anisole in the third reaction mixture remained unchanged. In the cisoid conformations (accompanying formulas) required for Diels–Alder reaction only the diene **12b** would be expected to be unreactive.[62]

A mixture of 74.1 mg. (0.451 mmole) of the diene **12a**, 44.2 mg. (0.451 mmole) of maleic anhydride, 1.5 mg. of 2,5-di-*t*-butylhydroquinone and 0.25 ml. of benzene was allowed to stand at room temperature under nitrogen for 3 days and then concentrated and diluted with hexane. Crystallization of the precipitated solid from benzene–hexane mixtures afforded 34 mg. (29%) of the crude crystalline adduct which was recrystallized several times to separate 2 mg. (1.7%) of the pure adduct as colorless prisms, m.p. 141.5–142.7° dec. (lit.,[59] 142.5°) with infrared absorption[63] at 1850 and 1775 cm.$^{-1}$ (C=O of anhydride in five-membered ring) and a series of weak ultraviolet maxima[64] ($\epsilon < 600$) in the region 250–270 mμ.

A mixture of the diastereoisomers of the saturated alcohol 14 was collected from appropriate reaction mixtures (Table VIII) by gas chromatography.[52] The material, containing a 74–26% mixture of the two diastereoisomers,[65] was shown to be identical with the subsequently described sample by comparison of the spectra and gas chromatograms[65] of the two samples.

To a cold solution of 10 ml. (22 mmoles) of a 2.2 *M* ethereal solution of ethylmagnesium bromide and 10 ml. of ether was added, with stirring under nitrogen, 1.350 g. (7.66 mmoles) of 4-phenyl-2-hexanone (**6c**). After the mixture had been stirred for 45 min. and the crude product isolated in the previously described manner, distillation afforded 1.415 g. (89.7%) of a 76–24% mixture of the diastereoisomers of **3-methyl-5-phenyl-3-heptanol** (**14**), b.p. 142° (21 mm.), n^{25}D 1.4995. The material has infrared absorption[41] at 3600 and 3490 cm.$^{-1}$ (unassoc. and assoc. O—H) with a series of low intensity ($\epsilon < 250$) in the region 240–270 mμ of the ultraviolet.[42]

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.90; H, 10.31. Found: C, 81.61; H, 10.61.

Authentic samples of 4-phenyl-2-butanone, b.p. 102–105° (6 mm.), n^{25}D 1.5126 [lit.,[66] b.p. 115° (13 mm.), $n^{21.7}$D 1.511], 2,4-dinitrophenylhydrazone m.p. 128.1–128.8° (lit.,[67] 128.5–129°), 1-phenyl-1-penten-3-ol, b.p. 125–127° (8 mm.), $n^{24.5}$D 1.5579 [lit.,[68] b.p. 123° (7.5 mm.), n^{31}D 1.5550], and *trans*-1-phenyl-1,3-butadiene, b.p. 79–81° (10 mm.), n^{25}D 1.6013 [lit.,[69] b.p. 83° (11 mm.), n^{25}D 1.6089] were prepared and shown[52] to be absent in all the product mixtures obtained from ethylmagnesium derivatives and the ketone **8b**.

The quantitative data, summarized in Table VII, were obtained as previously described utilizing gas chromatography[42] for product analyses. Unless otherwise noted, the percentages in Table VII are average values from two or more runs. In no case where average values are reported did the maximum deviation from the average value exceed 4%.

For the runs reported in Table VII, a known weight of anisole was added to each sample prior to analysis. From a knowledge of the area under the anisole peak in each case and appropriate calibration mixtures, the per cent yields for the products indicated in Table VII were calculated. In no case was the yield of the combined products indicated less than 90%. In two cases where substantial amounts of the saturated alcohol **14** were formed, the reaction mixtures were decomposed both by adding the reaction mixtures to saturated, aqueous ammonium chloride and by adding saturated, aqueous ammonium chloride to the reaction mixtures. Since the former procedure did not decrease the amount of alcohol **14** produced, we conclude that this product is formed in the original reaction mixture before any water has been added.

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(62) D. Craig, J. J. Shipman, and R. B. Fowler, *J. Am. Chem. Soc.*, **83**, 2885 (1961).

(63) Determined as a solution in chloroform.

(64) Determined as a solution in ether.

(65) The analysis was obtained with a 200-ft., Ucon-50 capillary column heated to 140°. We are indebted to Drs. H. E. Johnson and E. Rick of the Union Carbide Chemicals Corporation for this analysis.

(66) A. Klages, *Ber.*, **37**, 2301 (1904).

(67) G. D. Johnson, *J. Am. Chem. Soc.*, **73**, 5888 (1951).

(68) I. E. Muskat and M. Herrman, *ibid.*, **53**, 252 (1931).

(69) O. Grummitt and F. J. Christoph, *ibid.*, **73**, 3479 (1951).

The Chemistry of Carbanions. III. The Reaction of Organomagnesium Compounds with Saturated Ketones[1a]

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Both the product compositions and the rates of reaction have been studied for 3-pentanone and diisopropyl ketone with diethylmagnesium, ethylmagnesium bromide, and the ethylmagnesium alkoxides **6**. From these and other studies, we conclude that magnesium bromide does not catalyze addition of the ethylmagnesium reagents to the carbonyl functions but does suppress the tendency of ethylmagnesium alkoxides and/or magnesium dialkoxides to give by-products resulting from enolization and reduction.

In continuing our study of the reactions of organomagnesium compounds,[2] it was of interest to examine the behavior of simple ketones **5** with various organomagnesium compounds including the Grignard reagent **1**, a dialkylmagnesium compound **2**, and the product (possibly an alkylmagnesium alkoxide **3** or its dimer **4**) obtained by reaction of one molar equivalent of a dialkylmagnesium compound with one molar equivalent of a ketone. The reactions studied are summarized in Chart I.

