AN ISOTOPIC STUDY OF THE REDUCING ACTION OF THE GRIGNARD REAGENT[1]

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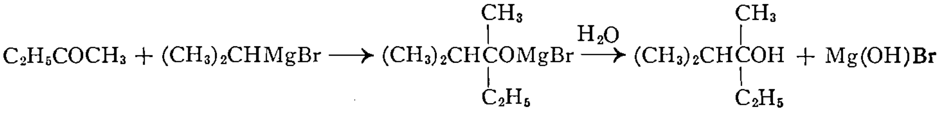
ABSTRACT

Benzophenone has been reduced to benzhydrol with three samples of isobutylmagnesium bromide containing deuterium in the *alpha*, *beta*, and *gamma* positions, respectively. Deuterium was found only in the benzhydrol obtained from β-deuteroisobutylmagnesium bromide. Comparison of the ratios of deuterium to protium in β-deuteroisobutylmagnesium bromide and in the benzhydrol obtained from it shows an isotope effect of about two. In the decarboxylation of hydroxyl-deuterated dimethylmalonic acid an isotope effect of 4.5 was observed. These results are considered in terms of the probable mechanisms of the reactions.

INTRODUCTION

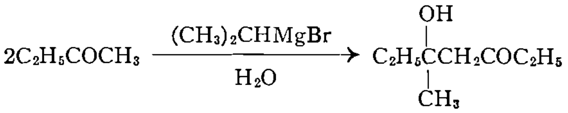
Of the many reactions of the Grignard reagent, the most familiar and probably the most used is the addition to a carbonyl group. It has long been known, however, that this reaction is frequently complicated by side reactions which may replace some or all of the addition. The three most important of these side reactions are commonly referred to as condensation, enolization, and reduction (8). They are illustrated below in terms of methyl ethyl ketone and isopropylmagnesium bromide (15).

Addition



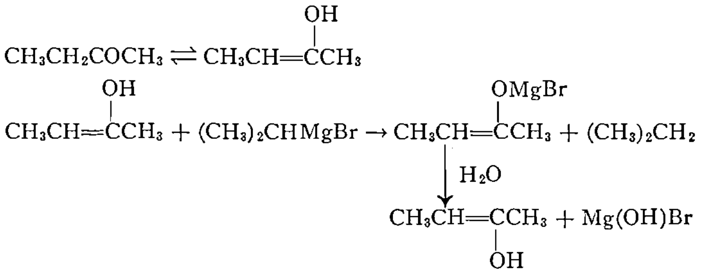
$$C_2H_5COCH_3 + (CH_3)_2CHMgBr \longrightarrow (CH_3)_2CH\underset{C_2H_5}{\overset{CH_3}{C}}OMgBr \xrightarrow{H_2O} (CH_3)_2CH\underset{C_2H_5}{\overset{CH_3}{C}}OH + Mg(OH)Br$$

Condensation



$$2C_2H_5COCH_3 \xrightarrow[H_2O]{(CH_3)_2CHMgBr} C_2H_5\underset{CH_3}{\overset{OH}{C}}CH_2COC_2H_5$$

Enolization



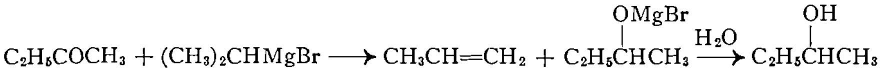
$$CH_3CH_2COCH_3 \rightleftharpoons CH_3CH{=}\overset{OH}{C}CH_3$$

$$CH_3CH{=}\overset{OH}{C}CH_3 + (CH_3)_2CHMgBr \rightarrow CH_3CH{=}\overset{OMgBr}{C}CH_3 + (CH_3)_2CH_2$$

$$\downarrow H_2O$$

$$CH_3CH{=}\underset{OH}{C}CH_3 + Mg(OH)Br$$

Reduction



$$C_2H_5COCH_3 + (CH_3)_2CHMgBr \longrightarrow CH_3CH{=}CH_2 + C_2H_5\overset{OMgBr}{C}HCH_3 \xrightarrow{H_2O} C_2H_5\overset{OH}{C}HCH_3$$

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The condensation reaction is, at least formally, analogous to the common base-catalyzed aldol condensation with the Grignard reagent as the base, and the enolization reaction is an example of the well-known tendency of the Grignard reagent to react with acidic hydrogen. The reduction reaction, however, shows a property of the Grignard reagent which is not illustrated among its better known reactions and, consequently, this side reaction has attracted more interest and experiment than the other two.

