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THE REACTION OF ETHYL GRIGNARD
REAGENT WITH HALO-BENZOIC ACIDS

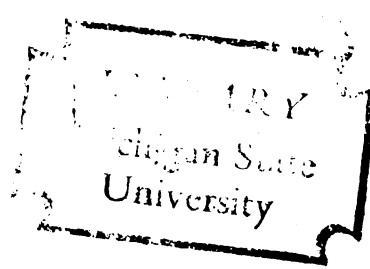
Thesis for the Degree of M. S.

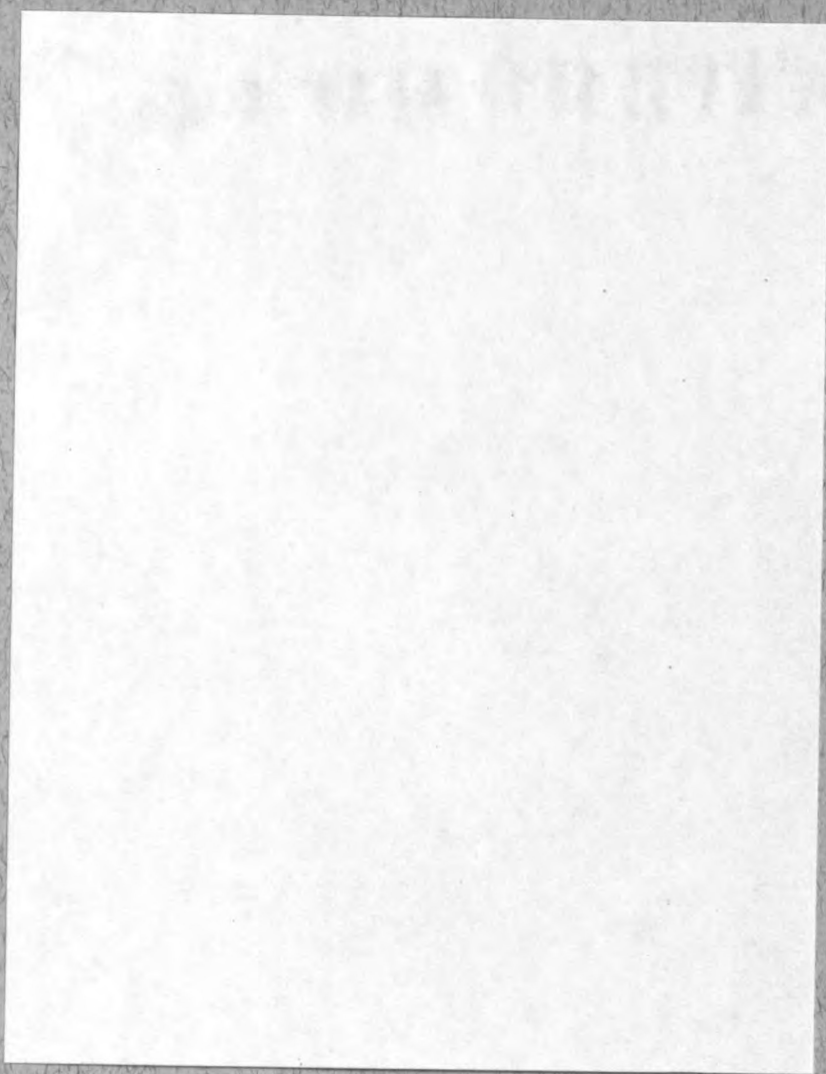
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THE REACTION OF ETHYL GRIGNARD REAGENT WITH HALO-BENZOIC ACIDS

by

EDWARD SIMON

A THESIS

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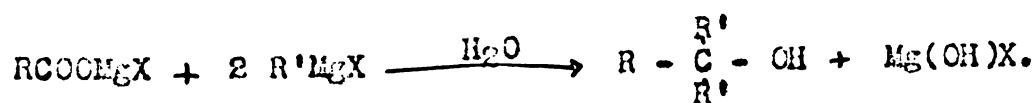
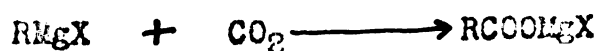
INTRODUCTION

Although the Grignard reaction is as old as the century, very few attempts have been made to investigate the reactions of acids with the Grignard reagent. The reasons are understandable: there is very little use for the tertiary alcohols that result, and the reactions of esters and ketones are more economical of the reagent. For these very reasons, the reactions of the Grignard reagent with esters and ketone have been thoroughly investigated -- and many controversies have raged over the proposed mechanisms of their reactions.

