(dd, $J = 11$ Hz, 6.5 Hz, 1 H, H_5), 3.95 (t, $J = 8$ Hz, 1 H, H_2), 4.49 (m, 1 H, H_7), 6.10 (s, 1 H, H_{12}), 6.79 (dd, $J = 8.9$ Hz, 6 Hz, 1 H, H_{15}), 7.0 (d, $J = 8.9$ Hz, 1 H, H_{14}) (norsecurinine numbering).

(−)-Norsecurinine (2a). In identical fashion with that described above for **2b**, the enantiomeric mesylate **52** (derived from D-proline) afforded (−)-norsecurinine (**2a**), also in homochiral form: $[\alpha]^{20}_{D} = -262°$, $c = 0.06$ (ethanol); spectral data identical with those given above for **2b**.

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Supplementary Material Available: Spectroscopic data for compounds *ent*-**11**, *ent*-**15**, **40**, **42**, **43**, **44**, *ent*-**39**, *ent*-**45**, *ent*-**45S**, *ent*-**47**, *ent*-**49**, *ent*-**50**, *ent*-**51**, *ent*-**52**, **2a**, **2b**, and tables of X-ray crystallographic data for compound *ent*-**51** (31 pages). Ordering information is given on any current masthead page.

Solvent Attack in Grignard Reagent Formation from Bromocyclopropane and 1-Bromohexane in Diethyl Ether

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Abstract: In the reaction of magnesium with bromocyclopropane in diethyl ether at reflux, intermediate cyclopropyl radicals attack the solvent, giving cyclopropane (20–30 mol/100 mol of bromocyclopropane consumed) and solvent-derived products. In contrast, the similar reaction of 1-bromohexane gives no more than 0.5 mol of hexane from solvent attack by hexyl radicals. These data are consistent with calculations based on a mechanism (D Model) with freely diffusing intermediate radicals, in which cyclopropyl and hexyl radicals have similar reactivities in their conversions to Grignard reagents, but the cyclopropyl radical is approximately 1000 times as reactive toward the solvent as the hexyl radical.

For Grignard reagent formation from magnesium and an alkyl halide (RX), the extent of reaction of the intermediate alkyl radical ($R^{\bullet}$) with the solvent (SH) is a critical issue related to the mechanism.[2-6] In general, solvent attack does not appear to be significant for ordinary alkyl halides reacting in diethyl ether. However, it may become significant when $R^{\bullet}$ or SH is sufficiently reactive.[7]

Figures 1 and 2 depict mechanisms currently under consideration. In the D (diffusion) Model (Figure 1), $R^{\bullet}$ diffuses freely in solution at all times.[2] In an A (adsorption) Model, $R^{\bullet}$ remains adsorbed at the magnesium surface. The mechanism proposed by Walborsky (Figure 2) is a basic A Model elaborated with additional hypotheses in order to accommodate certain experimental observations.[3]

The issues addressed here concern those aspects of mechanism and reactivity that determine the extent of solvent attack. In particular, we consider reactions of magnesium with a prototypical alkyl bromide, 1-bromohexane (HxBr), and a prototypical cyclopropyl bromide, bromocyclopropane (CpBr) itself. For these reactions, we have taken great care in analyzing the products.

HxBr provides a calibration point for typical alkyl bromides. CpBr is of particular interest because (1) Walborsky's mechanism is anchored in data for reactions of another cyclopropyl bromide, 1-bromo-1-methyl-2,2-diphenylcyclopropane (**1**),[3] and (2) $Cp^{\bullet}$ is more reactive in atom-transfer reactions, by factors of 10^2–10^4, than alkyl radicals such as $Hx^{\bullet}$.[8]

1

One question that arises in connection with **1** is that of typicality, that is, the question whether or not the behavior of **1** in Grignard reagent formation is representative of typical (simple) alkyl bromides, e.g., hexyl bromide. Not only is **1** a cyclopropyl bromide, so that the intermediate radical might be unusually reactive, but also it is highly unsaturated. The pseudoconjugation of the cyclopropyl ring with the phenyl groups could lend unusual stability to an intermediate anion radical of **1**, for which there is evidence in reductions in homogeneous solutions.[9]

We find little solvent attack for HxBr but large amounts for CpBr. The latter result contrasts with the data reported for **1** and suggests that the behavior of **1** in Grignard reagent formation

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(1) On leave from the Institute of Organic Chemistry, University of Veszprém, 8201 Veszprém, Hungary.

(2) (a) Garst, J. F.; Swift, B. L. *J. Am. Chem. Soc.* **1989**, *111*, 241. (b) Garst, J. F.; Swift, B. L.; Smith, D. W. *J. Am. Chem. Soc.* **1989**, *111*, 234. (c) Garst, J. F.; Deutsch, J. M.; Whiteside, G. M. *J. Am. Chem. Soc.* **1986**, *108*, 2490. (d) Garst, J. F. *Acc. Chem. Res.* **1991**, *24*, 95.

(3) (a) Walborsky, H. M. *Acc. Chem. Res.* **1990**, *23*, 286. (b) Rachon, J.; Walborsky, H. M. *Tetrahedron Lett.* **1989**, *30*, 7345. (c) Walborsky, H. M.; Rachon, J. *J. Am. Chem. Soc.* **1989**, *111*, 1896. (d) Boche, G.; Walborsky, H. M. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; John Wiley and Sons Ltd.: London, 1987; Chapter 12. (e) Walborsky, H. M. *Tetrahedron* **1981**, *37*, 1625. (f) Walborsky, H. M.; Aronoff, M. S. *J. Organomet. Chem.* **1973**, *51*, 33. (g) Walborsky, H. M.; Young, A. E. *Baskerville Chem. J.* **1965**, *14*, 1. (h) Walborsky, H. M.; Young, A. E. *J. Am. Chem. Soc.* **1964**, *86*, 3288.

