Cleavage by Organic Magnesium Compounds.

Maxwell Mcclelland Barnett

Louisiana State University and Agricultural & Mechanical College

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CLEAVAGE BY ORGANIC MAGNESIUM COMPOUNDS

I. THE CLEAVAGE OF MALONONITRILES

II. THE CLEAVAGE OF BETA HYDROXY KETONES
CLEAVAGE BY ORGANIC MAGNESIUM COMPOUNDS

A DISSERTATION

PRESENTED TO THE FACULTY

OF

LOUISIANA STATE UNIVERSITY

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR

THE DEGREE OF DOCTOR OF PHILOSOPHY

BY

MAXWELL M. BARNETT

BATON ROUGE, LOUISIANA

MAY, NINETEEN HUNDRED THIRTY SEVEN
This dissertation is dedicated to Dr. J.L.E. Erickson, under whose guidance it has been my privilege to work.

M.M. Barnett
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INTRODUCTION
Several investigators have observed that organic magnesium compounds may effect a characteristic cleavage of the C-C bond. The steps in this process have been outlined with certainty in several cases, but the reasons underlying the cleavage have remained obscure. This work was undertaken with the object of supplying additional information about the nature of this transformation through a study of the malononitriles and beta-hydroxy ketones, which are compounds of the type that cleave.

These substances were chosen for study because they permit a simplification of the problem. The number of possible substituents is reduced to two in the malononitriles; they therefore represent ideal compounds in which to determine the effect of various groups upon the rupture of the molecule. The beta-hydroxy ketones possess the advantage of being one step nearer cleavage than the beta-diketones.

Several alkaline addition reagents are known to cause cleavage. The organic magnesium compounds appear to be the most satisfactory reagents for this purpose. The reaction is irreversible, therefore its course may be followed with certainty. Moreover, the magnesium compounds are easily prepared and give well defined reaction products which can be isolated, purified, and identified.

The problem involved the preparation of several malononitriles and beta-hydroxy ketones. These were treated with phenyl magnesium bromide and the products investigated.
Special attention was given to accounting for the materials in a quantitative manner, particularly where more than one molecule of reagent was consumed indicating that cleavage had taken place.
REVIEW OF THE LITERATURE
Zelinsky\(^1\) investigated the reaction of methyl magnesium iodide with diacetyl, acetylacetone, and acetoxyacetone, representatives of alpha, beta, and gamma-diketones respectively. Diacetyl and acetoxyacetone yielded the corresponding glycols. With acetylacetone, however, there was obtained only a small quantity of liquid boiling at 100-102° under a pressure of 16 mm. This liquid had a composition corresponding approximately to C\(_7\)H\(_{16}\)O\(_2\). Zelinsky attributed the somewhat surprising behaviour of acetylacetone to the fact that it exists largely in the enol form.

Acetoacetic ester and its homologs yield no simple products with organic magnesium compounds\(^2\). A poor yield of, (CH\(_3\))\(_2\)C(OH)CH(C\(_2\)H\(_5\))CO\(_2\)C\(_2\)H\(_5\), is obtained from ethyl acetoacetic ester and methyl magnesium iodide.

Slavjanoff\(^3\) treated dimethylacetoacetic ester and dimethylmalonic ester with methyl magnesium iodide. Both esters furnished the same products with slight variations in yield. The following compounds were obtained:

Isobutyric acid, (CH\(_3\))\(_2\)CHCO\(_2\)H. I.

Tetramethylethylene lactic acid, (CH\(_3\))\(_2\)C(OH)C(CH\(_3\))\(_2\)CO\(_2\)H. II.

Hexamethyl trimethyleneglycol, (CH\(_3\))\(_2\)C(OH)C(CH\(_3\))\(_3\)C(CH\(_3\))\(_2\)OH. III.

Compounds II and III resulted from straight addition of the Grignard reagent to the carbonyl and carboxyloxy groups.

---

(1) Zelinsky, Ber., 35, 2138 (1902).
(2) Grignard, Compt. rend., 134, 649 (1902).
Slavenoff advanced no mechanism to account for the formation of isobutyric acid.

Zerevitinoff reported that one molecule of acetylacetone furnished 82 mols of methane with methyl magnesium iodide.

Smedley added methyl magnesium iodide to dimethyldibenzoyl-methane and obtained a product boiling at 120-125° under a pressure of 55 mm. The analysis corresponded to C_{18}H_{26}O_{2}. She considered it to be the tertiary alcohol, C_{16}H_{12}(CH_{3})COHC(CH_{3})_{2}C(OH)CH_{3}C_{6}H_{5}, without further evidence.

One cyclic beta-diketone, tetramethyl cyclobutanone, has been treated with the Grignard reagent.

\[
(CH_{3})_{2}C\overline{\begin{array}{c}CO \\ OC\end{array}}C(CH_{3})_{2} + C_{2}H_{5}MgBr \rightarrow (CH_{3})_{2}C\overline{\begin{array}{c}CO \\ OC\end{array}}C(CH_{3})_{2}
\]

The cyclic glycol was obtained in almost the theoretical yield.

Vorlander, Osterburg and Meye attempted to prepare the glycol, (C_{6}H_{5})_{3}C(OH)CH_{2}C(OH)(C_{6}H_{5})_{2}, from phenyl magnesium bromide and dibenzoylmethane. Their object was to convert it into tetraphenyl allene by dehydration. The reagent added to only one of the

(4) Zerevitinoff, Ber., 41, 2343 (1908).
(6) Wedekind and Miller, Ber., 41, 3285 (1911).
(7) Vorlander, Osterburg and Meye, Ber., 56, 1140 (1931).
carbonyl groups to yield, \((C_6H_5)_2C(OH)CH_2COC_6H_5\), a compound previously obtained from phenyl magnesium bromide and malonic ester. They stated that the hydroxy ketone did not enter into further reaction with the reagent.

Kohler and Erickson made a systematic investigation of the action of organic magnesium compounds on a number of beta-diketones. They found that normal addition products are obtained only in those cases where the compound is largely or completely enolic.

\[
\begin{align*}
C_6H_5COCH_2COC_6H_5 & \rightarrow C_6H_5C=CHCOC_6H_5 \rightarrow C_6H_5C=CH-C(C_6H_5)_2 \rightarrow C_6H_5COCH_2C(C_6H_5)_2OH \\
OMgX & \rightarrow OMgX \rightarrow OMgX
\end{align*}
\]

Compounds which contain a substituted methylene group invariably showed cleavage.

\[
\begin{align*}
C_6H_5COCH(C_6H_5)COC_6H_5 & \rightarrow C_6H_5COCH(C_6H_5)C(C_6H_5)_2 \rightarrow C_6H_5COCH(C_6H_5)C(C_6H_5)_2COOMgX \\
OMgX & \rightarrow OMgX
\end{align*}
\]

Kohler and Erickson discovered that the results reported by Smedley are probably in error. The compound which she considered to be the ditertiar y alcohol, \(C_6H_5(CH_3)COHC(CH_3)_2C(OH)CH_2C_6H_5\), was apparently a mixture of the cleavage products, \((CH_3)_2CHCOC_6H_5\), and \(C_6H_5CH_3CHOH\).

When dimethyldibenzoylmethane was treated with phenyl

(8) Dilthey and Last, Ber., 37, 2639 (1904).
magnesium bromide, the compound was cleaved and the expected products were isolated.

\[
\text{C}_6\text{H}_5\text{COC(CH}_3\text{)}_2\text{COC}_6\text{H}_5 \xrightarrow{\text{OMgX}} (\text{C}_6\text{H}_5)_2\text{C(OH)CH}_2\text{COC}_6\text{H}_5
\]

\[
\text{C}_6\text{H}_5\text{COC(CH}_3\text{)}_2 + (\text{C}_6\text{H}_5)_2\text{CO} \rightarrow (\text{C}_6\text{H}_5)_3\text{COH}
\]

The following table shows the compounds investigated and the products obtained from them.

<table>
<thead>
<tr>
<th>COMPOUND</th>
<th>PRODUCTS</th>
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</thead>
<tbody>
<tr>
<td>1. C\text{C}_6\text{H}_5\text{COCH}_2\text{COCH}_2\text{COC}_6\text{H}_5</td>
<td>(\text{C}_6\text{H}_5)_2\text{C(OH)CH}_2\text{COC}_6\text{H}_5</td>
</tr>
<tr>
<td>2. CH\text{C}_3\text{COCH}_2\text{COCH}_3</td>
<td>(\text{CH}_3)_2\text{C(OH)CH}_2\text{COCH}_3</td>
</tr>
<tr>
<td>3. C\text{C}_6\text{H}_5\text{COCH}(\text{C}_6\text{H}_5)\text{COCH}_2\text{COC}_6\text{H}_5</td>
<td>\text{C}_6\text{H}_5\text{COCH}_2\text{COC}_6\text{H}_5 + (\text{C}_6\text{H}_5)_3\text{COH}</td>
</tr>
<tr>
<td>4. C\text{C}_6\text{H}_5\text{COCH(CH}_3\text{)}_2\text{COC}_6\text{H}_5</td>
<td>\text{C}_6\text{H}_5\text{COCH}_2\text{CH}_3 + (\text{C}_6\text{H}_5)_2\text{COH}</td>
</tr>
<tr>
<td>5. CH\text{C}_3\text{COC(CH}_3\text{)}_2\text{COCH}_3</td>
<td>\text{CH}_3\text{COCH(CH}_3\text{)}_2 + (\text{C}_6\text{H}_5)_3\text{CH}_3\text{COH}</td>
</tr>
<tr>
<td>5a.</td>
<td>+ \text{CH}_3\text{COC}_6\text{H}_5(\text{CH}_3)_2</td>
</tr>
<tr>
<td>6. C\text{C}_6\text{H}_5\text{COCH(CH}_3\text{)}_2\text{COC}_6\text{H}_5</td>
<td>\text{C}_6\text{H}_5\text{COCH(CH}_3\text{)}_2 + (\text{C}_6\text{H}_5)_3\text{COH}</td>
</tr>
<tr>
<td>7. C\text{C}_6\text{H}_5\text{COC(CH}_3\text{)}_2\text{COC}_6\text{H}_5</td>
<td>\text{C}_6\text{H}_5\text{COCH(CH}_3\text{)}_2 + (\text{C}_6\text{H}_5)_3\text{COH}</td>
</tr>
<tr>
<td>8. C\text{C}_6\text{H}_5\text{COCBr}_2\text{COC}_6\text{H}_5</td>
<td>(\text{C}_6\text{H}_5)_2\text{COCHBrCOC}_6\text{H}_5</td>
</tr>
<tr>
<td>9. C\text{C}_6\text{H}_5\text{COCOCOCOC}_6\text{H}_5</td>
<td>\text{C}_6\text{H}_5\text{COCH(OR)C}_6\text{H}_5 + (\text{C}_6\text{H}_5)_3\text{COH}</td>
</tr>
</tbody>
</table>

(a) was run with mesityl magnesium bromide.

In contrast to dibenzoyl methane, the hydroxy compound formed from it is capable of cleaving. According to Vorlander, Osterburg and Meye\(^7\), the compound does not react with phenyl magnesium bromide. Actually, it reacted rapidly to form triphenyl carbinol and the glycol, (\text{C}_6\text{H}_5)_2\text{C(OH)CH}_2\text{C(OH)(C}_6\text{H}_5)_2. The cleavage reaction may be represented as follows:

\[
\text{PRODUCTS}
\]

---

(7) Vorlander, Osterburg and Meye, Ber., 56, 1140 (1921).
\[(C_6H_5)_2C(OH)CH_2COC_6H_5 \rightarrow (C_6H_5)_2C(OH)CH_2COC_6H_5 \rightarrow (C_6H_5)_2CO + CH_2=CHC_6H_5\]

It was found possible to avoid cleavage by operating at a sufficiently low temperature. Thus by proceeding in the reverse of the usual manner, adding phenyl magnesium bromide cautiously to phenyldibenzoylmethane and acidifying without delay, it was possible to obtain a fair yield of tetraphenyl propenone, formed by loss of water from the tertiary alcohol.

\[C_6H_5COCH(C_6H_5)C(C_6H_5)_2OMgX \rightarrow C_6H_5COCH(C_6H_5)C(C_6H_5)_2OH \rightarrow C_6H_5COC(C_6H_5)=C(C_6H_5)_2\]

The reaction with diphenylpropanetrione was as follows:

\[C_6H_5COCOCOC_6H_5 \rightarrow C_6H_5COCOCOC_6H_5 \rightarrow C_6H_5COC(OMgX)C_6H_5COC_6H_5 \rightarrow \]

Hydrogen is an addition reagent, and many of the compounds which are cleaved by organomagnesium compounds are also cleaved by hydrogen. The first investigators to report such a reaction were Sabatier and Mailhe, who used reduced nickel as a catalyst and hydrogenated in the vapor phase\(^\text{(10)}\). Acetone was hydrogenated at 150°, and yielded five products.

1. Acetaldehyde.
2. Acetone.
3. Ethanol.

---

\(^{\text{(10)}}\) Sabatier and Mailhe, Compt. rend., 144, 1086 (1907).
4. Isopropyl alcohol.

5. A colorless liquid boiling at 176-178°.

The last substance corresponded to about one-quarter of the acetylacetone used. It was shown to be, CH₃CHOHCH₂COCH₃, a compound already prepared by Claisen through a different route. The other three-quarters of the acetylacetone suffered cleavage according to the equation:

\[
\text{CH₃COCH₃COCH₃} + \text{H₂} \rightarrow \text{CH₃CHO} + (\text{CH₃})₂\text{CO}
\]

Methylacetylacetone was hydrogenated at about 170°. Four reactive products were isolated.

1. Acetaldehyde.
2. Ethanol.
4. 2-butanol.

There was also obtained a very small quantity of liquid boiling at 170°, which must have been the ketone alcohol corresponding to the starting material. The quantity was insufficient to work with further.

One alpha-diketone, diacetyl, was hydrogenated and found to yield the expected products, 2-butanol-3-one and 2,3-butanediol.

Bradley and Robinson submitted a number of unsymmetrical derivatives of dibenzoylmethane to cleavage with 1 per cent aqueous sodium hydroxide. The reactions were carried out to completion. According to them, a diketone, RCOCH₂COR, usually yields a mixture of RCO₂H, RCOCH₃, RCO₂H and RCOCH₃ on hydrolysis.

In general the stronger of the acids which might be formed was found in the greater relative amount. They proposed the following mechanism:

1. "The hydrolytic fission of dibenzoylmethane is a reaction characteristic of the diketone phase and does not occur in the keto-enolic modification. Satisfactory evidence is available in support of this proposition and it will suffice to note that compounds of fixed open chain beta-letonic structure are readily hydrolyzed by alkali, whereas substances having fixed keto-enolic structures and related to beta-diketones are relatively stable to hydroxyl ions.

2. On account of the considerations given in (1), the extent of enolization, great as it is, and the nature of the enols do not affect the result of hydrolytic fission as mentioned below.

3. The hydrolysis is probably the result of the decomposition of a complex anion formed from the diketone and hydroxyl ion.

\[
\begin{align*}
\text{RCOCH}_2\text{COR}_1 + \text{OH} & \rightarrow \text{R-C-CH}_2\text{COR}_1 \rightarrow \\
\text{OH} & \\
\text{RCO}_2 & + \text{HCH}_2\text{COR}_1
\end{align*}
\]

The complex ions may undergo other transformations of which the most important is the formation of the enolic modification.

4. Hence the chief factors controlling the direction of the change are:

(a) The rates of formation of the two possible complex anions, \(\text{RCO(OH)CH}_2\text{COR}_1\) and \(\text{RCOCH}_2\text{CO(OH)R}_1\).
(b) The extent to which each of these breaks down with the formation of carboxylate ions."

The table gives a summary of the results obtained by Bradley and Robinson.

\[
\begin{array}{|c|c|c|c|}
\hline
\text{R} & \text{R}_1 & \text{RCO}_2\text{H} & \text{R}_1\text{CO}_2\text{H} \\
\hline
\text{p-methoxyphenyl} & \text{phenyl} & 82.1 & 17.9 \\
\text{p-methoxyphenyl} & \text{phenyl} & 61.9 & 38.1 \\
\text{p-methoxyphenyl} & \text{phenyl} & 50.2 & 49.8 \\
\text{p-isopropoxyphenyl} & \text{phenyl} & 33.0 & 67.0 \\
\text{p-chlorophenyl} & \text{phenyl} & 63.7 & 36.3 \\
\text{p-chlorophenyl} & \text{phenyl} & 66.4 & 33.6 \\
\text{p-nitrophenyl} & \text{phenyl} & 82.0 & 17.7 \\
\text{2,4-dimethoxyphenyl} & \text{phenyl} & 74.7 & 25.3 \\
\text{3,4-dimethoxyphenyl} & \text{phenyl} & 50.2 & 49.2 \\
\hline
\end{array}
\]

Conner and Adkins\(^{12}\) investigated the cleavage resulting from the hydrogenation of a number of organic compounds. They found that the 1,3-glycols and beta-diketones suffer cleavage of the C-C bond in a number of instances.