This paper is written with an eye to filling the gaps in the knowledge of the Grignard reactions and -- within the limits of the title, to finding the most favorable conditions for the reaction of the Grignard reagent with aromatic acids -- as has previously been done in this laboratory with some of the aliphatic acids (44).

HISTORY

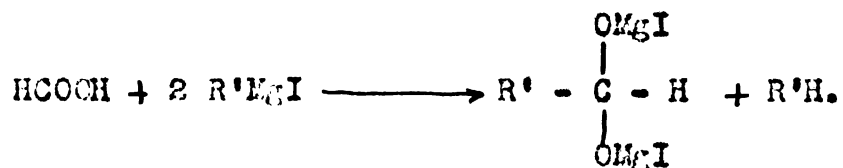
In the past fifty years since Grignard (33) showed that alkyl magnesium halides reacted with carbon dioxide to yield, upon hydrolysis, alkyl carboxylic acids, there have been some sporadic attempts to investigate the reaction of organic acids with organo-metallic halides. In 1904, Grignard (38) reacted the RCOOMgX complex formed from addition of carbon dioxide to alkyl magnesium halide to produce tertiary alcohols. He postulated a mechanism which involves the formation of a ketone intermediate to account for the products thus formed (see THEORY). In this wise, he made 2-methyl-5-ethyl-5-heptanol by reacting isoamyl magnesium bromide with carbon dioxide and further reacting the addition complex formed with two moles of ethyl magnesium bromide. A generalized formulation of the reaction:



Also in 1904, Grignard (34) produced diethyl phenyl carbinol by reacting phenyl magnesium bromide with carbon dioxide and the ensuing complex with ethyl magnesium bromide. He also obtained a small amount of the unsaturate of the alcohol (1-methyl-1-phenyl 2-methyl-ethylene). When he reacted the magnesium bromide, instead of the expected diethyl-benzyl carbinol, a great deal of gas (ethane) was evolved and the

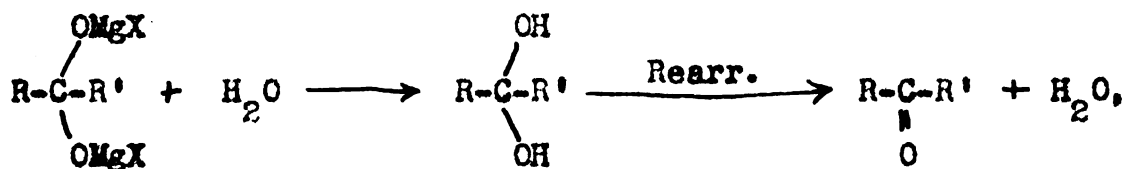
products were mostly toluene and dibenzyl. Only a minute amount of the expected alcohol was isolated. Grignard postulated that the methylenic group -- the only difference between the benzoic and phenylacetic acids, contained hydrogen atoms active enough to reduce the Grignard complex to the gas and thus form the complex $C_6H_5-CH(MgBr)-COOMgBr$.

In 1904 and 1905 Zelinsky (86) and Hauben (39) produced secondary alcohols by reacting alkyl magnesium compounds with formic acid. Grignard (34) also tried this reaction and postulated that the complex produced when two moles of the magnesium compound had reacted was of the structure:

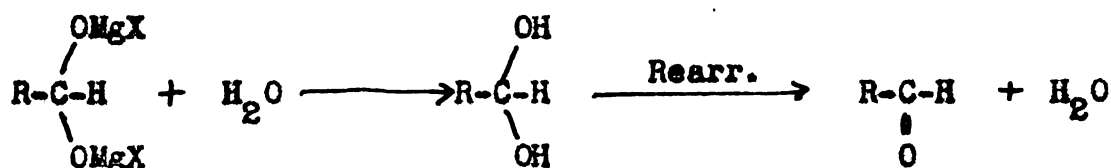


In 1906 Bayer and Company (81), through the efforts of Simonis and Arand, patented a process for making tertiary alcohols from benzoic acid and sodium benzoate by reaction with the Grignard reagent. They reported producing diethyl-phenyl carbinol.