We first examined reactions where the reactants were mixed by adding the ketone **5** to an excess of the organomagnesium compound (normal addition procedure where the organometallic is always in excess) and by adding the organomagnesium derivative to the ketone (inverse addition procedure where the ketone is in excess during at least the first half of the reaction). In the absence of magnesium bromide, the results (Tables I and II) are in agreement with the earlier suggestion of Mosher and co-workers[3,4] that a dialkylmagnesium compound reacts with a ketone to give primarily an addition product **7**, whereas the intermediate (possibly **3** or **4**) formed after consumption of the first alkyl group reacts with a ketone to give substantial amounts of enolization (as in **5**) and reduction (as in **9**) products as well as the addition product **7**. However, the differing product ratios obtained in the two steps of this reaction are greatly reduced when a molar equivalent of magnesium bromide is present in the reaction mixture. This observation is in accord with

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(1)(a) This research has been supported by grant no. 594-A from the Petroleum Research Fund; (b) supported by the U. S. Air Force Academy.

(2) H. O. House, D. D. Traficante, and R. A. Evans, *J. Org. Chem.*, **28**, 348 (1963).

(3) J. Miller, G. Gregoriou, and H. S. Mosher, *J. Am. Chem. Soc.*, **83**, 3966, 5051 (1961).

(4)(a) D. O. Cowan and H. S. Mosher, *J. Org. Chem.*, **27**, 1 (1962); (b) D. Cowan and H. S. Mosher, *ibid.*, in press.

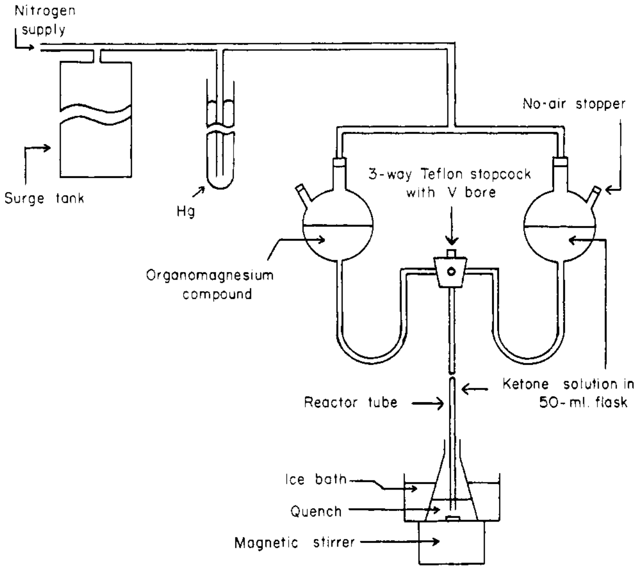

Figure 1

the earlier reports[5] that reactions of ketones with equivalent quantities of Grignard reagents give smaller amounts of by-products resulting from enolization and reduction in the presence of excess magnesium bromide. Recent studies[4b] have suggested that only one species is responsible for the observed reduction.

We next examined the rates of reaction of the ketones **5** with ethylmagnesium derivatives by employing a flowing stream reactor (Figure 1) which permitted study of reaction times within the range 0.01 to 0.1 sec. (Table III). Under these conditions, the reaction of diethyl ketone (**5a**) with diethylmagnesium proved too rapid for accurate measurement and the reaction of diisopropyl ketone (**5b**) with ethylmagnesium bromide was too slow for reliable measurement. However, our data in each case indicated that the ketone **5** reacted at least 50 times more rapidly with diethylmagnesium than with ethylmagnesium bromide. This order of reactivity (*i.e.*, **2** > **1**) is in agreement with previous studies.[6-8]

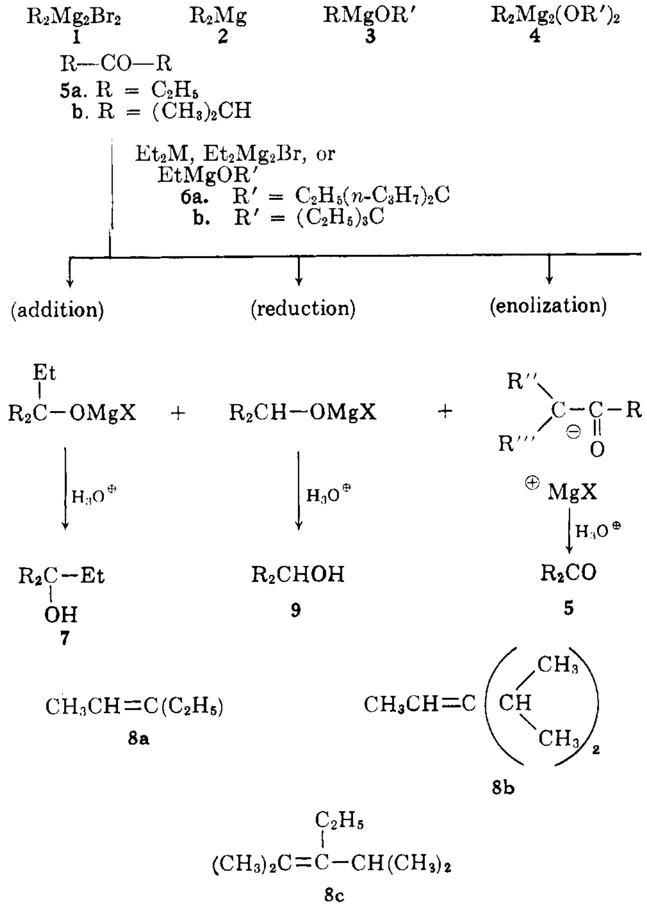

CHART I

The rate of reaction of diethyl ketone **5a** with ethylmagnesium bromide was dependent on the concentrations of both the ketone and the organomagnesium compound. The rate constants listed (Table III) were calculated using the expressions, rate = k [$Et_2Mg_2Br_2$] [ketone] (or rate = k [Et_2Mg] [ketone] in the absence of magnesium bromide), which appeared to give better agreement among calculated rate constants than the expressions, rate = k [$Et_2Mg_2Br_2$], rate = k $[Et_2Mg_2Br_2]^2$ [ketone], rate = k [EtMgBr] [ketone] or *rate* = k $[EtMgBr]^2$ [ketone]. Because of several possible sources of error in our rate measurements (see Experimental), we do not consider that we have established the kinetic order of the reactions studied. The intermediate alkylmagnesium alkoxide **6a** produced by reaction of diethylmagnesium with one molar equivalent of 4-heptanone proved to be substantially less reactive than diethylmagnesium toward 3-pentanone (**5a**).[9] Although calculation of a rate constant was unwarranted in view of a serious side reaction (enolization) which occurred under these conditions, it is nonetheless clear from the extent of the reaction (81% after 0.08 sec.) that the rate of this reaction is similar to the rate of reaction of ethylmagnesium bromide with 3-pentanone.

