

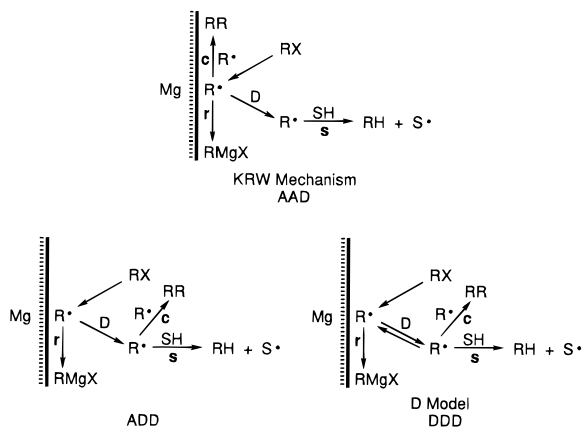
## Definitive Evidence of Diffusing Radicals in Grignard Reagent Formation

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In reactions of magnesium with alkyl halides (RX) in ether solvents (SH), intermediate alkyl radicals (R<sup>•</sup>) reduce to Grignard reagent (r), couple and disproportionate (c), and attack the solvent (s).<sup>2–14</sup> Possible mechanisms can be distinguished by the roles assigned to adsorption and diffusion for these steps. In an “A” (adsorption) step, the radicals remain adsorbed at the magnesium surface until they react. Otherwise, the step is “D” (diffusion), a reaction of radicals that diffuse in solution. Specifying the nature of the steps in the order rcs, three of the possible mechanisms are AAD [Kharasch–Reinmuth–Walborsky (KRW) mechanism],<sup>2–8</sup> ADD, and DDD (D model).<sup>9–14</sup>



Although a considerable body of data verifies quantitative predictions of the D model,<sup>9–13</sup> the KRW mechanism has not been disproved. It cannot be tested against such data because it does not support quantitative predictions. It does, however, provide a definite prediction of the effect of decreasing the rate constant ( $k_s$ ) for s; the product distribution will remain unchanged (because r, c, and desorption, and not s, are product-determining). In contrast, the D model predicts that decreasing  $k_s$  will increase the amount of r, c, or both at the expense of s.

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Since  $k_s$  can be decreased by appropriately deuterating the solvent (kinetic isotope effect), studies of solvent isotope effects can distinguish definitively between the KRW mechanism and the D model.

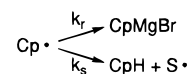
Cyclopropyl bromide (CpBr) is an appropriate substrate for such studies because in its reactions, unlike those of typical alkyl bromides, s is significant.<sup>6,13,14</sup> Accordingly, we have investigated the effects of solvent perdeuteration on reactions of cyclopropyl bromide (CpBr) in diethyl ether (DEE), MgBr<sub>2</sub>/DEE, THF, and MgCl<sub>2</sub>/THF.

In every case (Table 1), the yield of r (CpMgBr) or c (CpCp), or both, increases on solvent deuteration. This disproves the KRW mechanism.

Since it is generally agreed that s is a reaction of diffusing radicals, the observed increases of 12–14% in the yields of CpMgBr in MgBr<sub>2</sub>/DEE, THF, and MgCl<sub>2</sub>/THF demonstrate that at least 12–14% of the CpBr reacts to give diffusing radicals Cp<sup>•</sup> that are reduced to CpMgBr in the deuterated media. This proves that radicals that leave the magnesium surface can be converted to Grignard reagent, an essential element of the D model that has been disputed.<sup>7</sup>

D-model calculations can provide quantitative predictions of the effects of solvent deuteration as a function of the value of the isotope effect,  $k_s(\text{SH})/k_s(\text{SD})$ .<sup>10</sup> Consider MgBr<sub>2</sub>/DEE. The viscosity is higher than that of DEE, so the reaction is slower and c is negligible. For  $v = 2.0 \times 10^{-6} \text{ mol cm}^{-2} \text{ s}^{-1}$  ( $v$  = flux of radical formation at the magnesium surface) and the values of all other rate parameters except  $\delta$  the same as those used (and justified) previously for Cp<sup>•</sup>,<sup>13</sup> the experimental value of the yield of CpMgBr (71%) is matched by setting  $\delta$  to 0.010 Å<sup>-1</sup> ( $\delta = \kappa/D$ ;  $\kappa$  = heterogeneous rate constant for r;  $D$  = diffusion coefficient of Cp<sup>•</sup>). Decreasing  $k_s$  by factors from 2 to 10 leads to calculated yields of CpMgBr of 77–87%. The observed value in MgBr<sub>2</sub>/DEE-*d*<sub>10</sub>, 84%, is matched with an isotope effect of 6, a plausible value. Reactions in THF and MgCl<sub>2</sub>/THF are quantitatively similar.

