Kinetics and Mechanisms of Organomagnesium Reactions with Benzonitrile

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The reactions of diethylmagnesium and of ethylmagnesium bromide with benzonitrile in tetrahydrofuran at 30.00° were examined in detail, and kinetics and mechanisms for these reactions have been proposed. These reactions were followed by hydrolyzing aliquots in a known excess of acid and back-titrating with standard base. Only 50% of the ethyl groups in diethylmagnesium or in ethylmagnesium bromide reacted with benzonitrile and the remaining groups failed to give a positive Gilman test for unchanged Grignard reagent. Further, of the reactive ethyl groups, two distinct rates of reaction were observed. These results are best interpreted by postulating that diethylmagnesium reacts as $[(C_2H_5)_2Mg]_2$, and that the ethyls in ethylmagnesium bromide react from $(C_2H_5)_2Mg{\cdot}MgBr_2$ and also from $[(C_2H_5)_2Mg]_2$ in solution.

While the empirical formula, RMgX; adequately describes the Grignard reagent for synthetic purposes, it does not satisfactorily describe its structure. For example, the Grignard reagent has been considered as an equilibrium[3] between

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

but recently Dessy[4-6] and co-workers demonstrated that the magnesium in dialkylmagnesium does not exchange with the magnesium in magnesium halide. Thus, Dessy adopted the $R_2Mg{\cdot}MgX_2$ structure (which was originally proposed by Jolibois[7]) for the Grignard reagent and suggested that the following equilibrium takes place:

$$R_2Mg{\cdot}MgX_2 \rightleftharpoons R_2Mg + MgX_2 \qquad (2)$$

A consequence of rejecting the RMgX structure for the Grignard reagent is that any conclusions which have been based on this formula must also be modified. For example, mechanisms have been proposed for the reactions of Grignard reagents with ketones,[8,9] 1-alkynes,[10-14] and nitriles[8,15]; which all employ the RMgX structure as the reactive species for the Grignard reagent.

The purpose of this investigation was to study certain physical-chemical aspects of the reaction of ethylmagnesium compounds with benzonitrile in order to throw more light on the nature of the Grignard reagent in solution and in particular on the mechanism of the reaction with benzonitrile. This study also concerned itself with three ancillary questions. First, if the $R_2Mg.MgX_2$ structure exists, should the reactivities of both alkyl groups be identical? This has been reported not to be the case for diethylmagnesium,[14] but it has never been demonstrated for a Grignard reagent. Second, if the Grignard reagent is in equilibrium with dialkylmagnesium does part or all of the reaction proceed through the R_2Mg structure? Third, does the presence of magnesium bromide in the system (formed *in situ* from the Grignard reagent) affect the reaction mechanism or rate of polarizing the benzonitrile present? It has been reported that magnesium bromide can alter the course of reaction of Grignard reagents with sterically hindered ketones.[9]

This projected study required the development of an accurate and convenient analytical method; therefore an analytical investigation was also undertaken.

EXPERIMENTAL

A. *Syntheses, sources and purification of reagents.* The magnesium was obtained in ingot form from the Nelco Metals Co. and was reported to contain the following impurities: aluminum, 75 p.p.m.; copper, 10 p.p.m.; iron, 60 p.p.m.; calcium, 30 p.p.m.; silicon, 100 p.p.m.; boron 0.5 p.p.m.; manganese, 60 p.p.m. Turnings were prepared by milling the magnesium with a Carballoy cutting tool. Care was taken to prevent the turnings from coming into contact with other metal.

Ethyl bromide, benzonitrile, diethyl ether, and tetrahydrofuran were purified and dried by conventional techniques, details of which are found in the reference cited in footnote 1.

Magnesium bromide etherate. This was prepared from 9.39 g. (0.050 mole) of ethylene bromide, 1.22 g. (0.050 g.-atom) of magnesium turnings, and 100 ml. of anhydrous ether, by following the usual procedure for Grignard reagent. A gas (ethylene) was evolved during the addition of ethylene

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(2) To whom inquiries should be sent.

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(6) R. E. Dessy, *Chem. Eng. News*, **38**, No. 31, 42 (1960).

(7) P. Jolibois, *Compt. rend.*, **155**, 353 (1912).

(8) C. G. Swain, *J. Am. Chem. Soc.*, **69**, 2306 (1947).

(9) C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, **73**, 870 (1951).

(10) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, *J. Am. Chem. Soc.*, **77**, 103 (1955).

(11) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, *J. Org. Chem.*, **20**, 1545 (1955).

(12) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, *J. Am. Chem. Soc.*, **78**, 1221 (1956).

(13) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, *J. Org. Chem.*, **21**, 1063 (1956).

(14) R. E. Dessy, J. H. Wotiz, and C. A. Hollingsworth, *J. Am. Chem. Soc.*, **79**, 358 (1957).

(15) A. Bruylants, *Bull. soc. chim. France*, 1291 (1958).

bromide to the magnesium, and two liquid layers formed. Stirring was continued until gas was no longer liberated, and the mixture was allowed to stand under anhydrous conditions for 2 days. The product was filtered through a fine porosity fritted-glass funnel to remove the trace of unreacted magnesium remaining. The lower liquid layer (magnesium bromide etherate) was found to be 5.47 N in bromide ion (see section B).

Ethylmagnesium bromide (ether). The Grignard reagent was prepared in the conventional manner from ethyl bromide and magnesium turnings in diethyl ether. The resulting product was filtered under anhydrous conditions through a fine porosity fritted-glass funnel, yielding a pale yellow solution. Several such solutions were prepared and their ethyl and bromide concentrations were determined (see section B).

Diethylmagnesium (tetrahydrofuran). To 50 ml. of an ether solution of ethylmagnesium bromide (85.61 meq. of ethyl, 87.77 meq. of bromide) was added 7.81 ml. (88.6 meq.) of dioxane. The reaction vessel was sealed and the contents were stirred with a glass-enclosed magnetic stirrer for 24 hr. Precipitation occurred almost immediately and the solid assumed a white, crystalline appearance within a few minutes. At the end of 24 hr., the contents of the flask were filtered under anhydrous conditions through a fine porosity fritted-glass funnel. The filtrate was diluted with 100 ml. of tetrahydrofuran and the ether was fractionally distilled. The residual solution was found to contain no bromide ion (see section B).