Discussion

Both our data and other studies[6-8] indicate that the reaction of ketones with dialkylmagnesium compounds is markedly retarded by the presence of a molar equivalent of magnesium bromide or magnesium iodide. The presence of additional magnesium bromide causes a further decrease in the reaction rate.[7,10] Thus, the rate of the dialkylmagnesium–ketone reaction bears an inverse relationship to the concentration of magnesium bromide and the suggestion[5,8] that magnesium bromide catalyzes this addition is untenable. Furthermore, it is clear from the data presented in Tables I and II that the beneficial effect[3-5] of magnesium bromide in favoring addition rather than enolization and reduction results, not from catalyzing the addition of a dialkylmagnesium compound to a ketone, but from suppressing the tendency of the intermediate alkylmagnesium alkoxide **3** or **4** to give enolization and reduction products rather than addition. Since the rate

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[5] (a) C. G. Swain and H. B. Boyles, *J. Am. Chem. Soc.*, **73**, 870 (1951); (b) E. T. McBee, O. R. Pierce, and J. F. Higgins, *ibid.*, **75**, 1736 (1953).

[6] J. G. Aston and S. A. Bernhard, *Nature*, **165**, 485 (1950).

[7] N. M. Bikales and E. I. Becker, *Chem. Ind.* (London), 1831 (1961).

[8] (a) M. Anteunis, *J. Org. Chem.*, **26**, 4214 (1961); (b) *ibid.*, **27**, 596 (1962).

[9] S. J. Storfer and E. I. Becker, *ibid.*, **27**, 1868 (1962).

[10] Although not considered by the author (ref. 8), recalculation of the data given for the reaction of pinacolone with methylmagnesium bromide and with methylmagnesium bromide plus an additional molar equivalent of magnesium bromide indicates that the reaction was slower in the presence of excess magnesium bromide.

TABLE I

REACTIONS OF 3-PENTANONE (**5a**, 0.14 *M*) WITH ETHYLMAGNESIUM DERIVATIVES

Organomagnesium reactant	Mode of addition	Product composition, %: Ketone **5a** (enolization)	Alcohol **9a** (reduction)	Alcohol **7a** (addition)
0.29 *M* $Et_2Mg_2Br_2$	Normal	1	<1	99
	Inverse	1	1	98
.29 *M* Et_2Mg +	Normal	2	1	97
0.29 *M* $MgBr_2$	Inverse	4	1	95
.29 *M* Et_2Mg	Normal	2	<1	98
	Inverse	21	<1	79
.57 *M* EtMgOR[a,b]	Normal	25	5	70
	Inverse	26	5	69
.57 *M* EtMgOR[a,c]	Normal	18	7	75
	Inverse	67[d]	4	29[d]
.29 *M* Et_2Mg +	Normal	20	6	74
0.29 *M* $Mg(OR)_2$[a,e]	Inverse	66	3	31
.57 *M* EtMgOR[a,b]	Normal	4	1	95
+ 0.29 *M* $MgBr_2$	Inverse	27[f]	2	71[f]
.57 *M* EtMgOR[a,b]	Normal	3	1	96
+ 0.57 *M* $MgBr_2$	Inverse	8	1	91
.29 *M* Et_2Mg +	Normal	2	1	97
0.29 *M* $Mg(OR)_2$[a,e] + 0.29 *M* $MgBr_2$	Inverse	37	2	61

[a] R = C_2H_5 (n-C_3H_7)$_2$C. [b] This reagent was prepared by the addition of one molar equivalent of 4-heptanone to one molar equivalent of diethylmagnesium. When a solution of this reagent was hydrolyzed the product contained 79% of the tertiary alcohol ROH (addition) and 21% of 4-heptanone (enolization). The ratio of these two components was essentially unchanged in the reaction mixtures obtained from this reagent and 3-pentanone. [c] This reagent was prepared by the addition of one molar equivalent of ethyldi-*n*-propylcarbinol to one molar equivalent of diethylmagnesium. [d] In this case the duplicate values differed from one another by 4%. [e] This reagent was prepared by adding two molar equivalents of ethyldi-*n*-propylcarbinol to one molar equivalent of diethylmagnesium. [f] In this case the triplicate values differed from the average value by 11%.

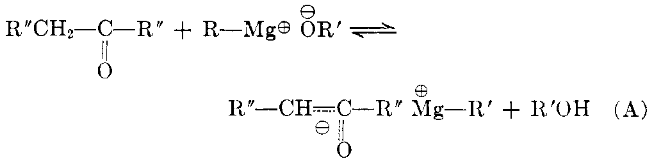
TABLE II

REACTIONS OF 2,4-DIMETHYL-3-PENTANONE (**5b**, 0.14 *M*) WITH ETHYLMAGNESIUM DERIVATIVES

Organomagnesium reactant	Mode of addition	Product composition, %: Ketone **5b** (enolization	Alcohol **9b** (reduction)	Alcohol **7b** (addition)
0.29 *M* $Et_2Mg_2Br_2$	Normal	<1	4	96
	Inverse	<1	5	95
.29 *M* Et_2Mg +	Normal	<1	9	91
0.29 *M* $MgBr_2$	Inverse	<1	9	91
.29 *M* Et_2Mg	Normal	1	6	93
	Inverse	3	28[a]	69[a]
.57 *M* EtMgOR[b,c]	Normal	19	53	28
	Inverse	31	47	22
.57 *M* EtMgOR[b,d]	Normal	8	75	17
	Inverse	22[e]	64	14[e]
.57 *M* EtMgOR[b,c]	Normal	<1	10	90
+0.57 *M* $MgBr_2$	Inverse	<1	10	90