(4) Ashby, E. D.; Oswald, J. J. *J. Org. Chem.* **1988**, *53*, 6068.

(5) (a) Root, K. S.; Hill, C. L.; Lawrence, L. M.; Whitesides, G. M. *J. Am. Chem. Soc.* **1989**, *111*, 5405. (b) Root, K. S.; Deutch, J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1981**, *103*, 5475. (c) Lawrence, L. M.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 2493. (d) Rogers, H. R.; Deutch, J.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 226. (e) Rogers, H. R.; Hill, C. L.; Fujiwara, Y.; Rogers, R. J.; Mitchell, H. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1980**, *102*, 217.

(6) (a) Bodewitz, H. W. H. J.; Schaart, B. J.; Van der Niet, J. D.; Blomberg, C.; Bickelhaupt, F.; den Hollander, J. A. *Tetrahedron* **1978**, *34*, 2523. (b) Bodewitz, H. W. H. J.; Blomberg, C.; Bickelhaupt, F. *Tetrahedron* **1975**, *31*, 1053. (c) Grootveld, H. H.; Blomberg, C.; Bickelhaupt, F. *Tetrahedron Lett.* **1971**, 1999.

(7) Kharasch, M. S.; Reinmuth, O. *Grignard Reactions of Nonmetallic Substances*; Prentice-Hall: New York, 1954; pp 63–66.

(8) Johnston, L. J.; Scaino, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 4877.

(9) (a) Boche, G.; Schneider, D. R.; Wintermayr, H. *J. Am. Chem. Soc.* **1980**, *102*, 5697. (b) Jacobus, J. *J. Chem. Soc. D* **1969**, 400.

Table I. Products of the Reaction of Magnesium with 1-Bromohexane in Diethyl Ether at Reflux under Nitrogen[a]

expt	$[HxBr]_0$	HxMgBr[b]	HxMgBr[c]	HxH[d]	HxH[e]	Hx(−H)[f]	HxHx[g]	Hx tot[h]
AU-52	0.41					0.8, 1.6		
AU-64	0.40	79.2	86.8	85.7		1.2	7.2	95–102
AU-106	0.18	78.2	82.6				7.9	94–98
AU-122	0.18	79.6					7.6	95
AU-132	0.40				1.5	1.0		
AU-135	0.40	74.1					11.8	
AU-137[i]	0.18	82.3					7.4	97+
most probable			82		1.5	1.0	8	100

[a] Hx = hexyl. Each yield is the amount (mole) of product formed for 100 mol of HxBr consumed. [b] By titration with (±)-2-butanol. [c] By acid titration. [d] After quenching with water. [e] Before quenching. [f] 1-Hexene. [g] Dodecane. [h] Hexyl groups (mol) in all products. [i] Using magnesium of 99.99% purity. The other experiments use "Grignard magnesium" (99.8%).

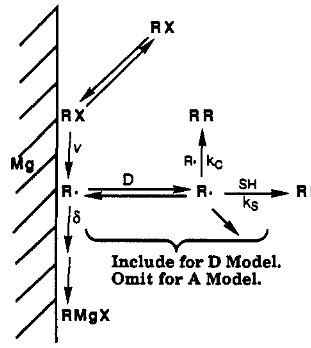

Figure 1. Basic D and A Models.

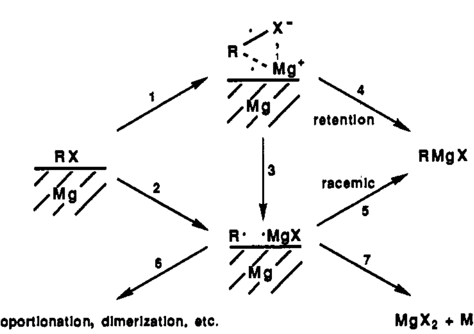

Figure 2. Elaborated version of the A Model proposed by Walborsky and co-workers.

is not that of a representative cyclopropyl bromide, much less that of a representative alkyl bromide.[3] Thus, conclusions drawn from studies of **1** should not be applied to reactions of typical cyclopropyl and other alkyl bromides without independent supporting evidence.

Our data are consistent with a mechanism of Grignard reagent formation in which $R^\bullet$ diffuses freely in solution. A D-Model analysis of the data indicates that the reactivity of $Cp^\bullet$ toward the solvent is about 10^3 times that of $Hx^\bullet$. However, the reactivities of $Cp^\bullet$ and $Hx^\bullet$ in the step in which they are reduced to Grignard reagents (governed by δ) are very similar.

Experimental Section

Reactions and associated manipulations were carried out under nitrogen (99.98%, dried by passing through 25-cm Drierite and P_4O_{10} columns) with oven-dried glassware (assembled hot with silicone grease) and by using Schlenk techniques.[10] Liquids were transferred with use of a nitrogen-purged stainless-steel cannula or a gas-tight Hamilton syringe.

Materials. Diethyl ether was freshly distilled from sodium benzophenone ketyl. 1-Bromohexane (Aldrich, 99%) and bromocyclopropane (Aldrich, 99%) were distilled under nitrogen. Magnesium turnings (Strem, 99.8%; Alfa, 99.99%) were used without preparation.

Reactions of Magnesium with Alkyl Bromides. All experiments were replicated. A dry Teflon-coated magnetic stirring bar and magnesium turnings (2.0 or 2.5 g) were placed in a three-necked jacketed (water at 34 °C) reaction vessel fitted with a reflux condenser (ice water), a silicon-disk-capped stopcock, and a stopper (when the reaction mixture was to be quenched on workup) or an adapter (when the reaction mixture was to be distilled without quenching). The adapter connected the reaction vessel through a closed 3-mm-bore stopcock to an evacuated cold (−79 °C) Schlenk tube. Diethyl ether was added, stirring begun, and the alkyl bromide (4.0 or 8.0 mmol) was injected (all at once) into the refluxing solvent. Reactions of 1-bromohexane start (increased reflux) within 1 min, and those of bromocyclopropane (gas evolution) within 5 min. After 30 min, the mixture was cooled to room temperature.