An attempt was made to synthesize diethylmagnesium in tetrahydrofuran from ethylmagnesium bromide that was prepared in tetrahydrofuran. The addition of a stoichiometric amount of dioxane resulted in the precipitation of only 80% of the bromide (as magnesium bromide bisdioxanate) and the addition of excess dioxane failed to precipitate the remaining bromide ion.

Ethylmagnesium bromide (tetrahydrofuran). Four methods were used to prepare these solutions. In one method, magnesium and ethyl bromide were allowed to react directly in tetrahydrofuran. In the second method, magnesium bromide (etherate) was added to ethylmagnesium bromide or to diethylmagnesium. Tetrahydrofuran was added, where necessary, and the ether was fractionally distilled from the solution. The third method involved the addition of tetrahydrofuran to an ether solution of ethylmagnesium bromide, followed by the fractional distillation of the ether. The fourth method was similar to the third, with the exception that a measured amount of dioxane was added to the ether solution of ethylmagnesium bromide (to remove part of the bromide ion), and the precipitated magnesium bromide bisdioxanate was filtered from the solution prior to the addition of tetrahydrofuran.

B. *Methods of analysis.* 1. *Gravimetric analysis of ketone.* a. *Reagents and solvents. Dinitrophenylhydrazine reagent.* This was a solution 0.01 N in 2,4-dinitrophenylhydrazine (DNP), and 2 N in hydrochloric acid in 50% (volume) aqueous alcohol.

Acid wash solvent. This was a 2 N hydrochloric acid solution in 50% (volume) aqueous alcohol.

Neutral wash solvent. This was 50% (volume) aqueous alcohol.

b. *Procedure.* An aliquot of the solution to be analyzed was added to a volume of DNP reagent containing sufficient reagent to react with all of the ketone present in the aliquot. The mixture was boiled gently for 5 min. to hydrolyze the organomagnesium compounds and to dissolve the magnesium salts. The solution was cooled slowly to 0° to crystallize the dinitrophenylhydrazone. The solid was collected in a tared, fritted-glass funnel, washed with ice-cold acid wash solvent to remove unchanged dinitrophenylhydrazine and then with ice-cold neutral wash solvent until the washings were chloride-free. After drying the funnel at 110° to constant weight (2–4 hr. were required), it was cooled to room temperature and weighed.

c. *Accuracy and precision of the method.* Known amounts of propiophenone were weighed and treated with a constant excess of DNP reagent. Each sample was worked up in the described manner and the yields of dinitrophenylhydrazine were found to be 99.0 ± 0.6% of theory. The ratio of dinitrophenylhydrazine to propiophenone (1.5–3.0), or the presence of benzonitrile and ether did not affect the yield. The melting points of the samples obtained generally were 189–191° (lit., m.p. 191°) although a few ranged from 184–187°.

2. *Volumetric analysis.* a. *Procedure.* An aliquot of the solution under study was hydrolyzed by adding it to a known excess of standard sulfuric acid (0.15 N), and the solution was boiled gently for 5–10 min. to digest the magnesium salts and to distill most of the tetrahydrofuran from the solution. After cooling to room temperature, the solution was back-titrated with 0.05 N sodium hydroxide solution using Methyl Red indicator.

b. *Precision of the method.* At least three aliquots of ethylmagnesium solutions were titrated in determining the ethyl concentrations of each solution. The average deviation of these determinations was usually ±0.002 N (as ethyl anion) and never was greater than ±0.003 N. Similar results were also obtained on titrating the products of the reaction of these reagents with benzonitrile.

c. *Comparison of the gravimetric and volumetric methods.* Three reactions of diethylmagnesium with benzonitrile in tetrahydrofuran were run under identical conditions. In one case, the reaction was followed by the gravimetric method of analysis; in the other two cases, by the volumetric method. A plot of the concentration of ketone *vs.* time was made for each run, and a comparison of the methods of analysis gave almost identical results throughout the course of the reaction.

3. *Volumetric analysis for bromide.* All analyses for bromide were performed by the Volhard method.[16] The following procedure was employed to prepare an organomagnesium sample for analysis: A 1-ml. aliquot was hydrolyzed in 10 ml. of water and boiled gently for 5–10 min. to distill the bulk of the tetrahydrofuran from the solution. The solution was allowed to cool to room temperature and was then acidified to a *p*H of 3–4 with 1 N nitric acid. A known excess of silver nitrate was added to the acidified solution and the mixture was back-titrated with 0.1 N potassium thiocyanate solution, using ferric sulfate as indicator.

C. *Reactivity of ethylmagnesium compounds.* 1. *Diethylmagnesium with benzonitrile and propiophenone.* To 2.00 ml. of 0.875 M diethylmagnesium (1.75 mmoles) in tetrahydrofuran was added 0.135 ml. (1.40 mmoles) of benzonitrile. At the end of 21 hr., 0.186 ml. (1.40 mmoles) of propiophenone was added, and the resulting solution was allowed to stand for 3 hr. longer. The concentration of propiophenone present in the solution at the end of this time was found to be 1.053 mmoles/ml. by gravimetric analysis.

2. *Diethylmagnesium with benzonitrile and benzaldehyde.* A solution containing 12 ml. of 0.28 M diethylmagnesium (3.4 mmoles) in tetrahydrofuran and 0.54 ml. (5.2 mmoles) of benzonitrile was allowed to stand for 4 days. To it was added 0.17 ml. (1.7 mmoles) of benzaldehyde, and the resulting solution was allowed to stand for 2 days longer. At the end of this time, the solution was hydrolyzed in 25 ml. of saturated ammonium hydrochloride solution and the tetrahydrofuran was distilled. The organic residue was extracted from the aqueous solution with ether and the ether solution was washed with saturated ammonium chloride and then dried over anhydrous magnesium sulfate. Distillation of the ether yielded an oil which was examined by infrared analysis. Absorption bands at 3400 m, 2220 m, 1680 s, 1120 *m* cm.$^{-1}$ were observed. No band at 2720 cm.$^{-1}$ was found.