[a] In this case the individual values differed from one another by 9%. [b] R = $(C_2H_5)_3C$. [c] This reagent was prepared by the addition of one molar equivalent of 3-pentanone to one molar equivalent of diethylmagnesium. When a solution of this reagent was hydrolyzed, the product contained 83% of the tertiary alcohol ROH (addition) and 17% of 3-pentanone (enolization). The ratio of these two components was essentially unchanged in the reaction mixtures obtained from this reagent and 2,4-dimethyl-3-pentanone. [d] This reagent was prepared by the addition of one molar equivalent of triethylcarbinol to one molar equivalent of diethylmagnesium. [e] In this case the individual values differed from one another by 6%.

of addition of the alkylmagnesium alkoxide **6a** with the ketone **5a** also is not enhanced by the presence of magnesium bromide, there is no reason to believe that this second addition step is catalyzed by magnesium bromide. Thus we are led to the conclusion that the intermediate alkylmagnesium alkoxides (and/or the magnesium dialkoxides **10** as in equation D) **3** or **4** are capable of reaction with ketones to lead to enolization and reduction by processes which are comparable in rate to addition. One obvious way by which the magnesium alkloxides **3** or **4** could catalyze enolization is illustrated in the accompanying equations A and B wherein the alkoxide ion serves as a



$$\text{R}''\text{CH}_2\text{—}\underset{\underset{\text{O}}{\|}}{\text{C}}\text{—R}'' + \text{R—Mg}^{\oplus}\ \overset{\ominus}{\text{O}}\text{R}' \rightleftharpoons \text{R}''\text{—CH}\overset{\ominus}{=}\underset{\underset{\text{O}}{\|}}{\text{C}}\text{—R}''\ \overset{\oplus}{\text{Mg}}\text{—R}' + \text{R}'\text{OH} \qquad \text{(A)}$$

$$\text{R}'\text{OH} + \text{R}_2\text{Mg} \longrightarrow \text{R—Mg}^{\oplus}\ \text{O}^{\ominus}\text{R}' + \text{R—H} \qquad \text{(B)}$$

$$\text{R—Mg}^{\oplus}\ {}^{\ominus}\text{OR}' + \text{MgBr}_2 \rightleftharpoons \text{R—Mg}^{\oplus}\ [\text{R}'\text{—O—MgBr}_2]^{\ominus} \qquad \text{(C)}$$

catalyst for the necessary proton transfers. As illustrated in equation C, the basic alkoxide ion should be effectively removed from the reaction medium by the presence of the Lewis acid, magnesium bromide. Although the magnesium salts of primary and secondary alcohols can promote reduction[11] by a process analogous to the Meerwein–Porndorf–Verley reduction, the tertiary magnesium alkoxides employed in this study could not promote the reduction of hindered ketones in this way. Since we have thus far been unable to measure the rate of reaction of the magnesium alkoxide **6b** with diisopropyl ketone **5b**, the possibility exists that addition of an alkylmagnesium alkoxide to less reactive ketones than 3-pentanone[12] is greatly retarded by steric (and possibly electronic) factors.[13] This retardation of the addition rate would permit reduction[3] to complete as a side reaction.

The possibility also exists that magnesium bromide serves as a catalyst for the equilibration depicted in equation D. Some indication that this equilibration

$$\underset{\mathbf{3}}{2\text{R—Mg—OR}'}\ [\text{or } \underset{\mathbf{4}}{\text{R}_2\text{Mg}_2\,(\text{OR}')_2}] \rightleftharpoons \underset{\mathbf{2}}{\text{R}_2\text{Mg}} + \underset{\mathbf{10}}{(\text{R}'\text{O})_2\text{Mg}} \qquad \text{(D)}$$

may be slow in the absence of magnesium bromide is provided by product composition experiments (Tables I and II) which utilized samples of ethylmagnesium alkoxide prepared in several ways. The product obtained from diethylmagnesium and one molar equivalent of a ketone behaved differently, especially in inverse addition experiments, from the alkoxide obtained by mixing diethylmagnesium with one molar equivalent of the corresponding tertiary alcohol or by mixing one molar equivalent of diethylmagnesium with two molar equivalents of the tertiary alcohol (to form **10**) followed by the addition of a second molar equivalent of diethylmagnesium.

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(11) R. Hamelin, *Bull. soc. chim. France*, 926 (1961).

(12) Support for the idea that the second alkyl group adds very slowly to less reactive ketones (ref. 7 and 8) and to nitriles (ref. 9) is found in other studies.

(13) R. Hamelin, *Bull. soc. chim. France*, 915 (1961).

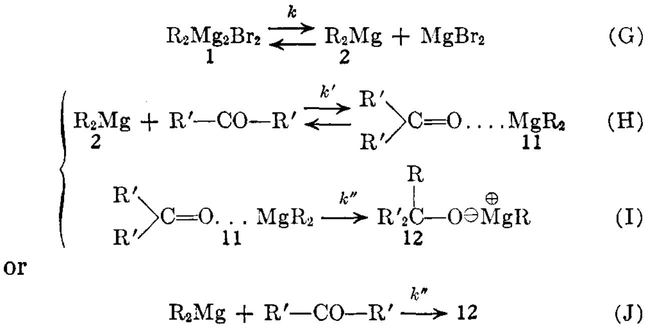
Our kinetic studies appear to be in best agreement with one of the kinetic expressions, rate = k [$R_2Mg_2Br_2$] [ketone] or rate = k [R_2Mg] [ketone], as have some of the data[7] for the reaction of benzophenone with methylmagnesium bromide. From a study of the reaction of methylmagnesium iodide with acetone,[6] the expression rate = k [RMgI] was reported and from the reactions of benzophenone and pinacolone with methylmagnesium bromide, the expression rate = k [RMgBr]^2 [ketone] was advocated.[8] As has been discussed elsewhere,[2,9] there exists rather compelling evidence that the one component not present in solutions of Grignard reagents is the monomeric species RMgBr. Consequently, we consider mechanistic arguments[8] requiring the presence of this species illogical irrespective of whether kinetic data appear to fit such a reactant. Since accurate quantitative data concerning the positions and rates of establishment of equilibria such as those illustrated in equations E and F are not available,[14] we believe it is most inappropriate at the present time to attach significance[8] to the *apparent* kinetic order of the organomagnesium compound other than to conclude that some alkylmagnesium compound is involved in the slow step of the addition reaction.

