analysis of the hydrolyzed Grignard reagent. The preparation of another Grignard reagent was necessitated by the difficulty in removing the oil from the SE-30 column of the gas chromatograph and because of the reaction of bromobenzene with phenylmagnesium bromide to form biphenyl.

The second Grignard reagent was prepared by adding 31.4 g. (0.2 mole) of bromobenzene, diluted with 40 ml. of diethyl ether, to 100 ml. of diethyl ether containing 4.86 g. (0.2 mole) of magnesium chips. The addition took one hour and was performed under the usual nitrogen atmosphere. The solution was filtered from the unreacted magnesium in an oxygen free system by passing the Grignard reagent through glass wool into a flask that had been flushed with nitrogen (fig. 4). This supply of Grignard reagent was exhausted in identification of products on the FFAP column by G. C. coinjection. Analysis
FILTRATION APPARATUS

Figure 4

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of the hydrolyzed Grignard reagent found no unreacted bromobenzene. The concentration of phenylmagnesium bromide was 1.64 M.

To decrease the possibility of having unreacted bromobenzene present in the solution, three changes were made in the reaction conditions for the formation of phenylmagnesium bromide. First, the solution was prepared in lower concentration. Second, a 100% excess of magnesium chips was used. Third, longer addition time was employed.

The Grignard reagent was then prepared by slowly adding 47.2 g. (0.3 mole) of bromobenzene, diluted with 500 ml. of diethyl ether, to 500 ml. of diethyl ether containing 14.4 g. (0.6 mole) of magnesium chips. The addition took 2.5 hours and was followed by refluxing the mixture for 5 hours. The Grignard reagent was filtered from the unreacted magnesium and stored under a nitrogen atmosphere. G. C. analysis of the hydrolyzed Grignard reagent indicated that all of the bromobenzene had reacted. The concentration of phenylmagnesium bromide was 0.22 M.

Saturation of Solutions with Ozone

In an attempt to dissolve ozone in solvents that could then be added to the Grignard reagent, 100 ml. of diethyl ether was ozonized at -78°C for different lengths of time at the same \( \text{O}_3, \text{O}_2 \) flow rate. In all the cases, the blue color of the solution disappeared within seconds after the ozone flow was shut off. This indicated that ozone
was reacting with diethyl ether. As indicated by Erickson, Hansen, and Harkins,\textsuperscript{22} this is an expected result since ozone reacts with ethers to form α-hydrotrioxides.

\[
\begin{align*}
R-C-OR + O_3 & \rightarrow R-C-OR_3H \\
\end{align*}
\]

(14)

In an effort to saturate heptane with ozone, ozone was bubbled through heptane for different lengths of time at the same \( O_3, O_2 \) flow rate. Upon reaction of the dissolved ozone with potassium iodide and titration with sodium thiosulfate, no constant concentrations were observed.

By passing ozone through heptane and then titrating an aliquot every 10 minutes over a period of one hour, it was discovered that the concentration remained constant if the solution was kept at \(-78^\circ C\), but was reduced to about 10\% of the original concentration when allowed to warm to room temperature.

It was found that nearly two times as much ozone could be dissolved in pentane as in heptane at \(-78^\circ C\). The concentration of ozone in pentane appeared to be equally stable at this temperature.

**Slow Addition of Ozone to Phenylmagnesium Bromide**

All reactions involving slow addition of ozone to phenylmagnesium bromide were conducted with the apparatus illustrated in figure 2. A
solution containing ozone was added dropwise to the Grignard reagent which had been cooled to \(-78^\circ C\). The reaction products obtained upon hydrolysis were then compared to products of the hydrolyzed Grignard reagent by vapor-phase chromatography employing 1,2,3,4-tetrahydro-naphthalene as an internal standard.

**Ozonation of Concentrated Phenylmagnesium Bromide in Diethyl Ether.** Although a concentrated Grignard reagent is not soluble in heptane, an experiment was conducted in which 5 ml. of the 2.46 M Grignard reagent was "mixed" with heptane at \(-78^\circ C\). The use of a high speed power stirrer was employed to keep the extremely viscous Grignard reagent separated into small particles. Addition of 2.06 mmoles of ozone took 68 minutes with an additional 25 minutes of reaction time allowed before the reaction product was hydrolyzed and acidified to pH 6. The organic layer was then separated from the water layer, dried with magnesium sulfate, and compared with the hydrolyzed Grignard reagent on an SE-30 gas chromatograph column. The internal standard was added before G. C. analysis was conducted.