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(16) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," revised ed., The Macmillan Co., New York, 1947, pp. 475-478, 573-574.

3. *Diethylmagnesium with benzonitrile and Michler's ketone.* To 12 ml. of 0.40 M diethylmagnesium (4.8 mmoles) in tetrahydrofuran was added 0.61 ml. (5.9 mmoles) of benzonitrile. At the end of 24 hr., 0.5 ml. of the solution was added to 0.5 ml. of 1% 4,4'-bis(N,N-dimethylamino)benzophenone in benzene. Application of the Gilman test[17] to the mixture gave a negative result.

The Gilman test was repeated on a solution of 0.25 ml. (2.4 mmoles) benzonitrile in 12 ml. of 0.40 M diethylmagnesium (4.8 mmoles) in tetrahydrofuran. A positive test was obtained in this case.

4. *Ethylmagnesium bromide with benzonitrile and Michler's ketone.* To 25 ml. of ethylmagnesium bromide (17.0 meq. of ethyl groups) in tetrahydrofuran was added 1.40 ml. (13.5 mmoles) of benzonitrile. At the end of 48 hr., the reaction product gave a negative Gilman test.

5. *Diethylmagnesium with propiophenone.* To 25 ml. of 0.305 M diethylmagnesium (7.6 mmoles) in tetrahydrofuran was added 1.50 ml. (11.3 mmoles) of propiophenone. Periodically, aliquots were withdrawn from the solution and examined by the gravimetric method of analysis. At the end of 1.0 hr., a precipitate of dinitrophenylhydrazine was obtained by this method; however, at the end of 3.0 hr., no precipitate formed.

D. *Kinetics.* 1. *Apparatus.* The reaction vessels used in these studies had the following specifications: the capacity of each vessel was 50–60 ml.; the walls were cylindrical, the bottom was flat, and the top was domed; attached to the top of each vessel was a Teflon stopcock with a 2-mm. bore through which a syringe could be inserted to introduce reagents or to withdraw samples.

All equipment was dried at 150° for a minimum of 8 hr. and was cooled to room temperature under vacuum before use.

2. *Reaction conditions.* Tetrahydrofuran was the solvent employed in these reactions and all kinetic studies were run at 30.00 ± 0.02°. The reactions were run in closed systems free from water and carbon dioxide. The reacting solutions were shaken in the water bath by means of a wrist-action shaker.

3. *Procedure.* Before starting a run, a measured volume of the standard organomagnesium solution in tetrahydrofuran was put into the vessel and, at zero time, the required volume of thermostatted benzonitrile (to give the desired benzonitrile:organomagnesium ratio) was added.

At regular intervals an aliquot was withdrawn from the reaction vessel and its basic concentration, N_t, was determined by the volumetric method of analysis. The values of N_t were then used to calculate the concentrations of reactants and products in the solution.

E. *Degree of association of diethylmagnesium in tetrahydrofuran.* Exactly 2.00 ml. of 0.2507 M fluorenone in tetrahydrofuran was allowed to come to equilibrium under isopiestic conditions with 25.12 ml. of 0.3219 M diethylmagnesium in tetrahydrofuran at 30.00°. The volume of the fluorenone solution increased to 2.05 ml. during the first 3 days, but remained constant thereafter. The final concentration of the organomagnesium solution was 0.3161 M as diethylmagnesium, and that of fluorenone was 0.2446 M.

RESULTS[18]

Analytical methods. Previous analytical methods for following the reaction of an alkylmagnesium with benzonitrile were rejected for the present investigation. Gasometric analysis[8] proved unwieldy and complicated. Ultraviolet spectrophotometric analysis of two Grignard-nitrile reactions required an arbitrary correction factor of 16%.[19]

Two relatively simple methods were developed, based on the knowledge that an ethylmagnesium compound reacts with benzonitrile to form a magnesium derivative of a ketimine. In method 1, aliquots of the reacting solutions were added directly to an acid solution of 2,4-dinitrophenylhydrazine. The ketimine salt was converted to the 2,4-dinitrophenylhydrazone, which was recrystallized, collected, and weighed.

In method 2, aliquots of the reacting solution were hydrolyzed in excess standard acid and back-titrated with base. Under the conditions used, the ketimine provided an equivalent of base (ammonia) in addition to those arising from hydrolysis of the Mg—C or Mg—N bonds. The nitrile did not interfere. Since both magnesium[20] and ammonium[21] hydroxides could be titrated to a Methyl Red endpoint, the consumption of ethyl groups could be followed by determining the increase in basicity.

The reliability of this method was tested. The average deviation of this method proved to be ±0.002 N and a comparison of the two methods of analysis showed them to give similar results.

The internal consistency of the results obtained in measurements of the stoichiometry of the reaction provided further evidence for the reliability of the volumetric method. This will be illustrated in section C.

B. *Calculations.* The initial concentration of organomagnesium in the reaction solution was of necessity calculated indirectly. Two procedures were used to obtain this value.

The first procedure involved the removal and hydrolysis of three or more samples during the first few minutes of reaction. The basic concentration, N_t, of each aliquot was determined, and a graphical plot of N_t *vs.* t (time) was made. Then, assuming that the rate of formation of ketimine was constant during this part of the reaction (less than 10% of the reaction had occurred), a straight line was constructed through these points and extrapolated back to zero time (t_0) to give the initial basic concentration, N_0.

The second procedure for determining N_0 required a knowledge of the stoichiometry of the reaction and of the final basic concentration, N_f. For example, if there were m equivalents of ethyl groups originally in a reacting solution, and if these reacted with n equivalents of benzonitrile, then since each equivalent of ketimine produces one

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(17) H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, **47**, 4002 (1925).

(18) More extensive detailed kinetic data, calculations, and graphs may be found in the reference cited in footnote 1.

(19) J. Vekemans, Dissertation for the degree Docteur en Science, Université Catholique de Louvain, Louvain, Belgium, January 1958. J. Vekemans and A. Bruylants, *Bull. soc. chim. Belges*, **68**, 541 (1959).

(20) H. Gilman, P. D. Wilkinson, W. P. Fishel, and C. H. Meyers, *J. Am. Chem. Soc.*, **45**, 150 (1923).

