SYNTHESIS OF ALKYL ARYL PINACOLS

USING MAGNESIUM AND IODINE

By

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THESIS AND ABSTRACT APPROVED:

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A C K N O W L E D G M E N T

The author wishes to express his sincere gratitude to Dr. Ernest M. Hodnett, upon whose suggestion and under whose direction this work has been carried out.

He also wishes to acknowledge the work done by his wife and members of the chemistry staff of Oklahoma A. and M. College for proof-reading this thesis.
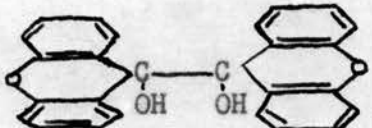
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INTRODUCTION

This work was undertaken in an attempt to synthesize some mixed pinacols by treating certain mixed ketones with magnesium and magnesium iodide in organic solvents. No record of pinacols prepared in this manner was found in the literature.
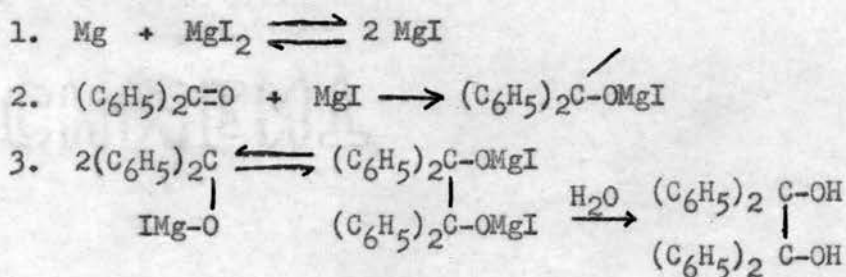
The hope of the author was ultimately to prepare some of the synthetic estrogens via the pinacol reduction of certain mixed ketones, this to be followed by dehydration of the pinacol and also demethylation when applicable.

HISTORICAL DISCUSSION

Bachmann (6), using the magnesium and iodine mixture in organic solvents, prepared a number of symmetrical aromatic pinacols. A partial list of these pinacols, along with the ketone they were prepared from, and the yields obtained follow:

Ketone	Pinacol	% Yield
Benzophenone	$(C_6H_5)_2C\text{---}C(C_6H_5)_2$ $\quad\quad\quad\;$ OH OH	99.6
4-Methylbenzophenone	$CH_3C_6H_4\diagdown$ $\diagup C_6H_4CH_3$ $\quad\quad\;\; C\text{---}C$ $\quad\quad\;\; /\; |\quad|\;\; C_6H_5$ $C_6H_5\;\; OH\; OH$	98
4,4'-Dimethylbenzophenone	$(CH_3C_6H_4)_2C\text{---}C(C_6H_4CH_3)_2$ $\quad\quad\quad\quad\;\;$ OH OH	94
Xanthone		92

The mechanism of the reactions involved in this work as typified by benzophenone follows:

1. $Mg + MgI_2 \rightleftharpoons 2\, MgI$

2. $(C_6H_5)_2C{=}O + MgI \longrightarrow (C_6H_5)_2C\text{-}OMgI$

3. $2(C_6H_5)_2C \rightleftharpoons (C_6H_5)_2C\text{-}OMgI$
$\quad\quad |$
$\quad\quad IMg\text{-}O \quad\quad (C_6H_5)_2C\text{-}OMgI \xrightarrow{H_2O} (C_6H_5)_2\;\; C\text{-}OH$
$\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad (C_6H_5)_2\;\; C\text{-}OH$

Other methods of preparing the pinacols studied in this work have been used. 2,3-Diphenyl-2,3-butanediol has been prepared by reduction of

acetophenone in isopropyl alcohol by letting the solution stand in the sun-
light for one month (8). This method is preferred to that of the action of
methylmagnesium iodide on benzil (1).

A 52% yield of the pinacol has been reported from the action of methyl-
magnesium iodide on benzil (3).

2,3-Diphenyl-2,3-butanediol was obtained in 43% yield when diacetyl in
ether was added to an ice-cold solution of phenylmagnesium bromide (14).

Acetophenone was reduced electrolytically in alkaline solution at many
different cathodes. The effect of the surface of the cathode material was
studied. The main product of the reduction was the pinacol (12).

In the condensation of ethyl dichloroacetate with acetophenone, accord-
ing to Darzens (4), 2,3-diphenyl-2,3-butanediol was obtained as a by-product
with yields of five to ten percent. Ethyl α-chloro-β-hydroxy-β-phenyl-
butyrate is the main product of this reaction.

Both low-melting (122-123°) and high-melting (168-169°) forms of
2,3-bis-(p-methoxyphenyl)-2,3-butanediol (9) have been prepared by the
electrolytic reduction of p-methoxyacetophenone in an alkaline aqueous medium
at the refluxing temperature and 110 volts. The high-melting isomer, was
also prepared by reduction of the ketone with aluminum amalgam in moist ether.

Both pinacols to be prepared in this work exist in two isomeric forms
of different melting points (9) (13).

PRELIMINARY DISCUSSION

Unsymmetrical ketones were selected for the preparation of certain pinacols in an attempt to obtain eventually synthetic estrogens related to stilbestrol. Runs were attempted using p-methoxyacetophenone and then acetophenone. p-Methoxyacetophenone had to be synthesized, while acetophenone was readily available. The greatest emphasis in this investigation was upon the method of synthesis of a particular compound; however, some qualitative analyses were made in order to determine the extent of side reactions occurring. Variations made in experimental conditions included a change of solvents between pure benzene and ether-benzene solution, change in temperature of the system, change in contact time and hydrolysis procedures. Different solvents were also used in extraction.

