Mechanism of Formation of Grignard Reagents. Kinetics of Reaction of Alkyl Halides in Diethyl Ether with Magnesium[1]

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Abstract: The rate of reaction of organic halides with magnesium is proportional to organic halide concentration and magnesium surface area. All organic iodides examined and many secondary alkyl bromides appear to react with magnesium at mass-transport or diffusion-controlled rates in diethyl ether. The rates of less reactive organic bromides (neopentyl, phenyl, cyclopropyl) contain contributions both from mass transport and from chemical reaction. Most organic chlorides react at rates which are not mass transport limited. Analysis of rate-structure profiles indicates that free carbanions and carbonium ions are not intermediates, and that the transition-state structure does not resemble an S_N2 reaction. Insertion of magnesium into the carbon-halogen bond also does not seem to occur. Soluble Mg(I) can be excluded as the only reactive species responsible for disappearance of alkyl halide. The two most plausible limiting rate-determining steps are halogen atom abstraction from the organic halide by the metal and electron transfer to the organic halide from the metal.

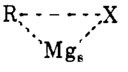
Introduction

The mechanism(s) of formation of Grignard reagents are poorly understood, and the experimental conditions normally used in carrying out the reaction reflect the accumulated experience of synthetic chemists, but not a clear understanding of the reaction mechanism.[5-7] A central difficulty in studying this heterogeneous reaction mechanism is that of obtaining interpretable kinetics information. This paper develops appropriate techniques and presents representative rate-structure profiles. Two accompanying papers extend these techniques[8,9] and establish that the rates of reaction of all alkyl iodides and of most secondary alkyl bromides with magnesium in diethyl ether, and of all alkyl bromides in polar solvents, appear to be mass transport limited. Rates of reaction of most alkyl chlorides are slower, and are not mass transport or diffusion limited. A third paper uses studies of the corrosion of magnesium surfaces to generate a qualitative description of the processes that remove magnesium atoms from the metal surface.[10] Work to be described in future papers,[11] and that reported by others,[12] characterizes the organic products of reaction, and reinforces the hypothesis made by Walborsky, and developed by Bickelhaupt and others, that radicals are intermediates in formation of Grignard reagents.

We have considered ten limiting transition states for the organic moiety, summarized by structures **1–10**. Here, Mg_s represents a magnesium atom of a magnesium metal surface, and Mg(n) represents a magnesium ion.

1 RX
2 $(RX)\cdot Mg_s$
3 $[RX]^{-}$
4 R^{-}
5 R^{+}

6 $R\cdot$
7 $Mg_s{-}{-}{-}R{-}{-}{-}X$ (S_N2)
8



9 RMgY
10 $R{-}{-}{-}X{-}{-}{-}Mg^{(I)}$

1. The unperturbed organic halide would represent the transition state if the overall rate of reaction were limited by the rate of encounter of this organic halide, either with the magnesium surface or with some other reactive species in solution.

2. The organic halide might adsorb at the metal surface in the rate-limiting step.

3. Electron transfer from the magnesium to the organic halide, either close to or adsorbed at the magnesium surface, might be rate limiting.

4–6. The carbon-halogen bond might be broken in the transition state.

7, 8. A magnesium atom at the metal surface (or possibly in solution) might displace halide from carbon in an S_N2-like reaction or insert into the carbon-halogen bond in a concerted process.

9. The rate-limiting step might involve a species with a covalent carbon-magnesium bond; for example, the rate of detachment of an organomagnesium species from the magnesium surface or diffusion of the product Grignard reagent from the surface might be rate determining.

10. A soluble, reactive, magnesium(I) species might cleave the carbon-halogen bond. The kinetics data that follow exclude any transition-state structure showing a large buildup of charge or large steric effects for the organic group, and establish that Mg(I) is not the sole species responsible for breaking carbon-halogen bonds. **3** and **6** remain the most plausible transition-state structures.

Throughout this work, we will be concerned with processes having velocities limited by the rate of encounter of reactants. These encounter rates are influenced both by mass transport (in turn determined primarily by the agitation of the solution) and by diffusion. The available evidence suggests that most of the mechanistically interesting reactions involving alkyl halides occur at the magnesium-solution interface. For convenience in what follows, we will refer to processes having rates limited by some combination of mass transport and diffusion as "transport limited", without specifying whether the process is homogeneous or heterogeneous.[13]

Results and Discussion

Kinetics Methods. The rate of reaction of organic halides with metallic magnesium depends, in principle, on the (measurable) concentration of organic halide in solution and on (presently undefined and unmeasurable) physical characteristics of the magnesium surface. The simplest expression for the rate of disappearance of an organic halide, R_1X, from solution would be eq 1, in which f(Mg) takes into account all the magnesium surface characteristics that influence this rate.[14]

$$-d(R_1X)/dt = k_1(R_1X)^{\alpha}f(Mg) \qquad (1)$$

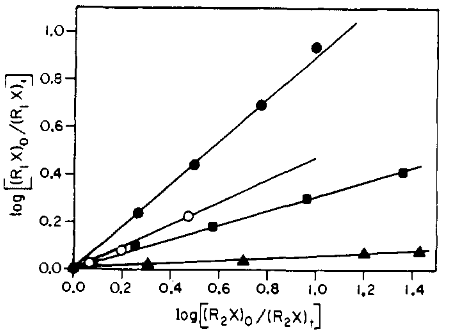


Figure 1. Four representative competitive Grignard reactions plotted according to eq 3—cyclohexyl bromide vs. cyclopentyl bromide (●); cyclopentyl chloride vs. cyclopentyl bromide (▲); *n*-pentyl chloride vs. cyclohexyl chloride (■); neopentyl bromide vs. cyclopentyl bromide (○). (The first member in each pair is plotted as R_1X, the second as R_2X).

$$-d(R_2X)/dt = k_2(R_2X)^{\alpha}f(Mg) \qquad (2)$$

$$\log [(R_1X)_t/(R_1X)_0] = (k_1/k_2) \log [(R_2X)_t/(R_2X)_0] \qquad (3)$$

We studied initially the relative rates of reaction of two organic halides present in the same solution at a common magnesium surface.[15] Assuming that f(Mg) is the same for two structurally similar organic halides competing for a magnesium surface, we write eq 2 for a second alkyl halide R_2X. Dividing eq 1 by eq 2, making the further assumption that $\alpha = 1$, and integrating we obtain eq 3; the correctness of the assumption that $\alpha = 1$ is confirmed experimentally using a different technique (vide infra). Plots of eq 3 are linear to >65% consumption of alkyl halide; representative data are shown in Figure 1. Deviations from linearity at high conversions, when observed, are due primarily to changes in the polarity of the medium at high concentrations of Grignard reagent.[8]

A representative ratio of the rate constants (k_1/k_2) obtained using eq 3 is insensitive to changes in magnesium sample size, purity, and surface area and to the addition of plausible impurities to the solution (Figure 2).[16] The inference from Figure 2 that the measured ratio of rates is independent of the extent of agitation is correct only for certain pairs of alkyl halides. In the specific instance in which one halide reacts at a transport-limited rate and the second does not, the ratio of rates measured *does* depend on ω, although it is entirely reproducible at a particular value of ω. All of the data collected here were obtained using $\omega = 600 \pm 100$ rpm; detailed discussion of the dependence of relative rates on ω is deferred to the end of this section. High concentrations of magnesium salts do influence the rate ratio by changing the polarity of the medium.[8,9] The scatter of points in Figure 2 provides a realistic illustration of the reproducibility of the data obtained using this technique. The observation of straight-line plots in Figure 1 confirms the insensitivity of k_1/k_2 to the concentration of alkyl halides, to low concentrations of magnesium salts and Grignard reagents in solution, and to the magnesium surface area, since all are changing during the course of a kinetic run.