(21) I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," revised ed., The Macmillan Co., New York, 1947, pp. 562–564.

equivalent of base on hydrolysis. This will be discussed further in the next section.

Using the value $N_t - N_0$, which is equal to the concentration of ketimine formed, it was possible to calculate the concentrations of the reactants as a function of time.

C. *Stoichiometry of the reaction.* In the reaction of benzonitrile with diethylmagnesium or with ethyl magnesium bromide (in tetrahydrofuran at 30°), the benzonitrile was quantitatively converted to the ketimine only when there were initially at least two ethyl groups present for each benzonitrile molecule. Thus, Equation 3 was found to hold when $n/m = 0.125$–0.250.

$$N_0 = \frac{m}{(m + n)} N_f \tag{3}$$

On the other hand, when there were less than two ethyl groups available for each benzonitrile (in practice, $n/m = 0.75$–3.99), the average value for N_f/N_0 was 1.52 ± 0.02. Since N_0 equals the original concentration of ethyl groups, and since $N_f - N_0$ equals the concentration of ketimine produced, this suggests that only half of the available ethyl groups are capable of converging benzonitrile to propiophenone ketimine under these conditions.

D. *Reactivity of organomagnesium–benzonitrile and organomagnesium–propiophenone compounds.* The reactivity of the remaining ethyl groups in the reaction products of benzonitrile with diethylmagnesium and with ethylmagnesium bromide were investigated. Both reaction products gave negative Gilman tests, and the diethylmagnesium–benzonitrile product did not further react with propiophenone. On the other hand, the diethylmagnesium–benzonitrile adduct was capable of further reaction with benzaldehyde to form ethylphenylcarbinol.

In another study, over half of the ethyl groups in diethylmagnesium were found to react with propiophenone, suggesting that the diethylmagnesium-propiophenone product could further react with propiophenone.

E. *Kinetics of the reaction of diethylmagnesium with benzonitrile.* Since the reaction of Grignard reagents with nitriles has been described as being first order with respect to each reagent,[8,19] it seemed reasonable to seek a similar dependency in the reaction between diethylmagnesium and benzonitrile. The appropriate plots were constructed for several runs, and rate constants were calculated by the method of least squares. In no case did the line representing the rate constant pass through the experimental points and the origin of the graph.

It was noted, however, that straight lines could be drawn through the points taken during the first 30% of the reaction or during the last 40%. The line connecting the initial points in each graph passed through the origin and the second line intersected the first one near the calculated value for 50% reaction (see Fig. 1). The decision to construct two straight lines was admittedly arbitrary; however, since these lines did fit the data and since no other simple rate equation could be found to do so, the assumption that two distinct reactions were occurring seemed reasonable. Consequently, each half of the over-all reaction was studied separately.

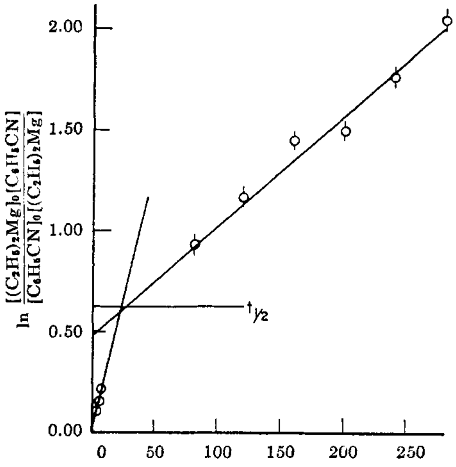

Fig. 1.—Second-order plot of the reaction between benzonitrile and diethylmagnesium (run 16)

1. *The first half of the reaction.* Several rate equations were proposed to fit the data for the first half of the reaction (see Table I). Only those rate equations which assumed the reaction to be first-order in benzonitrile were found to be valid when the initial concentration of diethylmagnesium was held constant. However, kinetics could not determine whether the reaction was first or second-order in diethylmagnesium monomer, or first order in diethylmagnesium dimer (the possibility that diethylmagnesium might exist as a dimer is based on the suggestion of Zeil[22]). The complexity of the reaction was further indicated by the fact that these calculated rate constants varied as the initial concentration of diethylmagnesium was changed.

2. *The second half of the reaction.* Of the several rate equations that were proposed to fit the data for the last portion of the reaction, only two were found to give linear graphical plots: one which was first-order each in diethylmagnesium monomer and benzonitrile, and one which was first-order only in diethylmagnesium monomer (see Table II). However, since the rate constants for these rate equations were calculated from experimental points taken when the over-all reaction was 65–90% complete,[23] only crude conclusions could be drawn

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(22) W. Zeil, *Z. Elektrochem.*, 56, 789 (1952).

(23) Subsequent calculations have shown that, assuming a consecutive, competitive second-order reaction, the first portion of the reaction is 99% complete when the over-all reaction is about 70% complete. It was therefore necessary to calculate rate constants for the latter portion of the reaction in the region chosen if the mechanism for the first portion of the reaction was to be ignored.

TABLE I

CALCULATION OF INITIAL RATE CONSTANTS

Case	Assumed Reaction	Assumed Rate Equation	Units of k
I.	$(C_2H_5)_2Mg + C_6H_5CN \longrightarrow$ product.	Rate $= k[(C_2H_5)_2Mg]\,[C_6H_5CN]$	l./mole-sec.
II.	$2(C_2H_5)_2Mg + C_6H_5CN \longrightarrow$ product $+ (C_2H_5)_2Mg$	Rate $= k[(C_2H_5)_2Mg]^2[C_6H_5CN]$	l.^{2}/mole^2-sec.
III.	$[(C_2H_5)_2Mg]_2 + C_6H_5CN \longrightarrow$ product	Rate $= k[[(C_2H_5)_2Mg]_2][C_6H_5CN]$	l./mole-sec