The equation written above for the reduction reaction indicates that the Grignard reagent is converted into olefin, and careful work by Noller, Grebe, and Knox has shown that, at least in the reduction of benzophenone by isobutylmagnesium bromide, the amounts of olefin and alcohol produced are exactly equivalent (14). It is also commonly observed that the double bond of the olefin has for one of its carbon atoms that one to which magnesium was originally attached. For example, γ-phenylpropylmagnesium bromide when used as a reducing agent is converted into allylbenzene (2). Evidently the net result of the reaction is the elimination of magnesium and hydrogen from adjacent carbon atoms. This conclusion is supported by the observation that, although the amounts of all three side reactions increase with increasing branching in the alkyl groups of both carbonyl and Grignard reagents, reduction does not occur when the Grignard does not contain a hydrogen atom on the carbon *beta* to magnesium (20).

Although the evidence considered above shows that the over-all result of the reduction is the transfer of the elements of magnesium halohydride from Grignard reagent to carbonyl compound, it does not, of course, prove that a hydrogen atom originally attached to the β-carbon of the Grignard is the one actually transferred to the carbonyl compound. It is conceivable that the actual hydrogen atom appearing in the carbinol product could come from the α- or γ-position of the Grignard reagent, from the solvent, or from the water used in the hydrolysis. However, in the absence of evidence to the contrary, attempts to devise a mechanism for the reduction have naturally been based on the simplest reasonable assumption: namely, that a hydride ion is transferred directly from the Grignard molecule to the carbonyl compound.

The objects of the present investigation have been: first, by substituting deuterium for hydrogen in various positions of the Grignard molecule to determine whether or not the hydrogen atom lost from the β-position of the Grignard reagent is, in fact, the one which appears in the carbinol product of the reduction; and, second, by observing the isotope effect in the hydrogen transfer to learn something about the sequence and relative speeds of the various steps in the reaction.

The reaction we have chosen to study is the reduction of benzophenone to benzhydrol by isobutylmagnesium bromide:

$$\begin{tikzcd}[column sep=small] (C_6H_5)_2CO + (CH_3)_2CHCH_2MgBr \arrow[r] & (CH_3)_2CH{=}CH_2 + (C_6H_5)_2CHOMgBr \arrow[d, "H_2O"] \\ & (C_6H_5)_2CHOH + Mg(OH)Br \end{tikzcd}$$

It was chosen for a number of reasons: (*a*) the ketone cannot undergo condensation or enolization and gives an almost quantitative yield of the reduction product; (*b*) this reaction is one of the very few for which it has been demonstrated that the amounts of olefin and alcohol produced are equivalent; (*c*) the Grignard has hydrogen in the α-, β-, and γ-positions which could, in principle, be transferred to the ketone; and (*d*) the halomagnesium salt of benzhydrol is insoluble in ether so that it can readily be separated from unreacted benzophenone and other reaction products, if any.

Three samples of isobutylmagnesium bromide were prepared which contained deuterium in the α-, β-, and γ-positions respectively. Benzophenone was reduced by each of these, using two equivalents of Grignard reagent to one of benzophenone. By analyzing the resultant benzhydrol samples for deuterium it could be determined whether or not hydrogen is transferred from the Grignard reagent and, if so, from which position in it. By comparing the deuterium to protium ratios in the Grignard reagent and in the benzhydrol obtained from it the isotope effect in the reaction could be determined.

EXPERIMENTAL

The deuterated Grignard reagents required for this work were prepared from deuterated isobutyl bromides obtained from the corresponding deuterated isobutyl alcohols. A variety of methods for the synthesis of these alcohols were explored, using undeuterated materials. The yields quoted in the procedures described below are those obtained from the undeuterated materials since the small quantities of deuterated compounds used were usually distilled directly into the reaction vessel for the next step in the synthesis without measurement.

