[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

Equilibrium Composition of Certain Grignard Reagents in *n*-Butyl Ether

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In connection with work in this Laboratory on the reaction of monochloramine with organomagnesium compounds (Coleman and Blomquist[2]) it was of interest to determine the apparent composition of the Grignard reagents used with respect to the following equilibrium

$$2RMgX \rightleftarrows R_2Mg + MgX_2 \qquad (1)$$

The dioxane precipitation method was used for comparison purposes although it had been shown that this method does not give true values.[3] Noller and Raney[4] had further shown that on the basis of the equilibrium constant for equation (1) determined by their method in a solution of *n*-butylmagnesium chloride in ethyl ether the percentage of di-*n*-butylmagnesium at equilibrium was very much less than the percentage obtained by the dioxane method.

The determination of equilibrium constants by the Noller and Raney method involves the assumption that the concentration of magnesium chloride etherate is the same in the Grignard solution as in pure ether. However, the authors call attention to the possibility that the solubility of magnesium chloride in the Grignard reagent may be greatly increased by the presence of the butylmagnesium chloride and the di-*n*-butylmagnesium. This suggestion was supported by the work of Doering and Noller[5] with magnesium bromide. The authors conclude that either the dioxane precipitation method does not give a true picture of the composition of the Grignard solutions or the solubility of the magnesium chloride is increased from a very low value to approximately one mole per mole of dibutylmagnesium. Further evidence on equation (1) is given in the work of Evans and Pearson[6] on the "Ionic Nature of the Grignard Reagent."

At the time the work with monochloroamine was reported some attention had been given in this Laboratory to a study of the equilibrium composition of the Grignard reagent from *n*-butyl chloride in *n*-butyl ether by the Noller and Raney method. Subsequently this work was extended and certain refinements in technique introduced. A study was also made of the equilibrium composition of the Grignard reagent from ethyl chloride in *n*-butyl ether. While there may be some uncertainty with respect to assumptions involved in the calculations by this method, the experimental results of this work are here reported.

Special precautions were used to prevent air from coming in contact with the Grignard solutions. However, in the light of a brief report by Noller and Castro[7] it appears that even greater care may be necessary to give true equilibrium values.

A relatively large number of determinations were made using solutions of varying concentration. Anhydrous magnesium chloride was added to some reaction tubes, but it was later established that this had little or no effect on the time required for apparent equilibrium to be established. Continuous shaking was used for a time, but it became evident that this had little effect on the rate of establishment of equilibrium. Equilibrium was apparently reached in about two hundred to two hundred and fifty hours. Observations were continued, however, for a much longer period.

The apparent equilibrium composition of *n*-butylmagnesium chloride and ethylmagnesium chloride in *n*-butyl ether are given in Table I and II. The solubility of anhydrous magnesium chloride in *n*-butyl ether was determined and found to be approximately 0.0002 mole per 1000 g. of solution. It may be noted in Table I that with the *n*-butyl chloride reagent a fairly satisfactory constant was obtained, with perhaps a slight increase observable with decreasing concentration. The equivalent percentage of the Grignard reagent in the form of di-*n*-butylmagnesium varied

TABLE I

EQUILIBRIUM COMPOSITION OF *n*-BUTYLMAGNESIUM CHLORIDE IN *n*-BUTYL ETHER[a]

Total Grig. concn.	Total Cl concn.	Bu_2Mg concn.	$K \times 10^{-4}$
1.9182	1.8273	0.0455	0.014
1.5897	1.5190	.0354	.015
1.4797	1.4148	.0325	.016
1.1566	1.1175	.0196	.016
1.0771	1.0455	.0158	.015
0.7740	0.7518	.0111	.020

TABLE II

EQUILIBRIUM COMPOSITION OF ETHYLMAGNESIUM CHLORIDE IN *n*-BUTYL ETHER[a]

Total Grig. concn.	Total Cl concn.	Et_2Mg concn.	$K \times 10^{-4}$
1.6650	1.4953	0.0849	0.038
1.2883	1.1371	.0756	.058
1.1905	1.0670	.0618	.054
1.0188	0.9146	.0521	.062
0.9721	.8697	.0512	.068
.7980	.7179	.0401	.078

[a] Concentrations are expressed in mg. equivalents per gram of solution with exception of Bu_2Mg which is expressed in mg. moles per gram of solution.

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(1) Present address: Socony Vacuum Oil Company, Paulsboro, N. J.

(2) Coleman and Blomquist, THIS JOURNAL, **63**, 1692 (1941).

(3) Noller and White, *ibid.*, **59**, 1354 (1937).

(4) Noller and Raney, *ibid.*, **62**, 1749 (1940).

(5) Doering and Noller, *ibid.*, **61**, 3436 (1939).

(6) Evans and Pearson, *ibid.*, **64**, 2865 (1942).