Run	$[C_2H_5]$ at t_0	$[C_6H_5CN]$ at t_0	$[C_6H_5CN]/[C_2H_5]$ at t_0	Calculated Rate Constants, Case I	II	III
17	0.414	0.106	0.250	0.00036	0.0020	0.00089
14	0.368	0.368	1.00	0.00031	0.0021	0.00081
11	0.399	0.798	2.00	0.00032	0.0020	0.00083
16	0.368	1.463	5.99	0.00034	0.0022	0.00082
19B	1.104	0.138	0.125	0.00052	0.0011	0.00122
20	1.092	0.273	0.250	0.00047	0.0011	0.00128

TABLE II

CALCULATION OF FINAL RATE CONSTANTS

Case	Assumed Reaction	Assumed Rate Equation	Units for k
I.	$(C_2H_5)_2Mg + C_6H_5CN \longrightarrow$ product	Rate $= k[(C_2H_5)_2Mg][C_6H_5CN]$	l./mole-second
IV.	$(C_2H_5)_2Mg + (C_6H_5CN) \longrightarrow$ product	Rate $= k[(C_2H_5)_2Mg]$	l.$^{-1}$

Run	$[C_2H_5]$ at r_0	$[C_6H_5CN]$ at t_0	$[C_6H_5CN]/[C_2H_5]$ at t_f	Calculated Rate Constants, Case I	IV
18	1.092	0.854	0.56	0.00012	0.00005
15	0.368	0.368	1.00	0.00015	0.00003
7	0.408	0.705	2.46	0.00019	0.00010
9	0.399	0.798	3.00	0.00013	0.00009
16	0.368	1.463	6.95	0.00007	0.00009

about their consistency over a wide range of concentrations.

According to the data in Table II, the rate constant for case I remains consistent through most of the range of concentrations tested, and appears to decrease when a large excess of benzonitrile is used. On the other hand, the rate constant for case IV approaches a maximum as the ratio of benzonitrile to ethyl groups increases.

F. *Degree of association of diethylmagnesium in tetrahydrofuran.* Solutions of diethylmagnesium and of fluorenone in tetrahydrofuran were allowed to come to equilibrium under isopiestic conditions at 30°. At equilibrium, the concentrations of diethylmagnesium (expressed as the monomer) and of fluorenone were found to be 0.3161 M and 0.2446 M, respectively.

If diethylmagnesium is assumed to exist partially as a dimer in solution—recognizing the fact that other assumptions may also be proposed to account for the observed results—it is possible to calculate an equilibrium constant for a monomer-dimer association. To illustrate, if $2M \rightleftharpoons D$, and $K = D/M^2$, where M represents the concentration of diethylmagnesium in the monomeric form, D its concentration in dimeric form, and K the corresponding equilibrium constant, then

$$M = 0.1731,\ D = 0.0715,\ \text{and } K = 2.38$$

G. *Kinetics of the reaction of ethylmagnesium bromide with benzonitrile.* Inasmuch as only half of the ethyl groups in ethylmagnesium bromide were found to react with benzonitrile, no effort was made to define the reaction as being first order in ethylmagnesium bromide and in benzonitrile. Instead, an attempt was made to determine whether the reaction was first order each in diethyl magnesium–magnesium bromide and in benzonitrile. However, second order plots (see Fig. 2) showed that a straight line could not be constructed to pass through all of the points and through the

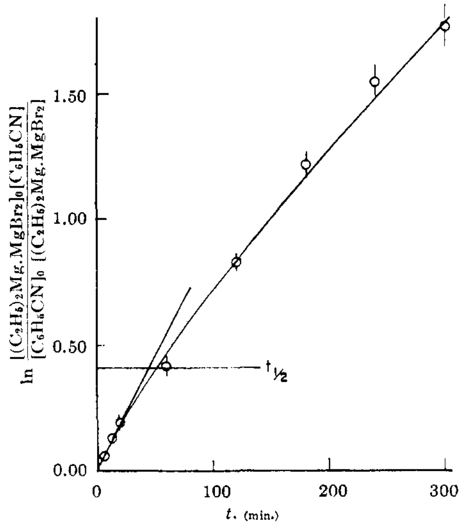

Fig. 2.—Second-order plot of the reaction between benzonitrile and ethylmagnesium bromide (run 36)

origin. Rather, the distribution of points suggested that the rate constant so defined decreased as the reaction progressed. Attempts were made to find a rate equation which could account for the results obtained, but without success. It was noted, however, that a straight line could be constructed through the points representing the first 30% of reaction and through the origin. Consequently, kinetic studies were directed primarily to this phase of the reaction.

In order to provide a correlation between diethylmagnesium reactions and Grignard reactions, the concentration of ethyl groups was calculated as if it were present only in the form $[(C_2H_5)_2Mg]_2$. Rate constants for the initial reaction were then calculated by assuming the reaction to be first-order each in benzonitrile and in $[(C_2H_5)_2Mg]_2$. The results are given in Table III.

TABLE III

CALCULATION OF THE RATE CONSTANT (k) WHERE RATE = $k[[(C_2H_5)_2Mg]_2][C_6H_5CN]$[a]

Run	A_0	B_0/A_0	$[Br_0]/(C_2H_5)$	$k \times 10^3$
17	0.106	1.00	0.000	0.89
21A	0.121	1.10	0.000	0.83
21B	0.121	1.00	0.000	0.82
12	0.092	3.90	0.000	0.81
14	0.092	4.00	0.000	0.81
10	0.100	8.02	0.000	0.86
11	0.100	8.02	0.000	0.83
16	0.092	15.90	0.000	0.82
Av.	0.103 ± 0.010			0.83 ± 0.02
28	0.139	1.00	0.000	0.92
23A	0.194	1.00	0.000	1.05
23B	0.194	1.00	0.000	1.13
Av.	0.194 ± 0.000			1.09 ± 0.04
19A	0.276	0.52	0.000	1.18
19B	0.276	0.50	0.000	1.22
22	0.281	0.50	0.000	1.29
20	0.273	1.00	0.000	1.28
Av.	0.276 ± 0.002			1.24 + 0.04
25A	0.148	1.00	0.074	1.04
25B	0.148	1.00	0.074	0.97
27A	0.149	1.00	0.200	1.22
27B	0.149	1.00	0.200	1.20
37	0.188	1.00	0.509	1.46
35	0.106	4.00	1.11	1.33
34	0.115	1.03	1.11	1.07
36	0.118	4.00	1.03	1.57
38	0.145	1.00	1.49	1.64
32	0.166	3.20	1.11	2.93
29A	0.170	1.00	1.01	2.21
29B	0.170	1.00	1.01	2.12
31B	0.174	4.00	1.04	2.50

[a] Key: k = l./mole-sec.; $A_0 = [(C_2H_5)_2Mg]_2$ at t_0; $B_0 = [C_6H_5CN]$ at t_0; $[Br_0]/(C_2H_5)_0$ = ratio at t_0.