EXPERIMENTAL

PRELIMINARY EXPERIMENTS

I. Preparation of Benzopinacol.

Materials used:

15 g. (0.62 g. atom) of powdered magnesium

100 cc. of ether, distilled from sodium

200 cc. of benzene

42 g. (0.33 g. atom) of iodine, dried over sulfuric acid

54.6 g. (0.3 mole) of benzophenone

The method used for this preparation is the same as that described by Gomberg and Bachmann (6). One hundred cubic centimeters of ether and 150 cc. of benzene were added to the powdered magnesium. To this mixture in the 500-cc. flask iodine was added in portions of several grams at intervals so as to keep the solution refluxing (under a calcium chloride guard tube) quite vigorously. The light-red solution of the magnesium salt was cooled and to it was added a solution of the benzophenone in 50 cc. of warm benzene. The heavy white precipitate of the ketone-magnesium iodide addition complex filled the flask. The flask was stoppered and shaken for 15 minutes. During this time the precipitate disappeared and a deep-red solution resulted. The complete disappearance of the precipitate indicated the reduction to be practically complete. When the flask was shaken for too long a time, the iodomagnesium pinacolate precipitated upon the metallic magnesium, making subsequent separation difficult. After the magnesium settled, the solution was filtered from the excess metal, the magnesium remaining was washed with a mixture of ether and benzene and this wash solution was filtered and added

to the main portion. Water was added to the solution of the pinacolate. The magnesium hydroxide formed in the hydrolysis was dissolved by the addition of dilute hydrochloric acid. A small amount of sodium bisulfite served to remove what iodine remained. The pinacolate was decomposed in a short time by shaking the mixture, and the liberated benzopinacol precipitated in large quantities. The solid benzopinacol was filtered off. The remaining mixture was treated with enough benzene to complete the separation of the pinacol. The organic solvents were combined and then dried over anhydrous sodium sulfate. The crude pinacol was digested with 100 cc. of ligroin at 40-60° to remove traces of benzophenone and then recrystallized from a mixture of alcohol and chloroform. Melting point, 190° (Literature value, 192-4°).

II. Preparation of Xanthopinacol.

A solution of 19.6 g. (0.1 mole) of xanthone in 100 cc. of hot benzene was added to the reddish-brown reaction mixture of 4 g. of magnesium and 15 g. of iodine in 100 cc. of ether-benzene. To aid in keeping the magnesium from being coated by the insoluble complex, $(C_{13}H_8O_2)_2 \cdot MgI_2 \cdot (C_2H_5)_2O$, which began to deposit, the mixture was heated on the steam bath until reaction began. The flask was then shaken at room temperature for 12 hours. If the magnesium does become so coated as to prevent it from reacting, the addition of a small amount of fresh metal induces reaction in a short time.

When the yellow pinacolate solution was decomposed with water, the greater part of the xanthopinacol precipitated in the layer of organic solvents. This was filtered off. Additional pinacol was obtained from the benzene solution. Xanthopinacol is not very soluble in alcohol or benzene. It crystallizes from toluene in shining white needles that are highly

refracting. The pure pinacol was obtained by digesting with hot benzene to remove the unreduced xanthone. It does not melt but decomposes at $185-187°$. (Literature value, $185-187°$).

III. Preparation of Intermediate Ketone, p-Methoxyacetophenone.

First Run: The procedure used here was that recommended by Noller and Adams (7). A solution of 0.5 mole (54.07 g.) of anisole in 200 cc. of carbon disulfide was placed in a 1-liter three-neck flask, fitted with a liquid-sealed mechanical stirrer, a dropping funnel, and a reflux condenser bearing a tube to carry off the hydrogen chloride evolved. The flask was then immersed in an ice bath to keep the temperature down to about $5°$ in order to prevent splitting the ether which occurs at the reflux temperature of the reaction mixture. One and one-tenth mole (146.7 g.) of aluminum chloride was added through one of the necks of the three-neck flask, and then with rapid stirring, 0.5 mole (50 ml.) of acetic anhydride was added slowly through the dropping funnel. This required about 45 minutes as the reaction mixture would heat up if the acetic anhydride were added faster. After the addition of all of the acetic anhydride, the stirring was continued with the chrome wire stirrer, to insure thorough mixing. After about five minutes of this continued stirring, the reaction mixture turned dark and suddenly became very viscous, stalling the electric stirrer. At this point, the electricity was cut off and the apparatus was dismantled. The tar formed had the nauseating odor of mercaptans, indicating that the acetic anhydride or the anisole had reacted with the solvent. Preparation was then made to continue the synthesis, but using this time a more inert solvent.
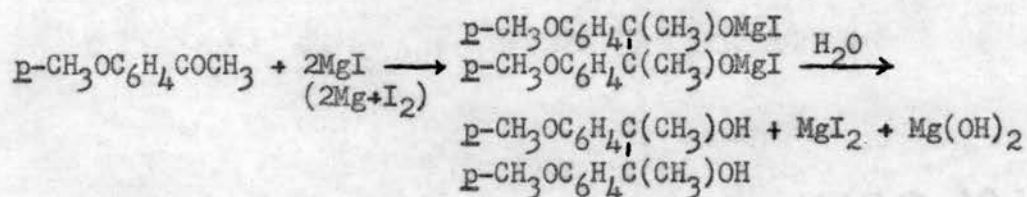
Second Run: In this run, the same quantities of anisole and aluminum chloride were used as in the first run, but instead of carbon disulfide as