The 1,3-glycols and beta-diketones may undergo hydrogenolysis to give four sets of reaction products.

\[
\text{R}_2\text{COH} + \text{R'}_2\text{COH} \rightarrow \text{R}_2\text{CHCH}_2\text{C(OH)}\text{R'}_2 + \text{H}_2\text{O} \\
\text{R}_2\text{COH} + \text{R'}_2\text{COH} \rightarrow \text{R}_2\text{C(OH)}\text{CH}_2\text{CH}_2\text{R'} + \text{H}_2\text{O} \\
\text{R}_2\text{COH} \rightarrow \text{R}_2\text{CHOH} + \text{R'}_2\text{C(OH)}\text{CH}_3 \\
\text{R}_2\text{COH} \rightarrow \text{R'}_2\text{CHOH} + \text{R}_2\text{C(OH)}\text{CH}_3
\]

A highly branched chain greatly facilitated hydrogenolysis.

It is interesting to note that cleavage of diacetone alcohol occurred so readily that it could not be hydrogenated to the glycol without formation of considerable isopropyl alcohol. It is possible that the oxide catalyst was sufficiently alkaline to cause a reversal of the reaction by which diacetone alcohol is formed.

\[ 2 \text{CH}_3\text{COCH}_3 \rightarrow \text{CH}_3\text{COCH}_2\text{C(OH)}\text{(CH}_3\text{)}_2 \]

A nickel catalyst which contained no alkali was found to give no isopropyl alcohol.

Several beta-ketoesters were hydrogenated. However, since hydrogenation of the carbonyl group takes place at much lower temperatures than does cleavage or hydrogenation of the carboxy group, the compounds actually undergoing hydrogenolysis were beta-hydroxy esters. Conner and Adkins postulated four possible reactions.

\[
\begin{align*}
\text{CH}_3 \\
| \\
\text{CHOH} + \text{H}_2 \\
| \\
\text{CR}_2 \\
| \\
\text{CO}_2\text{C}_2\text{H}_5 & \rightarrow \text{C}_2\text{H}_5\text{OH} + \text{R}_2\text{CHCH}_2\text{OH} \quad \text{I} \\
\text{CH}_3\text{CH(OH)}\text{CHR}_2 + \text{H}_2\text{O} \quad \text{II} \\
\text{CH}_3\text{CH(OH)}\text{CHR}_2 + \text{CH}_3\text{OH} \quad \text{III} \\
\text{CH}_3\text{CH}_2\text{CR}_2\text{CH}_3\text{OH} + \text{H}_2\text{O} \quad \text{IV}
\end{align*}
\]

Only reactions (II) and (IV) occurred with the monosubstituted acetoacetic esters. Reaction (I) took place, but only to a negligible degree. The table shows the ratio of carbon-carbon cleavage to carbon-oxygen cleavage.

<table>
<thead>
<tr>
<th>Compound</th>
<th>% C-C Cleavage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethyl acetoacetate</td>
<td>0</td>
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</tbody>
</table>
Malonic ester underwent carbob-carbon cleavage to a small degree, but the disubstituted malonic esters underwent 100 per cent cleavage to methanol and a dialkyl carbinol. The mono-substituted malonic esters were cleaved less completely. The results indicated that 20 per cent of butyl malonic, 32 per cent of benzyl malonic and 20 per cent of ethyl malonic ester had cleaved to give methanol.

Studies of the hydrogenation of beta-diketones were reported by Sprague and Adkins. A large number of substituted and unsubstituted beta-diketones were submitted to hydrogenation over Raney nickel. Many types of products were obtained, making it somewhat difficult to determine the effect of structure upon the mode of cleavage. They found that the ratio of products is primarily a function of the structure of the diketone and of the amount of hydrogen which the reaction mixture is allowed to take up. The temperature of hydrogenation, the kind, activity and amount of catalyst, the nature of the reaction medium and other factors played a lesser role.

Sprague and Adkins used temperatures of about 125° for the hydrogenation of unalkylated diketones and 50-60° for those having a substituent on the central carbon atom. In general, the unalkylated compounds required a higher temperature for reasonably rapid rate of reaction. Absorption of hydrogen was generally stopped after 1.6 - 1.8 moles had been used.

Four linkages in the beta-diketones are labile to hydrogen. These are indicated by dotted lines in the type formula given below:

\[ R-C(:=O)\cdots \text{CHR'}\cdots C(:=O)-R'' \]

The oxygen to carbon linkages (a) and (b) may be hydrogenated, and all four may be cleaved during hydrogenation. In most cases the linkages (a) and (b) were hydrogenated and the corresponding glycol was formed. In a few cases, the reaction stopped at the hydroxy ketone stage. Quite frequently monoketones were obtained. These must have resulted from hydrogenolysis of one of the carbonyl oxygen atoms.

Cleavage occurred many times at the (c) and (d) linkages. In five cases this amounted to 40-68 per cent of the hydrogenolysis. Four of the unalkylated diketones gave a cleavage of 6-25 per cent, and two of the unalkylated compounds gave 10-15 per cent.

The ease of cleavage of the carbon-carbon bond is a function of the number and kind of substituents. In a general way the order of increasing effectiveness is as follows:
The four monoalkyl diketones which showed the highest proportion of carbon to carbon cleavage contain an almost negligible quantity of the enolic form. However, two diketones (R is mesityl or furyl, R" is phenyl) which showed 20-25 per cent carbon cleavage, are apparently completely enolized.

Beckman and Adkins\textsuperscript{14} undertook to determine the relation of structure to the mode of cleavage of diketones under conditions complicated as little as possible by secondary and side reactions. They avoided the use of hydrogen chloride or sodium ethoxide as catalysts and used, instead, an alcoholic solution of the compound and hydrogen under 100 atmospheres pressure.

It was found, as the result of a number of experiments, that the proportion of acetyl cleavage was constant within the limits of experimental error so long as the temperature was maintained at 150-250°, with alcoholsysis from 6-25 per cent complete, and with ratios of diketone to ethanol varying from 1-1.3 to 1-1.5. The acetyl cleavage was also independent of whether or not the gas over the reaction mixture was hydrogen or nitrogen, and was also independent of the pressure.

Beckman and Adkins found, however, that the proportion of cleavage products was, within certain limits, a function of the catalysts present. Thus there was a greater proportion of acetyl cleavage in very dry alcohol than in alcohol containing .1 to .2 per cent of water. Other factors such as the material used in the

reaction vessel, affected the ratio of products. One very significant fact was discovered. The addition of any of several catalysts reduced the acetyl cleavage to a minimum characteristic of the diketone.

In an unsymmetrical diketone, CH₃CO....CHR....COR', cleavage occurred to a greater extent at (a) than at (b) when R' was phenyl or an alkyl group. The isopropyl group was an exception. In general, a greater proportion of acetyl cleavage was obtained from those alkyl groups having long and branched chains.

The rates of alcoholysis of a number of diketones were measured. The results are summarized in the table below.

<table>
<thead>
<tr>
<th>CH₃CO............CH(R).......COR'</th>
<th>a</th>
<th>b</th>
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<tbody>
<tr>
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<tr>
<td></td>
<td>a</td>
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The substitution of ethyl, n-butyl or benzyl groups on the central carbon atom decreased cleavage when R' was tertiary butyl. Two benzyl groups almost prevented alcoholysis under some conditions.

A study of the alcoholysis by hydrogen chloride of several beta-diketones was made by Adkins, Kutz and Coffman\(^{15}\). Their method was to dissolve approximately 0.01 mole of the diketone in dry ethanol and add a normal solution of hydrogen chloride so that the volume of the reaction mixture was 40 cc., and the desired amount of catalyst was present. If the amount of ethyl acetate expected in the reaction mixture was less than about 0.002 moles, the amounts of reactants were increased so that at least that much ester would be present in the solution to be analyzed. The reaction mixture was placed in a thermostat and held at 60° for the desired length of time. The reaction was stopped by adding 2 cc. of phenyl hydrazine. The ester formed was determined by distillation, saponification with a known quantity of alkali, and back titration of the excess. Determinations on samples containing from 0.001 to 0.01 moles of ethyl acetate showed 0.00015 mole of ethyl acetate was unaccounted for by the saponification value. The loss was probably due to mechanical losses and to saponification of the ester in the flask before distillation.

The rate of alcoholysis was independent of the ratio of diketone to alcohol when the value was varied from 1:1 to 1:40. It was also independent of whether ethanol or butanol was used. With secondary propyl, or tertiary butyl alcohol, the rate was lower, probably

because of reaction of the alcohols with hydrogen chloride.

The rate and extent of alcoholysis was found to be a function of the amount of hydrogen chloride present in the reaction mixture. A high ratio of catalyst to diketone (1:1) was necessary to complete alcoholysis in 48 hours.

The rate of hydrolysis of the substituted diacetyl methane fell off as the substituent was varied from γ-butyl, γ-propyl, ethyl, isopropyl, benzyl, diethyl and dibenzyl.

Dibenzoylmethane underwent almost no alcoholysis. Acetylbenzoylmethane underwent hydrolysis more slowly than did diacetyl methane.

Kutz and Adkins15 made some further investigations of the cleavage of mono-substituted beta-diketones with alcoholic hydrogen chloride. Their results are summarized in the table below.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Alcoholysis</th>
<th>Hyrsolysis</th>
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<tbody>
<tr>
<td></td>
<td>CH₃CO% RCO%</td>
<td>CH₃CO% RCO%</td>
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<tr>
<td>Acetyl butyryl methane</td>
<td>43.5 56.5</td>
<td>49 51</td>
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<tr>
<td>Acetyl valeryl methane</td>
<td>61.0 39.0</td>
<td>55 45</td>
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<tr>
<td>Acetyl 1-valeryl methane</td>
<td>65.5 34.5</td>
<td>67 33</td>
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<tr>
<td>Acetyl 2-valeryl methane</td>
<td>81 19.0</td>
<td>62 38</td>
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<tr>
<td>Acetyl benzoyl methane</td>
<td>100 0</td>
<td>58 42</td>
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<tr>
<td>Acetyl cyclohexanoyl methane</td>
<td>100 0</td>
<td>69 31</td>
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<tr>
<td>Acetyl furoyl methane</td>
<td>100 0</td>
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</table>

Kutz and Adkins concluded that there was no close correlation between the strengths and amounts of the acids produced in

Hydrolysis.

Beckham and Adkins\(^\text{(1)}\) summarizes the results obtained by Edkis and his co-workers on the alcoholysis of keto compounds.

1. The substitution of an alkyl group on the methylene carbon atom increased the rate of cleavage of the diketone or keto ester in basic solution or in the high temperature cleavage. For example, under similar conditions, diacetylmethane underwent 8 per cent reaction whereas the monomethyl derivative underwent 19 per cent reaction. The direction and extent of enolization is immaterial in the alkaline cleavage of symmetrical compounds.

2. The substitution of two alkyl groups on the methylene carbon atom increased the rate of basic cleavage as compared to the mono-substitution product. In this case the competing side reaction (enolization) is completely eliminated so that the basic cleavage will occur more rapidly.

3. The substitution of one alkyl group for a H of the methylene carbon atom decreased the rate of acidic split. As a particular example, diacetylmethane underwent 58 per cent reaction under conditions where the monoethyl derivative underwent 37 per cent cleavage. In acid solution the extent of enolization is one of the factors in the rate of cleavage. Diacetylmethane contains 83 per cent enol and ethylidiacetylmethane contains 28 per cent. Thus if we calculate to a constant enol basis, we find that ethylidiacetylmethane underwent reaction 1.9 times as fast as diacetylmethane.

4. Dialkyl derivatives cleaved more slowly in acid or high

---

temperature alcoholysis than did unsubstituted or mono-substituted diketones and keto esters. This corresponds to the fact that enolization, upon which acid cleavage depends, is impossible under such conditions.

The analysis in sections 1 to 4 makes it clear why, if a series of diketones is arranged in the order of decreasing ease of acid hydrolysis, it will be found that they have been arranged in general in the order of increasing ease of alkaline hydrolysis.

5. Acetoacetic ester did not undergo acid hydrolysis under conditions which cleaved diacetyl methane rapidly, and malonic ester was more stable to high temperature alcoholysis than was acetoacetic ester. In the presence of sodium ethoxide diacetyl-methane underwent alkaline alcoholysis two to three times as rapidly as acetoacetic ester and considerably higher temperatures were necessary for the cleavage of acetoacetic ester in the absence of a catalyst.

8. Substitution of C_6H_5 for CH_3 in diacetyl methane to form acetyl-benzoylmethane lowered the rate of acidic cleavage, but did not affect the relative basic rate. The two phenyl groups in dibenzoylmethane stopped acidic cleavage and increased basic cleavage.

The following mechanism was proposed for cleavage in basic solution:

---

* See also Ref. (11).
(C) is presumed to be the compound which undergoes cleavage, i.e.

\[
\begin{align*}
\text{(A)} & & \text{(B)} \\
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{O}
\end{array}
& \quad \begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \equiv \text{C} \equiv \text{R}^n
\end{array}
& \quad \begin{array}{c}
\text{O} \\
\text{H} \\
\text{O}
\end{array}
& \quad \begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \equiv \text{C} \equiv \text{R}^n
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{(C)} & & \text{(D)} \\
\begin{array}{c}
\text{OEt} \\
\text{R}
\end{array}
& \quad \begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \equiv \text{C} \equiv \text{R}^n
\end{array}
& \quad \begin{array}{c}
\text{OEt} \\
\text{R}
\end{array}
& \quad \begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \equiv \text{C} \equiv \text{R}^n
\end{array}
\end{align*}
\]

In the presence of acid, the following equilibria are established:

\[
\begin{align*}
\text{(A)} & & \text{(B)} \\
\begin{array}{c}
\text{O} \\
\text{H} \\
\text{O}
\end{array}
& \quad \begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \equiv \text{C} \equiv \text{R}^n
\end{array}
& \quad \begin{array}{c}
\text{O} \\
\text{H} \\
\text{O}
\end{array}
& \quad \begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \equiv \text{C} \equiv \text{R}^n
\end{array}
\end{align*}
\]

\[
\begin{align*}
\text{(C)} & & \text{(D)} \\
\begin{array}{c}
\text{OEt} \\
\text{R}
\end{array}
& \quad \begin{array}{c}
\text{R} \\
\text{C} \\
\text{C} \equiv \text{C} \equiv \text{R}^n
\end{array}
& \quad \begin{array}{c}
\text{OEt} \\
\text{R}
\end{array}
\end{align*}
\]

Equilibrium is established between (A) and (C) through (B) and (D) as intermediates and not directly as is the case in the presence of a base. This is presumably due to the difficulty of rapid direct addition of the comparatively neutral ethanol without some additional activating influence, possibly chelation.
(C) is the form which undergoes cleavage.

\[
\begin{array}{c}
\text{OH} & \text{R} & \text{C} & \text{O} & \text{C} & \text{R}^n + H \rightarrow \text{R} & \text{C} & \text{O} & \text{C} = \text{C} & \text{R}^n
\end{array}
\]

**ALPHA OXIDO KETONES AND ALPHA OXIDO ESTERS**

Kohler, Richtmyer and Hester\(^{(18)}\) made the first systematic investigation of cleavage by organic magnesium compounds. They treated alpha-oxido ketones and glycidic esters with the Grignard reagent and in every case studied observed cleavage of the molecule.

Alpha-oxido ketones: \(R_2\text{C} = \text{C}(\text{R})\text{COR}\)

Glycidic esters: \(R_2\text{C} = \text{C}(\text{R})\text{CO}_2\text{R}\)

They began their investigation with the oxide of benzalacetophenone, \(\text{C}_6\text{H}_5\text{CH} = \text{CHCOC}_6\text{H}_5\). When this was treated with phenyl magnesium bromide, two molecules of reagent were consumed and one molecule of triphenyl carbinol was formed. The oxide also reacted in a similar manner with ethyl magnesium bromide and gave diethylphenyl carbinol. In addition to the carbinol, the reaction between the oxide ketone and magnesium compounds yielded only resins, which were evidently due to extensive polymerization.

The oxide of anisalacetophenone showed a similar behaviour when added to an excess of phenyl magnesium bromide. Triphenylcarbinol

and a resin were formed, demonstrating that cleavage occurs between the carbonyl group and the oxide ring.

\[
\text{C}_6\text{H}_5\text{CH}=\text{COC}_6\text{H}_5 + \text{C}_6\text{H}_5\text{MgBr} \rightarrow (\text{C}_6\text{H}_5\text{C}_2\text{H}_2\text{O})\text{MgBr} + (\text{C}_6\text{H}_5)_3\text{CO} \\
(\text{C}_6\text{H}_5)_3\text{COMgBr}
\]

The fact that one of the primary cleavage products was a ketone was demonstrated by treating the oxide of benzal acetone with mesityl magnesium bromide. The acetomesitylene thus formed, due to steric hindrance, did not add more reagent and was obtained as a primary cleavage product.

\[
\text{C}_6\text{H}_5\text{CH}=\text{COC}_6\text{H}_5 + (\text{CH}_3)_3\text{C}_6\text{H}_5\text{MgBr} \rightarrow (\text{C}_6\text{H}_5\text{C}_2\text{H}_2\text{O})\text{MgBr} + \\
\text{CH}_3\text{COC}_6\text{H}_5(\text{CH}_3)_3
\]

Information as to the nature of the second cleavage product was secured through the oxido ketone, \((\text{C}_6\text{H}_5)_3\text{C}=\text{COC}_6\text{H}_5\), which gave well defined products with no resinous material. Both cleavage products were isolated in this case. With excess phenyl magnesium bromide, triphenyl carbinol and diphenyl acetaldehyde were obtained in good yield. The action of organic magnesium compounds upon oxido ketones can, therefore, be represented as follows:

\[
(\text{C}_6\text{H}_5)_3\text{C}=\text{COC}_6\text{H}_5 + \text{RMgX} \rightarrow (\text{C}_6\text{H}_5)_3\text{C}=\text{CH(OMgX)} + \text{RCOC}_6\text{H}_5
\]

\[
\text{C}_6\text{H}_5\text{CH}=\text{COC}_6\text{H}_5 + \text{RMgX} \rightarrow (\text{C}_6\text{H}_5\text{CH}=\text{CHOMgX})_n + \text{RCOC}_6\text{H}_5
\]

In a search for the underlying reason for the cleavage, the
procedure was reversed and the Grignard reagent added inversely to an ethereal solution of the oxido ketone at $-10^\circ$. The mixture was decomposed immediately with iced acid. The result was the formation of the oxido carbinol, $\text{C}_6\text{H}_5\text{CH}=\text{OCH}(\text{C}_6\text{H}_5)_2\text{OH}$.