Workup with Quenching. To the stirred reaction mixture was added anhydrous 1,10-phenanthroline (hexyl case, 1 mg) or 2,2′-biquinoline (cyclopropyl case, 1 mg) in diethyl ether (0.2 mL) as an indicator. The purple solution was titrated to the sharp end point (colorless)[11] with anhydrous (±)-2-butanol (Aldrich, 99%+) from a microburet, connected through the silicone-capped stopcock on the reaction vessel by a needle and Teflon spaghetti tubing. Octane (100 μL, Aldrich, 99%+, internal standard for GC) was added and the solution was transferred through a cannula into a 25-mL volumetric flask. Aliquots (2.50 or 5.00 mL) were added to 0.1 M hydrochloric acid (10 mL) and titrated (phenolphthalein) with 0.1 M NaOH. A sample from the volumetric flask was added to cold brine, and the nonaqueous layer was analyzed by gas chromatography.

Workup by Distillation. The volatile components were distilled into the cold (−79 °C) Schlenk tube by slowly opening the stopcock on the adaptor (room temperature) and gradually raising the temperature to 34 °C. After addition of octane (50 or 100 μL), the distillate was analyzed by GC.

Gas Chromatography. Analyses were performed on a Hewlett-Packard HP 5890 instrument with a 30-m, 0.32-mm i.d., SPB-1 fused-silica capillary column, helium carrier gas, flame-ionization detector, and splitless injection. Components were identified by coinjection of authentic samples of cyclopropane (Matheson), 1-cyclopropyl-1-ethoxyethane (prepared by the reaction of sodium 1-cyclopropylethanolate with ethyl iodide in DMSO),[12] 2,3-diethoxybutane (prepared from 2,3-butanediol (Aldrich)),[13] hexane (Aldrich), 1-hexene (Aldrich), 2-ethoxyoctane (prepared from sodium 2-octanolate and ethyl iodide in diethyl ether),[14] and ethyl vinyl ether (Aldrich). The identifications (except for ethyl vinyl ether) were verified by independent GC–MS analysis (Finnegan 4000 quadrupole instrument). Quantitative analyses were based on measured response factors using model mixtures of all components except bicyclopropyl, for which a response factor of 1.000 (by mass, relative to octane) was assumed. An oven temperature of −10 °C was used in the analysis for ethyl vinyl ether.

Reaction of Magnesium with Bromocyclopropane in the Presence of Ethyl Vinyl Ether. In a stirred, refluxing mixture of 21.4 mL of diethyl ether, 4 mmol of bromocyclopropane, 10 mmol of ethyl vinyl ether, and 2.0 g of magnesium turnings, oily droplets formed on the wall of the reactor within 30 min. GC analysis of a quenched sample showed that only 6 mmol of ethyl vinyl ether remained in solution. In a similar experiment in which the magnesium was activated with 4 mmol of 1,2-dibromomethane before the addition of bromocyclopropane, ca. 95% of the ethyl vinyl ether was consumed within 30 min and a sticky, acetone-soluble substance suspected of being polymeric was formed. In another experiment, 10 mmol of ethyl vinyl ether was added to a solution

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(10) Schriver, D. F.; Drezdzon, M. A. *The Manipulation of Air-Sensitive Compounds* 2nd ed.; Wiley-Interscience: New York, 1986.

(11) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(12) 1-Cyclopropyl-1-ethoxyethane: ^1H NMR ($CDCl_3$, 300 MHz) δ 3.63 (m, 1 H), 3.46 (m, 1 H), 2.73 (m, 1 H), 1.20 (t, 3 H), 1.17 (d, 3 H), 0.83 (m, 1 H), 0.55 (m, 1 H), 0.46 (m, 1 H), 0.05 (m, 1 H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.25, 15.87, 4.95, 4.03, 3.81, 1.02, 0.12 ppm.

(13) Helmkamp, G. K.; Lucas, H. J. *J. Am. Chem. Soc.* **1952**, *74*, 951.

(14) 2-Ethoxyacetone: ^1H NMR ($CDCl_3$, 250 MHz) δ 3.52 (m, 2 H), 3.37 (m, 1 H), 1.47 (m, 10 H), 1.16 (t, 3 H), 1.04 (d, 3 H), 0.88 (t, 3 H) ppm; ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ 75.16, 63.53, 36.74, 31.88, 29.40, 25.57, 19.74, 15.64, 14.08 ppm.

Table II. Products of the Reaction of Magnesium with 1-Bromocyclopropane in Diethyl Ether at Reflux under Nitrogen[a]

expt	$[CpBr]_0$	CpMgBr[b]	CpMgBr[c]	CpH[d]	CpCp[e]	CpS[f]	SS[g]	S(−H)[h]	Cp tot[i]
AU-118	0.18	51.5			1.5	4.3	7.0		
AU-119	0.18			40.8					
AU-123	0.18	50.4	53.6						
AU-138[j]	0.18	51.8			1.4	4.7	7.7		
AU-150/1	0.18	51		40	1.5	4.9	7.3		
most probable	0.18	51		41	1.5	4.6	7.3	(3)	100

[a] Cp = cyclopropyl. S = 1-ethoxyethyl. Each yield is the amount (mole) of product formed for 100 mol of CpBr consumed. [b] By titration with (±)-2-butanol. [c] By acid titration. [d] By GC before quenching. [e] Bicyclopropyl. [f] 1-Cyclopropyl-1-ethoxyethane. [g] 2,3-Diethoxybutane (1:1 ratio of meso and (±)). [h] Ethoxyethene (ethyl vinyl ether). [i] Cyclopropyl groups (mole) in all products. [j] Using magnesium of 99.99% purity. The other experiments use "Grignard magnesium" (99.8%).

of cyclopropylmagnesium bromide, from which the excess magnesium turnings had been removed. After refluxing for 5 h, the GC analysis of a quenched sample indicated the presence of 9.98 mmol of ethyl vinyl ether.

