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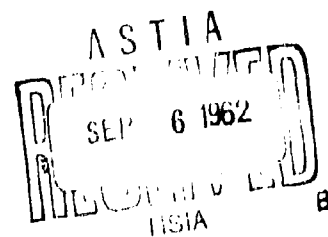
DANIEL D. TRAFICANTE
29502A Capt. USAF

Ph. D. Thesis

PART I Reactions of Organomagnesium Compounds
with α,β-Unsaturated Ketones.

PART II Reactions of Organomagnesium Compounds
with Saturated Ketones.

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PART I: REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH
           α, β-UNSATURATED KETONES

PART II: REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH
           SATURATED KETONES

by

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B.S., Syracuse University

(1955)

Submitted in Partial Fulfillment

of the Requirements for the

Degree of Doctor of Philosophy

at the

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

July 9, 1962

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                              Department of Chemistry, July 9, 1962

Certified by _____
                                                 Thesis Supervisor

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PART I: REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH
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Submitted in Partial Fulfillment of the Requirements for the Degree of
Doctor of Philosophy at the Massachusetts Institute of Technology,
July 9, 1962.

ABSTRACT

PART I: REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH
          α, β-UNSATURATED KETONES

The reactions of trans-4-phenyl-3-buten-2-one (8b) and trans-3-penten-2-one (8a) with dimethyl-, diethyl- and diphenylmagnesium have been studied. The ratio of conjugate to normal addition observed was decreased only slightly by the presence of magnesium bromide in the reaction mixture. In the reaction of the ketone 8b with diethylmagnesium, variations in the concentration of either reactant did not significantly alter the proportions of normal and conjugate addition products. The presence of cuprous ion favored conjugate addition both with the diaryl- and dialkyl-magnesiums and with the Grignard reagents. The presence of excess isoprene in the reaction mixtures did not reduce the proportion of conjugate addition.

PART II: REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH
          SATURATED KETONES

The reactions of 3-pentanone (2) and 2,4-dimethyl-3-pentanone (6) with diethyl- and alkoxyethylmagnesium (1) have been studied. The ratio of enolization and reduction to normal addition was significantly decreased by the presence of magnesium bromide in the reaction mixture. Kinetic data for these reactions have also been obtained. The order of reactivities

for the organomagnesium compounds was found to be diethylmagnesium greater than ethylmagnesium bromide or alkoxyethylmagnesium (1), and for the ketones, 3-pentanone (2) greater than 2,4-dimethyl-3-pentanone (6). A mixture of the alkoxyethylmagnesium compound (1) with magnesium bromide gave a rate comparable to ethylmagnesium bromide.

Thesis Supervisor: Herbert O. House

Title: Associate Professor of Chemistry

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PART I

REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH

α, β - UNSATURATED KETONES

I. INTRODUCTION

Recent investigations have provided evidence for the previous suggestion[1a] that Grignard reagents are solvated complexes 1 formed

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(1) For a discussion of earlier work with leading references see
(a) E. G. Rochow, D. T. Hurd, and R. N. Lewis, "The Chemistry of Organometallic Compounds, " John Wiley and Sons, Inc., New York, N. Y., 1957; (b) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances, " Prentice-Hall, Inc., New York, N. Y., 1954.

---

from dialkylmagnesium compounds and magnesium halides rather than equilibrating mixtures of alkylmagnesium halides 2, dialkylmagnesium

---

(2) R. E. Dessy, G. S. Handler, J. H. Wotiz, and C. A. Hollingsworth, J. Am. Chem. Soc., 79, 3476 (1957).

---

compounds 3 and magnesium halides 4.[1-5] Since the magnesium halide

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(3) (a) R. E. Dessy and G. S. Handler, J. Am. Chem. Soc., 80, 5824 (1958);
(b) R. E. Dessy, J. Org. Chem., 25, 2260 (1960).

(4) The lack of an appreciable concentration of free carbanions in dialkylmagnesiums is indicated by a study of the ultraviolet spectra of dicinnamylmagnesium [R. H. DeWolfe, D. L. Hagemann, and W. G. Young, J. Am. Chem. Soc., 79, 4795 (1957)]. See also J. E. Nordlander, W. G. Young, and J. D. Roberts, J. Am. Chem. Soc., 83, 494 (1961).

(5) For simplicity, the solvent molecules associated with the organomagnesium compounds (Ref. 1) have been omitted from the formulas.

---

4 are appreciably stronger Lewis acids than the dialkylmagnesium compounds 3,[1a] one is led to expect that the course of reactions of dialkylmagnesium compounds 3 with other reagents might be influenced by the

presence or absence of magnesium halide 4. This expectation is

supported by a number of observations where, in the absence of mag-

nesium halides, the following effects have been observed:

A.   An increased rate of reaction of

    1. diethylmagnesium with 1-hexyne[6]

    2. dimethylmagnesium with acetone[7]

    3. dimethylmagnesium with benzophenone[8,9]

B.   A decreased rate of addition of dialkylmagnesium compounds to nitriles.[10,11]

C.   An increased amount of enolization and reduction in the reactions of

    1. propylmagnesium bromide with diisopropyl ketone[12]

    2. dialkylmagnesium compounds with diisopropyl ketone[13,14].

D.   An increased amount of enolization in the reaction of acetomesitylene

    with dimethylmagnesium.[15]

(6)   (a) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, J. Org. Chem.,
21, 1063 (1956); (b) J. H. Wotiz, C. A. Hollingsworth and R. E.
Dessy, J. Am. Chem. Soc., 78, 1221 (1956); (c) R. E. Dessy, J. H.
Wotiz, and C. A. Hollingsworth, J. Am. Chem. Soc., 79, 358 (1957).

(7)   J. G. Aston and S. A. Bernhard, Nature, 165, 485 (1950).

(8)   N. M. Bikales and E. I. Becker, Chemistry and Industry, 1831 (1961).

(9)   (a) M. Anteunis, J. Org. Chem., 26, 4214 (1961); (b) M. Anteunis,
J. Org. Chem., 27, 596 (1962).

(10) (a) H. Gilman and R. E. Brown, J. Am. Chem. Soc., 52, 1181 (1930);
(b) H. Gilman and R. E. Fothergill, J. Am. Chem. Soc., 51, 3149 (1929).

(11) For more recent kinetic studies see (a) C. G. Swain, J. Am. Chem. Soc.,
69, 2306 (1947); (b) S. J. Storfer and E. I. Becker, J. Org. Chem.,
27, 1868 (1962); (c) J. Vekemans and A. Bruylants, Bull. Soc. Chim
Belges, 68, 541 (1959).

(12) C. G. Swain and H. B. Boyles, J. Am. Chem. Soc., 73, 870 (1951) E. T.
McBee, O. R. Pierce, and J. F. Higgins, J. Am. Chem. Soc., 74, 1736 (1952).

(13) (a) J. Miller, G. Gregoriou, and H. S. Mosher, J. Am. Chem. Soc., 82, 3966
(1961); (b) D. O. Cowan and H. S. Mosher, J. Org. Chem., 27, 1 (1962).

3.

(14)   A well known example of differing behavior is found in the reaction of epoxides with organomagnesium compounds. N. G. Gaylord and E. I. Becker, Chem. Revs., 49, 413 (1951).

(15)   G. F. Wright, J. Am. Chem. Soc., 61, 1152 (1939).

The addition of cuprous chloride has also been previously reported[16] as causing a very substantial increase in the amount of conjugate addition in the reactions of Grignard reagents with α,β-unsaturated ketones.

(16)   M. S. Karasch and P. O. Tawney, J. Am. Chem. Soc., 63, 2308 (1941).

The normal 5 and conjugate 6 addition products obtained from organomagnesium compounds 7 and α,β-unsaturated ketones 8 have been suggested[8,9,12,13,17] to result from the cyclic addition processes such as 9 and 10[18]. If these cyclic mechanisms are correct, normal addition

(17)   (a) R. E. Lutz and W. G. Reveley, J. Am. Chem. Soc., 63, 3180 (1941);

        (b) For a comprehensive review and discussion see Ref. 1b, p. 196.

(18)   The cyclic mechanism 10 for conjugate addition has been criticised by E. R. Alexander and G. R. Coraor [J. Am. Chem. Soc., 73, 2721 (1951)] on the grounds that such a process is sterically improbable for the observed conjugated addition of Grignard reagents to cyclohexenone.

should be facilitated by the presence of excess magnesium halide in the reaction mixture and impeded in its absence.[12,17b]

This thesis contains a study of various factors, including the presence or absence of magnesium bromide, which might be expected to influence the reaction of α, β-unsaturated ketones with organomagnesium compounds.

$$R_2 Mg \underset{Br}{\overset{Br}{\diamond}} Mg \rightleftharpoons R_2 Mg + Mg Br_2 \underset{}{\overset{}{\rightleftharpoons}} 2 \; RMg \; Br$$

$$\underline{1} \qquad\qquad \underline{3} \qquad \underline{4} \qquad\qquad \underline{2}$$
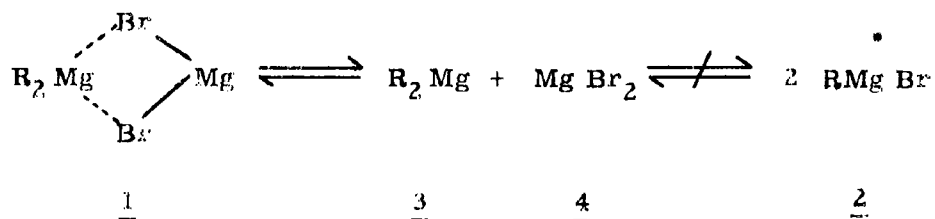
II.   DISCUSSION

An experimental test of the previously discussed prediction has been performed by reaction of unsaturated ketones 8 with organomagnesium compounds 7.   The proportions of products 5 and 6 obtained are summarized in Table I.   In this study each of the products 5 and 6 as well as the dienes 11 and 12 were isolated and characterized.   To avoid the analytical difficulties noted in previous studies,[18] gas chromatography was used for all product analyses save for the reaction of the phenylmagnesium compounds with benzalacetone 8b where infrared analysis was employed.

As will be noted in Table I, the predicted[17b] enhancement of conjugate addition to α, β-unsaturated ketones in the absence of magnesium bromide is valid, but the effect is very slight.   That the small effects observed are attributable to the absence of magnesium bromide rather than to the presence of varying amounts of impurities is indicated by a reversal of the effect when the dialkylmagnesium compounds are treated with an equimolar amount of magnesium bromide prior to reaction with the unsaturated ketone.   It was not possible to obtain meaningful data for reactions of the unsaturated ketones 8 with Grignard reagents containing excess magnesium bromide since the products 5 from normal addition were destroyed by the reaction conditions, presumably by dehydration of the unsaturated alcohols and subsequent polymerization of the dienes formed. . Thus, it is concluded that the suggested[17b] enhancement of normal addition by adding excess magnesium bromide or enhancement of conjugate addition by use of dialkylmagnesiums free from magnesium bromide has little preparative value.

Addition of 1-5 mole % of cuprous chloride caused a very sub-
stantial increase in the proportion of conjugate addition, both with
Grignard reagents as previously reported,[16] and with dialkyl- and
diarylmagnesium compounds. In two instances addition of excess iso-
prene to reaction mixtures, either in the presence or absence of cuprous
chloride, failed to alter significantly the proportion of conjugate addi-
tion. These observations suggest that cuprous ion-catalyzed conjugate
additions do not proceed via radical chain processes involving alkyl
or aryl free radicals.

Although the enhancement of conjugate addition by cuprous ion
might be interpreted as involving addition of an intermediate organo-
copper compound to the unsaturated ketone[19] it is difficult to understand

(19)   J. Munch-Peterson and V. K. Anderson, Acta. Chemica Scan-
        dinavia, 15, 271 (1961).

how the series of exchange reactions which would be required to explain
the effect of small percentages of cuprous halide could possibly be fast
enough to compete with the direct reaction of the organomagnesium
compound and the unsaturated ketone. For this reason some type of
radical chain process is considered as most probable.[20] The present

(20)   (a) M. S. Kharasch, L. Biritz, W. Nudenberg, A. Bhattacharya,
            and N. C. Youg, J. Am. Chem. Soc., 83, 3229 (1961).