The oxido carbinol could be heated for above its melting point without causing any change, and it was not decomposed by methyl alcoholic potassium hydroxide, although it was promptly cleaved by phenyl magnesium bromide, the final products being triphenyl carbinol and resin. The oxido carbinol could be made in any desired quantity by adding the ketone to an excess of reagent in the usual manner, provided that the operation was carried out at a sufficiently low temperature and the mixture was decomposed without delay. The cleavage, therefore, was not due to an excess of reagent. When only one equivalent of reagent was added at the usual temperature, no oxido carbinol was found. Instead there was obtained the usual cleavage products consisting of resin and benzophenone. The latter compound would have appeared as triphenyl carbinol had there been sufficient reagent to react with it.

Thus, it was established that cleavage involves the spontaneous decomposition of a magnesium compound formed by the addition of one molecule of reagent to the oxido ketone.

\[
\text{C}_6\text{H}_5\text{CH}=\text{OCH}(\text{C}_6\text{H}_5)_2 \longrightarrow \text{C}_6\text{H}_5\text{CH}=\text{OMgX} + (\text{C}_6\text{H}_5)_2\text{CO}
\]

One glycidic ester, $(\text{CH}_3)_2\text{C}=\text{OCHCO}_2\text{C}_2\text{H}_5$, was treated with phenyl magnesium bromide. The expected cleavage took place,
although only one cleavage product, triphenyl carbinol, was isolated.

Bergmann and Wolff\textsuperscript{19} confirmed some of the results of Kohler, Bichtmyer and Hester, but they reported two oxido ketones which did not cleave.

Phenyl magnesium bromide and benzal-$p$-phenyl acetophenone oxide, $\text{C}_6\text{H}_5\text{CH}–\text{CHCOC}_6\text{H}_4\text{C}_6\text{H}_5$, yield two products. One of these is the pinacol of phenyl biphenyl ketone.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C}_6\text{H}_4 & \quad \text{C}_6\text{H}_4\text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5\text{OH} & \quad \text{C}_6\text{H}_5\text{HO} \quad \text{C}_6\text{H}_5
\end{align*}
\]

the formation of this compound was caused by the reducing action of finely divided magnesium upon phenyl biphenyl ketone, which was obtained through cleavage. The second product was a well-defined compound, $\text{C}_{33}\text{H}_{28}\text{O}_2$, resulting from the addition of two moles of phenyl magnesium bromide to the ethylene oxide ring. Bergmann and Wolff proposed two possible formulas:

\[
\begin{align*}
\text{I} & \quad \text{II} \\
\text{C}_6\text{H}_5\text{CH}–\text{CHC}_6\text{H}_4\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5\text{CH}–\text{CHC}_6\text{H}_4\text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5\text{OH} & \quad \text{C}_6\text{H}_5\text{OH} \quad \text{C}_6\text{H}_5
\end{align*}
\]

Formula (II) seemed more probable to them in view of the known reactions of ethylene oxides with the Grignard reagent.

Addition without cleavage was again obtained with benzal-$p$-methoxy acetophenone oxide, $\text{C}_6\text{H}_5\text{CH}—\text{CHCOC}_6\text{H}_4\text{OCH}_3$, and the

compound, $C_{18}H_{26}O_2$, was formed. This was assigned the structure below:

$$
\begin{align*}
\text{C}_6\text{H}_5\text{CH-CH-} & \quad \text{C} \quad \text{C}_6\text{H}_4\text{OCH}_3 \\
\text{OH C}_6\text{H}_5 & \quad \text{OH C}_6\text{H}_5
\end{align*}
$$

Dickel\(^a\) made a more thorough investigation of the compound obtained by Bergmann and Wolff from benzal-$\mu$-methoxy acetophenone oxide. Oxidation with chromic acid yielded benzophenone and $\mu$-methoxy benzophenone. Only two compounds, (III) and (IV) would give these oxidation products.

\begin{align*}
\text{(C}_6\text{H}_5)_2\text{CH-CH-} & \quad \text{C} \quad \text{C}_6\text{H}_5 \\
\text{OH HO C}_6\text{H}_4\text{OCH}_3 & \\
\text{III} \\
\text{(C}_6\text{H}_5)_2\text{C-CH}_2- & \quad \text{C} \quad \text{C}_6\text{H}_5 \\
\text{OH HO C}_6\text{H}_4\text{OCH}_3 & \\
\text{IV}
\end{align*}

Compound (III) may be formed by addition of the Grignard reagent to the opened oxide ring. Compound (IV) would result by addition of phenyl magnesium bromide to the ketone resulting from rearrangement of the oxide.

The beta-diketone, $C_6H_6C\equiv CH_2COC_6H_5OCH_3$, was prepared and compound (IV) synthesized from it according to the equations:

\begin{align*}
\text{C}_6\text{H}_5\text{COCH}_2\text{COC}_6\text{H}_5\text{OCH}_3 + \text{C}_6\text{H}_5\text{MgBr} & \rightarrow \text{C}_6\text{H}_5\text{COCH}_2\text{COC}_6\text{H}_5\text{OCH}_3 \\
\text{C}_6\text{H}_6\text{COCH}_2\text{COC}_6\text{H}_5\text{OCH}_3 + \text{C}_6\text{H}_5\text{Li} & \rightarrow \text{IV}
\end{align*}

The structure was confirmed by oxidation to benzophenone and $p$-methoxy benzophenone. The carbinol was not identical with that obtained from the $p$-methoxy oxide. Therefore, by elimination, the structure of the product obtained by Bergmann is represented by (III).

When the $p$-methoxy oxide was treated with phenyl lithium, results were obtained which corresponded to the action of the Grignard reagent upon benzal acetophenone oxide. In cold solution the hexanol was the only product; at room temperature the expected cleavage took place.

Kohler and Biekel\textsuperscript{21} made a study of the oxanols, $\text{C}_8\text{H}_8\text{CH}(-\text{CHC(OH)}\text{C}_6\text{H}_5)_2$ and $\text{C}_8\text{H}_8\text{CH(OH)}\text{CH}(-\text{C(C}_6\text{H}_5)_2$. They found that both of them readily form metallic derivatives by replacement of hydroxyl hydrogen by a metal. At low temperatures these compounds may be regenerated from the metallic derivatives by hydrolysis with acids. At higher temperatures all of the metallic derivatives decompose into benzophenone and the corresponding metallic derivative of diphenyl acetaldehyde. The Grignard reagent, phenyl lithium, and sodium in liquid ammonia were used in this investigation.

**Beta Hydroxy Ketones and Beta Hydroxy Esters**

Franks and Kohn\textsuperscript{22} published a series of papers on the reaction of beta-hydroxy aldehydes and ketones with the Grignard reagent.

\textsuperscript{22} Franks and Kohn, Ber., 37, 4730 (1904).
They made pentanediol-2,4 in good yield with aldol and methyl magnesium iodide.

\[ \text{CH}_3\text{CH(OH)CH}_2\text{CHO} + \text{CH}_3\text{MgI} \rightarrow \text{CH}_3\text{CH(OH)CH}_2\text{CH(OH)CH}_3 \]

Diacetone alcohol reacted smoothly with methyl magnesium iodide to give the corresponding beta-glycol\(^{33}\).

\[(\text{CH}_3)_2\text{C(OH)CH}_2\text{COCH}_3 + \text{CH}_3\text{MgI} \rightarrow (\text{CH}_3)_2\text{C(OH)CH}_2\text{C(OH)(CH}_3)_2 \]

With one mole of formisobutyraldol and two moles of methyl magnesium iodide there was obtained the expected glycol\(^{34}\).

\[\text{HOCH}_2\text{C(CH}_3)_2\text{CHO} + \text{CH}_3\text{MgI} \rightarrow \text{HOCH}_2\text{C(CH}_3)_2\text{CH(OH)CH}_3 \]

Ethyl magnesium bromide and phenyl magnesium bromide gave similar addition products.

\[\text{HOCH}_2\text{C(CH}_3)_2\text{CHO} + \text{C}_6\text{H}_5\text{MgBr} \rightarrow \text{HOCH}_2\text{C(CH}_3)_2\text{CH(OH)C}_6\text{H}_5 \]

\[\text{HOCH}_2\text{C(CH}_3)_2\text{CHO} + \text{C}_6\text{H}_5\text{MgBr} \rightarrow \text{HOCH}_2\text{C(CH}_3)_2\text{CH(OH)C}_6\text{H}_5 \]

Baeyer\(^{35}\) treated several hydroxy phenyl compounds with the Grignard reagent as a means of preparing derivatives of triphenyl carbinol. He reported only the formation of normal addition products. \(\alpha\)-Hydroxy triphenyl carbinol was prepared from methyl salicylate and phenyl magnesium bromide; \(\alpha\)-\(\alpha\)-dihydroxy triphenyl carbinol from phenyl magnesium bromide and dihydroxy

\(^{(23)}\) Franke and Kohn, Monatsh., 28, 967 (1907).
\(^{(24)}\) Franke and Kohn, ibid., 27, 1087 (1906).
\(^{(25)}\) Baeyer, Ann., 354, 167 (1907).
benzophenone, and \( \beta \)-\( \beta \)-dihydroxy triphenyl carbinol from phenyl magnesium bromide and dihydroxy benzophenone.

Abelmann\(^{26}\) treated 3-methyl-4-butanol-2-one with methyl, ethyl and \( \mu \)-propyl Grignard reagents and obtained the corresponding beta-glycols. Purification for analysis offered certain difficulties and careful fractionation of the products was necessary. The yields were fairly small, mainly because of the formation of high boiling polymerization products.

Lemaire\(^{27}\) treated diacetone alcohol with methyl magnesium iodide and obtained a 75 per cent yield of the corresponding glycol. He was apparently unaware of the work of Franke and Kohn (Ref. 18) with the same compounds.

Several beta-hydroxy esters were treated with the Grignard reagent by Berberian\(^{28}\). Methyl magnesium iodide and beta-beta-diphenyl-beta-hydroxy propionic ester furnished the corresponding glycol.

\[
HOC(C_6H_5)_2CH_2CO_2C_2H_5 + CH_3MgI \rightarrow HOC(C_6H_5)_2CH_2C(OH)(CH_3)_2
\]

A small quantity of the hydrocarbon, \((C_6H_5)_2C=C=CH(CH_3)_2\), was also obtained. The same ester was treated with ethyl and phenyl magnesium bromides.

\[
HOC(C_6H_5)_2CH_2CO_2C_2H_5 + C_2H_5MgBr \rightarrow HOC(C_6H_5)_2CH_2C(OH)(C_2H_5)_2
\]

\(^{26}\) Abelmann, Ber., 42, 2500 (1909).
\(^{27}\) Lemaire, Rec. trav. chim., 22, 22 (1910).
\(^{28}\) Berberian, Bull. soc. romane stiin., 22, 11 (1914).
No mention of any but normal reaction products was made.

McKenzie and Martin prepared several glycols from beta-hydroxy-beta-phenyl propionic acid. They reported only the formation of normal addition products.

\[
\text{C}_8\text{H}_8\text{CH(OH)CH}_2\text{CO}_2\text{H} + \text{C}_6\text{H}_5\text{MgBr} \rightarrow \text{C}_8\text{H}_8\text{CH(OH)CH}_2\text{C}(\text{C}_6\text{H}_5)_2\text{OH}
\]

Maitland and Tucker studied the reaction of 9-fluorenyl magnesium bromide with diacetone alcohol and found that several products were produced. One of these, 9-fluorenyl dimethyl carbinol, was produced either by cleavage or by the action of the Grignard reagent upon acetone contained as an impurity in the diacetone alcohol. Four compounds were isolated.

1. Alpha-9-fluorenyl-alpha-gamma-gamma-trimethyl trimethylene glycol, \((\text{C}_8\text{H}_4)_2\text{CHC(OH)CH}_3\text{CH}_2\text{C(OH)(CH)}_3\)

2. A phototropic substance, \(\text{C}_{19}\text{H}_{18}\), melting at 80-82°.

3. A substance, \(\text{C}_{19}\text{H}_{18}\), melting at 58-61°.


The yields of the above substances were small and a considerable amount of uncrystallizable oil was obtained. The glycol, which would appear to be the first product of the reaction, was...

(30) McKenzie and Martin, ibid., 1913, 112 (1913).
isolated on one occasion only, and then in very small quantity. It lost water readily to yield the two isomeric hydrocarbons listed above.

Maitland and Tucker state that the 9-fluorenyl dimethyl carbinoa was probably the product of the direct action of the Grignard reagent upon acetone, either originally contained in admixture with the diacetone alcohol, or formed from it during the reaction. They were of the opinion that the Grignard reagent may have acted in the manner of a base and transformed part of the diacetone alcohol back into acetone.

\[
(CH_3)_2C(OH)CH_2COCH_2 \rightarrow (CH_3)_2CO
\]

Beta-hydroxy-1,8,9-alpha-dimethyl propion aldehyde\(^{44}\) gave the corresponding glycols in yields of about 50 per cent when treated with the Grignard reagent.

\[
\text{HOCH}_2\text{C(CH}_3)_2\text{CHO} + \text{l-C}_7\text{H}_{13}\text{MgBr} \rightarrow \text{HOCH}_2\text{C(CH}_3)_2\text{CH(OH)C}_7\text{H}_{13}
\]

\[
\text{HOCH}_2\text{C(CH}_3)_2\text{CHO} + \text{l-C}_6\text{H}_{11}\text{MgBr} \rightarrow \text{HOCH}_2\text{C(CH}_3)_2\text{CH(OH)C}_6\text{H}_{11}
\]

\[
\text{HOCH}_2\text{C(CH}_3)_2\text{CHO} + \text{l-C}_6\text{H}_{13}\text{MgBr} \rightarrow \text{HOCH}_2\text{C(CH}_3)_2\text{CH(OH)C}_6\text{H}_{13}
\]

Kohler and Erickson\(^9\) have been shown that the beta-hydroxy ketone, \((C_6H_5)_2C(OH)CH_2COC_6H_5\), undergoes both cleavage and addition when treated with phenyl magnesium bromide. This reaction has already been discussed in connection with the beta-diketones.

Jacquemain\(^{31}\) treated diacetone alcohol with several RMgX

\(^{44}\) Sebastien, Sabety and Blegor, Bull. soc. chim., (4) 47, 885 (1950).


\(^{31}\) Jacquemain, Compt. rend., 192, 1315 (1931).
compounds and obtained glycols of the type,
(CH₃)₂C(OH)CH₂C(OH)CH₂R. He used Grignard reagents in which R
was CH₂CH₃, (CH₃)₂CH₂, (CH₃)₃CH₂, (CH₃)₄CH₂, CH(CH₃)₂ and
(CH₃)₅CH(CH₃)₂.

Bickel treated (C₆H₅)₂C(OH)CH₂COC₆H₄OH₂, and
C₆H₅COCH₂C(OH)(C₆H₅)C₆H₄CH₃ with phenyl lithium. He obtained
the corresponding hydroxy compounds and apparently did not
observe cleavage.

MALONIC ESTERS

Soon after the discovery of the Grignard reaction, Valeur investigated the reaction of ethyl magnesium iodide with ethyl
malonate. He obtained an unsaturated alcohol, C₁₁H₂₂O₂, boiling
at 177-178°. He concluded that the tertiary glycol,
(C₂H₅)₂C(OH)CH₂C(OH)(C₂H₅)₂, is first formed. The glycol then
yields the unsaturated alcohol by loss of water.

Slavjanoff treated dimethyl acetoacetic ester and dimethyl
malonic ester with methyl magnesium iodide. Both esters gave
the same products with slight variations in yield. The following
compounds were obtained:
Isobutyric acid, (CH₃)₂CHCO₂H  I.
Tetramethyl ethylene lactic acid, (CH₃)₄C(OH)C(CH₃)₂CO₂H  II.
Hexamethyl trimethylene glycol, (CH₃)₂C(OH)C(CH₃)₃C(CH₃)₃OH  III.

Compounds (II) and (III) resulted from straight addition of the
Grignard reagent. Compound (I) may have been formed as the
result of cleavage by the Grignard reagent.

Vorlander and Siebert\textsuperscript{33} treated methyl malonate with phenyl magnesium bromide and obtained a compound which melted at 119°. They were unable to convert this substance into tetraphenyl allene by the action of acetic anhydride, and they made no further attempt to determine the constitution of their compound.

A study of the preparation of glycols from substituted malonic esters was made by Kalishev\textsuperscript{34}. He used a ratio of four moles of reagent $R^\text{m} \text{MgX}$ to one mole of ester, $R^\text{n} \text{R} = \text{C} (\text{CO}_2 \text{C}_2 \text{H}_5)_2$. The reaction went to completion yielding glycols only when $R^\text{m}$ and $R^\text{n}$ were methyl groups, although, even in this case, one of the carbethoxy groups was less reactive than the other. Hydroxy esters were obtained exclusively when all of the $R$s were not methyl. The organomagnesium compounds used by Kalishev in this investigation were methyl magnesium iodide, ethyl magnesium iodide, propyl magnesium iodide, and phenyl magnesium iodide. The esters were dimethyl malonate, diethyl malonate, and dipropyl malonate.

