into a flask containing 50 cc. of water and 10 cc. of a 10% aqueous solution of potassium iodide. The liberated iodine then was titrated with 0.1 N sodium thiosulfate.

For the indirect method of titration an excess of the 0.1 N bromine solution in alcohol, which had been cooled to -7 to $-10°$, was added to the cold alcohol-hexane solution of the keto ester. The excess bromine was decolorized immediately by titration with a 10% solution of β-naphthol in absolute alcohol. To this point approximately fifteen seconds were required from the time the equilibrium was frozen by the cold alcohol. Then 15 cc. of a 10% solution of potassium iodide was added and the resulting solution warmed to 25–30° for five minutes, after which time the liberated iodine was titrated with 0.1 N sodium thiosulfate.

Summary

The enol contents of a number of alkyl acetoacetates and of some α,γ-dialkyl substituted ethyl acetoacetates are reported.

MADISON, WISCONSIN RECEIVED JUNE 16, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Precipitation of Phenylmagnesium Bromide by Pyridine and by Dioxane

BY ARTHUR C. COPE

The accuracy of the Schlenk dioxane precipitation method[1] for determining the position of Grignard equilibria ($2RMgX \rightleftarrows R_2Mg + MgX_2$) is still open to question. The method depends upon precipitation of insoluble dioxanates of the RMgX and MgX_2 components, and this precipitation must be rapid compared to the rate of equilibration in order to avoid shifting the equilibrium in the direction of the less soluble dioxanate during precipitation. Recent work has shown that the compositions of the solution and the precipitate change if the two remain in contact,[2] presumably because of the reaction: $2RMgX \cdot \text{dioxane (insoluble)} \rightleftarrows R_2Mg \text{ (soluble)} + MgX_2 \cdot \text{dioxane (insoluble)}$. If the precipitation is used as an analytical method for determining the position of the original Grignard equilibrium, the latter reaction must be minimized by rapid removal of the precipitate.

In this investigation a number of ethers, sulfides and tertiary amines were added to ether solutions of phenylmagnesium bromide in an effort to find other precipitants for the halomagnesium components, thus making it possible to compare analyses obtained with two or more precipitants. Phenylmagnesium bromide was chosen because in this Laboratory arylmagnesium halides have given consistent analyses by dioxane precipitation.

Pyridine produces a precipitate with phenylmagnesium bromide which is grossly similar to the one obtained with dioxane. The precipitate can be separated by centrifuging, and the solution analyzed for basic magnesium and halogen. Typical data are plotted in Fig. 1, which shows the percentage of basic magnesium and bromide ion left in solution after the addition of a definite number of equivalents of pyridine, together with similar data for dioxane. The behavior of the two precipitants is very different in several respects. Dioxane precipitates the halomagnesium components more completely than does pyridine. Diphenylmagnesium is not precipitated by dioxane even when the latter is in large excess and high concentration. Pyridine precipitates only

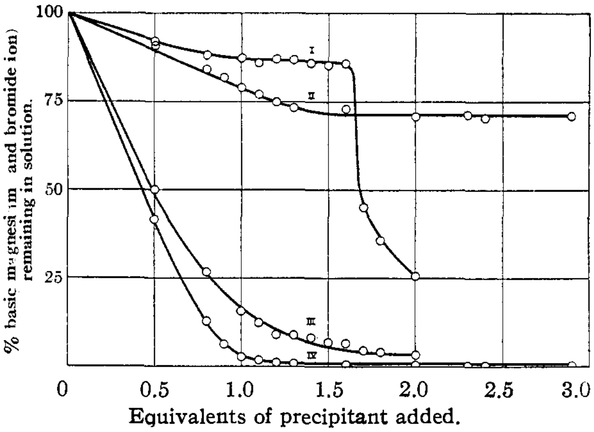

Fig. 1.—Precipitation of a phenylmagnesium bromide solution 0.2325 N in basic magnesium and 0.2402 N in bromide ion. The equivalents of precipitants are based on the normality in bromide ion. Curve I, % basic magnesium remaining in solution after precipitation with pyridine; II, % basic magnesium in solution after dioxane precipitation; III, % bromide in solution after pyridine precipitation; IV, % bromide in solution after dioxane precipitation.

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[1] Schlenk and Schlenk, *Ber.*, **62**, 920 (1929); Schlenk, *ibid.*, **64**, 734 (1931).

[2] (a) Noller and White, THIS JOURNAL, **59**, 1354 (1937); (b) Cope, *ibid.*, **57**, 2238 (1935).

phenylmagnesium bromide and magnesium bromide up to a molar ratio of pyridine to bromide ion of 1.6, with the concentrations employed: with ratios higher than 1.6 diphenylmagnesium is also precipitated, and in large amount (note the point of inflection in Curve I).