Equation 3 is not useful in trying to examine the influence of solvent composition, solvent viscosity, or temperature on the reactivity of a single organic halide toward magnesium. For studies of this type, we used a different procedure. A quantity of magnesium very large compared to the quantity of organic halide to be used (a 20-25-fold excess) was immersed in solvent, and its surface cleaned by etching using either 1,2-dibromoethane or an alkyl halide. The reaction of magnesium metal with organic halides normally generates relatively smooth, polished surfaces:[10] that is, for limited extents of reaction, the surface area of the magnesium changes very little. It is thus possible to bring a small quantity of one organic halide into contact with the etched magnesium surface, follow its disappearance with time, remove the solvent containing the initially formed Grignard reagent and replace it with fresh solvent, add a second halide, and follow its disappearance with time, all without significantly changing the surface area of the magnesium. Although the numbers obtained from these experiments have no absolute significance, they can be compared with one another, since f(Mg) in eq 1 can be assumed constant over the course of the experiments. The apparatus used in these studies is that shown in Figure 3. Variations in the rate of stirring established that the values of the apparent rate constant for certain alkyl bromides (e.g., cyclopentyl bromide) increased with the stirring frequency ω (Figure 4A).[17] The rates were reproducible at a particular value of ω. Data were ordinarily collected using $\omega = 140$ rpm. To ensure the reproducibility of the method, measurements were made at least in duplicate; that is, using the same magnesium assembly, kinetic runs were carried out in succession with R_1Br, R_2Br, R_1Br, and R_2Br (or, when studying the influence of solvent on the rate of reaction of a single alkyl halide, in succession with solvents A, B, A, and B). These experiments are more complex and less accurate than the competitive kinetics experiments. Nevertheless,

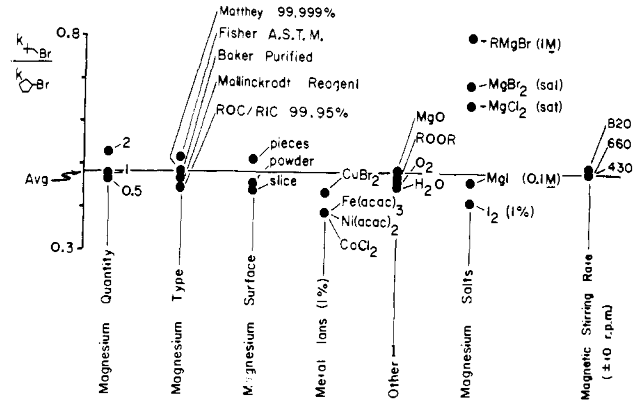


Figure 2. The relative rates of reaction of neopentyl bromide and cyclopentyl bromide with magnesium are insensitive to magnesium type, quantity, and surface area, and to a number of potential contaminants. They are influenced by high concentrations of magnesium halides and Grignard reagents. The line indicated as "avg" represents the average value obtained from several determinations of the relative rate in diethyl ether at 0 °C with Baker purified magnesium (standard conditions for all the competitive kinetics experiments).

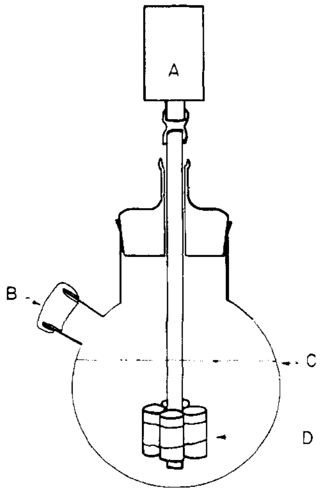


Figure 3. Apparatus for following the reaction of a single organic halide with a large excess of magnesium. (A) High-torque, adjustable speed stirrer. (B) Sampling and inert gas inlet through a No-air stopper. (C) Level of reaction solvent (typically ca. 300 mL). (D) Four (originally) 1.00 × 0.625 in. reagent grade (99.9%) magnesium rods bound to the central stirring rod by two pieces of 18-gauge stainless steel wire.

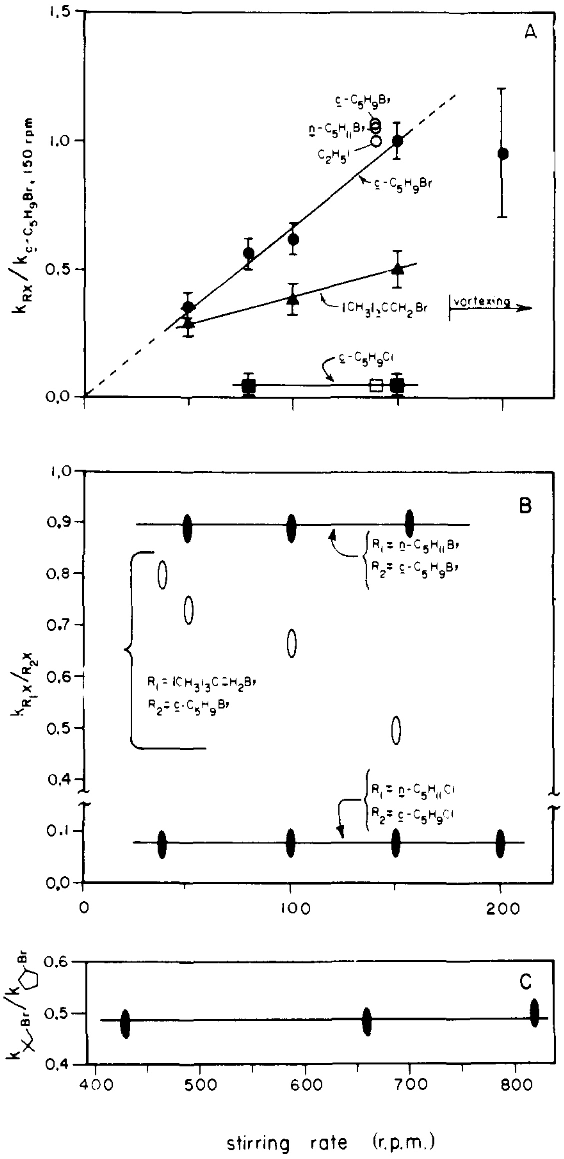


Figure 4. (A) Variation in the apparent first-order rate constant for disappearance of cyclopentyl bromide in diethyl ether at 0 °C with stirring rate obtained using the constant-surface kinetics technique. The same scale of stirring rates apply to (A) and (B). Above ca. 150 rpm, vortexing limits the accuracy of this method when applied as in (A). Filled symbols represent data obtained as part of a systematic study of the influence of ω on rate constant; open symbols represent single experiments obtained under roughly comparable conditions. (B) Variation in the relative rate constants for reaction of two alkyl halides with magnesium, as a function of stirring rate. The two alkyl halides were present in the same solution and the data were collected and analyzed using the competitive kinetics technique, but the experimental configuration used for stirring was that typical of the constant-surface technique (Figure 3). The top set of data in this figure (●, n-C_5H_{11}Br vs. c-C_5H_9Br) represents a competition between two bromides both reacting at or close to a transport-limited rate. The central set (O, $(CH_3)_3CCH_2Br$ vs. c-C_5H_9Br) gives data for experiments in which only one halide is clearly transport limited. The bottom set (●, n-C_5H_{11}Cl vs. c-C_5H_9Cl) gives results for competitions in which neither halide is transport limited. (C) The ratio of rates of reaction of neopentyl bromide and cyclopentyl bromide in diethyl ether, as a function of stirring rate, obtained using the competitive technique (magnetic stirring bar and magnesium turnings).

agreement between runs was usually ±10%, with no evidence for an important systematic decrease in rate due to a decrease in magnesium surface area. Typical data are shown in Figure 5.

Since data obtained using each of the two kinetics techniques will be utilized in the discussions that follow, it is useful to have a descriptive label for each. We will call the first procedure described—the competition of two organic halides present in a single solution for the same magnesium surface—the "competitive technique". The second procedure—the comparison of data obtained from successive reaction carried out so that a magnesium surface of approximately constant area is maintained—will be referred to as the "constant-surface technique".

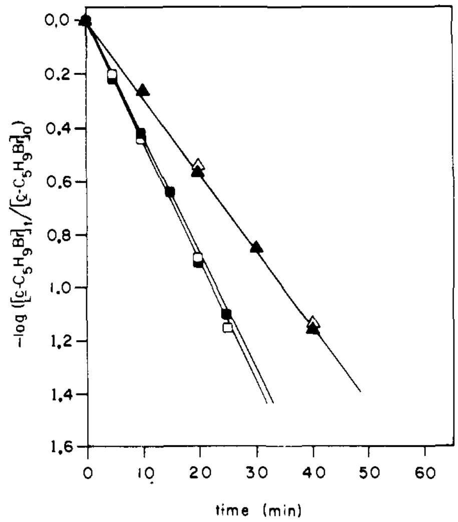


Figure 5. Pseudo-first-order plots for the disappearance of cyclopentyl bromide in diethyl ether obtained in four consecutive experiments using the constant-surface technique (■, first run; □, third run) and tetrahydrofuran (▲, second run; △, fourth run).

The constant-surface technique serves several useful functions. First, it permits the comparison of rates of reaction of a single organic halide with magnesium in different solvents and at different temperatures. Second, it provides a direct experimental measure of the exponent α in eq 1 and 2: since a plot of log $(RBr)_t/(RBr)_0$ vs. time is linear (Figure 5), α equals 1. Third, it provides a method of checking results gathered using the simpler competitive techniques based on eq 3. The ratios of rate constants obtained by measurements of two alkyl halides in sequence using this more complex technique agree (perhaps fortuitously) with those inferred from the simple competitive procedure. For example, measurement of the rates of reaction of cyclopentyl chloride and cyclopentyl bromide in sequence using the constant surface procedure gave the ratio $k_{C_5H_9Cl}/k_{C_5H_9Br} = 0.053$; measurement based on the competitive kinetics technique and eq 3 gave 0.055.

This last observation is directly relevant to a general question concerning the competitive kinetics methods (eq 3) which is particularly important for this work: viz., what is the significance of the relative rates measured using this technique when one of the competing substrates reacts at a transport-limited rate and the second reacts at a rate slower than diffusion or mass transport?[17] Consider the influence of agitation in the three possible limiting rate regimes for reaction of two alkyl halides (A and B) with magnesium. If A and B both react at transport-controlled rates, and both have similar diffusion constants (as is the case in virtually all of this work),[18] $k_A/k_B \sim 1$ will be independent of the stirring rate. If A and B both react at rates that are much less than transport controlled, k_A and k_B will be independent of mass transport and k_A/k_B will be independent of stirring rate. If, however, A reacts at a rate less than mass transport but B reacts at a mass-transport-controlled rate, the analysis of relative rates becomes complicated: k_A will be independent of stirring rate, k_B will depend on mass transport and will increase with increasing stirring rate, and k_A/k_B will decrease with increasing stirring rate.