Mirau\textsuperscript{35} treated ethyl di-p-tolyl malonate with an excess of phenyl magnesium bromide and obtained triphenyl carbinol and ethyl di-p-tolyl acetate. Doubtless, in the first step, ethyl benzoate and the enolate of ethyl di-p-tolyl acetate are formed. The latter cannot react further with the Grignard reagent, and the former is converted into triphenyl carbinol.

\[
\begin{align*}
(C_6H_5CH_3)_2C(C_2O_2C_2H_5)_2 + C_6H_5MgBr & \rightarrow (C_6H_4CH_3)_2C=CO_2C_2H_5 + \text{C}_6H_5MgBr
\end{align*}
\]

\[
\begin{align*}
(C_6H_4CH_3)_2C(C_2O_2C_2H_5)_2 + C_6H_5MgBr & \rightarrow (C_6H_5)_3COH
\end{align*}
\]

\textsuperscript{33} Vorlander and Siebert, Ber., 39, 1035 (1906).
\textsuperscript{34} Kalishev, J. Russ., Phys. Chem. Soc., 46, 427 (1914).
\textsuperscript{35} Mirau, Thesis, Berlin, 1937.
Leroide made a study of the behaviour of alpha, alpha-di-substituted esters towards the Grignard reagent, particularly propyl magnesium bromide. One of the compounds which he investigated was dimethyl malonic ester, which he found gave only a small quantity of glycol. The chief reaction was cleavage resulting from the addition of the magnesium compound.

\[
(CH_3)_2C(CO_2C_2H_5)_2 + C_3H_7MgBr \rightarrow (CH_3)_2CHCO_2C_2H_5 + C_3H_7CO_2C_2H_5
\]

ALPHA CYANO KETONES AND ALPHA CYANO ESTERS

Blaise investigated the reaction of ethyl magnesium bromide with ethyl cyanoacetate. The reaction proceeded in two stages, the first step being the formation of hydrocarbon by reaction with an enolic hydroxyl.

\[
\text{CH}_3\text{C} = \text{C} = \text{N-Br} + \text{C}_2\text{H}_5\text{MgBr} \rightarrow \text{CH}_3\text{C} = \text{C} = \text{N} = \text{O} + \text{C}_2\text{H}_5
\]

The CN group was attacked if an excess of reagent was present.

\[
\text{CH}_3\text{C} = \text{C} = \text{N-Br} + \text{C}_2\text{H}_5\text{MgBr} \rightarrow \text{CH}_3\text{C} = \text{C} = \text{N-Br} + \text{C}_2\text{H}_5\text{COCH}_2\text{CO}_2\text{C}_2\text{H}_5
\]

Ethyl propionyl and butyryl acetates were prepared in this way.

(37) Blaise, Compt. rend. 152, 978 (1901).
Mavrodin studied the action of organic magnesium compounds upon the substituted cyanoacetic esters. He began his investigation with ethyl ethylcyanoacetate, \( \text{NOCH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_6\text{H}_5 \). The only reaction observed at the boiling point of ether was that of enolization.

\[
\text{NCCHCO}_2\text{C}_2\text{H}_5 + \text{RMgX} \rightarrow \text{NC} = \text{C}(\text{OMgX})\text{OC}_2\text{H}_5
\]

The cyanide group was caused to react by heating in toluene, and the beta-diketone, \( \text{RCOCH}(\text{C}_2\text{H}_5)\text{COR} \), was obtained. Mavrodin postulated the following reactions:

\[
\begin{align*}
\text{NCCHCO}_2\text{C}_2\text{H}_5 + \text{RMgX} & \rightarrow \text{NC} = \text{C}(\text{OMgX})\text{OC}_2\text{H}_5 + \text{RMgX} \\
\text{NC} = \text{C} & \left( \text{OMgX} \right) \text{OC}_2\text{H}_5 & \xrightarrow{3 \text{RMgX}} & \text{X} = \text{C}(\text{OMgX})\text{C} = \text{R} + \text{OMgX} + \text{H}_2\text{O} \\
\text{RCOCH}(\text{C}_2\text{H}_5)\text{COR} & \text{with yield of ethyl dibenzoylmethane.}
\end{align*}
\]

The ethyl dipropionyl methane thus formed boiled at 91-93°C under a pressure of 10 mm, and was obtained in 25-30 per cent yield. Phenyl magnesium bromide furnished a 60 per cent yield of ethyl dibenzoylmethane.

\[
\text{NCCH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5 + \text{C}_6\text{H}_5\text{MgBr} \rightarrow \text{C}_6\text{H}_5\text{COCH}(\text{C}_2\text{H}_5)\text{CO}_2\text{C}_6\text{H}_5
\]

---

(58) Mavr din, Compt. rend., 1504 (1959)
In a second paper on the subject\textsuperscript{39}, Mavrodin reported the results of an investigation of diethylcyanoacetic ester, a compound in which enolization is not possible. The reaction with phenyl magnesium bromide is as follows:

\[
\text{NCC(C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5 + \text{C}_6\text{H}_5\text{MgBr} \rightarrow \text{C}_6\text{H}_5\text{CN} + \text{BrMgC(C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5
\]

The benzonitrile reacted with the excess of reagent which was present to form benzophenone.

\[
\text{C}_6\text{H}_5\text{CN} + \text{C}_6\text{H}_5\text{MgBr} \rightarrow (\text{C}_6\text{H}_5)_2\text{CO}
\]

The magnesium complex was considered to condense with itself.

\[
2\text{BrMgC(C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5 \rightarrow \text{BrMgC(C}_2\text{H}_5)_2\text{COC(C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5
\]

Mavrodin compared the cleavage reaction to one observed by Grignard\textsuperscript{40} with diethylacetoacetic ester.

\[
\text{CH}_3\text{COC(C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5 + \text{CH}_3\text{MgI} \rightarrow (\text{CH}_3)_3\text{CO} + \text{IMgC(C}_2\text{H}_5)_2\text{CO}_2\text{C}_2\text{H}_5
\]

Two reactions were found to take place with ethyl magnesium bromide. One of these involved a cleavage of the molecule, as in the case of phenyl magnesium bromide, to form diethyl ketone. Self condensation of the residue produced ethyl alpha-di-thyl-gamma-diethylacetylacetate. The other reaction gave the hydroxy

\textsuperscript{39} Mavrodin, Compt. rend., 191, 1064 (1951).
\textsuperscript{40} Grignard, ibid., 187, 1036 (1926).
In the course of the reaction this partially decomposed into diethylacetonitrile and diethyl ketone. The excess of reagent transformed the latter product into triethyl carbinol.

Mavrodin also treated phenacyl cyanide with ethyl and phenyl magnesium bromides and obtained the expected beta-diketones.  

\[
\text{SCCH}_2\text{CO CeH}_5 + \text{C}_2\text{H}_5\text{MgBr} \rightarrow \text{C}_2\text{H}_5\text{COCH}_3\text{CO CeH}_5
\]

Mavrodin also treated phenacyl cyanide with ethyl and phenyl magnesium bromides and obtained the expected beta-diketones.  

\[
\text{NCCH}_2\text{CO CeH}_5 + \text{C}_2\text{H}_5\text{MgBr} \rightarrow \text{C}_2\text{H}_5\text{COCH}_3\text{CO CeH}_5
\]

Doremus investigated the cleavage of phenyl, diphenyl, dibenzyl and dimethyl -cyanoacetic esters by phenyl magnesium bromide.

Phenyl cyanoacetic ester reacted in the enolic form at room temperature to produce a complex from which it was regenerated upon hydrolysis. At the temperature of boiling benzene, the enolic form reacted further with the reagent to furnish the ketimine of benzoylphenylacetic ester and the monoimine of phenyldibenzoylmethane. Doremus proposed two mechanisms:

\[
\text{NCCCH(C}_6\text{H}_5)\text{CO}_2\text{C}_2\text{H}_5} \rightarrow \text{NCC(C}_6\text{H}_5)=\text{C}_2\text{H}_5\text{MgX} + \text{C}_6\text{H}_5\text{MgX}
\]

\[
\text{NCC(C}_6\text{H}_5)=\text{C}_2\text{H}_5\text{MgX} + \text{C}_6\text{H}_5\text{MgX} \rightarrow \text{C}_6\text{H}_5\text{C}-\text{C(C}_6\text{H}_5)=\text{C}_2\text{H}_5\text{MgX} + \text{C}_2\text{H}_5\text{OMgX}
\]

\[
\text{N-MgX} + \text{H}_2\text{O} \rightarrow \text{C}_6\text{H}_5\text{C}-\text{CH(C}_6\text{H}_5)-\text{CO CeH}_5
\]

The second mechanism involves enolization to the nitrogen atom.

\[
N=N(CH(C_6H_5)CO_2C_2H_5) \rightarrow XMgN=C(C_6H_5)CO_2C_2H_5
\]

\[
(XMg)_2NC(C_6H_5)=C(C_6H_5) \rightarrow C_6H_5 + C_6H_5OMgX
\]

Doremus considered the second scheme to be quite unlikely as it is quite probable that the keto group would not survive at the temperature of boiling benzene. Support for the first mechanism was obtained through the reaction of the potassium derivative of the enol form of diphenylacetic ester with phenyl magnesium bromide. Ethoxyl magnesium bromide was split off and diphenylacetoepheneone was formed.

\[
(C_6H_5)_2C=CO_2C_2H_5 + C_6H_5MgBr \rightarrow (C_6H_5)_2C=CO_2C_2H_5 + C_6H_5OMgBr
\]

The ketimine of benzoylphenylacetic ester was probably formed through normal addition of the Grignard reagent to the CN group. Diphenylcyanoacetic ester was readily cleaved. From the products isolated, it appears that cleavage took place from both ends of the molecule.
Dibenzylcyanoacetic ester was cleaved in a similar manner. No t of the cleavage resulted from addition to the CN group, although some triphenyl carbinol was isolated, demonstrating that cleavage also took place through the ester end of the molecule.

Dimethylcyanoacetic ester suffered cleavage from the nitrile end of the molecule. However, the corresponding alpha-cyano ketone, $C_6H_5COC(CH_3)_2CN$, was cleaved from the keto end, a result to be expected from a comparison of the relative reactivities of the carbonyl and nitrile groups.

Erickson and Coffman treated several alpha-cyano ketones with phenyl magnesium bromide. Phenacyl cyanide underwent enolization to the oxygen atom, and normal addition to the cyanide group.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{COCH}_2\text{CN} & \quad \xrightarrow{\text{O-MgX}} \quad \text{C}_6\text{H}_5\text{C}=\text{C}(\text{C}_6\text{H}_5)-\text{C}≡\text{N} \\
\text{C}_6\text{H}_5\text{C}=\text{C}(\text{C}_6\text{H}_5)-\text{C}≡\text{N} & \quad \xrightarrow{\text{O-MgX}} \quad \text{C}_6\text{H}_5\text{C}=\text{CH}-\text{C}-\text{C}_6\text{H}_5
\end{align*}
\]

(43) Erickson and Coffman, Unpublished work.
A similar reaction was observed with desyl cyanide:

\[
\begin{align*}
\text{C}_6\text{H}_5\text{COCH(C}_6\text{H}_5)\text{CN} & \xrightarrow{\text{OMgX}} \text{C}_6\text{H}_5\text{C}≡\text{C}\text{(C}_6\text{H}_5)\text{CN} \\
\text{C}_6\text{H}_5\text{C}≡\text{C}\text{(C}_6\text{H}_5)\text{CN} & \xrightarrow{\text{OMgX}} \text{N}\text{MgX} \\
\text{C}_6\text{H}_5\text{C}≡\text{C}\text{(C}_6\text{H}_5)\text{C}≡\text{C}\text{H}_5
\end{align*}
\]

Benzoyldiphenylacetonitrile was cleaved with the formation of benzophenone and the magnesium derivative of the imino form of diphenylacetonitrile.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CO(C}_6\text{H}_5)\text{C-CN} & \xrightarrow{\text{OMgX}} \text{C}_6\text{H}_5\text{C}-\text{C(C}_6\text{H}_5)\text{C-CN} \\
\text{C}_6\text{H}_5\text{CO(C}_6\text{H}_5) + (\text{C}_6\text{H}_5)\text{C}-\text{C=N-MgX}
\end{align*}
\]

Both primary cleavage products reacted further with the reagent. The benzophenone yielded triphenylcarbinol and the ketene imine compound gave diphenylacetophenone.

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CO(C}_6\text{H}_5) + \text{C}_6\text{H}_5\text{MgX} & \xrightarrow{\text{OMgX}} (\text{C}_6\text{H}_5)\text{C-OH} \\
(\text{C}_6\text{H}_5)\text{C}-\text{C=N-MgX} + \text{C}_6\text{H}_5\text{MgX} & \xrightarrow{\text{OMgX}} (\text{C}_6\text{H}_5)\text{C}-\text{C=N(MgX)} \\
(\text{C}_6\text{H}_5)\text{C}≡\text{C-NH}_2 + \text{H}_2\text{O} & \xrightarrow{\text{H}_2\text{O}} (\text{C}_6\text{H}_5)\text{C}-\text{C}≡\text{C} + \text{NH}_3
\end{align*}
\]
MALONONITRILES

No work has been done on the cleavage of the malononitriles other than that reported in this Dissertation.
THEORETICAL DISCUSSION
GENERAL

A survey of the literature has shown that several types of compounds undergo cleavage when treated with organic magnesium compounds. Although the functional groups are quite varies, it will be noted that in every case a certain fundamental linkage is present which is part of a chain of three carbon atoms. Each of the terminal carbon atoms is also part of an unsaturated group capable of reacting with the reagent.

\[
\begin{align*}
R & \quad \text{beta-diketones} \\
O=\overset{\text{C}}{\text{C}}-\overset{\text{C}}{\text{C}}=\overset{\text{O}}{\text{O}} \\
R & \quad \text{malonic esters} \\
O=\overset{\text{C}}{\text{C}}-\overset{\text{C}}{\text{C}}=\overset{\text{O}}{\text{O}} & \quad \text{alpha-cyano esters}
\end{align*}
\]
It has been shown that the first reaction is the addition of one molecule of reagent. The magnesium derivative is unstable and decomposes with rupture of the carbon chain. This may be illustrated conveniently with the beta-ketones:
The unsubstituted beta-diketones do not cleave, but react in the enolic form to yield a stable magnesium complex

\[
\begin{align*}
\text{R-C-C-C-R} & \rightarrow \text{R-C=O-C-R} & \rightarrow \text{R-C-C-C-R} \\
\text{R} & \quad \text{H} & \quad \text{H}
\end{align*}
\]

Similar reactions may be written for the other types of compounds which exhibit cleavage. Fundamentally the decomposition of these unstable magnesium derivatives is analogous to a reversal of the aldol condensation.

\[
\begin{align*}
\text{R-C-C-C-R} & \rightarrow \text{R-C=O-C-R} + \text{C-R} \\
\text{R} & \quad \text{R} & \quad \text{R'}
\end{align*}
\]

It is also possible that the cleavage of the beta-diketones by sodium ethyl takes place through the formation of an unstable intermediate similar to the magnesium compounds.

\[
\begin{align*}
\text{R-C-C-C-R} + \text{NaOC}_2\text{H}_5 & \rightarrow \left[ \begin{array}{c} \\
\text{O} \\
\text{R-C-O-C}_2\text{H}_5 \\
\end{array} \right] \rightarrow \\
\text{R-C=O-C}_2\text{H}_5 + (\text{R})_2\text{C}=\text{C-R}
\end{align*}
\]
Beckham and Adkins\textsuperscript{17} have proposed essentially the same mechanism as a result of their studies of the cleavage of beta-diketones with sodium ethylate.

\[
\begin{align*}
\text{R-C-C-C-R} + \text{OC}_2\text{H}_5 & \rightarrow \text{[C}_2\text{H}_5\text{O-} \text{C-C-C-R}] \\
\text{R-C-OC}_2\text{H}_5 & \rightarrow \text{R}_2\text{C=C} \\
\end{align*}
\]

Why, then, are these metallic derivatives unstable? The answer to this question is not a parent, although the decomposition of these compounds may be correlated with other, somewhat similar, reactions. Schmidt has pointed out in a series of several publications\textsuperscript{45} that a general relationship exists as to the point of fission in a carbon chain containing double bonds. This is obvious from a consideration of the following compounds. The arrow indicates the position at which cleavage takes place.

\[
\text{CH}_2=\text{CH-CH}_2/\text{CH}_2-\text{CH}_2-\text{CH}_3
\]

dihexene

\textsuperscript{17} Beckham and Adkins, J. Am. Chem. Soc., 56, 1119 (1934).
\textsuperscript{45} Schmidt, Ber., 67, 1780 (1934); ibid., 66, 60 (1935); 68, 795 (1935); Chem. Rev., 17, 137 (1934).
\[
\text{CH(OH)} = \text{C(OH)} - \text{CHOH-CHOH-CHOH-CH}_2\text{OH}
\]

enol form of glucose

\[
\text{CH}_2 = \text{CH-CH}_2 - R
\]

allyl compounds

(R denotes halogen, O, N, etc.)