A comparison of the dioxane and pyridine precipitation data (Table I) gives two independent evaluations of the extent of disproportionation of phenylmagnesium bromide. The most accurate analyses should be those in which there is least bromide ion left in solution, or those with 1.2 to 20.0 equivalents of dioxane and 1.2 to 1.6 equivalents of pyridine. These dioxane and pyridine values show 70–74% and 78–79% disproportionation,[3] respectively. The results do not indicate a high degree of accuracy for the dioxane precipitation method, but the approximate checks obtained with the two precipitants suggest that in this case the order of magnitude at least is correct.

TABLE I

DISPROPORTIONATION OF PHENYLMAGNESIUM BROMIDE

Molar ratio precipitant/Br^-	% disproportionation[a] from dioxane precipitation A		from pyridine precipitation A	
		B		B
1.0	76.2	78.9	71.7	87.3
1.1	75.2	77.0	73.6	86.0
1.2	73.8	74.9	78.1	87.1
1.3	72.5	73.3	77.9	86.8
1.4	..	..	77.8	85.9
1.5	..	..	78.5	85.3
1.6	72.4	72.9	79.3	85.8
2.0 to 20.0	70–72	70–72	..	..

[a] In this calculation it is necessary to make some assumption concerning the bromide ion left in solution, which is an appreciable quantity in all cases with pyridine, and with dioxane if less than 1.2 equivalents is used. The values recorded are calculated from the data of Fig. 1. The values in the columns headed A are calculated assuming that all the remaining bromide ion is present as phenylmagnesium bromide, and those headed B assuming that it is all magnesium bromide. The A values are more nearly correct, since magnesium bromide dioxanate appears to be less soluble than phenylmagnesium bromide dioxanate, but the true values are probably somewhere between the two extremes.

Pyridine cannot be recommended as a precipitant for preparing dialkylmagnesium solutions from Grignard reagents for synthetic purposes, because it does not remove bromide ion as completely as does dioxane, nor is it as convenient a reagent for use in analyses. If its behavior with phenylmagnesium bromide is typical of Grignard reagents in general, it may serve a useful purpose in checking analyses made by the Schlenk method.

Oddo[4] has reported that the addition of two moles of pyridine to an ether solution of phenylmagnesium bromide causes precipitation of the definite compound, $C_6H_5MgBr\cdot(C_2H_5)_2O\cdot 2C_5H_5N$. This and most of the other work on addition compounds of tertiary amines and other "donor" molecules with Grignard reagents[5] was done prior to Schlenk's demonstration of the existence of the Grignard equilibrium, and the addition compounds were usually analyzed after some purification, with no thought of a possible separation of the supposedly homogeneous reagent during precipitation. It is possible that in other cases like the above, where definite compounds are reported, analysis of the original precipitate or the residual solution after precipitation would disclose a differential precipitation of the components of the equilibrium.

Experimental Part[6]

The phenylmagnesium bromide solutions were prepared in the usual manner under dry nitrogen in a flask fitted with a filter tube,[2b] and filtered with nitrogen pressure directly into the reservoir of a specially designed buret (Fig. 2). During filtration the reagent was protected by a counter current of nitrogen introduced through the tip of the buret, the top half of the ground glass seal being removed and tube A stoppered temporarily. The solutions were standardized by acidimetric[7] and Volhard titrations.

Among the substances investigated which gave no precipitate with phenylmagnesium bromide in ether solution were the following: dimethyldioxane,[8] *p*-thioxane, *p*-dithiane, diphenylpiperazine, dimethylaniline, diethylaniline, N-phenylmorpholine and nicotine. Quinoline, α-picoline, N-methylmorpholine and diphenyl sulfoxide gave varying amounts of oily or gelatinous precipitates which could not be handled quantitatively.

The pyridine and dioxane analyses were made in the following manner. Twenty cubic centimeters of the Grignard solution (at 20°) was measured from the buret into a dry, nitrogen-filled centrifuge tube of 50-cc. capacity, made with a constricted neck. The access of air during transfer was prevented by a nitrogen mantle (shown in Fig. 2), and the tube was tightly stoppered as soon as it was removed from the mantle. Solutions of pyridine or dioxane were made up to contain the desired number of equivalents of precipitant in 10 cc. of dry ether solution, and this volume was added to the 20-cc. samples as rapidly as possible from a buret with a wide orifice, the sample

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(3) According to assumption A above. With assumption B the values are 70–75% and 85–87%.

(4) Oddo, *Atti accad. Lincei*, [5] **13**, II. 100 (1904); *Gazz. chim. ital.*, **34**, II. 420 (1904).

(5) *Cf.* the references given by Hepworth, *J. Chem. Soc.*, **119**, 1249 (1921).

(6) The author wishes to express his indebtedness for a grant from the Wolcott Gibbs fund of the National Academy of Sciences for apparatus essential to this investigation.