**Ozonation of Dilute Phenylmagnesium Bromide in Diethyl Ether.** Three reactions of this type were conducted, the first of which involved addition of 2.60 mmoles of ozone to 5 ml. of the 2.5 M Grignard reagent which had been diluted with 50 ml. of diethyl ether. The addition of ozone to the Grignard reagent took 70 minutes. An additional 25 minutes of reaction time was allowed before the reaction
product was hydrolyzed and acidified to pH 6. The organic layer was then separated from the water layer, dried with magnesium sulfate, and compared with the hydrolyzed Grignard reagent on an SE-30 gas chromatograph column. The internal standard was added before G. C. analysis.

The second reaction of this type involved addition of 3.50 mmoles of ozone in pentane to 10 ml. of the 1.64 M Grignard reagent which had been diluted with 50 ml. of diethyl ether. The addition of ozone to the Grignard reagent took 30 minutes after which an additional 20 minutes of reaction time was allowed. The reaction product was hydrolyzed and acidified to pH 6. The internal standard for G. C. analysis was added. The organic layer was then separated from the water layer, dried with magnesium sulfate, and compared with the hydrolyzed Grignard reagent on an FFAP gas chromatograph column.

The third reaction of this type used the Grignard reagent that had been prepared in a 0.22 M concentration. A solution of pentane containing 3.12 mmoles of ozone was added to 25 ml. of the Grignard reagent which had been diluted with 25 ml. of diethyl ether. The addition time was 50 minutes with an additional 20 minutes of reaction time allowed before hydrolysis with a saturated solution of ammonium chloride. The internal standard for G. C. analysis was added, the organic layer was then separated from the water layer, dried with magnesium sulfate, and compared with the hydrolyzed Grignard reagent on the gas chromatograph using an FFAP and an SE-30 column.
Ozonation of Phenylmagnesium Bromide Diluted with Dimethoxy­methane. Phenylmagnesium bromide prepared in diethyl ether in a 2.43 M concentration was used in this reaction. Heptane containing 2.67 mmoles of ozone was added dropwise to 3 ml. of the Grignard reagent which had been diluted with 50 ml. of dimethoxymethane. The addition time was 56 minutes. An additional 30 minutes of reaction time was allowed before hydrolysis. The reaction product was acidified to pH 6. The organic layer was then separated from the water layer, dried with magnesium sulfate, and compared with the hydrolyzed Grignard reagent by vapor-phase chromatography using an SE-30 column. The internal standard was added before G. C. analysis. Attempts to prepare phenylmagnesium bromide in dimethoxymethane resulted in an extremely low yield of Grignard reagent.

Rapid Addition of Ozone to Phenylmagnesium Bromide

The reaction involving rapid addition of ozone to phenylmagnesiu bromide was conducted with the apparatus illustrated in figure 3. Ozone which had been separated from oxygen by selective adsorption on silica gel at -78°C was bubbled through the Grignard reagent at -78°C with a stream of nitrogen. An undetermined amount of ozone was bubbled through 25 ml. of the 0.22 M Grignard reagent which had been diluted with 25 ml. of diethyl ether. Addition of the ozone to the Grignard reagent took 8 minutes after which the reaction
mixture was hydrolyzed with a saturated solution of ammonium chloride. The internal standard for G. C. analysis was added, the organic layer separated from the water layer, dried with magnesium sulfate, and compared with the hydrolyzed Grignard reagent on an SE-30 and an FFAP column on the gas chromatograph.

Rapid Addition of Oxygen to Phenylmagnesium Bromide

For this reaction 310 ± 10 mmols of oxygen was bubbled through 25 ml. of the 0.22 M Grignard reagent which had been diluted with 25 ml. of diethyl ether. Addition of the oxygen to the Grignard reagent which had been cooled to -78°C took 17 minutes. Hydrolysis and G. C. analysis were conducted in the same way as in the above reaction involving rapid addition of ozone.