The effect of diffusion can be evaluated by comparing the D-model calculation with one based on a (pseudo)-first-order kinetic model for competing r and s. For a decrease in  $k_s$  by a factor of 6, the first-order model predicts an



increase in the yield of CpMgBr from 71% to 94%, a significant overestimate. Relative to the first-order model, diffusion attenuates the rate of r in the D model, reducing the calculated yield of CpMgBr from 94% to 84%.

Among the media studied, pure DEE is unique in that its deuteration increases c by a factor of nearly 4 but r only marginally. Here s is coupled strongly to c but weakly (if at all) to r, a result that is predicted by the ADD mechanism. There are several plausible explanations. (1) The mechanism in DEE is ADD. It is not clear why it should be ADD in one medium and DDD in the others. (2) The mechanism is DDD in all media, but in pure DEE the buildup of polar solutes (MgBr<sub>2</sub>, RMgBr) adjacent to the magnesium surface creates a zone that radicals do not often re-enter, once they have left it. If most of the s and c occur outside that zone, then the observed behavior results. Indeed, we have found two liquid phases in the product mixture from some reactions in DEE.<sup>15</sup> One of these could lie adjacent to the magnesium and constitute a viscous, polar zone that could have these effects. (3) The early part of the reaction in pure DEE involves mostly s and c, consistent with the proposition that r requires the presence of MgBr<sub>2</sub>, which builds

(15) Unpublished observations of R. Batlaw in our laboratories.

**Table 1.** Effects of Solvent Deuteration on Products of Reactions of Cyclopropyl Bromide with Magnesium<sup>a</sup>

	<i>n</i>	[MgX <sub>2</sub> ] <sub>0</sub>	CpMgBr	CpCp	CpS	SS
				DEE		
SH	6	0.0	52 (49–57)	3 (1–4)	3 (3–4)	7 (4–8)
SD	3	0.0	54 (52–55)	14 (13–14)	3	1.2 (1.0–1.6)
SH	3	2.6	71 (70–72)	2 (1–3)	2	5 (2–8)
SD	2	2.6	84 (84–85)	4	0.3	0.04 (0.03–0.05)
				THF		
SH	7	0.0	58 (55–61)	<i>b</i>	10 (6–18)	16 (7–25)
SD	2	0.0	70 (69–71)	<i>b</i>	3	0.3
SH	4	0.5	68 (65–74)	<i>b</i>	6 (3–9)	4 (2–6)
SD	2 <sup>c</sup>	0.5	80 (78–82)	<i>b</i>	6 (3–9)	0.07 (tr–0.14)

<sup>a</sup> [CpBr]<sub>0</sub> = 0.40 M; temperature = 37 °C. [MgX<sub>2</sub>]<sub>0</sub> is the initial molar concentration of MgBr<sub>2</sub> (DEE) or MgCl<sub>2</sub> (THF). *n* is the number of replicate experiments. For CpMgBr, CpCp, and CpS, the yield is the percentage of Cp groups (of the CpBr consumed) accounted for in the product. For CpS and SS, the yield is the percentage of Cp groups accounted for as residues (S) of solvent attack by Cp\*. Grignard reagent was determined by titration with 2-butanol; CpCp, CpS, and SS were determined by GC.<sup>13,14</sup> The tabulated yields are averages. The limits of observed variations are given in parentheses. Where no limit is given, the range was zero (for the tabulated number of significant figures). <sup>b</sup> Solvent interference prevented reliable GC analyses for CpCp; the yields appear to be low. <sup>c</sup> For one of these experiments, [CpBr]<sub>0</sub> = 0.57 M and [MgCl<sub>2</sub>]<sub>0</sub> = 0.7 M.

up as the reaction proceeds.<sup>14</sup> Deuterating DEE would divert some *s* to *c*, but not *r*, during the early part of the reaction. The effects of deuteration during the later part, when *r* is more important, would be attenuated by the effects involving *s* and *c* only in the early part. These and perhaps other possible explanations deserve further exploration.

As noted previously,<sup>11</sup> quantitative predictions of the D model do not depend on whether or not there is *transient* adsorption of intermediate alkyl radicals at the magnesium surface, provided that *r* is their only surface reaction. The D model will accommodate such adsorption if it becomes necessary to invoke it to account for the partial retention of configuration that is found for reactions of optically active 1-bromo-1-methyl-2,2-

diphenylcyclopropane (\*CpBr).<sup>3–8</sup> This is not necessary at present because there are several viable alternatives, including a minor retention pathway along which \*Cp\* is not an intermediate, as is suggested by Walborsky.<sup>3–8</sup>

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