Results

Table I gives the products of stirred reactions of magnesium turnings with HxBr in diethyl ether, under a nitrogen atmosphere in a reaction vessel thermostated at 34 °C. Reflux occurs during the reactions. "Grignard grade" magnesium (99.8%) was used in most experiments. A higher purity magnesium (99.99%) gave similar results (experiment AU-137).

To avoid confusion over the yield basis, we report each yield as the amount (mole) of product formed from 100 mol of RBr. We use three methods for determining the yield of HxMgBr: (1) titration with (±)-2-butanol (1,10-phenanthroline indicator), (2) titration with acid, and (3) quenching following by GC analysis. All methods give yields in the range 78–87 mol, but there are probable systematic errors in each. A small amount of water in the (±)-2-butanol titrant would lead to systematically low values. This may account for the fact that these titrations always give slightly lower values than the other methods. Control experiments show that the reaction of 1,2-dibromoethane alone gives a small nonzero acid titration. Thus, uncorrected values from acid titrations may be a little high. Also, the HxH determined by GC after quenching includes the HxH (1.5 mol) present before quenching, so these uncorrected values are also too high. The "most probable" yield given in Table I takes all of these factors into account.

The yields are 82 mol of HxMgBr and 9 mol of HxHx (including the HxHx equivalent of disproportionation products). These results are not surprising. With appropriate identifications, they are identical with those reported by Bickelhaupt for similar reactions of 5-hexenyl bromide (at a higher initial RBr concentration, ~2.1 M): 81 ± 5 mol of RMgBr (including both 5-hexenyl- and (cyclopentylmethyl)magnesium bromide), and 9.5 ± 2.5 mol of RR (including disproportionation products), where Bickelhaupt's data are converted to the present yield basis and corrected for radical disproportionation, using our data for 1-bromohexane.

We detect no products containing S (1-ethoxyethyl), suggesting very little attack of $Hx^\bullet$ on the solvent. Since the disproportionation of $Hx^\bullet$ gives equal amounts of hexane (HxH) and 1-hexene (Hx(−H)), any solvent attack would produce an excess of HxH over Hx(−H). However, adventitious protonation is another source of excess HxH. Our best experiment (AU-132, aimed especially at this determination) gave 0.5 mol of excess HxH. Since we cannot be absolutely certain that we have eliminated all traces of adventitious protonation of HxMgBr, this figure should be regarded as an upper limit of the HxH yield from solvent attack. A previously reported D-Model calculation, using an approximate value of k_S (4.4×10^3 s^{-1}), predicts 0.12 mol of HxH from solvent attack, which is in satisfactory agreement with the present experiments.[2a]

Table II gives the results of similar experiments with CpBr. Many other experiments, not reported here in detail, were carried out under an atmosphere of CpH so that the CpH yield could be determined by gas-volumetric analysis. Those results are consistent with the ones reported in Table II, but we consider the gas-volumetric analyses for CpH to be less accurate due to uncertainty in some of the many corrections required. The yield of cyclopropane is so high that it can be seen clearly in the ^{1}H NMR spectrum (at δ 0.2 ppm) of an unquenched reaction mixture.

Table III. Products of Reactions of Magnesium with 1-Bromo-1-methyl-2,2-diphenylcyclopropane (**1**) in Diethyl Ether and Methanol-*O*-*d*[a]

solvent	RMgBr	RH	R(−H)	R_2	ref
$(C_2H_5)_2O$	25	1.4[b]	*c*	*c*	3f
CH_3OD	87[d]	0[e]			3c

[a] Values are the amounts (mole) of products per 100 mol of RBr consumed. [b] RD for a reaction in diethyl-d_{10} ether. The combined yield of RH and RD is reported as 20.2%, 6.7% of which is RD. [c] Detected. [d] RD formed in solvent CH_3OD. [e] RH formed in solvent CH_3OD.

These results *are* surprising. Reports for reactions of **1** suggest very little solvent attack, on the order of 2 mol or less.[3] In contrast, CpBr gives 41 mol of cyclopropane (CpH), along with 52 mol of CpMgBr and some CpCp, CpS, SS, and S(−H) (ethyl vinyl ether). The high yield of CpH and the concomitant formation of CpS, SS, and S(−H) clearly indicate that solvent attack by $Cp^\bullet$ is a major source of CpH.

The mass balance on Cp groups is excellent, but half of the hydrogen atoms donated by $Cp^\bullet$ are unaccounted for by residues of their sources. This introduces uncertainty into the detailed interpretation of the product distribution. The most likely products that might account for the missing H are cyclopropene, SMgBr ((1-ethoxyethyl)magnesium bromide), and ethyl vinyl ether.

Cyclopropene, a product of $Cp^\bullet$ disproportionation, would not survive the reaction conditions.[15] However, no Cp groups are missing, so missing cyclopropene cannot account for the missing residues of hydrogen atom sources.

If SMgBr forms and survives, its protonation on workup would lead to diethyl ether, which would be undetected. However, the literature indicates that SMgBr decomposes giving ethanolate and 2-butene.[16] In our experiments, there is no GC peak where *trans*-2-butene would appear, and the Grignard and acid titers, when the latter are corrected for bases introduced from the magnesium, are nearly identical, indicating that no significant amount of ethanolate is formed in a CpBr reaction, so the formation and decomposition of SMgBr does not provide a likely account of the missing residues.

This leaves ethyl vinyl ether as the product that is most likely missing. Control experiments show that ethyl vinyl ether *is* reactive under the reaction conditions and that it may polymerize. Thus, the small amount (3 mol) of monomeric ethyl vinyl ether that we determined in one experiment is probably not all that is formed. If all of the missing H is assumed to be accounted for by missing ethyl vinyl ether, then its actual yield is estimated as 11 mol.