α-*Deuteroisobutyl Alcohol*

This compound was made by reduction of isobutyraldehyde with lithium aluminum deuteride. Isobutyraldehyde (4.2 gm., 0.058 mole) in 20 ml. of dry ether was added dropwise to a stirring solution of 0.65 gm. (0.017 mole) of lithium aluminum deuteride in 20 ml. of ether. A 45 min. reflux period was followed by hydrolysis with dilute hydrochloric acid and extraction of the aqueous layer with ether. The dried ether extracts were evaporated and the residue distilled. The yield of isobutyl alcohol boiling in the range 96–107°C. was 70%.

β-*Deuteroisobutyl Alcohol*

This compound was synthesized by the following series of reactions:

$$CH_3CH(COOEt)_2 \xrightarrow[CH_3I]{\text{NaOEt}} (CH_3)_2C(COOEt)_2 \xrightarrow{\text{KOH}} (CH_3)_2C(COOH)_2 \xrightarrow{D_2O} (CH_3)_2C(COOD)_2$$

$$(CH_3)_2C(COOD)_2 \xrightarrow[-CO_2]{\text{heat}} (CH_3)_2CDCOOD \xrightarrow{LiAlH_4} (CH_3)_2CDCH_2OH$$

Methylmalonic acid diethyl ester (26.0 gm., 0.16 mole) was added to a solution of 3.8 gm. of sodium (0.16 gm-atom) in 100 ml. of absolute ethanol. Then 22.7 gm. (0.16 mole) of methyl iodide was added dropwise. After a three-hour reflux period 2 ml. of methyl iodide was added and refluxing continued for another hour. Ethanol was distilled off and the residue treated with water.

From ether extracts of the aqueous solution there was obtained 9.1 gm. of dimethylmalonic acid diethyl ester boiling at 186–190°C., a yield of 68%.

This ester was saponified by refluxing it for 2.5 hr. with an equal weight of potassium hydroxide dissolved in its own weight of water. Unsaponified ester was removed by extraction with ether. Dimethylmalonic acid was isolated by extracting the acidified aqueous solution with ether, evaporating the ether, and crystallizing the residue from benzene. It melted at 188–190°C. Yields were 90% or better. Recrystallization from ether raised the melting point to the literature value of 192–193°C. Neutral equivalent was 67.5±2.0 as compared to calculated values of 66 for dimethylmalonic acid and 59 for methylmalonic acid.

Dimethylmalonic acid (21.5 gm., 0.163 mole) was equilibrated with deuterium oxide by dissolving it in 60 ml. of dioxane (purified by the method of Fieser (4), containing 3.3 gm. (0.165 mole) of heavy water[3] and allowing the solution to stand at room temperature for 70 hr. Dioxane and water were removed at 90°C. under reduced pressure, and the residue of deuterodimethylmalonic acid was decarboxylated by heating the distilling flask containing it above 195°C. in an oil bath. The deuteroisobutyric acid which distilled over had a neutral equivalent of 91±2 compared to the calculated value of 89. The over-all yield of exchange and decarboxylation was 85%.

Deuteroisobutyric acid (12.0 gm., 0.14 mole) in 15 ml. of dry ether was added dropwise with stirring to a suspension of lithium aluminum hydride (7.0 gm., 0.14 mole) in 45 ml. of ether. The mixture was refluxed for an hour, then hydrolyzed with water, and acidified. From the ether layer was obtained 6.1 gm., a 60% yield, of β-deuteroisobutyl alcohol, b.p. 96–107°C.

γ-*Deuteroisobutyl Alcohol*

This compound was prepared by the following series of reactions:

$$(CH_3)_2CO \xrightarrow{D_2O} (CD_3)_2CO \xrightarrow{LiAlH_4} (CD_3)_2CHOH \xrightarrow{PBr_3} (CD_3)_2CHBr \xrightarrow{Mg}$$

$$(CD_3)_2CHMgBr \xrightarrow{CO_2} (CD_3)_2CHCOOH \xrightarrow{LiAlH_4} (CD_3)_2CHCH_2OH$$

Acetone (30 gm., 0.52 mole) was equilibrated with deuterium oxide (30 gm., 1.5 mole) containing 0.2 gm. of sodium hydroxide. After 48 hr. at room temperature the mixture was distilled through a 9×1.5 cm. column packed with 3 mm. glass helices, distillate being collected up to 95°C. This deuteroacetone was dried over calcium sulphate and filtered.