Figure 4B shows rate data obtained using pairs of alkyl halides that fit these three limiting conditions. These data were

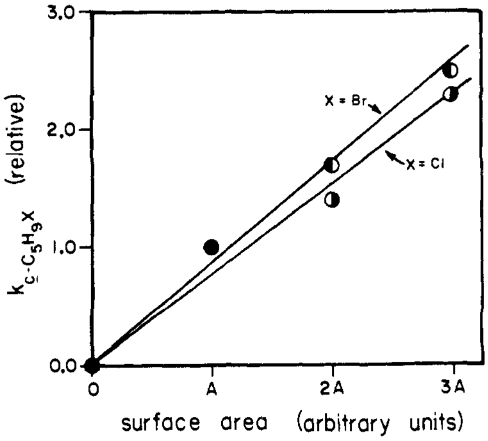


Figure 6. The relative rates of reaction of cyclopentyl bromide (◑) and cyclopentyl chloride (◐) with magnesium is proportional to the exposed surface area of the magnesium.

obtained using the apparatus shown in Figure 3 (to facilitate comparison with Figure 4A) but using the competitive kinetic technique; that is, both alkyl halides of a competing pair were present in solution at the same time, and reacting at the same magnesium surface. Evidence presented later in this paper and in a following paper[8] indicates that cyclopentyl bromide reacts at a transport-controlled rate; *n*-pentyl bromide is on the verge of transport control (its rate is ca. 90% that of cyclopentyl bromide); neopentyl bromide reacts significantly more slowly than a transport-controlled rate (ca. 50% that of cyclopentyl bromide); *n*-pentyl chloride and cyclopentyl chloride react much more slowly than cyclopentyl bromide. Figure 4A demonstrates that the rate of reaction of neopentyl bromide with magnesium shows a considerably smaller dependence on ω than does that of cyclopentyl bromide, and confirms that transport limitations are less important with the former than with the latter. As expected, the measured values of $k_{n\text{-}C_5H_{11}Br}/k_{c\text{-}C_5H_9Br}$ and $k_{n\text{-}C_5H_{11}Cl}/k_{c\text{-}C_5H_9Cl}$ are independent of stirring rate, while that for $k_{(CH_3)_3CCH_2Br}/k_{c\text{-}C_5H_9Br}$ decreases as the stirring rate increases. The value measured for $k_{(CH_3)_3CCH_2Br}/k_{c\text{-}C_5H_9Br}$ using the standard competitive kinetics technique was found to be independent of the magnetic stirring frequency in the range used (400–800 rpm, Figure 4C). A similar value was measured for this ratio of rates using the hybrid experimental technique that forms the basis for Figure 4B with a stirring frequency of ca. 150 rpm. Both of these rate ratios superimpose mass transport effects on the intrinsic reactivities of the two compounds, and neither value provides an absolute measure of these intrinsic reactivities. Nonetheless, the data of Figure 4 indicate that the measured rate ratio from either technique should be insensitive to small changes in stirring frequencies, and that the stirring frequencies used in the standard competitive and constant surface protocols (600 ± 100 and 140 ± 5 rpm, respectively) yield consistent and comparable data.

Preliminary Observations. Evidence for first-order dependence of rate on the concentration of organic halide has already been presented (Figure 5); evidence concerning the dependence on magnesium surface is more qualitative. If the rate of disappearance of cyclopentyl bromide or cyclopentyl chloride is followed for reaction mixtures containing equal weights, but different exposed surface areas, of magnesium, the rate is directly proportional to the surface area (Figure 6). Thus, the empirical rate law for disappearance of alkyl halide is given by eq 4; here S_{Mg} is the surface area of the magnesium (note that this expression has the form assumed in eq 1, with $\alpha = 1$).

$$-d(RX)/dt = k_{RX}(RX)S_{Mg} \qquad (4)$$

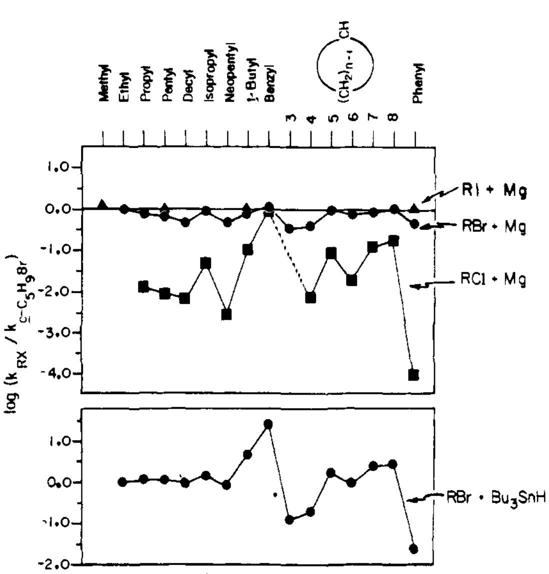


Figure 7. Structure-reactivity profiles for the reaction of organic chlorides, bromides, and iodides with magnesium (top) and organic bromides with tri-*n*-butyltin hydride (bottom). The ring size of the cycloalkyl halides is denoted by "*n*". All reactions were run in diethyl ether at 0 °C. The point represented by *tert*-butyl for reaction of alkyl chloride with magnesium was obtained using 2-methyl-2-butyl chloride: cf. footnote *b*, Table I.

The most important conclusion from this rate law is that the rate-determining step in the reaction requires reaction of organic halide at the magnesium surface. In particular, it excludes several conceivable reaction mechanisms involving generation of soluble Mg(I) by reaction of Mg(0) and Mg(II),[19,20] either in the rate-determining step or in a prior equilibrium (eq 5–7). In the first instance, the reaction rate would be independent of organic halide concentration. In the second, the rate would depend upon the concentration of magnesium-containing species in solution, but would be independent of the quantity of magnesium metal present, since the thermodynamic activity of magnesium metal in the system is independent of its mass as long as some amount of the metal is present and as long as the concentration of Mg(I) is truly at equilibrium. Thus, structures such as **10** can be discarded as *exclusive* representations for the transition state for this reaction. Note, however, that the kinetic analysis outlined in a following paper[8] suggests that some homogeneous reaction may contribute to the disappearance of alkyl halide in competition with the heterogeneous reaction with magnesium. A magnesium(I) species must still be considered a candidate for this possible competing reaction.

$$\text{Mg(metal)} + \text{Mg(II)} \longrightarrow 2\text{Mg(I)} \qquad (5)$$

$$\text{Mg(I)} + \text{RX} \rightleftarrows \text{R}\cdot + \text{Mg(II)} + \text{X}^- \qquad (6)$$

$$\text{R}\cdot \rightsquigarrow \text{RMgX} \qquad (7)$$

The structure of the organic group has little effect on the rate of reaction of alkyl halides with magnesium: positively charged, negatively charged, and S_N2-like transition states are not involved. The relative reactivities of a number of organic halides in diethyl ether were determined using the competitive technique (Figure 7 and Table I). Figure 7 also includes relative rates for the free-radical reduction of the same group of alkyl bromides by tri-*n*-butyltin hydride ($h\nu$, AIBN, Et_2O).[21,22] Tables of relative rates obtained by competition experiments may contain large, cumulative, systematic errors when long sequences of comparisons are required. Several checks suggest that, in general, the accuracy of the data of Figure 7 is good, although the accuracy of particular compounds may be lower (vide infra). First, the rate–structure

Table I. Relative Rates of Reaction of Organic Halides, RX, with Magnesium and Tri-*n*-butyltin Hydride and Diethyl Ether[a]

R	magnesium			*n*-Bu_3SnH
	X = Cl	X = Br	X = I	X = Br
1. CH_3			≤1.2	
2. CH_3CH_2		1.0	1.1	1
3. $CH_3(CH_2)_2$	0.013	0.83		1.1
4. $CH_3(CH_2)_4$	0.0094	0.88	0.92	1.1
5. $CH_3(CH_2)_9$	0.0072	0.84		0.97
6. $(CH_3)_2CH$	0.050	0.93	0.95	1.47
7. $(CH_3)_3CCH_2$	0.0029	0.48	0.89	0.80
8. $R'(CH_3)_2C$[b]	0.10	0.97		4.7
9. 1-adamantyl		0.56		1.4
10. 2-adamantyl		0.50		1.3
11. $C_6H_5CH_2$	≤1.2[c]	≤1.2[c]		23
12. $CH_2{=}CHCH_2$		≤1.5[c]		
13. c-C_3H_5		0.37		0.11
14. c-C_4H_7	0.0071	0.41		0.20
15. c-C_5H_9	0.055	1	0.99	1.62
16. c-C_6H_{11}	0.030	0.95		0.97
17. c-C_7H_{13}	0.13	0.94		2.4
18. c-C_8H_{15}	0.19	1.05		2.7
19. C_6H_5	0.00010	0.48	1.1	0.024
20. $CH_2{=}CBrCH_2CH_3$		0.19		
21. XCH_2CH_2	0.16[d,e]	1.2[c,e,f]		3.5[d,g]
22. $XCH_2CH_2CH_2$	0.010	0.75[d,e]	1.1[c,e,f]	
23. $XCH_2CH_2CH_2CH_2$	0.011	0.64[d]	≤1.2[c]	