(7) Gilman, Zoellner and Dickey, THIS JOURNAL, **51**, 1576 (1929).

(8) Kindly furnished by the Carbide and Carbon Chemicals Corp.

again being protected from the air with a nitrogen mantle. The tubes were stoppered immediately, shaken vigorously and centrifuged at 2800 r. p. m. for ten minutes. The clear supernatant liquid was decanted into a flask containing 75 cc. of water. A 20-cc. portion of dry ether was added to the solid residue remaining in the centrifuge tube, which was again shaken, centrifuged for five minutes and decanted into the flask containing water. Further washing of the precipitate with ether failed to remove significant quantities of basic magnesium or halogen, showing that there was little if any occlusion, except in analyses using pyridine in quantities sufficient to precipitate diphenylmagnesium. In the latter case the amount of basic magnesium taken into solution increased with each washing of the precipitate, so that the analyses with more than 1.6 equivalents of pyridine have no exact quantitative significance.

In the pyridine analyses, the ether was first boiled off, after which the aqueous mixture was boiled for thirty minutes to remove the pyridine, acidified with an excess of standard sulfuric acid, again boiled for five minutes and back titrated with standard alkali. Bromide analyses were made on the same samples, after cooling, by Volhard titration. The method was proved to be accurate by analysis of a Grignard reagent of known normality after the addition of pyridine. The end-points in the acidimetric titration were not as sharp as in the dioxane analyses. Solutions precipitated with dioxane were acidified initially with an excess of standard sulfuric acid and boiled long enough to expel completely the ether before back titrating with standard alkali.

Precipitations with Isoquinoline.—Isoquinoline gives a bulky solid precipitate with phenylmagnesium bromide in ether solution. The precipitate may be separated by centrifuging, and the solutions analyzed as in the pyridine procedure if they are boiled for one hour before acidification, although the end-points are obscure in the acidimetric titration. Interpretation of the analyses is difficult, because a relatively large proportion of the bromide ion remains in solution. The following data are representative. A solution of phenylmagnesium bromide 0.2060 *N* in basic magnesium and 0.2138 *N* in bromide ion was precipitated as described above with 1.0 and 1.1 equivalents of isoquinoline. The solutions after centrifuging contained: (1 equivalent of isoquinoline) basic magnesium 0.1720 *N* (with respect to the volume of the original sample); bromide ion 0.0522 *N;* (1.1 equivalents of isoquinoline) basic magnesium 0.1690 *N;* bromide ion 0.0443 *N.*

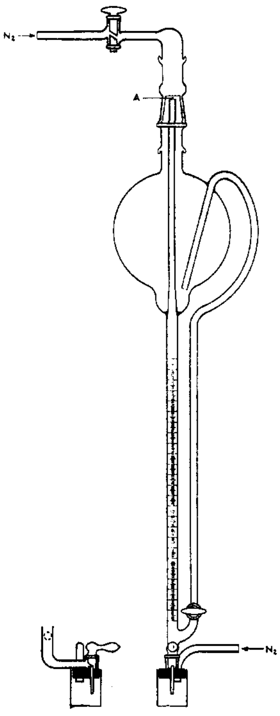


Fig. 2.—Apparatus.

Summary

Pyridine behaves like dioxane in precipitating the halomagnesium components of the equilibrium, $2C_6H_5MgBr \rightleftarrows (C_6H_5)_2Mg + MgBr_2$. The two precipitants indicate 78–79% and 70–74% disproportionation in the above equilibrium, respectively. This rough check with two different precipitants indicates that the Schlenk dioxane precipitation method, for this Grignard reagent at least, gives approximately correct results.

BRYN MAWR, PENNSYLVANIA RECEIVED JUNE 18, 1938

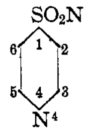
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE CALCO CHEMICAL COMPANY, INC.]

Sulfanilamide Derivatives. I. Aminoarylsulfonamidoarylsulfonic Acids and Aminoarylsulfonamidoarylcarboxylic Acids*

BY M. L. CROSSLEY, E. H. NORTHEY AND MARTIN E. HULTQUIST

Nomenclature of Sulfanilamide Derivatives.—Chemical and medical literature on sulfanilamide derivatives suffers from a confusion of names and naming systems which is bewildering to the medical reader and often misleading to chemists. The name "sulfanilamide" has been adopted officially by the American Medical Association and is now generally used. It would seem desirable, therefore, to continue with this and relate the names of new derivatives, where possible, to the parent sulfanilamide. In the interest of setting up such a system, we have corresponded with Austin M. Patterson, who has given valuable suggestions on the following:

a. Naming as substituted sulfanilamides



In sulfanilamide the sulfonamide group, being the principal functional group, occupies the 1-posi-

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(*) Presented in part before the Division of Medicinal Chemistry, A. C. S., April 20, 1938.