Certain observations could be made from these data. First, when A_0 and $[Br_0]/[(C_2H_5)_0]$ were held constant, k was independent of B_0/A_0. Second, k increased as A_0 or as $[Br_0]/[(C_2H_5)_0]$ was increased.

The method of synthesizing the Grignard reagents apparently had little, if any, effect on the rate constants obtained. For example, the reagents used in Runs 29A, 29B, and 36 were prepared by adding tetrahydrofuran to an ether solution of ethylmagnesium bromide and removing the ether by fractional distillation. The reagents used in runs 31B and 32 were prepared directly from magnesium and ethyl bromide in tetrahydrofuran and those used in runs 34 and 35 were made by adding magnesium bromide etherate to a diethylmagnesium solution in tetrahydrofuran and distilling the ether from the reagent.[18] Comparison of the rate constants obtained in runs 34, 35, and 36, or those obtained in runs 29A, 29B, 31B, and 32, indicated that the source of the reagent was of little importance on the kinetics of the reaction.

DISCUSSION

Several experimental systems were examined before selecting this system for study. Benzonitrile was selected because it reacts relatively slowly with Grignards, and because it does not undergo significant side reactions. Tetrahydrofuran was used as the solvent because of its ability to keep the reactants and products in solution. Ether was unsuitable since acetone, benzophenone, and benzonitrile, each with ethylmagnesium bromide in ether, gave precipitates during the course of reaction.

In the reaction of diethylmagnesium or of ethylmagnesium bromide with benzonitrile in tetrahydrofuran, only half of the ethyl groups were found to undergo reaction. These results not only confirmed the hypothesis that there should be a difference in reactivity of the ethyl groups in these organomagnesium compounds (although we did not anticipate so great a difference), but it considerably simplified the subsequent kinetic studies.

The nonreactivity of the second ethyl group led to tests of its possible reaction with other "Grignard active" compounds. A selectivity was found. The second alkyl group did not react with benzonitrile, Michler's ketone, or propiophenone, but did react with benzaldehyde.

It was especially interesting to discover that the unchanged ethyl groups in the diethylmagnesium-benzonitrile and ethylmagnesium bromide–benzonitrile addition products could not be detected by the Gilman test.[17] In his study of the relative reactivities of Grignard reagents with nitriles in ether, Gilman[24] employed this test to determine when the reactions were complete. Of course, the results obtained in tetrahydrofuran do not prove that similar results would occur in ether; on the other hand, the results do provide sufficient reason

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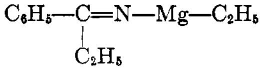
(24) H. Gilman, E. L. St. John, N. B. St. John, and M. Lichtenwalter, *Rec. trav. chim.*, **55**, 577 (1936).

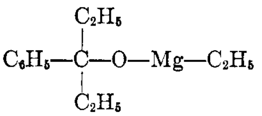
to question the assumption that Grignard reagents react quantitatively with nitriles in ether.

The low reactivity of the second ethyl group in the reaction with nitriles, as compared to what is normally seen in the reaction with ketones, may be explained by applying Swain's mechanism[8] to each reaction. If the first step in the reaction of the second ethyl group of these monoaddition products with a second mole of nitrile or ketone involves the rapid and reversible formation of a complex, then the relative reactivities of these monoaddition products may depend upon the electron deficiencies of their respective magnesium atoms. A comparison of the monoaddition products of diethylmagnesium with benzonitrile (A) and with propiophenone (B)



$C_6H_5{-}C(C_2H_5){=}N{-}Mg{-}C_2H_5$

A



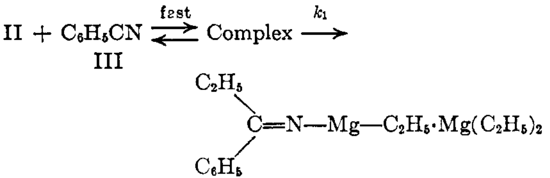
$C_6H_5{-}C(C_2H_5)_2{-}O{-}Mg{-}C_2H_5$

B

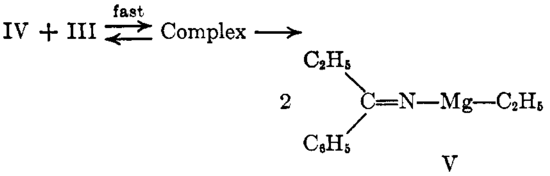
suggests that the electron deficiency of the magnesium atom in A will be more readily satisfied internally, so that A will be less likely to complex with a second mole of nitrile or ketone than with B.[25] This is a matter of degree since benzaldehyde does react with A although benzonitrile and propiophenone do not, while propiophenone can react with B.

Kinetically, the reaction of diethylmagnesium with benzonitrile follows no simple rate law. A plot employing first-order dependence on diethylmagnesium shows that the reactive ethyl groups are consumed at two different rates (see Fig. 1). The data thus require that three reactivities for the ethyl groups be rationalized by the mechanism; two which have different reactivities and one which is unreactive depending upon the stage of the reaction. A dimer of diethylmagnesium appears to be the simplest entity to fit these requirements. Since the molecular weight suggests that diethylmagnesium may be in equilibrium with its dimer, the following sequence of steps may be projected:

$$\underset{\mathrm{I}}{2(C_2H_5)_2Mg} \rightleftharpoons \underset{\mathrm{II}}{[(C_2H_5)_2Mg]_2} \qquad (4)$$



$$\mathrm{II} + \underset{\mathrm{III}}{C_6H_5CN} \overset{\text{fast}}{\rightleftharpoons} \text{Complex} \xrightarrow{k_1} \underset{\mathrm{IV}}{(C_2H_5)(C_6H_5)C{=}N{-}Mg{-}C_2H_5 \cdot Mg(C_2H_5)_2} \qquad (5)$$



$$\mathrm{IV} + \mathrm{III} \overset{\text{fast}}{\rightleftharpoons} \text{Complex} \longrightarrow 2\,\underset{\mathrm{V}}{(C_2H_5)(C_6H_5)C{=}N{-}Mg{-}C_2H_5} \qquad (6)$$

(or a dimer)

The equilibrium that apparently exists between the monomeric and dimeric forms of diethylmagnesium complicates the kinetic study of the reaction with benzonitrile since no convenient method is currently available to measure directly the actual concentration of either species of diethylmagnesium in solution. It is possible, however, to solve this problem by indirect means, and the following paragraphs will describe the method employed.