$$R_2Mg_2Br_2 \rightleftharpoons R_2Mg + MgBr_2 \qquad (E)$$

$$(R_2Mg)_2 \rightleftharpoons 2\ R_2Mg \qquad (F)$$

In an effort to learn what the positions of equilibria D and E might be, we examined the n.m.r. signal of the methylene group next to magnesium in ethereal solutions of diethylmagnesium, ethylmagnesium bromide, and the ethylmagnesium alkoxide **6a**. However, these measurements, made at 25°, proved uninformative since the position and pattern (see Experimental) of the n.m.r. signal was essentially the same for each of the three solutions. We have thus far been unable to obtain measurements at low temperatures in an effort to learn whether we have observed only the average signal from rapidly exchanging ethyl groups.[15]

From the available kinetic studies of the ketone–Grignard reagent reaction, two features seem particularly noteworthy. First is the aforementioned inverse dependence of the reaction rate on the magnesium bromide concentration, and second is the fact that the reaction rate is dependent on the ketone concentration[16] with ketones of low[7,8] and moderate (this study) reactivity but becomes independent of the ketone concentration with the very reactive ketone, acetone.[6,17] Consideration of these features suggests that a slight modification (equations G, H, and I or G, and J) of the reaction mechanism originally suggested by Aston and Bernhard[6,18] provides the most satisfactory explanation for the data currently available. If in this sequence $k > k''$ as would be anticipated with relatively unreactive ketones, the observed kinetic dependence on ketone concentration would be expected. However, use of a very reactive ketone could well reverse this order of reactivities (*i.e.*, $k'' > k$) and cause the reaction to be dependent only on the concentration of the Grignard reagent **1**. The equilibrium G would obviously be displaced to the left by the addition of excess magnesium bromide lowering the effective concentration of diethylmagnesium **2** and reducing the over-all rate of addition. Although this scheme does not incorporate the rather popular idea[2,3,5,7,8,13] that at least one molecule of magnesium bromide should be included in the transition state leading to addition, our findings concerning the reason for suppression of enolization and reduction as side reactions in the presence of magnesium bromide appear to remove the only compelling reason[5] for including magnesium bromide in the transition state.



$$\underset{1}{R_2Mg_2Br_2} \overset{k}{\rightleftharpoons} \underset{2}{R_2Mg} + MgBr_2 \qquad (G)$$

$$\underset{2}{R_2Mg} + R'{-}CO{-}R' \overset{k'}{\rightleftharpoons} R'_2C{=}O\ldots \underset{11}{MgR_2} \qquad (H)$$

$$\underset{11}{R'_2C{=}O\ldots MgR_2} \xrightarrow{k''} \underset{12}{R'_2C(R){-}O^{\ominus}\overset{\oplus}{Mg}R} \qquad (I)$$

or

$$R_2Mg + R'{-}CO{-}R' \xrightarrow{k''} 12 \qquad (J)$$

The evidence concerning the possible intervention of a complex **11** (as in equations H and I)[18] rather than a direct bimolecular reaction (as in equation J)[19] is rather meager. As has been reported for other systems,[8,20] we observed a transient yellow color in the reactions of diethylmagnesium[20] with diisopropyl ketone which persisted only as long as the unchanged ketone was present. We thus far have not found a system which would permit us to maintain this transient color long enough to measure the spectra of the species responsible and can only speculate that this colored species may represent a charge-transfer complex formed from the ketone and the organomagnesium compound. The question of whether this colored species is an intermediate or only the result of a competing equilibrium clearly can not be answered with the data presently available.

Experimental[21]

Reagents.—Solutions of ethylmagnesium bromide, diethylmagnesium, and magnesium bromide were prepared and analyzed as previously described.[2] Commercial samples of 3-pentanone

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[14] See ref. 9 and R. E. Dessy, *J. Org. Chem.*, **25**, 2260 (1960).

[15] C. R. McCoy and A. L. Allred, *J. Am. Chem. Soc.*, **84**, 912 (1962).

[16] Unlike the previously mentioned uncertainties about the interpretation of the apparent kinetic order of organomagnesium compounds, the *apparent first order dependence on the ketone concentration* observed in the present study and in previous work (ref. 7 and 8) is probably safety ascribed to a transition state containing a single ketone molecule, since there is no reason to except the ketones studied to be significantly associated with themselves and at least one of the ketones studied (ref. 7) appears not to be associated with magnesium bromide in the reaction mixture.

[17] From the data provided (ref. 6) we estimate the reaction of acetone with methylmagnesium iodide to be about fifty times more rapid than the reaction of 3-pentanone with ethylmagnesium bromide.

[18] A sequence comparable to equations H and I has been suggested for the reaction of organolithium compounds with ketones. C. G. Swain and L. Kent, *J. Am. Chem. Soc.*, **72**, 518 (1950).

[19] (a) R. E. Dessy and R. M. Salinger, 140th National Meeting of the American Chemical Society, Chicago, Ill., September 3–8, 1961, Abstracts of Papers, p. 9Q; (b) R. E. Dessy and F. Paulik, 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September 9–14, 1962, Abstracts of Papers, p. 6Q.

[20] (a) The coloration in solutions of ethylmagnesium bromide prevented observation of this transient color in the case we studied; (b) see R. MacLeod and co-workers, "Petroleum Research Fund Reports," 1959, p. 93; 1961, p. 50.