        (b) M. S. Kharasch, M. Weiner, W. Nudenberg, A. Bhattacharya,
            T. Wang, and N. C. Yang, J. Am. Chem. Soc., 83,
            3232 (1961).

data indicate that, if such a process is correct, the radical carrying
species is not reactive toward isoprene. Alternatively, enhancement of
conjugate addition could be attributed to rapid, reversible complexing

$R_2 M_g$

8a, R=CH$_3$
b, R=C$_6$H$_5$

7a, R=CH$_3$
b, R=C$_2$H$_5$
c, R=C$_6$H$_5$

10

H$_2$O

R_1
CH CH$_2$ CO CH$_3$
R_2

6a, R$_1$=R$_2$=CH$_3$
b, R$_1$=CH$_3$, R$_2$=C$_6$H$_5$
c, R$_1$=C$_2$H$_5$, R$_2$=C$_6$H$_5$
d, R$_1$=R$_2$=C$_6$H$_5$

MgBr$_2$

9

H$_2$O

5a, R$_1$=R$_2$=CH$_3$
b, R$_1$=CH$_3$, R$_2$=C$_6$H$_5$
c, R$_1$=C$_6$H$_5$, R$_2$=CH$_3$
d, R$_1$=C$_6$H$_5$, R$_2$=C$_2$H$_5$
e, R$_1$=R$_2$=C$_6$H$_5$

11a, R$_1$=R$_2$=CH$_3$
b, R$_1$=C$_6$H$_5$, R$_2$=CH$_3$
c, R$_1$=C$_6$H$_5$, R$_2$=C$_2$H$_5$

12a, R$_1$=H, R$_2$=CH$_3$
b, R$_1$=CH$_3$, R$_2$=H
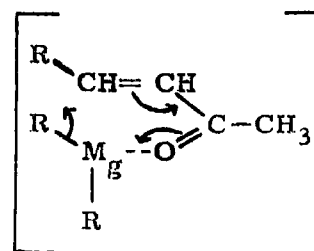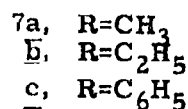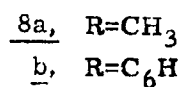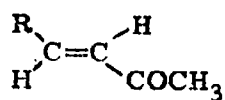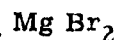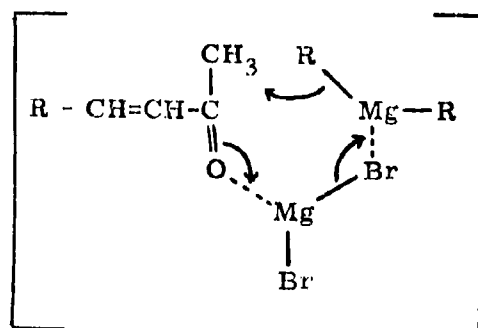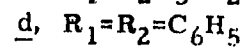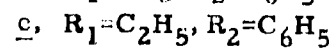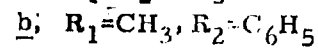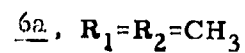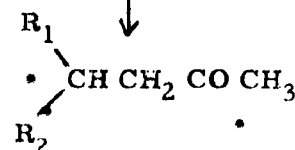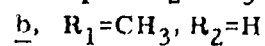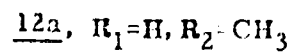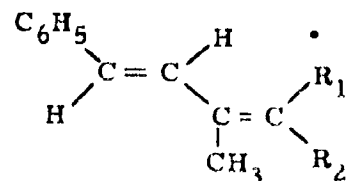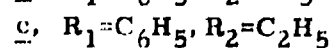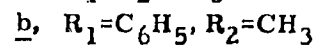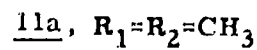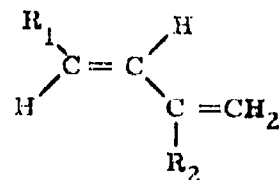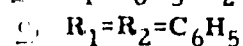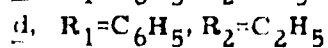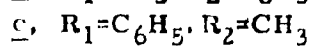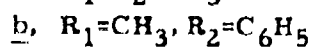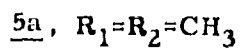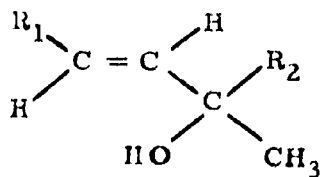
TABLE I

REACTION OF ORGANOMAGNESIUM

COMPOUNDS WITH α, β - UNSATURATED KETONES

Organomagnesium compound[b]	% Normal addition[a]	
	$CH_3CH=CHCOCH_3$	$C_6H_5CH=CHCOCH_3$
$(CH_3)_2Mg \cdot MgBr_2$	93	94 $(95)^c$
$(CH_3)_2Mg$	91	89
$(C_2H_5)_2Mg \cdot MgBr_2$	--	20
$(C_2H_5)_2Mg$	--	15
$(C_6H_5)_2Mg \cdot MgBr_2$	50 $(53)^c$	77 $(70)^c$
$(C_6H_5)_2Mg$	47	43

[a] The numbers listed, which are the average values from two or more runs, represent the percent alcohol 5 (including any dienes 11 and 12 derived from the alcohols 5) in the product. The values in this table are derived from reaction of two equivalents of the organomagnesium compound with one equivalent of the unsaturated ketone. [b]For the numbers not enclosed in parentheses, the formulas $R_2Mg \cdot MgBr_2$ refer to the Grignard reagent prepared in the usual manner. [c]For the numbers enclosed in parentheses, the formulas $R_2Mg \cdot MgBr_2$ refer to the reagent obtained by mixing two equivalents of the dialkylmagnesium compound with two equivalents of magnesium bromide.

between cuprous ion and the unsaturated ketone to greatly catalyze conjugate addition.

The possible effect of concentration changes on the ratio of conjugate to normal addition have also been examined. In two cases (7c + 8a and 7b + 8b) mixing the reactants by slowly adding the organomagnesium compound to the ketone (i.e. inverse addition), a procedure which insures that the ketone will be in excess during the first half of the reaction, did not significantly alter the proportion of conjugate addition. The use of a flow system[21] for mixing ethylmagnesium bromide

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(21)   A description of this apparatus and of the studies of the reaction of alkylmagnesium compounds with saturated ketones is the subject of Part II.

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with benzalacetone (8b) also did not significantly alter the ratio of conjugate to normal addition. 'Finally, the possible effects of changing the absolute concentrations of either the organometallic or the ketone in the reaction of ethylmagnesium derivatives (7b) with benzalacetone (8b) were examined. These studies, summarized in Table II, were conducted in such a way that there was always a ten-fold excess of diethylmagnesium present (assuming that only one ethyl group will react). In this way the concentration of the organometallic remained essentially constant thereby insuring that reactions involving only the first, more reactive[7-9, 22]

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(22)   This method for comparing kinetic orders of competing reactions has been used by Mosher and co-workers (Ref. 14) in a study of competing addition and reduction reactions involving organomagnesium compounds and saturated ketones.

---

ethyl group of the diethylmagnesium were being studied.

Suppose the mechanism is:

$$aG + bK \xrightarrow{k_1} C$$

$$aG + bK \xrightarrow{k_2} N$$
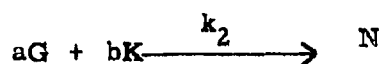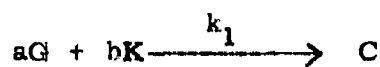
Then

$$\frac{dC}{dt} = k_1 G^a K^b$$

$$\frac{dN}{dt} = k_2 G^a K^b$$

$$\frac{dC}{dN} = \frac{k_1}{k_2} \quad \text{and} \quad \frac{C}{N} = \frac{k_1}{k_2}$$

where G is the organometallic, K the ketone, C the conjugate addition product and N the normal addition product. The products will appear in a constant ratio despite the order of the reaction, assuming only that the orders are the same.

For those reactions conducted in the absence of magnesium bromide, it is abundantly clear that neither changes in ketone concentration nor changes in the organometallic concentration alter the ratio of conjugate to normal addition. Thus, it can be concluded that the kinetic order of both reactions in the organometallic compound and in the ketone is the same, and it is therefore possible to determine the relative rate constants, $k_1/k_2 \approx 6$. Furthermore, the fact that the ratio was not altered by an inverse order of mixing where the alkylmagnesium alkoxide 13 is present accompanied by unchanged ketone indicates either that the kinetic order for consumption of the ethyl group of the alkoxide 13 ($R=C_2H_5$) is the same for both normal and conjugate additions or that the intermediate alkoxide 13 ($R=C_2H_5$) does not react with benzalacetone (8b) under the reaction conditions employed.

The concentration effects observed (Table II) in the reaction
when magnesium bromide is present are small but appear to be real.
The observed ratios of conjugate to normal addition, namely, 2.0, 2.6,
and 3.4, differ by much too small factors to be consistent with the
simple kinetic expressions, k_c [ketone] $[Et_2Mg_2Br_2]^n$ and k_n [ketone]
$[Et_2Mg_2Br_2]^{n+1}$ for conjugate and normal addition, respectively.

Of incidental interest in the reaction of ethylmagnesium deriva-
tives with benzalacetone (8b), was the formation of the saturated alcohol
14. 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 the saturated, aqueous ammonium chloride to the reaction mix-
tures. Since the former procedure did not decrease the amount of
alcohol 14 produced, it is concluded that this product is formed in the
original reaction mixture before any water has been added. This
material became the major product when large excesses of diethyl-
magnesium or long reaction times were employed. However, none of
this product was formed when the reactants were mixed in a flow system
permitting short reaction times. This saturated alcohol is apparently
formed in a relatively slow reaction between the initially formed enolate
15 and diethylmagnesium.[23] In support of this idea, essentially the

(23)   (a) R. C. Fuson, T. San and J. Dickmann, J. Org. Chem., 27,
             1221 (1962);
        (b) In our studies the possible formation of the alcohol 14
        during the isolation procedure [cf. R. E. Lyle and F. J. Tres-
        cianiec, J. Org. Chem., 24, 333 (1959)] was excluded (see
        Experimental).

TABLE II

EFFECT OF CONCENTRATION ON PRODUCT RATIO

$$C_6H_5CH=CHCOCH_3 + (C_2H_5)_2Mg \longrightarrow C_6H_5CH=CH\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-C_2H_5$$

8b   7c   5d

$$C_6H_5\underset{\overset{|}{C_2H_5}}{C}HCH_2COCH_3 + C_6H_5\underset{\overset{|}{C_2H_5}}{C}HCH_2\underset{\underset{OH}{|}}{\overset{\overset{CH_3}{|}}{C}}-C_2H_5$$

6c   14
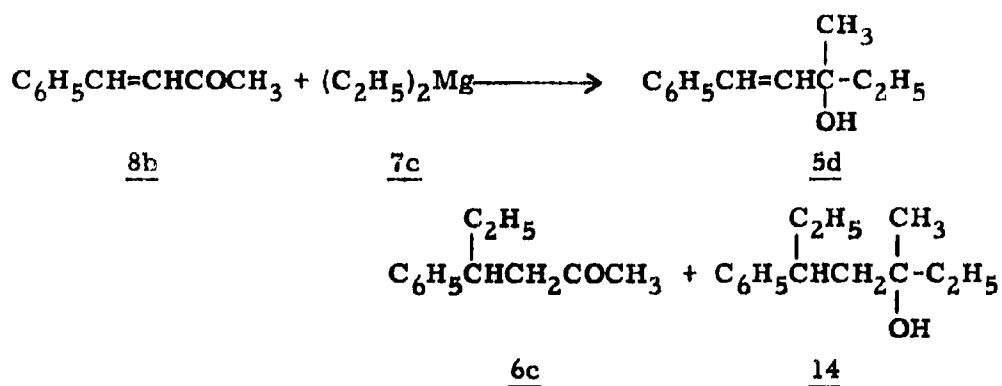
Molarity of 8b	Molarity of 7c	Molarity[b] of MgBr$_2$	Conjugate addition[a] % (of product)
0.075	0.75	--	86
0.015	0.75	--	86
0.015	0.15	--	88
0.075	0.75	0.75	67
0.015	0.75	0.75	72
0.015	0.15	0.15	77

[a]The figures listed are the averages of two or more runs and include 6c plus 14. [b]The magnesium bromide is that present in the preparation of the Grignard reagent.

same mixture of diastereoisomers of structure 14 was produced in the
reaction with benzalacetone (8b) and with the saturated ketone 6c.

$$RMgOR' \quad\quad C_6H_5CH\text{-}CH\overset{\overset{\displaystyle C_2H_5}{|}}{=\!=}C\text{-}CH_3 \quad\longrightarrow\quad C_6H_5CH\text{-}CH\overset{\overset{\displaystyle C_2H_5}{|}}{\underset{\theta}{}}\overset{O}{\overset{\|}{C}}\text{-}CH_3$$

13   15
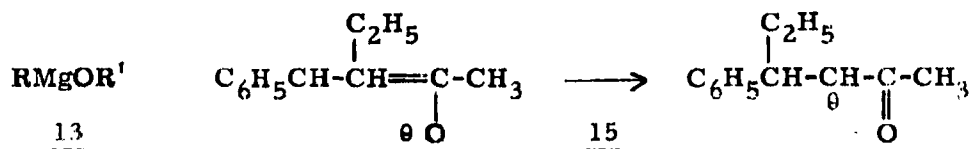
The absence of substantial effects from concentration changes
or added magnesium salts suggests that the transition states for normal
and conjugate addition of organomagnesium compounds to unsaturated
ketones are derived from the same reactants and are similar in character.
Consequently, the major obstacle to the interpretation of the mechanisms
of these reactions at the present time is the uncertainty about the mech-
anism of normal addition. From a number of kinetic studies[6-9, 21, 24] it

(24)   R. E. Dessy and R. M. Salinger, 140th Meeting of the American
Chemical Society, Chicago, Illinois, September 3-8, 1961,
Abstracts of Papers, p. 9Q.

has become clear that the order of reactivity of various organomagnesium
compounds towards addition to ketones is: $R_2Mg > R_2Mg_2Br_2 \gg RMgOR'$
(or the dimers or polymers of these structures). The addition of excess
magnesium bromide further retards the rate of the addition reaction.[8]
Thus, any assumption that magnesium bromide catalyzes the addition of
a dialkylmagnesium to a ketone is unwarranted.

The observation that addition may be favored at the expense of
reduction and enolization by adding excess magnesium bromide (Ref. 12)
has often been interpreted as evidence for including magnesium bromide
as an important component in the transition state for normal addition.

The kinetic data are clearly not compatible with this interpretation. The finding (Ref. 21) that the pronounced tendency of alkylmagnesium alkoxides 13 to give reduction and enolization products rather than addition may be mitigated by the addition of magnesium bromide provides an explanation for the increased amount of addition found in the presence of magnesium bromide.