Deuteroacetone (14.0 gm., 0.24 mole) was dissolved in 20 ml. of dry diethyl carbitol and the solution was added slowly to a suspension of 3.0 gm. (0.08 mole) of lithium aluminum hydride in 20 ml. of diethyl carbitol. At the end of 1.5 hr. the mixture was acidified with dilute hydrochloric acid and distilled, distillate bieng collected up to 95°C. This distillate was redistilled through a 9×1.5 cm. column packed with 3 mm. glass helices. The yield of deuteroisopropyl alcohol boiling at 79–81°C. was 11.4 gm. (80%).

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[3] *Heavy water was obtained from the Commercial Products Division of Atomic Energy of Canada, Ltd., and was reported by the supplier to contain 99.73 atom-% deuterium.*

Deuteroisopropyl alcohol was converted to the corresponding bromide, b.p. 56–60°C., in 55% yield by the method described below for converting deuteroisobutyl alcohol to its bromide.

Deuteroisopropyl bromide (24.5 gm., 0.20 mole) was converted to the Grignard reagent with 0.22 gm-atom of magnesium in 60 ml. of dry ether in the usual way. The yield by titration with standard acid was 85%. This was poured into a slurry of crushed Dry Ice in ether; the mixture was acidified and extracted with ether. From the ether extracts was obtained 11.6 gm. (78%) of deuteroisobutyric acid boiling at 145–150°C.

Deuteroisobutyric acid was reduced to γ-deuteroisobutyl alcohol by means of lithium aluminum hydride in ether as described above under β-deuteroisobutyl alcohol. The yield was 65%.

Conversion of Deuteroisobutyl Alcohols to Deuteroisobutyl Bromides

Phosphorus tribromide (19.5 gm., 0.072 mole) was added dropwise with stirring to 12.8 gm. (0.173 mole) of isobutyl alcohol over a period of 45 min. while the reaction was being cooled in an ice–salt bath. The mixture was then distilled, distillate being collected up to 96°C. This distillate was cooled to 0°C., washed with cold concentrated sulphuric acid, cold sodium carbonate solution, and cold water in turn, then dried and distilled. Yields of the various deuterated isobutyl bromides boiling at 88–92°C. ranged from 40% to 50%.

Reduction of Benzophenone by Deuterated Grignard Reagents

The three deuterated isobutyl bromides obtained from the above reactions were diluted with ordinary isobutyl bromide where necessary to give enough material for the subsequent reductions, then analyzed for deuterium. Three reductions with each bromide were attempted. In a typical run 3.0 gm. (0.022 mole) of deuterated isobutyl bromide in 5 ml. of dry ether was added to a 10% excess of magnesium (0.53 gm.) in 25 ml. of dry ether. Reaction was initiated by gentle warming, and completed by refluxing for three hours. Titration with standard acid showed the yield to be 75%. To this solution was added slowly one-half of the equivalent quantity (1.51 gm., 0.0083 mole) of benzophenone dissolved in 10 ml. of dry ether. The solution turned deep red as soon as the ketone was added, but the color disappeared when the addition was complete and the solution had been refluxed for a few minutes. After a few hours of reflux, the bromomagnesium salt of benzhydrol was allowed to settle out, filtered, washed with ether, and hydrolyzed with dilute acid. The liberated benzhydrol was extracted with ether and recrystallized from ligroin. The yield of benzhydrol melting at 66°C. was 1.2 gm. (80%).

Deuterium Analyses

The samples were burned in a standard macrocombustion apparatus using a Vycor tube and a plug of silver wool to trap halogens. The water of combustion was collected in a Dry Ice trap and purified by the method of Keston, Rittenberg, and Schoenheimer (6) except that calcium oxide and potassium permanganate were used instead of chromium trioxide and potassium hydroxide. The density of the water of combustion was determined by the gradient density tube method described by Anfinsen (1). Two gradients were used, one covering the range 0–8% D_2O for samples rich in deuterium and another covering the range 0–2% D_2O for less concentrated samples.

