

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF IOWA STATE COLLEGE]

## THE OXIDATION OF ARYLMAGNESIUM HALIDES

BY HENRY GILMAN AND AGNES WOOD<sup>1</sup>

RECEIVED DECEMBER 21, 1925

PUBLISHED MARCH 5, 1926

In connection with studies involving some relationships between anti-septic action and chemical constitution, it was necessary to prepare a number of new phenols. The oxidation of arylmagnesium halides was tried as one of several possible methods.

It has long been known that the following general reaction occurs when Grignard reagents are treated with air or oxygen:  $\text{RMgX} + (\text{O}) \longrightarrow \text{ROMgX}$ . On hydrolysis, the  $\text{ROMgX}$  compound gives the corresponding hydroxyl compound. The reaction is capable of wide application. In particular, excellent yields of alcohols are obtainable by the oxidation of alkylmagnesium halides.<sup>2</sup> Equally good yields of the analogous compounds are obtained when both alkyl- and arylmagnesium halides are treated with sulfur, selenium and tellurium.<sup>3</sup>

However, Bodroux<sup>4</sup> got very low yields of phenols when he oxidized arylmagnesium halides. Even after trying a variety of conditions he could not get the yield of phenol<sup>5</sup> to exceed 18%. Eight arylmagnesium halides were oxidized and the highest yield of phenolic compound, 22%, was obtained from the monomagnesium derivative of 1,4-dibromonaphthalene. Wuyts,<sup>6</sup> in a careful study, showed that peroxides were very probably formed as intermediate compounds. In addition to phenol, from the oxidation of phenylmagnesium bromide, he obtained benzene, diphenyl, *p*-diphenylbenzene, phenols other than  $\text{C}_6\text{H}_5\text{OH}$ , phenylmethyl carbinol and ethyl alcohol. Porter and Steele,<sup>7</sup> in a study of the mechanism of the reaction, determined the influence of temperature upon the yield of phenol and chief by-products.

Inasmuch as there is no present explanation for the unusually wide differences in yields in the oxidation of alkylmagnesium halides as contrasted

<sup>1</sup> This paper is an abstract of a part of a thesis presented by Agnes Wood in partial fulfilment of the requirements for the degree of Master of Science in Chemistry at Iowa State College.

<sup>2</sup> Bouveault, *Bull. soc. chim.*, **29**, 1051 (1903). Grignard, *Compt. rend.*, **138**, 1048 (1904). Barbier and Grignard, *Bull. soc. chim.*, **31**, 840 (1904). Hesse, *Ber.*, **39**, 1126 (1906). Houben, *Ber.*, **39**, 1700 (1906).

<sup>3</sup> Giua and Cherchi, *Gazz. chim. ital.*, **50**, I, 362 (1920); *C. A.*, **15**, 521 (1921). Taboury, *Bull. soc. chim.*, **29**, 761 (1903). Wuyts and Cosyns, *ibid.*, [3] **29**, 89 (1903). Wuyts, *ibid.*, [4] **5**, 405 (1909). Gilman and King, *THIS JOURNAL*, **47**, 1136 (1925), give other references.

<sup>4</sup> Bodroux, *Compt. rend.*, **136**, 158 (1903).

<sup>5</sup> Bodroux, *Bull. soc. chim.*, **31**, 33 (1904).

<sup>6</sup> Wuyts, *Compt. rend.*, **148**, 930 (1909).

<sup>7</sup> Porter and Steele, *THIS JOURNAL*, **42**, 2650 (1920).

with arylmagnesium halides, a quantitative study has been made of the yield of phenol obtained under various conditions. It was found possible to improve the yield over that obtained by Porter and Steele.<sup>7</sup> However, the yield was still quite unsatisfactory, even though it was shown by the color test described by Gilman and Schulze<sup>8</sup> that all of the phenylmagnesium bromide was used up. This prompted a re-investigation of the by-products, particularly because the color changes noted by others<sup>5,7</sup> during the oxidation of phenylmagnesium bromide were not observed in our work.

The explanation of the low yield is associated almost entirely with the formation of large quantities of phenylmethyl carbinol ( $C_6H_5CHOHCH_3$ ).<sup>6</sup> This by-product was not described by Porter and Steele.<sup>7</sup> It owes its formation unquestionably to the preliminary oxidation of the ether used as a medium. Clover<sup>9</sup> has shown that the auto-oxidation of ethyl ether gives  $\alpha$ -ethoxyethyl hydrogen peroxide ( $C_2H_5OC(H)(CH_3)OOH$ ). This ether peroxide, which is not to be confused with diethyl peroxide,<sup>10</sup> can give by various decompositions acetaldehyde, its mono-ethyl acetal, acetic acid, ethyl alcohol and carbon dioxide. Acetaldehyde and its acetal should react with phenylmagnesium bromide, according to well-known reactions, to give the phenylmethyl carbinol. Undoubtedly any undecomposed ether peroxide would give the same secondary alcohol. This, however, accounts for only a part of the  $RMgX$  compound. The large amounts of benzene obtained can be most satisfactorily explained on the basis of an active hydrogen that would decompose phenylmagnesium bromide in the customary manner into benzene and basic magnesium halide. Such hydrogen is present in the ether peroxide, the mono-acetal, ethyl alcohol and acetic acid. It could not have come from the very carefully dried oxygen that was used.

