Kinetics of Formation of Alkyl Grignard Reagents: Evidence for Rate-Determining Electron Transfer

Summary: A technique for obtaining relative rates of reaction of organic halides with metallic magnesium has been developed, and rate data obtained using this technique have been interpreted to indicate that the rate-determining step for formation of alkyl Grignard reagents involves electron transfer from the metal to alkyl halide.

Sir: The mechanism of the reactions between alkyl halides and metallic magnesium in ethereal solvents has proved difficult to investigate, in part because in this, as in other surface processes, the influence of the structure of the organic reactant on the rate of the reaction is not easily characterized using absolute kinetics techniques. Organic radicals have been implicated as intermediates in these reactions by stereochemical, CIDNP, and product studies, but the relevance of these radicals to the principal reaction path leading to Grignard reagent, the strength of their interaction with the magnesium surface, and the nature of the rate-determining step for the overall reaction remain unsolved problems. Here we report that reliable relative rate data for these reactions may be obtained using competition techniques and present evidence suggesting that electron transfer from magnesium to the alkyl halide occurs in the rate-limiting step.

The principal difficulty in studying the kinetics of the reaction of an alkyl halide, RX, with magnesium is that of accounting for the unknown and variable effective surface area of the metal (S_{Mg}). We have hypothesized that an expression having the form of eq 1 might prove adequate to describe this reaction. If this hypothesis is correct, it should be possible to write precisely analogous expressions (eq 1 and 2) containing the same value of S_{Mg} for two structurally similar organic halides competing in the same reaction mixture for a common magnesium surface.

\[
-k_1[R,X]\frac{d[R,X]}{dt} = k_{1'}[R,X]'S_{Mg}
\]  
(1)

\[
-k_2[R,X]\frac{d[R,X]}{dt} = k_{2'}[R,X]'S_{Mg}
\]  
(2)

\[
\ln\left(\frac{[R,X]/[R,X]_0}{[R,X]/[R,X]_0}\right) = k_1/k_2\ln\left(\frac{[R,X]/[R,X]_0}{[R,X]/[R,X]_0}\right)
\]  
(3)

where \(k_1/k_2\) is a constant attributed to the magnesium surface or by decomposition of 2.

Comparison of the rate-structure profiles produced by the kinetic data generated using this procedure (Figure 1) with profiles for reactions proceeding by SN2 and anionic mechanisms establishes that the rate of the Grignard reaction is much less sensitive to the structure of the organic moiety than are members of these classes of reactions and confirms that the transition state for the formation of alkyl Grignard reagents is not similar to transition states typical of these classes. The exceptionally small influence of the structure of the organic moiety on the rate of reaction is compatible with a diffusion-controlled reaction; however the absolute rates of the Grignard reactions are less than diffusion controlled. Since these observations exclude heterolytic and diffusion-limited mechanisms for the reaction, and since the predominant loss of stereochemistry at carbon observed by others on reaction of diastereomeric alkyl halides with magnesium argues against concerted insertion of a surface magnesium atom into a carbon-halogen bond (1), two basic types of transition states for the reaction remain to be considered. One (2) would resemble an alkyl halide radical anion, produced by one-electron reduction of the alkyl halide by the metal; a second (3) would approximate an alkyl radical, either free or surface-bound, and might be generated by abstraction of a halogen atom by the magnesium surface or by decomposition of 2.

Generalizable reaction-rate profiles for radical reactions are difficult to obtain, since many methods of generating radicals—including, in principle, the reaction considered here—impose polar character on their transition states. We have used the reduction of alkyl halides with tri-n-butyltin hydride to model 3 (Figures 1 and 2) and find that, although the rates of both the tin hydride and Grignard reactions are relatively insensitive to variations in structure, only a poor correlation exists between them: the latter are significantly less responsive to changes in structure than are the former, and, while the structure-rate profiles for the two reactions are similar in general form, they differ markedly at specific compounds.
the energy required to convert RX to RX⁻ (2), we have used half-wave potentials, \( E_{1/2} \), for reduction of alkyl halides.¹¹ For a reaction generating 2, the log of the rate of electron transfer to RX at constant potential should be approximately proportional to \( E_{1/2} \), provided, as we observe, that the rate is not diffusion limited. The correlation between \( \log (k_{RX}/k_{EBR}) \) from the Grignard reactions and \( E_{1/2} \) for the corresponding alkyl bromides is again not particularly close over the limited range of compounds for which consistent electrochemical data are available, but appears better than that characterizing the tri-n-butyltin hydride reductions.¹² ¹³

These rate studies indicate that the rate-determining transition state in the formation of an alkyl Grignard reagent does not involve a heterolytic fission of the C-X bond, nor is it diffusion limited. The superiority of the tri-n-butyltin hydride is established that the difference persists in ethereal solvents.⁹ The bulk of the available evidence suggests one-electron transfer from the electrode to the alkyl halide as the potential-determining step; cf. C. K. Mann, J. L. Webb, and H. M. Walborsky, J. Amer. Chem. Soc., 92, 2042 (1970), and A. J. Fry and R. G. Reed, ibid., 94, 8475 (1972), for discussion of this point.

All of the \( E_{1/2} \) values included in Figure 2 are taken from a single source: F. L. Lambert and K. Kobayashi, J. Amer. Chem. Soc., 82, 5224 (1960). This study employed a dropping mercury electrode, DMF solvent, and \( Bu_4N^+ | as supporting electrolyte. Our efforts to obtain \( E_{1/2} \) data in ethereal solvents have not been successful: C. L. Hill, unpublished work.

The origin of the differences in the slopes of the lines correlating \( E_{1/2} \) with \( \log (k_{RX}/k_{EBR}) \) for primary and secondary alkyl moieties is not obvious, but does not deserve speculation until it has been established that the difference persists in ethereal solvents.


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