The observation of asymmetric induction in a Grignard addition reaction carried out in an optically active solvent[25] provides compelling

(25)   N. Allentoff and G. F. Wright, J. Org. Chem., 22, 1 (1957).

evidence that at least one molecule of solvent is bonded to some atom (presumably magnesium) in the transition state leading to addition.[26]

(26)   For further discussion of the mechanism and the role of the
        solvent see (a) A. Kirrmann and R. Hamelin, Compt. rend.,
        251, 2990 (1960); (b) R. Hamelin, Bull. soc. chim. France,
        684, 915, 926 (1961).

In the absence of rigorous contradictory evidence, the best working hypothesis for the mechanism for reaction of the first alkyl group of a dialkylmagnesium with a ketone is considered to be the counterpart of the mechanism proposed for the normal addition of lithium reagents to ketones.[27] In particular, there seems to be no justification

(27)   C. G. Swain and L. Kent, J. Am. Chem. Soc., 72, 518 (1950).
        The argument used by these authors for supposing different
        mechanisms for the Grignard-ketone reaction (Ref. 11a) was
        based on reports that benzophenone forms a complex with the
        first equivalent of added Grignard reagent but does not react
        until a second equivalent of the organometallic is added. These
        reports are now known (Ref. 8) to be incorrect.

for incorporating a molecule of magnesium bromide into the preferred transition state for normal addition (as in $\underline{9}$ or its equivalent[26]) and no compelling reason (ignoring esthetics) to formulate either normal or conjugate addition as a cyclic, six-centered process.

III. EXITERIMENTAL [28]

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(28) All melting points are corrected and all boiling points are
uncorrected. The infrared spectra were determined with
either a Baird, Model B, or a Perkin Elmer, Model 21, infra-
red recording spectrophotometer fitted with a sodium chloride
prism. The ultraviolet spectra were determined with a Cary
recording spectrophotometer, Model 11MS. The microanalyses
were performed by Dr. S. M. Nagy and his associates and by
the Scandinavian Microanalytical Laboratory. Unless otherwise
stated magnesium sulfate was employed as the drying agent.

Preparation of the Organomagnesium Compounds -- Ethereal solu-
tions of the Grignard reagents from methyl bromide, ethyl bromide and
bromobenzene were prepared under nitrogen in the usual way. After the
mixtures had been allowed to stand overnight to permit the settling of
undissolved solids, the solutions were transferred to volumetric flasks
which were sealed and stored in such a way that they were protected from
light. To determine the concentration of the reagents, aliquots were
decomposed in excess standard hydrochloric acid and back titrated with
standard sodium hydroxide. The concentrations of the reagents varied
over the following ranges: methyl Grignard reagent, 1.45 $\underline{M}$ to 2.69 $\underline{M}$;
ethyl Grignard reagent, 2.20 $\underline{M}$; phenyl Grignard reagent, 1.76 M to
1.91 $\underline{M}$. A 2.59 $\underline{M}$ ethereal solution of magnesium bromide was pre-
pared by reaction of 1,2-dibromoethane with magnesium. After aliquots
of the solution had been quenched in water, the bromide ion concentration
was determined by titration with standard silver nitrate solution using
potassium chromate as an indicator. The ethereal solutions of dimethyl-,
diethyl- and diphenylmagnesium were prepared from the organomercury
compounds as previously described[29] and analyzed by the same method
used for the Grignard reagents. The concentrations of the reagents

(29)   W. Schlenk, Ber., 64, 736 (1931).

varied over the following ranges: dimethylmagnesium, 0.157 M to

0.866 M; diethylmagnesium, 0.93 M; diphenylmagnesium, 0.203 M

to 1.51 M. The dimethylmercury, b.p. 91 - 92.5° (lit. [30] 92°),

(30)   C. S. Marvel and V. L. Gould, J. Am. Chem. Soc., 44, 153
        (1922).

diethylmercury, b.p. 158 - 161° (lit. [31] 159°), and diphenylmercury,

(31)   E. Frankland and B. F. Duppa, Ann., 130, 104 (1864).

m.p. 122.9 - 124.6° (lit. [32] 121 - 123°), were all prepared by the general

(32)   H. O. Calvery, Org. Syntheses, Coll. Vol. 1, 228 (1951).

procedure of Gilman and Brown[33] or by a slightly modified procedure in

(33)   H. Gilman and R. E. Brown, J. Am. Chem. Soc., 52, 3314
        (1930).

which a tetrahydrofuran solution of mercuric chloride was added directly

to the Grignard reagent. In all cases a sufficient vol .me of the organo-

magnesium reagent was prepared so that all runs with a given unsaturated

ketone were done with the same batch of organomagnesium compound. In

this way any effects resulting from the possible presence of trace

impurities in the magnesium were kept constant.

    Reaction of Methylmagnesium Derivatives with <u>trans</u>-3-Penten-2-one (8a), --<u>trans</u>-3-Penten-2-ol, b.p. 39.5 - 41° (17 mm.), $n_D^{27.5}$ 1.4245 (lit. [34] 116 - 121°, n_D^{20} 1.4280), acid phthalate derivative, m.p. 89.5 - 90°

(34)   E. R. Alexander and R. W. Kluiber, <u>J. Am. Chem. Soc.</u>, <u>73</u>, 4304 (1951).

(lit. [35] 90 - 90.5°), was oxidized at -5° with aqueous chromium trioxide and

(35)   H. W. J. Hills, J. Kenyon and H. Phillips, <u>J. Chem. Soc.</u>, 576 (1936).

sulfuric acid to yield <u>trans</u>-3-penten-2-one, b.p. 110°, n_D^{29} 1.4314 (lit. [36]

(36)   A. L. Wilds and C. Djerassi, <u>J. Am. Chem. Soc.</u>, <u>68</u>, 1715 (1946).

121 - 122.5°, n_D^{20} 1.4342), semicarbazone m.p. 140 - 141° (lit. [38] 142°),

(38)   S. Krapiwin, <u>Bulletin de la Society Imperiale des Naturalistes de Moscou</u>, 1 (1908), <u>Chem. Zentr.</u>, 81 I, 1335 (1910).

containing[37] 99 % of the desired unsaturated ketone. Alternatively, a

(37)   A gas chromatography column packed with 4-methyl-4-nitropimelo-nitrile suspended on ground firebrick was employed.

sample of 3-penten-2-one, b.p. 115 - 118°, n_D^{25} 1.4352-1.4392, containing[37] 96 % of the desired ketone, was isolated by fractional distillation of the product mixture from the aldol condensation of acetaldehyde with acetone.[39]

(39)   The author is indebted to the Union Carbide Chemicals Corporation for a sample of this mixture.

To a solution of the Grignard reagent prepared from 1.032 g.
(0.043 g.-atom) of magnesium, excess methyl bromide and 30 ml. of
ether was added, dropwise and with stirring under a nitrogen atmos-
phere at 0°, a solution of 1.80 g. (0.021 mole) of 3-penten-2-one in
20 ml. of ether. After the mixture had been stirred for 30 min., it was
washed with a cold, saturated, aqueous solution of ammonium chloride
to which sufficient aqueous ammonium hydroxide had been added to bring
the solution to pH 7.5 to 8. The ether layer was dried and concentrated
by distillation of the ether through an 80-cm. Vigreux column. Fractional
distillation of the crude residue separated 1.025 g. of a fraction, b.p. 51°
(24 mm.), $n_D^{29.5}$ 1.4240 [lit.[40] b.p. 37° (13 mm.), n_D^{17} 1.4285], con-

(40)   R.C.R. Bacon and E. H. Farmer, J. Chem. Soc., 1065 (1937).

taining[37] 96 % of the allylic alcohol 5a as well as 0.417 g. (total yield
1.442 g. or 67 %) of fractions, b.p. 47 – 51° (24 mm.), $n_D^{29.5}$ 1.4189–
1.4224, containing[37] the ketone 6a as well as the alcohol 5a. The alcohol
exhibits infrared absorption[41] at 3580 cm.$^{-1}$ (unassoc. O-H), at 3340 cm.$^{-1}$

(41)   Determined as a solution in carbon tetrachloride.

(assoc. O-H) and 970 cm.$^{-1}$ (trans CH=CH) with weak end absorption
(ϵ 65 at 210 mμ) in the ultraviolet.[42]   Reaction of a 1.5 g. (0.015 mole)

(42)   Determined as a solution in 95 % ethanol.

sample of the alcohol 5a with the cyanic acid generated[43] from 5 g.

(43)   H. W. Blohm and E. I. Becker, Chem. Rev., 51, 471 (1952).

(0.04 mole) of cyanuric acid afforded the crude allophanate which was
taken up in ether. The pure allophanate crystallized from ether as
white needles, m.p. 116.5 - 118.5°, yield 0.25 g. (9 %).

Anal. Calcd. for $C_8H_{14}O_3N_2$: C, 51.60; H, 7.58; N, 15.04.

Found: C, 51.58; H, 7.64; N, 15.28

An authentic sample of methyl isobutyl ketone 6a, b.p. 116.5°,
n_D^{26} 1.3940 (lit.[44] b.p. 118.5°, n_D^{20} 1.3956), semicarbazone m.p. 132.5 -

(44)   D. M. Cowan, G. H. Jeffery, and A. I. Vogel, J. Chem. Soc.,
       171 (1940).

133° (lit.[45] 134°), was prepared by the hydrogenation of mesityl oxide

(45)   H. D. Law, J. Chem. Soc., 101, 1016 (1912).

over platinum. This sample was shown to be identical with a sample of
the ketone collected[37] from the organometallic reaction by comparison
of the infrared spectra of the two samples.

An authentic sample of the diene 11a, b.p. 76° n_D^{27} 1.4399 (lit.[46]

(46)   G. S. Whitby and W. Gallay, Cand. J. Res., 6, 280 (1932);
       Chem. Zentr., 103 II, 1425 (1932).

b.p. 76 - 77°, n_D^{20} 1.4418) was obtained by distillation of the allylic alco-
hol 5a from potassium bisulfate. The diene has infrared absorption[41]
at 1610 cm.$^{-1}$ (conj. C=C), at 965 cm.$^{-1}$ (trans CH=CH) and at 885 cm.$^{-1}$
(C=CH$_2$) with an ultraviolet maximum [42] at 227 mµ (ϵ 17,100).

For the quantitative experiments summarized in Table III, the
desired quantity of organomagnesium compound and any additives were

diluted with ether and then the unsaturated ketone plus sufficient ether to make the total reaction volume 25 ml. were added. The resulting reaction mixtures were stirred under a nitrogen atmosphere at room temperature for 45 min. and then washed with an aqueous solution of ammonium chloride and ammonium hydroxide. The ethereal solutions were dried and then analyzed by gas chromatography[37] employing columns which had been calibrated with known mixtures. The percentages of normal addition in Table III are the average values obtained from two or more runs. In no case did the deviation of an individual run from the average value exceed 2 %. In the runs containing cuprous chloride, the low solubility of this salt resulted in only partial solution of the cuprous chloride in the initial reaction mixture. The molarity values in Table III and subsequent tables are calculated from the quantity of cuprous chloride added to the reaction mixture. In none of the cases summarized in Table III was the diene 11a detected in the reaction mixtures.

Reaction of Phenylmagnesium Derivatives with trans-3-Penten-2-one (8a). --- Reaction of 50 ml (0.095 mole) of a 1.91 $\underline{M}$ ethereal solution of phenylmagnesium bromide with 4.01 g. (0.048 mole) of the unsaturated ketone for 30 min. followed by the previously described isolation procedure afforded 5.462 g. (70 %) of the product mixture, b.p. 67.5 - 130° (0.2 mm.), containing[47] biphenyl, 2-phenyl-trans-3-penten-

(47)   A gas chromatography column packed with 1540 Carbowax suspended on basewashed 80-100 mesh Chromosorb was employed.

TABLE III

REACTIONS OF METHYLMAGNESIUM COMPOUNDS WITH

TRANS-3-PENTEN-2-ONE (8a).

Molarity of Ketone	Molarity of Methylmagnesium Compound	Molarity of Added Substance (s)	Normal addition, % (of product)
0.29 M	0.29 M $Me_2Mg_2Br_2$	--	93
0.16 M	0.16 M Me_2Mg	--	91
0.39 M	0.38 M $Me_2Mg_2Br_2$	0.04 M CuCl	27
0.19 M	0.19 M $Me_2Mg_2Br_2$	0.04 M CuCl 4 M isoprene	18
0.19 M	0.19 M $Me_2Mg_2Br_2$	4 M isoprene	92

2-ol (5b), and 4-phenyl-2-pentanone (6b) as well as other unidentified

minor components. Chromatography of a 3.75-g. sample from this

mixture on 150 g. of Woelm neutral alumina (activity III) separated

0.187 g. of biphenyl, m.p. 69.2 - 70.3°, 0.613 g. of the ketone 6b

and 1.455 g. of the allylic alcohol 5b as well as 1.301 g. of fractions

containing various mixtures of these three components. The alcohol 5b,

after further purification by distillation through a short path still

$[n_D^{26.5}$ 1.5284, lit. [48] n_D^{18} 1.5327], exhibits infrared absorption[41] at

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(48)   V. Levy and H. Normant, Compt. rend., 244, 202 (1957).

_____

3600 cm.$^{-1}$(unassoc. O-H), at 3460 cm.$^{-1}$(assoc. O-H) and at 975 cm.$^{-1}$

(trans CH=CH) with a series of low intensity (ϵ 140 to 280) maxima in

the 240 to 270 mμ region of the ultraviolet.[42]

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70.

Found: C, 81.73; H, 8.65.

The ketone 6b was shown to be identical with a subsequently

described sample by comparison of the gas chromatograms and the infra-

red spectra of the two samples.

