[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Oxidation of Grignard Reagents

BY M. T. GOEBEL AND C. S. MARVEL

The oxidation of Grignard reagents by air and by oxygen was reported as early as 1903 and is a well-recognized reaction. However, the fact that the oxidation is extremely rapid and that it causes serious losses in connection with the use of the Grignard reagent are points which do not yet seem to be fully recognized. The experiments which are reported here are presented to call attention to these two considerations.

Attention was first directed to this problem by Bodroux,[1] who observed that arylmagnesium halides were readily oxidized by oxygen or air and that poor yields of the corresponding phenols were obtained by decomposing the oxidation products with acids. Shortly afterward Bouveault[2] found cyclohexanol as a by-product in the preparation of hexahydrobenzoic acid from the action of carbon dioxide on cyclohexylmagnesium chloride. In his experiments the by-product was formed to the extent of 20%. He thought that the alcohol was probably produced by oxidation of the Grignard reagent, and confirmed this view by oxidizing another Grignard reagent, benzylmagnesium chloride. This gave a yield of 80% of the theoretical amount of benzyl alcohol. Barbier and Grignard[3] obtained borneol by the oxidation of the Grignard reagent from pinene hydrochloride. Since these earlier papers, most of the oxidation studies[4] have dealt with aryl compounds which yield very complex mixtures of products.

Wuyts[4,5] studied both aromatic and aliphatic Grignard reagents and demonstrated with some degree of certainty that peroxides are intermediate products in the oxidation reaction. Under his experimental conditions ethylmagnesium bromide and cyclohexylmagnesium bromide were oxidized to give 88 and 81%, respectively, of the theoretical amounts of alcohol. Meisenheimer and Schlichenmaier[6] have studied the oxidation of methyl-, ethyl- and phenylmagnesium iodides and have reported the formation of the iodides along with the hydroxyl compounds when the oxidations were carried out in dilute solutions. In concentrated solutions the iodides were not obtained. Gilman and his students[7] have shown that several different Grignard reagents are slowly oxidized in boiling ether solutions and have pointed out that this reaction causes loss of yields

---

(1) Bodroux, *Compt. rend.*, **136**, 158 (1903).

(2) Bouveault, *Bull. soc. chim.*, [3] **29**, 1051 (1903).

(3) Barbier and Grignard, *Bull. soc. chim.*, [3] **31**, 840 (1904). See also Hesse, *Ber.*, **39**, 1127 (1906); Houben, *ibid.*, **39**, 1700 (1906).

(4) Wuyts, *Compt. rend.*, **148**, 930 (1909); Porter and Steele, THIS JOURNAL, **42**, 2650 (1920); Ivanov, *Bull. soc. chim.*, [4] **39**, 47 (1926); Gilman and Wood, THIS JOURNAL, **48**, 806 (1926).

(5) Wuyts, *Bull. soc. chim. Belg.*, **36**, 222 (1927).

(6) Meisenheimer and Schlichenmaier, *Ber.*, **61**, 2029 (1928).

(7) Gilman and Wood, THIS JOURNAL, **48**, 806 (1926); Gilman and St. John, *Bull. soc. chim.*, [4] **45**, 1091 (1929); Gilman and Hewlett, *Rec. trav. chim.*, **48**, 1124 (1929).

in synthetic work. Gilman and Zoellner[8] have also noted that oxidation may cause losses in the carbonation of Grignard reagents.

None of these experiments indicated clearly the extreme ease with which Grignard reagents were oxidized at low temperatures. Our attention was directed to this fact by the results of attempts to combine cetylmagnesium bromide with 2,3-dibromopropene-1. The reaction was carried out in the usual manner[9] by preparing the Grignard reagent in ether, cooling this solution and adding the 2,3-dibromopropene-1. Among the products of the reaction, a large amount of cetyl alcohol was always obtained. After a number of trials it was found that this was caused by oxidation of the Grignard reagent by air. In the usual Grignard reaction the ether vapors prevent the easy access of air to the organomagnesium halide and thus oxidation is almost completely prevented. In all cases where the Grignard reaction mixture is cooled to a low temperature before the addition of another reagent, the ether vapors are largely condensed and if the reaction mixture is stirred in air a large loss of Grignard reagent due to oxidation will follow. Under ordinary circumstances this side reaction will not be recorded by the experimenter because the reagents most commonly used are the lower ones and the alcohols produced by the oxidation are lost in the low boiling fractions during purification. These statements are borne out by the experiments recorded in this paper on the absorption of oxygen by various Grignard reagents in diethyl ether.

