

## Salt and Polar Effects in the Grignard Reaction. The Reaction of Arylmagnesium Reagents with Benzonitrile

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We have investigated the kinetics of the reactions of arylmagnesium reagents with benzonitrile in tetrahydrofuran. The two-part study involved an investigation of Hammett substituent polar effects on phenylmagnesium bromide at 30° and of a salt effect over a temperature range of 10–50°. In all cases, the rate followed simple second-order kinetics and the expected products were obtained. The rate of reaction of Grignard species was strongly dependent on the ratio of magnesium bromide to diphenylmagnesium over the temperature range of 10–50°. Furthermore, Arrhenius plots for the various concentration ratios produced curves which suggested specific mechanistic interpretations.  $\Delta H^\ddagger$ ,  $\Delta S^\ddagger$ , and  $\Delta F^\ddagger$  have been determined for five concentrations, which shed light on the nature of the transition state. *p*-CH<sub>3</sub>O-, *p*-CH<sub>3</sub>-, *p*-H-, *p*-F-, and *p*-Cl-substituted phenylmagnesium bromide were treated with benzonitrile and the rate constants correlated with Taft  $\sigma^\ddagger$  values. A  $\rho$  of -2.85 was obtained in keeping with the theoretical considerations of the phenyl carbanion character of phenylmagnesium bromide.

Although Victor Grignard discovered the organomagnesium reagent which bears his name over 60 years ago, the mechanism of its reactions and the structure of the reagent is still in question today. A breakthrough in the structural configuration occurred in 1957, when Dessy and co-workers<sup>3,4</sup> reported findings to show that the monomer "RMgX" did not exist in solution, but that the magnesium bonded to the R group was different from the magnesium bonded to the halide, and that the Grignard reagent must exist in the form R<sub>2</sub>Mg and MgX<sub>2</sub>. This interpretation of structure gave rise to a number of new investigations in the field, many<sup>5–16</sup> in agreement with the dimer structure and many not in agreement.<sup>17–23</sup> Whereas nuclear magnetic resonance and infrared studies give results which are conflicting,<sup>9,14,15,21</sup> vapor pressure measurements<sup>18,19</sup> and fractional crystallization experiments<sup>17</sup> tend to show the Grignard reagent as a monomer. In light of the above findings, Dessy re-

cently repeated and extended his original experiments, but without definitive result<sup>24</sup> and found that the Grignard reagent does have nonequivalent magnesium, which means the magnesium-carbon bond is not distinguishable from the magnesium-halide bond and that the first experiments are now subject to question.

In view of this state of conflicting evidence based on both physical measurements of the Grignard and mechanistic interpretations based on kinetic data, it appears that workers in the field agree<sup>13,17c</sup> that there is at present no conclusive evidence to accept either species. Part of the difficulty of understanding the mechanism of the Grignard reaction is due to the possibility of having different active organomagnesium species in solution which may vary as a function of solvent,<sup>23</sup> salt effects, nature of the R group, purity of materials, the substrate with which it is treated, concentration of Grignard,<sup>17b</sup> and temperature.

The purpose of this investigation was to study the rate of reaction of arylmagnesium reagents with the substrate, benzonitrile, as a function of purity of materials, temperature, and salt and polar effects. It was hoped that by altering the Grignard reagent in a systematic way more insight could be gained of the active species and the mechanism by which Grignard reagents react with benzonitrile in tetrahydrofuran.

### Experimental Section

**A. Starting Materials.** 1. **Bromobenzene.**—Fisher certified reagent grade bromobenzene was shaken with cold, concentrated sulfuric acid, followed by saturated bicarbonate, and finally with water. The material was then stored over anhydrous calcium chloride and finally distilled at 156° under argon into a storage bottle containing activated molecular sieves (Linde, Type 4A).

2. ***p*-Bromoanisole.**—Matheson Coleman and Bell *p*-bromoanisole was stored over anhydrous magnesium sulfate and then distilled into a dry storage bottle containing molecular sieves, bp 216°.

3. ***p*-Fluorobromobenzene.**—Pierce *p*-fluorobromobenzene was stored over molecular sieves and then distilled over dry argon at 152° into a storage bottle containing molecular sieves.

4. ***p*-Bromotoluene.**—Matheson Coleman and Bell *p*-bromotoluene was repeatedly fractionally crystallized at room temperature until only a white crystalline solid phase remained. The solid was then distilled at 185° over argon into an addition tube for use on a vacuum system.

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5. *p*-Chlorobromobenzene.—Matheson Coleman and Bell *p*-chlorobromobenzene was sublimed twice and then sublimed directly into an addition tube for use directly on a vacuum system, bp 196°.

All aryl halides, as well as ethers and benzonitrile were analyzed for purity by vapor phase chromatography. Only one peak was observed when the instrument was run at highest sensitivity.

6. Tetrahydrofuran.—Fisher certified grade tetrahydrofuran (THF) was shaken with successive portions of potassium hydroxide pellets until water white, then stored in a distillation flask which contained previously prepared phenylmagnesium bromide and distilled as needed prior to use.

7. Diethyl Ether.—Mallinckrodt diethyl ether was stored over active phenylmagnesium bromide, previously prepared, and distilled as needed prior to use.

8. Benzonitrile.—Fisher certified reagent grade benzonitrile was washed successively with cold, dilute hydrochloric acid, saturated sodium carbonate solution, dried over anhydrous sodium sulfate for 4 days, and then distilled at 190° (lit.<sup>25</sup> 190.7°).