It is evident from these examples that the C-C bond next to a double linkage remains unbroken, and instead, rupture always occurs in the one following it. Schmidt has proposed that there is an alternation of bond strength in a carbon chain containing a double linkage. The bond next to the double linkage is strengthened and the following one is weakened. This change from stronger to weaker bonds is perpetuated with diminishing intensity throughout the molecule. Thus in the carbon chain, \( C_1 - C_2 = C_3 - C_4 - C_5 - C_6 - C_7 - C_8 \), bonds 1-2, 3-4, 5-6, and 7-8 are
strengthened abd bonds 4–5 and 6–7 are weakened.

Oda has suggested that Schmidt's double bond rule is capable of quite general application. He ascribes the reactivity of the methylene hydrogen atoms in malonic ester, cyanoacetic ester, and acetoacetic ester to the effect of the two doubly bonded oxygen atoms upon the strength of the C–H bond. He assumes that the bond between hydrogen and the methylene carbon atom is weakened so that enolization readily occurs.

\[
\begin{align*}
&\text{RO}\cdot\text{C}^\bullet\text{C}^\bullet\text{C}^\bullet\text{OR} \underset{\text{H}}{\xleftrightarrow{}} \text{RO}\cdot\text{C}^\bullet\text{C}^\bullet\text{C}^\bullet\text{OR} \\
&\text{NC}\cdot\text{C}^\bullet\text{C}^\bullet\text{C}^\bullet\text{OR} \underset{\text{H}}{\xleftrightarrow{}} \text{NC}\cdot\text{C}^\bullet\text{C}^\bullet\text{C}^\bullet\text{OR} \\
&\text{CH}_3\cdot\text{C}^\bullet\text{C}^\bullet\text{C}^\bullet\text{OR} \underset{\text{H}}{\xleftrightarrow{}} \text{CH}_3\cdot\text{C}^\bullet\text{C}^\bullet\text{C}^\bullet\text{OR}
\end{align*}
\]

The high reactivity of CH₃=CH–CH₂–I and CH₂=CH–CH₂–I is explained according to the same principles. It is also known that CH₂=CH–CH₂–Cl is less reactive than CH₂=CH₂–CH₂–Cl, so that the theory of alternation in reactivity is in good accordance with fact.

Oda explains the double bond effect in terms of partial valence.

\[
\begin{align*}
\text{strong} & & \text{strong} \\
C_1 & \equiv & C_2 & \equiv & C_3 & \equiv & C_4 & \equiv & C_5 & \equiv & C_6 \\
\text{weak} & & \text{weak}
\end{align*}
\]

The heat of formation of the ethylene bond is about 21 Cal. smaller than that of two simple bonds. All of the energy of the carbon valencies is not utilized, but remains as a partial valence or residual affinity. The valence force of \( C_3 \) is attracted by the residual valence of \( C_1-C_2 \). Therefore, the simple bond next to the double bond is strengthened and the following one is weakened. Bond \( C_5-C_6 \) is weakened, and bond \( C_4-C_5 \) is strengthened in a similar manner by the attraction between the valence forces of \( C_5 \) and \( C_4 \). The effect is thus transmitted throughout the molecule with diminishing intensity.

It now becomes of interest to apply Schmidt’s rule to cleavage by organic magnesium compounds and other alkaline reagents. The unstable magnesium derivatives of the beta-diketones

\[
\begin{align*}
\text{OMgX R} \\
\text{R-C-C-C=O} \\
\text{R R R}
\end{align*}
\]

undergo fission at the point predicted by Schmidt’s theory,
provided that a doubly bonded oxygen atom acts in the same way as C=O in weakening the bond that breaks. The same considerations apply to the alpha-cyano ketones, alpha-cyano esters, and malonic esters, although the situation is somewhat different.

\[
\begin{array}{c}
\text{R} \\
\text{N} = \text{C} - \text{C} - \text{C} - \text{R} \\
\text{R} \\
\end{array}
\begin{array}{c}
\text{R} \\
\text{N} = \text{C} - \text{C} - \text{C} - \text{R} \\
\text{R} \\
\end{array}
\begin{array}{c}
\text{R} \\
\text{R} \\
\text{C}_2\text{H}_5\text{O} \\
\text{R} \\
\end{array}
\]

with the nitrogen compounds since they contain the C≡N linkage instead of C=O.

The malononitriles, however, furnish unstable magnesium derivatives of a different sort.

\[
\begin{array}{c}
\text{R} \\
\text{N} = \text{C} - \text{C} - \text{C} - \text{R} \\
\text{R} \\
\end{array}
\]

The molecule contains one double and one triple bond in positions such that, according to Schmidt's rule, each should tend to neutralize the effect of the other, unless it is assumed that the triple bond exerts a greater influence than the double bond. This is, of course, highly problematical.

The unstable magnesium derivatives of the alpha-oxido ketones and alpha-oxido esters also represent a special case since the oxygen at m of the ethylene oxide ring is not unsaturated in
The same sense as C=O, but apparently owes its activity to the strain inherent in a three-membered ring.

THE CLEAVAGE OF MALONONITRILES

All of the malononitriles used in this investigation, with the exception of diphenylmalononitrile, were prepared by well-known methods. The literature contains no reference to the diphenyl compound, however, so that it became necessary to devise a synthesis. Two unsuccessful attempts were made before a scheme was evolved.

The first of these involved condensation of cyanogen bromide with the sodium salt of diphenylacetonitrile.

\[
(C_6H_5)_2CHCN \xrightarrow{NaNH_2} \left(\frac{(C_6H_5)_2CCN}{Na}\right) \xrightarrow{CNBr} (C_6H_5)_2C(CN)_2
\]

In the second method, diphenylchloroacetamide was treated with mercuric cyanide. The expected product, diphenylcyanooacetamide, should yield diphenylmalononitrile when reacted with phosphorous pentachloride.

\[
(C_6H_5)_2CClCONH_2 \xrightarrow{Hg(CN)_2} (C_6H_5)_2C(CN)CONH_2 \xrightarrow{PCl_5} (C_6H_5)_2C(CN)_2
\]
Both methods are unsatisfactory as the products are a mixture of high melting substances, insoluble in most solvents and difficult to fractionally crystallize. It was therefore necessary to turn to another scheme. This was found in the dehydration of diphenylmalonoamide with phosphorous pentachloride, which furnishes a fair yield of diphenylmalononitrile.

\[
(C_6H_5)_2C(CONH_2)_2 \xrightarrow{PCl_3} (C_6H_5)_2C(CN)_2
\]

The usefulness of the method depends upon the availability of the amide. A satisfactory synthesis of this compound was developed which begins with diphenylmalonic acid.

Diphenylmalonic acid was prepared by Morsman in 1935. Several derivatives were known previous to that time, but the free acid had never been isolated. Hydrolysis of the methyl ester, or the acid chloride with dilute base leads to a cleavage of the molecule.

\[
(C_6H_5)_2C(CO_2R)_2 \xrightarrow{H_2O} (C_6H_5)_2CHCO_2R + HO-C-OR
\]

\[
(C_6H_5)_2C(COCl)_2 \xrightarrow{H_2O} (C_6H_5)_2CHCO_2H + HO-C-OH
\]

However, Morsman showed that it is possible to avoid cleavage of

(48) Staudinger, Ber., 47, 44 (1914).
The acid chloride by hydrolysis with water. The acid chloride is slowly hydrolyzed and is completely converted into pur diphenylmalonic acid after seventeen hours shaking. The synthesis is detailed below:

\[ 2 \text{C}_6\text{H}_5\text{CHO} \xrightarrow{\text{KCN}} \text{C}_6\text{H}_5\text{COCH(OH)}\text{C}_6\text{H}_5 \xrightarrow{\text{HNO}_3} \text{C}_6\text{H}_5\text{OCOC}_6\text{H}_5 \]

\[ \text{C}_6\text{H}_5\text{OCOC}_6\text{H}_5 \xrightarrow{\text{NH}_3\text{NH}_2} \text{C}_6\text{H}_5\text{C} = \text{C}_6\text{H}_5 \xrightarrow{\text{HgO}} \text{C}_6\text{H}_5\text{C} = \text{C}_6\text{H}_5 \]

Diphenyl ketone, \((\text{C}_6\text{H}_5)_2\text{C}=\text{C}=0\), was converted into diphenyl malonyl dichloride by treatment with oxalyl chloride. The resulting acid chloride was then hydrolyzed as described above.

\[ (\text{C}_6\text{H}_5)_2\text{C}=\text{C}=0 + \text{ClC} = \text{C} = \text{Cl} \xrightarrow{\text{heat}} (\text{C}_6\text{H}_5)_2\text{C(OCI)}_2 + \text{CO} \]

\[ (\text{C}_6\text{H}_5)_2\text{C(OCI)}_2 \xrightarrow{\text{H}_2\text{O}} (\text{C}_6\text{H}_5)_2\text{C(CO}_2\text{H)}_2 \]

The overall yield by this method is poor, and a long time is required to carry it out. A much more rapid and convenient

(49) Schroter, Ber., 42, 2346 (1909).
(48) Staudinger, Ber., 47, 44 (1914).
Synthesis was developed from diphenylmethane which furnishes diphenylmalonic acid in good yields.

Morton and Hechenbleikner\textsuperscript{50} have shown that when toluene is treated with amyl sodium and the product is carbonated, the sodium salts of phenylacetic and phenylmalonic acids are obtained. The formulate the following reactions:

\[
\begin{align*}
C_6H_{11}Cl + 2 \text{Na} & \rightarrow C_6H_{11}\text{Na} + \text{NaCl} \\
C_6H_5CH_3 + C_6H_{11}\text{Na} & \rightarrow C_6H_5CH_2\text{Na} + C_6H_{12} \\
C_6H_5CH_2\text{Na} + C_6H_{11}\text{Na} & \rightarrow C_6H_5\text{CHNa}_2 + C_6H_{12} \\
C_6H_5CH_2\text{Na} + \text{CO}_2 & \rightarrow C_6H_5CH_2\text{CO}_2\text{Na} \\
C_6H_5\text{CHNa}_2 + 2 \text{CO}_2 & \rightarrow C_6H_5\text{CH(}\text{CO}_2\text{Na})_2
\end{align*}
\]

Morton and Hechenbleikner also treated diphenylmethane with amyl sodium in the same manner and reported that no diphenylmalonic acid is obtained; instead, the sole product of the reaction is diphenylactic acid, which they obtained in good yield. However, it is probable that they actually had diphenylmalonic acid in hand but failed to recognize it because of the ease with which it loses carbon dioxide and is converted into diphenylacetic acid.

Their experimental work was not repeated as diphenylmalonic acid had already been obtained when their paper on the subject appeared. The success of the reaction is greatly dependent upon temperature and it is possible that their lack of success in preparing diphenylmalonic acid was due to this cause, since they operated at room temperature. A temperature of about 0° is most suitable and can be readily maintained with an ordinary freezing mixture. Under this condition a yield of 3.6 g. of pure diphenylmalonic acid can be consistently secured from 10 g. of diphenylmethylene. This is accompanied by about 4.0 g. of diphenylacetic acid. The two acids may be separated through the difference of their solubilities in benzene, diphenylacetic acid being considerably more soluble in this solvent.

\[
(C_6H_5)_2CH_2 + 2 C_6H_{12}Na \rightarrow (C_6H_5)_2CNa_2 + 2 C_6H_{12}
\]

\[
(C_6H_5)_2CNa_2 + CO_2 \rightarrow (C_6H_5)_2C(CO_2Na)_2
\]

\[
(C_6H_5)_2C(CO_2Na)_2 + H_2SO_4 \rightarrow (C_6H_5)_2C(CO_2H)_2
\]

The acid is easily converted into the acid chloride by treatment with phosphorus pentachloride, and a fair yield of the amide may be obtained through the reaction of the acid chloride with ammonia.
(C₆H₅)₂C(CO₂H)₂ → PCl₅ → (C₆H₅)₂C(COCl)₂

(C₆H₅)₂C(COCl)₂ → NH₃ → (C₆H₅)₂C(CONH₂)₂

The cleavage of the following malononitriles was investigated:

NC-CH₂-CN
malononitrile

NC-CH(C₆H₅)-CN
phenylmalononitrile

NC-C(CH₃)₂-CN
dimethylmalononitrile

NC-C(CH₂C₆H₅)₂-CN
dibenzyLMalononitrile

NC-C(C₆H₅)₂-CN
diphenylmalononitrile

Malononitrile is the simplest member of the series.

Surprisingly enough, it forms no addition products with phenyl magnesium bromide. Instead, an insoluble magnesium derivative is obtained which stubbornly resists further action of a liberal excess of reagent, even when the operation is carried out at 75° and for a period of several hours. Upon hydrolysis, an almost quantitative yield of malononitrile is recovered.
It is probable that the nitrile reacts in the imino form to yield a magnesium complex from which it is regenerated upon hydrolysis.

\[
\text{NaN} \rightarrow \text{NMC-CH}=\text{C}=\text{NMgX} \rightarrow \text{NMC-CH}=\text{C}=\text{CSN}
\]

Evidence in favor of this hypothesis was obtained through a determination of active hydrogen by the method of Zerewitinoff.

Approximately one-half mole of gas is liberated and the same quantity of reagent is consumed.

Dibenzylmalononitrile undergoes cleavage when added to an ethereal solution of phenyl magnesium bromide, and benzophenone and diphenylacetonitrile are obtained upon hydrolysis. The first step in the reaction is addition of the reagent to one of the nitrile groups. The resulting magnesium compound is unstable, and decomposed immediately in a manner presumably like that of the magnesium derivatives from beta-diketones.

\[
\begin{align*}
\text{CH}_2\text{C}_6\text{H}_5 & \quad \text{CH}_2\text{C}_6\text{H}_5 \\
\text{NC} & \quad \text{C} \quad \text{CN} \\
\text{CH}_2\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5 \quad \text{C} \quad \text{CN} \\
 & \quad \text{NMgBr} \quad \text{CH}_2\text{C}_6\text{H}_5 \\
+ \text{C}_6\text{H}_5\text{CN} & \quad \text{(C}_6\text{H}_5)_2\text{C}=\text{NMgBr}
\end{align*}
\]

An examination of the structure of the ketene imine cleavage product shows that it possesses a twinned double linkage not unlike that found in ketenes. If the reaction is carried out
In ether, the ketene imine compound survives for an almost indefinite length of time, while benzonitrile, the other cleavage product, reacts with more of the reagent. Yet such linkages are known to be quite reactive. Diphenyl ketene adds a variety of reagents to the terminal unsaturated group.

Gilman, Kirby and Kinney51 have recently published some generalizations on the addition of the Grignard reagent to compounds of this type. They consider that all addition reactions of the Grignard reagent to compounds possessing terminal cumulative unsaturated groups show two marked similarities:

1. "In each case addition takes place to the ultimate unsaturated group of those types of compounds having terminal cumulated unsaturated groups.

2. The reaction stops at this unsaturated group, even with a liberal excess of phenyl magnesium bromide at the low temperature given by ether as a medium."

The magnesium derivatives of ketene imines presumably react in a very sluggish manner. However, upon replacing the ether with benzene and operating at a higher temperature, both the ketene imine compound and benzonitrile consume more of the reagent to give, upon hydrolysis, excellent yields of diphenylacetophenone and benzophenone.

Diphenylmalononitrile is cleaved in a manner similar to dibenzylmalononitrile. The products in this case are diphenylacetonitrile and benzophenone.

The extent to which cleavage occurs depends entirely upon the stability of the primary Grignard addition product. The extreme ease with which these magnesium derivatives decompose is indeed surprising. If decomposition takes place at all, it usually does so immediately. However, from a comparison of the results obtained by Leroide\(^{(36)}\) and Slavjanoff\(^{(3)}\) with disubstituted malonic

\[\text{(56)} \text{Leroide, Ann. chim., 16, 354 (1931).}\]
and acetoacetic esters, it is reasonable to suppose that the complexity of the reagent is an appreciable factor. Kuntz and Adkins\(^{16}\), however, in their experiments with dialkyl beta-diketones and keto esters, have conclusive evidence that the rate of alkaline alcoholysis varies with the nature of the substituted alkyl group. The experiments with dimethylmalononitrile and phenyl magnesium bromide indicate that these groups influence greatly the rate of decomposition of the magnesium derivative. When dimethylmalononitrile is added to an ethereal solution of phenyl magnesium bromide in the usual manner, cleavage is almost entirely avoided, as the product consists almost wholly of the diketimine of dimethyldibenzoylmethane, with only a trace of benzophenone imine, but when, inversely, the compound is added to but one equivalent of the reagent, only the cleavage products, benzonitrile and isobutyronitrile are obtained, thus affording additional evidence as to the manner in which fission of the molecule occurs.

\[\text{CH}_3\text{C}==\text{C}==\text{CN} \xrightarrow{\text{CH}_3\text{C}==\text{C}==\text{C}==\text{C}==\text{CH}_3} (\text{CH}_3)_2\text{C}==\text{C}==\text{NMgBr} + \text{C}_6\text{H}_5\text{CN}\]

\[\text{C}_6\text{H}_5\text{C}==\text{C}==\text{C}==\text{C}_6\text{H}_5\]

\[\text{NMgBr} \quad \text{NMgBr} \quad \text{NMgBr} \]

With the monosubstitution products of malononitrile, the outcome is quite definite, but entirely different. Upon adding phenylmalononitrile to an ethereal solution of phenylmagnesium bromide, all of the material is recovered. Quantitative determinations, however, show that it liberates one mole of methane. If the operation is carried out at an elevated temperature, three equivalents of the reagent are consumed, and it becomes possible to secure a good yield of a red crystalline substance, which proved to be the diketimine of phenylidibenzoylmethane. The reaction then must be represented as follows:

\[
\begin{align*}
\text{HC} = \text{C} - \text{CH} - \text{CN} & \xrightarrow{\text{C}_6\text{H}_5} \text{HC} = \text{C} - \text{NMgBr} \xrightarrow{\text{C}_6\text{H}_5} \text{C}_6\text{H}_5\text{C} - \text{CH} - \text{C} = \text{N} (\text{MgBr})_2 \\
\text{C}_6\text{H}_5\text{C} - \text{CH} - \text{C} = \text{N} (\text{MgBr})_2 & \xrightarrow{\text{C}_6\text{H}_5\text{NH}} \text{C}_6\text{H}_5\text{C} - \text{CH} - \text{C} = \text{N} (\text{MgBr})_2
\end{align*}
\]

THE CLEAVAGE OF BETA HYDROXY KETONES

The beta-hydroxy ketones possess the structure, \((R)_2\text{C(OH)} - \text{C(R)}_2 - \text{COR}\). A magnesium derivative which should cleave is obtained if the hydrogen of the hydroxyl group is replaced by MgX.
Indeed, the unstable magnesium complex thus formed is identical with that obtained from the addition of one molecule of reagent to a beta-diketone, and which is known to undergo cleavage.