In diethyl ether at room temperature the oxidation of 0.006 mole of Grignard reagent was 80–90% complete in one hour. At 0° with slow stirring the Grignard reagent was completely oxidized in six to eight minutes and with rapid stirring four to five minutes was sufficient time for the reaction to go to completion. It is of interest to note that phenylmagnesium bromide is more slowly and less completely oxidized than is the case for any of the alkyl magnesium halides which have been studied. These figures must of course be considered as qualitative rather than strictly quantitative as no elaborate precautions were taken in carrying out the experiments.

The completeness of the oxidation and the fact that an alcoholate was produced was demonstrated by oxidizing 0.242 mole of *n*-octylmagnesium bromide in diethyl ether and the isolation of 0.21 mole of *n*-octyl alcohol. Similarly cetylmagnesium bromide gave about 60% of the theoretical amount of cetyl alcohol.

Experimental

Preparation of Grignard Reagents.—The ether solutions of these reagents were prepared and standardized by titration by the methods recommended by Gilman and his students.[10]

---

[8] Gilman and Zoellner, THIS JOURNAL, **53**, 1945 (1931).

[9] Lespieau and Borguel, "Organic Syntheses," Vol. VI, 1926, p. 20.

[10] Gilman and others, THIS JOURNAL, **45**, 150, 159, 2462 (1923): **51**, 1576 (1929).

Experiments on Oxidation at Room Temperature.—An Erlenmeyer flask, mounted on a shaking machine, was connected with a gas measuring buret. The apparatus was filled with oxygen and 35 cc. of dry ether was introduced into the flask through a dropping funnel. The pressure was adjusted by a leveling bulb. Then a measured quantity of a standard solution of the Grignard reagent was added through the dropping funnel. The flask was vigorously agitated by the shaker and the absorption of oxygen was noted by the change in pressure. A thermometer in the ether gave the temperature.

TABLE I

OXIDATION OF GRIGNARD REAGENTS IN DIETHYL ETHER AT ROOM TEMPERATURE

No.	Grignard reagent	Temp., °C.	Reagent used, mole	Total cc. O_2 abs. (uncorr.)	Per cent. of total absorption after minutes					
					10	20	30	40	50	60
1	Ethyl MgBr	26	0.00645	66.5	25	38	53.7	63.4	79.5	87.2
2	Ethyl MgBr	26	.00645	75.5	34	54	69.5	85.1	95.9	98.1
3	Ethyl MgBr	29	.00516	56	23.2	46.4	60.7	82.1	91.1	93.4
4	Phenyl MgBr	28	.00602	51	24.5	38	54	65	71.6	80
5	Octyl MgBr	27	.00605	67	26.9	47.7	62.7	72.8	79.1	83.6