9. Magnesium.—Ingots of sublimed magnesium (Dow) (reported to have the following analysis, in ppm: Al 3, Fe 100, Si 100, Ag 3, Sn 10, and Ti 0.09) were milled as described by Storfer.<sup>5</sup>

10. Dioxane.—Dioxane was purified according to the method of Fieser.<sup>26</sup>

11. 1,2-Dibromoethane.—Eastman White Label grade ethylene dibromide was distilled from phosphorus pentoxide at 131° into a storage vessel over argon.

12. Argon.—Prepurified argon (Matheson) was passed through a tower of copper wool at 500°, then bubbled through sulfuric acid, and finally passed through phosphorus pentoxide.

13. Phenylmagnesium Bromide.—Phenylmagnesium bromide was prepared by conventional bench-top techniques from bromobenzene and magnesium in THF over argon. At the completion of the reaction, the product was allowed to stir for 4 hr and was then filtered under positive pressure through a medium-porosity fritted-glass filter. The resultant solution was brown to amber and showed a Tyndall effect.

A high vacuum system was constructed utilizing a two-stage oil diffusion pump which could evacuate an all-glass reaction manifold down to below 10<sup>-5</sup> mm. It was used to prepare Grignard reagents according to the following procedures. (1) All-glass surfaces exposed to the preparation of Grignard reagent were degassed. (2) The magnesium turnings at temperatures high enough to sublime the magnesium were degassed. (3) All liquid solvents and reaction materials were degassed and purified by vacuum distillation. (4) The formation of Grignard reagent was then allowed to occur under the vapor pressure of THF. (5) The resulting Grignard reagent was then filtered through a sintered-glass funnel in the apparatus directly into a storage vessel without contacting the atmosphere. This was carried out in the apparatus shown in Figure 1.

By use of preheated charcoal, prepared according to Dushman,<sup>27</sup> the liquid aryl halides and ethers were effectively degassed so that trace amounts of oxygen were removed. In addition, the ethers and aryl halides were degassed by repeated freezing in liquid nitrogen and vacuum pumping. In all cases, the vacuum over the surface of the frozen liquid was allowed to reach at least 2 × 10<sup>-5</sup> mm before thawing and recycling the process. The liquids were cycled at least three times before final distillation into the reaction vessel. When the THF was vacuum distilled into the reaction flask containing the sublimed magnesium turnings, and the halide was added at ice-water temperatures, the reaction was started immediately without initiators. After final addition of the halide, the mixture was stirred for 4–6 hr at room temperature. Colorless, water-white phenylmagnesium bromide was obtained after filtration, which showed no Tyndall effect at concentrations of 0.8–1.0 N.

Similarly, colorless Grignard reagents free of Tyndall effects were obtained from *p*-bromotoluene, *p*-chlorobromobenzene, *p*-fluorobromobenzene, and *p*-bromoanisole.

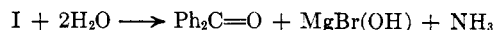
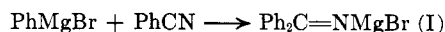
14. Diphenylmagnesium in THF.—The above vacuum system technique was used to prepare phenylmagnesium bromide

in diethyl ether. An equivalent amount of dioxane plus a 1% excess was slowly added to the Grignard and then stirred overnight. The ether was then replaced by THF by distillation according to the method of Storfer.<sup>5</sup>

15. Magnesium Bromide in THF.—1,2-Dibromoethane was added to magnesium turnings in THF using the high-vacuum system. When the barometer showed a positive ethylene pressure, the vacuum system was opened to the atmosphere through a molecular sieve drying tube. When the reaction was finished, the tube was placed 1 cm below the surface of clean mercury in a beaker so that the atmosphere would not back up at pressure equilibrium. A saturated solution of magnesium bromide was shown to be 0.476 *N* at 30.0° and gave a negative Michler's ketone test for active Grignard.<sup>28</sup>

16. Preparation of Organomagnesium Reagents with Variable Magnesium Bromide Concentration.—For organomagnesium reagents other than diphenylmagnesium and phenylmagnesium bromide prepared directly from bromobenzene, the calculated amount of magnesium bromide was added to a premeasured volume of known diphenylmagnesium or phenylmagnesium bromide. Thus, to obtain a solution of the ratio (Ph<sub>2</sub>Mg):(MgBr<sub>2</sub>) equal to 1.00:0.50, diphenylmagnesium was employed, and to obtain a solution of the ratio (Ph<sub>2</sub>Mg):(MgBr<sub>2</sub>) equal to either 1.00:1.35 or 1.00:1.62, the calculated amount of MgBr<sub>2</sub> solution was added to analyzed phenylmagnesium bromide solutions. All solutions were analyzed for bromide:arylmagnesium ratios. The upper level of bromide concentration was limited by the solubility of magnesium bromide in 0.380 *N* arylmagnesium in THF at 20.0° and this is the value 1.62 obtained above.

B. Methods of Analysis. 1. Kinetics.—The rate of formation of benzophenone ketimine magnesium bromide (I) was followed by the method of Storfer.<sup>5</sup> Upon hydrolysis, every molecule of bromomagnesium ketimine salt liberates one molecule of ammonia, one of benzophenone, and 1 equiv of magnesium hydroxide. Residual nitrile does not liberate ammonia in this mild hydrolysis. The ammonia was conveniently estimated by a simple acid base back titration.



As an independent check of the acid-base titration, the benzophenone formed was then converted to its dinitrophenylhydrazone according to the method of Storfer.<sup>5</sup> The two methods agreed within ±0.3% of each other.