In 1909, Simonis and Arand (82) reviewed the reactions of the Grignard reagent with organic acids. They objected to Grignard's hypothesis of the $RC(OMgX)_2R'$ complex intermediate claiming that, if it does exist, a ketone should be realized through the hydrolysis of the complex after addition of the first two moles of the Grignard Reagent:

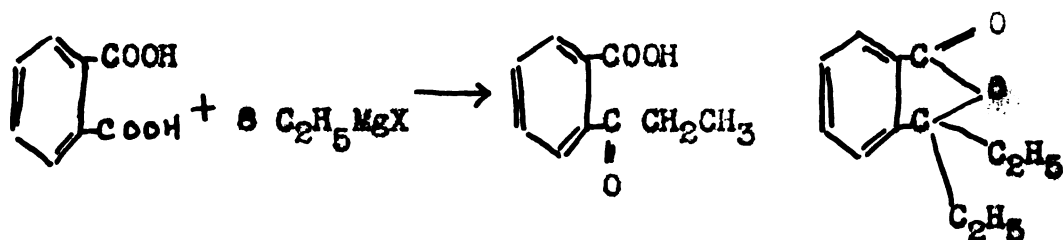


and an aldehyde when formic acid was used:



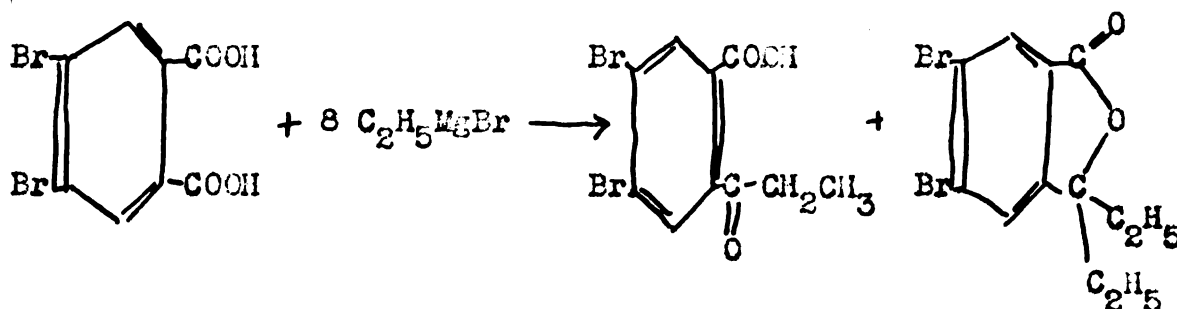
They found no ketone upon hydrolyzing their reaction at that stage.

Simonis and Arand went on to investigate the products of the reaction of dicarboxylic acids with the Grignard reagent feeling that only those acids as a class hadn't been investigated. One mole of phthalic acid was reacted with 8 moles of ethyl Grignard to yield 30% diethyl phthalide and 20% propiophenone-o-carboxylic acid:

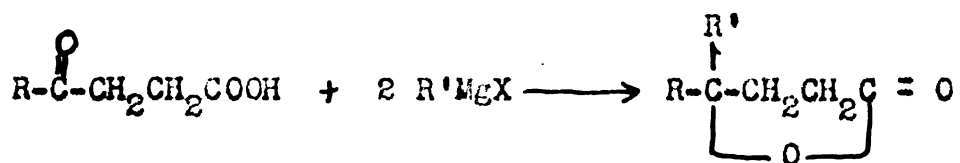


The products produced were the same as those obtained when Bauer (7) had phthalic anhydride react with ethyl magnesium bromide. When 4, 5-dibromophthalic acid was reacted with