solvent, ligroin was used. After all the acetic anhydride was added, the
mixture was stirred for two hours to insure complete reaction. At the end
of this time there was practically no evolution of gas. The slightly warm
reaction mixture was then cooled to room temperature and was decomposed by
pouring into a 2000-cc. beaker of cracked ice. After the decomposition,
which was carried out under the hood, the mixture was cooled and extracted
with a small portion of ether. The ether layer was washed first with water,
then with 10% sodium hydroxide, and finally again with water. It was then
dried over calcium chloride, the solvent distilled, and the residue subjected
to distillation under reduced pressure (1 mm.). The fraction which boiled
at 120-125° at this pressure was collected and cooled in an ice bath. White
crystals plated out in a short time; they melted at 36-37°. (Literature
value, 38-39°). The compound was purified by recrystallization from alcohol.
Twelve and one-half grams of p-methoxyacetophenone (13.2% yield) was obtained.

Attempted Preparation of 2,3-Bis(p-methoxyphenyl)-2,3-butanediol.

The reactions involved here are as follows:

$$p\text{-}CH_3OC_6H_4COCH_3 + 2MgI \xrightarrow[(2Mg+I_2)]{} \begin{array}{l} p\text{-}CH_3OC_6H_4C(CH_3)OMgI \\ p\text{-}CH_3OC_6H_4C(CH_3)OMgI \end{array} \xrightarrow{H_2O}$$

$$\begin{array}{l} p\text{-}CH_3OC_6H_4C(CH_3)OH + MgI_2 + Mg(OH)_2 \\ p\text{-}CH_3OC_6H_4C(CH_3)OH \end{array}$$

I. First Run: A solution of 7.5 g. (0.05 mole) of p-methoxyacetophenone
in 50 cc. of warm benzene was added to the light-red reaction mixture of
2 g. of magnesium (0.0822 g. atom) and 7.5 g. (0.059 g. atom) of iodine in
50 ml. of ether-benzene (Note 1). To aid in keeping the magnesium from
becoming coated by the insoluble complex, the mixture was heated on the
steam bath until reaction began. The flask was then shaken for six hours
at room temperature. As the magnesium became coated with the insoluble

complex, the reaction stopped, but with the addition of more magnesium, the reaction continued.

When the reaction mixture was decomposed with water, the greater part of the pinacol precipitated in the layer of organic solvents (Note 2). This was filtered off by arranging a jacket about a Hirsch funnel and filling the jacket with ice water to prevent the melting of the pinacol as it came in contact with the filter paper. Three hundred twenty-one milligrams of a waxy substance (melting point, 40-45°) which had a yellowish color was obtained. This substance was then refluxed with ligroin to remove the unreacted ketone. The refluxing was continued for about 15 minutes, then the solution was filtered (Note 3). After filtering, an attempt was made to recrystallize the pinacol from the ligroin, but this attempt at purification failed as the same discolored material as before was obtained.

The yellow waxy substance was then dissolved in alcohol, and water was added drop by drop to precipitate the compound from solution. This resulted in the formation of an oil. This oil was extracted and taken up in ether and dried overnight with anhydrous sodium sulfate. The ether was distilled off, and the apparatus set up for vacuum distillation. The system was connected to a mercury diffusion pump equipped with a McLeod-type manometer. The pressure was reduced to 1 mm. of mercury and the distillation was continued until the residue began to decompose. The product distilled between 290-315° under a pressure of 1 mm. This product retained a yellowish color so an attempt was made to purify it further by recrystallization from chlorofrom and alcohol. A few rhomboidal crystals were obtained which melted from 165 to 175°. These were so few in number that it was impossible to further characterize them.

Notes

(1) The color of the reaction mixture goes through a series of color
changes on addition of the ketone. When the ketone is first
added, the light-red solution of magnesium and iodine changes
to yellow in five to ten seconds. When shaken, the yellow
solution changes to green and then to brown in a few minutes.

(2) When water was added to the organic layer an additional layer
was formed which was dark in appearance, and was much more
viscous than the other layer of organic solvents above it.
The two organic layers were separated and treated like the
organic solvent layer mentioned above.

(3) Note here the variation from the procedure used in preparing
the pinacols from the symmetrical aromatic ketones. The mixed
ketones, in the presence of acid, undergo the pinacolone
rearrangement, so the solution is not acidified to dissolve
the magnesium hydroxide.

II. Second Run: To the clear red reaction mixture of 1 g. (0.04 g. atom)
of magnesium and 3.25 g. (0.025 g. atom) of iodine in ether-benzene (50 cc.)
was added 3.75 g. (0.025 mole) of p-methoxyacetophenone in 50 cc. of warm
benzene.

The procedure followed in this run was varied somewhat from that
followed in the first run. It was noted in run one that the reaction mixture
darkened on heating, indicating decomposition of products, so this run was
carried out avoiding heat.