[a] All reactions were carried out in diethyl ether at 0 °C. Relative rates were determined by the competitive kinetics technique. The experimental uncertainty in these data is estimated to be ±10%, unless indicated otherwise. Rates of reaction with magnesium are all relative to cyclopentyl bromide, because this halide was the object of the detailed studies reported in ref 8. Note that c-C_5H_9Br and C_2H_5Br have the same relative rate. Rates of reaction with tri-*n*-butyltin hydride are relative to ethyl bromide. [b] For X = Cl, $R' = CH_3CH_2$; for X = Br, $R' = CH_3$. [c] Qualitative data. These numbers are probably too high, because processes other than reaction with magnesium also appear to consume these halides. [d] These rates have been corrected statistically for the presence of two equivalent halide atoms by dividing the observed rate by 2.0. [e] The products of these reactions have lost the elements of X_2: no stable organomagnesium compound is formed. [f] Statistically uncorrected. [g] This datum is consistent with the value of $k_{CH_3CHBrCHBrCH_3}/k_{CH_3CHBrCH_2CH_3} = 4.8\text{-}7.6$ measured by R. J. Strunk, P. M. DiGiacomo, K. Aso, and H. G. Kuivila, *J. Am. Chem. Soc.*, **92**, 2849 (1970).

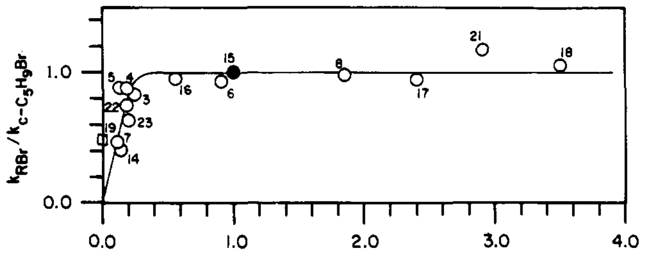


Figure 8. A plot of the relative rates of reaction of organic bromides with magnesium against the corresponding relative rates of reaction of organic chlorides follows a smooth curve, and suggests that neither set of data contains large experimental errors. Numbers on the plot refer to entries in Table I. Data from this table for which uncertainty is abnormally large (benzyl and allyl halides) have been omitted. The one nonaliphatic point on this plot (phenyl) is indicated by □. Typical precision in measuring a single ratio of rates is ca. ±10%. Values for $k_{RCl}/k_{c\text{-}C_5H_9Cl}$ were calculated from the data in Table I. The slope of the rising portion of the curve is ca. 4.

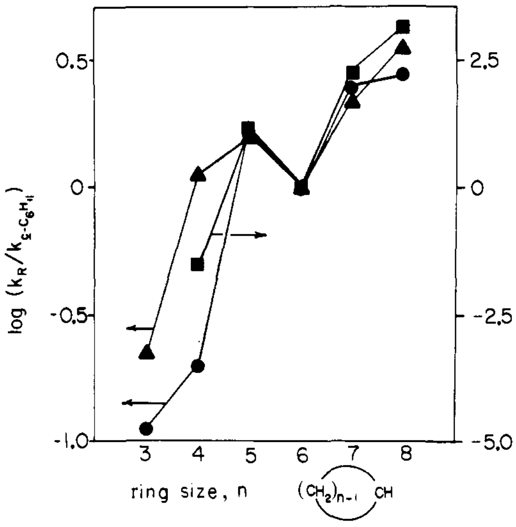


Figure 9. Dependence of the rate of formation of cycloalkyl radicals on ring size from three independent studies: (●) tri-*n*-butyltin hydride reduction of alkyl bromides; (▲) abstraction of bromine atoms from alkyl bromides by phenyl radical;[24] (■) thermal decomposition of cycloalkylazonitriles.[23]

profiles for the reaction of alkyl chlorides and alkyl bromides with magnesium were obtained independently. Plotting the relative rates of one against those of the other indicates that, although the two are not linearly related, there is a smooth correlation between them (Figure 8). Second, comparisons of relative rates of reaction of representative pairs of organic halides by competitive and constant-surface techniques yield the same values. Third, comparison of the rate-structure profile for reduction of cycloalkyl bromides by tri-*n*-butyltin hydride with data for other reactions that generate a free radical shows an adequate correlation (Figure 9).[23-26]

The experimental uncertainties in the relative rates of reaction of benzylic and allylic halides is larger than that for most of the compounds in Table I. These rates are not entirely reproducible, and consumption of the unreacted alkyl halides by already formed Grignard reagent occurs at a rate that is competitive with their rate of reaction with magnesium. Similar reactions may also occur with some of the alkyl iodides and with 1,2-dibromoethane. The error in these data is thus such that the values in Table I for benzylic and allylic halides, alkyl iodides, and 1,2-dibromoethane are too high by an unknown but probably small (<50%) factor. A different un-

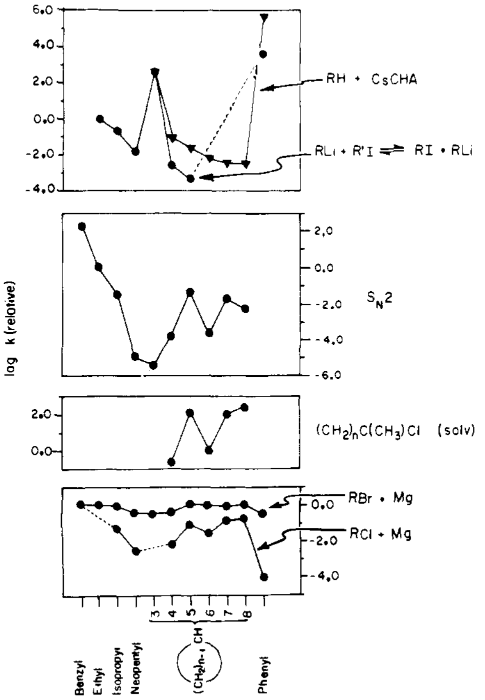


Figure 10. A comparison of structure-reactivity profiles for several reaction types. At the top are two reactions involving a carbanion intermediate—anionic exchange of hydrogen atoms with cyclohexylamine catalyzed by cesium cyclohexylamide and metal-halogen interchange. Second from the top is an S_N2 reaction—displacement of bromide ion from alkyl bromides by iodide ion in acetone. Third from the top is an S_N1 reaction (carbonium ion intermediate)—solvolysis of 1-methyl-1-chlorocycloalkanes in aqueous ethanol. At bottom are the reactions of alkyl bromides and alkyl chlorides with magnesium.

certainty is attached to reactions of the α,ω-dihalides. First, 1,2-dibromo- and 1,2-dichloroethane react readily with magnesium, but yield no detectable Grignard reagent; only ethylene is formed. Similarly, 1,3-dibromo- and 1,3-dichloropropane yield hydrocarbons rather than Grignard reagents.[27] Only 1,4-dibromobutane and 1,4-dichlorobutane, of the α,ω-dihalides examined, react normally and yield (ultimately) butane-1,4-di(Grignard reagents). Second, as we have already indicated, many, but not all, organic bromides react with magnesium at a transport-controlled rate. The experimentally observed rates for the alkane α,ω-dichlorides have been corrected statistically for the presence of two equivalent reactive halides in order to compare the reactivities of their individual carbon-halogen bonds with those of monochloroalkanes. A statistically corrected rate constant is also listed in Table I for 1,3-dibromoethane or for 1,3-diiodopropane (implying transport-limited reactions) for two reasons. First, statistically uncorrected rate constants for 1,3-dibromopropane and 1,2-diiodopropane would be higher than the rate transport-limited reaction of cyclopentyl bromide and would therefore be physically unreasonable. Second, the statistically corrected rate constants fit squarely on the correction line of Figure 8. Thus, although we have not explicitly tested the reactions of 1,3-dibromopropane or 1,4-dibromobutane for diffusional or mass transport limitations, we are confident, from the arguments outlined, that they do *not* react at a transport-controlled rate.