Quantitative Analysis by Vapor-Phase Chromatography

Since the area of a peak on a gas chromatogram is proportional to the amount of substance injected, the ratio of areas observed for two compounds would be proportional to the ratio of masses of the two compounds. However, since a thermal conductivity detector is used in this work to determine the presence of a compound, this proportionality would be an equality only if the thermal conductivities of all compounds were the same. Generally, a proportionality constant is needed to account for the inequality. If one of these substances was designated as a standard, the mathematical relationship describing the
proportionality would be:

\[
\frac{\text{Area of Compound}}{\text{Area of Standard}} = \frac{\text{Mass of Compound}}{\text{Mass of Standard}} \times \text{constant} \quad (15)
\]

1,2,3,4-Tetrahydronaphthalene was used as an internal standard for G. C. analysis. Using 1,2,3,4-tetrahydronaphthalene as the internal standard, Phillip G. Marsh determined the proportionality constants for benzene, phenol, and biphenyl using the SE-30 column. In all cases the proportionality constant was determined to be close to 1. The yields listed in Chapter III were determined with the use of the above mathematical relationship by assuming that the proportionality constant was equal to 1.00 for all products.

The best separation of components on both the FFAP column and the SE-30 column was accomplished by using a temperature program. The start of the program involved maintaining the temperature at ambient temperature for 1.5 minutes. This was followed by a constant increase of 20°C/min. until 240°C was attained. The 240°C temperature was then held until all components had exited from the column. The flow rate of helium, the carrier gas, was held at 100 cc./min.

The use of the two columns enabled complete separation of all components found in the reaction mixture except two, as mentioned in Chapter III. This separation was possible since the FFAP column had a relatively high affinity for the polar components whereas the SE-30
column allowed the constituents to be separated according to boiling points.

Identification of Products

Two methods were used to identify the reaction products. Both methods involved vapor-phase chromatography.

G. C. Coinjection. Products were identified by comparing chromatograms of the reaction mixture with chromatograms of the reaction mixture to which a small amount of known substance had been added. Positive identification was insured by using both the FFAP and the SE-30 columns for this method.

Spectroscopic Analysis. The reaction mixture was concentrated by removing the solvent with a Rinco rotary evaporator. Products were purified for spectroscopic analysis by separation on the FFAP Prep column and SE-30 Prep column. The best separation of components for collection was accomplished with the same temperature program used for quantitative analysis by vapor-phase chromatography. The flow rate of helium used for separation on the FFAP Prep and SE-30 Prep columns was 200 cc/min.
CHAPTER III

RESULTS

Products of Ozonation of Phenylmagnesium Bromide

The hydrolyzed ozonation products of phenylmagnesium bromide were identified by G. C. coinjection and spectroscopic analysis as previously described (page 23). Other products were not identified but have been assigned theoretical molecular weights on the basis of G. C. retention times for the purpose of quantitative measurement (see figure 5 for representative chromatogram).

Reaction Type I: Diethyl Ether as Solvent. Five ozonation reactions were conducted in which phenylmagnesium bromide was dissolved in diethyl ether (reactions 1, 2, 3, and 5, Table I and one not listed). Use of the FFAP and SE-30 gas chromatographic columns enabled separation of the compounds obtained upon hydrolysis of the product mixture into nine peaks (figure 5). Benzene was identified by G. C. coinjection. Bromobenzene, phenol, and phenylmethyl carbinol were identified by G. C. coinjection and IR spectroscopy. Biphenyl and diphenyl ether were observed to have the same retention time on both the FFAP and SE-30 columns. Consequently, only the combination yield has been reported (see Table I). Four unknown products were observed (unknowns 1, 2, 3, and 4). In only one reaction in which diethyl ether was the
VAPOR-PHASE CHROMATOGRAPHY

10% SE-30
0°-240° @ 20°/Min.
Flow: 100 cc/Min.

[Diagram showing peaks for Phenylmethyl Carbinol, Phenol, Tetralin, Biphenyl, and others.]

10% FFAP
0°-240° @ 20°/Min.
Flow: 100 cc/Min.

[Diagram showing peaks for Phenylmethyl Carbinol, Tetralin, Phenol, Biphenyl, and others.]

Figure 5

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solt solvent (reaction 2, Table I) a product was formed upon allowing the hydrolyzed reaction mixture to sit in a refrigerator overnight (unknown 6). G. C. analysis indicated that the formation of this material accompanied a decrease in the concentration of one of the other components (unknown 1). Yields of all products for reactions 1, 2, 3, and 5 have been reported (Table I). Since too much internal standard was added to the hydrolyzed reaction mixture for the ozonation of concentrated phenylmagnesium bromide (page 18), yields were not recorded for this reaction.