The minimum possible yield of CpH from the reaction of $Cp^\bullet$ with SH is that of the S residues actually determined, 20 mol (including 3 mol S(−H) determined in an experiment not tabulated in Table II). The maximum is 30 mol (if the actual yield of S(−H) is 11 mol).

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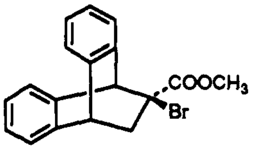
(15) Wiberg, K. B.; Bartley, W. J. *J. Am. Chem. Soc.* **1960**, *82*, 6375.

(16) Taeger, E.; Fiedler, C.; Chiari, A.; Berndt, H. P. *J. Prakt. Chem.* **1965**, *28*, 1.

Discussion

Solvent Attack and Retention of Configuration for 1, 2, and 3. Walborsky and co-workers report very little solvent attack in reactions of magnesium with 1-bromo-1-methyl-2,2-diphenylcyclopropane (**1**) in diethyl ether or CH_3OD (Table III) or from similar reactions of **2** and **3** in CH_3OD.[3] Optically active **1**, **2**, and **3** give RMgBr with partial retention of configuration in ethereal solvents, and in CH_3OD they give RH with partial retention (**1**, 23% optical purity; **2**, 60%; **3**, 11%).[3c,f] Walborsky and Rachon interpret these data as evidence against the D Model and support for the mechanism of Figure 2: "if the radicals left the surface of the magnesium, then the reactive σ radicals formed from the chiral bromides **1**...[and **2**]...would react with the solvent [CH_3OD] to abstract a hydrogen atom from the methyl group to yield RH...As one might expect the more reactive σ radicals are adsorbed more strongly than π radicals [formed from **3**] on the magnesium surface [giving less racemization for σ radicals]."[3c] The hypotheses underlying this reasoning seem to be (1) that adsorbed radicals do not react with the solvent, (2) that radicals that leave the magnesium surface *do* react with the solvent, and (3) that σ radicals (such as Cp•) are more strongly adsorbed than π radicals (such as Hx•). According to Walborsky,[3] radicals couple, disproportionate, and are converted to Grignard reagents at the magnesium surface, but do not react there with the solvent. The few that react with the solvent do so by separating from the magnesium surface. Similar hypotheses are made by Kharasch and Reinmuth.[7]

2



3

Applying hypotheses 1–3 to Hx• and Cp• leads to the clear prediction that there will be more solvent attack by Hx• than by Cp• during Grignard reagent formation from HxBr and CpBr. In fact, we find at least 40 times as much solvent attack from CpBr as from HxBr, and the most probable ratio is even higher. Thus, hypotheses 1–3 are invalid (as a group) for Grignard reagent formation from HxBr and CpBr in diethyl ether.

The falsification of this set of hypotheses as a group does not falsify A Models in general. An A Model can accommodate the present data by allowing solvent reaction by surface-bound radicals, by not requiring radicals that leave the surface to react with the solvent, or by not specifying that σ radicals are adsorbed more strongly than π radicals. However, if either of the first two of these accommodations is made, then some of the arguments that have been raised in favor of A Models vanish,[3] and if the last accommodation is made, then the smaller extent of retention in reactions of **3**, compared to **1** and **2**, remains unaccounted for.[3c]

These considerations highlight the fact that A Models, in their present states, are mostly theories of accommodation.[2d] Accommodation is achieved by auxiliary hypotheses designed specifically to account for experimental observations on a case by case basis. A Models do not have much predictive power and, consequently, are not very useful and are not falsifiable by many readily accessible methods.

Walborsky's mechanism itself shows how the observed potential retention of configuration can be accounted for without invoking adsorption of R•. If the magnesium surface is erased from the intermediates in Figure 2, the resulting mechanism still accommodates partial retention. The surface is not necessary for racemization along the lower branch of Figure 2 nor for retention along the upper branch. In fact, there is experimental evidence of a pathway similar to the upper branch of Figure 2 in homogeneous solution reductions of **1** by alkali naphthalenes, where partial retention is observed.[9]

Partial retention could also be accounted for by the basic D Model. All that is needed is a sufficiently high reactivity of R• at Mg_Z. However, our data indicate that the reactivities of Cp• and Hx• at Mg_Z are similar (see below), corresponding to median lifetimes of R• of 10^{-7}–10^{-8} s. These lifetimes are too long to allow partial retention to be accounted for in this way.

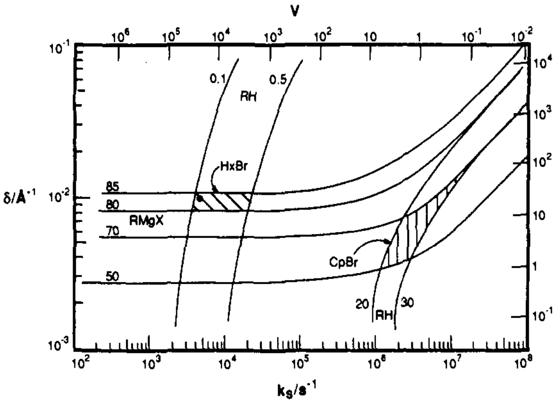


Figure 3. Calculated yields (mol/100 mol of RBr) of RMgX (horizontally trending lines) and RH from solvent attack by R• (vertically trending lines) according to an idealized D Model in which the intermediate radicals R• and S• have the same diffusion coefficients and reactivities in analogous processes. The shaded areas correspond to observed product distributions for 1-bromohexane (HxBr) and bromocyclopropane (CpBr). The left boundary of the shaded area for HxBr is somewhat arbitrarily chosen. The CpBr data presented in this work lie along the lower boundary of the shaded area; some of the rest applies to other experiments under different reaction conditions. The dark spot marks the calculation used previously in fitting the 6-bromo-1-hexene data of Bickelhaupt.[2a,6b] The scales on the top and right sides are for the dimensionless parameters V and F (see text). On the bottom and left are scales for the rate constant k_S (solvent attack by R•) and the parameter δ (reactivity of R• in its conversion to RMgX) for $D = 3.0 \times 10^{-5}$ cm^2 s^{-1}, $v = 2.0 \times 10^{-5}$ mol cm^{-2} s^{-1}, and $2k_C = 3.0 \times 10^9$ M^{-1} s^{-1}.