The quantitative experiments, summarized in Table IV, were

performed as in the previous case utilizing gas chromatography[47] for

the product analyses. In no case did the deviation of an individual run

from the average values reported in Table IV exceed 2 % . A blank

experiment utilizing a known mixture of the alcohol 5b and the ketone 6b

demonstrated that the isolation and analytical procedures employed did

not alter the amounts of ketone and alcohol present.

TABLE IV

REACTIONS OF PHENYLMAGNESIUM COMPOUNDS WITH

TRANS-3-PENTEN-2-ONE (8a)

Molarity of Ketone	Molarity of Phenylmagnesium Compound	Molarity of Added Substance	Normal addition, % (of product)
0.19 M	0.19 M $Ph_2\overline{Mg}_2Br_2$	--	50
0.95 M	0.95 M $Ph_2\overline{Mg}_2Br_2{}^a$	--	55
0.19 M	0.19 M $Ph_2\overline{Mg}_2Br_2{}^a$	--	56
0.19 M	0.19 M $Ph_2\overline{Mg}_2Br_2{}^b$	--	56
0.19 M	0.19 M $Ph_2\overline{Mg}$	--	47
0.19 M	0.19 M $Ph_2\overline{Mg}$	0.19 M $\overline{MgBr}_2$	53
0.19 M	0.19 M $Ph_2\overline{Mg}_2Br_2$	0.02 M $\overline{CuCl}$	11
0.19 M	0.19 M $Ph_2\overline{Mg}$	0.02 M $\overline{CuCl}$	22

[a] In these runs the unsaturated ketone was added dropwise over 75 min.

[b] In these runs, the organomagnesium reagent was added to the unsaturated ketone (i.e. inverse addition).

Reaction of Methylmagnesium Derivatives with trans-4-Phenyl-
3-buten-2-one (8b). -- Reaction of 43 ml. (0.132 mole) of a 3.06 M
ethereal solution of methylmagnesium bromide with a solution of 9.6 g.
(0.066 mole) of the unsaturated ketone 8b in 20 ml. of ether for 1 hr.
followed by the usual isolation procedure yielded 9.5 g. (89 %) of the
crude, undistilled product mixture. A series of fractional crystallizations
from petroleum ether at Dry Ice temperatures separated 1.06 g. (9.9 %)
of the pure allylic alcohol 5c as colorless needles, m.p. 34.7 - 36° (lit. [49]

.

(49)   E. A. Braude and C. J. Timmons, J. Chem. Soc., 2000 (1950).

36 - 37°). The material exhibits infrared absorption[41] at 3610 cm.$^{-1}$
(unassoc. O-H), at 3380 cm.$^{-1}$ (assoc. O-H) and at 970 cm.$^{-1}$ (trans
CH=CH) with an ultraviolet maximum[42] at 251 mμ (ε 18,600). From a
comparable reaction of 153 ml. (0.292 mole) of a 1.91 M ethereal
solution of methylmagnesium bromide with 21.5 g. (0.147 mole) of the
unsaturated ketone 8b in 75 ml. of ether, distillation of the crude pro-
duct afforded 18.29 g. of fractions, b.p. 59 - 104° (0.20 to 0.25 mm.),
containing mixtures of the alcohol 5c, the ketone 6b and the diene 11b.
Fractional distillation of this mixture separated 4.17 g. of the diene 11b,
b.p. 114.5 - 115.5° (19 mm.), which crystallized from petroleum ether
at Dry Ice temperatures as colorless needles, m.p. 32.5 - 33° (lit. [50] 28°).

(50)   K. Auwers and G. Peters, Ber., 43, 3094 (1910).

The diene has infrared absorption[41] at 1608 cm.$^{-1}$ (conj. C=C), at
965 cm.$^{-1}$ (trans CH=CH) and at 890 cm.$^{-1}$ (C=CH$_2$) with ultraviolet
maxima[42] at 273 mμ (ε 28,600) and 281 mμ (ε 29,600)[lit. [49,51] 273 mμ

(51)   The previous workers (Ref. 49) stated that their product was impure.

(ϵ 20,200) and 279 mμ (ϵ 20,200)]. After reaction of 36 ml. (0.110 mole) of a 3.06 $\underline{M}$ ethereal solution of methylmagnesium bromide with 20 ml. of an ethereal solution containing 8.05 g. (0.055 mole) of the ketone $\underline{8b}$ in the presence of 1.090 g. (0.011 mole) of cuprous chloride, distillation of the crude product afforded 4.125 g. of fractions, b.p. 115 - 120° (17 mm.), containing[47] from 45 to 65 % of the ketone $\underline{6b}$. A pure sample of the ketone $\underline{6b}$, collected from a gas chromatograph,[52]

(52)   A gas chromatography column packed with 20 $\underline{M}$ Carbowax suspended on ground firebrick was employed.

exhibits infrared absorption[41] at 1720 cm.$^{-1}$ (C=O) with a series of low intensity (ϵ 310) maxima in the 250-270 mμ region of the ultraviolet.[42] The ketone $\underline{6b}$ formed a 2,4-dinitrophenylhydrazone, m.p. 74.1 - 75.2° (lit.[53] 71 - 72°), and a semicarbazone, m.p. 131.3 - 132.8° (lit.[53]

(53)   M. C. Chiang, J. Chinese Chem. Soc., 18, 65 (1951); $\underline{C}$. $\underline{A}$., 46, 4472 (1952).

133 - 134°).

The quantitative studies, summarized in Table V, were performed as in previous cases utilizing gas chromatography[47] for product analyses. In no case did the deviation of an individual run from the average values reported in Table V exceed 2 %.

TABLE V

REACTIONS OF METHYLMAGNESIUM COMPOUNDS WITH

TRANS-4-PHENYL-3-BUTEN-2-ONE (8b)

Molarity of Ketone	Molarity of Methylmagnesium Compound	Molarity of Added Substance	Normal Addition, % (of product)
0.59 M	0.54 M $Me_2\overline{Mg}_2Br_2$	--	94
0.59 M	0.54 M $Me_2\overline{Mg}_2Br_2$	0.06 M CuCl	72
0.35 M	0.35 M $Me_2\overline{Mg}$	--	89
0.26 M	0.27 M $Me_2\overline{Mg}$	0.26 M $MgBr_2$	95

Reaction of Phenylmagnesium Derivatives with trans-4-Phenyl-3-buten-2-one (8b) -- For the quantitative data summarized in Table VI, the previously described reaction and isolation procedures were employed. The solvent was removed from the ethereal solution of the crude products at room temperature under reduced pressure and a 0.500-g. sample of the residual oil was diluted to 5.00 ml. with carbon tetrachloride. The optical densities of these solutions at 1715 and 970 cm.$^{-1}$ in the infrared were measured and compared with working curves[54] prepared from known

(54)   R. A. Evans, S. M. Thesis, Mass. Inst. of Tech. (1959).

mixtures of the alcohol 5e and the ketone 6d to determine the percentages of these components in the mixtures. Neither biphenyl nor isoprene interfered with this analytical procedure and the absence of the starting ketone 8b, which would have interfered, was demonstrated by the absence of absorption at 1680 cm.$^{-1}$. The deviation of individual runs from the average values reported in Table VI did not exceed 3 % .

Reaction of Ethylmagnesium Derivatives with trans-4-Phenyl-3-buten-2-one (8b). -- After reaction of 150 ml. (0.330 mole) of a 2.20 **M** ethereal solution of ethylmagnesium bromide with 50 ml. of an ethereal solution containing 23.4 g. (0.160 mole) of the ketone 8b for 1 hr. followed by the usual isolation procedure, a 10.25-g. portion of the crude product (28.902 g.) was chromatographed on 400 g. of Woelm neutral alumina (activity III). The fractions separated (analyzed by gas chromatography[52]) were a mixture of olefins 11c, 12a, and 12b (2.139 g.), the ketone 6c (4.777 g.), a mixture of the ketone 6c and the alcohol 5d (2.765 g.) and finally the alcohol 5d (0.401 g.) corresponding to yields of 21 % olefins, 58 % ketone, and 8 % alcohol. Distillation of the alcohol fractions afforded the pure alcohol 5d, b.p. 119° (9 mm.) [lit.[55] 124- 125°

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(55)   A. Klages, Ber., 39, 2587 (1906).

(11 mm.)], n_D^{25} 1.5359, which has infrared bands[41] at 3620 cm.$^{-1}$ (unassoc. O-H) at 3470 cm.$^{-1}$ (assoc. O-H) and at 972 cm.$^{-1}$ (trans CH=CH) with an ultraviolet maximum[42] at 251 mμ (ϵ 16,900).

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15.

Found: C, 81.68; H, 9.32.

Distillation of the ketone fractions afforded the pure ketone 6c, b.p. 115° (9 mm.) [lit. [56] 130° (18 mm.)], $n_D^{24.6}$ 1.5015, with infrared

(56)   E. P. Kohler, Am. Chem. J., 38, 511 (1907).

absorption[41] at 1718 cm.$^{-1}$ (C=O) and a series of low intensity (ϵ 232) maxima in the 250 - 270 mμ region of the ultraviolet.[42]

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15.

Found: C, 81.94; H, 9.32.

Gas chromatographic analysis[52] of the diene fraction indicated the presence of 11c (20 %), 12b (30 %), and 12a (50 %, components listed in order of increasing retention time). Each of the dienes was collected[52] and further purified by distillation through a short-path still. The olefin 11c, b.p. 100 - 105° (14 mm.), mol. wt. 158 (mass spectrum), has infrared absorption[41] at 960 cm.$^{-1}$ (trans CH=CH) and 890 cm.$^{-1}$ (C=CH$_2$) with an ultraviolet maximum[42] at 281 mμ (ϵ 27,000). The NMR spectrum (60 mc.)[41] of the sample has a multiplet centered at 2.68τ (aromatic C-H), a pair of doublets (J=16 c.p.s.) at 3.70 and 3.43τ and at 3.35 and 3.08τ (trans CH=CH), a partially resolved multiplet at 4.97τ (C=CH$_2$) and a triplet centered at 8.85τ plus a quadruplet centered at 7.67τ (-CH$_2$CH$_3$).

The diene 12b, b.p. 112 - 118° (12 mm.), mol. wt. 158 (mass spectrum), has infrared absorption[41] at 963 cm.$^{-1}$ (trans CH=CH) with an ultraviolet maximum[42] at 289 mμ (ϵ 26,800); the NMR spectrum (60 mc.)[41] has a multiplet centered at 2.73τ (aromatic C-H), a doublet (J=16 c.p.s.) at 3.70τ and 3.43τ (trans CH=CH, second doublet apparently is obscured by the aromatic C-H absorption, one peak of the presumed doublet being discernible at 3.02τ), a quadruplet (J~6 c.p.s.) centered

TABLE VI

REACTIONS OF PHENYLMAGNESIUM COMPOUNDS WITH TRANS-4-PHENYL-3-BUTEN-2-ONE (8b)

Molarity of Ketone	Molarity of Phenylmagnesium Compound	Molarity of Added Substance (s)	Normal Addition, % (of product)
0.35 $\underline{M}$	0.35 M $Ph_2\overline{Mg}_2Br_2$	--	77
0.26 $\underline{M}$	0.26 M $Ph_2\overline{Mg}_2Br_2$	--	71
0.29 $\underline{M}$	0.31 M $Ph_2\overline{Mg}$	--	43
.0.31 $\underline{M}$	0.31 M $Ph_2\overline{Mg}$	0.31 $\underline{M}$ $Mg\overline{Br}_2$	70
0.33 $\underline{M}$	0.33 M $Ph_2\overline{Mg}_2Br_2$	0.014 $\underline{M}$ CuCl	28
0.33 $\underline{M}$	0.33 $\underline{M}$ $Ph_2\overline{Mg}_2Br_2$	2 $\underline{M}$ isoprene	70
0.33 $\underline{M}$	0.33 M $Ph_2\overline{Mg}_2Br_2$	2 $\underline{M}$ isoprene 0.$\overline{019}$ $\underline{M}$ CuCl	30

at 4.57τ (olefinic proton of C=$\underline{CH}$-CH_3) and a pair of peaks at 8.25 and 8.13τ apparently resulting from a doublet (J~ 6 c.p.s., methyl group of C=CH-$\underline{CH}_3$) and a singlet (or unresolved multiplet) centered at 8.13τ ($\underline{CH}_3$-C=CH-CH_3).

The diene $\underline{12a}$, b.p. 121 - 128° (12 mm.), n_D^{25} 1.6020 [lit. [57] b.p.
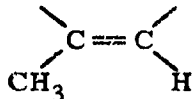
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(57)   (a) A. V. Dombrovskii, Doklady Akad. Nauk. S.S.S.R., 111, 827 (1956); C. A., 51, 9508 (1957). (b) A. V. Dombrovskii, Zhur. Obshchei Khim., 27, 3041 (1957); C.A., 52, 8087(1958). This author did not establish the stereochemistry of his diene nor did he establish that only one isomer was present.