The most striking feature of the data summarized in Figure 7 for the reaction of organic halides with magnesium is the low sensitivity of these rates to the structure of the organic moiety: the reaction of organic bromides and iodides with magnesium is among the least selective of organic reactions.[28] This low selectivity argues against several of the possible remaining transition-state models (**1–9**). Figure 10 compares structure-reactivity profiles for several representative reactions types with the analogous profiles for reactions of alkyl bromides and alkyl chlorides with magnesium.[29,30] The very small range of rates characterizing the organic bromides suggests that no transition state showing either a large charge separation or significant steric effects (**4, 5, 7, 8, 9**) describes their reaction with magnesium. Organic chlorides show a larger range in rates. Again, however, the differences between the structure-reactivity profiles for reactions involving authentic carbanions and for reactions forming organomagnesium chlorides is such that transition states bearing significant negative charge (**4**, probably **9** and **8**) can be excluded. The observation that rates of reaction of phenyl, cyclobutyl, and *tert*-butyl chlorides all react with magnesium at rates comparable to typical primary and secondary alicyclic chlorides argues strongly against S_N1- and S_N2-like transition states (**5** and **7**).[31] The unexceptional reactivity of 1-adamantyl and cyclopropyl bromides within the series of organic bromides also supports this general conclusion.

The rates of reaction of all alkyl iodides examined, of many, but not all, alkyl bromides, and of benzyl chloride with magnesium in diethyl ether are mass transport or diffusion limited. Analysis of the rate-structure profiles summarized in Figure 7 requires an initial segregation of these data into rates that are transport limited and those that are not. Three lines of evidence, discussed in detail in an accompanying paper,[8] establish that the reaction of cyclopentyl bromide with magnesium in diethyl ether falls in the former group. First, the rate of this reaction, measured using constant-surface techniques, is inversely proportional to solution viscosity and proportional to stirring rate. Second, the activation energy for the reaction (E_a = 2.3 kcal/mol) is that expected for diffusion.[32] Third, the relative rates summarized in Figure 7 establish that a number of organic halides having unrelated structures—cyclopentyl bromide, cyclohexyl bromide, isopropyl bromide, several organic iodides, benzyl bromide, benzyl chloride—react at experimentally indistinguishable rates, and none of the compounds examined react at faster rates. We conclude that all of the compounds which share this upper limit are reacting at rates determined by their transport and diffusion to the magnesium surface.

With the single exception of benzyl chloride, alkyl chlorides react significantly more slowly than cyclopentyl bromide and the other alkyl halides whose rates are limited by transport. The diffusion constants of alkyl chlorides should be larger than those of the corresponding alkyl bromides. Thus, the rates of reaction of the organic chlorides examined (excepting benzyl chloride) are not limited by diffusion. It is not clear how many of the alkyl bromides are reacting at rates limited by processes other than diffusion. Neopentyl bromide[8] and phenyl bromide[9] have been established to react at rates less than transport limited in diethyl ether, although these rates become transport limited in other solvents. Cyclopropyl bromide, cyclobutyl bromide, and probably 1- and 2-adamantyl bromide also react at rates less than those at which they encounter the magnesium surface. The primary alkyl bromides appear to be on the border between these two rate regimes. This distribution of rates according to structure is best appreciated by reference to the curve of Figure 8: those organic bromides on the rising part of this curve appear to react at rates less than mass transport or diffusion; those on the plateau are transport limited. The kinetics of reaction of organic bromides with magnesium are thus remarkable: small changes in the structure of the organic group shift the overall rate-limiting step for disappearance from mass transport and diffusion to some other step.

Chlorine-atom abstraction or single-electron transfer appear to be the most probable rate-limiting steps for reaction of organic chlorides with magnesium in diethyl ether. The rates of reaction of alkyl chlorides with magnesium provide a rate-structure profile which is not complicated by transport limitations. Transition states resembling **4, 5, 7,** and **9** can be discarded as rate determining in these reactions, on the grounds that the rate-structure profile for this reaction bears little similarity to rate-structure profiles for model reactions. The reaction is not transport limited: **1** can also be excluded. The remaining possible state structures include adsorbed organic halide (**2**), organic halide radical anion resulting from single-electron transfer (**3**), free radical (**6**), and concerted insertion of magnesium into the carbon-chlorine bond (**8**). These possibilities are not necessarily mutually exclusive; for example, electron transfer to the carbon-halogen σ^* orbital of an organic halide could be effectively concerted with carbon-halogen bond breaking,[33,34] and adsorption of organic chloride to magnesium with the carbon-chlorine bond parallel to the surface could well merge with magnesium atom insertion into this bond.

In another study, we have examined the capability of rate-structure profiles based on the range of organic structures represented in Table I to distinguish between halogen-atom abstraction and electron-transfer mechanisms.[35] In brief, these studies indicate that rate-structure profiles for reaction of alkyl chlorides with magnesium, of alkyl chlorides with tri-*n*-butyltin hydride, and of alkyl bromides with lithium 4,4′-dimethylbenzophenone ketyl are all linearly correlated, and suggest that outer-sphere, single-electron reduction of alkyl halides proceeds with extensive carbon-halogen bond breaking in the transition state. Thus **3** and **6** are not distinguishable by this approach, and **3** may not correspond to a species having a finite lifetime.[36]

Conclusions

The experimental evidence summarized in this paper limits the possibilities for the overall rate-determining transition state for reaction of an organic halide with magnesium.

(1) The rate of reaction of organic bromides and chlorides with magnesium is proportional to organic halide concentration and magnesium surface area. This observation implies that reaction occurs, at least in part, at the metal-solution interface.

(2) The rates of reactions of organic bromides and iodides with magnesium are either mass transport and/or diffusion limited or are close to these rates.[8,9] The small structure dependence that characterizes those substances that do not react at transport-limited rates (aryl,[9] vinyl, cyclopropyl, cyclobutyl, neopentyl,[8] and possibly primary alkyl bromides) reflect competitive reaction and transport. The fact that the rate-structure profile observed for those alkyl bromides which react at less than transport-limited rates is qualitatively similar to that observed for alkyl chlorides suggests, however, that the two classes of compounds share similar mechanisms for the cleavage of carbon-halogen bonds.

(3) The structure-reactivity profile for alkyl chlorides is not an artifact of reaction rates close to mass transport limited: although the reaction is fast, it is approximately a factor of 100 slower than the reaction of alkyl bromides with magnesium, and therefore is at least this much slower than mass transport.

(4) Comparison of the rate-structure profile for the Grignard reaction with rate-structure profiles for carbonium ion, carbanion, and S_N2 processes permits structures of type **4, 5,** and **9** to be discarded as models for the transition state for the formation of Grignard reagents from alkyl chlorides, and from those alkyl bromides that react at rates slower than mass transport. Concerted insertion of a magnesium atom into a carbon-halogen bond that involves sufficient redistribution of charge to resemble the organomagnesium product (**8**), also seems unlikely: the rate-structure profile for this type of mechanism should reflect more sensitivity to alkyl moiety structure and more negative charge on the carbon atom in the transition state than is observed for the reactions.

(5) The rate expression excludes mechanisms in which a rate-limiting or preequilibrium step generates a soluble magnesium(I) or other reactive magnesium species which becomes the sole substance responsible for breaking the carbon-halogen bond; it does not exclude involvement of magnesium(I) in side reactions, or after the overall rate-limiting step.

(6) Present evidence[35] does not permit a choice between halogen abstraction and generation of an alkyl halide radical anion by single-electron transfer as the initial step in carbon-halogen bond cleavage. It is, in fact, unclear whether electron transfer and carbon-halogen bond breaking can be considered as separate events.[35,36]

(7) Adsorption of the alkyl halide onto the magnesium surface with limited carbon-halogen bond breaking is difficult to exclude rigorously for those compounds which react at less than transport-limited rates but seems improbable. Reaction rates show no clear evidence for steric effects around the carbon-halogen bond. The low susceptibility of Grignard formation to poisoning argues against competitive adsorption by other solution components.

In summary, this work provides sufficient evidence to exclude many of the transition states conceivable for the rate-limiting step for reactions of alkyl halides with magnesium. For alkyl iodides and most alkyl bromides transport to the magnesium surface is overall rate limiting; the rate of reaction of alkyl chlorides is slower and is not transport limited. It appears from our work on the latter stages of the reaction, and from work by others, that an alkyl radical rather than a carbanion or an organomagnesium compound is produced initially as an intermediate.[11,12] Presently available evidence does not differentiate between initial electron transfer from magnesium to the organic halide and collision of the organic halide with the magnesium followed by halogen abstraction. Detailed consideration of the kinetics of these reactions indicates that certain other, more complex, types of mechanisms also cannot be excluded at present.[8]

These mechanistic ambiguities notwithstanding, these studies establish the most basic features of the transition state for consumption of organic halides by reaction with magnesium. They also indicate the remarkable balance of the rates of this reaction between mass transport limited regimes, and suggest that the reaction of organic bromides with magnesium should prove to be a very useful reaction, both for exploring the details of the transition region between mass transport limited and reaction-limited reactions and for studying the kinetic characteristics of heterogeneous organic reactions.