**Reaction Type II: Dimethoxymethane as Solvent.** A reaction involving slow addition of ozone to phenylmagnesium bromide in dimethoxymethane was investigated (reaction 4) in hopes that side reactions involving the solvent would be eliminated or reduced. At least one product (unknown 5) was formed in this reaction that was uncommon to the above reactions. Other products may have been present that were not observed since the use of the FFAP column was not employed. Products identified were benzene, bromobenzene, phenol, phenylmethyl carbinol, and the composite of biphenyl and diphenyl ether. Because the retention time of unknown 5 on the SE-30 column was similar to that of phenylmethyl carbinol, unknown 1 and unknown 2, yields have been reported by grouping the total yields of products in this region (see Table I). Unknown 4 was observed for this reaction. Since full investigation of this reaction would involve preparation of
phenylmagnesium bromide in dimethoxymethane, and because an attempt to
do so as previously mentioned (page 20) resulted in an extremely low
yield of Grignard reagent, the study of this reaction was terminated.
Hence, no effort was made to identify the unknown products.

Products of Oxygenation of Phenylmagnesium Bromide

The products obtained upon rapid addition of oxygen to a solu-
tion of phenylmagnesium bromide in diethyl ether (reaction 6) were
largely the same as those obtained for the ozonation reaction. Three
products were not observed in the oxygen reaction that were found in
the corresponding ozonation reaction (unknowns 1, 2, and 3). Yields
were obtained for the products of this reaction (Table I).

Relation of Addition Rates and Grignard Reagent Concentration to
Reaction Yields

The relationship of the yield of phenol to the concentration of
Grignard reagent and to the rate of addition of ozone has been out-
lined in Table II. The reaction in which ozone was bubbled through
the Grignard reagent (reaction 5) was conducted without flow measure-
ments. Nevertheless, the quantity of Grignard reagent used during this
reaction was about the same as that used for the reaction in which
ozone was added slowly (reaction 3). It could be assumed then that
about the same amount of ozone was used in each reaction. The ozone
addition time in reaction 5 was 8 minutes, whereas in reaction 3 it
was 65 minutes.

The yield of phenol increased with increased concentration of phenylmagnesium bromide and faster ozone addition rate. This study did not determine the optimum conditions for phenol production.

Stoichiometry of Ozone Uptake

Stoichiometric measurements were only possible for the slow addition reactions (reactions 1, 2, 3, and 4, Table II), since the quantity of ozone was measured only for these reactions. Reactions 1, 2, and 4 used about 1 mole of ozone for every 2 moles of phenylmagnesium bromide. In reaction 3 the relationship was about 1 mole of ozone for each mole of phenylmagnesium bromide.
### TABLE I. PRODUCT RATIOS

<table>
<thead>
<tr>
<th>Product</th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5.</th>
<th>6.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bromobenzene</td>
<td>3.6%</td>
<td>19.7%</td>
<td>5.0%</td>
<td>2.6%</td>
<td>5.7%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Phenol</td>
<td>31.4%</td>
<td>43.8%</td>
<td>9.3%</td>
<td>31.4%</td>
<td>66.7%</td>
<td>69.4%</td>
</tr>
<tr>
<td>Phenylmethyl Carbinol</td>
<td></td>
<td></td>
<td>11.2%</td>
<td>21.8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown 1</td>
<td>29.4%</td>
<td>8.9%</td>
<td>4.0%</td>
<td></td>
<td>0.7%</td>
<td></td>
</tr>
<tr>
<td>Unknown 2</td>
<td></td>
<td>Trace</td>
<td>2.6%</td>
<td></td>
<td>Trace</td>
<td></td>
</tr>
<tr>
<td>Unknown 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown 3</td>
<td>1.4%</td>
<td>Unk. b</td>
<td>11.8%</td>
<td></td>
<td>4.7%</td>
<td></td>
</tr>
<tr>
<td>Biphenyl-Diphenyl Ether</td>
<td>10.6%</td>
<td>5.1%</td>
<td>15.0%</td>
<td>35.2%</td>
<td>3.6%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Unknown 4</td>
<td></td>
<td>Unk. b</td>
<td>8.7%</td>
<td>2.0%</td>
<td>1.0%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Benzene c</td>
<td>23.6%</td>
<td>11.2%</td>
<td>21.8%</td>
<td>12.8%</td>
<td>8.8%</td>
<td>10.3%</td>
</tr>
<tr>
<td>Unknown 6</td>
<td></td>
<td>0.1%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Slow Addition of Ozone in Heptane to Phenylmagnesium Bromide in Diethyl Ether (yields calculated by G. C. analysis on a SE-30 column).