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80 - 82° (2 mm.), n_D^{20} 1.5900], mol. wt. 158 (mass spectrum), has infrared absorption[41] at 962 cm.$^{-1}$ (trans CH=CH) with an ultraviolet maximum[42] at 286 mμ (ε 29,500). The NMR spectrum (60 mc.)[41] of the sample has a multiplet centered at 2.77τ (aromatic C-H), a pair of doublets J=16 c.p.s.) at 3.12 and 3.38τ and at 3.55 and 3.83τ (trans CH=CH), a quadruplet (J~ 6 c.p.s.) centered at 4.40τ (olefinic proton of C=$\underline{CH}$-CH_3) and a pair of bands at 8.30 and 8.20 apparently composed of a doublet (J~ 6 c.p.s., methyl group of C=CH-$\underline{CH}_3$) and a singlet (or unresolved multiplet) centered at 8.20τ ($\underline{CH}_3$-C=CH-CH_3). These NMR data permit the assignments of stereochemistry to the dienes $\underline{12}$ since the position (8.13τ) of the methyl resonance in diene $\underline{12b}$, containing the structural unit [structure: C=C with CH₃ and H], occurs at 0.07τ lower field than the methyl resonance (8.20τ) of the diene $\underline{12a}$, containing the structural unit [structure: CH₃, C=C, H] [58]. Also, the position of the olefinic proton

(58)   R. B. Bates and D. M. Gale, J. Am. Chem. Soc., 82, 5749 (1960).

resonance (4.57τ) in diene **12b** ($\overset{\diagup}{\underset{CH_3}{\diagdown}}C == C\overset{\diagup}{\underset{H}{\diagdown}}$) occurs at 0.17τ higher

field than the position (4.40τ) of the corresponding peak in diene **12a**
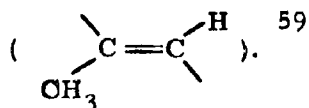
($\overset{\diagup}{\underset{CH_3}{\diagdown}}C == C\overset{H}{\diagdown}$). [59]

(59)   S. L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 121.

Additional evidence confirming these stereochemical assignments were obtained by mixing known quantities of each of the pure dienes **11c**, **12a**, and **12b** with a weighed quantity of anisole (employed as an internal standard) in benzene solutions. Each of the solutions was treated with approximately one equivalent of maleic anhydride, sealed under nitrogen, allowed to stand at room temperature for three days and then analyzed by gas chromatography.[52] No unchanged diene was detected in the solution prepared from dienes **11c** and **12a** but the ratio of diene **12b** to anisole in the third reaction mixture remained unchanged. In the cisoid conformations (accompanying formulas) required for Diels-Alder

11c   Ph   12a   Ph   12b   Ph
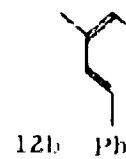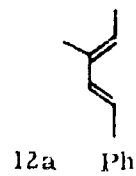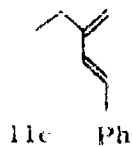
reaction only the diene 12b would be expected to be unreactive.[60]

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

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° d. (lit. [57] 142.5°), with infrared absorption[61]

(61)   Determined as a solution in chloroform.

at 1850 and 1775 cm.$^{-1}$ (C=O of anhydride in 5-membered ring) and a series of weak ultraviolet maxima[62] ($\epsilon < 600$) in the region 250-270 mμ.

(62)   Determined as a solution in ether.

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,[63] was shown to be identical with the subsequently

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

described sample by comparison of the infrared spectra and gas chromatograms[63] of the two samples.

To a cold solution of 10 ml. (22 mmoles) of 2.2 $\underline{M}$ 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_D^{25} 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 (ϵ < 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_D^{25} 1.5126 [lit.[64] b.p. 115° (13 mm.), $n_D^{21.7}$ 1.511], 2,4-

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(64)   A. Klages, $\underline{Ber.}$, $\underline{37}$, 2301 (1904).

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dinitrophenylhydrazone m.p. 128.1 - 128.8° (lit.[65] 128.5 - 129°),

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(65)   G. D. Johnson, J. Am. Chem. Soc., $\underline{73}$, 5888 (1951).

1-phenyl-1-penten-3-ol, b.p. 125 - 127° (8 mm.), $n_D^{24.5}$ 1.5579 [lit.[66]

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(66)   I. E. Muskat and M. Herrman, J. Am. Chem. Soc., $\underline{53}$, 252 (1931).

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b.p. 123° 1.5550], and trans-1-phenyl-1,3-butadiene, b.p. 79 - 81°
(10 mm.), n_D^{25} 1.6013 [lit. [67] b.p. 83° (11 mm.), n_D^{25} 1.6089] were

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(67)   O. Grummitt and F. J. Christoph, J. Am. Chem. Soc., 73,
       3479 (1951).

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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 percent 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, it is concluded that this product is formed in the original
reaction mixture before any water has been added.

TABLE VII

REACTIONS OF ETHYLMAGNESIUM COMPOUNDS WITH TRANS-4-PHENYL-3-BUTEN-2-ONE (8b)

Molarity of Ketone	Molarity of Ethylmagnesium Compound	Product Composition %				
		Dienes 11c, 12a and 12b	unsaturated alcohol 5d	ketone 6c	saturated alcohol 14	Conjugate Addition 6c and 14
0.185 M	0.186 M Et$_2$Mg	0	15	64	21	85
0.185 M	0.185 M Et$_2$Mg	3	13	48	36	84[a]
0.185 M	0.925 M Et$_2$Mg	2	11	29	58	87[b]
0.075 M	0.075 M Et$_2$Mg	1	13	25	61	86
0.015 M	0.075 M Et$_2$Mg	1	13	28	58	86
0.015 M	0.15 M Et$_2$Mg	2	10	30	58	88

37.

Table VII (Cont.)

Molarity of Ketone	Molarity of Ethylmagnesium Compound	Product Composition %					
		Dienes 11c, 12a and 12b	unsaturated alcohol 5d	ketone 6c	saturated alcohol 14	Conjugate Addition 6c and 14	
0.22 M	0.11 M Et$_2$Mg$_2$Br$_2$	0	22	78	0	78	
0.22 M	0.22 M Et$_2$Mg$_2$Br$_2$	0	20	67	13	80	
0.157 M	0.157 M Et$_2$Mg$_2$Br$_2$	13	4	83	0	83[c]	
0.075 M	0.75 M Et$_2$Mg$_2$Br$_2$	31, 25, 3[d]	2, 5, 34	43, 50, 38	24, 20, 25	67	
0.015 M	0.75 M Et$_2$Mg$_2$Br$_2$	24, 6[d]	2, 25	47, 48	27, 21	72	
0.015 M	0.15 M Et$_2$Mg$_2$Br$_2$	1, 2[d]	20, 23	43, 49	36, 26	77	

[a] In these runs, the organomagnesium compound was added to the unsaturated ketone. [b] A reaction time of 7 days was employed for these reactions. [c] In these runs the reagents were mixed in a flow system (Ref. 21) and the reaction mixture was quenched in aqueous methanol. [d] Percentage values from individual runs. Within each column the numbers are in the same order.

REFERENCES

1. For a discussion of earlier work with leading references see (a) E. G. Rochow, D. T. Hurd, and R. N. Lewis, "The Chemistry of Organometallic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1957; (b) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Inc., New York, N. Y., 1954.

2. R. E. Dessy, G. S. Handler, J. H. Wotiz, and C. A. Hollingsworth, J. Am. Chem. Soc., 79, 3476 (1957).

3. (a) R. E. Dessy and G. S. Handler, J. Am. Chem. Soc., 80, 5824 (1958); (b) R. E. Dessy, J. Org. Chem., 25, 2260 (1960).

4. The lack of an appreciable concentration of free carbanions in dialkylmagnesiums is indicated by a study of the ultraviolet spectrum of dicinnamylmagnesium [R. H. DeWolfe, D. L. Hagemann, and W. G. Young, J. Am. Chem. Soc., 79, 4795 (1957)]. See also J. E. Nordlander, W. G. Young, and J. D. Roberts, J. Am. Chem. Soc., 83, 494 (1961).

5. For simplicity, the solvent molecules associated with the organomagnesium compounds (Ref. 1) have been omitted from the formulas.

6. (a) J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, J. Org. Chem., 21, 1063 (1956); (b) J. H. Wotiz, C. A. Hollingsworth and R. E. Dessy, J. Am. Chem. Soc., 78, 1221 (1956); (c) R. E. Dessy, J. H. Wotiz, and C. A. Hollingsworth, J. Am. Chem. Soc., 79, 358 (1957).

7. J. G. Aston and S. A. Bernhard, Nature, 165, 485 (1950).

8. N. M. Bikales and E. I. Becker, Chemistry and Industry, 1831, (1961).

9. (a) M. Anteunis, J. Org. Chem., 26, 4214 (1961); (b) M. Anteunis, J. Org. Chem., 27, 596 (1962).

10. (a) H. Gilman and R. E. Brown, J. Am. Chem. Soc., 52, 1181 (1930); (b) H. Gilman and R. E. Fothergill, J. Am. Chem. Soc., 51, 3149 (1929).

11. For more recent kinetic studies see (a) C. G. Swain, J. Am. Chem. Soc., 69, 2306 (1947); (b) S. J. Storfer and E. I. Becker, J. Org. Chem., 27, 1868, (1962); (c) J. Vekemans and A. Bruylants, Bull. Soc. Chim. Belges, 68, 541 (1959).

12. C. G. Swain and H. B. Boyles, J. Am. Chem. Soc., 73, 870 (1951). See also E. T. McBee, O. R. Pierce, and J. F. Higgins, J. Am. Chem. Soc., 74, 1736 (1952).

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

14. A well known example of differing behavior is found in the reaction of epoxides with organomagnesium compounds. N. G. Gaylord and E. I. Becker, Chem. Revs., 49, 413 (1951).

15. G. F. Wright, J. Am. Chem. Soc., 61, 1152 (1939).

16. M. S. Karasch and P. O. Tawney, J. Am. Chem. Soc., 63, 2308 (1941).

17. (a) R. E. Lutz and W. G. Reveley, J. Am. Chem. Soc., 63, 3180 (1941); (b) For a comprehensive review and discussion see Ref. 1b, p. 196.

18. The cylcic mechanism 10 for conjugate addition has been criticised by E. R. Alexander and G. R. Coraor [J. Am. Chem. Soc., 73, 2721 (1951)] on the grounds that such a process is sterically improbable for the observed conjugated addition of Grignard reagents to cyclohexenone.

19. J. Munch-Peterson and V. K. Anderson, Acta. Chemica Scandinavia, 15, 271 (1961).

20. (a) M. S. Kharasch, L. Biritz, W. Nudenberg, A. Bhattacharya, and N. C. Youg, J. Am. Chem. Soc., 83, 3229 (1961).

    (b) M. S. Kharasch, M. Weiner, W. Nudenberg, A. Bhattacharya, T. Wang, and N. C. Yang, J. Am. Chem. Soc., 83, 3232 (1961).

21. A description of this apparatus and of the studies of the reaction of alkylmagnesium compounds with saturated ketones is the subject of Part II.

22. This method for comparing kinetic orders of competing reactions has been used by Mosher and co-workers (Ref. 14) in a study of competing addition and reduction reactions involving organomagnesium compounds and saturated ketones.

23. (a) R. C. Fuson, T. San and J. Dickmann, J. Org. Chem., 27, 1221 (1962); (b) In our studies the possible formation of the alcohol 14 during the isolation procedure [cf. R. E. Lyle and F. J. Trosclaniec, J. Org. Chem., 24, 333 (1959)] was excluded (see Experimental).

24. R. E. Dessy and R. M. Salinger, 140th Meeting of the American Chemical Society, Chicago, Illinois, September 3-8, 1961, Abstracts of Papers, p. 9Q.

25. N. Allentoff and G. F. Wright, J. Org. Chem., 22, 1 (1957).

26. For further discussion of the mechanism and the role of the solvent see (a) A. Kirrmann and R. Hamelin, Compt. rend., 251, 2990 (1960); (b) R. Hamelin, Bull. soc. chim. France, 684, 915, 926 (1961).

27. C. G. Swain and L. Kent, J. Am. Chem. Soc., 72, 518 (1950). The argument used by these authors for supposing different mechanisms for the Grignard-ketone reaction (Ref. 11a) was based on reports that benzophenone forms a complex with the first equivalent of added Grignard reagent but does not react until a second equivalent of the organometallic is added. . These reports are now known (Ref. 8) to be incorrect.

28. All melting points are corrected and all boiling points are uncorrected. 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 11MS. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory. Unless otherwise stated magnesium sulfate was employed as the drying agent.

29. W. Schlenk, Ber., 64, 736 (1931).

30. C. S. Marvel and V. L. Gould, J. Am. Chem. Soc., 44, 153 (1922).

31. E. Frankland and B. F. Duppa, Ann., 130, 104 (1864).

32. H. O. Calvery, Org. Syntheses, Coll. Vol. 1, 228 (1951).

33. H. Gilman and R. E. Brown, J. Am. Chem. Soc., 52, 3314 (1930).

34. E. R. Alexander and R. W. Kluiber, J. Am. Chem. Soc., 73, 4304 (1951).

35. H. W. J. Hills, J. Kenyon and H. Phillips, J. Chem. Soc., 576 (1936).

36. A. L. Wilds and C. Djerassi, J. Am. Chem. Soc., 68, 1715 (1946).

37. A gas chromatography column packed with 4-methyl-4-nitro-pimelonitrile suspended on ground firebrick was employed.

38. S. Krapiwin, Bulletin de la Society Imperiale des Naturalistes de Moscou, 1 (1908), Chem. Zentr., 82, 1315 (1910).

39. The author is indebted to the Union Carbide Chemical Corporation for a sample of this mixture.

40. R. G. R. Bacon and E. H. Farmer, J. Chem. Soc., 1065 (1937).

41. Determined as a solution in carbon tetrachloride.

42. Determined as a solution in 95% ethanol.

43. H. W. Blohm and E. I. Becker, Chem. Revs., 51, 471 (1952).

44. D. M. Cowan, G. H. Jeffery, and A. I. Vogel, J. Chem. Soc., 171 (1940).

45. H. D. Law, J. Chem. Soc., 101, 1016 (1912).

46. G. S. Whitby and W. Gallay, Canad. J. Res., 6, 280 (1932); Chem. Zentr., 105 II, 1425 (1932).

47. A gas chromatography column packed with 1540 Carbowax suspended on basewashed 80-100 mesh Chromosorb was employed.

48. V. Levy and H. Normant, Compt. rend., 244, 202 (1957).

49. E. A. Braude and C. J. Timmons, J. Chem. Soc., 2000 (1950).

50. K. Auwers and G. Peters, Ber., 43, 4094 (1910).

51. The previous workers (Ref. 49) stated that their product was impure.

52. A gas chromatography column packed with 20 M Carbowax suspended on ground firebrick was employed.

53. M. C. Chiang, J. Chinese Chem. Soc., 18, 65 (1951); C. A., 46, 4472 (1952).

54. R. A. Evans, S. M. Thesis, Mass. Inst. of Tech. (1959).

55. A. Klages, Ber., 39, 2587 (1906).

56. E. P. Kohler, Am. Chem. J., 38, 511 (1907).

57. (a) A. V. Dombrovskii, Doklady Akad. Nauk. S.S.S.R., 111, 827 (1956); C. A., 51, 9508 (1957). (b) A. V. Dombrovskii, Zhur. Obshchei Khim., 27, 3041 (1957); C. A., 52, 8087 (1958). This author did not establish the stereochemistry of his diene nor did he establish that only one isomer was present.