Thus the beta-hydroxy ketones represent a stage one step nearer to cleavage than the beta-diketones. Surprisingly enough, only two cases of cleavage by the Grignard reagent have been reported.

Kohler and Erickson showed the following reactions take place with diphenyl phenacyl carbinol:

\[
\begin{align*}
(C_6H_5)_2C-CH_2-C-C_6H_5 & \rightarrow \left[ \begin{array}{c} O \text{MgX} \\ \text{(R)}_2C-C\text{(R)}_2-C\text{R} \end{array} \right] \\
O & \rightarrow \left[ \begin{array}{c} O \text{MgX} \\ \text{(R)}_2C-C\text{(R)}_2-C\text{R} \end{array} \right]
\end{align*}
\]

Maitland and Tucker isolated 9-fluorenyldimethyl carbinol.

(9) Kohler and Erickson, J. Am. Chem. Soc., 53, 3301 (1931)
among other compounds, from the reaction of 9-fluorenyl magnesium bromide with diacetone alcohol. They attributed the formation of this compound either to acetone contained as an impurity in the starting material, or to a reversal of the reaction

$$2 \text{CH}_3\text{COCH}_3 \rightarrow (\text{CH}_3)_2\text{C(OH)CH}_2\text{COCH}_3$$

by the Grignard reagent. It may also be explained as due to cleavage.

Quite probably other cases of cleavage have been overlooked by investigators who did not expect cleavage products, and therefore made no search for them. A second explanation is that very few compounds which are favourable to cleavage have been studied.

The following beta-hydroxy ketones were used in this investigation:

$$\text{CH}_3-\text{CH(OH)}-\text{CH}_2-\text{CO-CH}_3 \quad (I)$$

hydracetylaceton e

$$(\text{CH}_3)_2\text{C(OH)}-\text{CH}_2-\text{CO-CH}_3 \quad (II)$$
diacetone alcohol
Hydracetyl acetone and diaceton alcohol were made by well known methods. The other compounds, however, were synthesized by the method recently developed by Colonge. The condensing agent is an amino magnesium compound, usually phenyl amino magnesium bromide. This substance is readily prepared from methyl aniline and ethyl magnesium bromide.

\[ C_6H_5(CH_3)NH + C_2H_5MgBr \rightarrow C_6H_5(CH_3)N\cdotMgBr \]

A large number of ketones may be condensed to furnish beta-hydroxy ketones by its use. Colonge represents the reaction as taking place in two stages: the first step involves addition of the amino magnesium compound to one molecule of ketone.

In the second stage, the amine is regenerated by the action of a second molecule of ketone upon the magnesium amino complex, and the magnesium derivative of a beta-hydroxy ketone is obtained.

\[
\begin{align*}
\text{R-C-CH}_3 + \text{X} \text{Mg} \rightarrow \text{R-C-N(CH}_3)_2 \text{C}_6 \text{H}_5 & \rightarrow \text{R-C-N(CH}_3)_2 \text{C}_6 \text{H}_5 \\
\text{CH}_3 & \\
\end{align*}
\]

Compound (VII) yields a beta-hydroxy ketone upon hydrolysis. Thus this magnesium derivative is one which should cleave, and is, as a matter of fact, the compound to be expected from the reaction of the origination reagent with the hydroxyl group of the beta-hydroxy ketone. It is probable that some cleavage does take place in the course of the reaction, and the fact that low yields are usually obtained is evidence in favor of this assumption.

Two unsuccessful attempts were made to prepare the completely phenylated hydroxy ketone, \((\text{C}_6 \text{H}_5)_2 \text{C(OH)} \rightarrow \text{C} \rightarrow \text{C}_6 \text{H}_5 \rightarrow \text{CO} \rightarrow \text{C}_6 \text{H}_5\). The first scheme involved the alkylation of diphenylacetophenone with bromodiphenylmethane:

\[
\begin{align*}
(\text{C}_6 \text{H}_5)_2 \text{CBr} + (\text{C}_6 \text{H}_5)_2 \text{CH-CO-C}_6 \text{H}_5 & \rightarrow \text{NaOC}_2 \text{H}_5 \\
(\text{C}_6 \text{H}_5)_2 \text{C-CO-C}_6 \text{H}_5 & \rightarrow \text{CH(C}_6 \text{H}_5)_2
\end{align*}
\]
Only the starting material was recovered when the alkylation was carried out, making it impossible to proceed beyond the first stage.

The second scheme seemed more promising, but failure was again encountered, this time because the Friedel Crafts reaction with benzene and diphenyldimethyl dichloride could not be successfully carried out.

\[
(C_6H_5)_2C(OCOCl)_2 + HCl \rightarrow C_6H_5-CO-C(C_6H_5)_2-CO-C_6H_5
\]

\[
C_6H_5-CO-C(C_6H_5)_2-CO-C_6H_5 + C_6H_5MgX \rightarrow (C_6H_5)_2C(OH)-C(C_6H_5)_2-CO-C_6H_5
\]

Hydrazacyclonexetone reacts in the normal manner with phenylmagnesium bromide to furnish the corresponding glycol.
Hindrance to addition in this compound is very small, so that little, if any, cleavage is to be expected.

Diacetone alcohol, however, undergoes both cleavage and addition. Addition is obtained when the compound is added to the reagent in the normal manner so that an excess of phenyl magnesium bromide is always present. However, when the manner of addition is reversed and the reagent added to the compound, both cleavage and addition take place.

Only cleavage products were isolated from the reaction of (III) with phenyl magnesium bromide.
Compounds (IV) and (V) react in a totally unexpected manner. Neither addition nor cleavage takes place, but enolization of the carbonyl oxygen so that they are both recovered unchanged after hydrolysis. These results were confirmed by a Zerewitinoff determination which revealed the presence of two active hydrogen atoms in each molecule.

It is probable that the steric hindrance around the carbonyl oxygen atom is so great that addition of the reagent is impossible. Consequently, the molecule reacts in the enol form to give a dimagnesium complex from which it is recovered upon hydrolysis.

Compound (VI) reacts in the ordinary manner to yield the corresponding glycol.
The same product is obtained whether the addition of the compound is normal or inverse.
EXPERIMENTAL

PART I. THE MALONONITRILES
Malononitrile, NCCCH₂CN

Malononitrile was prepared according to the method described in Organic Syntheses\(^{(52)}\).

**Action of Phenyl Magnesium Bromide upon Malononitrile at the Boiling Point of Ether**

An ethereal solution of 3.3 g. (.06 mole) of malononitrile was added to a solution of phenyl magnesium bromide prepared from 6.1 g. (.25 atom) of magnesium and 44 g. of bromobenzene. There was a vigorous reaction accompanied by the formation of a heavy precipitate. The supernatant liquid was decanted and the precipitate was washed with ether and decomposed with ammonium chloride solution. It was necessary to neutralize the alkaline solution in order to extract the regenerated malononitrile. The solution was placed in a continuous liquid extractor and extracted with ether. A 90 per cent recovery of the nitrile was obtained. Admixture of the product with an authentic sample of malononitrile caused no depression of the melting point, m.p. 31°.

**Action of Phenyl Magnesium Bromide upon Malononitrile at the Boiling Point of Benzene**

The above experiment was repeated, except that after the compound was added the ether was displaced with benzene until the boiling point of the solution rose to 75°. The precipitate which was present did not go into solution, even after 2.5 hours of refluxing. The benzene layer was decanted and the precipitate treated as before. The recovery of malononitrile amounted to 85

per cent of the theoretical value. A mixed melting point with an authentic sample showed no depression. Refractive index of known = 1.412. Refractive index of recovered material = 1.4155.

Phenylcyanoacetic Ester, \( \text{NCCH(C}_6\text{H}_5\text{)CO}_2\text{C}_2\text{H}_5 \)

This ester was prepared by the method of Hessler\(^{53}\) which involves the condensation of benzy1 cyanide with diethyl carbonate in the presence of metallic sodium. The substitution of sodium ethylate for metallic sodium was found to give better yields.

Preparation Using Metallic Sodium

Sodium wire (10.9 g.) was forced into a solution of 50 g. of diethyl carbonate in 500 cc. of absolute ether. The flask was cooled with water and 50 g. of benzy1 cyanide was added in several portions. The mixture was allowed to stand overnight and was then acidified with dilute hydrochloric acid. The ethereal solution was separated, washed with water, dried over calcium chloride, and distilled. The yield was 56.1 g. of ester which boiled at 105° under 20 mm. pressure. The yield was 47.5 per cent of the theoretical value.

Preparation Using Sodium Ethylate

Sodium ethylate was prepared by dissolving 34.8 g. of sodium in 500 cc. of absolute alcohol. A mixture of 175 g. of diethyl carbonate and 175 g. of benzy1 cyanide was added in small portions to the alcoholic solution. The flask was placed on a steam bath

and heated for three hours. Alcohol was evaporated with the aid of a water pump and the semi-solid mass remaining in the flask was neutralized with dilute hydrochloric acid. An oil separated which was extracted with ether. The ethereal solution was washed with a little water, dried over calcium chloride, and the ether evaporated off. The yield of crude ester was 182 g., or 64 per cent of theory.

Phenylcyanoacetamide\(^5\), NC\((\text{C}_6\text{H}_5)\text{CONH}_2\)

Hesslers method was used for the preparation of this compound. 143.2 g. of phenylcyanoacetic ester was dissolved in 150 cc. of concentrated ammonium hydroxide. The solution became quite warm, and crystals of the amide gradually separated. These were filtered off at the end of 15 hours and dried. The product melted at 147\(^\circ\) after crystallization from ethyl alcohol. The yield was 75.5 g., or 62 per cent of the theoretical.

In a second experiment, 150 g. of the ester was used. The yield of amide amounted to 80 g.

Phenylmalononitrile\(^5\), NC\((\text{C}_6\text{H}_5)\text{CN}\)

42.5 g. of phenylcyanoacetamide was introduced into a Claisen flask which contained sufficient phosphorus pentachloride to give a ratio of 5 molecules of the amide to 2 of the chloride. The mixture was heated by means of a metal bath until reaction ceased. Hydrogen chloride and phosphorus oxychloride were removed with the aid of a suction pump, and the product was distilled under diminished pressure. The yield was 21 g. or

56.5 per cent of the theoretical. The product melted at 68-69° after crystallisation from ether and petroleum ether.

In a second experiment, 50 g. of the amide was used. The yield of nitrile was 22.5 g.

**Action of Phenyl Magnesium Bromide upon Phenylmalononitrile at the Boiling Point of Ether**

The Grignard reagent was prepared from 3.3 g. of magnesium and 80.6 g. of bromobenzene. An ethereal solution of 3.7 g. of the nitrile was added slowly. A vigorous reaction took place and a bulky white precipitate was formed. The mixture was refluxed for three hours and decomposed with ammonium chloride solution. It was necessary to neutralize the aqueous solution after decomposition in order to completely extract the nitrile which was recovered quantitatively.

**Action of Phenyl Magnesium Bromide upon Phenylmalononitrile at the Boiling Point of Benzene**

An ethereal solution of 7.1 g. of phenylmalononitrile was added to a solution of phenyl magnesium bromide containing 0.4 atom of magnesium. The mixture was refluxed for one hour. Circulation of water through the condenser was discontinued and the ether in the flask was displaced with benzene at a sufficient rate to maintain a constant level. Circulation was started again when the temperature reached 73°, and the mixture was refluxed at this temperature for three hours. The precipitate, which was originally present, went into
Decomposition was effected with ice and concentrated hydrochloric acid. A reddish tar separated. The benzene layer was decanted and the aqueous layer heated on the steam bath for one hour. A mass of white crystals separated. The tar was heated with 1:1 hydrochloric acid and furnished a second crop of crystals which was combined with the first and crystallized from benzene. m.p. 148-149°. A mixed melt with phenyldibenzoylmethane showed no depression. The yield was 5.7 g. (38 per cent of theory).

Phenyldibenzoylmethane Diketimine

The above experiment was repeated except that decomposition of the magnesium derivative was effected with cold ammonium chloride solution. A red solid separated. This was filtered off and washed well with concentrated ammonium chloride solution. The product was crystallized from methyl alcohol and ether. The yield was 3.9 g. or 45 per cent of the theoretical. The compound melted at 167-168° with decomposition.

Analysis of Phenylidibenzoylmethane Diketimine

Calcd. for C_{32}H_{18}N_{2}: C, 84.55; H, 6.06; N, 9.39.

Found - C, 84.62; H, 6.13; N, 9.27.

Hydrolysis of phenylidibenzoylmethane Diketimine

0.85 g. of the diketimine was dissolved in 25 cc. of 20 per cent hydrochloric acid, imparting a reddish color to the solution. Upon heating on the steam bath, the color faded gradually, a colorless solution remaining at the end of an hour, and a mass of colorless crystals separated. These were collected and dried, and when crystallized from benzene and petroleum ether they melted at 149°. A comparison with an authentic sample of phenylidibenzoyl-
methane on hand proved them to be identical. The yield was quantitative.

Zerewitinoff Determination of Active Hydrogen in Phenylmalononitrile

1 m. mole of compound produced .99 m. mole of methane.
1 m. mole of compound consumed 1.02 m. mole of reagent.

Dibenzylcyanoacetamide

This compound was prepared according to the method of Errera. A solution of sodium ethylate from 5.5 g. of sodium and 150 g. of absolute alcohol was added to a warm solution of 10 g. of cyanoacetamide dissolved in 150 cc. of absolute alcohol. The mixture was cooled in an ice bath and treated with 50 g. of benzyl chloride. The solution lost its alkaline reaction after a few minutes and the reaction was completed by heating on the steam bath for one hour. Alcohol was evaporated under diminished pressure yielding a mixture of the amide and sodium chloride. The latter compound was removed by washing with water and the precipitated amide was crystallized from alcohol. The yield was 40 g. or 55 per cent of the theoretical.

Dibenzylmalononitrile, NC(CH₂C₆H₅)₂CN

An intimate mixture of 25 g. of dibenzylcyanoacetamide and the theoretical quantity of phosphorous pentoxide was heated to 170-180° for one hour. The product was extracted with water and the residue crystallized from alcohol. The yield was almost quantitative. m.p. 130°.

(54) Errera, Gazz. chim. ital., 26, 234 (1856).
Action of Phenyl Magnesium Bromide upon Dibenzylmalononitrile at the Boiling Point of Ether

The Grignard reagent was prepared from 22.4 g. of bromobenzene and 3.5 g. of magnesium. A solution of 7.0 g. of the nitrile was added. There was only slight evidence of reaction. The mixture was refluxed for one hour and allowed to stand for twelve. It was the poured slowly with stirring into 30 cc. of concentrated hydrochloric acid and 400 g. of cracked ice. The ether layer was separated and the aqueous layer was extracted with 300 cc. of ether. The combined ether extracts were washed once with 100 cc. of water, dried over calcium chloride and evaporated. The residue crystallized when the flask was immersed in an ice bath. The crystals were washed with petroleum ether and recrystallized several times from methyl alcohol. The yield of dibenzylacetonitrile melting at 92° was 5 g. or 79.5 per cent of theory.

When the aqueous solution was heated, benzophenone, which was present as the hydrochloride of the ketimine, was precipitated. This was extracted with ether. The yield was almost quantitative.

Action of Phenyl Magnesium Bromide upon Dibenzylmalononitrile at the Boiling Point of Benzene

The same quantities of materials were used as in the preceding experiment. An ethereal solution of the nitrile was added to the reagent and the eth r displaced with benzene until the boiling point rose to 70—75°. The solution was refluxed at this temperature for one-half hour. It was allowed to cool and poured with vigorous shaking into a slush of cracked ice and hydrochloric acid. A precipitate of dibenzylacetophenone settled out. This was
collected on a filter, dried and recrystallized from methyl alcohol. m.p. 75°. It was identified by a mixed melting point determination with an authentic sample. The yield was 3.1 g., or 36.6 per cent of the theoretical.

Benzophenone was obtained from the aqueous layer as before.