(7) Noller and Castro, *ibid.*, **64**, 2509 (1942).

according to these results from 2.9 in the more dilute solutions to 4.8 in the more concentrated.

In the case of the ethyl chloride reagent, Table II, there is a definite increase in the constant from the more concentrated to the more dilute solutions. The equivalent percentage of the Grignard reagent in the form of diethylmagnesium was very close to 10 for all the solutions studied.

Experimental

Purification of *n*-Butyl Ether.—Butyl ether was distilled through an efficient fractionating column and the portion boiling between 138–141° collected. This fraction was refluxed over sodium for six hours. The ether was then redistilled and the portion boiling between 139–141° collected and stored over bright sodium wire.

Purification of Nitrogen Gas.—To remove impurities in nitrogen that react with Grignard reagents, the gas was passed through a purification train containing alkaline pyrogallol, water, concentrated sulfuric acid and finally solid sodium hydroxide.

Preparation of Grignard Reagents.—The Grignard reagents were prepared under purified nitrogen from ethyl chloride and *n*-butyl chloride and magnesium turnings in *n*-butyl ether without the use of catalysts. The solutions were centrifuged before being transferred to equilibrium tubes.

Solubility of Anhydrous Magnesium Chloride.—Anhydrous magnesium chloride was prepared by the method described by Noller and Raney.[4] The solubility in *n*-butyl ether was determined by shaking an excess of the powdered material with *n*-butyl ether until equilibrium was reached. The chloride content of the solution was determined by the Volhard method using 0.01 *N* solutions of silver nitrate and potassium thiocyanate. The solubility was found to be approximately 0.0002 mole of magnesium chloride per 1000 g. of solution.

Equilibrium Determination.—In general the procedure for determining the equilibrium composition was similar to that of Noller and Raney.[4] Pyrex glass tubes of about 80 ml. capacity, equipped with stopcocks, were used. Purified nitrogen gas was used in all transfers and special precautions were taken throughout to prevent the solutions from coming in contact with air or moisture.

Anhydrous magnesium chloride was placed in some equilibrium tubes. It soon became evident, however, that this had little or no effect on the rate at which equilibrium was established and it was therefore not continued. Constant shaking was used for a time but as this was apparently unnecessary it was also discontinued.

The time required for equilibrium apparently to become established was about two hundred hours for solutions of *n*-butylmagnesium chloride and about two hundred fifty hours for ethylmagnesium chloride. Observations were continued for a much longer period, in some cases up to thirteen hundred hours. The solutions were analyzed for active Grignard reagent and for chloride ion. The Volhard method was usually used for the chloride analysis, but this was checked in several cases by gravimetric determinations.

Summary

Determinations have been made of the equilibrium compositions of Grignard reagents prepared from *n*-butyl chloride and ethyl chloride in *n*-butyl ether. Concentrations were varied from about 0.6 to 1.9 equivalents per 1000 g. of solution.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Periodate Oxidation of Certain Active Methylene Groups[1,1a]

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In applying the periodate oxidation technique to the problem of structural proof of an aldonic acid benzimidazole,[2] it was noted that more periodate was consumed than could be accounted for by the well-known cleavage of 1,2-glycols, ketols and 1,2-diketones.[3] Further study indicated that an activated α-hydrogen was being oxidized. Smith and Duke[4] have reported a reaction of this general nature when using perchlorato-ceric acid in the presence of perchloric acid but data for this reaction are not given for periodic acid. Oxidation of active α-hydrogens by lead tetraacetate is well known.[5,6]

The present studies give evidence for a new reaction of periodate in aqueous solution, *i.e.*, the oxidation of active α-hydrogens such as those found in malonic acid. The reaction was investigated by both macrodeterminations of periodate consumption and carbon dioxide evolution in the presence of small molar excesses of periodate, and by microdeterminations of carbon dioxide evolution by means of the Warburg respirometer in the presence of large molar excesses of periodate. A number of compounds of related structure were studied, and the probable mechanism of this reaction is indicated.

Malonic acid, on treatment at room temperature with an excess of sodium metaperiodate (6 to 8 molar equivalents (ME)), evolved slightly less than 2 ME of carbon dioxide within two hours (Fig. 1, Curve I). Three ME of periodate were consumed in the reaction during the same time

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(2) C. F. Huebner, R. Lohmar, R. L. Dimler, S. Moore and K. P. Link, *J. Biol. Chem.*, **150**, 503 (1945).

(3) E. L. Jackson in R. Adams, "Organic Reactions," Vol. II, John Wiley and Sons, New York, N. Y., 1944, p. 341.

(4) G. F. Smith and F. R. Duke, *Ind. Eng. Chem., Anal. Ed.*, **15**, 120 (1943).

(5) O. Dimroth and R. Schweizer, *Ber.*, **56**, 1375 (1923).

(6) R. C. Hockett, M. H. Nickerson and W. H. Reeder, III, THIS JOURNAL, **66**, 472 (1944).