The ketone was added to the magnesium and iodine in the ether-benzene
solution and the reaction was allowed to proceed at room temperature for a

few minutes, but when it became too vigorous, water was run over the flask
to prevent decomposition of the pinacol. Intermittent shaking speeded the
reaction. When the reaction was completed, the solvent was decanted from
the excess magnesium into a separatory funnel. The magnesium was washed
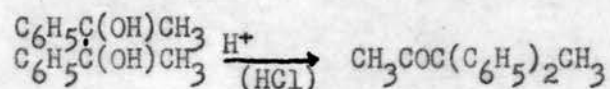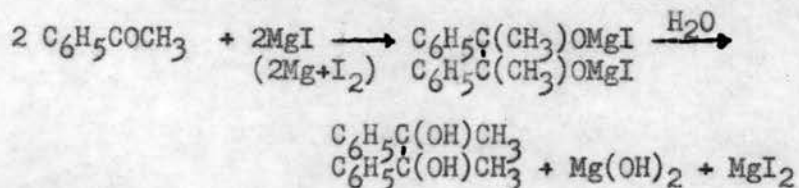with ether and the latter was added to the main portion of solvent.

Water was added to the benzene-ether solution, whereupon two precipi-
tates formed. One of these precipitates was magnesium hydroxide, the other
the pinacol. When the mixture was shaken for fifteen minutes, the light-tan
precipitate of the pinacol dissolved in the organic layer. This layer was
then filtered to remove the magnesium hydroxide. The organic solvents were
evaporated under reduced pressure (1 mm.) to avoid heating. The remaining
substance was then dissolved in ether and dried with anhydrous sodium sulfate
overnight. The ether was distilled off leaving a brown oily material which
contained a few white flaky crystals. The mixture was dissolved in carbon
disulfide and an attempt was made to recover the crystals from the solution.
Only a few were isolated and these were not of high purity. Melting point,
162-173°. Too few crystals were isolated for further study.

The oxime was prepared by dissolving some of the crude product in
alcohol (5 ml.) along with 0.2 g. of hydroxylamine hydrochloride, and adding
5 ml. of pyridine. The solvents were then removed by evaporation. The
residue was triturated thoroughly with 5 ml. of cold water, and the mixture
filtered. The oxime formed was recrystallized from an ethanol-water mixture
(10). Melting point, 192-94°. The oxime of 3,3-dianisyl-2-butanone melts
at 192-94° (9). This ketone could be formed as the result of the rearrange-
ment of the pinacol. This indicated that the conditions of the reaction
induced the pinacolone rearrangement.

At this point in the investigation, due to the low yield of pinacol and the lack of starting material (p-methoxyacetophenone), study of the reaction of acetophenone with magnesium and iodine was undertaken.

Attempted Preparation of 2,3-Diphenyl-2,3-butanediol

Reactions involved in the following runs are:

$$2\ C_6H_5COCH_3 + 2MgI \longrightarrow \begin{array}{c} C_6H_5C(CH_3)OMgI \\ C_6H_5C(CH_3)OMgI \end{array} \xrightarrow{H_2O}$$
$$(2Mg+I_2)$$

$$\begin{array}{c} C_6H_5C(OH)CH_3 \\ C_6H_5C(OH)CH_3 \end{array} + Mg(OH)_2 + MgI_2$$

$$\begin{array}{c} C_6H_5C(OH)CH_3 \\ C_6H_5C(OH)CH_3 \end{array} \xrightarrow[(HCl)]{H^+} CH_3COC(C_6H_5)_2CH_3$$

I. First Run: Material used:

36.04 g. (0.3 mole) acetophenone

15 g. (0.62 g. atom) of magnesium

42 g. (0.33 g. atom) of iodine

The procedure used in this preparation was much the same as that used by Gomberg and Bachmann for the preparation of benzopinacol (q.v.), except for modifications due to differences in solubility of 2,3-diphenyl-2,3-butanediol and benzopinacol. Upon addition of the acetophenone to the magnesium and iodine in the ether-benzene solution, two distinct layers were formed above the excess magnesium in the flask. The bottom layer was a black viscous oil insoluble in ether or benzene. These two layers were hydrolyzed separately. When the magnesium pinacolate was hydrolyzed, the pinacol did not precipitate in the layer of organic solvents as in the case of the hydrolysis of the benzopinacolate. A few milliliters of dilute hydrochloric acid was added to dissolve the magnesium hydroxide in the aqueous layer. The dark-brown oil formed on hydrolysis turned to light tan

on the addition of sodium bisulfite. This light-tan oily layer was separated, washed with water, and dried overnight with anhydrous sodium sulfate. The organic solvents were then distilled off under a pressure of approximately 10 mm. using a mercury diffusion pump. Reduced pressure was used in order to avoid heat which caused darkening of the oil, indicating decomposition. After the organic solvents had been distilled off, a light-tan oil remained which was set in the refrigerator for three days to induce crystallization. At the end of this time, the flask was removed and small needle-like crystals were noted suspended in the syrupy liquid. The mixture was then divided into several smaller portions and various solvents were tried to effect separation of the crystals from the oil. Results are shown in Table I.

Since only a few crystals of the compound were obtained from the solvents that were suitable agents for extraction, it was deemed desirable to run a detailed qualitative analysis on the mixture to identify the various compounds formed as side products.