**Dimethylcyanoacetic Ester**

11.5 g. of sodium was dissolved in 200 cc. of absolute alcohol contained in a 1-liter three-necked flask equipped with a mechanical stirrer, dropping funnel and reflux condenser. The flask was cooled with ice water and the theoretical quantities of ethyl cyanoacetate and methyl iodide were added. The cooling bath was removed and the mixture allowed to stand at room temperature until neutral. This required about one-half hour. A further quantity of 11.5 g. of sodium in 300 cc. of absolute alcohol was added as before. The mixture was heated on the steam bath until neutral. Alcohol was removed in vacuo and the residual liquid was treated with water, extracted with ether, dried, and fractionally distilled. The boiling point was 170-176° at 4-6 mm., and the yield was 41.8 g.

**Dimethylcyanoacetamide**

Errera prepared this amide by alkylating cyanoacetamide with methyl iodide in the presence of sodium ethylate. The following method was found to be more suitable.

41.5 g. of dimethylcyanoacetic ester was poured into 500 cc.

(56) Errera, Gazz. chim. ital., 26, 308 (1896).
concentrated aqueous ammonia. Solution required about twenty hours, and a few drops of undissolved oil still remained at the end of this time. This seemed to be an impurity as it could not be made to go into solution. The ammoniacal solution was decanted, evaporated on the steam bath and cooled. The crystals which separated were collected on a filter and dried. The yield was 14.1 g. or 42.5 per cent of the theoretical.

**Dimethylmalononitrile**$^\text{65}$, NCC(CH$_3$)$_2$CN

An intimate mixture of 14.1 g. of dimethylcyanoacetamide and 10.4 g. of phosphorous pentachloride was placed in a Claisen flask and heated by means of a metal bath. The nitrile distilled readily under the vacuum of a water pump. The yield was 8.4 g. (71 per cent of the theory) m.p. 30-31°.

**Action of Phenyl Magnesium Bromide upon Dimethylmalononitrile**

To a solution of phenyl magnesium bromide containing 8.3 g. of magnesium was added gradually 8.4 g. of the nitrile dissolved in ether. Each drop produced a vigorous reaction, accompanied by a slight precipitate which dissolved immediately. The resulting solution was hydrolyzed at once with iced acid. Needle-like crystals separated, probably the hydrochloride of the diketimine of dimethyldibenzoylmethane. They hydrolyzed rapidly, the product going into the ether layer. The ethereal solution was concentrated and upon addition of petroleum ether 4.3 g. of colorless crystals separated, which when recrystallized from alcohol, melted at 90°. When mixed with an authentic sample of dimethyldibenzoylmethane,

---

the melting point was unaltered. Warming of the aqueous layer caused the separation of 1.3 g. of benzophenone.

**Action of One Mole of Phenyl Magnesium Bromide, Inverse Grignard Reaction upon Dimethylmalononitrile**

In this experiment the operation was reversed and the reaction was carried out below -15°. A solution of phenyl magnesium bromide containing 2 g. of magnesium was added, slowly, to 6 g. of the nitrile dissolved in anhydrous ether. The mixture was allowed to stand for five minutes, and was then decomposed with cold dilute hydrochloric acid. The ether layer gave an oil, which was separated into two fractions by distillation. The first fraction consisted of 5.1 g. of a liquid boiling at 185-189°, and was identified as benzonitrile by hydrolyzing the product to benzamide. The second fraction, boiling at 104-109° contained 1.1 g. of isobutyronitrile, which was converted to the corresponding amide for purposes of identification.

**Diphenylacetonitrile**

The nitrile was prepared from the amide, which in turn was prepared from the acid chloride. No difficulties were experienced with these preparations and the yields corresponded to those reported in the literature.

**Action of Cyanogen Bromide upon the Sodium Salt of Diphenylacetonitrile**

5 g. (.0359 mole) of the nitrile was dissolved in 150 cc. of

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(57) Neure, Ann., 250, 142 (1888).
(58) Klingeman, Ann., 275, 84 (1883).
Absolute ether contained in a three-necked flask equipped with a stirrer, reflux condenser and dropping funnel. The sodium salt was prepared by adding 1.5 g. of sodamide and refluxing for three hours. An etheral solution of .0259 mole of cyanogen bromide was then added. A bulky white solid separated. The mixture was refluxed for fifteen minutes and treated with 200 cc. of water. The solid was collected on a filter and crystallized from benzene and ether. mp. 169-172°C. Fractional crystallization showed at least two compounds to be present. One melted at 169-172°C, and the other melted higher but was not obtained pure. Analysis showed a much greater amount of carbon in the 170° compound than corresponds to diphenylmalononitrile.

Calcd. for C_{13}H_{10}N_{2}: C, 82.57; H, 4.59. Found: C, 89.97; H, 5.56.

Action of Mercuric Cyanide upon Diphenylchloroacetamide.

A mixture of 3.3 g. of the amide and 3.4 g. of the cyanide was heated for 24 hours at 115-120°C. The resulting mass was extracted with chloroform to separate the organic compounds and the chloroform solution was evaporated. A mixture of several substances was obtained, none of which could be isolated in the pure state.

Diphenylmalonic Acid, (C_{6}H_{5})_{2}C(CO_{2}H)_{2}

Several runs were made to determine the optimum conditions for this preparation. Two of these will be described to illustrate the effect of temperature upon the yield of acid.

Preparation at Room Temperature

The reaction was carried out in the usual Grignard apparatus.
under an atmosphere of pure dry nitrogen.

30 g. of sodium was cut in the form of chips approximately 1 cm. square and 1 mm. thick. These were placed in the flask with 10 g. of diphenylmethane and 200 cc. of petroleum ether. The flask was flushed out with nitrogen and 35 g. of amyl chloride was run in over a period of two hours. Reaction began immediately and the solution became quite green. However, the color gradually changed to a deep yellow. After standing overnight, 50 cc. of dry ether was added and the product carbonated with dry carbon dioxide gas. The yellow color disappeared in the course of about fifteen minutes leaving a colorless suspension of sodium salts. The suspension was separated from the sodium chips by pouring the contents of the flask into an open filter funnel which readily allowed the ethereal suspension to drain through into a flask below. The suspension was shaken with 500 cc. of water and the ether layer separated and discarded. The aqueous layer was cooled and carefully acidified with dilute sulfuric acid. A mixture of 0.4 g. of diphenylmalonic acid and 1.2 g. of diphenylacetic acid separated. The acids were filtered off, and the water layer was extracted with three 50 cc. portions of ether. The extract was dried with calcium chloride and evaporated to a volume of about 5 cc. in vacuo. Addition of petroleum ether precipitated 0.5 g. of almost pure diphenylmalonic acid, which was identified by the neutral equivalent and the preparation of the methyl ester, acid chloride and acid amide.

Preparation at 0°

The yield was considerably increased by carrying out the reaction
At 0°. The same quantities of reagents were used as in the preceding experiment.

The sodium chips, diphenylmethane and petroleum ether were placed in the flask which was cooled with a bath of ice and concentrated hydrochloric acid. Amyl chloride was added at such a rate that the temperature was maintained at 0°. This required about two hours. When all of the amyl chloride was added, the bath was removed and the stirrers allowed to operate for about three hours longer. Then the mixture was allowed to stand overnight. 50 cc. of dry ether was added to destroy any amyl sodium present and the product was carbonated with dry carbon dioxide gas. The suspension of sodium salts was decanted and treated with 500 cc. of water. The ether layer was discarded and the aqueous layer cooled and carefully acidified with dilute sulfuric acid.

The acid solution was extracted with three 50 cc. portions of ether; the ether evaporated in vacuo and the solid residue extracted three times with 100 cc. portions of benzene. Diphenylmalonic acid is much less soluble in benzene than diphenylacetic acid; hence this property offers a convenient method for the separation of the two compounds. The residue was dissolved in the smallest possible amount of ether and precipitated by addition of petroleum ether. The yield of pure diphenylmalonic acid was 3.6 g. Naut. equiv. Caled: 138. Found: 130.

0.12 g. of the acid was methylated with diazomethane. The yield of dimethyl ester melting at 85-84° amounted to 0.09 g.

Diphenylmalonyl Dichloride, \((C_6H_5)_2C(COCl)_2\)

Thionyl chloride is too inactive to react with diphenyl-
Malonic acid at low temperatures, and the sole product is diphenylacetyl chloride at high temperatures. Phosphorous pentachloride reacts readily, however, to give a good yield of diphenylmalonyl dichloride.

An intimate mixture of 3.6 g. of diphenylmalonic acid and 6.0 g. of phosphorous pentachloride was placed in a flask with 5 cc. of benzene. The latter acted only as a solvent. Reaction began immediately at room temperature and was almost complete after 1.5 hours. The diphenylmalonic acid went into solution and the reaction was completed by heating on the steam bath for 30 minutes. The solvent and phosphorous oxychloride were removed with the aid of a suction pump and the residue was distilled. The yield of diphenylmalonyl dichloride, boiling at 160° under 2 mm. pressure, amounted to 3.3 g. It is not advisable to attempt the distillation of large amount of the acid chloride because of its tendency to decompose.

**Diphenylmalonoamide**\(^{59}\), \((C_6H_5)_2C(CONH_2)\_2\)

10.5 g. of diphenylmalonoamide was dissolved in anhydrous ether and treated with an excess of gaseous ammonia. A precipitate separated immediately, which was collected on a filter and extracted with water. The residue was crystallized from ethyl alcohol. The yield of diamide was 3.3 g. m.p. 243°.

**Diphenylmalononitrile**, \((C_6H_5)_2C(CH_2)\_2\)

A mixture of 3.3 g. of diphenylmalonoamide and 5.5 g. of phosphorous pentachloride was placed in a balloon flask and

heated gently with a free flame. A reaction began immediately and the mixture soon liquified. Gentle heating was continued for 30 minutes. The product was triturated with water and the residue crystallized from methyl alcohol. The yield of dinitrile was 0.5 g. m.p. 86-87°C. It crystallizes in long colorless needles.

**Analysis of Diphenylmalononitrile**

Calcd. for C₁₆H₁₈N₂: C, 82.53; H, 4.63; N, 12.86.

  Found : C, 82.27; H, 4.84; N, 12.73.

**Action of Phenyl Magnesium Bromide upon Diphenylmalononitrile**

An ethereal solution of 1.1 g. of the dinitrile was added to a solution of phenyl magnesium bromide prepared from 4.0 g. of bromobenzene and 1.0 g. (an excess) of magnesium. Some heat was allowed to stand for 12 hours and hydrolyzed with ice and hydrochloric acid. The ether layer furnished 0.7 g. of diphenylacetonitrile. m.p. 75-76°C. A mixed melting point with an authentic sample showed no depression. The aqueous layer yielded 0.1 g. of benzophenone when it was warmed and extracted with ether.
EXPERIMENTAL

PART II. THE BETA-HYDROXY KTONES
Hydracetylaceitone, $\text{CH}_3\text{CH(OH)}\text{CH}_2\text{C} = \text{CH}_2$

105 g. of acetone was cooled to $-12^\circ$ and treated with 5 g. of KCN dissolved in 10 cc. of water. The solution was stirred vigorously and 40 g. of freshly distilled acetaldehyde poured in. After standing for thirty minutes, 75 cc. of alcohol-free ether was added to precipitate the KCN. Claisen recommends that the reaction product be allowed to stand for 7 hours in the ice box before adding ether, but it was found advantageous to proceed immediately as there is less tendency to form resinous products. The ether layer was separated from the aqueous potassium cyanide layer and washed twice with saturated sodium chloride solution, dried over calcium chloride, and distilled. There was obtained 10 g. of the compound boiling at 77-79$^\circ$ at 20 mm.

Action of Phenyl Magnesium Bromide upon Hydracetylaceitone

The Grignard reagent was prepared from 39.2 g. of bromobenzene and 6.7 g. of magnesium. It was filtered through glass wool before use.

An ethereal solution of 5.1 g. of hydracetylaceitone was added slowly through the dropping funnel. Each drop caused the formation of a precipitate which eventually dissolved. After all of the compound had been added, the solution was allowed to stand for one hour. The magnesium complex was decomposed with ammonium chloride and ice and the ether layer worked up in the customary manner. There was obtained 3.6 g. of liquid boiling at 16-140$^\circ$ which was shown to be the glycol by analysis. The yield was 40 per

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(60) Claisen, Ann., 306, 324 (1889).
cent of the theoretical. The compound is a colorless, very viscous liquid which resisted all attempts to crystallize it.

**Analysis of the Glycol**

Calcd. for C$_{11}$H$_{16}$O$_2$: C, 73.33; H, 8.80. Found: C, 73.18; H, 9.03.

Diacetone Alcohol, (CH$_3$)$_2$C(OH)CH$_2$COCH$_3$

Diacetone alcohol was prepared according to the method described in *Organic Syntheses*\(^{(1)}\) and was freshly distilled before use. The boiling point was 73-74° under 3 mm. pressure.

**Action of Phenyl Magnesium Bromide upon Diacetone Alcohol**

An ethereal solution of 7.5 g. of diacetone alcohol was added slowly to a solution of phenyl magnesium bromide prepared from 7.9 g. of magnesium. There was a vigorous reaction, after which the solution was refluxed for a short time and allowed to stand at room temperature for several hours. The magnesium complex was decomposed with ammonium chloride and ice and the ether evaporated under diminished pressure. The residue was distilled at 3 mm. pressure. Diphenyl came over first, and then 7.7 g. of compound boiling at 115-118°, which solidified to a colorless crystalline mass. The yield was 61.5 per cent of the theoretical, and the compound melted at 51-52°.

**Analysis of the Glycol, or 54°-56° Compound**

Calcd. for C$_{12}$H$_{18}$O$_2$: C, 74.17; H, 9.35. Found: C, 74.30; H, 9.36.

**Action of Phenyl Magnesium Bromide upon Diacetone Alcohol, Inverse Addition of the Reagent**

The experiment immediately preceding this one was repeated except that the amount of diacetoalcohol was increased to twenty grams, and exactly one mole of phenyl magnesium bromide was added to it. Actually, no acetone could be isolated, but only diacetoalcohol and the glycol.

1,3-diphenyl-3-hydroxy-1-butane $^{62}$, C$_6$H$_5$-(CH$_3$)C(OH)CH$_2$COC$_6$H$_5$ (I)

The method of preparation was that developed by Colonge. The condensing agent was prepared by adding 35 g. of methyl aniline to a Grignard reagent made from 50 g. of ethyl bromide, 6 g. of magnesium and 120 cc. of anhydrous ether. The solution was filtered through a plug of glass wool into a flask which contained 0.67 mole of acetophenone and 180 cc. of benzene. The resulting mixture was allowed to stand for one hour, and was then treated with the theoretical amount of hydrochloric acid. The ether layer was separated, washed with water, and dried over sodium sulfate. Ether and benzene were removed under a vacuum of 1 mm. to remove acetophenone. The residue was dissolved in petroleum ether and cooled. Crystals were deposited after some time which melted at 59-60°. The yield was 18 g.

Action of Phenyl Magnesium Bromide upon (I), Inverse Addition of the Reagent

An ethereal solution of phenyl magnesium bromide which contained 2.5 g. of magnesium was filtered into a dropping funnel and added drop by drop to an ethereal solution of (I). A white granular

precipitate was formed. The solution was allowed to stand for two hours and then hydrolyzed with ice and ammonium chloride. The ether layer was evaporated and the residue, when vacuum distilled, gave 0.5 g. of a product which was proved to be acetophenone. A higher boiling fraction consisted of 2.5 g. of diphenylmethyl carbinol which distilled at 128-130°. The latter compound was identified by comparison with an authentic sample, and the acetophenone was identified by the preparation of its semicarbazone which melted at 201°.

**Action of Phenyl Magnesium Bromide upon (I)**

In a second experiment, an etheral solution of 5.0 g. (0.0308 mole) of (I) was added to a solution of phenyl magnesium bromide which contained 2.5 g. (60.104 atom) of magnesium. There was a vigorous reaction accompanied by the formation of a precipitate which eventually dissolved. The mixture was allowed to stand for two hours and then decomposed with ammonium chloride and ice. The ether layer was separated and worked up in the usual manner. There was obtained 2.4 g. of diphenylmethyl carbinol, melting at 80-81°, as the sole product. A mixed melting point determination with an authentic sample showed no depression. No other product was isolated.

**9-hydroxy-9-fluorenyl-α-acetophenone**, *(C₆H₄)_αC(OH)CH₂COC₆H₅* (II)

The condensing agent was prepared as in the preceding experiment from 6.0 g. of methyl aniline, 6.1 g. of ethyl bromide and 1.5 g. of magnesium. It was then filtered into a flask

containing 10 g. of fluorenolone and 6.7 g. of acetophenone. The mixture was allowed to stand with stirring for two hours and then hydrolyzed with 18 cc. of concentrated hydrochloric acid and ice. After working up the products in the usual way, there was obtained 2.5 g. of the hydroxy ketone melting at 112°.

**Action of Phenyl Magnesium Bromide upon (II)**

2.5 g. of (II) was added to the filtered solution of phenyl magnesium bromide prepared from 7.0 g. of bromobenzene and an excess of magnesium. The solution was poured into ice and ammonium chloride after stirring for one hour. The ether layer was separated, washed, dried, and concentrated under diminished pressure. The addition of petroleum ether caused the separation of an oil which crystallized on standing. The product formed white crystals which melted at 95—96°. Analysis showed it to be the glycol. The yield was 2.5 g. or 79 per cent of the theoretical.

**Analysis of the 95—96° Compound**

Calcd. for C_{17}H_{22}O_2: C, 85.72; H, 5.82. Found: C, 85.56; H, 5.71.