Experimental Section

General Methods. Reagent grade magnesium turnings (Mallinckrodt or Eastman) were used for the competitive kinetic studies. Other magnesium samples used were Matthey 99.999%, ROC/RIC 99.95%, Fisher A.S.T.M., and Baker purified grades. Reagent grade magnesium rods (Fisher) 0.625 in. in diameter were used for the "constant surface" kinetics studies. Alkyl chlorides, bromides, and iodides were used as received unless GLC analysis indicated impurities. Impure alkyl chlorides were purified by distillation through a column of glass helices. Impure alkyl bromides and iodides were filtered through a column of either Woelm activity I alumina or activity I silica gel and distilled through a column of glass helices. All solvents used in kinetics studies were distilled under argon directly into dry storage flasks equipped with Teflon stopcocks which had been flamed dry and allowed to cool under a stream of argon. Reagent grade diethyl ether and tetrahydrofuran (THF) were distilled from dark purple solutions containing disodium benzophenone dianion. Xylene (a mixture of isomers) was distilled from sodium. Solvent transfers were made using standard cannulae techniques.[37] Solvents were used within 3 days of distillation. Stirring rates were measured using a General Radio Model 1531-AB Strobotac.

Methods for Competitive Kinetics. Grignard Reaction. Similar procedures were used in all experiments in which two alkyl halides were allowed to compete for the same magnesium surface. A representative procedure follows. To a three-necked, 50-mL, round-bottomed flask, equipped with a 0.75-in. magnetic stirring bar, was added 1.0 g (0.040 g-atom) of reagent grade magnesium turnings. The flask was capped with three No-air stoppers, and a 20-gauge stainless steel syringe needle was inserted through one of the stoppers as a vent. A rapid stream of argon introduced from another 20-gauge syringe needle inserted through a No-air stopper was maintained in the flask for 5 min; then the flask was flamed dry and allowed to cool under this stream of argon. The syringe needle acting as a vent was removed and the flask, under argon, was charged with 10 mL of anhydrous ether. The surface of the magnesium turnings was activated if necessary by the addition of ca. 0.05 mL of ethyl bromide. The resulting reaction mixture was stirred at 0°C (ice-water bath) for 10 min. The reaction whose kinetics were to be determined was initiated by adding a mixture of the cooled halides (5.0 mmol of *n*-pentyl bromide and 5.0 mmol of cyclohexyl bromide) and internal standard (0.25 g of *n*-decane) to the reaction mixture in one portion by syringe. The reaction mixture was stirred rapidly (ca. 600 rpm). In all cases with alkyl bromides, reaction began quickly and proceeded to completion in less than 10 min; reactions with certain alkyl chlorides required hours to go to completion. Aliquots were withdrawn at appropriate times by removing ca. 0.6 mL of the reaction mixture by syringe and adding it slowly to a vial containing ca. 0.5 g of sodium chloride and ca. 1 mL of ice-water. The vial was capped and shaken. The ethereal phase containing all the unreacted halides and internal standard was filtered through a plug of glass wool in a micropipet, placed in the sampling vials of an automatic GLC sample injector, and analyzed by GLC. Five to eight aliquots were withdrawn in each kinetics experiment, and each aliquot was sampled three times.

When possible, rates of alkyl bromides were measured relative to cyclopentyl bromide. Alkyl chlorides were measured in pairs that minimized the rate difference between the reacting members. The relative rates of reaction of the organic bromides and chlorides were established by comparisons of the rates of reaction of cyclopentyl bromide and cyclopentyl chloride. The rate difference between these compounds is large ($k_{c\text{-}C_5H_9Cl}/k_{c\text{-}C_5H_9Br} = 0.053$) but not so large as to preclude accurate rate measurements using competitive techniques.

Methods for Competitive Kinetics. Tri-*n*-butyltin Hydride Reductions. A 50-mL, three-necked, round-bottomed flask equipped with a 0.75-in. magnetic stirring bar was flame dried and allowed to cool under a stream of argon. After cooling, 0.1 g of AIBN was added to the flask, the necks were capped with No-air stoppers, and the argon flow was resumed. After 5 min, 10 mL of anhydrous ether was added to the flask by cannula, and the flask was placed in an ice-water bath at 0 °C. The two halides (5.0 mmol of each) and alkane internal standard (0.25 g) were added to the flask by syringe, and the contents of the flask was stirred at 0 °C for 10 min. The first aliquot (0.6 mL) was withdrawn by syringe at this time. The reaction was initiated by addition of 3.58 g (11 mmol) of tri-*n*-butyltin hydride to the reaction flask that was irradiated with a long-wavelength, low-intensity ultraviolet light (Mineralite, UVSL 25). Aliquots (0.6 mL) were removed every 5 min for 30 min. Each aliquot was added to a vial for the automatic sampler that contained ca. 1 mL of carbon tetrachloride: carbon tetrachloride reacts with tin hydrides a factor of 20–30 times faster than the alkyl bromides that were studied and provides effective quenching for the reaction mixtures.[21] The vials were capped, shaken, placed on the automatic sampler, and analyzed by GLC.

Methods for Constant-Surface Kinetics. The constant-surface kinetics method utilized an approximately 20–25-fold molar excess of magnesium metal relative to alkyl halide and produced pseudo-first-order plots for disappearance of alkyl halide (cf. Figure 5). A reagent grade magnesium rod 0.625 in. in diameter was polished with medium-grade sandpaper until the original oxidized surface had been removed. The polished magnesium rod was then cut into sections 1.00 in. long, and two deep notches were made in each section using a hacksaw or fiber bandsaw. Four of these sections were wired to the end of a glass stirring rod by passing two pieces of stainless steel wire through the two sets of notches on the magnesium, then tightening the wires with pliers. The reaction vessel used for the constant-surface kinetics method consisted of a 500-mL round-bottomed flask with a 24/40 standard-taper ground-glass joint, and an additional 60/50 ground glass joint (Figure 3). The glass stirring rod with the four pieces of magnesium could just pass through this 60/50 opening into the reaction vessel. The other end of the glass rod was attached to a high-torque, constant-speed stirrer and an appropriate adapter joined the stirring rod collar to the 60/50 joint. The 24/40 outlet was fitted with a No-air stopper containing a 12-gauge syringe needle as a vent. Argon, 1,2-dibromoethane, alkyl halides, and solvents were introduced and removed from the reaction vessel by cannulae through the 24/40 opening.

After the magnesium and the stirring rod were inserted through the 60/50 opening, the reaction vessel was flushed with argon for 5 min, flame dried, and allowed to cool under a stream of argon. Diethyl ether (ca. 400 mL) was then added to the cooled flask, followed by ca. 5.0 mL of 1,2-dibromoethane. The reaction with the dibromoethane was controlled by immersing the reaction vessel in an ice-water bath periodically. This reaction was allowed to go nearly to completion; at this point >90% of the original magnesium surface was visibly etched. The ethereal solution of magnesium bromide was removed by cannula under a positive pressure of argon and replaced with 300 mL of fresh anhydrous ether. The freshly corroded magnesium surface was darkened by the operation of removing the magnesium bromide solution and adding fresh ether. A small quantity of 1,2-dibromoethane (0.5 mL) introduced into the reaction vessel by syringe immediately removed the dark material on the magnesium surface and rendered the surface shiny once again. The reaction vessel was then cooled in an ice-water bath (0 °C) for 30 min and the glass stirring rod with the magnesium was rotated at 140 rpm. The reaction whose kinetics were to be studied was initiated by the addition of 0.053 mol of alkyl halide and 4.0 mL of alkane internal standard in one portion by syringe. The first aliquot was taken immediately after addition of the alkyl halide, and subsequent aliquots were taken at 2-min intervals for the alkyl bromides and at 5–30-min intervals for the alkyl chlorides, depending on the reactivity of the particular alkyl chloride being studied. Immediately upon conclusion of the reaction, the ice-water bath was removed, the Grignard solution was removed by cannula under a positive pressure of argon, and 300 mL of fresh anhydrous ether was added by cannula, followed by 0.5 mL of dibromoethane. The reaction vessel was again cooled to 0 °C for 30 min, then the second halide whose kinetics were to be studied and alkane internal standard were added in one portion by syringe. Aliquots were withdrawn in the same manner described for the reaction of the first alkyl halide. The entire operation was repeated a second time for the first halide and then the second halide. The rates of the first and third reactions on the magnesium surface—reaction with the first alkyl halide—were comparable, and the rates of the second and fourth reactions on the magnesium surface—reactions with the second alkyl halide—were comparable. Up to seven reactions could be run in sequence on a single assembly of dibromoethane-activated magnesium rods, and the rates of reaction for one halide were nearly always reproducible within ±10%.

Sequential reactions involving one halide in different solvents with one magnesium surface of constant activity gave reproducible results. Dibromoethane activation was carried out in diethyl ether in the usual manner. The ethereal magnesium dibromide was removed by cannula, then solvent A was introduced. After 0.5 mL of 1,2-dibromoethane was added to reactivate the surface, the reaction flask was cooled and the reaction carried out and analyzed as described above in the general procedure. On completion of the reaction, the Grignard solution in solvent A was removed and fresh solvent B was added to the reaction vessel. The second reaction was carried out in solvent B, the third in A, the fourth in B, and so forth. The rates of reaction of the one halide in the same solvent were reproducible within ±10%. Sequential reactions involving the reaction of one halide with one magnesium surface of constant activity in the same solvent at different temperatures gave reproducible rates for reaction at each temperature. Stirring rates above ca. 170 rpm produced vortices in the stirred ether solution that exposed some of the reacting magnesium to the argon atmosphere. The higher the stirring rate was above 170 rpm, the less the reacting magnesium surface was exposed to the ethereal alkyl halide solution. A stirring rate of 140 rpm was used in all the experiments reported in this work.

