[CONTRIBUTION NO. 1000 FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PITTSBURGH]

The Constitution of the Grignard Reagent

BY RAYMOND E. DESSY,[1] GEORGE S. HANDLER, JOHN H. WOTIZ AND C. A. HOLLINGSWORTH

RECEIVED JANUARY 12, 1957

The equilibria $Et_2Mg \cdot MgBr_2 \rightleftarrows Et_2Mg + MgBr_2 \rightleftarrows 2EtMgBr$ have been investigated by employing magnesium bromide labeled with radioactive magnesium. Only a small amount of exchange was noted between Et_2Mg and Mg^*Br_2. These results, in conjunction with the fact that the same species seems to be present in a solution of Et_2Mg and $MgBr_2$ as is present in the Grignard reagent prepared in the usual manner, indicate that the ethyl Grignard reagent is better represented by a complex $Et_2Mg \cdot MgBr_2$ than by EtMgBr.

Despite the fact that the Grignard reagent has been known and utilized for over fifty years, its structure, particularly in ether solution, is unknown. The most widespread hypothesis considers the equilibria[2]

$$R_2Mg \cdot MgX_2 \rightleftarrows R_2Mg + MgX_2 \rightleftarrows 2RMgX \quad (1)$$

The addition of dioxane to a Grignard solution results in the precipitation of virtually all of the halogen and part of the magnesium, leaving R_2Mg in the supernatant liquid.[2] It also has been shown[3,4] that equimolar mixtures of diethylmagnesium and magnesium bromide in ether yield almost instantaneously a solution having the same relative rate of reaction and kinetics in a reaction with a given substrate, hexyne-1, as does the Grignard reagent prepared in the normal manner from ethyl bromide and magnesium. This would seem to imply that the same species is/are present in the two solutions. Recalling these two pieces of information, it therefore seemed of interest to investigate equation 1 [R = ethyl, X = Br] employing radioactive magnesium as a tracer, using, for example, Mg^*Br_2.

Methods and Results

Radioactive magnesium (Mg^{28}, $t_{0.5}$ = 21.25 hr.) was prepared by a spallation reaction involving proton irradiation of potassium chloride. The magnesium, diluted with carrier, was separated as the oxinate and ignited to the oxide. The latter was converted to magnesium chloride, and exchange between this and elemental magnesium was accomplished by heating the mixture to 800°. The resulting labeled magnesium metal was then treated with bromine in dry ether to yield magnesium bromide. The specific activity of the magnesium in an aliquot was determined as a function of time. Table I lists the specific activities of the magnesium in the magnesium bromide used in two entirely separate experiments.

Equimolar amounts of this magnesium bromide and diethylmagnesium (prepared from ordinary magnesium) were dissolved in ether so as to give a solution 1.0 *M* in magnesium. The resulting solution was permitted to stand for ten minutes or 36 hr. and an excess of dioxane added, so as to precipitate the elements of magnesium bromide, leaving diethylmagnesium in the supernatant liquid. The specific activity of the magnesium in an aliquot of the diethylmagnesium solution was determined as a function of time. Table I also lists these specific activities, corrected to the same time of counting as the corresponding magnesium bromide sample and corrected for the small amount of magnesium bromide left unprecipitated by the dioxane.

TABLE I

RADIOACTIVITY EXCHANGE BETWEEN $(C_2H_5)_2Mg$ AND Mg^*Br_2

Run	Specific activity (counts/sec.-*mg.* Mg)		Contact *time,* min.	Activity ratio	% Migration	% Exchange (based on statistical exchange)
	Mg^*Br_2	Et_2Mg^a				
1	1.65	0.089	10	19:1	5	10
2a	13.05	.444	10	29:1	3	6
2b	4.20	.178	36 hr.	24:1	4	8

[a] The specific activity of the magnesium in the diethylmagnesium sample has been adjusted to the same counting time as that of the companion magnesium in the magnesium bromide sample by means of log (activity) *versus* time plots. It also takes into account the $MgBr_2$ present as a result of incomplete precipitation by the dioxane. This accounted for about 1% of the magnesium present in the sample.

