copper were found to be ineffective as catalysts in the synthesis of hexestrol dimethyl ether from anethole hydrobromide and Grignard reagents.

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Factors Determining the Course and Mechanism of Grignard Reactions. VII. Analysis of Gases Formed During the Reaction of Phenylmagnesium Bromide with Organic Halides in the Presence of Cobaltous Halides

BY M. S. KHARASCH, DANIEL W. LEWIS AND W. B. REYNOLDS

The catalytic effect of small quantities of certain metallic halides upon the reaction of Grignard reagents with organic halides has been previously reported from this Laboratory.[1] In most cases, the normal coupling is not increased; instead, there is initiated a chain reaction, at one stage of which the metal in the catalyst appears in an active sub-valence state. This active "subhalide" is then reoxidized by the organic halide; an organic free radical is thus produced. The series of reactions involved is illustrated below for the cobaltous chloride catalyzed reaction of phenylmagnesium bromide with ethyl bromide.

$$\text{(A)}\quad C_6H_5MgBr + CoCl_2 \longrightarrow C_6H_5CoCl + MgClBr$$
$$\text{(B)}\quad 2C_6H_5CoCl \longrightarrow C_6H_5\text{–}C_6H_5 + 2CoCl\cdot$$
$$\text{(C)}\quad CoCl\cdot + C_2H_5Br \longrightarrow CoClBr + C_2H_5\cdot$$

Since the gases evolved in this and similar reactions have not yet been quantitatively examined, it seemed desirable to undertake such a study in order further to elucidate the mechanism of these reactions. Accordingly, the reactions of phenylmagnesium bromide with methyl bromide, ethyl bromide, propyl bromide, *n*-butyl bromide and tertiary butyl chloride in the presence and absence of cobaltous chloride were studied.

Analyses of Gases Formed.—The reactions were carried out in a 500-ml. three-neck flask equipped with ground-glass joints. The center joint was fitted with a mercury-seal stirrer; one of the side joints carried an efficient Friedrichs condenser; the other side joint carried a wide, straight, adapter-shaped dropping funnel fitted with an auxiliary nitrogen inlet tube extending slightly into the flask. After the set-up had been thoroughly dried, it was filled with dry nitrogen (oxygen-free), and the Grignard reagent was introduced. The flask was cooled by surrounding it with an ice-pack. Anhydrous cobaltous chloride (5 mole per cent.) was next added. Nitrogen gas was then passed into the flask for three to five minutes; then the nitrogen inlet tube was closed. The alkyl halide was next added slowly through the dropping funnel. From the condenser outlet, the evolved gases passed through a short calcium chloride tube and a trap surrounded by ice (except in the butyl chloride experiments where the trap was maintained at 10°). The gases were finally collected over water from which air had been removed by boiling. Usually the first 500 ml. of gas (which was mostly nitrogen) was discarded. The gases were all hydrocarbons and could be completely analyzed by determination of molecular weight and percentage unsaturation. These determinations were made in the vacuum-line apparatus of Fig. 1.

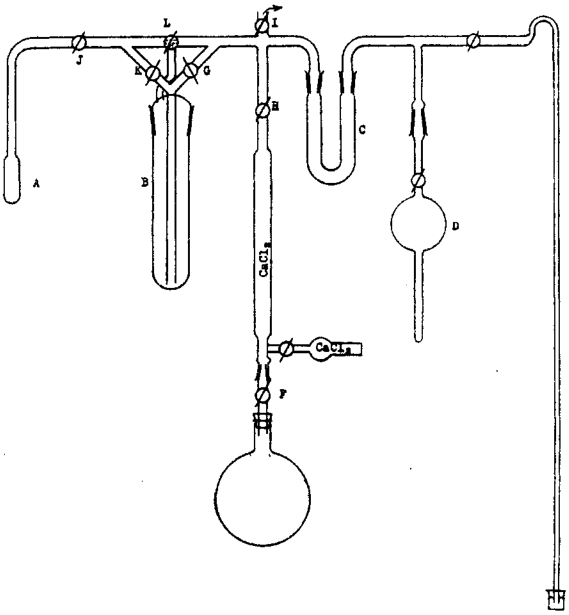

Fig. 1.—Vacuum line gas analysis apparatus.

Molecular weights were determined by the Dumas method in bulb (D). This bulb was first evacuated to 10^{-6} mm. and accurately weighed. After it had been replaced on the line, the entire system was evacuated down to stopcock (F). After stopcocks (G) and (K) had been closed and (L) adjusted so that tube (A) was connected to the system but trap (B) eliminated, stopcock (I) was closed, and the gas sample was slowly admitted to the system through (F). Stopcock (H) was then closed, and a liquid nitrogen trap was placed at (A). The gas sample condensed and solidified in (A) while the manometer rose rapidly to within a millimeter of its high-vacuum reading.