[21] All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated, magnesium sulfate was employed as a drying agent The infrared spectra were determined with either a Baird, Model B, or a Perkin–Elmer, Model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The n.m.r. spectra were determined at 60 Mc. with a Varian, Model A-60, n.m.r. spectrometer. The mass spectra were obtained with a CEC, Model 21-130, mass spectrometer.

and 2,4-dimethyl-3-pentanone, b.p. 124°, $n^{25}\text{D}$ 1.3973 [lit.,[22] b.p. 125°, $n^{25}\text{D}$ 1.39759], which contained more than 99% of the desired ketone,[23] were employed. From the reaction of 9.46 g. (0.11 mole) of 3-pentanone (**5a**) with 0.22 mole of ethylmagnesium bromide in 125 ml. of ether was obtained, after fractional distillation, 7.642 g. (60%) of pure triethylcarbinol **7a**, b.p. 138–142°, $n^{25}\text{D}$ 1.4272° (lit., b.p. 139–142°,[24] $n^{20}\text{D}$ 1.4294[25]).

Heating a mixture of 1.0 g. (8.6 mmoles) of the alcohol **7a** and 1.0 g. of potassium acid sulfate produced 0.584 g. (68%) of 3-ethyl-2-pentene (**8a**), b.p. 89°, $n^{25}\text{D}$ 1.4122 [lit.,[26] b.p. 95–98°, $n^{18}\text{D}$ 1.4140], with an ultraviolet maximum[27] at 189 mμ (ϵ 7,500) and a molecular weight of 98 (mass spectrum). A sample of 3-pentanol, b.p. 111°, $n^{25}\text{D}$ 1.4075 (lit.,[28] b.p. 114.4° $n^{20}\text{D}$ 1.4104) was obtained from the reaction of ethylmagnesium bromide with propionaldehyde. The 4-ethyl-4-heptanol, b.p. 78–79° (20 mm.), $n^{25}\text{D}$ 1.4310 [lit. b.p. 76–78° (17 mm.),[29] $n^{20}\text{D}$ 1.4332[30]] used to prepare some of the ethylmagnesium alkoxide **6a** solutions employed in this series of reactions was obtained in 71% yield from the reaction of 4-heptanone with ethylmagnesium bromide.

From the reaction of 1.60 g. (0.011 mole) of 2,4-dimethyl-3-pentanone (**5b**) with 0.022 mole of ethylmagnesium bromide and 0.022 mole of magnesium bromide in 31 ml. of ether was obtained, after fractional distillation, 0.487 g. (31%) of pure ethyldiisopropylcarbinol (**7b**), b.p. 116° (125 mm.), $n^{25}\text{D}$ 1.4411 [lit.,[31] b.p. 117.5° (125 mm.), $n^{20}\text{D}$ 1.4440]. Reduction of 2,4-dimethyl-3-pentanone (**5b**) with excess lithium aluminum hydride in ether afforded, after fractional distillation, 71% of diisopropylcarbinol (**9b**), b.p. 137–137.5°, $n^{25}\text{D}$ 1.4229 [lit.,[32] 137–138°, $n^{25}\text{D}$ 1.4246]. From heating a mixture of ethyldiisopropylcarbinol and potassium acid sulfate 55% of a mixture of olefins **8b** and **8c**, b.p. 110–122°,[33] was obtained and a sample of each olefin was collected.[34] The olefin **8b** (first eluted from the column) has an ultraviolet maximum[27] at 190 mμ (ϵ 9,900) with n.m.r. absorption[35] at 4.86 τ [1H, quadruplet (J = 7 c.p.s.), vinyl C—H] with a multiplet in the region 7.0 to 8.0 τ (2H, tertiary C—H), a doublet (J = 7 c.p.s.) at 8.40 τ (3H, allylic CH_3) and a doublet (J = 8 c.p.s.) at 9.02 τ (12H, CH_3) and a molecular weight of 126 (mass spectrum). The olefin **8c** has an ultraviolet maximum[27] at 192 mμ (ϵ 8,900) with no n.m.r. absorption[35] attributable to vinyl C—H and a singlet at 8.38 τ (allylic CH_3) and a series of partially resolved peaks (apparently a triplet and a doublet each with J = 7 c.p.s.) centered at 9.05 τ (CH_3). The material has a molecular weight of 126 (mass spectrum).

Procedure for Quantitative Studies.—All reactions were run under a nitrogen atmosphere, and the solutions of reactants were maintained at 25° prior to mixing. For the reactions employing normal addition, approximately 15 ml. of an ethereal solution of the ketone was added, with stirring and over a period of 60 ± 5 sec., to approximately 16 ml. of an ethereal solution of the organomagnesium compound. The volumes of ether employed were such that the final volume of the reaction mixture was 31 ml. The concentrations listed in the tables refer to the calculated final concentrations in the reaction mixture if no reaction had occurred. For reactions employing inverse addition the same general procedure was followed except that a solution of the organomagnesium compound in approximately 16 ml. of ether was added to a solution of the ketone in approximately 15 ml. of ether. A weighed quantity of an internal standard (anisole for the 3-pentanone experiments and *p*-methylanisole for the 2,4-dimethyl-3-pentanone experiments) was present in each ethereal solution of the ketone. The reaction mixtures were stirred for 45 min. at room temperature and then washed with an aqueous solution of ammonium chloride and ammonium hydroxide (pH 7.5 to 8.0). The ether solutions were analyzed by gas chromatography[34] using a column which had been calibrated with known mixtures of products and standards. The products from representative runs were identified both by retention times and by comparison of the infrared spectra of collected samples with the spectra of the previously described authentic samples. In all cases the calculated yields (from internal standards) of products exceeded 90%. The numbers listed in the tables represent the average values of two or more runs. Except as noted, the duplicate values agreed to within ±3%.