Upon treatment of the distilled reaction mixture with bromine and carbon tetrachloride (11), the bromine-carbon tetrachloride solution was decolorized. The odor of hydrogen bromide was not detected which indicated addition of bromine. The compound resulting from this addition was separated from the carbon tetrachloride by addition of an ethanol-water mixture and filtration; after drying overnight it was found to melt over the range 139-149°. This corresponds approximately to the melting point of 1,4-dibromo-2,3-diphenyl-2-butene reported in the literature as melting at 149-150° (14).
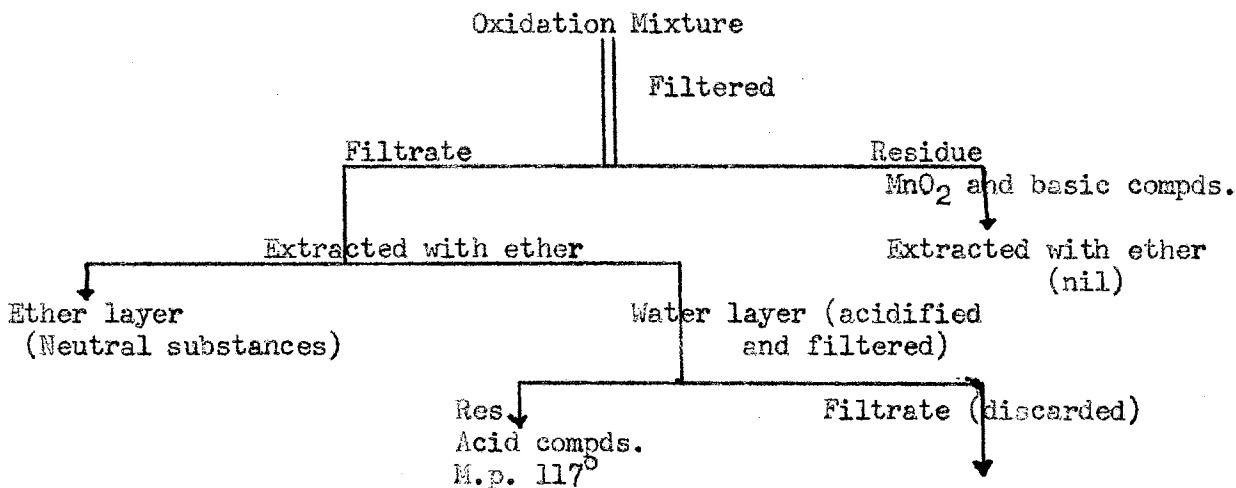
A neutral 10% potassium premanganate solution was added to the distilled reaction mixture. Apparently there was no reaction until the mixture was heated slightly, at which time the permanganate color was discharged.

TABLE I
SOLUBILITIES OF REACTION MIXTURE AFTER VACUUM DISTILLATION

SOLVENT	SOLUBILITIES	USEFULNESS AS CRYSTALLIZING MEDIUM
Ether	V.s. at room temp.: v.s. at 0°	Poor
Acetone	V.s. when warmed: fairly soluble at 0°	Fair
95% Ethanol	Sl. sol. at room temp.: sol. at b.p.[*]	Poor
Methanol	Sl. sol. at room temp.: sol. at b.p.[*]	Poor
Pyridine	Insol. at room temp.: v.s. at b.p.	Poor
Chloroform	V.s. at room temp.: insol. at acetone dry ice temp.[*]	Poor
Carbon tetra-chloride	V.s. at room temp.: v.s. at 0°	Poor
Dioxane	V.s. at room temp.: v.s. at 0°	Poor
n-Butyl alcohol	V. sl. s. at room temp.: sl. sol. at b.p.	Poor
Carbon disulfide	Insol. at room temp.: sol. when warm	Good
Acetic anhydride	Insol. at room temp.: sol. at b.p.	Good
Glacial acetic acid	Insol. at room temp.: sl. sol. at b.p.	Good
Benzene	V.s. at room temp.: sol. when cold	Poor
Ligroin	Sl. sol. at room temp.: insol. at 0°	Poor

[*] Insoluble portion appeared as an oil.