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[1] For previous references see Kharasch and Fields, THIS JOURNAL, 63, 2316 (1941).

Table I

Summary of Data from Reactions of Phenylmagnesium Bromide with Alkyl Halides in Ether Solution

Halide	$CoCl_2$	Extent of reaction, %	Yield of gas,[a] %	Mol. wt. orig. gas	% Unsat.	Mol. wt. unsat. removed	Compn. of sample, %	Biphenyl, g.	Poly-phenyl, g.	RC_6H_5, g.
CH_3Br	+	90	67	21.0	20	18.5	CH_4, 62 C_2H_6, 18 C_2H_4, 20	14.5	2.5	...
	−	<10	None	..	..	..		...	...	Trace
C_2H_5Br	+	45	80	31.0	60	32.0	C_2H_6, 40 C_2H_4, 60	5.1	3.0	2.0
	−	5	..	..	..	..		...	...	Trace
n-C_3H_7Br	+	62	66	43.8	46	44.9	C_3H_8, 54 C_3H_6, 46	6.8	2.9	2.8
	−	5	..	..	..	..		...	...	Trace
n-C_4H_9Br	+	83	73	58.5	46	59.0	C_4H_{10}, 54 C_4H_8, 46	10.5	2.0	3.6
	−	14	..	..	..	..		1.0	0.4	2.5
t-C_4H_9Cl	+	?	75	58.7	20	63.5	i-C_5H_{12}, 80 i-C_5H_{10}, 20	13.5	4.0	None
	−	?					i-C_5H_{10}	Trace	Trace	4.0

[a] The yield is based upon the amount of reacted alkyl halide; this amount was determined by halogen titration (Volhard). Tertiary butyl chloride could not be thus estimated because this halide hydrolyzes too readily.

If the manometer reading at this stage was more than one or two millimeters, the presence of nitrogen in the gas sample was indicated, and this impurity was pumped off through (I). After (I) was closed, the liquid nitrogen trap was removed from (A) and the system was allowed to come to equilibrium at room temperature. Bulb (D) was then closed off, and the gas remaining in the system was condensed in (A) for storage. (J) was then closed; air was admitted to the line, and bulb (D) was removed and weighed. From the known volume, temperature, and gas weight the molecular weight was calculated. (D) was then replaced on the line, and the line was evacuated and closed off at (I). With the liquid nitrogen trap still at (A), stopcocks (D) and (J) were opened and the sample was entirely condensed in (A). Stopcocks (G) and (K) were then opened, and stopcock (L) was set so that it was open across the line and also into the trap. The manometer at this point indicated less than a millimeter pressure. The liquid nitrogen trap was then removed from (A), and the system was allowed to reach equilibrium; at this point the manometer reading was noted. With (G) open, (K) closed, and (L) set so that the upper trap was connected with (A) but not with the rest of the line, the liquid nitrogen trap was placed at (A). The gas was thereby bubbled through the trap and condensed in (A). (K) was then opened, (G) closed, and (L) set to open from the trap toward (D). The liquid nitrogen trap was then placed at (D) and the gas from (A) was bubbled through the trap and condensed in (D). The bubbling of the gas back and forth through the trap was continued until all unsaturates were removed. The end of the absorption was indicated by constancy in the manometer readings at equilibrium, with all stopcocks except (H) and (I) open. Usually two or three round-trip passes were sufficient. The apparatus was tested with pure methane, butane, butylene, and ethylene. In all of these test runs, the molecular weights were checked to within 3% and the unsaturation to within 5%. The absorbent solution in (B) consisted of concentrated sulfuric acid containing silver sulfate and nickel sulfate as recommended by Tropsche and Dittrich.[2] This mixture removed even ethylene rapidly and quantitatively. The U-shaped trap (C) contained "Drierite." In order to facilitate recharging, this tube was connected to the line by ground glass joints.

Table I summarizes the results of these experiments.

