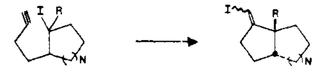
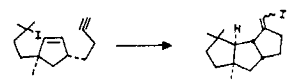
Table I. Isomerization of Hexynyl Iodides

hexynyl iodide	vinyl iodide	E/Z	conditions[a]	yield[b]
				
$R_1 = R_2 = CH_3$		15/1	A	84%
		15/1	B	c
		15/1	C	95%
$R_1 = CH_3$, $R_2 = H$		3.3/1	A	67%
		3.3/1	C	87%
$R_1 = R_2 = H$		-	A	67%
		-	B	70%
		-	C	77%
				
N = 1, $R = CH_3$		24/1	A	22%[d,e]
N = 2, $R = CH_3$		19/1	A	40%[d,e]
N = 1, R = H		1.3/1	A	42%[d,e]
N = 2, R = H		5/1	A	40%[d,e]
		6/1	B	74%[d]

[a] A: 10% Bu_3SnH, 5% AIBN (added in two separate portions at 1-h intervals), C_6D_6, reflux, 2 h. B: 10% $Me_3SnSnMe_3$, PhH, reflux, 10 h. C: 10% $Bu_3SnSnBu_3$ hr 275-W sunlamp, PhH, 70–75 °C, 30 min. [b] Yields refer to ^1H NMR or GC yield against an internal standard unless otherwise indicated. [c] Rapid decomposition of starting material was observed. [d] Isolated yield after flash column chromatography. [e] Yield is reduced due to difficulties in obtaining pure iodide.

is several orders of magnitude greater than the rate constants for the alkyl radical/alkyl iodide transfer illustrated in eq 2.[5,9]

A variety of other hexynyl iodides were isomerized to the corresponding (iodomethylene)cyclopentanes and the results are collected in Table I. To avoid the presence of even a small amount of H atom donor (Bu_3SnH), other initiation conditions were also investigated. While dark initiation with hexabutylditin/AIBN was successful in several cases, more rapid conversion was observed by irradiating a solution of the alkynyl iodide (~0.3 M, PhH) and 10% $Bu_3Sn{-}SnBu_3$ with a 275-W GE sunlamp.[4c] Sufficient heat was produced to raise the reaction temperature to 70–75 °C. Vinyl iodides were not formed in the absence of organotin additives and heating of **1** with or without AIBN in the light or dark led only to unidentified decomposition products.

Note that primary, secondary, and tertiary alkyl iodides all serve as useful substrates for the atom-transfer cyclization. In addition, modest to good selectivities are observed for formation of the (*E*)-vinyl iodide. This is readily rationalized by assuming that the rapidly inverting vinyl radical[10] abstracts an iodine atom from the less hindered side. Finally, the last entry demonstrates that tandem radical cyclizations may also be terminated by iodine atom transfer.[11]

In conclusion, this alkyl iodide → cyclic vinyl iodide isomerization provides a powerful method for termination of a radical cyclization sequence by an iodine atom transfer. The synthetic utility of this atom-transfer cyclization is enhanced by the versatility of the resultant vinyl iodide which is the synthetic equivalent for both a vinyl anion and a vinyl cation and may also be used to regenerate a vinyl radical in a subsequent step. We are presently investigating the generality of this particular atom-transfer cyclization and the possibility for the extension of the basic principles outlined above to the design and development of related radical chain reactions.

Acknowledgment. We thank the National Institutes of Health (GM-33372) for funding of this work. We also thank American Cyanamid and Stuart Pharmaceuticals for unrestricted financial support.

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$$(CH_3)_2C{=}CH\cdot + Bu_3SnH \xrightarrow{k_H} (CH_3)_2C{=}CH_2 + Bu_3Sn\cdot$$

$$k_H = 3.5 \times 10^8 \text{ mol}^{-1}\text{ s}^{-1} \text{ at } 30\text{ °C}$$

(9) Evidence that related phenyl radicals will rapidly abstract iodine from alkyl iodides is available, see ref 5a,c.

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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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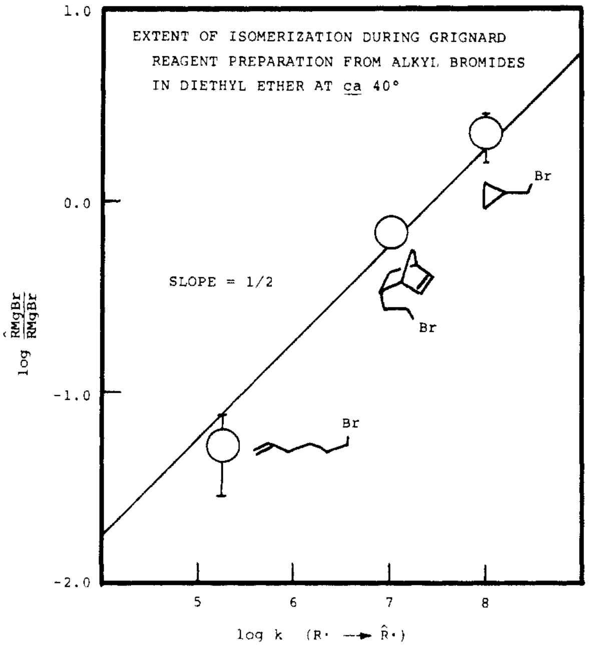

Figure 1. Test of eq 6 for isomerizations occurring during Grignard reagent formation in deithyl ether from primary alkyl bromides. Sources of data: 5-Hexenyl bromide; ref 4, 5d. 5-Hexenyl radical; ref 10. Norbornenylethyl bromide and radical; Ashby, E. C.; Pham, T. N. *Tetrahedron Lett.* **1984**, 4333. 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 R̂MgX, as a function of k, with experimental results could be informative. Such a comparison is reported here. Ratios R̂MgX/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 R̂· (eq 2) is governed by the same first-order rate constant k that applies in homogeneous solution. Both R· and R̂· 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

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

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

yield ratio R̂MgX/RMgX. These solutions of the relevant diffusion-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

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

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 (R̂MgX/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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[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.

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