2. Bromide Analysis.—Bromide was estimated argentometrically by a modified potentiometric method<sup>29</sup> using a silver wire, glass electrode, and a Beckman Zeromatic pH meter. An aliquot of halide-containing solution was syringed into ca. 25 ml of distilled water in a 100-ml beaker and gently boiled to codistill the volatile organic materials. The solution was then made acid with dilute nitric acid until the pH meter showed no additional reflection with added acid. Standard silver nitrate was then added from a buret with stirring and the deflection of the needle of the pH meter was observed. At the first excess of silver nitrate solution, an easily observable break was seen by a large swing of the needle. The high acid concentration essentially renders the glass electrode a constant potential reference electrode and the system is sensitive only to the silver-silver bromide potential. The author found that this method gave results of comparable precision and accuracy as the Volhard method. In addition, one less standard solution (KSCN) is required.

C. Kinetics. 1. Apparatus and Procedure.—Reaction vessels of approximately 25–50-ml capacity were used. A 2-mm bore Teflon stopcock, affixed at the top, was opened to introduce reagent, benzonitrile and to withdraw aliquots of the reaction mixture, during the course of the reaction. Becton-Dickinson 1-ml tuberculin syringes, which were accurate to 1%, were used with 15.25 cm, no. 22 gauge, stainless steel needles to withdraw samples. All equipment was dried overnight at 150° and allowed to cool in an argon atmosphere. After a known volume of assayed Grignard reagent was added to the vessel, the reaction vessel was placed in a mechanical wrist shaker and allowed to come to thermal equilibrium in a constant-tempera-

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ture water bath. At time zero, the benzonitrile was introduced and aliquots were withdrawn at measured intervals. The temperature of the water bath was controlled to  $\pm 0.02^\circ$ .

2. **Analytical Procedure.**—The aliquots of reaction mixture were syringed into a known excess of dilute sulfuric acid. The solution was then gently boiled to digest the magnesium salts, and back-titrated with standard base.

3. **Calculation of Data.**—A FORTRAN IV program was written for the IBM 7040 computer so that a rate constant could be conveniently computed using the method of least squares. The time and number of milliliters of base were read into the program in addition to the normality of the base and its acid equivalent. Second-order kinetics were assumed. In addition, all results were plotted graphically to check the linearity of the curves and to determine that no points had greater error than four times the standard deviation. All thermodynamic data were calculated both graphically and by the method of least squares.

## Results

Five diphenylmagnesium magnesium bromide solutions of varying arylmagnesium: $\text{MgBr}_2$  ratios were studied in reaction with benzonitrile in THF over a temperature span of  $10.0$ – $50.0^\circ$ . The reaction went to at least 90% completion based on the yield of ketone produced from diarylmagnesium, and the products remained in solution during each run. The reaction of Grignard reagents with benzonitrile has been reported to be second order by other workers,<sup>5,30–32</sup> first order in nitrile and first order in Grignard reagent.

We have found straight-line kinetics for the first 25% of the reaction, first order in benzonitrile and first order in either the monomer “ $\text{PhMgBr}$ ” or the dimer “ $(\text{PhMgBr})_2$ .” The slope curved downward from 25 to 90% reaction. For reason of comparison with diphenylmagnesium which must exist in the simplest form as  $\text{Ph}_2\text{Mg}$ , the data here are reported as the dimer  $\text{Ph}_2\text{Mg}\cdot\text{MgBr}_2$ . Owing to the complications of possible secondary kinetic effects after the first 25% of reaction, no attempt was made to utilize the data based on the 25–90% reaction. No implication based on kinetics is made about the nature of the bond between the  $\text{Ph}_2\text{Mg}$  and the  $\text{MgBr}_2$ , and no inference based on kinetic reaction order is made as to whether “ $\text{PhMgBr}$ ” or “ $\text{Ph}_2\text{Mg}\cdot\text{MgBr}_2$ ” is the actual reacting species in solution. At the temperature range the reaction was run, the second phenyl group of the dimer does not appear to be reactive enough in tetrahydrofuran to react with another molecule of benzonitrile, since one would expect the yield of final product to be in the range of 100–200% (calculated as the dimer).

Any mechanistic inferences about the reaction studies will be based on thermodynamic data such as Hammett and Arrhenius plots and  $\Delta S^\ddagger$ ,  $\Delta F^\ddagger$ , and  $\Delta H^\ddagger$ , which, it should be noted, do not depend upon intermediate equilibria before reaction, but on the difference between the initial reactants and the reaction complex. Thus “ $\text{PhMgBr}$ ” is the same, thermodynamically speaking, as  $0.5(\text{Ph}_2\text{Mg}\cdot\text{MgBr}_2)$ . The Schlenk formulation<sup>33</sup> has recently been found to be valid<sup>17b</sup> in THF and would rationalize any formulation of classical Grignard reagent formed from diphenylmagnesium bromide, *e.g.*



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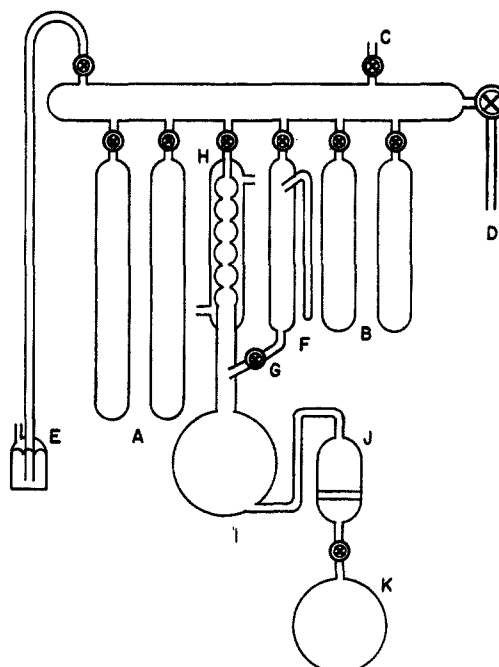


Figure 1.—High vacuum system: A, degassing tubes for solvent; B, degassing tubes for aryl halide; C, McLeod gauge; D, to vacuum and diffusion pump; E, mercury barometer; F, addition tube; G, Newman stopcock; H, water-cooled condenser; I, reaction flask; J, sintered-glass funnel; and K, storage vessel.