**2,2-dimethyl-5,5-diphenyl-5-hydroxy-2-pentanone**

(C₈H₅)₂C(OH)CH₂COC(CH₃)₂ (III)

The condensing agent was prepared from 30.1 g. of methyl aniline, 34.0 g. of ethyl bromide and 8.5 g. of magnesium. 51 g. of benzophenone was dissolved in 100 cc. of benzene and the condensing agent added to it. This solution was then treated with 28.2 g. of pinacolin and allowed to stand for 24 hours. It was then hydrolyzed with the theoretical quantity of hydrochloric

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acid. The solvents were separated, and the product was worked up in the usual way. A semi-solid residue was obtained which was triturated with petroleum ether and allowed to crystallize spontaneously. The yield was 2.0 g. melting t 102°.

**Action of Phenyl Magnesium Bromide upon (III)**

The Grignard reagent was prepared from 5.6 g. of bromobenzene and 1.0 g. of magnesium. It was filtered as usual, and 2.0 g. of (III) was added to it in the solid state. There was a vigorous reaction. The product was allowed to stand for four hours, and was then decomposed with ice and ammonium chloride. 1.5 g. of the starting material was recovered. No other product was found.

**Zerewitinoff Determination of Active Hydrogen in (III)**

1 m. mole of compound produced 1.78 m. mole of methane.

**2,5-dimethyl-9-hydroxy-9-l-fluroeny-2-butanone**

\[(C_6H_4)_2C(OH)CH_2COC(CH_3)_3 \text{ (IV)}\]

The condensing agent was prepared from 14.9 g. of methyl aniline, 15.2 g. of ethyl bromide, and 3.7 g. of magnesium. This was added to a solution of 25.0 g. of fluorenone in benzene. 15.0 g. of pinacolin was added immediately, and the product was allowed to stand for sixteen hours. Hydrolysis was effected with ice and the theoretical quantity of hydrochloric acid. The acid solution was discarded, and the benzene layer was washed with water, dried over calcium chloride, and evaporated under diminished pressure. The residue was crystallized from petroleum ether. 12.0 g. of the compound was obtained which melted at 95-97°.

Action of Phenyl Magnesium Bromide upon (IV)

6.0 g. of (IV) was dissolved in ether and added to a solution of phenyl magnesium bromide prepared from 17.0 g. of bromobenzene and 3.0 g. of magnesium. No precipitate was formed, but the Grignard solution became quite fluorescent. Hydrolysis was effected with ice and ammonium chloride. All but 0.3 g. of the starting material was recovered.

Zerewitinoff Determination of Active Hydrogen in (IV)
1 m. mole of compound produced 1.07 m. mole of methane.

Attempted Alkylation of Diphenylacetophenone with Diphenylmethyl Bromide

11.0 g. of diphenylacetophenone was added to a solution of sodium ethylate prepared from 1.0 g. of sodium and 100 cc. of absolute alcohol. A solution of 10.0 g. of diphenylmethyl bromide in absolute alcohol was then added, and the mixture was refluxed on the steam bath until neutral. Only diphenylacetophenone (9.0 g.) was obtained when the product was worked up.

Friedel Crafts Reaction with Diphenylmalonyl Dichloride in Benzene

Aluminum chloride (3.5 g.) was added in small portions to a solution of 6.0 g. of the acid chloride dissolved in 10 cc. of dry benzene. There was immediate reaction and a large quantity of hydrogen chloride was evolved. The product was heated for one hour to complete the reaction, and was hydrolyzed with ice and isolated. It was evident that extensive decomposition had taken place.
Friedel Crafts Reaction with Benzene and Diphenylmalonyl Dichloride in Nitrobenzene Solution

4.7 g. of aluminum chloride was added to a mixture of 15 cc. of nitrobenzene and 10 cc. of dry benzene. Diphenylmalonyl dichloride (5.0 g.) was then added. There was no spontaneous reaction at room temperature, but hydrogen chloride was slowly evolved when the mixture was heated to 60°. The product was decomposed with ice and concentrated hydrochloric acid after heating for three hours. No crystalline compound could be found, but only a tar similar to that previously obtained.
SUMMARY
The reactions between phenyl magnesium bromide and several malononitriles and beta-hydroxy ketones have been studied.

Dibenzylmalononitrile and diphenylmalononitrile add one equivalent of reagent to yield a magnesium compound, which decomposes into two cleavage products; each subsequently then consumes one equivalent of the reagent. Dimethylmalononitrile behaves in a similar manner.

Phenylmalononitrile consumes three equivalents of reagent to form an addition product.

Malononitrile forms an insoluble magnesium compound from which the former is recovered upon hydrolysis.

Addition of the reagent to a ketene imine linkage is described.

Hydracetylacetone and 9-hydroxy-9-fluorenyl-ω-acetophenone undergo normal addition to the carbonyl group and furnish the corresponding glycols.

Diacetone alcohol undergoes both cleavage and addition. Only cleavage products are obtained from 1,3-diphenyl-3-hydroxy-1-butanolone.

Magnesium enolates are obtained with 2,2-dimethyl-5,5-diphenyl-5-hydroxy-3-pentanone and 3,3-dimethyl-9-hydroxy-9,1-fluorenyl-2-butanolone which are not susceptible to cleavage.

A synthesis of diphenylmalonic acid and diphenylmalononitrile is described.
(1) Zelinsky, Ber., 35, 2138 (1902).
(2) Grignard, Compt. rend., 134, 849 (1902).
(4) Zerewitinoff, Ber., 41, 2243 (1908).
(6) Wedekind and Miller, Ber., 44, 3285 (1911).
(7) Vorlander, Osterburg and Meye, ibid., 56, 1140 (1931).
(8) Dilthey and Last, ibid., 37, 2639 (1904).
(10) Sabatier and Mailhe, Compt. rend., 144, 1086 (1907).
(13) Sprague and Adkins, ibid., 56, 2669 (1934).
(14) Beckham and Adkins, ibid., 56, 2676 (1934).
(15) Adkins, Kutz and Coffman, ibid., 52, 4036 (1930).
(16) Kutz and Adkins, ibid., 52, 3212 (1930).
(17) Beckham and Adkins, ibid., 56, 1119 (1934).
(18) Kohler, Richtmyer and Hester, ibid., 53, 205 (1931).
(19) Bergmann and Wolff, ibid., 54, 1644 (1932).
(20) Bickel, ibid., 59, 325 (1937).
(21) Kohler and Bickel, ibid., 57, 1073 (1935).
(22) Franke and Kohn, Ber., 37, 4730 (1904).
(23) Franke and Kohn, Monatsh., 28, 397 (1907).
(24) Franke and Kohn, ibid., 27, 1097 (1906).
(26) Abelmann, Ber., 42, 2500 (1909).
(30) McKenzie and Martin, ibid., 103, 112 (1913).
(31) Jacquemain, Compt. rend., 199, 1315 (1934).
(32) Valeur, ibid., 162, 833 (1901).
(33) Vorlander and Siebert, Ber., 39, 1035 (1906).
(37) Blaise, Compt. rend., 132, 978 (1901).
(38) Mavrodin, ibid., 188, 1504 (1929).
(39) Mavrodin, ibid., 191, 1064 (1931).
(40) Grignard, ibid., 187, 1026 (1928).
(43) Erickson and Coffman, Unpublished Work.
(45) Schmidt, Ber., 67, 1780 (1934); 68, 60 (1935); 69, 795 (1935);
22, 47 (1933).
(48) Staudinger, Ber., 47, 44 (1914).
(49) Schroter, ibid., 48, 2648 (1909).
(54) Errera, Gazz. chim. ital., 26, 224 (1896).
(56) Errera, Gazz. chim. ital., 26, 208 (1896).
(57) Neure, Ann., 250, 142 (1888).
(58) Klingemann, ibid., 273, 84 (1893).
(60) Claisen, Ann., 306, 324 (1899).
BIOGRAPHY
Maxwell McClelland Barnett was born April 19, 1915 at Lake Charles, Louisiana. At an early age he moved to Baton Rouge, Louisiana where he attended the public schools. In 1929 he was graduated from Baton Rouge Senior High School, and in the fall of the same year he entered Louisiana State University. He received the degree of B.S. in chemical engineering in June 1933, and in September began work leading to the degree of Master of Science. During the course of this work he was appointed to a teaching fellowship in chemistry. He received the M.S. degree from Louisiana State University in August 1934. He spent the 1934-35 session at Louisiana State University, the 1935-36 session at Iowa State College, and the 1936-37 session at Louisiana State University. During these three years, he worked toward the degree of Doctor of Philosophy.
Various types of compounds are known to undergo cleavage when treated with organic magnesium compounds. The object of this work was to determine whether or not such a reaction takes place with the malononitriles and beta-hydroxy ketones - compounds which are of a type which may be expected to cleave.

Five malononitriles were treated with phenyl magnesium bromide: malononitrile, NC-CH$_2$-CN (I), phenylmalononitrile, NC-CH(C$_6$H$_5$)-CN (II), dimethyl malononitrile, NC-C(CH$_3$)$_2$-CN (III), dibenzylmalononitrile, NC-C(CH$_2$C$_6$H$_5$)$_2$-CN (IV), and diphenylmalononitrile, NC-C(C$_6$H$_5$)$_2$-CN (V). A rapid and convenient synthesis of diphenylmalonic acid from diphenylmethane was developed for the preparation of (V).

Benzophenone and dibenzylacetonitrile were obtained as cleavage products when dibenzylmalononitrile was added to an ethereal solution of phenyl magnesium bromide. The first step in the reaction is addition of the reagent to one of the nitrile groups. The resulting magnesium compound is unstable, and decomposes immediately in a manner presumably like that of the magnesium derivatives from beta-diketones.

\[
\begin{align*}
\text{NC-CH}_2\text{CN} & \quad \text{NC-C-CN} \quad \text{C}_6\text{H}_5\text{C} \quad \text{C-CN} \quad (\text{C}_6\text{H}_5\text{CH}_2)_2\text{C}=\text{C}=\text{NMgBr} (\text{VI}) \\
\text{CH}_2\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5\text{C} \quad \text{CH}_2\text{C}_6\text{H}_5 \\
\text{CH}_2\text{C}_6\text{H}_5 & \quad \text{NMgBr} \quad \text{CH}_2\text{C}_6\text{H}_5
\end{align*}
\]

An examination of the structure of the ketene imine cleavage
product (VI) shows that it possesses a twinned double linkage, not unlike that found in ketenes. If the reaction is carried out in ether, (VI) survives for an almost indefinite length of time in the presence of an excess of phenyl magnesium bromide, while benzonitrile, the other cleavage product, reacts with more of the reagent. The magnesium derivatives of ketene imines presumably react in a very sluggish manner, as this is apparently the end of the process. Yet from general considerations, one would expect this ketene imine to be capable of further reaction with phenyl magnesium bromide, and such was found to be the case. Upon replacing the ether with benzene and operating at a higher temperature, both (VI) and benzonitrile consume more of the reagent to give, upon hydrolysis, excellent yields of dibenzylacetophenone and benzophenone.

\[
\begin{align*}
(C_6H_5CH_2)_2C=CMgBr & \rightarrow (C_6H_5CH_2)_2C=N(MgBr)_2 \\
(C_6H_5CH_2)_2C=CH-C=NH & \rightarrow (C_6H_5CH_2)_2CH-C=O
\end{align*}
\]

The extent to which cleavage occurs depends entirely upon the stability of the primary Grignard addition product. The extreme ease with which these magnesium compounds decompose is indeed surprising. If decomposition takes place at all, it usually does so immediately. However, when dimethyldimethyldialkylether-
nitrile is added to an ethereal solution of phenyl magnesium bromide in the usual manner, cleavage is almost entirely avoided, as the product consists almost wholly of the diketimine of dimethyldibenzoylmethane, with only a trace of benzophenone imine, but when, inversely, the compound is added to but one equivalent of reagent, only the cleavage products, benzonitrile and isobutyronitrile are obtained, thus affording additional evidence as to the manner in which fission of the molecule occurs.

\[
\begin{align*}
&\text{CH}_3 \\
\text{C}_6\text{H}_5\text{C} - \text{C-CN} \quad \text{C}_6\text{H}_5\text{C} - \text{C-CN} \quad \text{C}_6\text{H}_5\text{CN} + (\text{CH}_3)_2\text{C} = \text{C} = \text{NMgBr} \\
&\quad \text{NMgBr} \quad \text{NMgBr} \\
&\quad \text{NMgBr} \quad \text{NMgBr}
\end{align*}
\]

The extent to which the molecule is cleaved, therefore, depends upon the relative rates of decomposition of the primary magnesium derivative and of addition of more reagent to the unattacked cyanide group.

Diphenylmalononitrile is apparently completely cleaved. In this case the products are diphenylacetonitrile and benzophenone.
With the monosubstitution products of malononitrile, the outcome is quite definite, but entirely different. Upon adding phenylmalononitrile (II) to an ethereal solution of phenyl magnesium bromide, all of the material is recovered. Quantitative determinations, however, show that it liberates one mole of methane. If the operation is carried out at an elevated temperature, three equivalents of reagent are consumed, and it becomes possible to secure a good yield of a red crystalline compound which proved to be the diketimine of phenyldibenzoylmethane. The reaction then must be represented as follows:

\[
\begin{align*}
\text{NC-CH-CN} & \rightarrow \text{NC-C=NMgBr} \rightarrow \text{C}_6\text{H}_5 \text{C}=\text{C}=\text{C-N(1gBr)}_2 \rightarrow \\
\text{C}_6\text{H}_5 \text{C}=\text{C}=\text{C-N(1gBr)}_2 & \rightarrow \text{C}_6\text{H}_5 \text{C}=\text{C}=\text{C-N(1gBr)}_2 \\
\text{C}_6\text{H}_5 \text{C}=\text{C}=\text{C-N(1gBr)}_2 & \rightarrow \text{C}_6\text{H}_5 \text{C}=\text{C}=\text{C-N(1gBr)}_2 \\
\end{align*}
\]

Strangely enough, the simplest member of the series, malononitrile itself, forms no addition product with phenyl magnesium bromide. Instead, an insoluble magnesium derivative is obtained which stubbornly resists further action of a liberal excess of the reagent, even when the reaction is carried out at 75°, and
for a period of several hours. Upon hydrolysis, an almost quantitative yield of malononitrile is recovered. The reasons for the abnormal behaviour of malononitrile are not apparent.

Six beta-hydroxy ketones were studied: hydracetylacetone, $\text{CH}_2\text{COCH}_2\text{CH(OH)CH}_3$ (VII), diacetone alcohol, $\text{CH}_3\text{COCH}_2\text{C(OH)(CH}_3)_3$ (VIII), 1,3-diphenyl-3-hydroxy-1-butane, $\text{C}_6\text{H}_5(\text{CH}_3)\text{C(OH)CH}_2\text{COC}_6\text{H}_5$ (IX), 2,2-dimethyl-5,5-diphenyl-5-hydroxy-3-pentanone, $(\text{C}_6\text{H}_5)_2\text{C(OH)CH}_2\text{COC}(\text{CH}_3)_3$ (X), 3,3-dimethyl-9-hydroxy-9,1-fluorenyl-3-butane, $(\text{C}_6\text{H}_5)_2\text{C(OH)CH}_2\text{COC(\text{CH}_3)_3}$ (XI), and 9-hydroxy-9-fluorenyl-ω-acetophenone, $(\text{C}_6\text{H}_5)_2\text{C(OH)CH}_2\text{COC}_6\text{H}_5$ (XII).

Hydracetylacetone is not cleaved, but reacts normally to furnish the corresponding glycol, as does (XII).

Diacetone alcohol undergoes both normal addition and cleavage, depending upon the conditions of the experiment. In the former
case the product is a glycol; in the latter acetone and dimethylphenyl carbinol are formed.

\[
\begin{align*}
(CH_3)_2C-CH_2-C-CH_3 & \xrightarrow{OMgBr} (CH_3)_2C-CH_2-C-CH_3 & (CH_3)_2C-CH_2-C(CH_3)C_6H_5 \\
(CH_3)_2C(CH_3)C_6H_5 & \xrightarrow{OMgBr} (CH_3)_2CO + CH_3C=CH_2 & (CH_3)_2C-CH_2-C(CH_3)C_6H_5
\end{align*}
\]

Compound (IX) undergoes cleavage exclusively.

\[
\begin{align*}
C_6H_5(CH_3)C-CH_2-C-C_6H_5 & \xrightarrow{OMgBr} C_6H_5(CH_3)C-CH_2-C-C_6H_5 \\
(CH_3)_2CO + CH_2=C-C_6H_5 & \xrightarrow{OMgBr} (CH_3)_2C(CH_3)C_6H_5
\end{align*}
\]

Compounds (X) and (XI) reacted in the enol form to yield magnesium derivatives of a type which cannot cleave.
It is probable that the steric hindrance around the carbonyl oxygen atom is so great that addition of the reagent is impossible. In agreement with the above mechanism, quantitative determinations with methyl magnesium iodide show the presence of two active hydrogen atoms in each molecule.
Louisiana State University

The Graduate School

Thesis Report

Name of Candidate: Maxwell M. Barnett

Major Field: Organic Chemistry

Title of Thesis: Cleavage by Organic Magnesium Compounds.

I. The Cleavage of Malononitriles. II. The Cleavage of Beta Hydroxy Ketones.

Approved:

J. E. Einhorn
Major Professor and Chairman

Charles W. Pipke
Dean of the Graduate School

Examinining Committee:

E. A. Fugita

A. C. Elphick

P. J. Robichaux

J. M. Horton

Jesse Brates

O. E. Croft

Arthur Stenhouse

Lloyd W. Morris

Richard C. Keen

R. L. Mervill

M. S. Sturdivant

Date: May 8, 1937