Discussion

Assuming, on the basis of the rate data mentioned previously,[3,4] that an equimolar mixture of diethylmagnesium and magnesium bromide yields the same species as that to which we assign the name "ethyl Grignard" and considering equation 1, one would conclude that in a mixture of $(C_2H_5)_2Mg$ and Mg^*Br_2 there should be a 50% migration of the label (100% exchange). This would arise because of the fact that in the species C_2H_5MgBr we have an equilibrium partner in which all of the magnesium atoms are equivalent. The low percentage of exchange actually found[5] would seem to indicate that forms such as those represented by RMgX in equation 1 play little or no part in the constitution of the ethyl Grignard reagent. Although one is limited by the short

---

(1) Department of Chemistry, The Ohio State University, Columbus 10, Ohio.

(2) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954.

(3) J. H. Wotiz, C. A. Hollingsworth and Raymond E. Dessy, *J. Org. Chem.*, **21**, 1063 (1956).

(4) Raymond E. Dessy, J. H. Wotiz and C. A. Hollingsworth, THIS JOURNAL, **79**, 358 (1957).

(5) It is impossible at the present to explain why a low percentage of migration, rather than no migration at all was found. One possible explanation would be of course to assume that a very small amount of the species C_2H_5MgBr was present and that the disproportionation of this to the species $(C_2H_5)_2Mg$ and $MgBr_2$ occurs very slowly. However, it is also very likely that a considerable amount of precipitation exchange occurs, that is, migration occurring during the vigorous exothermic precipitation of the $MgBr_2$. The actual mechanism of this step is unknown.

The low percentage of exchange found is also most unexpected in view of the appreciable conductivity of ether solutions of $(C_2H_5)_2Mg$ and $MgBr_2$ (*cf.* Evans and Pearson, THIS JOURNAL, **64**, 2865 (1942)).

half-life of the tracer, the fact that the activity ratios after a contact time of ten minutes or 36 hr. were sensibly the same indicates that equilibrium 2 is at most a very unimportant side

$$(C_2H_5)_2Mg + MgBr_2 \rightleftharpoons 2C_2H_5MgBr \tag{2}$$

reaction with respect to the over-all picture. The results are compatible with an equilibrium of the type

$$(C_2H_5)_2Mg + MgBr_2 \rightleftharpoons (C_2H_5)_2Mg{\cdot}MgBr_2 \tag{3}$$

Along the same lines it is interesting to note that the diethylcadmium–cadmium bromide system in tetrahydrofuran shows no exchange under similar conditions.[6]

A more comprehensive investigation of Grignard systems is being contemplated, employing stable isotopes as tracers.

Experimental

Diethylmagnesium.—The diethylmagnesium in ether was prepared by the action of dioxane on an ether solution of ethylmagnesium bromide,[7] followed by removal of the solvents and dissolution in ether.

Labeled Magnesium Bromide.—Mg^{28} was prepared by a spallation reaction involving proton irradiation of a one cc. single crystal of potassium chloride[8] for 1 hr. at a radius equivalent to 350 Mev. in the Synchrocyclotron of the Carnegie Institute of Technology. The crystal was permitted to stand for 2 hr. after it was dismounted from the probe to allow any short-lived material to decay, and it was then dissolved in 50 ml. of water, along with 100 mg. of $Al(NO_3)_3$ and 500 mg. of $MgBr_2$ to serve as carriers. The solution was heated to the boiling point and adjusted to *p*H 8 with ammonium hydroxide in order to precipitate aluminum hydroxide, which was filtered off. The filtrate was diluted to 125 ml. and heated to 60° and 35 ml. of 6 *N* ammonium hydroxide added. Then 30 ml. of 5% 8-hydroxyquinoline in 2 *N* acetic acid was added slowly. The suspension was brought to the boiling point and then permitted to settle for a few minutes. The oxinate of magnesium was collected by filtration and dried.

The greenish-yellow oxinate was mixed intimately with an equal volume of oxalic acid and placed in a fused silica crucible. Careful ignition with a blast burner yielded magnesium oxide as a fine white powder. The magnesium oxide was dissolved in concentrated hydrochloric acid and any excess acid destroyed by adding a few shavings of magnesium metal.