Added confirmation for this explanation is found in a large run oxidation of *p*-tolylmagnesium bromide. In addition to the expected *p*-cresol, there was obtained a large quantity of *p*-tolylmethyl carbinol and an approximately corresponding amount of toluene.

The small amount of peroxide obtained by Clover in the auto-oxidation of ether makes it difficult to account for the large quantities of secondary alcohols obtained from the oxidation of the Grignard reagent. However, he found that the formation of the peroxide from ethyl ether was very favorably affected by the presence of acetaldehyde, a compound that is quite susceptible to auto-oxidation. It is probable that the arylmagnesium halides which are readily oxidized or peroxidized<sup>6,7</sup> accelerate in like manner the peroxidation of ethyl ether.

<sup>8</sup> Gilman and Schulze, *THIS JOURNAL*, **47**, 2002 (1925).

<sup>9</sup> Clover, *ibid.*, (a) **44**, 1107 (1922); (b) **46**, 419 (1924). Also (c) Poleck and Thümmel, *Ber.*, **22**, 2863 (1889).

<sup>10</sup> Gilman and Adams, *THIS JOURNAL*, **47**, 2816 (1925).

It is apparent that there is a fixed upper limit to the yield of phenols obtainable by the oxidation of arylmagnesium halides when these reagents are prepared in ether. Even when the quantity of ether used is not larger than one mole per mole of bromobenzene, the yield of phenol is no higher than that obtained when a large excess of ether is used. Obviously, a most promising way of improving the yield of phenols is to dispense with the use of ether. There appears to be a limited advantage in the use of other aliphatic ethers, because Clover<sup>9</sup> has shown that the rapidity of peroxide formation appears to increase with increasing size of the ether molecule.<sup>11</sup> Unfortunately, it is almost impossible to prepare the so-called individual RMgX compounds in good yields in solvents such as benzene or dimethylaniline.<sup>12</sup> It is highly significant that a good yield of phenol is obtainable by the oxidation of phenylmagnesium bromide prepared in phenetole,<sup>11</sup> because Clover<sup>9b</sup> proved that anisole and phenetole show no evidence of auto-oxidation.

### Experimental Part

**Procedure.**—Practically all of the experiments were made with 0.1 molecular equivalent of bromobenzene and magnesium. The bromobenzene in 50 cc. of ether was added to the magnesium covered with an equal volume of ether and contained in a 3-necked flask provided with a stirrer, condenser and separatory funnel that was later replaced by an entry tube for the oxygen. It is probable that an optimum yield of phenylmagnesium bromide was obtained in each run.<sup>13</sup> The oxygen was passed through a train consisting of concd. sulfuric acid, sodium hydroxide and phosphorus pentoxide and was admitted just over the surface of the ether.<sup>14</sup>

**Analysis.**—Phenol was estimated by the standard method used by Porter and Steele<sup>7</sup> in their work. This method of titration with potassium bromate and bromide may give results that are somewhat high because of the presence of phenolic compounds other than phenol.<sup>8</sup> Indications of this error were found in some of the large runs where the phenol was extracted, distilled and weighed. The yields thus obtained were lower than those of the smaller runs made under corresponding conditions. Mechanical losses may account for much of the difference. However, the error is not serious because of the essentially comparative nature of the results.

### Discussion and Conclusions

**Temperature.**—Porter and Steele<sup>7</sup> found that the optimum temperature was 0° and the average yield of phenol at this temperature was 22.9%. The average yield in our work was 26% at 0° and it increased to 29% at -5°. Cooling to about -60° with carbon dioxide snow actually caused

<sup>11</sup> The yield of phenol from phenylmagnesium bromide prepared in phenetole was 45%. This work was done by F. Schulze and the quantity of phenylmagnesium bromide was determined by the method of Gilman, Wilkinson, Fishel and Meyers [THIS JOURNAL, 45, 150 (1923)].

<sup>12</sup> Studies are now in progress on the activation of magnesium in order to prepare RMgX compounds in good yields in the absence of ether.

<sup>13</sup> Gilman and Meyers, THIS JOURNAL, 45, 159 (1923). Also, Gilman and McCracken, *ibid.*, 45, 2462 (1923).

<sup>14</sup> Gilman and Parker, *ibid.*, 46, 2816 (1924).

a drop in yield to about 21.2%. Here, however, the time of addition of oxygen was one hour and not the three-hour periods used in the 0° and -5° experiments. From these results it is apparent that little is gained in cooling below 0°.