D-Model Calculations. The steady-state kinetics of the D Model have been solved in closed form for an ideal case in which all of the radical intermediates have the same reactivities in analogous reactions.[2b] Where radical–radical reactions and (pseudo-)-first-order radical reactions both compete with Grignard reagent formation, the solutions to the kinetic equations are sufficiently complex so that they are best evaluated by means of a computer program (a BASIC version is available).[2b]

When the intermediate radicals do not isomerize, and when all of the intermediate radicals in a particular reaction have the same reactivities in analogous steps, there are five rate parameters: D (cm^2 s^{-1}), diffusion coefficient of radicals; v (mol cm^2 s^{-1}), flux of formation of R• from RX; δ (cm^{-1}), κ/D, where κ (cm s^{-1}) is the activation-control heterogeneous rate constant for the conversion of R• to RMgX at Mg_Z; k_C (cm^3 mol^{-1} s^{-1}), rate constant for coupling/disproportionation of like radicals; and k_S (s^{-1}), pseudo-first-order rate constant for the reaction of R• with the solvent. However, the calculated product distributions are determined completely by only two composite parameters, the scaled reaction flux V and the scaled radical–surface reactivity Δ. Another composite parameter F is also significant and will be used here (instead of Δ) in displaying the results of D-Model calculations.

$$V = [4k_C/3(k_S{}^3D)^{1/2}]v \tag{1}$$

$$\Delta = (D/k_S)^{1/2}\delta \tag{2}$$

$$F = \Delta^3/V = 3D^2\delta^3/4k_Cv \tag{3}$$

Figure 3 shows some of the calculated variations of the yields of RMgX and RH (from solvent attack) with parameters V and F (scales on upper and right sides). The shaded regions are those for V and F values that fit the data for HxBr and CpBr. For the CpBr data presented here (Table II), the values lie along the lower edge of the shaded region. The upper parts of the shaded region for CpBr correspond to experiments under other conditions, not reported here, in which the yield of CpMgBr is as high as 70 mol.

The spot in the HxBr region marks the parameter values used in earlier calculations that fit the product distribution from 6-

Table IV. Comparisons of Observed and Calculated Yields for Reactions of 1-Bromohexane and Bromocyclopropane[a]

RBr		RMgBr	RH[b]	RR[c]	RS[d]	SS[d]	δ[e]	k_S[f]
HxBr	observed	82	<0.5	9	0	0		
	calculated	84	0.12	8.0			0.010	4.4×10^3
CpBr	observed	51	20–30	1.5	>4.6	>7.3		
	calculated	52	34	3.9	6.2	6.3	0.0050	4.4×10^6

[a] Amount (mole) of product formed for 100 mol of RBr consumed. All calculations are for the same values of D (3.0×10^{-5} cm^2 s^{-1}), v (2.0×10^{-5} mol cm^{-2} s^{-1}), and $2k_C$ (3.0×10^9 M^{-1} s^{-1}). [b] Includes only the RH formed in the reaction of R$^\bullet$ with the solvent (SH, diethyl ether at reflux). [c] Includes products of radical disproportionation as well as coupling. [d] Calculation includes products of radical disproportionation as well as coupling. [e] Å^{-1}. [f] M^{-1} s^{-1}.

bromo-1-hexene.[2a] Small variations in the value of k_S, which affects V but not F, would not affect the goodness of fit of these calculations, so the value of V is not very well determined by this analysis. Our HxH data for HxBr, however, show that V is not less than 10^3 for HxBr or 6-bromo-1-hexene.

Along the bottom and left sides of Figure 3 are scales that represent values of k_S and δ, provided that the values of v, D, and k_C are the same for CpBr as those used earlier for 6-bromo-1-hexene: $v = 2.0 \times 10^{-5}$ mol cm^{-2} s^{-1}, $D = 3.0 \times 10^{-5}$ cm^2 s^{-1}, and $2k_C = 3.0 \times 10^9$ M^{-1} s^{-1}. This is probably an excellent approximation. Variations in D and k_C among small molecules in fluid solvents are small. Whitesides has found that bromocyclopropane reacts with magnesium at a rate near that for 1-bromohexane. And surprisingly but favorably for the present considerations, v appears to be nearly independent of RBr concentration when magnesium pieces are used in reactions at reflux.[17] (This contrasts with the direct proportionality of v with [RBr] that is found in reactions of rotating disks of magnesium at 0 °C.)[5b] In our laboratories, reactions of 6-bromo-1-hexene under the same conditions as the experiments reported in Tables I and II give a product distribution consistent with a value of v of 1.4×10^{-5} mol cm^{-2} s^{-1},[19] near that which best fits the data of Bickelhaupt.[2a]

In the D-Model analysis (Figure 3), the data correspond to a value of k_S for Cp$^\bullet$ of at least 10^6 s^{-1}, possibly somewhat higher. At the same time, the value of δ is clearly *not* much higher for Cp$^\bullet$ than for Hx$^\bullet$ (0.010 Å^{-1}).[2a] If anything, δ is probably slightly smaller for Cp$^\bullet$, perhaps as small as 0.004 Å^{-1}. Table IV gives comparisons of observed and some calculated yields for reactions of HxBr and CpBr. The parameters for the HxBr calculation are those that give the best fit to Bickelhaupt's data for 6-bromo-1-hexene. The calculated yields of all products from HxBr, other than RH, are not sensitive to the value of k_S as long as it is sufficiently small. For CpBr, the same values are used except for δ (which is half of that for HxBr) and k_S (which is 10^3 times that for HxBr).