GLC analysis of the aliquots taken during "constant-surface" kinetics studies determined the loss of alkyl halide relative to internal standard as a function of time. All the experiments that were carried out using the constant-surface technique yielded first-order plots for the rate of alkyl halide consumption.

Methods for Rate vs. Surface Area Determinations. To a 50-mL round-bottomed flask equipped with a 0.75-in. magnetic stirring bar was added either a single 1.5-g slice of magnesium rod (0.625 in. o.d., surface area *A*), two 0.75-g slices (surface area 2*A*), or three 0.5-g slices (surface area 3*A*). The flask was fitted with a No-air stopper, purged with argon for 15 min, flame dried and cooled to room temperature under a stream of argon, and placed under a slight positive pressure of argon. The flask was charged with 10 mL of anhydrous ether and 0.2 mL of 1,2-dibromoethane was added to activate the magnesium surface. After the 1,2-dibromoethane had reacted, as indicated by cessation of ethylene evolution, the ethereal magnesium bromide was removed under argon by cannula and 10 mL of fresh anhydrous ether and 0.5 mL of *n*-nonane (internal GLC standard) were added. With vigorous magnetic stirring (ca. 400 rpm) the flask was equilibrated to 0 °C (ice-water bath) for 15 min. Cyclopentyl bromide (10 mmol, precooled to 0 °C) was added and a ca. 0.8-mL sample was immediately removed, and the additional aliquots were taken at 5-15-min intervals. The workups and analysis were identical with those used for the constant-surface kinetics experiments (vide supra). The method employed using cyclopentyl chloride differed in the quantities of magnesium used: for surface area *A*, 1.0 g of reagent grade magnesium metal turnings and two 1.0-g slices of 0.625-in. o.d. bar (total = 3.0 g of Mg) were used; surface area 2*A* and 3*A* were, respectively, 2.0 g of turnings plus one 1.0-g slice of bar and 3.0 g of turnings.

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References and Notes

(1) Supported by the National Science Foundation through Grants GP 28586X, GP 14247, MPS 74-20956, and 7711282CHE.

(2) Texaco Fellow, 1975-1976.

(3) Texaco Fellow, 1974-1975.

(4) National Institutes of Health Predoctoral Fellow, 1966-1969.

(5) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-Metallic Compounds", Prentice-Hall, Englewood Cliffs, N.J., 1954.

(6) G. E. Coates, M. L. H. Green, and K. Wade, "Organometallic Compounds", Vol. 1, Methuen, London, 1967, Chapter 2.

(7) J. L. Wardell, *Chem. Soc., Spec. Publ.*, **5**, 19 (1976).

(8) H. R. Rogers, J. E. Deutch, and G. M. Whitesides, *J. Am. Chem. Soc.*, following paper in this issue. A preliminary report discussed electron-transfer and halogen-abstraction mechanisms for formation of Grignard reagents (R. J. Rogers, H. C. Mitchell, Y. Fujiyama, and G. M. Whitesides, *J. Org. Chem.*, **39**, 857 (1974)). The arguments outlined in this paper were based on the assumption that none of the reported rates was mass transport limited. The current studies establish this assumption to be incorrect, and the conclusions of the earlier paper should be disregarded in favor of those outlined here.

(9) H. R. Rogers, R. J. Rogers, H. L. Mitchell, and G. M. Whitesides, *J. Am. Chem. Soc.*, accompanying paper in this issue.

(10) C. L. Hill, J. Vander Sande, and G. M. Whitesides, *J. Org. Chem.*, in press.

(11) C. L. Hill, Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, Mass., 1975; H. R. Rogers, Y.-S. Shih, J. F. Garst, J. E. Deutch, K. Root, J. Barber, L. Lawrence, and G. M. Whitesides, to be published.

(12) H. M. Walborsky and M. S. Aronoff, *J. Organomet. Chem.*, **51**, 31 (1973); H. W. H. J. Bodewitz, C. Blomberg, and F. Bickelhaupt, *Tetrahedron*, **31**, 1053 (1975), and references cited in each.

(13) The influence of mixing, mass transport, and diffusion on selectivity are discussed by P. Rys, *Acc. Chem. Res.*, **9**, 345 (1976); *Angew. Chem., Int. Ed. Engl.*, **16**, 807 (1977); G. W. Roberts in "Catalysis in Organic Synthesis", P. N. Rylander and H. Greenfield, Eds., Academic Press, New York, 1976, p 1; C. D. Johnson, *Chem. Rev.*, **75**, 755 (1975).

(14) M. Kilpatrick and H. P. Simons, *J. Org. Chem.*, **2**, 459 (1937); F. C. Gyzemski and M. Kilpatrick, *ibid.*, **5**, 264 (1940).

(15) The use and interpretation of competitive kinetics in studying heterogeneous catalysis are reviewed by J. K. A. Clarke and J. J. Rooney, *Adv. Catal.*, **25**, 125 (1976). Note in particular that rates derived from competitive heterogeneous kinetics techniques may be almost uninterpretable mechanistically if adsorption to the surface and reaction of adsorbed species at the surface are both important in determining rates. We see no evidence that adsorption prior to reaction is important for organic halides on magnesium.

(16) We emphasize that there is no indication in our data that traces of transition metals have any influence on the *kinetics* of reaction of alkyl halides with magnesium, although they may influence the yields of Grignard reagents and clearly influence the reactions of the Grignard reagents once formed (E. C. Ashby and J. L. Wiesemann, *J. Am. Chem. Soc.*, **100**, 189 (1978)).

(17) Related experiments which measured relative rates of reaction of organic halides with lithium incidentally during other studies have suggested that these rates are independent of stirring frequency above a certain value. Since these experiments were not designed to test explicitly for the frequency dependence of the rate, the observed variation in rate might have contained unrecognized contributions from vortexing or other artifacts of stirring. G. G. Cameron and A. J. S. Milton, *J. Chem. Soc., Perkin Trans. 2*, 378 (1976).

(18) For diffusion constants of representative organic compounds, see D. W. Brubaker and K. Kammermeyer, *Ind. Eng. Chem.*, 733 (1954); D. F. Evans, C. Chan, and B. C. Lamartine, *J. Am. Chem. Soc.*, **99**, 6492 (1977).

(19) M. D. Rausch, W. E. McEwan, and J. Kleinberg, *Chem. Rev.*, **57**, 417 (1957); M. Krumpett, J. Fischer, and I. Johnson, *J. Phys. Chem.*, **72**, 506 (1968).

(20) W. J. James, *Adv. Corros. Sci. Technol.*, **4**, 85 (1974); E. Heitz, *ibid.*, **4**, 185 (1974).

(21) The rate-limiting step in the reduction of alkyl bromides is probably the abstraction of hydrogen from tri-*n*-butyltin hydride by alkyl radicals rather than abstraction of bromine atoms by tri-*n*-butyltin radicals.[22] Nonetheless, since two alkyl halides are present in the same solution, the relative rates of their disappearance reflect the relative rates at which they are converted to alkyl radicals by tri-*n*-butyltin radical.

(22) D. J. Carlsson and K. U. Ingold, *J. Am. Chem. Soc.*, **90**, 7047 (1968).

(23) C. G. Overberger, H. Biletch, A. B. Finestone, J. Liker, and J. Herbert, *J. Am. Chem. Soc.*, **75**, 2078 (1953).

(24) W. C. Danen and K. A. Rose, *J. Org. Chem.*, **40**, 619 (1975). A limited number of data are also available for abstraction of iodine atoms from alkyl iodides by phenyl radicals: W. C. Danen and R. L. Winter, *J. Am. Chem. Soc.*, **93**, 716 (1971).

(25) C. Rüchardt, *Angew. Chem., Int. Ed. Engl.*, **9**, 830 (1970); B. Criese, *ibid.*, **16**, 215 (1977).

(26) W. H. Davis, J. H. Gleaton, and W. A. Pryor, *J. Org. Chem.*, **42**, 7 (1977).

(27) The products of these reactions have not been carefully established, but cyclopropane is the major product: M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances", Prentice-Hall, Englewood Cliffs, N.J., 1954, p 33; R. West and E. G. Rochow, *J. Org. Chem.*, **18**, 1739 (1953); L. C. Costa, Ph.D. Thesis, Massachusetts Institute of Technology, 1976.

(28) Reaction of carbenes with hydrocarbons shows similar low selectivity: B. M. Herzog and R. W. Carr, Jr., *J. Phys. Chem.*, **71**, 2688 (1967); W. von E. Doering, R. G. Buttery, R. G. Laughlin, and N. Chaudhuri, *J. Am. Chem. Soc.*, **78**, 3224 (1956); D. B. Richardson, M. C. Simmons, and I. Dvoretzky, *ibid.*, **82**, 5001 (1960); J. W. Simons, C. J. Mazoc, and G. W. Taylor, *J. Phys. Chem.*, **72**, 749 (1968); D. B. Richardson, L. R. Durrett, J. M. Martin, Jr., W. E. Putnam, S. C. Slaymaker, and I. Dvoretzky, *J. Am. Chem. Soc.*, **87**, 2763 (1965).