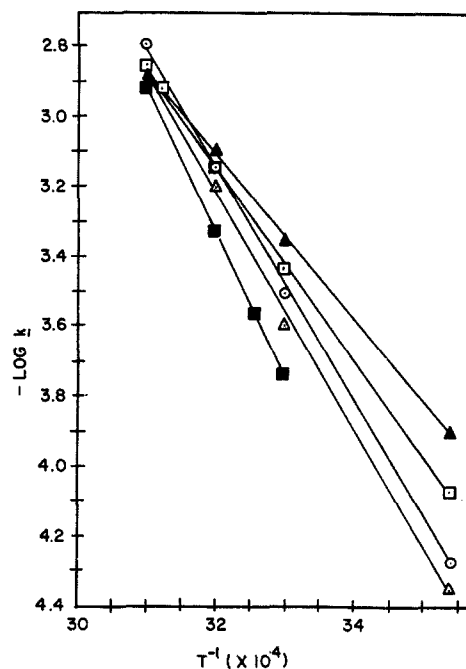


Figure 2.—Arrhenius plots of arylmagnesium reagents in reaction with benzonitrile in tetrahydrofuran:  $\blacktriangle$ ,  $\text{Ph}_2\text{Mg}$ ;  $\square$ ,  $\text{Ph}_2\text{Mg}\cdot 0.50\text{MgBr}_2$ ;  $\circ$ ,  $\text{Ph}_2\text{Mg}\cdot\text{MgBr}_2$  (Grignard reagent);  $\triangle$ ,  $\text{Ph}_2\text{Mg}\cdot 1.35\text{MgBr}_2$ ;  $\blacksquare$ ,  $\text{Ph}_2\text{Mg}\cdot 1.62\text{MgBr}_2$ .

The rate constants are given in Table I. The concentration of benzonitrile is either equal to the initial concentration of the diarylmagnesium or two times in excess. Table II lists the calculated activation energies, free energies of activation and the entropies of activation for the five linear plots of  $\text{Ph}_2\text{Mg}$ ,  $\text{Ph}_2\text{Mg}\cdot 0.50\text{MgBr}_2$ ,  $\text{Ph}_2\text{Mg}\cdot\text{MgBr}_2$  (Grignard reagent),  $\text{Ph}_2\text{Mg}\cdot 1.35\text{MgBr}_2$ , and  $\text{Ph}_2\text{Mg}\cdot 1.62\text{MgBr}_2$ . Figure 2 is a plot of  $1/T$  vs.  $\log k_{\text{rate}}$  for the various organomagnesium-magnesium halide reagents with benzonitrile.

TABLE I  
RATE CONSTANTS FOR THE REACTION OF BENZONITRILE WITH PHENYLMAGNESIUM  
REAGENTS OF VARYING SALT CONCENTRATION

Species	10°			20°			30°			40°			47.5°			50°		
	$k_{rate}^a$	$n^b$	b:c <sup>c</sup>	$k_{rate}^a$	$n^b$	b:c <sup>c</sup>	$k_{rate}^a$	$n^b$	b:c <sup>c</sup>	$k_{rate}^a$	$n^b$	b:c <sup>c</sup>	$k_{rate}^a$	$n^b$	b:c <sup>c</sup>	$k_{rate}^a$	$n^b$	b:c <sup>c</sup>
Ph <sub>2</sub> Mg	1.25 ± 0.030	6	1.0	4.45 ± 0.10	6	1.0	...	...	6.58 ± 0.20	4	1.0	...	...	...	13.4 ± 0.4	4	1	
Ph <sub>2</sub> Mg·0.500MgBr <sub>2</sub>	0.853 ± 0.009	3	1.0	3.66 ± 0.026	2	1.0	...	...	7.27 ± 0.19	2	1.0	...	...	...	14.0 ± 0.25	2	1	
Ph <sub>2</sub> Mg·1.00MgBr <sub>2</sub> <sup>d</sup>	0.54 ± 0.006	5	1.0	3.12 ± 0.053	17	1.0	...	...	7.63 ± 0.11	5	1.0	...	...	...	16.1 ± 0.08	5	1	
Ph <sub>2</sub> Mg·1.35MgBr <sub>2</sub>	0.452 ± 0.0	2	1.0	2.52 ± 0.11	3	1.0	...	...	6.54 ± 0.24	3	1.0	...	...	...	13.5 ± 0.15	2	1	
Ph <sub>2</sub> Mg·1.62MgBr <sub>2</sub>	...	...	...	1.86 ± 0.046	3	1.0	2.71 ± 0.018	3	1	4.76 ± 0.19	2	1.0	...	...	12.6 ± 0.20	3	1	

<sup>a</sup> × 10<sup>-4</sup> l. mole<sup>-1</sup> sec<sup>-1</sup>. <sup>b</sup> Number of runs. <sup>c</sup> Ratio of [PhCN]:[Ph<sub>2</sub>Mg]. <sup>d</sup> Grignard reagent.