TABLE II

OXIDATION OF GRIGNARD REAGENT IN DIETHYL ETHER AT 0°

Grignard reagent used	RMgX mole	O_2 abs. 0°, 760 mm., cc.	Mole of O_2 per 1 mole of RMgX	Per cent. O_2 absorbed 3 min.	5 min.	10 min.
Slow Stirring						
C_2H_5MgBr	0.0054	53	0.876	80	93	100
C_2H_5MgBr	.0054	55	.909	81	93	100
C_2H_5MgBr	.0108	97	.801	78	94	100
C_2H_5MgBr	.0162	145	.801	73	90	100
C_2H_5MgBr	.0113	108	.857	75.5	87	100[a]
C_2H_5MgBr	.0113	106	.840	71	87	100[a]
$C_6H_5CH_2MgBr$	.0078	91	1.04	81	94	100[b]
$C_6H_5CH_2MgBr$	.0078	89	1.02	78.5	90	100
n-$C_{16}H_{33}MgBr$	.0072	83	1.03	80	94	100[c]
n-$C_{16}H_{33}MgBr$	.0060	72	1.07	82	95	100[b]
Rapid Stirring						
C_2H_5MgBr	0.0054	53	0.876	90	100	...
C_2H_5MgBr	.0054	51	.843	90	99	100[d]
C_2H_5MgBr	.0054	51	.843	89	98	100
n-$C_8H_{17}MgBr$	.0077	78	.905	90	97	100[d]
n-$C_8H_{17}MgBr$	.0077	86	1.0	91	97	100[d]
$C_6H_5CH_2MgBr$	.0078	91	1.04	83	94	100[c]
n-C_4H_9MgCl	.0052	49	0.845	90	97	100[d]
n-C_4H_9MgCl	.0052	51	.879	88	97	100
n-$C_{16}H_{33}MgBr$	.0060	61	.908	97	100	...
n-$C_{16}H_{33}MgBr$	.0060	56	.833	97	100	...
n-$C_{16}H_{33}MgBr$	.0060	57	.848	91	97	100[b]
C_6H_5MgBr	.0060	46	.636	90	97	100[d]

[a] Air was used in these experiments in place of oxygen. [b] No oxygen absorbed after seven minutes. [c] No oxygen absorbed after eight minutes. [d] No oxygen absorbed after six minutes.

While no attempt was made to regulate this closely, the original temperature and the final temperature were the same.

The data are reported in Table I.

Oxidation at 0°.—The apparatus was essentially the same as before but was more carefully assembled and the reaction vessel in which the oxidation was carried out was equipped with a stirrer and surrounded by an ice-bath held at 0°. Again no elaborate thermostat was used but the temperature was controlled within the range of about 1°. The oxygen was taken from an ordinary tank of compressed gas and purified by passing successively through a concentrated solution of potassium hydroxide, a soda lime tower, a concentrated sulfuric acid wash bottle and a tube of anhydrite.

The data are given in Table II.

Preparation and Isolation of Alcohols. (a) ***n*-Octyl Alcohol.**—A solution containing 0.242 mole of *n*-octylmagnesium bromide in 200 cc. of ether was oxidized by bubbling pure dry oxygen through the solution, which was cooled in an ice-bath. After two hours the reaction mixture was poured into 300 cc. of water and 10 cc. of concentrated hydrochloric acid. The water solution was extracted with three 100-cc. portions of ether. The extract was evaporated on the steam-bath and distilled. Twenty-seven grams (0.21 mole) (85% of the theoretical amount) of octyl alcohol boiling at 195–198°, and entirely soluble in cold concentrated sulfuric acid, was recovered. The melting point of the phenyl urethan (72–73°) compared well with the melting point (74°) which has been reported for this derivative.[11]

(b) **Cetyl Alcohol.**—An ether solution containing 0.07 mole of cetylmagnesium bromide was oxidized for two hours, decomposed and taken up in ether as above. The ether was evaporated and the product distilled under reduced pressure. Ten grams (59% of the theoretical amount) of material, distilling at 150–190° (2 mm.), but melting at 45–48°, was recovered. This material showed no depression of melting point when mixed with known cetyl alcohol. As a residue from the vacuum distillation, 8 g. of dotriakontane, melting at 68° was recovered.

Summary

1. The rates of oxidation of certain Grignard reagents have been determined under various conditions.

2. At low temperatures (0°) where the vapor pressure of ether is not high enough to prevent free access of air to the solution the oxidation has been found to proceed at a very rapid rate and may become a serious side reaction in the use of the Grignard reagent.

3. *n*-Octyl- and cetylmagnesium bromides have been oxidized by dry oxygen to give good yields of the corresponding alcohols.

URBANA, ILLINOIS

RECEIVED NOVEMBER 7, 1932
PUBLISHED APRIL 6, 1933

---

[11] Bouveault and Blanc, *Compt. rend.*, **136**, 1676 (1903).