First, rate constants were calculated for the

$$\text{Rate} = kAB, \qquad (7)$$

where A was the *total* concentration of diethylmagnesium present, assuming the dimeric form, and B was the concentration of unchanged benzonitrile. A new rate equation,

$$\text{Rate} = k_i DB, \qquad (8)$$

was set up in which D represented the actual concentration of I present, and k_i was the corresponding rate constant. The rate of reaction being independent of the rate equation proposed to account for it, it was possible to combine equations 7 and 8 to solve for k_i:

$$k_i = kA/D = k/Q \qquad (9)$$

where

$$Q = D/A \qquad (10)$$

Expressing A in terms of the concentrations of the dimer D and the monomer M, and assuming an equilibrium between monomer and dimer, there are then

$$A = D + {}^1/_2M, \qquad (11)$$

and

$$K = \frac{D}{M^2} \qquad (12)$$

Combining equations 10, 11, and 12 gives K in terms of A and Q.

$$K = \frac{Q}{4A(1 - Q)^2} \qquad (13)$$

The values for k_i and K may now be calculated. Let k represent the rate constant for a run in which the initial concentration of diethylmagnesium is A, and let k' be the corresponding value for A'. Then, from equation 9,

$$\frac{k'}{k} = \frac{Q'}{Q} \qquad (14)$$

and, from equation 13,

$$\frac{(1 - Q)^2}{(1 - Q')^2} = \frac{A'/A}{Q'/Q} \qquad (15)$$

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[25] It is recognized, of course, that the electron-deficiency of the magnesium atom is compensated for in solution by the presence of the solvent molecules—ether or tetrahydrofuran. However, the oxygen atoms of either solvent are probably not as basic as that of propiophenone and should be displaced readily. Consequently, no attempt has been made to include the solvent molecules in the equations.

equations 14 and 15 may then be combined and solution for Q gives

$$Q = \frac{(A'/A)^{1/2} - (k'/k)^{1/2}}{(k'/k)(A'/A)^{1/2} - (k'/k)^{1/2}} \tag{16}$$

Once Q is known, k_1 and K may then be calculated by using equations 9 and 13, respectively.

Using data averages given in Table 3, Q was calculated and gave values of $Q_{av} \pm 0.38 \pm 0.05$. The value of Q' for each of the other concentrations was calculated by introducing Q_{av} into equation 9 and the values of K were calculated using equation 8 to give the value $K_{av} = 2.5 \pm 0.2$. Finally, the value for k_1 was calculated from equation 6 and was found to be $k_t = 2.2 \times 10^{-3}$ l./mole-sec.

To check the equilibrium constant for diethylmagnesium by some nonkinetic means, the isopiestic method of determination was used, since the conditions of the measurement approximated those of the reactions. The equilibrium constant calculated by this technique, 2.4, proved to be in agreement with the value calculated from kinetic determinations.

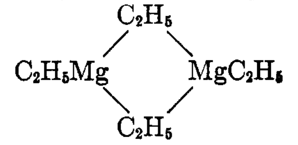
The mechanism given in equations 5 and 6 implies consecutive competitive second-order reactions and, consequently, cannot be solved without resorting to certain approximations. Preliminary calculations show that the first step of the reaction is over 99% complete when the over-all reaction is about 70% complete; it was therefore decided to study the second step in the region where the over-all reaction was 60–85% complete. Calculation of the concentration of IV during this portion of the reaction was simplified by the fact that, if the first step is assumed to be complete, this concentration is numerically identical to the calculated concentration of unchanged diethylmagnesium.

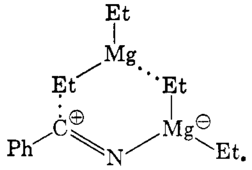
Assuming the mechanism described by equation 6 to be correct, the rate equation for this step of the reaction is then

$$\text{Rate} = k_{tt}\,[\text{III}]\,[\text{IV}] \tag{17}$$

The values for k_{tt} have been calculated in Table II. It is interesting to note that equation 17 is applicable primarily when the ratio of III/IV is small; as the ratio is increased, the reaction becomes first order in IV and zeroth order in III.

These results are in accord with the mechanism proposed in equation 6. It may be assumed that III and IV combine rapidly and reversibly, and in relatively low conversion, to give the intermediate complex which then rearranges to give the product V. This mechanism suggests a second order reaction only so long as the relative concentrations of III and IV are of the same order. If the concentration of one component, III in this case, becomes considerably greater than that of the other, it may be expected that the equilibrium will be shifted to favor the formation of the complex. Then, the concentration of complex will be numerically equal to that calculated for IV and the reaction will follow first-order kinetics. Thus, when the second step follows second-order kinetics, the rate constant k_{tt} is 1.5×10^{-4} l./mole-sec; when the second step follows *pseudo*-first-order kinetics, the rate constant k'' is 9.3×10^{-5} sec.$^{-1}$.

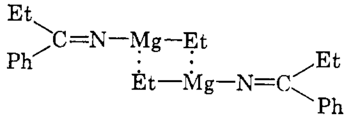
Some speculation may be made regarding the structures of the reactants, intermediates and products of equations 5 and 6. Zeil[22] had originally suggested that an equilibrium between the monomeric and dimeric forms of diethylmagnesium might exist and proposed that  $C_2H_5Mg\overset{C_2H_5}{\underset{C_2H_5}{\diamond}}MgC_2H_5$ best described the structure of the dimer. The rapid, reversible reaction of the dimer II with benzonitrile III to give the complex may be regarded as an acid-base reaction in which the electron-rich nitrogen of III displaces an ether of solvation from one of the magnesium atoms of II to give complex VI.