For reactions employing ethylmagnesium alkoxides, a cold (0°) ethereal solution of diethylmagnesium was treated with the calculated amount of ketone or alcohol under a nitrogen atmosphere and the resulting solution was stirred at room temperature for 30 min. prior to use. An aliquot of each of these solutions was hydrolyzed and analyzed as previously described. For organomagnesium solutions containing added magnesium bromide, the solution obtained after addition of magnesium bromide was stirred for 45 min. prior to use.

Procedure for Kinetic Studies.—A diagram of the apparatus employed is presented in Figure 1. For determining reaction times, the reagent reservoirs were fitted with auxiliary 150-ml. bulbs and the time required to pass measured volumes of ether through the apparatus at various pressures and reaction tube lengths was measured. From these data and the measured volume of the reaction tubes and the stopcock, the time required for the two streams of ether to pass from the point of mixing to the outlet of the reaction tube was calculated.[36] A series of measurements with representative solutions of reactants demonstrated that under the conditions employed, a 15.0-ml. aliquot of the ketone solution was mixed with from 13.6 to 15.0 ml. of the organomagnesium solution depending on the concentration and nature of the reagent. The efficiency of mixing was demonstrated by mixing a deep blue solution of Thymolphthalein and sodium ethoxide in ether with an ethereal solution of *p*-toluenesulfonic acid. Since the blue color of the indicator was no longer discernible in the reaction tube, even at the highest pressures employed, mixing was judged to be complete within the stopcock. The efficiency of mixing also follows from the fact that the reaction of diethylmagnesium with 3-pentanone was complete even at the shortest reaction times employed.

For the kinetic runs, 15 ml. of a solution (thermostated to 25.0°)[37] of the ketone and the appropriate internal standard in ether was placed in one flask and 20 ml. of a solution (thermostated to 25.0°) of the organomagnesium compound was placed in the second flask. The system was placed under nitrogen pressure and the stopcock was opened in such a way that the organomagnesium solution preceded the ketone solution into the mixing chamber. The end of the reaction tube was immersed in a cold (0°) quenching bath containing 20 ml. of methanol and 15 ml. of water, a mixture which kept the quenched reaction mixture homogeneous.

After the run was complete, a sufficient quantity of saturated aqueous ammonium chloride (adjusted to pH 7.5 to 8.0 by addition of ammonium hydroxide) was added to dissolve the magnesium salts and cause the mixture to separate into two layers. The aqueous layer was extracted with ether and the combined organic layers were dried and concentrated by distillation through a 30-cm. Holzmann column. The concentrated solution then was analyzed by gas chromatography as previously described utilizing the same internal standards. Appropriate blank

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(22) R. R. Dreisbach and R. A. Martin, *Ind. Eng. Chem.*, **41**, 2875 (1949).

(23) A gas chromatographic column packed with Dow Corning silicone fluid, no. 550, was employed for this analysis.

(24) W. W. Moyer and C. S. Marvel, "Organic Syntheses," Coll. Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 602.

(25) F. C. Whitmore and D. E. Badertscher, *J. Am. Chem. Soc.*, **55**, 1559 (1933).

(26) I. N. Nasarow, *Ber.*, **70**, 617 (1937).

(27) Determined in *n*-heptane.

(28) F. C. Whitmore and J. D. Surmatis, *J. Am. Chem. Soc.*, **62**, 995 (1940).

(29) J. M. Church, F. C. Whitmore, and R. V. McGrew, *ibid.*, **56**, 176 (1934).

(30) J. Stas, *Bull. soc. chim. Belges*, **35**, 379 (1926).

(31) F. C. Whitmore and R. S. George, *J. Am. Chem. Soc.*, **64**, 1239 (1942).

(32) F. C. Whitmore and F. Johnson, *ibid.*, **60**, 2265 (1938).

(33) The pure olefin **8b** is reported to boil at 138°, $n^{25}\text{D}$ 1.4328, and the pure olefin **8c** is reported to boil at 130°, $n^{25}\text{D}$ 1.4211. F. L. Howard, T. W. Mears, A. Fookson, P. Pomerantz, and D. B. Brooks, *J. Res. Natl. Bur. Std.*, **38**, 365 (1947) (Research Paper No. 1779); *Natl. Advisory Comm. Aeron., Tech. Note*, no. **1247**, 56 pp. (1947).

(34) A gas chromatographic column packed with 20 M Carbowax suspended on ground firebrick was employed.

(35) Determined in carbon tetrachloride solution.

(36) The rate of flow of the ether through the reaction tube exceeds the minimum critical velocity for turbulent flow by at least a factor of 100. See F. J. W. Roughton and B. Chance in S. L. Friess and A. Weissberger, "Technique of Organic Chemistry," Vol. VIII, Interscience Publishers, Inc., New York, N. Y., 1953, pp. 669–738.

(37) The kinetic runs were, of necessity, adiabatic in character. Consequently, the temperature of the reaction mixtures may well have increased by as much as 10° during the course of some of the kinetic runs. As a result, calculated apparent rate constants for runs where an appreciable fraction of the total reaction has occurred may be too large by as much (see ref. 7 and 8) as a factor of two. Since the reaction times encountered in this study are on the borderline for effective quenching (ref. 36), our apparent rate constants may be too large for this reason also.