The manganese dioxide was filtered off and the separation scheme carried out
in the following manner:

```
                        Oxidation Mixture
                              │║
                          Filtered
                              │║
         Filtrate             ║                    Residue
              └──────────┐    ║                    MnO₂ and basic compds.
                         │    ║                         │
             Extracted with ether                  Extracted with ether
              │                   │                        (nil)
              ▼                   │
      Ether layer          Water layer (acidified
   (Neutral substances)        and filtered)
                          │                         │
                      Res │                    Filtrate (discarded)
                      Acid compds.                    │
                      M.p. 117°                       ▼
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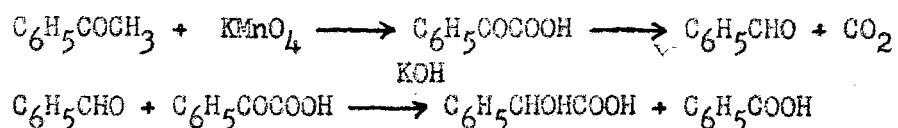
The neutral substances extracted with ether were treated with 2,4-dinitro-
phenylhydrazine; the melting point of the resulting product was 190-200°.
This wide range was taken to indicate a mixture of hydrazones.

The oily neutral compound was then distilled to remove the unreacted
acetophenone. A white waxy substance remaining which melted at 45° was
treated with hydroxylamine hydrochloride in pyridine to form the oxime (10).
This oxime melted at 150° which corresponds to the oxime of 1,2-diphenyl-
2-methyl-1-propanone (3). (Literature value, 151.2-2.2°). This indicates
rearrangement of the pinacol due to heating. The 2,4-dinitrophenylhydrazone
of this second neutral compound decomposed at approximately 260°. The
2,4-dinitrophenylhydrazone of 1,2-diphenyl-2-methyl-1-propanone is not
reported in the literature.

The literature value given for the melting point of mandelic acid is
117°. The acid extracted above melted at 117°. The anilide prepared from
this acid melted at 150° (Literature value, 151-52°), and the p-nitrobenzyl

ester melted at 125° (Literature value, 124°). The melting point of the mandelic acid was not depressed when mixed with this compound. Mandelic acid was the only one of these compounds isolated in appreciable amount (0.426 g.).

After the ketones were removed by the addition of 2,4-dinitrophenylhydrazine in alcohol, the compounds remaining were treated with permanganate in the manner described above. This did not produce any mandelic acid. This indicated that the mandelic acid was formed originally by the action of the permanganate on the acetophenone. This reaction could possibly occur in the following steps:

$$C_6H_5COCH_3 + KMnO_4 \longrightarrow C_6H_5COCOOH \longrightarrow C_6H_5CHO + CO_2$$

$$C_6H_5CHO + C_6H_5COCOOH \xrightarrow{KOH} C_6H_5CHOHCOOH + C_6H_5COOH$$

The mandelic acid sublimes in the sunlight, leaving the benzoic acid behind.

Second Run: The quantities of materials used in this run were the same as those used in the first run. The procedure was modified somewhat due to the lack of success on the previous runs.

As in the first run, extreme caution was taken to exclude all moisture from the reactants. It was found in the previous runs that moisture in the system interfered with the process. This finding is contrary to the statements of Gomberg and Bachmann, who report that the presence of water, even in considerable amounts, did not reduce the yields of pinacols they prepared (6).

The iodine was added to the powdered magnesium in 200 cc. of dry benzene contained in a 500-cc. flask to which was attached a condenser. The iodine was added in portions of several grams each, in order to keep the solution boiling quite vigorously. The solution formed here was not colorless as described by Gomberg and Bachmann but did become translucent.

The color changed from almost black at first to a clear red. This solution of the magnesium salt was cooled and to it was added 34.9 cc. (0.3 mole) of acetophenone. As the acetophenone came in contact with the magnesium-iodine solution in benzene, a light-tan precipitate formed which disappeared as soon as the flask was shaken. After the addition of the acetophenone, the solution was shaken for fifteen minutes; then a 100-cc. portion of anhydrous ether was added. Upon addition of the ether, the solution became warm and the reaction mixture underwent color changes similar to those noted in the preparation of the benzopinacol. The precipitate was light-tan changing to green, to brown, and finally to red. The color changes occurred during about 35 seconds. It was also noted here that the precipitate obtained when the ether is added had a dark-brown color which disappeared when shaken.

After the flask was shaken, there were observed two distinct layers above the excess magnesium in the flask. The layer immediately above the magnesium was black and very viscous. The top layer was light red and translucent in appearance.

These two layers were then decanted into a large separatory funnel, separated, and hydrolyzed separately. After the magnesium settled, the red solution was filtered from it and added, with vigorous stirring, to an equal volume of water. The magnesium was washed with benzene, filtered, and the filtrate was added to the light-red layer.

Each of the above layers was poured, with vigorous stirring, into equal volumes of water in order to hydrolyze the pinacolate. The heavy black viscous layer was diluted with ether before hydrolyzing, in order to emulsify the substance and thereby afford closer contact with the water.

The magnesium hydroxide formed on hydrolysis was dissolved by the
addition of dilute hydrochloric acid, as in the preparation of benzopinacol.
On addition of the hydrochloric acid, the organic layer darkened. A small
amount of sodium bisulfite was added to remove the free iodine that was
present. No precipitate was formed in the organic layer as was the case