RESULTS

Table I lists the analytical results. The three runs with α-deuteroisobutyl bromide used the same starting material so that the three analyses of α-deuteroisobutyl bromide are, in effect, triplicate analyses of the same material. Thus the three analyses illustrate the reproducibility of the method.

TABLE I

DEUTERIUM ANALYSES

Source of water sample	Run No.	Weight-% D_2O*	Atom ratio D/H in labelled position
α-Deuteroisobutyl bromide	1	0.70	0.029
	2	0.68	0.028
	3	0.69	0.029
Benzhydrol from α-deuteroisobutyl bromide	1	0.00	0.000
	2	0.00	0.000
	3	0.00	0.000
β-Deuteroisobutyl bromide	1	1.38	0.126
	2	1.48	0.137
	3	—	—
Benzhydrol from β-deuteroisobutyl bromide	1	0.65	0.076
	2	0.78	0.092
	3	—	—
γ-Deuteroisobutyl bromide	1	20.65	0.397
	2	21.32	0.418
	3	—	—
Benzhydrol from γ-deuteroisobutyl bromide	1	0.00	0.000
	2	0.03	0.003
	3	0.00	0.000
α-Deuteroisobutyric acid (dimethylmalonic acid)	1	14.16	1.072
	2	14.41	1.109
	3	14.39	1.107
β-Deuteroisobutyl alcohol	1	3.06	0.382
	2	3.08	0.384
	3	—	—

**A blank space indicates that a run or analysis was lost by accident.*

It is seen from the table that the benzhydrols obtained by reduction of benzophenone with β-deuteroisobutyl Grignard reagents contain deuterium while those obtained from α- and γ-deutero Grignard reagents do not. Therefore, the reduction occurs by hydrogen transfer from the β-position of the Grignard reagent, as has long been supposed.

The fact that the ratio of deuterium to protium in the labelled position of the benzhydrol is less than that in the β-deuteroisobutyl bromide from which it was obtained indicates that there is an isotope effect in the transfer.[4] The numerical value of the isotope effect can be calculated from the following considerations. If the reaction is assumed to be first order with respect to Grignard reagent, then

$$k_{\mathrm{H}}t = \ln\,[a/(a-x)] \quad \text{and} \quad k_{\mathrm{D}}t = \ln\,[a'/(a'-x')]$$

are the rate expressions for the reactions of normal and deutero Grignard reagents, respectively, where k_{H} is the rate constant for the transfer of hydrogen, k_{D} is the rate constant for the transfer of deuterium, a is the initial concentration of non-deuterated Grignard, a' is the initial concentration of deuterated Grignard, x is the concentration of non-deuterated product at time t, and x' is the concentration of deuterated product at time t. The isotope effect, $k_{\mathrm{H}}/k_{\mathrm{D}}$, is then given by the expression

$$[1] \qquad \frac{k_{\mathrm{H}}}{k_{\mathrm{D}}} = \frac{\log[a/(a-x)]}{\log[a'/(a'-x')]}.$$

If the substitutions $a'/a = A$, $x'/x = X$, and $(x+x')/(a+a') = P$ are made, the above expression becomes

$$[2] \qquad \frac{k_{\mathrm{H}}}{k_{\mathrm{D}}} = \frac{\log(1+X)-\log[1+X-P(1+A)]}{\log(1+1/X)-\log[1+1/X-P(1+1/A)]}$$

where A is the ratio of deuterium to protium in the labelled position of the reactant, X is the ratio of deuterium to protium in the labelled position of the product, and P is the fraction of reaction completed.

Since purified benzhydrol was isolated corresponding to 80% or more of the benzophenone used in the reactions, it is evident that the reduction of benzophenone must have been close to quantitative. And since two equivalents of Grignard were used to one of benzophenone, the fraction of Grignard reacted is one-half. Using this value for P and the values of X and A from Table I, the isotope effect, $k_{\mathrm{H}}/k_{\mathrm{D}}$, is found to be 2.0 in Run 1, and 2.2 in Run 2.

