

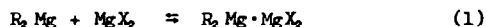
THE CONSTITUTION OF THE GRIGNARD REAGENT

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During the past year the sixty year old problem involving the structure of the ethereal Grignard reagent, a vexing controversy which was thought to have been solved by tracer studies in 1956, reopened as an apparently insolvable and irreconcilable dichotomy. The tracer results¹ involving the observation that mixtures of Et_2Mg and Mg^*Br_2 in ether led to little exchange of Mg between the two species, and kinetic and electrochemical data suggesting that these mixtures contained the same species as that produced by EtBr and Mg in ether² supported a modified Schlenk equilibrium



This formulation agreed, or at least was compatible with numerous kinetic findings^{3,4}, product stereochemistry and

¹ R. E. Dessy, G. S. Handler, J. H. Wotiz and C. A. Hollingsworth, *J. Am. Chem. Soc.*, **79**, 3476 (1957); R. E. Dessy and G. S. Handler, *ibid.* **80**, 5824 (1958).

² R. E. Dessy, *J. Org. Chem.*, **25**, 2260 (1960).

³ N. M. Bikales and E. I. Becker, *Chem. & Ind.*, 1831 (1963), S. J. Storfer and E. I. Becker, *J. Org. Chem.*, **27**, 1869 (1962).

⁴ M. Anteunis, *J. Org. Chem.*, **26**, 4214 (1961); **27**, 596 (1962).

mechanistic observations ^{5,6}, particularly those indicating effective utilization of only one alkyl group per ($R_2Mg \cdot X_2$), and apparent differences in product distribution from utilization of the first 50% of available alkyl groups as compared to the second half. The $R_2Mg \cdot MgX_2$ formulation was thus extended to other R groups, and to other solvent systems, such as THF.

Facts which eventually lead to conflict with this are associated with the "monomeric"⁷ molecular weights exhibited in dilute ethereal solutions by many Grignard reagents as recently reported from two separate laboratories ^{8,9}, and "monomeric" molecular weights exhibited over a wide range of concentrations in THF; more concentrated ethereal solutions tend toward the "dimeric". In addition, two studies on crystalline organomagnesium compounds suggest $RMgX$ units ^{9,10}, one of these entailing an X-Ray analysis of $\emptyset MgBr \cdot 2Et_2O$.

⁵ J. Miller, G. Gregorian and H. S. Mosher, J. Am. Chem. Soc., 83, 3966 (1961); D. O. Cowan and H. S. Mosher, J. Org. Chem., 27, 1 (1962).

⁶ H. O. House, D. D. Traficonte and R. A. Evans, J. Org. Chem., 28, 343, 355 (1963).

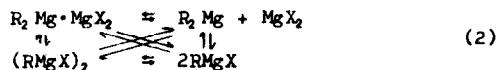
⁷ The extension of measured apparent molecular weights, really a measure of total concentration of species in solution, to the structure of organomagnesium solutions is difficult, and the term "monomeric" refers to a solution giving rise to one particle per R, Mg, X combination thus $RMgX$ and $R_2Mg + MgX_2$ are indistinguishable. Dimeric refers to a situation giving 1/2 particle per R, Mg, X combination. Thus $R_2Mg \cdot MgX_2$ and $(RMgX)_2$ are indistinguishable.

⁸ A. D. Vreugdenhil and C. Blomberg, Rec. trav. chim. des Fay-Bas, 82, 454, 461 (1963).

⁹ E. C. Ashby and W. E. Becker, J. Am. Chem. Soc., 85, 118 (1963); E. C. Ashby, personal communication.

¹⁰ R. E. Rundle, J. Am. Chem. Soc., 85, 1003 (1963).

Although such evidence is not transferable to solution, they do add weight to an argument calling for a Schlenk equilibrium:



Evidence for RMgX in the crystalline phase studies and the tracer work, showing no RMgX equilibrium member are the only direct conflicts. However, more deep seated problems are involved, since the solubility of MgX₂ in ethers may preclude a near zero value for the equilibrium constant of (1) as the cause of "monomeric" molecular weights suggesting that "monomeric" molecular weights and RMgX content are often related.

At present the occurrence of RMgX units has only been "proven" in THF solution. In ether the "monomeric" form (R₂Mg + MgX₂ or 2RMgX) is in evidence at low concentrations, normally below the solubility limit of MgX₂. At higher concentrations association (R₂Mg·MgX₂ or perhaps (RMgX)₂) is observed. Yet kinetic results in THF show distinct differences in reactivity of the first and second R group, as do ether ¹¹ reactions, facts which are cited above.

Since the basic evidence for R₂Mg·MgX₂ formulation is the exchange work, kinetic and mechanistic data being more subject to preconceived structural beliefs, the report in the early exchange work of a single experiment which yielded complete exchange, suggestive of RMgX, or an ionic or non-ionic pathway for exchange, assumed greater importance.