In several runs no oxygen was passed through and the phenylmagnesium bromide solution was protected from the air by an ordinary calcium-chloride-soda-lime drying tube. The effect of diffused air is quite significant because after refluxing the mixture in ether for eight hours the average yield of phenol was 6.8%. Under like conditions when most of the ether was replaced by benzene and the solution refluxed for eight hours at 78° the yield of phenol was 16.1%. The yield increased to 21.9% when refluxing was carried out in toluene at 108° for six hours. These experiments emphasize the great danger in protracted refluxing of RMgX compounds<sup>15</sup> unless more than ordinary precautions are taken to exclude air. Not only is the RMgX compound used up in significant quantities by such air oxidation, but numerous by-products are introduced.<sup>6</sup>

**Time.**—When the phenylmagnesium bromide was hydrolyzed immediately after its preparation and without passing in oxygen, the yield of phenol was 2.9%. Porter and Steele,<sup>7</sup> under like conditions, obtained 2.8% of phenol. In this connection, an experiment was carried out with ether that was treated with dry oxygen at 0° for seven hours; 200 cc. of this ether was added to 0.1 mole of phenylmagnesium bromide and the amount of phenol obtained after immediate hydrolysis was 6.9%.

In another experiment the oxygen was passed in during the formation of the phenylmagnesium bromide and the yield of phenol was 16.4%. The external temperature in this run was 0°.

The rate of addition of oxygen to prepared Grignard reagent appears to have little effect on the yield of phenol. Under corresponding conditions the yield after a 25-minute period was equal to that after a three-hour period, namely, 26.2%. However, even though the RMgX compound was shown to be used up<sup>8</sup> at the end of 25 minutes, using 0.1 molecular quantity, a slight improvement was noted after oxygen was passed in for eight hours. In this connection, it is worthy of note that the end of reaction is reasonably definitely marked by a clearing up of the white turbidity and a sharp drop in temperature when an ice or ice-salt bath is used for cooling.<sup>16</sup>

**Quantity of Ether.**—Earlier studies<sup>17</sup> showed that it is possible to prepare phenylmagnesium bromide in about 50% yields when only *one* molecular equivalent of ether is used, and in 92% yield when 4 equivalents of ether are used. With both of these solutions, the yield of phenol, based

<sup>15</sup> Gilman, Beaber and Meyers, *THIS JOURNAL*, **47**, 2047 (1925).

<sup>16</sup> The same kind of an end-point has been noted in the preparation of acids from alkylmagnesium halides and carbon dioxide. "Organic Syntheses," John Wiley and Sons, vol. 5, 1925, p. 75.

<sup>17</sup> Work of Roy McCracken.

on the quantity of phenylmagnesium bromide present, was approximately equal to that obtained when a liberal excess of ether was used under corresponding conditions. These experiments emphasize the drawbacks to the use of ether even in minimal quantities.

**By-Products.**—From the oxidation of one mole of phenylmagnesium bromide, 3% of diphenyl and 18% of phenylmethyl carbinol were obtained. The carbinol was characterized by the urethan prepared with phenylisocyanate. Under corresponding conditions, one molecular equivalent of *p*-tolylmagnesium bromide gave 15.3% of *p*-cresol, 16% of *p*-ditolyl, 11% of toluene and 11% of *p*-tolylmethyl carbinol. No study was made of other by-products.

**Phenylmagnesium Bromide and Metallic Oxides.**—Yellow mercuric oxide was refluxed with an ether-toluene solution of phenylmagnesium bromide at 108° for 19 hours; the yield of phenol was 15.1%. Silver oxide refluxed with an ether solution for ten hours gave 18% phenol, and sodium peroxide refluxed with an ether solution for five hours gave 14.5% of phenol. The extent of oxidation due directly to these metallic oxides is probably less than the percentages of phenol indicate, because other experiments (see above under **Time**) show that some phenol is formed by merely protracted digestion when air is not excluded.

### Summary

In a study of the optimal conditions for the preparation of phenols by the oxidation of arylmagnesium halides it is shown that the yields are strictly limited by the oxidation of ethyl ether. The ether peroxide so formed reacts with unaltered RMgX compound to give a secondary alcohol.

AMES, IOWA

---

[CONTRIBUTION FROM THE DRUG CONTROL LABORATORY IN COÖPERATION WITH THE COLOR LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE]

## IDENTIFICATION OF PHENOLS BY MEANS OF THE SPECTROSCOPE. II

BY H. WALES AND S. PALKIN

RECEIVED DECEMBER 22, 1925

PUBLISHED MARCH 5, 1926

In a previous paper<sup>1</sup> absorption-spectra data were given for the azo dye derivatives of a number of simple phenols. A method was there outlined for the identification of those phenols based on coupling them with *p*-nitrobenzene diazonium chloride, extracting the dye acid with a suitable solvent and measuring the absorption spectra of the potassium salts in three different solvents. In another publication<sup>2</sup> a further applica-

<sup>1</sup> THIS JOURNAL, 46, 1488 (1924).

<sup>2</sup> *Ibid.*, 47, 2005 (1925).