58. R. B. Bates and D. M. Gale, J. Am. Chem. Soc., 82, 5749 (1960).

59.   S. L. M. Jackman, "Applications of Nuclear Magnetic Resonance
        Spectroscopy in Organic Chemistry," Pergamon Press, New York,
        N. Y., 1959, p. 121.

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

61.   Determined as a solution in chloroform.

62.   Determined as a solution in ether.

63.   The Analysis was obtained with a 200-ft., Ucon-50 capillary
        column heated to 140°. The author is indebted to Drs. H. E.
        Johnson and E. Rick of the Union Carbide Chemicals Corporation
        for this analysis.

64.   A. Klages, Ber., 37, 2301 (1904).

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

66.   I. E. Muskat and M. Herrman, J. Am. Chem. Soc., 53, 252 (1931).

67.   O. Grummitt and F. J. Christoph, J. Am. Chem. Soc., 73,
        3479 (1951).

PART II

REACTIONS OF ORGANOMAGNESIUM COMPOUNDS WITH SATURATED KETONES

I. INTRODUCTION

In 1947 Swain reported[1] that the reaction of n-butylmagnesium

(1)   C. G. Swain, J. Am. Chem. Soc., 69, 2306 (1947).

bromide with benzonitrile followed second order kinetics. He proposed
that a Grignard complex was formed which was in rapid equilibrium with
the Grignard and ketone, and that the rate determining step was the
rearrangement of this complex into product.

Later he proposed[2] that the reaction of Grignard reagents with

(2)   C. G. Swain and H. B. Boyles, J. Am. Chem. Soc., 73,
870 (1951).

ketones required one mole of Grignard per mole of ketone to form the
reduction product, but that the formation of the normal addition product
required two moles of Grignard per mole of ketone. The first mole
complexes with the carbonyl as in reduction, and the second mole then
attacks the polarized carbon to form the product.

$$R_2CO + R'M_gX \;\rightleftarrows\; \overset{R}{\underset{R}{>}}C = O \ldots M_g\overset{R'}{\underset{X}{<}} \;\xrightarrow{R'M_gX}\; R - \underset{\underset{O}{\|}}{C} \cdots \rightarrow$$

$$R_2R'COM_gX + R'M_gX$$
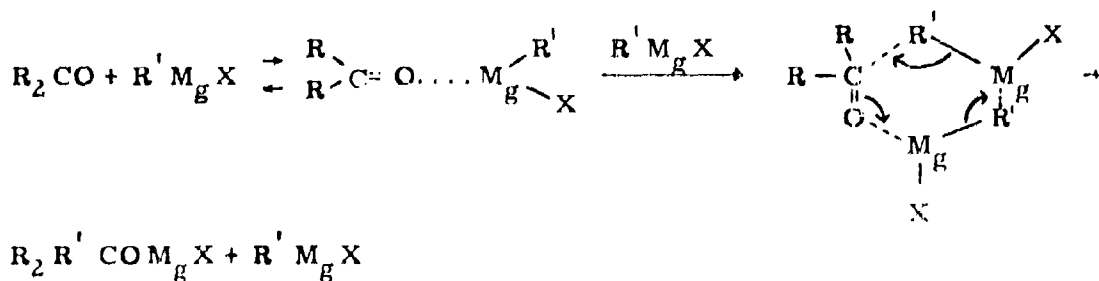
He reasoned that since magnesium bromide is a stronger Lewis acid than Grignard reagents, it should complex more readily with the carbonyl, and if a Grignard reagent is then added it would give a higher yield of normal addition product and a lower yield of reduction product.

As a test of this prediction, Swain reacted propylmagnesium bromide with diisopropyl ketone and found 3 % enolization, 63 % reduction, and 30 % addition. When the ketone was first mixed with magnesium bromide and then with the Grignard, he found 1 % enolization, 26 % reduction and 65 % addition.

Anteunis supported[3] the Swain mechanism when he found that

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(3)   M. Anteunis, J. Org. Chem., 26, 4214 (1961).

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the reaction of methylmagnesium bromide with pinacolone or benzophenone was a third order reaction.

$$v = k_3 (G)^2 (K)$$

However, Aston and Bernhard found[4] that acetone reacted approx-

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(4)   J. G. Aston and S. A. Bernhard, Nature, 165, 485 (1950).

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imately fifty times faster with dimethylmagnesium than with methylmagnesium iodide. This increase in rate by the use of dimethylmagnesium was confirmed by Bikales and Becker when they reported[5] that dimethyl-

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(5)   N. M. Bikales and E. I. Becker, Chemistry and Industry, 1831 (1961).

magnesium reacted about two times faster with benzophenone than methylmagnesium bromide, and that dimethylmagnesium plus an equivalent amount of magnesium bromide gave the same results as methylmagnesium bromide. Excess magnesium bromide gave a decrease in rate and was not complexed with the ketone, measured spectrophotometrically, which contradicts the Swain mechanism.

The specific rate of the reaction of methylmagnesium bromide with benzophenone when more than one-half of the methyl groups had reacted was 1.2% that of the initial rate. They attributed this to the lower reactivity of the alkoxide complex (1) formed. Their results could not be fitted to any simple rate law.
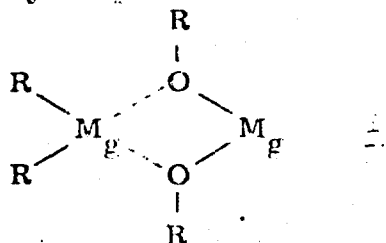
These results were confirmed by Anteunis when he reported[6] that

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(6)   M. Anteunis, J. Org. Chem., 27, 596 (1962).

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dimethylmagnesium reacted ten times faster with benzophenone than methylmagnesium bromide. The rate of the reaction decreased with time and he further found that the reaction stopped halfway when equivalent amounts of dimethylmagnesium and benzophenone were used. He also attributed this to the complex formation of the dimethylmagnesium with the formed alkoxide (1).

The effects of the alkoxide complex (1) were further investigated by Storfer and Becker who found[7] that one mole of diethylmagnesium gave

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(7)   S. I. Storfer and E. I. Becker, J. Org. Chem., 27, 1868 (1962).

a complete reaction with one mole of benzonitrile, but when two moles of benzonitrile were used, where there was no excess of ethyl groups, they obtained only one-half reaction. Although the remaining reactive ethyl group present in the mixture did not react with benzonitrile or propiophenone, it did react with the more reactive benzaldehyde to form phenylethylcarbinol. Furthermore, propiophenone reacted with the ethyl group from diethylmagnesium with propiophenone as evidenced by the complete reaction of one mole of diethylmagnesium with two moles of propiophenone.

The reaction of diethylmagnesium with benzonitrile showed a higher rate for the first 50% of the reaction than for the last 40% and the break in rates, determined by the extrapolation of the two rates from an appropriate plot, appeared at approximately the half reaction. They were unable to decide whether the reaction was first or second order in diethylmagnesium monomer for the first half of the reaction, but they found that the reaction was first order in diethylmagnesium monomer for the second half.

For the reaction of diethylmagnesium bromide with diisopropyl ketone, it was found[a] that the rate of addition to reduction was invariant

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

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with the concentration and ratio of reactants when the ketone was in excess, but when the Grignard was in excess the ratio was a function of the ratio of the reactants and their absolute concentrations. Although the same kinetic description applied for addition and reduction

when the ketone was in excess the same kinetic description did not apply when the Grignard was in excess, which proceeded by consecutive second-order kinetics.

The use of dialkylmagnesium compounds rather than Grignard reagents has been found[9] to give an increase in enolization and reduction

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(9)   D. O. Cowan and H. S. Mosher, J. Org. Chem., 27, 1 (1962).

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at the expense of addition.

The yields of products from the reaction of ethylmagnesium bromide with 2-butanone, 3-pentanone, 3-pentanone and diisopropyl ketone have been found[10] by Hamelin to depend upon the experimental

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(10)   R. Hamelin, Bull. Soc. Chim. France, 915 (1961).

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conditions employed.   Namely, the use of ether as a solvent, concentrated Grignard solutions, low temperatures and normal addition of the reactants (i.e., addition of the ketone to the Grignard) resulted in higher yields of the normal addition product.   Hamelin noted that these four conditions also favored the association phenomena in Grignard solutions and therefore proposed that the degree of association of the Grignard influences its chemical properties, and that the Grignard-ketone complex gives enolization and reduction if the magnesium is not associated, and normal addition if it is associated.   He proposed the following mechanism for normal addition.

49.

$$\underset{Br}{\overset{O=C}{\underset{Mg}{\diagup}}\overset{R}{\underset{Mg}{\diagdown}}R} \quad \longrightarrow \quad \underset{Mg}{\overset{C}{\underset{Br}{\diagup}}\overset{R}{\diagdown}} \quad + \quad \underset{Br}{\overset{}{\diagdown}}\underset{Mg}{\overset{}{\diagdown}}R$$
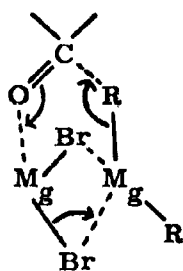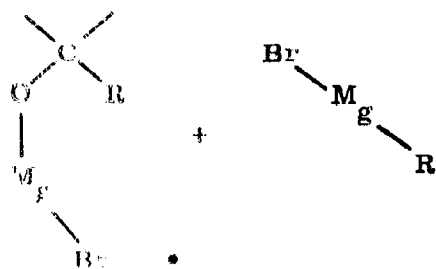
II. DISCUSSION

The amounts of enolization, reduction and addition products from the reactions of diethylmagnesium, ethylmagnesium bromide and an alkoxyethylmagnesium compound with diethyl ketone 2 have been determined. The following scheme summarizes the reaction.

$$Et\,M_g\,Br + Et_2\,CO \rightarrow Et_2\,CO + \text{...} CHOH + \text{...} COH$$
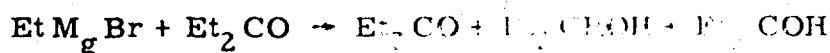
2
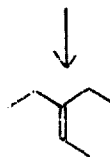
The results given show that ethylmagnesium bromide, either prepared in the normal way or from equimolar amounts of diethylmagnesium and magnesium bromide, gave predominately the normal addition product, 4, when either normal or inverse addition was used. However, diethylmagnesium gave a similar product distribution only when normal addition was used, and gave increased amounts of enolization in the case of inverse addition.

A possible explanation of this effect, considering the results obtained by Bikales and Becker, by A. Tsukamoto[5], and by Storfer and Becker[7], is that in the case of normal addition only diethylmagnesium is reacting with the ketone, at least during the early part of the reaction. In the case of inverse addition, however, both the diethylmagnesium and the alkoxide compound are competing for the ketone, even during the early part of the reaction. If these assumptions are

that the alkoxide complex is reactive enough to compete with the
diethylmagnesium and that its reaction with the ketone largely yields
the enolization product as a side reaction.

Although some alkoxide complexes cannot successfully com-
pete with Grignard reagents for compounds such as benzonitrile or
benzophenone, they will react with more reactive compounds such as
benzaldehyde[7]. Since methyl ketones are quite reactive, Table VI,
one may expect that it will be less reactive toward ethylmagnesium
and the alkoxide complex.

Since ethylmagnesium bromide gives predominately the alcohol $\underline{4}$
even when inverse addition is used, it seems that the presence
of magnesium bromide may gave the reaction the alkoxide complex.

Tests of this explanation were carried out by treating an alko-
xide complex with diethyl ketone. The complexes was prepared by the
three methods shown below.

1. $(n-Pr)_2 CO + Et_2 Mg$

2. $ROH + Et_2 Mg$ ——

3. $2 ROH + Et_2 Mg \rightarrow Mg(OR)_2$
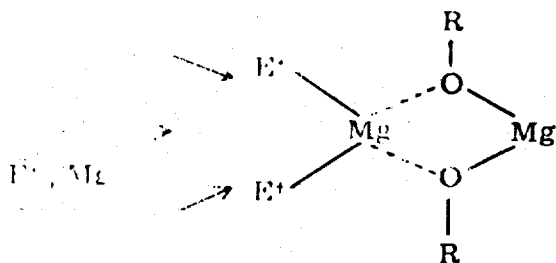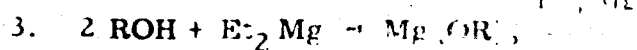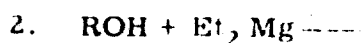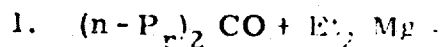
$$R = C_2H_5(n-C_3H_7)_2C \cdots \quad \text{reactions.}$$

It is clear from these results that the complexes formed by methods
2 and 3 are identical, and that the complex formed by method 1 appears
to be different. For this reason the reactions listed in Tables I,
II and VI were performed using the complex prepared by method 1, since
this complex probably corresponds to that formed in the inverse

addition of diethylmagnesium to diethyl ketone. The complex formed
was reactive towards diethyl ketone, and gave increased amounts of
enolization as predicted.