with the aromatic symmetrical ketones described earlier. Instead of this
precipitate, a light-tan heavy oil formed in the benzene layer. Upon
addition of ether, this oil went into solution. This organic layer was
then separated and dried over anhydrous sodium sulfate. The two organic
layers from the separate hydrolyses were then combined and the organic
solvents distilled off. The unreacted acetophenone was distilled off under
reduced pressure (1 mm.) and the residue was then dissolved in ether,
filtered, and the ether was evaporated. A few slender white needles separa-
ted; the melting point of these is 119°.

The residue above, after the separation of the needles, was distilled.
A white waxy solid melting from $71-75^{\circ}$ was obtained in minute amounts. It
is reported in the literature that 2,3-diphenyl-2,3-butanediol decomposes,
when distilled over infusorial earth in vacuo at $500-550^{\circ}$, to 2-phenyl-3-
methylindene, melting at 75°. The compound prepared above when treated with
an alcohol-picric acid solution, formed a picrate which melting at 116°
but this has not been tried for authentic 2-phenyl-3-methylindene. The
mechanism for the decomposition of the pinacol as proposed by Blum-
Bergmann is as follows: (2)
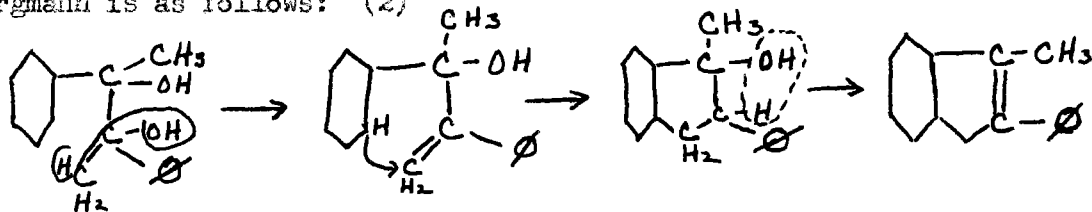
It was decided at this point to attempt another run, using increased amounts of starting materials in order to isolate enough of these needles to characterize them more fully.

Third Run: Material used:

    120.2 g. (1 mole) acetophenone

    48.64 g. (2 g. atoms) of powdered magnesium

    126.9 g. (1 g. atom) of iodine

    300 cc. of ether

    600 cc. of benzene

Molar quantities were used in this run as indicated above. Upon addition of the acetophenone, in 150 cc. of benzene, to the reaction mixture in a two-liter round-bottom flask, the mixture went through the series of color changes as observed before. On addition of the acetophenone, there was first formed the light-yellow precipitate which went into solution on mild agitation. The final color of the mixture was reddish brown. As observed in the previous runs two layers formed above the excess magnesium. The bottom layer was not so dark as in the previous runs, assuming this time a dark-red color. The top ether-benzene layer had a pale-yellow color. As before, the lower layer was very viscous. The reaction mixture was then allowed to stand for one week in order to afford longer contact with the magnesium and iodine.

The two liquid layers were then decanted through a Pyrex glass-wool filter into a larger separatory funnel in order to remove the excess magnesium present. The magnesium was then washed with ether and this ether was added to the top layer mentioned above. These two layers were hydrolyzed separately.

After hydrolysis of the pinacolate, 100 cc. of ether was added to dissolve the pinacol and the ether solution was filtered to remove the magnesium hydroxide suspended in it. Acidification was avoided in order to prevent rearrangement of the pinacol to 1,2-diphenyl-2-methyl-1-propanone. It was observed that the magnesium hydroxide goes through ordinary filter paper, so a special filter was prepared by dispersing small bits of crepe filter paper in water, filtering this and then washing with acetone and then dispersing in ether. Upon filtration, the magnesium hydroxide was adsorbed on the surface of the filter paper particles and remained behind. The filtrate was then dried over anhydrous sodium sulfate. The organic solvents were distilled off and the residue distilled in vacuo (1 mm.) to remove the unreacted acetophenone. The dark oily substance remaining was allowed to cool to room temperature. Small colorless needles appeared suspended in this substance. These needles were extracted with glacial acetic acid and filtered. The needles then took on a yellowish appearance due to the presence of the oily substance. The melting point of these crystals is 110-119°. The residue was then dissolved in ether and filtered. When the ether was evaporated, a few colorless needles were isolated. These melted at 119°.

The remainder of the residue from the glacial acetic acid was then placed in a 50-cc. distilling flask and heated in an attempt to purify by distillation. Sublimation instead occurred at 170°. Only 0.0025 g. of this pale yellow substance was isolated. It was hoped that this substance would absorb light in the visible range, so it was dissolved in capryl alcohol and the absorption spectrum was determined in the visible range, but the results were negative. The ultraviolet lamp was then used as the

light source, but since capryl alcohol absorbs light in this range, the results were inconclusive.

It was noted that some of the yellow precipitate formed on addition of the acetophenone to the mixture adhered to the surface of the magnesium. This mixture was dried and separated into two batches.
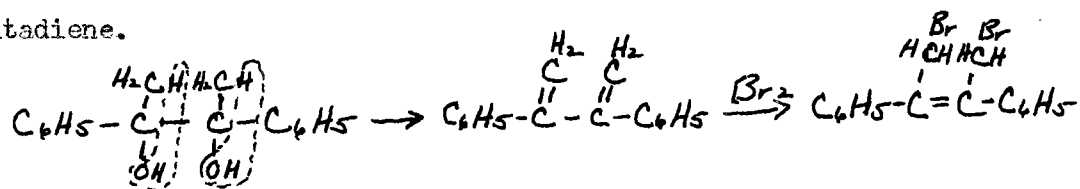
The first batch was hydrolyzed and ether was added to dissolve the pinacol formed and thereby separate it from the magnesium hydroxide formed. The ether layer was pipetted off, filtered, and poured onto a watch glass to evaporate. The brown oily material similar in appearance to the substance extracted in the previous runs was obtained. Analysis as described before showed the presence of 1,2-diphenyl-2-methyl-1-propanone, acetophenone, and a dark brown oil.

The second batch of the magnesium mixture was hydrolyzed overnight. Some white flacky crystals of different appearance from the magnesium hydroxide were noted floating atop the solution. These were picked off and dissolved in ether and filtered. As the ether dried, needles formed which melted at 117-119°.