Equation [2] can also be used to calculate what fraction of the reduction could have taken place by transfer of hydrogen from the α- and γ-positions of the Grignard without producing a detectable amount (0.01% by weight) of deuterium in the water of combustion from the resulting benzhydrol. If it is assumed that the isotope effect in these hypothetical reductions is six, a value near the maximum allowed by theory and experience (3), then it is found that the maximum per cent of reduction which could have escaped detection is 17% from the α-position and 1% from the γ-position. The value is large in the α-position because a short supply of lithium aluminum deuteride necessitated a low concentration of deuterium in the α-deuteroisobutyl bromide. However, it seems reasonable to suppose that the reaction takes place by one mechanism and not several, and since it is evident that the reduction does involve the β-hydrogen and that not more than 17% of it can involve α-hydrogen, it is highly probable that the reduction takes place by transfer of β-hydrogen exclusively.

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[4] *That deuterium is not lost from the alkyl groups of alkyl halides or alcohols during formation or hydrolysis of metal derivatives is shown by the work of Shiner (16).*

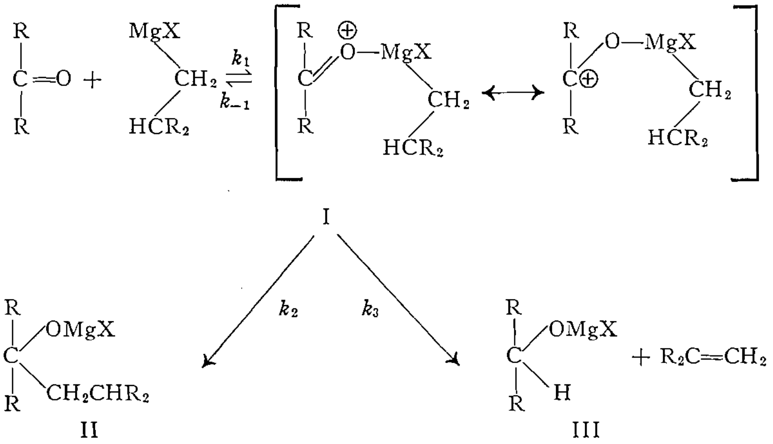
The deuterium analyses on dimethylmalonic acid and β-deuteroisobutyl alcohol can be used to calculate the isotope effect in the decarboxylation reaction

$$(CH_3)_2C(COOD) \xrightarrow[-CO_2]{\text{heat}} (CH_3)_2CDCOOD \xrightarrow{LiAlH_4} (CH_3)_2CDCH_2OH.$$

Here it is desired to compare the D/H ratio in the carboxyl groups of dimethylmalonic acid with that on the α-carbon atom of the isobutyric acid obtained from it. Since only carbon dioxide is lost during the decarboxylation itself, the over-all deuterium to protium ratio in the two compounds will be the same. Actually, isobutyric acid was analyzed and the result applied to both acids. Analysis of the isobutyl alcohol obtained from the isobutyric acid gave the D/H ratio on the β-carbon of the alcohol, which should be the same as that on the α-carbon of the isobutyric acid. Use of these ratios in Equation [2] gave a calculated isotope effect, k_H/k_D, of 4.5.

DISCUSSION

A variety of mechanisms have been suggested for the reducing action of the Grignard reagent, and these have been reviewed recently by Kharasch and Reinmuth (8). Probably the most satisfactory of these is the mechanism proposed by Whitmore, or some modification of it. Whitmore proposed (19) that the carbonyl oxygen co-ordinates with the Grignard magnesium forming a six-membered ring complex, I, which can either rearrange to addition products, II, or transfer a hydrogen from the β-carbon of the Grignard to the carbonyl carbon to give reduction products, III. This mechanism of reduction,



or something very like it, is given strong support by the asymmetric reductions accomplished by Mosher and LaCombe (12).

Our experimental results tend to support the Whitmore mechanism since they show that the reducing hydrogen does come from the β-carbon of the Grignard reagent as Whitmore (and many others) proposed. They do not, of course, support or contradict the theory that reduction takes place through hydrogen transfer within a complex. However, if it is assumed that such a complex is involved in the reaction, then our results show that the complex is in equilibrium with reactants, and that the rate of attainment of equilibrium is greater than the rate of decomposition of complex to reduction products. This is evident from the following considerations. The substitution of deuterium for protium on the β-carbon of the Grignard reagent should have no significant effect on the rate of co-ordination between magnesium and oxygen; hence deuterated and undeuterated complex should be formed in the ratio in which deuterated and undeuterated Grignard reagents were introduced. Then if every complex decomposed into reduction products (in our reaction there were no other products) the ratio of deuterium to protium in the labelled position of benzhydrol would be the same as that in the isobutyl bromide from which it was made. But an isotope effect of about two was observed, so that not every complex can decompose to alcoholate and olefin. That is, k_{-1} in the mechanism scheme above must be greater than k_3.