The calculations for CpBr agree reasonably well with all of the observed yields, but are best for CpMgBr and CpH. The yield of CpCp is overestimated and that of SS is underestimated. The calculation assumes that S$^\bullet$ and Cp$^\bullet$ are equally reactive in their conversions to Grignard reagent at Mg$_Z$. The deviations of the observed from the calculated yields are the expected ones if the radical S$^\bullet$ is actually less reactive than Cp$^\bullet$ at Mg$_Z$. Perhaps S$^\bullet$ does not give a Grignard reagent at all under these conditions. If so, then S$^\bullet$ builds up to higher steady-state concentrations than Cp$^\bullet$ and reacts with some cyclopropyl radicals that otherwise would have coupled. The steady-state concentrations of S$^\bullet$ are increased at the expense of Cp$^\bullet$, so that more products of radical–radical reactions of S$^\bullet$ and less of reactions of Cp$^\bullet$ result, as observed.

Rate Constants for Solvent Attack by Radicals. The value of k_S for Cp$^\bullet$ that is derived from our data through a D-Model analysis is near 10^6 s^{-1} (Figure 3). This is the order of magnitude expected on the basis of other studies of atom-transfer reactions of Cp$^\bullet$. Thus, the second-order rate constant for the reaction of Cp$^\bullet$ with THF at 25 °C is 5.5×10^5 M^{-1} s^{-1}, corresponding to a first-order rate constant k_S (THF solvent at 12 M) of 7×10^6 s^{-1}, which is approximately 10^3 times the reported value of k_S for the octyl radical, 6×10^3 s^{-1} at 22 °C. Similarly, 10^6 s^{-1} (approximate value of k_S for Cp$^\bullet$ in diethyl ether, from this work) is 10^3 times 10^3 s^{-1} (approximate value of k_S for the octyl radical in diethyl ether at 22 °C).[20]

It is noteworthy that reactions of magnesium with alkyl halides, coupled with D-Model analyses, can provide means of measuring the rate constants of certain reactions of intermediate radicals. If an independent determination of k_S for Cp$^\bullet$ agrees with the value calculated here, then the method will be validated for this example.

Reactivities of Hexyl and Cyclopropyl Radicals in Conversions to Grignard Reagents at the Magnesium Surface. Although Cp$^\bullet$ is much more reactive toward SH than is Hx$^\bullet$, D-Model calculations require values of δ (governing reactivity in the conversion of R$^\bullet$ to a Grignard reagent) that are similar for Cp$^\bullet$ and Hx$^\bullet$. This is one of the most interesting findings of this work.

Why don't the factors that make Cp$^\bullet$ much more reactive than Hx$^\bullet$ in atom-transfer reactions also make it much more reactive in its conversion to a Grignard reagent? Presumably, the high degree of s character of the singly occupied orbital of Cp$^\bullet$ enhances its reactivity in atom transfers. This might be expected to enhance the stability of the carbanion Cp$^-$ or a related (carbanionoid) organometallic compound such as a Grignard reagent. If so, then the enhanced stability is not reflected in the rate constant for the conversion of Cp$^\bullet$ to CpMgBr. Why not?

Several possible answers are evident. (1) The conversion of R$^\bullet$ to RMgX may be diffusion controlled. (2) It may be controlled by reaction-site availability. (3) It may be controlled by reorganization in the medium. All of these possibilities are viable.

The value of δ derived from the data corresponds to a median radical lifetime of 10^{-7}–10^{-8} s (D-Model calculations)[21] and is clearly less than a diffusion-control value. Thus, δ is the limit of α/λ as λ approaches zero, where λ is the encounter boundary (the distance from Mg$_Z$ to which an R$^\bullet$ must diffuse following a collision with Mg$_Z$ to terminate an encounter with Mg$_Z$) and α is the probability that R$^\bullet$ will react at Mg$_Z$ during a particular encounter.[2a] If $\lambda = 5$ Å is chosen to define an encounter, then $\alpha = 0.05$ (approximately) for $\delta = 0.010$ Å^{-1} (the experimentally determined value for Hx$^\bullet$). This means that only one-twentieth of the encounters so defined lead to reaction. The fraction is even smaller if a smaller value of λ is chosen. "Diffusion control" implies a value of α near unity, so the observed value of δ is distinctly less than a diffusion-control value.

However, this could be an illusion. Perhaps reactive sites are sparsely distributed over the magnesium surface. Suppose that R$^\bullet$ reacts at every encounter at an active site, but not at other encounters. Such a system would probably give a reasonable fit to D-Model calculations even though the basic D Model assumes a uniform reactivity of Mg$_Z$. The active-site sparseness would give an apparent value of δ that would be less than the diffusion-control limit, as observed, simply because many encounters with Mg$_Z$ would not be with active sites.

If active sites are dense on Mg$_Z$ or if the reactivity is uniform, they could still be rendered unavailable to an R$^\bullet$ by the adsorption of another molecule, perhaps a solvent molecule, or perhaps RMgX, X$^-$, MgX$_2$, or something else. In such a case, desorption of the hindering molecules could determine the rate at which R$^\bullet$

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(17) Whitesides and co-workers have directly observed the insensitivity of the rate to the (high) alkyl bromide concentration.[18] It is reflected in the insensitivity of product distributions to (high) alkyl bromide concentrations, as observed in the present work and by Ashby and Oswald.[4]

(18) Whitesides, G. M. Personal communication, 1990.

(19) Ungváry, F.; Lawrence, K. E.; Batlaw, R.; Garst, J. F. Unpublished results, 1989–91.

(20) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1988**, *29*, 3449.

(21) Garst, J. F. Unpublished calculations for $\delta = 0.01$ Å^{-1}, 1990.

reaches the surface (and the active sites there).