The mitigating effect of the presence of magnesium bromide is
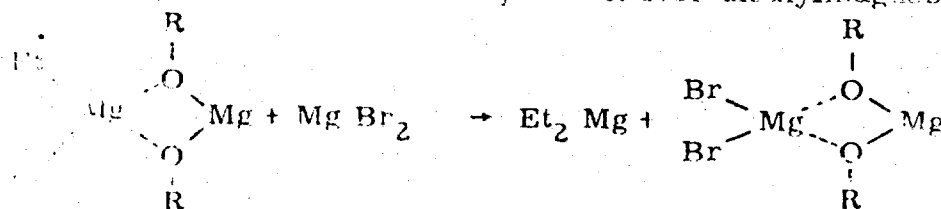also shown in Table I and the amount of this effect is dependent upon the
amount of magnesium bromide present. When the amount of magnesium
bromide added was equivalent to the amount of diethylmagnesium
present in the complex, the results obtained were similar to those
obtained from diethylmagnesium, and when this amount of magnesium
bromide was doubled, the results were similar to those obtained from
ethylmagnesium bromide. This can be explained if one supposes that
the first mole of magnesium bromide prefers to complex with the mag-
nesium alkoxide, rather than the diethylmagnesium, to form a magnesium
bromide-magnesium alkoxide complex and free diethylmagnesium.

$$
\begin{array}{ccc}
\underset{\displaystyle R}{\overset{\displaystyle R}{|}} & & \\
Mg \underset{O}{\overset{O}{\Big\rangle}} Mg + Mg\,Br_2 & \rightarrow & Et_2\,Mg + \quad \underset{Br}{\overset{Br}{\Big\rangle}} Mg \underset{O}{\overset{O}{\Big\langle}} Mg
\end{array}
$$

This is not unreasonable considering that magnesium bromide is a
stronger Lewis acid than diethylmagnesium, and that the oxygen atoms
are more electronegative than the magnesium atom in diethylmagnesium.
This amount of magnesium bromide then, should give results similar to
those obtained with diethylmagnesium, as actually observed.

When a second mole of magnesium bromide is added it has no
alternative but to complex with the diethylmagnesium, accounting
for results similar to those obtained with ethylmagnesium bromide.

The results obtained with diisopropyl ketone, summarized in Table II, are not very different except that the main side reaction is reduction instead of enolization.

$$Et\ Mg\ Br + (i-Pr)_2\ CO \rightarrow (i-Pr)_2CO + (i-Pr)_2\ CHOH + Et(i-Pr)_2\ COH$$

<div style="text-align:center">

6   **7**   **8**

</div>

9   +   **10**
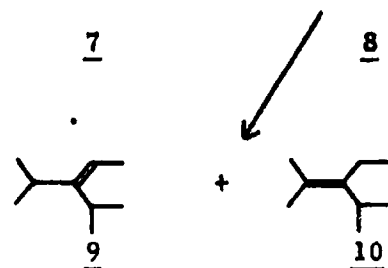
An interesting observation was noted in the reactions with diisopropyl ketone. For all the reactions, except those involving ethylmagnesium bromide which has a brown color, the organomagnesium solutions were clear and colorless. During the course of these reactions a transient yellow color formed which was visible for approximately three seconds. This color may be due to a polarized complex, and has previously been noted[3] for benzophenone.

The kinetic runs summarized in Table VI are consistent with the above explanation for the effect of magnesium bromide. The rate constant for the reaction employing the alkoxide complex was not calculated because of the complexity of two competing reactions, addition and enolization, where neither rate constant is known. However, when magnesium bromide was added to the alkoxide complex the rate was comparable to the rate obtained with ethylmagnesium bromide, and which would be expected on the basis of the previous explanation of the effect of magnesium bromide.

The kinetic runs utilizing 0.261 $\underline{M}$ ethylmagnesium bromide are consistent with the results of Bikales and Becker[5] and of Anteunis[6], in that the runs employing longer reaction times have the lowest rates.

It was not possible, because of the limitations of the apparatus employed, to measure the rate of diethylmagnesium with diethyl ketone, even at the shortest reaction time (0.0185 sec., k > 1570) nor the rate of ethylmagnesium bromide with diisopropyl ketone even at the longest reaction time (0.429 sec., k < 0.95).

Neither was it possible to obtain results for the reaction of diisopropyl ketone with the alkoxide complex from method 2 with magnesium bromide, since in two attempts a large amount of a crystalline solid separated from the ether solution of the complex when magnesium bromide was added.

III. EXPERIMENTAL[11]

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(11)   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 deter-
mined 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 NMR
spectra were determined at 60 mc. with a Varian, Model A-60,
NMR spectrometer. The mass spectra were obtained with a CEC,
Model 21-130, Mass spectrometer. The microanalyses were
performed by Dr. S. M. Nagy and his associates and by the Scan-
dinavian Microanalytical Laboratory

Preparation of the Organomagnesium Compounds -- Solutions of

ethylmagnesium bromide, diethylmagnesium and magnesium bromide were

prepared and analyzed as previously described. [12]

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(12)   See Experimental, Part I

For the 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 resul-

ting mixture was stirred at room temperature for 30 min. prior to use.

An aliquot of each of these solutions was hydrolyzed and analyzed by gas

chromatography. [13] For organomagnesium solutions containing added

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(13)   A gas chromatographic column packed with 20M carbowax sus-
pended on ground firebrick was employed.

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magnesium bromide, the solution obtained after addition of magnesium

bromide was stirred for 45 min. prior to use.

Reaction of Ethylmagnesium Derivatives with 3-Pentanone (2) --
A commercial sample of 3-pentanone, which contained more than 99 %
of the desired ketone,[13] was used for all runs.

From the reaction of 9.46 g. (0.11 mole) of 3-pentanone with
0.22 mole of ethylmagnesium bromide in 125 ml. of ether was obtained,
after fractional distillation, 7.642 g. (60 %) of pure triethylcarbinol (4),
b.p. 138-142°, n_D^{25} 1.4272 [lit. b.p. 139-142°[14], n_D^{25} 1.4294[15]].

(14)   W. W. Moyer and C. S. Marvel, Org. Syntheses, Coll. Vol. 2,
        602 (1946).

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

From the reaction of 2.02 g. (0.035 mole) of propionaldehyde
with 0.042 mole of ethylmagnesium bromide in 40 ml. of ether, was
obtained, after fractional distillation, 2.523 g. (89 %) of pure diethyl-
carbinol (3), b.p. 111°, n_D^{25} 1.4075 [lit.[16] b.p. 114.4°, n_D^{20} 1.4104].

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

Heating a mixture of 1.0 g. (8.6 mmoles) of the alcohol 4 and
1.0 g. of potassium acid sulfate produced 0.584 g. (68 %) of 3-ethyl-2-
pentene (5), b.p. 89°, n_D^{25} 1.4122 [lit.[17] b.p. 95-98°, n_D^{18} 1.4140],

(17)   I. N. Nazarow, Ber., 70, 617 (1937).

with ultraviolet absorption[18] at 189 mμ (ε 7,500), and a molecular weight

(18)   Determined in n-heptane.

of 98 (mass spectrum).

The 4-ethyl-4-heptanol, b.p. 78-79° (20 mm.), n_D^{25} 1.4310 [lit. b.p. 76-78° (17 mm.),[19] n_D^{20} 1.4332[20]] used to prepare some of

(19)   J. M. Church, F. C. Whitmore and R. V. McGrew, J. Am. Chem. Soc., 56, 176 (1934).

(20)   J. Stas, Bull. Soc. Chim. Belges, 35, 379 (1926).

the ethylmagnesium alkoxide (1) solutions employed in this series of reactions was obtained in 71% yield from the reaction of 57 g. (0.55 mole) of 4-heptanone with 0.75 mole of ethylmagnesium bromide in 500 ml. of ether.

Reaction of Ethylmagnesium Derivatives with 2,4-Dimethyl-3-pentanone (6). -- A sample of 2,4-dimethyl-3-pentanone, b.p. 124° n_D^{25} 1.3973 [lit.[21] b.p. 125°, n_D^{25} 1.39759], which contained more than

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

99% of the desired ketone,[13] was isolated by fractional distillation of a commercial sample.

From the reaction of 1.60 g. (0.011 mole) of 2,4-dimethyl-3-pentanone (6) 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 (8),

b.p. 116° (125 mm.), n_D^{25} 1.4411 [lit.[22] b.p. 117.5° (125 mm.), n_D^{20}

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

1.4440].

Reduction of 2,4-dimethyl-3-pentanone (6) with excess lithium aluminum hydride in ether afforded, after fractional distillation, 71% of diisopropylcarbinol (7), b.p. 137-137.5°, n_D^{25} 1.4229 [lit.[23] b.p.

(23)   F. C. Whitmore and F. Johnston, J. Am. Chem. Soc., 60, 2265 (1938).

137-138°, n_D^{25} 1.4246].

From heating a mixture of ethyldiisopropylcarbinol and potassium acid sulfate, 55% of a mixture of olefins 9 and 10, b.p. 110-122°,[24]

(24)   The pure olefin 9 is reported to boil at 138°, n_D^{25} 1.4328 and the pure olefin 10 is reported to boil at 130°, n_D^{25} 1.4
F. L. Howard, T. W. Mears, A. Fookson, P. Pomerantz and D. B. Brooks, J. Research Natl. Bur. Standards, 38, 365 (1947) (Research Paper No. 1779); Natl. Advisory Comm. Aeronaut., Tech. Note No. 1247, 56 pp (1947).

was obtained and a sample of each olefin collected.[13] The olefin 9, (first eluted from the column) has ultraviolet absorption[18] at 190 m μ (ϵ 9,900), with NMR absorption[25] at 4.86τ [1H, quadruplet (J = 7 c.p.s.),

(25)   Determined in carbon tetrachloride solution.

vinyl C-H] with a multiplet in the region 7.0 to 8.0τ (2H, tertiary C-H),
a doublet (J = 7 c.p.s.) at 8.40τ (3H, allylic CH_3) and a doublet
(J = 8 c.p.s.) at 9.02τ (12H, CH_3), and a molecular weight of 126 (mass
spectrum). The olefin 10 has ultraviolet absorption[18] at 192 mu (ε 8,900),
with no NMR absorption[25] attributable to vinyl C-H and a singlet at
8.38τ (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 9.05τ (CH_3).
The material has a molecular weight of 126 (mass spectrum).

Procedure for Quantitative Product 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 volumes of the
reaction mixture was 31 ml. The concentrations listed in the tables refer
to the calculated final concentration in the reaction mixture if no reac-
tion had occurred. For reactions employing inverse addition, the same
general procedure was followed, except that a solution of the organo-
magnesium 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-pen-
tanone experiments) was present in each ethereal solution of the ketone.

The reaction mixtures were stirred for 45 min. at room temper-
ature 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[3] 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%.

Procedure for Kinetic Studies. -- A diagram of the apparatus employed is presented in Figure I. 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 were 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 from the following formula:

$$\frac{(V_1 + V_2) \, t}{V_3} = \text{reaction time}$$

where: V_1 = volume of the reaction tube (0.647 ml., 1.738 ml., or 6.857 ml., determined from its weight filled with water).

V_2 = volume of the stopcock bore (0.072 ml., calculated from its dimensions).

V_3 = total volume of ether passed in t seconds.

t = time required to pass V_3 ml. of ether.

The results of these measurements are summarized in Table III. To correct the reaction times and the mixing ratios determined with pure ether for the slightly increased viscosity of the reaction mixtures,

Table I

Reactions of 3-Pentanone ($\underline{2}$, 0.155$\underline{M}$) with Ethylmagnesium Derivatives (0.261$\underline{M}$)

Organomagnesium Reactant	Type of Addition[a]	Molarity of MgBr$_2$	Product Composition,%		
			Ketone $\underline{2}$	Alcohol $\underline{3}$	Alcohol $\underline{4}$
Et$_2$Mg	N		2	<1	98
	I		21	<1	79
Et$_2$Mg$_2$Br$_2$	N		1	<1	99
	I		1	1	98
Et$_2$Mg	N	0.261	2	1	97
	I	0.261	4	2	95
Et$_2$Mg·Mg(OR)$_2$ [b,c]	N		25	6	70
	I		26	5	69
Et$_2$Mg·Mg(OR)$_2$ [b,d]	N		18	7	75
	I		67[e]	4	29[e]
Et$_2$Mg·Mg(OR)$_2$ [b,f]	N		20	6	74
	I		66	3	31
Et$_2$Mg·Mg(OR)$_2$ [b,c]	N	0.261	4	1	95
	I	0.261	27[g]	2	71[g]
Et$_2$Mg·Mg(OR)$_2$ [b,c]	N	0.522	3	1	96
	I	0.522	8	1	91
Et$_2$Mg·Mg(OR)$_2$ [b,f]	N	0.261	2	1	97
	I	0.261	37	2	61

[a] N indicates normal addition (i.e., the ketone was added to the organo-magnesium compound) and I indicates inverse addition. [b] R=C$_2$H$_5$(n-C$_3$H$_7$)$_2$C. [c] 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 components was essentially unchanged in the reaction mixtures from this reagent and 3-pentanone. [d] This reagent was prepared by the addition of one molar equivalent of ethyldi-n-propylcarbinol to one molar equivalent of diethylmagnesium. [e] In this case the duplicate values differed from one another by 4%. [f] This reagent was prepared by adding two molar equivalents of ethyldi-n-propylcarbinol to one molar equivalent of diethylmagnesium, and then adding this mixture to another equivalent of diethylmagnesium. [g] In this case the triplicate values differed from the average by 11%.