The solution was extracted with 100 cc. of ether in 25-cc. portions, which were combined and filtered using the filter technique described above to remove the suspended magnesium hydroxide. The ether was evaporated and the brown oil was combined with the hydrolysis product of the first batch. Glacial acetic acid was then added and the solution filtered. The dark tan crystals remaining were then dissolved in ether, filtered, and the ether evaporated. Approximately 0.05 g. of colorless crystals in the form of needles, remained on the watch glass. The melting point of these crystals is 119°. Bromination of a group of these crystals in boiling

chloroform formed a compound which crystallized from alcohol and water and melted at 149-150°. The melting point given in the literature for 1,4-dibromo-2,3-diphenyl-2-butene is 149-50° (14). According to the same authors this compound forms on bromination of 2,3-diphenyl-2,3-butanediol in boiling chloroform.

A possible explanation for the formation of this compound would be a dehydration of the pinacol, followed by a 1,4-addition to the substituted butadiene.

$$C_6H_5 - \underset{\underset{OH}{|}}{\overset{\overset{H_2C}{|}}{C}} + \underset{\underset{OH}{|}}{\overset{\overset{H_2C}{|}}{C}} - C_6H_5 \longrightarrow C_6H_5 - \underset{\overset{||}{C}}{\overset{H_2}{C}} - \underset{\overset{||}{C}}{\overset{H_2}{C}} - C_6H_5 \overset{Br_2}{\longrightarrow} C_6H_5 - \underset{|}{\overset{H\,CH}{\overset{Br}{C}}} = \underset{|}{\overset{H\,CH}{\overset{Br}{C}}} - C_6H_5$$

DISCUSSION OF RESULTS

The results of this investigation gave evidence of the formation of the pinacols of p-methoxyacetophenone as well as that of acetophenone.

New substances were isolated in the reduction attempted, but only in minute amounts. These substances as noted in the runs using p-methoxyacetophenone were impure as indicated by the spread in their melting point. It was noted quite early in the investigation that the rearrangement product of the pinacol was obtained, the oxime of the pinacolone derived from p-methoxyacetophenone having been prepared.

Some impure crystals were obtained which corresponded approximately in melting point to 2,3-bis(p-methoxyphenyl)-2,3-butanediol. The melting point of this compound as given in the literature (9) is 168-169°. This is the high-melting form.

It is not quite clear why different groups migrate when the two pinacols undergo the pinacolone rearrangement. The p-anisyl group shifts in the case of 2,3-bis(p-methoxyphenyl)-2,3-butanediol while a methyl group shifts on rearrangement of 2,3-diphenyl-2,3-butanediol. A list of the migration tendencies of certain groups in the pinacolone rearrangement follows (5):

p-anisyl > p-tolyl, p-biphenylyl, $\propto$ -naphthyl > p-isopropylphenyl > p-ethylphenyl, p-fluorophenyl > phenyl. It may be assumed from this that the migration tendency of the methyl group is intermediate between the p-anisyl and the phenyl group.

Because of its ready availability, acetophenone was used most extensively in these investigations. It was noted a rise in temperature of the system promoted much decomposition. In the cases investigated,

side products were so numerous that it was impossible to completely separate and identify them.

The color changes involved as the reaction proceeded indicated that the reaction goes via a free-radical mechanism, in the formation of these mixed pinacols, just as with the aromatic pinacols.

It was found that all moisture had to be excluded from the reactants in order for the reaction to proceed, and that upon hydrolysis of the pinacolates formed, acid must not be used to neutralize and dissolve the magnesium hydroxide formed. Acid media encourage rearrangment of the pinacol.

From the results of this investigation, it may be concluded that the pinacols of the mixed ketones are formed to some extent. The author believes that the proper experimental conditions and separation techniques can be developed and that this reaction will be of preparative value for alkyl aryl pinacols.

SUMMARY

Benzopinacol and xanthopinacol were prepared initially, using the method of Gomberg and Bachmann, in order to acquire technique in the later-attempted preparations.

2,3-Bis($\underline{p}$-methoxyphenyl)-2,3-butanediol and 2,3-diphenyl-2,3-butanediol have been prepared in minute amounts from $\underline{p}$-methoxyacetophenone and acetophenone respectively by the use of magnesium and iodine. The pinacolone-rearrangement products of these compounds were obtained in substantial amounts, when the solutions were acidified; this is believed to be the most damaging side reaction. Evidence indicated the absence in the reaction mixture of any olefinic compound.

Sufficient quantity of the pinacol of acetophenone to form a derivative in identifiable amounts was obtained after tripling the quantity of reactants. Several of the more common organic solvents were used in an effort to effect satisfactory separation of the pinacols.

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BIOGRAPHY

Joseph William Bowers was born April 17, 1922 in Greenville, Texas. He attended the Greenville Public Schools and graduated from Greenville High School in June 1940. Soon after graduating from high school, he enrolled in East Texas State Teachers College, Commerce, Texas.

He enlisted in the United States Army Air Force on October 15, 1942. After attending various colleges, where he received training in basic electrical engineering, he was graduated from the Eastern Signal Corps School at Ft. Monmouth, New Jersey and after training in radio operations, he was assigned to duty with the First Air Force and helped install direction-finding equipment along the eastern coast of North America.

He was discharged from the Air Force on January 6, 1946, and reentered East Texas State Teachers College. He received the Bachelor of Arts degree in June, 1947 and soon after was employed as an analyst for Sheffield Steel Corporation of Texas at Houston, Texas.

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He is married to Hazel Marie Peek and has a daughter seven years old.

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