The most interesting possibility may be that the rate of reaction of R$^\bullet$ at Mg_Z is controlled by a requirement of solvent or other reorganization of the medium. Bickelhaupt has given evidence in a special case that the mechanism of conversion of R$^\bullet$ to RMgX may involve an initial reduction of R$^\bullet$ to a carbanion (or carbanionoid species) R$^-$, which is then converted to RMgX.[22] The rates of reactions that drastically redistribute charge (such as an oxidation or reduction) can be especially sensitive to the extents and rates of reorganization of the solvent.[23,24] In principle, the reorganization need not be limited to the solvent. It could include ionic aggregation or dissociation, for example. Such reorganization could be R-structure-independent and could largely determine the value of δ.

Summary. The important findings and implications include the following.

(1) The extent of solvent attack by a typical alkyl radical intermediate (Hx$^\bullet$) is clarified. The upper limit of 0.5 mol is consistent with the prediction (ca. 0.12 mol) of the D Model.[2a]

(2) CpBr gives 20–30 mol of CpH derived from the attack of Cp$^\bullet$ on diethyl ether, accompanied by other solvent-derived products (CpS, SS, and S(–H)) as well as CpMgBr. It is clear that CpBr does not behave as a typical alkyl bromide and that **1**, which is reported to give much less solvent attack, does not behave as a typical cyclopropyl bromide, much less a typical alkyl bromide. Conclusions drawn from studies of **1** and similar halides should not be extended to either typical cyclopropyl halides or typical alkyl halides.[3]

(3) The data for CpBr and HxBr falsify the combination of hypotheses (1) that adsorbed radicals do not react with the solvent, (2) that radicals that leave the magnesium surface *do* react with the solvent, and (3) that σ radicals (such as Cp$^\bullet$) are more strongly adsorbed than π radicals (such as Hx$^\bullet$).

(4) A D-Model analysis of the data for CpBr indicates a value of k_S for Cp$^\bullet$ near 10^6 s^{-1}, about 10^3 larger than the value for Hx$^\bullet$. This agrees with estimates based on other data.[8]

(5) The values of δ for Cp$^\bullet$ and Hx$^\bullet$ derived from the data are similar. The lack of dependence of δ on radical structure could be a consequence of (1) diffusion control (with sparsely distributed reactive sites on Mg_Z), (2) rate-limiting desorption of some species to make reaction sites available, or (3) rate control by reorganization in the medium, accompanying the reduction of R$^\bullet$ to R$^-$ (or some related process that drastically redistributes charge).

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[22] (a) de Boer, H. J. R.; Akkerman, O. S.; Bickelhaupt, F. *Angew. Chem.* **1988**, *100*, 735. (b) Markies, P. M.; Akkerman, O. S.; Bickelhaupt, F.; Smeets, W. J. J.; Spek, A. L. *J. Am. Chem. Soc.* **1988**, *110*, 4284.

[23] (a) Zhang, X.; Yang, H.; Bard, A. J. *J. Am. Chem. Soc.* **1987**, *109*, 1916. (b) Zhang, X.; Leddy, J.; Bard, A. J. *J. Am. Chem. Soc.* **1985**, *107*, 3719.

[24] Weaver, M. J.; McManis, G. E., III *Acc. Chem. Res.* **1990**, *23*, 294.

Viscosity-Dependent Cage Reactions. Multiple Substitutions in Radical-Chain Chlorinations[1]

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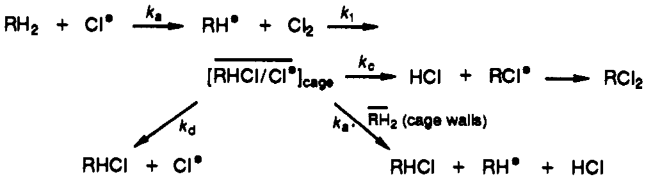
Abstract: The mechanism by which the free-radical chlorination of alkanes produces polychlorides has been explained by the assumption that the geminate chlorine atom–chloroalkane pair react in their solvent cage at rates competitive with their diffusion from, and rotation in, the cage in which they are born. The major piece of evidence supporting this mechanism is that as the concentration of alkane is increased, polyhalogenation decreases. As the hydrocarbon that makes up the "cage walls" becomes more concentrated, the surrounding hydrocarbon scavenges the caged chlorine atoms before they react with their geminate chloroalkane. In the inert solvents in which these reactions take place, CCl_4 or various Freons, the viscosity of the solvent is decreased with increasing concentration of hydrocarbon, and the diffusion rates are therefore increased. The diffusion dependence (i.e., viscosity) of the amount of polychlorination is an important component of the observed concentration dependence. The influence of the changing viscosity upon the production of polychlorination becomes more important as the hydrocarbon (neopentane, 2,3-dimethylbutane, or cyclohexane) makin up the cage walls becomes less reactive. The viscosity dependence of cage rotation was observed in solvents of high viscosity for the least reactive hydrocarbon, neopentane.

Introduction

Several years ago Skell[6] recognized that geminate cage halogenation could account for the anomalously high amounts of polychlorinated alkanes produced in the solution-phase photochlorinations of a number of hydrocarbons. Since the substitution reactions of chloroalkanes are less favorable than those of their parent hydrocarbons,[7] the large amount of polychlorination made it appear that the chlorination of a chloroalkane was not deactivated.

Scheme I



When the chlorinations of the hydrocarbons cyclohexane, isobutane, neopentane, or 2,3-dimethylbutane were carried out

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[1] Presented in part at the 73rd Canadian Institute of Chemistry Congress, Halifax, N.S., July 15–20, 1990.

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[6] Skell, P. S.; Baxter, H. N., III. *J. Am. Chem. Soc.* **1985**, *107*, 2823.

[7] Poutsma, M. L. *Methods in Free-Radical Chemistry*; Hyser, E. S., Ed.; Marcel Dekker: New York, 1969; Vol. 1.