Discussion

In the absence of cobaltous chloride, the reaction of phenylmagnesium bromide with alkyl halides is very slow at room temperature. Within twenty hours, it reacts with methyl, ethyl and butyl bromides only to the extent of 5 to 10%. No gases are evolved, no biphenyl is formed (except what is already present in the Grignard reagent), and only the coupling compounds (the alkylbenzenes) can be isolated. On the other hand, in the presence of 3–5 mole per cent. of cobaltous chloride, the reaction of the phenylmagnesium bromide is so vigorous that the alkyl halide must be added to the phenylmagnesium bromide–cobaltous chloride mixture in small portions. Here (see Table I), methyl, ethyl, propyl and n-butyl bromides react to the extent of 90, 46, 62, and 83%, respectively. (If an excess of Grignard reagent is used, the alkyl halide reacts completely.) Only small amounts of the normal coupling products are obtained; on the other hand, biphenyl and gases are formed in quantities sufficiently close to equivalent proportions to suggest their common origin.

The gases formed in these reactions are of

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[2] Tropsche and Dittrich, *Brennstoff-Chemie*, **6**, 169–177 (1925); *J. Soc. Chem. Ind.*, **44B**, 793 (1925).

considerable interest because of their bearing on the hypothesis which assigns to cobaltous subhalide the function of a chain carrier. If the function of the alkyl halide is to regenerate the cobaltous halide, then it must at the same time form a free alkyl radical. The behavior of these free alkyl radicals is of general interest because of the light it throws on reactions involving free radicals in solution. Our experiments with the ethyl, propyl and *n*-butyl halides indicate that the corresponding radicals do not dimerize to any appreciable extent (if at all), but disproportionate to the alkanes and alkenes. The slight deviations from the one to one ratio of these substances are probably due to the experimental error (±5%) inherent in our analytical method. The *t*-butyl free radical probably decomposes similarly to alkane and alkene, but the isobutylene, thus formed, probably polymerizes considerably. The composition of the collected gas (80% isobutane and 20% isobutylene) is thus explained. That isobutylene polymerizes more readily than the straight chain alkenes has been well established.

The composition of the gas formed in the reactions involving the methyl radical (60% methane, 20% ethane, 20% ethylene) is best explained by assuming two distinct reactions. The faster one is the capture by the methyl radical of a hydrogen atom from the solvent. Methane is thus formed. The slower one is the attack of the methyl radical on the oxygen atom of the ether molecule. This reaction leads to the formation of methyl ethyl ether and ethyl radicals; the latter disproportionate to ethylene and ethane. The formation of equal quantities of these two gases supports the assumption of their common origin.

Experimental Part

In all experiments here recorded, 0.3 mole of the organic halide dissolved in anhydrous ether solution was added during ten minutes to 0.3 mole of phenylmagnesium bromide (kept at 0°). In the cobaltous chloride catalyzed experiments, 0.015 mole of this halide was added to the Grignard reagent (kept at 0°) before the addition of the organic halide. The evolved gases were collected and analyzed. The reaction mixtures were allowed to come to room temperature after one hour, and were decomposed with water and acetic acid at the end of twenty hours. Ethylene was determined as ethylene dibromide (b. p. 131°, n^{20}_D 1.538); propylene, as 1,2-dibromopropane (b. p. 140°, n^{20}_D 1.520); butene-1, as *s*-butyl bromide (b. p. 91°, n^{20}_D 1.434); isobutylene, as *t*-butyl bromide (b. p. 74°, n^{20}_D 1.428).

Summary

1. The gases formed by the reaction of phenylmagnesium bromide on alkyl halides in the presence of cobaltous chloride have been analyzed.

2. A chain mechanism to explain the formation of these gases is suggested.

3. The methyl radical differs from the other alkyl radicals studied in that it attacks the solvent (ethyl ether) in two ways. One of these leads to the formation of methane, the other to the formation of ethane, ethylene and (probably) methyl ethyl ether.

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Factors Determining the Course and Mechanisms of Grignard Reactions. VIII. The Effect of Metallic Halides on the Reaction of Grignard Reagents with Aromatic Acyl Halides

BY M. S. KHARASCH, WALTER NUDENBERG AND S. ARCHER

Introduction

Recent publications from this Laboratory have described the effect of small amounts of certain metallic halides on the course of Grignard reaction.[1] The results were explained on the basis of a chain reaction involving free radicals and a metallic subhalide as the chain carrier. In view of the novelty of these results, it was of interest to investigate the reactions of aromatic acid chlorides with phenylmagnesium bromide in the presence of cobaltous halides.

Previous Studies

Treatment of benzoyl chloride with sodium in dry ether is reported to give an excellent yield of ethyl benzoate.[2] The substitution of sodium amalgam for metallic sodium causes the reaction

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(1) For earlier references see Kharasch and Fields, THIS JOURNAL, **63**, 2316 (1941).

(2) Pearl, Evans and Dehn, *ibid.*, **60**, 2479 (1938).