The Arrhenius plot for all species except Ph<sub>2</sub>Mg·1.62MgBr<sub>2</sub> ranges from 10 to 50°. Because of the limited solubility of MgBr<sub>2</sub> in 0.380 *N* arylmagnesium solution at 20°, the temperature range was limited in this case to from 30 to 50° with four temperature determinations. Figure 3 is a plot of  $\Delta H^*$  vs.  $\Delta S^*$  which gives an isokinetic temperature of 42° (315°K).

TABLE II  
ACTIVATION ENERGIES OF ARYLMAGNESIUM REAGENTS IN  
REACTION WITH BENZONITRILE

Organomagnesium reagent	$E_a$ , kcal/mole	$\Delta H^*$ , kcal/mole	$\Delta F^*$ , kcal/mole	$\Delta S^*$ , eu
Ph <sub>2</sub> Mg	11.28	10.68	22.4	-39.9
Ph <sub>2</sub> Mg·0.500MgBr <sub>2</sub>	12.6	12.0	22.8	-35.6
Ph <sub>2</sub> Mg·MgBr <sub>2</sub>	14.3	13.7	22.6	-29.9
Ph <sub>2</sub> Mg·1.35MgBr <sub>2</sub>	15.6	15.0	22.8	-25.8
Ph <sub>2</sub> Mg·1.62MgBr <sub>2</sub>	18.8	18.2	22.9	-15.5

Four *p*-substituted phenylmagnesium bromide reagents were found suitable for kinetic studies with benzonitrile at 30°. A plot of  $\log k/k_0$  vs.  $\sigma$  (various values) was obtained. Taft<sup>34</sup>  $\sigma^0$  values gave a satisfactory straight-line plot for the four substituents which passes through the origin for H ( $\sigma$  0.0), whereas all other recent values<sup>35</sup> gave erratic results. The calculated  $\rho$  value for the reaction is -2.85. See Table III and Figure 4.

TABLE III  
RATE CONSTANTS FOR SUBSTITUTED PHENYLMAGNESIUM  
BROMIDE AND TAFT  $\sigma^0$  VALUES

Substituent	$k \times 10^4$ , l. mole <sup>-1</sup> sec <sup>-1</sup>	No. of runs	$\log k/k_0$	b:c <sup>a</sup>	$\sigma^{0b}$
<i>p</i> -CH <sub>3</sub> O	8.60 ± 0.094	4	0.441	1.0	-0.16
<i>p</i> -CH <sub>3</sub>	4.69 ± 0.16	5	0.177	1.0	-0.15
H	3.12 ± 0.085	17	0.00	1.0	0.00
		1		2.0	
<i>p</i> -F	0.740 ± 0.016	4	-0.624	1.0	+0.17
<i>p</i> -Cl	0.337 ± 0.0061	3	-0.966	1.0	+0.27
		1		1.2	

<sup>a</sup> Ratio of [PhCN]:[Ph<sub>2</sub>Mg]. <sup>b</sup> Reference 34.

### Discussion

Most of the physical chemical studies on Grignard reagents have been done with aliphatic groups attached to magnesium as opposed to aryl. Aryl Grignard reagents have probably been avoided owing to colloidal nature of the colored phenylmagnesium bromide solutions obtained by careful conventional methods, which usually yield clear, water white aliphatic reagents. In 1942 Evans and Pearson stated that "The colloidal nature of the aromatic Grignards is further shown by the dark color of their ether solutions and their pronounced Tyndall effect. Ethylmagnesium bromide and *n*-butylmagnesium bromide solutions were water white, optically clear liquids after settling through glass wool. The conclusion is that while aliphatic Grignards form true solutions, the aromatic Grignards are in part colloidal."<sup>36</sup> We have corroborated their results as to the colloidal nature of conventionally made phenylmagnesium bromide. Using

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the amber-to-brown phenylmagnesium bromide in reaction with benzonitrile we obtained rate constants which were different with each new batch (from 2.0 to  $2.5 \times 10^{-4}$  l. mole $^{-1}$  sec $^{-1}$ ). When the same pre-purified starting materials were subjected to the rigorous purification methods of the vacuum system technique, clear, water white solutions were obtained. The rate data obtained with these clear solutions were reproducible for 18 runs to  $\pm 2.7\%$  and yield a rate constant of  $3.12 \times 10^{-4}$  l. mole $^{-1}$  sec $^{-1}$ . The fact that the pure reagent was faster by this amount is an indication that the colloidal material slowed the rate, perhaps by decreasing the effective concentration of organometallic reagent, and was rate controlling. When crushed glass was added to the colloidal Grignard solution, the rate increased from  $2.2$  to  $2.6 \times 10^{-4}$  l. mole $^{-1}$  sec $^{-1}$ . Therefore, surface effects cannot be considered a prominent factor in the reaction mechanism, since the crushed glass increased the surface by a factor of  $6.7 \times 10^2$ .

Many impurities have been reported as side products in the Grignard reagent, most arising from oxygen and water in the starting materials. Some of the materials found have been magnesium phenoxides,  $\text{ROOMgX}$ ,  $(\text{MgX})_2\text{O}$ ,  $\text{Mg}_4\text{Br}_6\text{O} \cdot 4\text{C}_6\text{H}_{10}\text{O}$ , and  $\text{Mg}(\text{OH})\text{Br}$ .<sup>37-41</sup> It is quite feasible for the active Grignard to complex with one or all of the above oxygen-containing substances in such a way that the relative reactivity is decreased. Oxygen in the starting materials in small amounts can give rise to free-radical-initiated compounds such as were found by Platt<sup>42</sup> in amber-colored phenylmagnesium bromide. He isolated 2-phenyltetrahydrofuran and showed it to be absent from "vacuum line" produced Grignard reagent. When 2-phenyltetrahydrofuran is added to the colorless Grignard reagent, the latter turned amber upon standing. Workers have found polyaromatic, highly colored materials when benzene is refluxed in the presence of Lewis acids and oxygen.<sup>43</sup> Evans<sup>44</sup> electrolyzed alkylmagnesium halides and arylmagnesium halides to produce free radicals which then gave various coupling products. Whereas the aliphatic Grignard reagents yielded coupling or disproportionation products, the phenylmagnesium bromide solution yielded coupling products followed by an additional attack by radicals upon the coupled product to give as final products aromatic polyphenyls.