(29) Data for these rate profiles were obtained from the following sources: A. Streitwieser, Jr., "Solvolytic Displacement Reactions", McGraw-Hill, New York, 1962; A. Streitwieser, Jr., and W. R. Young, *J. Am. Chem. Soc.*, **91**, 529 (1969), and references cited therein; D. E. Applequist and P. F. O'Brien, *ibid.*, **85**, 743 (1963); J. Hine, "Physical Organic Chemistry", 2nd ed., McGraw-Hill, New York, 1962, p 165. Values for S_N2 reactions are Streitwieser's "average" values. The data for exchange of hydrocarbons with CsCHA have not been related to the rate of exchange of ethane. Since only the general forms of these profiles are important, the relative rate of exchange of cyclopropane has arbitrarily been given the same value as the equilibrium constant for metal-halogen exchange between ethyllithium and cyclopropyl iodide. Also included are data on the solvolysis of 1-methyl-1-chlorocycloalkanes in aqueous ethanol—a reaction believed to take place by an S_N1 mechanism [H. C. Brown, R. S. Fletcher, and R. B. Johannesen, *J. Am. Chem. Soc.*, **73**, 212 (1951); H. C. Brown and M. Borkowski, *ibid.*, **74**, 1894 (1952)].

(30) It would also be desirable to have a structure-reactivity profile for a reaction that involves frontside electrophilic cleavage of an alkyl halide with retention of stereochemistry at the carbon atom bonded to the leaving group. However, the most likely system that reacts by this mechanism and could yield useful structure-reactivity data—the protonolysis or electrophilic cleavage of organomercurials—is of little use. Despite the fact that some relative data exist for acid cleavage of alkylmercurials, the mechanism of the acid cleavage and the relative order of cleavage of the various alkyl moieties change with the acidic reagent used. As a consequence, the rate data taken from different studies are often hard to interpret mechanistically and cannot be compared. For references, see F. R. Jensen and B. Rickborn, "Electrophilic Substitution of Organomercurials", McGraw-Hill, New York, 1968, Chapter 3; M. H. Abraham and P. L. Grellier, *J. Chem. Soc., Perkin Trans. 2*, 1132 (1973); and references cited in each.

(31) An S_N2-like transition state has been proposed for formation of organolead compounds by cathodic reduction at a lead electrode: H. E. Ulery, *J. Electrochem. Soc.*, **116**, 1201 (1969).

(32) The activation energy of diffusion, E_D, is in the range of 3-5 kcal mol^{-1} for most liquids: cf. S. Glasstone, K. J. Laidler, and H. Eyring, "The Theory of Rate Processes", McGraw-Hill, New York, 1941, pp 522-525; S. W. Benson, "The Foundations of Chemical Kinetics", McGraw-Hill, New York, 1960, p 499; D. Shooter in "Comprehensive Chemical Kinetics", Vol. 1, C. H. Bamford and C. F. H. Tipper, Eds., Elsevier, Amsterdam, 1969, p 253.

(33) Cyclic voltametry indicates that reduction of alkyl halides is irreversible on that time scale: M. Fleischmann, D. Pletcher, and C. S. Vance, *J. Electroanal. Chem.*, **29**, 325 (1971). Pulse radiolysis studies have been interpreted as providing indirect evidence for short-lived alkyl halide radical anions (E. J. Hart and M. Anbar, "The Hydrated Electron", Wiley-Interscience, New York, 1970, p 138 ff; J. K. Thomas, *J. Phys. Chem.*, **71**, 1919 (1967); M. Anbar and E. J. Hart, *ibid.*, **71**, 3700 (1967), and quantitative interpretations suggested that the lifetime of $(CH_3I)^{-}\cdot$ must be less than

8×10^{-8} s at 25 °C in water (S. P. Mishra and M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 391 (1973)). The lifetime of $CH_3Br^{-}\cdot$ is less than 10^{-9} s in cyclohexane, and the lifetime of $CH_3Cl^{-}\cdot \simeq 3 \times 10^{-8}$ s in cyclohexane (P. P. Infelta and R. H. Schuler, *J. Phys. Chem.*, **76**, 987 (1972)).

(34) S. Bank and D. A. Jackson, *J. Am. Chem. Soc.*, **98**, 7742 (1976).

(35) J. Barber and G. M. Whitesides, *J. Am. Chem. Soc.*, accompanying paper in this issue.

(36) M. C. R. Symons, *J. Chem. Res.* (*S*), 360 (1978).

(37) H. C. Brown, G. W. Kramer, and M. M. Midland, "Organic Synthesis via Boranes", Wiley, New York, 1975.

Mechanism of Formation of Grignard Reagents. The Rate of Reaction of Cyclopentyl Bromide with Magnesium Is Transport Limited in Diethyl Ether[1]

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Abstract: Three observations indicate that the rate of reaction of cyclopentyl bromide with metallic magnesium in several ethereal solvents is limited by the rate of its encounter with the metal. First, the rate of disappearance of cyclopentyl bromide is dependent on the first power of the organic halide concentration, the magnesium surface area, and rate at which the solution is stirred, and is inversely dependent on the solution viscosity ($-d[RBr]/dt \propto [RBr]^1, A^1, \omega^1, \eta^{-1}$). Second, the activation energy for the reaction in diethyl ether ($E_a \simeq 2.3$ kcal/mol) is consistent with mixing and diffusion as rate limiting. Third, a number of representative alkyl halides react with magnesium in diethyl ether at very similar rates; no organic halides examined react faster than this rate. The dependence of the rate of reaction of neopentyl bromide on solution dielectric constant illustrates transition from transport-limited to non-transport-limited rates, and suggests appreciable charge separation in the chemical step which breaks the carbon–bromine bond.

Introduction

An examination of the relative rates of reaction of organic halides with magnesium in diethyl ether solution established that reaction occurred (at least in major part) at the magnesium-solution interface, and suggested the existence of a well-defined upper limit to the rates:[3] all alkyl iodides examined, many alkyl bromides, and one particularly reactive alkyl chloride (benzyl chloride) reacted in diethyl ether at rates that were experimentally almost indistinguishable; no organic halide tested reacted faster than this rate.[3] This paper rationalizes the observation of an upper limit to these reaction rates by demonstrating that cyclopentyl bromide—a representative alkyl bromide whose rate of reaction falls at this upper limit—reacts with magnesium in a number of solvents (including diethyl ether) at a mass transport limited rate. Comparisons of the rates of reaction of cyclopentyl bromide and neopentyl bromide (one of the alkyl bromides which reacts significantly more slowly in diethyl ether than the observed upper limit) in solvents of a range of polarities indicates that the magnitude of the rate of reaction of the latter bromide is sensitive to dielectric constant, and that an increase in dielectric constant from $\epsilon < 10$ to $\epsilon > 10$ changes its rate from one slower than transport to one limited by transport. An accompanying paper demonstrates that the rate of reaction of aryl bromides with magnesium also changes from non-transport-limited to transport limited as the solvent polarity increases.[4]

Rates and Discussion

The rate of reaction of cyclopentyl bromide with magnesium in several solvents is inversely proportional to viscosity. The rate of a diffusion-limited homogeneous reaction is characterized by an inverse proportionality to the solution viscosity.[5] Identification of an encounter-limited solid–liquid heterogeneous reaction is more complicated, because both mass transport of reactant from bulk solution to the vicinity of the interface (convection) and diffusion of reactants through the stationary fluid boundary layer immediately adjacent to the solid surface contribute to the rate. We have not separated these contributions, and both mass transport and diffusional contributions are evident in certain experiments. For convenience in what follows, we will refer to any reaction whose overall rate is limited by the encounter of soluble reactant with the solid surface as "transport limited", without distinguishing between mass transport and diffusion.

We have examined the relative rates of reaction of solutions of cyclopentyl bromide in a number of solvents with metallic magnesium using the "constant-surface" kinetics technique described in detail in an accompanying paper.[3,6] The determination of the relative rates of reaction in two solvents using this technique typically involved four experiments. First, the disappearance of the halide was followed in one solvent, during reaction with a mass of magnesium sufficiently large that its surface area remains effectively constant during the reaction. This reaction was experimentally first order in cyclopentyl bromide and pseudo zero order in magnesium. The initial solvent was then replaced with a second solvent, and the reaction repeated. The ratio of the pseudo-first-order rate constants from these two experiments measured the relative rates of reaction in the two solvents. The procedure was carried through at least twice with each solvent with the same piece of magnesium to check for consistency. This technique provides information about the relative rates of reaction in solvents of different viscosity or polarity, at different temperatures, and under different conditions of agitation. Typical experimental data are given in Figure 1.

Relative Rates as a Function of Solvent Viscosity. Table I summarizes relative rates obtained by applying these techniques of cyclopentyl bromide in several solutions. The essential features of these data are summarized in Figure 2 as a plot of relative rate vs. the inverse of the shear viscosity. These solvent systems cover only a factor of 5 in viscosity, but constitute the widest range we could devise in which the formation of cyclo-

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