2. Slow Addition of Ozone in Pentane to Phenylmagnesium Bromide in Diethyl Ether (yields calculated by G. C. analysis on an FFAP column).


4. Slow Addition of Ozone in Heptane to Phenylmagnesium Bromide in
TABLE I. (Continued)

Dimethoxymethane (yields calculated by G. C. analysis on a SE-30 column).

5. Rapid Addition of Ozone by Bubbling through Phenylmagnesium Bromide in Diethyl Ether (yields calculated by G. C. analysis on SE-30 and FFAP columns).


* 

a. Product ratios were calculated as percent of total products observed. Yields were not determined on the basis of Grignard reagent used since the method employed did not distinguish between benzene formed upon hydrolysis of the unreacted phenylmagnesium bromide and the benzene produced by side reactions that occurred during the ozonation and oxygenation reactions.

b. Unknowns 3 and 4 were not measured because not enough time was given for them to exit from the FFAP column.

c. Yields of benzene were not directly measured. Since the precursor of phenylmethyl carbinol may be the same as the precursor of benzene (see page 4) the assumption was made that benzene was produced in the same yield as phenylmethyl carbinol for reactions in which this value was determined, and 80% of total combined yields of phenylmethyl carbinol, unknown 1, unknown 2, and unknown 5 for reactions 1 and 4.
TABLE II. COMPARATIVE YIELDS OF PHENOL

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Concentration of Grignard reagent (mole/1)</th>
<th>Rate of Addition of ozone (mmole/min.)</th>
<th>Yield$^2$ of phenol</th>
<th>Percent$^b$ of starting material accounted for</th>
<th>Moles of MgBr$^-$ moles of O$_3^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>0.224</td>
<td>0.372</td>
<td>31.4%</td>
<td>95.5%</td>
<td>2.02</td>
</tr>
<tr>
<td>2.</td>
<td>0.274</td>
<td>1.17</td>
<td>43.8%</td>
<td>23.2%</td>
<td>1.72</td>
</tr>
<tr>
<td>3.</td>
<td>0.110</td>
<td>0.48</td>
<td>9.3%</td>
<td>116.0%</td>
<td>0.86</td>
</tr>
<tr>
<td>4.</td>
<td>0.138</td>
<td>0.460</td>
<td>31.4%</td>
<td>48.0%</td>
<td>1.65</td>
</tr>
<tr>
<td>5.</td>
<td>0.110</td>
<td>3.0</td>
<td>66.7%</td>
<td>117.0%</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>0.110</td>
<td>18.2</td>
<td>69.4%</td>
<td>121.0%</td>
<td></td>
</tr>
</tbody>
</table>

1. Slow Addition of Ozone in Heptane to Phenylmagnesium Bromide in Diethyl Ether.
2. Slow Addition of Ozone in Pentane to Phenylmagnesium Bromide in Diethyl Ether.
4. Slow Addition of Ozone in Heptane to Phenylmagnesium Bromide in Dimethoxymethane.
5. Rapid Addition of Ozone by Bubbling through Phenylmagnesium Bromide in Diethyl Ether.
6. Rapid Addition of Oxygen by Bubbling through Phenylmagnesium Bromide in Diethyl Ether.

*: Values are taken from Table I (see footnote a, Table I).

b. With the use of G. C. analysis, the moles of Grignard reagent used in the reactions and the total moles of products were measured. The percent of starting material accounted for was determined by...
TABLE II. (Continued)

relating these two values. A possible source of error in these calculations might be the fact that the proportionality constant was assumed to be 1.00 for all products (see page 22).
The Ozonation and Oxygenation Products of Phenylmagnesium Bromide

Three products were found in the reactions of ozone with phenylmagnesium bromide in diethyl ether (reactions 1, 2, 3, and 5) that were not common to the oxygenation reaction. These products have been indicated in Table I as unknowns 1, 2, and 3. Although identification has not been made for these products, polarities of two of these products (unknowns 1 and 2) appear to be similar to that of phenylmethyl carbinol (see figure 5).