It would appear then that both aliphatic and aromatic Grignard reagents are susceptible to free-radical attack, and traces of oxygen and water give many side products capable of complexation, but that the aromatic free radical by-products are highly colored, and offer a built-in warning of impurity.

**Thermodynamics of Salt Effects.**—The Arrhenius plot of  $\log k_{\text{rate}}$  vs.  $1/T$  for the reaction of  $\text{Ph}_2\text{Mg}$  and  $\text{Ph}_2\text{Mg} \cdot \text{MgBr}_2$  with benzonitrile in THF showed an inversion point at  $42^\circ$  (Figures 2 and 4). It is generally believed that nitriles react faster with Grignard

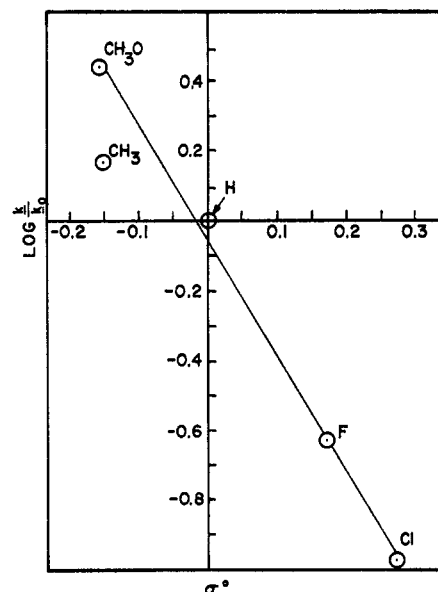


Figure 3.—A Hammett plot of *para*-substituted phenylmagnesium bromide in reaction with benzonitrile in tetrahydrofuran at  $30.0^\circ$ . The slope is equal to  $-2.85$ .

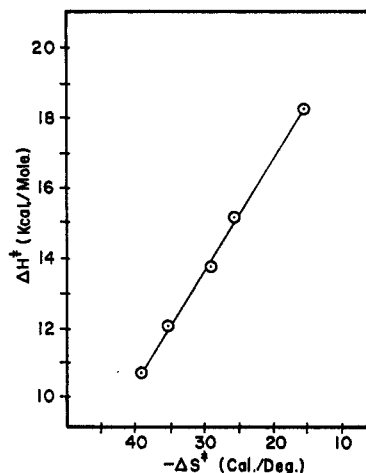


Figure 4.—An isokinetic relationship for the various arylmagnesium species in reaction with benzonitrile in tetrahydrofuran. The slope is equal to  $315^\circ\text{K}$ .

reagent than with  $\text{R}_2\text{Mg}$ . This is based on work by Storfer<sup>5</sup> and Gilman.<sup>45</sup> We find this true only at temperatures above the inversion point of  $42^\circ$  for the aromatic reagents.

Reactions of organomagnesium compounds with butynes,<sup>46</sup> ketones,<sup>6,47,48</sup> and benzylpyridines<sup>49</sup> are all faster with the species  $\text{R}_2\text{Mg}$  than with Grignard reagent and it seemed inconsistent to have the reverse phenomena with nitriles. Rochow<sup>50</sup> states, "The considerations in Chapter Two indicate that the carbon metal bond is more reactive in  $\text{R}_2\text{Mg}$  than in  $\text{RMgX}$ ." Chapter Two contains the theoretical considerations of organometallic bonds with respect to chemical reactivity based on electronegativity and per cent ionicity. The oft-quoted landmark investigation of Gilman and

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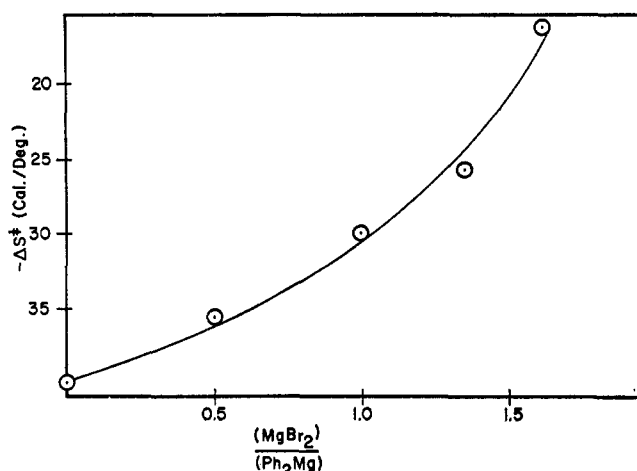


Figure 5.—A plot of  $(\text{MgBr}_2)/(\text{Ph}_2\text{Mg})$  vs.  $\Delta S^*$ .