VI

The rate-determining step of equation 5 then involves the rearrangement of VI, possibly by a cyclic mechanism to give IV.

Similarly, the reaction of IV with a second molecule of III to give the complex VII may be explained by assuming it to be an acid-base reaction. Rearrangement of VII to give the product V is best described as involving a four-center reaction, so that V possesses the structure shown.



Kinetically, it makes no difference whether V is really a dimer, as depicted, or a monomer; however, the assumption of a dimeric product also serves to explain the relative stability of the unreacted ethyl groups.

Before attempting to propose a mechanism for the Grignard reaction studied, some understanding of the structure of the Grignard reagent is necessary. It is believed that the Grignard reagent consists of a complex mixture of several species in equilibrium with each other. The following series of equations, which are a modification of those proposed by Zeil[22] and Dessy[4,6] are proposed to describe best the constitution of the reagent:

$$(R_2Mg)_2 \rightleftharpoons 2R_2Mg; \qquad (18a)$$

$$(MgX_2)_2 \rightleftharpoons 2MgX_2; \qquad (18b)$$

$$R_2Mg + MgX_2 \rightleftharpoons R_2Mg{\cdot}MgX_2; \qquad (18c)$$

$$R_2Mg{\cdot}MgX_2 \xrightarrow{\text{electrolysis}} RMg^+ + RMgX_2^-(?) \qquad (18d)$$

These equations satisfactorily account for the nonequivalency of magnesium,[4] the increase in apparent molecular weight of the Grignard reagent with rising concentration,[26] the dissociation products on electrolysis,[5] the independence of the ratio of diethylmagnesium to "RMgX" as a function of the total Grignard reagent present,[3] and the presence of magnesium halide in its dimeric form.[22] The hypothesis that dialkylmagnesium exists in part as a dimer is also included in these equations.

It seems reasonable to assume that if diethylmagnesium is present in a Grignard reagent, at least part of the reaction should proceed through this intermediate. Examination of Figure 2 suggests that this must be the case since, if it were absent, a straight line should have been obtained.

On the other hand, it is doubtful that I is the sole reactive species, since about a threefold increase in k was found with an increase in the $[Br_0/(C_2H_5)_0]$ ratio from zero to one. This rise cannot be attributed solely to an enhancement in reactivity of benzonitrile by magnesium bromide since excess magnesium bromide did not cause any further increase in the rate constant. Possibly, the rise in the rate constant may come from a shift in equilibrium from $[(C_2H_5)_2Mg]_2$ to (C_2H_5)-$Mg.MgBr_2$ (VIII) or to changes in dielectric constant of the medium as the reaction proceeds. These alternatives have not been differentiated in the present study.

Acknowledgment. We wish to thank the Eastman Kodak Co., Inc., for generous support for one of us (S.J.S.).

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(26) J. Meisenheimer and W. Schlichenmaier, *Ber.*, **61**, 720 (1928).

A Study of Alkyl Nitratocarbonates. An Improved Synthesis of Nitrate Esters

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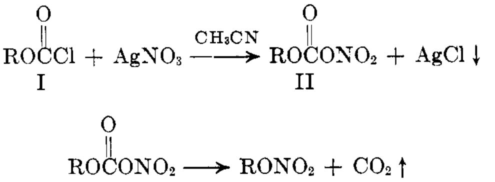
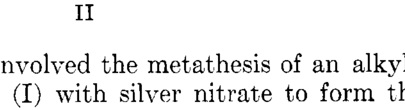
An alkyl nitratocarbonate, postulated as an unstable intermediate in the reaction of silver nitrate with an alkyl chloroformate, has been prepared in solution by using a catalyst in the cold. It decomposes completely upon warming to room temperature to give an alkyl nitrate and carbon dioxide. The pyridine-catalyzed reaction of silver nitrate with alkyl chloroformates constitutes a quick, mild, quantitative synthesis of alkyl nitrate esters.

In connection with studies of this laboratory, it became of interest to attempt the preparation and isolation of alkyl nitratocarbonates (II). After this work had been begun, Boschan's[1] work was published in which he shows that the nitratocarbonate structure is unstable and decomposes by an intramolecular cyclic mechanism to give alkyl nitrate and carbon dioxide. The synthesis and decomposition of a nitratocarbonate appeared to be stepwise, as follows:



$$\underset{\text{I}}{RO\overset{O}{\overset{\|}{C}}Cl} + AgNO_3 \xrightarrow{CH_3CN} \underset{\text{II}}{RO\overset{O}{\overset{\|}{C}}ONO_2} + AgCl\downarrow \qquad (1)$$



$$\underset{\text{II}}{RO\overset{O}{\overset{\|}{C}}ONO_2} \longrightarrow RONO_2 + CO_2\uparrow \qquad (2)$$

Step 1 involved the metathesis of an alkyl chloroformate (I) with silver nitrate to form the nitratocarbonate as an unstable intermediate (II) which then decomposed in step 2. Boschan believed that II had a finite lifetime since the kinetics of the over-all reaction were slightly less than second order.

In order to be able to prepare II, it seemed advisable to separate kinetically the two proposed steps of the reaction and to determine their relative rates. One way of determining the rate of step 1 is to follow the disappearance of chloroformate I in the reaction mixture. This could be done by vapor chromatography. The over-all rate of steps 1 and 2 could be followed by evolution of carbon dioxide. In addition to the rate information, vapor chromatography would also give a product analysis.

Using this approach, some preliminary experiments were carried out in acetonitrile using n-propyl chloroformate. Boschan's results were confirmed. In addition, it was found that reaction 2 roughly paralleled reaction 1 at high temperatures (40°), but was much slower than reaction 1 at temperatures below zero. However, reaction 1 was too slow to be useful at these temperatures. It was reasoned that if step 1 could be made to proceed more rapidly at low tempera-

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[1] R. Boschan, *J. Am. Chem. Soc.*, **81**, 3341 (1959).