Radical Isomerization during Grignard Reagent Formation. A Quantitative Treatment

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Alkyl group isomerizations during Grignard reagent formation from magnesium metal and alkyl halides in diethyl ether occur through intermediate alkyl radicals (eq 1–3).[1-9] Mechanistic

$$RX + Mg \rightarrow R\cdot \qquad (1)$$

$$R\cdot \xrightarrow{k} \hat{R}\cdot \qquad (2)$$

$$R\cdot \rightarrow RMgX \qquad (3a)$$

$$\hat{R}\cdot \rightarrow \hat{R}MgX \qquad (3b)$$

details that are not specified here are uncertain. One question concerns the mobility of the intermediate alkyl radicals: Are they adsorbed on the magnesium surface,[1,9] or do they diffuse freely

in solution?[5,8d]

Kinetic considerations bear on this point. For isomerizations of many alkyl radicals, values of rate constants k are known.[10]

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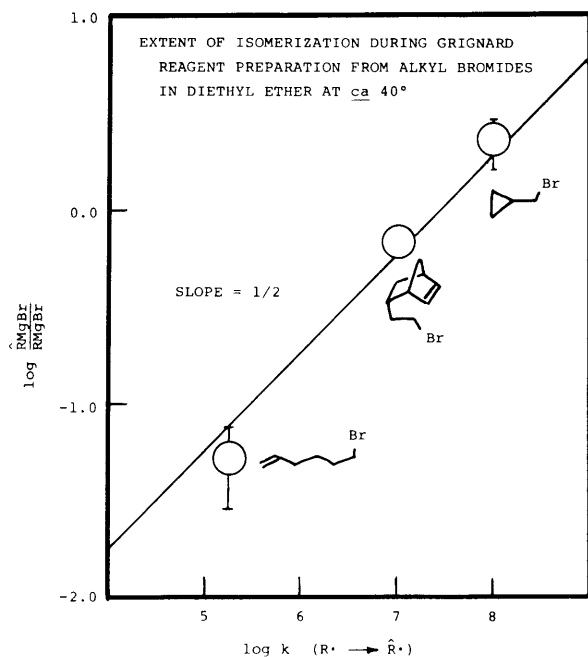
Figure 1. Test of eq 6 for isomerizations occurring during Grignard reagent formation in deithyl ether from primary alkyl bromides. Sources of data: 5-Hexenyl bromide; ref 4, 5d. 5-Hexenyl radical; ref 10. Norbornenylethyl bromide and radical; Ashby, E. C.; Pham, T. N. *Tetrahedron Lett.* **1984**, 4333. Cyclopropylcarbinyl bromide; ref 3. Cyclopropylcarbinyl radical; ref 10. The vertical bars represent limits of experimental variation.

Comparisons of quantitative predictions of the extent of formation of $\hat{R}MgX$, as a function of k, with experimental results could be informative. Such a comparison is reported here. Ratios $\hat{R}MgX/RMgX$ of products formed from primary alkyl bromides in diethyl ether conform to predictions based on a model in which the intermediate alkyl radicals diffuse freely in solution. This "D Model" is closely related to the detailed mechanism favored by Bickelhaupt and co-workers.[5]

The D Model. In reaction 1, RX is converted at the magnesium surface to R·, which is initially at a distance s from the surface. Isomerization of R· to $\hat{R}$· (eq 2) is governed by the same first-order rate constant k that applies in homogeneous solution. Both R· and $\hat{R}$· diffuse freely in solution at all times. Standard diffusion equations are assumed to apply at all distances from the surface. Radicals *must return to the surface* in order to be converted there to Grignard reagent or a precursor thereof (eq 3). Formation of byproducts, e.g., alkyl dimers, is neglected,[11] as is agitation of the solution by mechanical stirring, convection, or boiling.[12]

For this model, eq 4 and 5 describe the dependence on k of the

$$\frac{\hat{R}MgX}{RMgX} = \frac{1}{\phi}\left(\frac{(k/D)^{1/2}}{\delta} + 1 - \phi\right) \qquad (4)$$

$$\phi = \exp(-s(k/D)^{1/2}) \qquad (5)$$

yield ratio $\hat{R}MgX/RMgX$. These solutions of the relevant dif-

(11) Since yields of Grignard reagents from primary alkyl bromides in diethyl ether are high (ca. 90%), side reactions are small perturbations.

(12) On the relevant time and space scales (radical lifetimes and near the magnesium surface), diffusion may be the major mechanism of molecular transport normal to the surface.

fusion-reaction equations are taken from the literature,[13] but they can be obtained also through the molecular approach of Noyes.[14] Here D is the diffusion coefficient of the radicals and δ (Naqvi's b/D)[13] governs the reactivity of R· at the surface in reaction 3. When ϕ is near unity, eq 4 reduces to eq 6, which is analogous

$$\frac{\hat{R}MgX}{RMgX} \simeq \left(\frac{1}{\delta} + s\right)(k/D)^{1/2} \qquad \phi \simeq 1 - s(k/D)^{1/2} \quad (6)$$

to the well-known square-root law for scavening radicals or ions that would otherwise undergo geminate recombination.[15] For values of k, D, and s that are appropriate here, eq 6 is an excellent approximation to eq 4. Note that s must be equal to or less than about 4 Å, the diameter of a bromide ion. Since the maximum value of $(k/D)^{1/2}$ is about 0.02 Å^{-1}, $s(k/D)^{1/2}$ is no greater than about 0.08.

According to eq 6, a plot of log $(\hat{R}MgX/RMgX)$ vs. log k will be a straight line of slope $^1/_2$, provided that δ is constant. Figure 1 shows that experimental data for Grignard reagent formation from three primary alkyl bromides in diethyl ether conform to this prediction; the line is drawn with slope $^1/_2$.

If D is 3×10^{11} Å^2 s^{-1}, then the value of δ derived from Figure 1 is 0.01 Å^{-1}. This can be given the following interpretation:[14b] when an R· comes to the magnesium surface, its probability of undergoing reaction 3a *before* diffusing to a distance of 5 Å from the surface is ~ 0.05 (5δ).

If the intermediate alkyl radicals are not surface bound, then why don't they undergo more reaction with the solvent during Grignard reagent formation?[1] It is because the reactions with solvent are too slow to compete with reaction 3. In DME, the pseudo-first-order rate constant k_s for the reaction of a 5-hexenyl radical with the solvent is at least an order of magnitude less than the rate constant (10^5 s^{-1}) for radical cyclization.[16] Figure 1 shows that when $k_s = 10^4$ s^{-1}, the predicted yield of products from solvent attack is only about 2%.

More data, obtained under uniform and carefully controlled conditions, are needed before the correlation of Figure 1 can be accepted as definitive. However, it reinforces observations of CIDNP,[5] viscosity effects,[5d] and radical trapping,[8d] all of which point to freely diffusing radical intermediates.

Even more important, eq 4–6 show that special characteristics of reaction-diffusion kinetics should be taken into account in interpreting data on Grignard reagent formation and similar reactions. It is difficult for even a freely diffusing radical to escape reaction at a sufficiently reactive surface when it is generated near that surface. It is not necessary to invoke surface adsorption of radicals to account for every observation of the near absence of reactions that are favored when radicals of the same kind are formed in homogeneous solution.

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