Brown<sup>45</sup> may have been run above the inversion temperature. If this proves to be so, their conclusion that the Grignard reagents react more rapidly than diphenylmagnesium would be true only above the isokinetic temperature. The difference in the purity of materials and method of preparation have changed in the interim, and the method of analysis is now in question.<sup>5</sup>

Arrhenius plots can be used to obtain significant mechanistic interpretations about a reaction series. If a straight line is obtained when  $\log k_{\text{rate}}$  is plotted over a range of temperature, the series is following one reaction path or mechanism in that temperature interval.<sup>51</sup> We have obtained for five Arrhenius plots, five straight lines over the temperature interval 10–50° (see Figure 2). The slope of the Arrhenius plot for the reaction of diphenylmagnesium with benzonitrile is the smallest of all the series, and the slope increases for the other plots as a function of added magnesium bromide. A plot of  $\Delta H^*$  vs.  $\Delta S^*$  gives a straight line with a slope of 315°K or 42°. Bunnett<sup>52</sup> states that, when a straight-line relationship is observed for a plot of  $\Delta H^*$  vs.  $\Delta S^*$ , the reaction series all occur by the same mechanism. For our data this means that the classical Grignard reagent "PhMgBr," or  $(\text{PhMgBr})_n$  where  $n$  equals 2 or some small number, reacts over the temperature range in the same way, probably as an arylmagnesium carbanion, and that the magnesium bromide has a simple polarity effect and does not drastically change any mechanistic pathway by its presence.

The  $\Delta S^*$  and the  $\Delta H^*$  are consistent with this hypothesis. The entropy of activation for diphenylmagnesium is calculated to be -39.9 eu and, for diphenylmagnesium with a molar ratio of 1:1.62 of magnesium bromide, -15.5 eu. The Grignard reagent was found to have a  $\Delta S^*$  of -29.4 eu. These data show an entropy of activation which increases with increasing salt concentration. Assuming that the increasing salt concentration increases the polarity of the solvent (THF dielectric constant at 30°, 7.76<sup>53</sup>), the  $\Delta S^*$  values give a good indication of a transition state

in which the more polar the media, the easier a charged transition complex can be stabilized.<sup>54</sup>

A plot of the molar ratio of magnesium bromide to diphenylmagnesium versus  $\Delta S^*$  gives a smooth curve which shows a definite correlation between increasing salt concentration and increasing entropy of activation. We believe this effect is due to an increase in the polarity of the solvent as a function of added salt. Dessy and Jones<sup>55</sup> have measured the dielectric constants of diethylmagnesium and ethylmagnesium bromide in ether at 25°. They found a  $\epsilon$  of 6.6 and 11 for the reagents at 0.500 *N*, respectively. For a concentration of 1.00 *N* (or 0.500 *M* as the dimer), a dielectric constant of 35 was obtained. The dielectric constant of pure ethyl ether is about 4.3.<sup>56</sup> Hence, whereas diethylmagnesium increases the dielectric constant by a factor of 1.5, Grignard reagent increases the dielectric constant by a factor of 8.1.

A correlation between the dielectric constant of a solvent and the decreasing entropy of reaction has been shown by Pearson.<sup>57</sup> He has explained the decreasing negative entropy with decreasing polarity as due to a "freezing" of solvent molecules around the incipient ions in the activated complex. Nonpolar solvent media suffer a greater loss in entropy in such "freezing" than polar solvents (see Figure 5).

By inspection, the plot of  $\Delta S^*$  vs.  $(\text{MgBr}_2)/(\text{Ph}_2\text{Mg})$  is a smooth curve including the value for zero concentration of magnesium bromide. This is consistent with the assumption that diphenylmagnesium itself is the only species reacting during the early part of this reaction, or that it is the species largely reacting at this stage of the reaction. Essentially, then, the data point to diphenylmagnesium is the active reagent under these conditions. This would rule out any prereaction equilibria between active monomer  $\text{Ph}_2\text{Mg}$  and possible telomers as the rate-determining step.

Since  $\text{MgBr}_2$  is an ionic salt in aqueous media, it is possible that the salt in THF exerts only a simple Debye-Hückel salt effect. The dielectric constant of THF is comparable to that of diethyl ether (7.76 and 4.3, respectively), and ionization of  $\text{MgBr}_2$  should be similar in both solvents. Dessy<sup>55</sup> measured the specific conductance of  $\text{MgBr}_2$ ,  $\text{Et}_2\text{Mg}$ , and ethylmagnesium bromide in ether at 25°. He found a constant of  $0.092 \times 10^{-4}$  for 0.500 *M*  $\text{Et}_2\text{Mg}$ ,  $0.056 \times 10^{-4}$  for  $\text{MgBr}_2$  at 0.139 *M*, and  $2.26 \times 10^{-4}$  ohm<sup>-1</sup> cm<sup>-1</sup> for 0.500 *M*  $\text{Et}_2\text{Mg} \cdot \text{MgBr}_2$ . In water, 0.10 *M*  $\text{MgBr}_2$  has a specific conductance<sup>58</sup> of approximately 0.01 ohm<sup>-1</sup> cm<sup>-1</sup>, which means that the ionization of  $\text{MgBr}_2$  in THF is suppressed by a factor of approximately  $5 \times 10^{-4}$ . It is interesting to note that Dessy comments on this increased ionization of ethylmagnesium bromide over the separate ionization of  $\text{MgBr}_2$  and diethylmagnesium solutions as support for a Lewis acid-base ionization of the dimeric species  $\text{Et}_2\text{Mg} \cdot \text{MgBr}_2$ . We believe the polarity effect of added  $\text{MgBr}_2$  to  $\text{Ph}_2\text{Mg}$  in THF to be similarly due to a Lewis acid-base type of interaction.