The solution of magnesium chloride was transferred to a graphite crucible enclosed in a Vycor capsule along with 10 g. of Dow atomized magnesium pellets. The capsule was then attached to a vacuum line and carefully pumped out. The capsule was then heated to 800° and kept at that temperature for 1 hr. in order to cause exchange between the Mg and $Mg^{*}Cl_2$. The contents of the crucible were permitted to cool, and the capsule was forced open. Under the conditions employed the Mg was obtained as a clean crystalline plug, which had distilled or sublimed from the hot furnace area of the crucible to cooler portions. This plug was crushed and added to 100 ml. of Mallinckrodt Anhydrous Ether in a three-necked flask equipped with a stirrer, addition funnel and Dry Ice–acetone condenser. Bromine was added slowly to the suspension until a considerable quantity of the magnesium had been utilized. Magnesium bromide and ether, in these concentrations, form a two-phase system.[9] The darker lower layer which contains 485 mg. of $MgBr_2$ per ml. at 25° was used.

Exchange Reactions.—The concentrated magnesium bromide solution and the concentrated diethylmagnesium solution were added to a sufficient volume of ether to yield a solution 0.5 molar in each component (1.0 molar in magnesium). This was permitted to stand for various time periods, and then 1.5 mole equivalents of 1,4-dioxane was added slowly over a 15-minute period with constant agitation. The suspension was agitated slowly for 15 minutes and then centrifuged at 2000 r.p.m. for five minutes. The supernatant solution was analyzed for basic magnesium using the technique described by Gilman[10] and was found to be approximately 0.5 *M* in magnesium. A potentiometric titration for halogen indicated that the supernatant liquid was approximately 0.01 *M* in bromine.[11]

Sampling and Counting.—A portion of the supernatant liquid was transferred to a glass planchet, air hydrolyzed, treated with concentrated hydrobromic acid and dried. A similar planchet was prepared from the original magnesium bromide solution.

The activity of the samples was determined using an Amperex Type 200 CB halogen filled Geiger tube. The activity of the samples was followed for 60 hr. A plot of log(activity) *versus* time indicated high radiochemical purity and a $t_{0.5}$ of 21.2 hr. The reported $t_{0.5}$ of Mg^{28} is 21.25 hr.[12]

Acknowledgment.—The authors are indebted to the staff and crew of the Carnegie Institute of Technology Synchrocyclotron at Saxonburg, Pennsylvania, for their aid and coöperation.

---

[6] A. B. Garrett, Arthur Sweet, Wm. L. Marshall, David Riley and Anis Touma, *Rec. Chem. Progr.*, **13**, 155 (1952).

[7] J. H. Wotiz, C. A. Hollingsworth and Raymond E. Dessy, THIS JOURNAL, **78**, 1221 (1956).

[8] M. Lindner, *Phys. Rev.*, **89**, 1150 (1953).

[9] W. E. Doering and C. R. Noller, THIS JOURNAL, **61**, 3436 (1939).

[10] H. Gilman, *ibid.*, **51**, 1576 (1929).

[11] It was very difficult to obtain reliable data on the halogen concentration in the solutions when only one-ml. samples were available. However, determinations made during blank runs which did not involve the radioactive tracer and hence could be run on a larger scale indicated similar results.

[12] G. Friedlander and J. W. Kennedy, "Nuclear and Radiochemistry," John Wiley and Sons, Inc., New York, N. Y., 1955.

PITTSBURGH, PENNA.

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Condensation of Grignard Reagents with 3-Pyridyl and 3-Quinolyl Ketones

BY REYNOLD C. FUSON AND JOHN J. MILLER

RECEIVED JANUARY 18, 1957

Phenylmagnesium bromide was found to condense in the 1,4-manner with 3-benzoyl-, 3-mesitoyl- and 3-duroylpyridine and with 3-benzoyl- and 3-mesitoylquinoline. Benzylmagnesium chloride reacted in a similar way with the hindered pyridyl ketones, but gave the 1,2-addition product with 3-benzoylpyridine. The products with the phenyl reagents were the corresponding dihydro aromatic compounds; they were dehydrogenated readily with chloranil. 2-Azafluorenone (III) was produced when either 3-mesitoyl-4-phenylpyridine or 3-duroyl-4-phenylpyridine was treated with polyphosphoric acid. The action of polyphosphoric acid on 3-mesitoyl-4-phenylquinoline provided 3,4-benzo-2-azafluorenone (X).

In a search for diaryl ketones that might be unusually receptive to conjugate attack by Grignard reagents, attention was directed to the 3-pyridyl ketones. That these compounds would undergo condensation with organomagnesium halides in the 1,4-manner was indicated clearly by the