Although biphenyl was not distinguishable from diphenyl ether as previously mentioned (page 24), it was assumed that only a small amount of the diphenyl ether was formed since no quinone was observed. As previously mentioned (page 3), Porter and Steel indicated that quinone is formed by the reaction of atomic oxygen with diphenyl peroxide. The production of atomic oxygen is accompanied by the formation of diphenyl ether. 23

The formation of bromobenzene in the ozonation and oxygenation of phenylmagnesium bromide may be explained by the production of bromine in the reaction which can then react with phenylmagnesium bromide according to the reaction previously mentioned (reaction 10).
Meisenheimer and Schlichenmaier suggested that iodine was produced during the oxygenation of phenylmagnesium iodide. A 19.5% yield of iodobenzene was observed in this reaction.\(^{24}\)

**Effects of Addition Rates and Grignard Reagent Concentration**

From the experiments which were run, a relationship can be proposed concerning the effect of rate of addition of ozone to phenylmagnesium bromide. For dilute solutions of phenylmagnesium bromide in ether rapid addition of ozone produced a higher yield of phenol than did slow addition, as illustrated in Table II by the comparison of reactions 1, 2, 4, and 5. Results of reaction 3 appear to disagree with this conclusion, but closer investigation reveals that the concentration of the Grignard reagent was lower than for reactions of comparable rates of addition (reactions 1 and 4).

The effect of concentration of Grignard reagents may then be studied. Observations support the idea that for the same rate of addition of ozone the more concentrated Grignard reagent would yield more phenol, as illustrated by the comparison of reactions of similar rates of addition of ozone (reactions 1, 3, and 4, Table II). This has been shown in part by the literature previously mentioned (page 3) for the oxygenation reaction. Low yields were obtained except in the inverse reaction in which the yield of phenol was as much as 46%.\(^{25}\)

It has been shown that rapid addition of oxygen to phenylmagnesium
bromide produced phenol in a 66% yield (see Table I). Since the method of quantitative measurement by vapor-phase chromatography was superior to the "wet laboratory" method for product determination, these results appear somewhat compatible.

During the ozonation of phenylmagnesium bromide in diethyl ether, the ozone that is present is being used up by two competing reactions (see pages 37 and 17).

\[ \text{Rate constant} = k_1 \]

\[ \text{Rate constant} = k_2 \]

If it is assumed that \( k_1 \) and \( k_2 \) are not greatly different, then the change in the concentration of ozone would most greatly affect equation 16 since the concentration of diethyl ether is greater than the concentration of phenylmagnesium bromide in even the most concentrated Grignard reagent. This observation supports the conclusion that an increase in the rate of ozone addition increases the yield of phenol since phenol is a direct product of phenyltrioxymagnesium bromide.

The net reactions for the decomposition of phenyltrioxymagnesium bromide may be illustrated by the equations below (see page 38).
Equation 19 supports the observation that the production of phenoxy-magnesium bromide is directly related to the concentration of Grignard reagent. If equation 18 describes the logical decomposition of phenyltrioxymagnesium bromide, the quantity of phenoxy-magnesium bromide produced is solely dependent upon the rate of the reaction described by equation 16. The importance of the concentration of Grignard reagent would be enhanced if equation 19 has a significant contribution.

In addition to the reaction of ozone with phenylmagnesium bromide and the disproportionation reaction (equation 19), another reaction exists which involves the Grignard reagent.

\[
\text{CH}_3\text{CH}_2\text{O}-\text{CHCH}_3 + \text{O}_3\text{H} \rightarrow \text{CH}_3\text{O}-\text{MgBr} \rightarrow \text{CH}_3\text{O}-\text{MgBr} + \text{CH}_3\text{CH}_2\text{OH} + \text{O}_2
\]  

(Rate constant = \(k_5\))

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The observation that increasing the concentration of phenylmagnesium bromide enhances the production of phenol indicates that \( k_4 \gg k_5 \), since phenol is produced upon hydrolysis of phenoxy magnesium bromide.