TABLE II

Reactions of 2, 4-Dimethyl-3-pentanone ($\underline{6}$, 0.155 $\underline{M}$) with Ethylmagnesium Derivatives (0.261 $\underline{M}$)

Organomagnesium Reagent	Type of Addition[a]	Molarity of $MgBr_2$	Product Composition %		
			Ketone 6	Alcohol 7	Alcohol 8
Et_2Mg	N		1	6	93
	I		3	28[b]	69[b]
$Et_2Mg_2Br_2$	N		<1	4	96
	I		<1	5	95
Et_2Mg	N	0.261	<1	9	91
	I	0.261	<1	9	91
$Et_2Mg \cdot Mg(OR)_2$[c,d]	N		19	53	28
	I		33	47	22
$Et_2Mg \cdot Mg(OR)_2$[c,d]	N	0.522	<1	10	90
	I	0.522	<1	10	90
$Et_2Mg \cdot Mg(OR)_2$[c,e]	N		8	71	17
	I		22[f]	64	14[f]

[a] N indicates normal addition (i.e., the ketone was added to the organomagnesium compound) and I indicates inverse addition. [b] In this case the individual values differed from one another by 9%. [c] $R = (C_2H_5)_3C$ [d] 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 from the reagent and 2, 4-dimethyl-3-pentanone. [e] This reagent was prepared by the addition of one molar equivalent of triethylcarbinol to one molar equivalent of diethylmagnesium. [f] In this case the individual values differed from one another by 6%.

measurements were made of the time required to pass a given volume
of the reaction mixtures through the apparatus. These results are
summarized in Table IV.

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) of the ketone and the appropriate internal standard in ether was
placed in one flask and 20 ml. of a solution (thermostated to 25.0^0) 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 (0^0) 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 was then analyzed by gas chromatography as pre-
viously described.[3]

TABLE III

Calculated Reaction Times (sec.) for Pure Ether

Nitrogen pressure (cm. of Hg)	Reactor Length (cm.)	Volume Passed (ml.)	t (sec.)	Reaction Time (sec.)
32. 1	10. 6	334	13. 7	0. 0266
32. 1	30. 2	331	15. 8	0. 0832
45. 0	121. 5	315	17. 2	0. 375
52. 9	10. 6	340	11. 0	0. 0211
52. 9	30. 2	332	12. 0	0. 0630
73. 6	10. 6	342	9. 3	0. 0177
73. 6	30. 2	340	10. 4	0. 0532
92. 2	10. 6	340	8. 3	0. 0158
92. 2	30. 2	338	9. 4	0. 0481

TABLE ...

Reaction ... ... Factors

Organomagnesium Reactant	Ketonic Reactant	Gas Pressure, mm Hg	Reaction Length, cm.	Reaction Time, sec.	Factor [a]	Mixing Ratio [b]
0.261 M Et$_2$Mg$_2$Br$_2$	0.xxx M Me$_2$CO	45	30.2	0.0811	1.175	13.97
0.261 M Et$_2$Mg$_2$Br$_2$	0.077 M Et$_2$CO	30	30.2	0.0983	1.143	--
0.131 M Et$_2$Mg$_2$Br$_2$	0.077 M Et$_2$CO	30	30.2	0.0935	1.087	15.02
0.261 M Et$_2$Mg	0.155 M (i-Pr)$_2$CO	45	30.2	0.0821	1.190	13.55
0.261 M Et$_2$Mg·Mg(OR)$_2$	0.155 M Et$_2$CO	45	30.2	0.0814	1.180	13.71
0.261 M Et$_2$Mg·Mg(OR)$_2$ Plus 0.322 M MgBr$_2$	0.155 M Et$_2$CO	45	10.6	0.0269	1.160	13.80

a Calculated by dividing the listed reaction time by the corresponding reaction time obtained with pure ether.
b These figures represent the ml. of organomagnesium solution mixed per 15 ml. of the ketone solution.

Appropriate blank experiments demonstrated that this analytical procedure did not inadvertently fractionate the reaction products. The results of these experiments are summarized in Table V.

TABLE V.

Analytical Procedure Results

Component	Weight (mg.)	Actual %[a]	Analyzed %[a] Before	After
3-Ethyl-2-pentene (5)	71.7	10.7	11.8	9.1
3-Pentanone (2)	121.7	16.9	18.9	17.3
3-Pentanol (3)	81.3	12.0	14.0	13.2
Triethylcarbinol (4)	251.9	29.6	28.3	28.3
Anisole	596.8	----	----	----

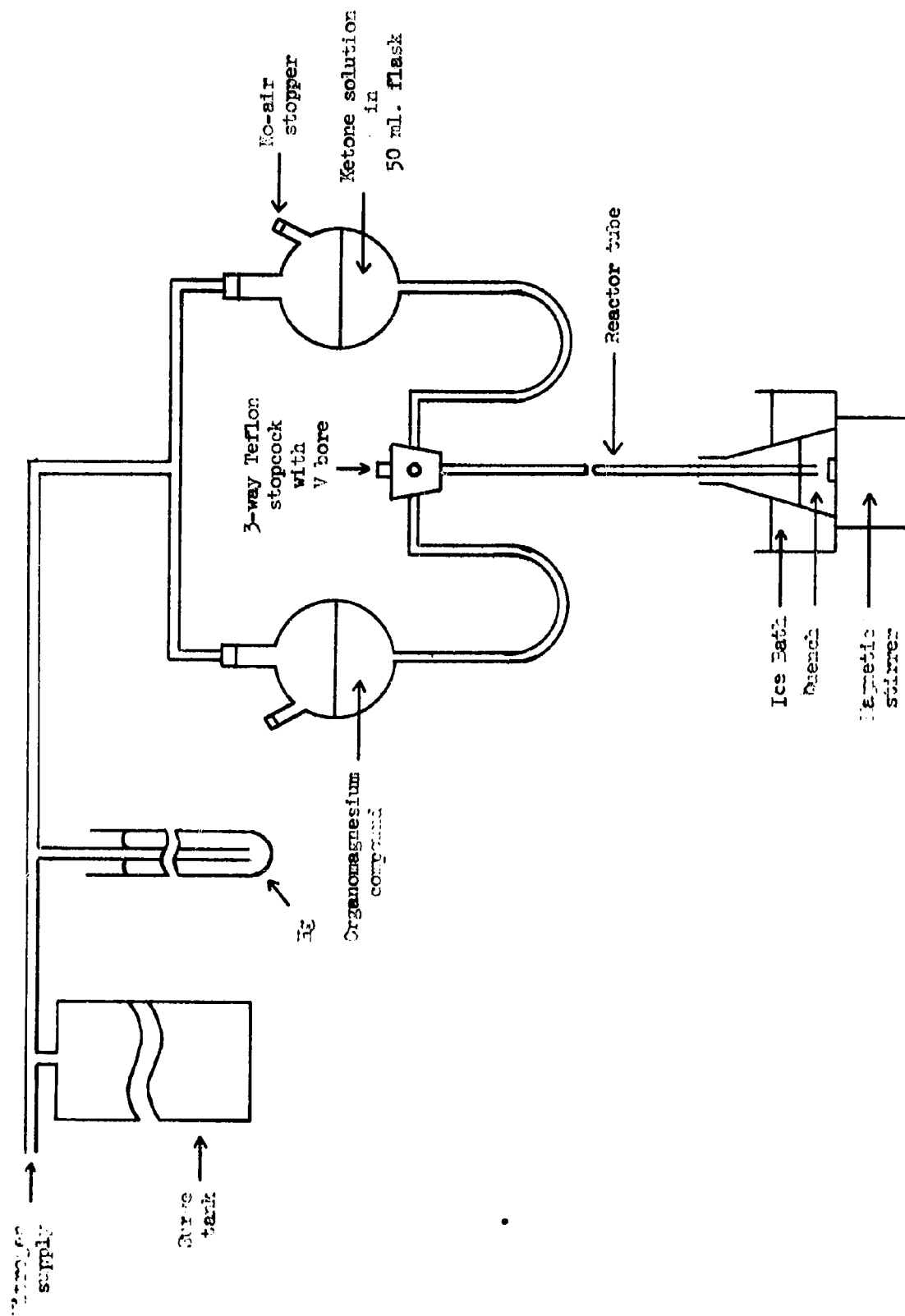[a] All percentages are relative to anisole, used as the internal standard.

Figure II

TABLE VI

Reactions of 3-Pentanone (2) with Organomagnesium Derivatives

Organomagnesium Reactant	Molarity of $MgBr_2$	Molarity of Ketone Reactant	Reaction Time (sec.)	k^a ($l. mole^{-1} sec^{-1}$)	Product Composition, % Ketone 2	Alcohol 3	Alcohol 4
0.261 M Et_2Mg		0.155	0.0186	>1570	0	0	100
0.261 M $Et_2Mg_2Br_2$		0.155	0.101	37	46(1)[b]	0(1)[b]	54(98)[b]
0.261 M $Et_2Mg_2Br_2$		0.155	0.0312	50	69	0	31
0.261 M $Et_2Mg_2Br_2$		0.155	0.0186	44	83	0	17
0.261 M Et_2Mg	0.261	0.155	0.0186	44	83	0	17
0.261 M $Et_2Mg_2Br_2$		0.077	0.0789	28	58	0	42
0.261 M $Et_2Mg_2Br_2$		0.077	0.0320	48	68	0	32
0.137 M $Et_2Mg_2Br_2$		0.074	0.0935	45	60	0	40
0.261 M $Et_2Mg \cdot Mg(OR)_2$[c,d]		0.155	0.0814	--	34	4	63
0.261 M $Et_2Mg \cdot Mg(OR)_2$[c,e]		0.155	0.0814	--	42(26)[b]	2(5)[b]	56(69)[b]
0.261 M $Et_2Mg \cdot Mg(OR)_2$[c,e]	0.522	0.155	0.0269	46	74(1)[b]	0(1)[b]	26(98)[b]

a-c See Footnote of Table VII.

TABLE VII

Reactions of 2,4-Dimethyl-3-pentanone (6) with Diethylmagnesium

Molarity of Et_2Mg	Molarity of Ketone Reactant	Reaction Time (sec.)	k^a (l. mole^{-1} sec.$^{-1}$)	Product Composition, %		
				Ketone (6)	Alcohol (7)	Alcohol (8)
0.261	0.155	0.0821	33	54(0)[b]	2(6)[b]	43(94)[b]
0.261	0.077	0.0821	39	47	2	50
0.137 $(Et_2Mg \cdot Et_2)$	0.074	0.429	<0.95	100	0	0

a   The values of k were calculated on the assumption that the reaction is first order in organomagnesium dimer and first order in ketone.   This assumption gave the most consistent values for k.   b The results in parentheses were obtained by allowing the mixture to flow into a dry, nitrogen filled flask, and then quenching after 15 min.   c $R = C_2H_5(C_3H_7)_2C$.   d This reagent was prepared by the addition of one molar equivalent of ethyldi-n-propylcarbinol to one molar equivalent of diethylmagnesium.   This was a single run and was not duplicated.   e This reagent was prepared by the addition of one molar equivalent of 4-heptanone to one molar equivalent of diethylmagnesium.

REFERENCES

1. C. G. Swain, J. Am. Chem. Soc., 69, 2306 (1947).

2. C. G. Swain and H. B. Boyles, J. Am. Chem. Soc., 73, 870 (1951).

3. M. Anteunis, J. Org. Chem., 26, 4214 (1961).

4. J. G. Aston and S. A. Bernhard, Nature, 165, 485 (1950).

5. N. M. Bikales and E. I. Becker, Chemistry and Industry, 1831 (1961).

6. M. Anteunis, J. Org. Chem., 27, 596 (1962).

7. S. J. Storfer and E. I. Becker, J. Org. Chem., 27, 1868 (1962).

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

9. D. O. Cowan and H. S. Mosher, J. Org. Chem., 27, 1 (1962).

10. R. Hamelin, Bull. Soc. Chim. France, 915 (1961).

11. 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 NMR spectra were determined at 60 mc. with a Varian, Model A-60, NMR spectrometer. The mass spectra were obtained with a CEC, Model 21-130, Mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

12. See Experimental, Part I.

13. A gas chromatographic column packed with 20M carbowax suspended on ground firebrick was employed.

14. W. W. Moyer and C. S. Marvel, Org. Syntheses, Coll Vol. 2, 602 (1946).

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

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

17. I. N. Nasarow, Ber., 70, 617 (1937).

18. Determined in n-heptane.

19. J. M. Church, F. C. Whitmore and R. V. McGrew, J. Am. Chem. Soc., 56, 176 (1934).

20. J. Stas, Bull. Soc. Chim, Belges, 35, 379 (1926).

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

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

23. F. C. Whitmore and F. Johnston, J. Am. Chem. Soc., 60, 2265 (1938).

24. The pure olefin 9 is reported to boil at 138°, n_D^{25} 1.4328 and the pure olefin 10 is reported to boil at 130°, n_D^{25} 1.4211

   F. L. Howard, T. W. Mears, A. Fookson, P. Pomerantz and D. B. Brooks, J. Research Natl. Bur. Standards, 38, 365 (1947) (Research Paper No. 1779), Natl. Advisory Comm. Aeronaut., Tech. Note No. 1247, 56 pp (1947).

25. Determined in carbon tetrachloride solution.