An interesting modification of the Whitmore mechanism has been proposed by Swain (17). From a consideration of the order of reactivity of a series of Grignard reagents toward nitriles and carbonyl compounds he concludes that, while reduction takes place by the decomposition of a complex as proposed by Whitmore, addition must take place by attack of a second Grignard molecule on the complex. Support for this theory was found in the observation that when magnesium bromide is added to the carbonyl solution prior to the Grignard reagent the yield of addition product is increased at the expense of reduction (18). This is explained by pointing out that magnesium bromide should be a better complexing agent than the Grignard reagent, and that a complex between carbonyl compound and magnesium bromide would be incapable of reductive hydrogen transfer but would still be subject to attack by a Grignard molecule leading to addition.[5]

McBee, Pierce, and Meyer have shown by a series of vapor pressure measurements in phenetole that magnesium bromide does complex some ordinary aldehydes and ketones, but that no complex is formed with analogous fluorinated carbonyl compounds (11). Since Grignard reagents should complex less readily than magnesium bromide, these authors conclude that reduction of fluorinated carbonyl compounds takes place without intermediate complex formation. Nevertheless, McBee, Pierce, and Higgins have shown that added magnesium bromide favors addition and hinders reduction of fluorinated aldehydes and ketones just as with non-fluorinated compounds (10). This seems to throw some doubt on the interpretation by Swain and Boyles of the mechanism of the action of added magnesium bromide.

However, it may be noted that the vapor pressure measurements on solutions of magnesium bromide and fluorinated carbonyl compounds actually show that the equilibrium concentration of complex is very low, not that no complex is formed. So long as the rate of attainment of equilibrium is fast the

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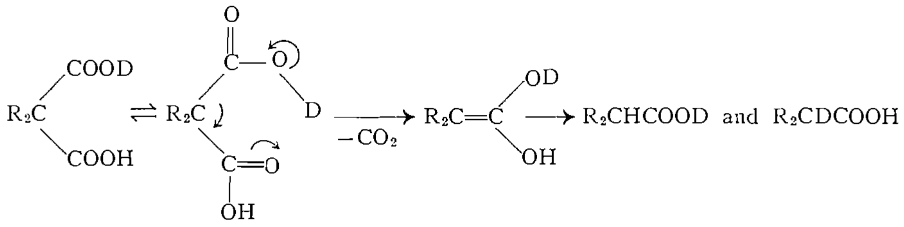
[5] *It has long been thought that magnesium halide is also in equilibrium with the Grignard reagent itself (5, 7).*

$$2RMgX \rightleftharpoons R_2Mg + MgX_2$$

If both RMgX and R_2Mg enter into reaction with carbonyl compound, and if R_2Mg is a better reducing agent (or poorer adding agent) than RMgX, then the results of Swain and Boyles can be explained simply by the effect of added magnesium bromide on this equilibrium. Some support, but certainly not proof, is given this alternative explanation by the work of Noller on the reducing action of diisobutylmagnesium on benzophenone (13).

reduction could still take place through a complex even though its concentration were never large. Thus the interpretation of the effect of added magnesium bromide could still be that of Swain and Boyles. The isotope effect observed in the present work shows that if a complex is formed it does reach equilibrium with its components rapidly, at least in the case of benzophenone and isobutylmagnesium bromide. Hence the possibility that Grignard reduction of fluorinated carbonyl compounds takes place through a complex is still open.

The isotope effect observed in the decarboxylation of dimethylmalonic acid throws little light on the mechanism of that reaction. A reasonable mechanism has been proposed by King (9) which predicts the observed isotope effect:



Indeed, the symmetry of the molecule is such that it is difficult to devise a mechanism which does not predict an isotope effect. The fact that one does exist is simply noted in passing.

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