**Mechanism of Ozonation of Phenylmagnesium Bromide**

Additional investigation is necessary to fully clarify the mechanism for the ozonation of phenylmagnesium bromide. Nevertheless, because of the electrophilicity of ozone as indicated by Belew and Augustine \(^{26}\) and because of the electron-dense carbon of the carbon-magnesium bond, it was assumed that the ozonolysis of phenylmagnesium bromide was an electrophilic substitution reaction. The most probable mechanism would involve a \( \sigma \)-complex as seen below.

\[
\begin{align*}
\sigma^+ & \text{MgBr} \\
\end{align*}
\]

It is reported \(^{27}\) that the large majority of electrophilic substitution reactions with an aromatic compound involve the \( \sigma \)-complex mechanism. An example of electrophilic substitution involving this mechanism is the hydrolysis of phenyl magnesium bromide. \(^{28}\)

The \( \sigma \)-complex produced upon ozonation could then lead to the intermediate phenyltrioxymagnesium bromide.

\[
\begin{align*}
\text{O-O-O-MgBr} \\
\end{align*}
\]
This intermediate could break down by a homolytic pathway according to one or more of the equations below.

\[
\text{OP: } \quad \text{O}^\cdot \text{O}^- \text{MgBr} \rightarrow \text{O}^\cdot + \text{O}_2 + \cdot \text{MgBr} \tag{23}
\]

\[
\text{MgBr} \quad \rightarrow \quad \text{O}^\cdot + \cdot \text{OMgBr} \tag{24}
\]

\[
\text{MgBr} \quad \rightarrow \quad 2 \text{O}^\cdot + \cdot \text{OMgBr} \tag{25}
\]

Alternatively, the intermediate could break in a heterolytic manner.

\[
\text{OP: } \quad \text{O}^- \text{O}^- \text{MgBr} \rightarrow \text{O}^- \text{O}^- + \cdot \text{O}_2 \tag{26}
\]

A possible mechanism by which phenoxy magnesium bromide is produced from the phenyltrioxymagnesium bromide intermediate without the accompanying formation of molecular oxygen would involve intermolecular disproportionation.

\[
\text{O}^- \text{O}^- \text{MgBr} + \text{O}^- \text{O}^- \text{MgBr} \rightarrow \text{O}^- \text{O}^- \text{MgBr} + 2 \text{O}^- \text{O}^- \text{MgBr} \tag{27}
\]

\[
\text{O}^- \text{O}^- \text{MgBr} + \text{O}^- \text{O}^- \text{MgBr} \rightarrow 2 \text{O}^- \text{O}^- \text{MgBr} \tag{28}
\]
Synthetic Utility

The ozonation and oxygenation reactions proved to have potential synthetic utility in the formation of phenols from aromatic Grignard reagents, although the superiority of one over the other cannot be determined without additional studies.

Synthesizing phenol in good yield by this procedure would involve rapid addition of ozone or oxygen to Grignard reagents which are in high concentration. It has been indicated by this study that the preparation of phenylmagnesium bromide in concentrated form may result in a low yield of Grignard reagent accompanied by an abundance of unreacted bromobenzene. This complication may be overcome if dilute Grignard reagent is prepared after which it may be concentrated by evaporation of solvent.
CHAPTER V

SUMMARY

The reaction of ozone with phenylmagnesium bromide at \(-78^\circ\text{C}\) was investigated. The effect of different rates and methods of addition of the reagents as well as different ether solvents was studied. Products formed from these reactions were compared to the oxygenation products.

Quantitative measurements and identification of products were made by vapor-phase chromatography. Three products were formed in low yield during the analogous oxygenation reaction. These products were not identified.

The use of dimethoxymethane as a solvent for the ozonation reaction proved to be of no advantage in the production of phenol. Since the yield of Grignard reagent prepared in dimethoxymethane was very low, the study of this reaction was not completed.

The reaction of aromatic Grignard reagents with either ozone or oxygen may be synthetically useful for the production of phenols. As indicated, the yield of phenol may be increased by an increase of ozone addition rate and with an increase in the concentration of the Grignard reagent.
REFERENCES

5. Ibid., p. 6035.
8. Ibid., p. 808.
12. Ibid.
17. Ibid., p. 35.

20. Ibid., p. 231.

21. Ibid., p. 177.


28. Ibid., p. 440.