¹¹ R. E. Dessy and R. M. Salinger, J. Am. Chem. Soc., 83, 3530 (1961).

This single experiment involved Mg^{25} as a tracer instead of the Mg^{24} used in the other experiments, and the exchange was attributed to impurities in the Mg^{25} sample not present in the Mg^{28} sources.

Repetition of the Mg^{28} exchange studies, under a number of conditions has led to the compilation of the data in Table I which includes all runs made from 1956 to date. Except for the variations noted all runs were made in what appears to be the same manner. Both no exchange results and statistical exchange results have been found in two systems.

There appears to be no direct correlation except the fact that the earlier ^{1a, 1b} no-exchange results correlate with the employment of a specific Mg source, Dow Atomized Shot. The entire series of recent runs employing other sources of magnesium show statistical exchange. Since Dow Shot is intermediate in purity between triply-sublimed material and commercial turnings, and negative catalysis of exchange is unpalatable, it would appear sounder to seek other sources for the dichotomy. However, inhibition of an exchange catalyst by trace impurities is not an impossibility. Perhaps the answer lies in $R_2Mg/MgBr_2$ ratios, sequence of addition, or alkoxide content. No obvious relationship between separation method, or method of preparation of $MgBr_2$ and the variable results appears evident. γ -Ray spectroscopy has confirmed the isotope employed.

In view of the large number of variables other investigations will have to suggest key experiments.

Specifically, one is faced with the problem of whether the statistical exchange data above result from RMgX intermediates, or equilibrium members, or are the result of non-ionic or ionic pathways for exchange; alternatively, one might consider whether $\text{R}_2\text{Mg} + \text{MgX}_2 \rightarrow$ always yields the same species as $\text{RX} + \text{Mg}$. Since the evidence cited above², as well as kinetic data provided by Becker³, and unpublished observations by Mosher indicate that the two pathways can lead to the same species, an explanation for no-exchange/statistical exchange could be in the fact that the two pathways do not always lead to the same species. In more general terms it is still difficult to reconcile the findings of Mosher⁵ and House⁶ in ether solvent with other than a $\text{R}_2\text{Mg}, \text{MgX}_2$ system at present. In THF there may be some merit in considering the suggestion of Anteunis⁴ that utilization of only one-half the available R groups might be associated with a product organomagnesium complex which effectively removes one available R- Mg unit per R- Mg unit that reacts.

TABLE I
 $R_2Mg + Mg^*Br_2 \rightleftharpoons$

R_2Mg	Method of Prep. ¹	Mg^*Br_2 Source ²	$MgBr_2$ Prep. ³	Sol-vent	Separation Reagent ⁴	No. Runs	Result
Et_2Mg	A	B	A	Et_2O	Dioxane	3	No Exc.
Et_2Mg	A	B+C	A	Et_2O	Dioxane	1	No Exc.
Et_2Mg	A	B	A	Et_2O	Electrolysis	1	No Exc.
Et_2Mg	A	C	A	Et_2O	Dioxane and Electrolysis	1	Stat.Exc. (Mg^{2+})
Et_2Mg	A	A	A	Et_2O	Dioxane	1	Stat.Exc.
Et_2Mg	A	A	B	Et_2O	Dioxane	1	Stat.Exc.
Et_2Mg	A	A	B	THF	Bipyridyl	1	Stat.Exc.
Me_2Mg	B	A	B	THF	Bipyridyl	1	Stat.Exc.
Me_2Mg	B	A	A	Et_2O	Dioxane	1	Stat.Exc.
Me_2Mg	B	A	A	Et_2O	Bipyridyl	1	Stat.Exc.
ϕMg	A	B	A	Et_2O	Dioxane	1	No Exc.

¹ R_2Mg was prepared by either method (A) " $RMgX$ " $\xrightarrow[\text{Ether}]{\text{Diox.}}$ or (B) $R_2Hg \xrightarrow{Mg}$

² The Mg used as carrier was (A) Dow Triply Sublimed, (B) Dow Atomized Shot, or (C) Grignard Grade Turnings, a typical analysis of which is:

	Max. Impurities in ppm		
	A	B	C
Al	<39	<39	<39
Cu	4	16	25
Cr	<4	<4	<4
Fe	41	310	310
Mn	<4	70	310
Ni	<20	<20	<20
Si	<73	<73	<73
Ti	<20	<20	<20

It is to be noted that sublimation of the carrier is normally involved as part of the labeling process. In one no exchange experiment this labeled sublimate was mixed with commercial turnings before preparation of $MgBr_2$.

³ $MgBr_2$ was produced by (A) $Mg + Br_2 \xrightarrow{Et_2O}$, or (B) $C_2H_4Br_2 \xrightarrow{Mg}$

⁴ The separation reagent is that used to separate R_2Mg from $MgBr_2$ or to isolate a unique Mg species from solution.