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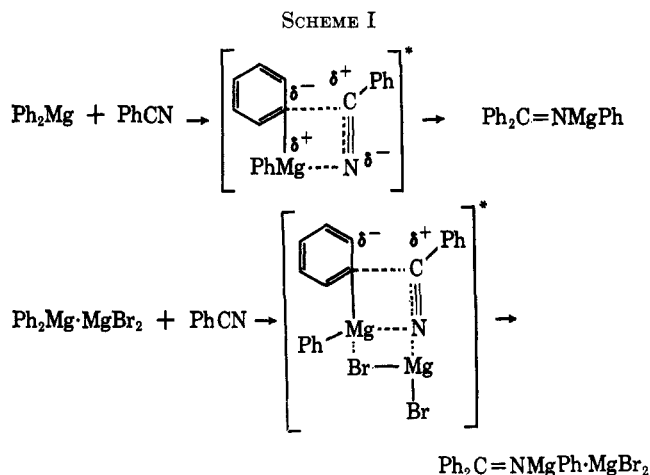
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A mechanism which is consistent with the data for the  $\Delta S^*$  is that in which  $MgBr_2$  helps to increase the polarity and hence decrease the order of the transition state by dispersing the charge which develops from the rearrangement of electrons in the activated complex, *e.g.*,<sup>59</sup> Scheme I.



Most Hammett  $\sigma$  values deal with the combined inductive and resonance interactions in a substituted

(59) A referee has suggested an alternative mechanism. The effect of  $MgBr_2$  on  $\Delta S^*$  may be to increase the order of the solvent molecules in the ground state so that the solvent medium does not suffer so great a loss in entropy in going to the "frozen" state of the activated complex. In other words, the solvent molecules already are effectively "frozen" to a degree in the ground state by the  $MgBr_2$ . Therefore, the change in the degree of freedom from ground state to the transition state is less with magnesium bromide present than it is with the neat solvent.

benzene ring.<sup>35</sup> Taft  $\sigma^0$  values are calculated as inductive effect constants in which no direct conjugative enhancement can occur.<sup>34</sup> If it is assumed that a carbanion attack on the nitrile carbon is a reasonable mechanism for Grignard-benzonitrile reactions, it should follow that only inductive effects on the carbanion should influence the rate of reaction. More specifically, a phenyl carbanion should be composed of two electrons occupying the carbon  $\sigma$  orbital *para* to the point of substitution, and any electronic effect which is due to resonance can operate only by  $p-\pi$  interaction up to the carbon atom involved, *but can not* resonate with a  $\sigma$   $sp^2$  bond which holds the two electrons. Whereas substituted phenolate ions can have resonance interaction up to the  $p-\pi$  oxygen orbitals, only inductive effects are operative on a phenyl carbanion.

A negative  $\rho$  of  $-2.85$  is in keeping with the notion of an attacking carbanion which is activated by electron-releasing groups and conversely is deactivated by electron-withdrawing groups. Citron and Becker<sup>60</sup> found a  $\rho$  of  $+1.6$  for the reaction of diethylmagnesium and *para*-substituted benzonitriles in THF at  $30^\circ$ , which positive value would be expected for the converse of our reaction.

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## The Norbornenyl-Nortricyclyl Radical System

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The reduction of norbornenyl bromide (**4b**) and chloride (**4c**) and of nortricyclyl bromide (**5b**) and chloride (**5c**) with tri-*n*-butyltin hydride provides the same mixture of norbornene and nortricyclene indicating the existence of common intermediates in the reaction. With triphenyltin hydride, nortricyclyl bromide yields a higher ratio of nortricyclene to norbornene in the absence of solvent than in pentane solution indicating the presence of discrete nortricyclyl and norbornenyl free radicals. Relative rates of reaction of cyclic bromides and chlorides (figures in parentheses) with the tri-*n*-butyltin radical at  $45^\circ$  follow: cyclopentyl, 1.0 (1.0); cyclopent-3-enyl, 1.73; cyclohexyl, 0.62 (0.399); *exo*-bicyclo[2.2.1]hept-2-yl, 0.81; *exo*-bicyclo[2.2.1]hept-2-en-5-yl, 1.40; *endo*-bicyclo[2.2.1]hept-2-en-5-yl, 0.37; and tricyclo[2.2.1.0<sup>2,2</sup>]hept-3-yl, 0.31. Thus no significant degree of anchimeric assistance attends the reaction.

A number of investigations have been carried out to determine whether nonclassical free radicals, analogous to nonclassical carbonium ions, appear as reaction intermediates. Bornyl or norbornyl radicals have been prepared by decomposition of 2-azobornane,<sup>2</sup> in the halogenation of norbornane,<sup>3</sup> in the addition of hydrogen bromide to 2-bromonorbornene,<sup>4</sup> and from the

norborn-2-ylcarboxy radical.<sup>5,6</sup> The norborn-2-en-5-yl radicals (**1**) have been generated from the norborn-2-en-5-yl carboxy radical,<sup>5,6</sup> in the decarbonylation of norborn-2-en-5-carboxaldehyde,<sup>7</sup> in the addition of thiols,<sup>8-10a</sup> arenesulfonyl halides,<sup>10b</sup> and other substances<sup>8</sup> to norbornadiene. The uniform conclusion has been that delocalization of the unpaired electron by either  $\sigma$  participation by a neighboring alkyl or  $\pi$  par-

(1) (a) Supported in part by Public Health Service fellowships (4-FL-GM-19,157) to C. R. W. and (1-FL-GM-28,104) to R. J. S. from the National Institute of General Medical Sciences; (b) taken in part from the Ph.D. dissertation of C. R. W., University of New Hampshire, April 1964; (c) to whom correspondence should be addressed at the Department of Chemistry, State University of New York at Albany, Albany, N. Y. 12203.

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