TABLE III

RATES OF REACTION WITH 3-PENTANONE (**5a**) AND 2,4-DIMETHYL-3-PENTANONE (**5b**)

Organomagnesium reactant	Ketone	Reaction time, sec.	k,[a] l. mole^{-1} sec.$^{-1}$	Product composition, %		
				5	**9** (reduction)	**7** (addition)
0.261 M $\mathrm{Et_2Mg}$	0.155 M **5a**	0.0251	...	3	<1	97
.261 M $\mathrm{Et_2Mg}$	.155 M **5a**	.0186	>2500	3	<1	97
.261 M $\mathrm{Et_2Mg_2Br_2}$	.155 M **5a**	...[b]	...	1	1	98
.261 M $\mathrm{Et_2Mg_2Br_2}$	.155 M **5a**	.101	37	46	<1	54
.261 M $\mathrm{Et_2Mg_2Br_2}$	.155 M **5a**	.0312	50	69	<1	31
.261 M $\mathrm{Et_2Mg_2Br_2}$	.155 M **5a**	.0186	44	83	<1	17
.261 M $\mathrm{Et_2Mg_2Br_2}$	.077 M **5a**	.0789	28	58	<1	42
.261 M $\mathrm{Et_2Mg_2Br_2}$	.077 M **5a**	.0320	48	68	<1	32
.137 M $\mathrm{Et_2Mg_2Br_2}$	.074 M **5a**	.0935	45	60	<1	40
		average	43 ∓ 6			
.261 M $\mathrm{Et_2Mg}$ + 0.261 M $\mathrm{MgBr_2}$	.155 M **5a**	.0186	44	83	<1	17
.261 M $\mathrm{Et_2Mg_2(OR)_2}$[c,d]	.155 M **5a**	...[b]	...	26	5	69
.261 M $\mathrm{Et_2Mg_2(OR)_2}$[c,d]	.155 M **5a**	.0814	...[e]	42	2	56
.261 M $\mathrm{Et_2Mg_2(OR)_2}$[c,d] + 0.522 M $\mathrm{MgBr_2}$	.155 M **5a**	...[b]	...	1	1	98
.261 M $\mathrm{Et_2Mg_2(OR)_2}$[c,d] + 0.522 M $\mathrm{MgBr_2}$	.155 M **5a**	.0269	46	74	<1	26
.261 M $\mathrm{Et_2Mg_2(OR)_2}$[c,f]	.155 M **5a**	.0814	...[g]	34	4	62
.261 M $\mathrm{Et_2Mg}$	.155 M **5b**	...[b]	...	0	6	94
.261 M $\mathrm{Et_2Mg}$	.155 M **5b**	.0821	33	54	2	43
.261 M $\mathrm{Et_2Mg}$	.077 M **5b**	.0821	39	47	2	50
.137 M $\mathrm{Et_2Mg_2Br_2}$	.074 M **5b**	.429	<0.2	100	<1	<1

[a] These rate constants were calculated using the expressions rate = $k\,[\mathrm{Et_2Mg_2Br_2}]\,[\mathrm{ketone}]$ or rate = $k\,[\mathrm{Et_2Mg}]\,[\mathrm{ketone}]$ for experiments performed in the absence of magnesium bromide. For the reactions of ethylmagnesium bromide with 3-pentanone (**5a**) first-order rate constants, calculated using the expression rate = $k[\mathrm{Et_2Mg_2Br_2}]$, ranged from 1.7 to 6.4 sec.$^{-1}$. The reactants were brought to 25.0° prior to mixing. See ref. 37. [b] These runs, used to determine the product composition after complete reaction, were made by mixing the reactants in the flowing-stream apparatus and collecting the product from the exit under nitrogen in a dry flask. After the mixtures had been allowed to stand for 15 min. they were quenched and analyzed in the usual way. [c] R = $\mathrm{C_2H_5(}n\mathrm{\text{-}C_3H_7)_2C}$. [d] See Table I, footnote *b*. [e] Because of the extensive amount of enolization as a side reaction, no effort was made to calculate a rate constant. However, the data indicate that the addition reaction was 81% complete in this time period. [f] See Table I, footnote *c*. [g] These data, the result of a single run, indicate that the ethylmagnesium alkoxide **6a** prepared in this way (footnote *f*) is not substantially more or less reactive than the reagent obtained by reaction of ethylmagnesium with one equivalent of 4-heptanone (footnote *d*).

experiments demonstrated that this analytical procedure did not inadvertently fractionate the reaction products.

To correct the reaction times (Table III) determined with pure ether for the slightly increased viscosity of the reaction mixtures, duplicate measurements were made of the time required to pass a given volume of representative reaction mixtures through the apparatus. The molar concentration values listed in Table III refer to the concentration of the reactants *after mixing* if no reaction had occurred. In each case the values have been corrected for the experimentally determined mixing ratios of the reactants. The data listed in Table III are average values from two determinations. In every case the calculated yields (or recovery) of products exceeded 90% and the deviations of individual value from the average values listed in Table III did not exceed 3%.

N.m.r. Spectra.—Although the peaks attributable to the methyl groups of the various ethylmagnesium derivatives, as approximately 1 M solutions in ether, were obscured by solvent absorption, the peaks attributable to the methylene groups were readily discernible. The diethylmagnesium solution has a quartet (J = 8 c.p.s.) of doublets (J = 1 c.p.s.) centered at 10.63 τ, the ethylmagnesium bromide has a quartet (J = 8 c.p.s.) of doublets ($J \sim 1$ c.p.s.) centered at 10.68 τ and the ethylmagnesium alkoxide **6a** has a quartet (J = 8 c.p.s.) of doublets ($J \sim 1$ c.p.s.) centered at 10.67 τ.

The Chemistry of Carbanions. IV. The Stereochemistry of Conjugate Grignard Addition[1]

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The reaction of $\Delta^{8,9}$-octal-1-one with phenylmagnesium bromide, either in the presence or absence of cuprous chloride has been found to yield mixtures of the allylic alcohol **5** and the saturated ketone having the stereochemistry indicated in structure **9**. Arguments are presented in support of the view that the conjugate addition of organomagnesium compounds is comparable to the Michael reaction and does not proceed *via* a six-membered cyclic transition state.

In continuing our study of the addition of organometallic compounds to conjugated ketones,[2] we were interested in learning the preferred stereochemistry of conjugate addition. Although previous studies of the cuprous ion-catalyzed addition of methyl Grignard reagents to the $\Delta^{1,9}$-octal-2-one system **1**[3] had led to the

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(2) H. O. House, D. D. Traficante, and R. A. Evans, *J. Org. Chem.*, **28**, 348 (1963) and references cited therein.

(3)(a) R. F. Church, R. E. Ireland, and D. R. Shridhar, *ibid.*, **27**, 707 (1962); (b) A. J. Birch and R. Robinson, *J. Chem. Soc.*, 501 (1943).