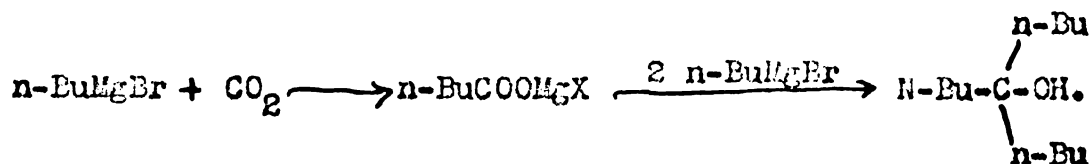
8 moles of ethyl Grignard reagent, the products were 3,3-diethyl-5,6-dibromophthalide and 4,5-dibromo-2-propioophenone-1-carboxylic acid:



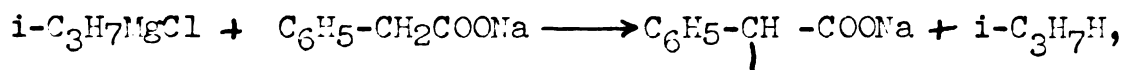
In 1923, P. M. Porter (76) investigated the reaction of γ -keto acids with the Grignard reagent to see if the product was the same as that produced when the usual esters were used, i.e., the γ -alkyl substituted lactone as obtained by Grignard and Moissans (35). When levulinic acid was reacted with methyl magnesium iodide 35.1% iso-caproic lactone was produced. The yield reported by Grignard was 35%. The general reaction:



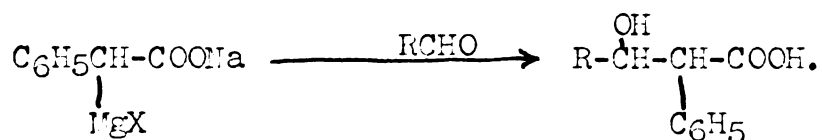
Ivanov (49) extended the original carbonation reaction of Grignard by reacting three moles of normal butyl magnesium bromide with one mole of carbon dioxide and obtaining 5-butyl-5-nonanol. His formulation:



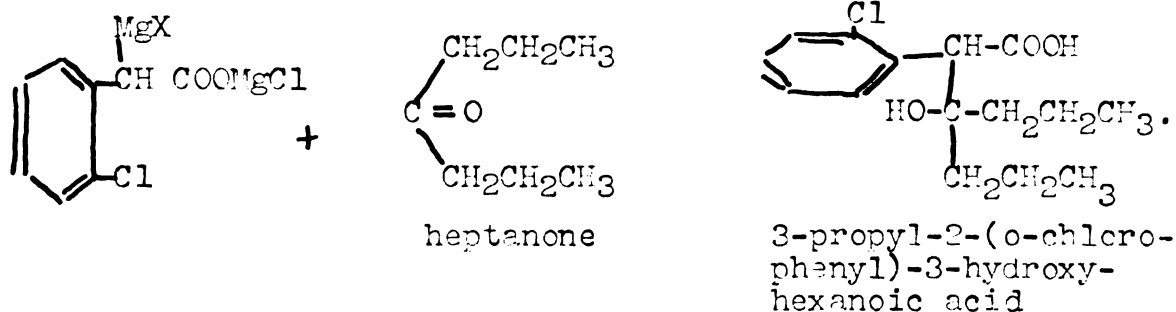
In 1932, Ivanov working with Nicoloff (50) utilized the active methylenic group of phenylacetic acid to form the reactive complex $\text{C}_6\text{H}_5\text{CH}(\text{MgX})\text{COONa}$:



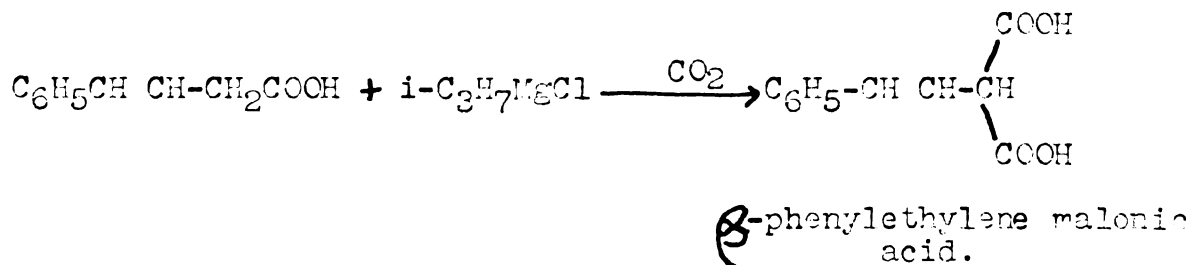
and reacted the complex with saturated aldehydes to obtain 65% yields of α -phenyl- β -lactic acids:

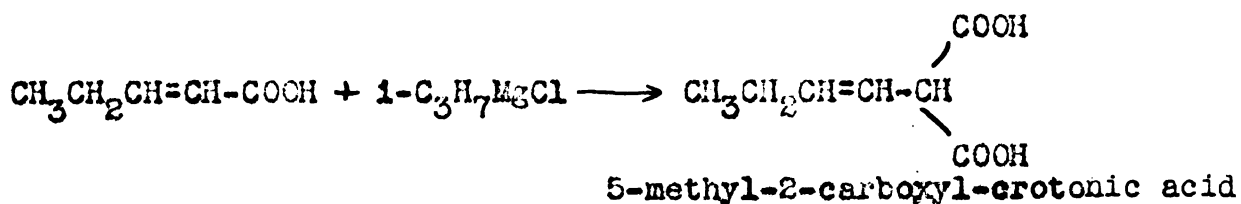


In the same year, with Mihova and Christova, Ivanov (51) reacted o -chlorophenyl- $\text{CH}(\text{MgX})\text{-COOMgCl}$ with saturated ketones to obtain α -chlorophenyl- β -lactic acids:



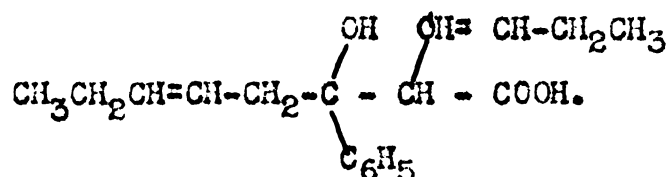
In 1933, Ivanov worked with Pehenichni (52) to investigate the possibilities of 1,4 addition to α - β -unsaturated acids:





which indicates that only the usual 1,2-addition takes place.

However, when 3-butenyl carboxylic acid was reacted with phenyl magnesium bromide and the complex treated with carbon dioxide, the product was 3-phenyl-2(α -butenyl)-3-hydroxy-5-octeno-1-oic acid:



In 1934 Ivanov and Spassov (47) while investigating the evolution of propane when adding esters to various Grignard reagents, investigated the evolution of ethane when benzoic acid was added to ethyl magnesium bromide. They found that only the calculated amount (one mole) of ethane was evolved due to the active hydrogen of the carboxylic group.

In 1946, Huston and Bailey (44) investigated the reactions of some of the aliphatic acids with various Grignard reagents and investigated the conditions for the best yields. They found that addition of the acid to an excess of Grignard reagent and stirring the reaction mixture two hours in refluxing ethyl ether gave the largest yields of the tertiary alcohols (average 65%). The reaction also produced an average of 10%

ketone. For example, when 0,5 moles of butyric acid were added to 1.75 moles of ethyl magnesium halide, propyl diethyl carbinol was obtained in 64.6% yield and ethyl propyl ketone in 10% yield.

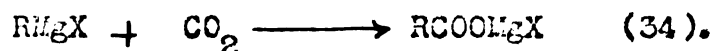
THEORETICAL

The reaction of organic acids with the Grignard reagent is usually written:

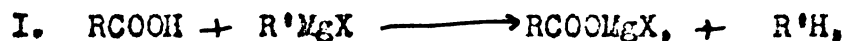


This formulation explains very little of the reaction and gives no indication of the by-products obtained.

Huston and Bailey (44) follow the lead of Grignard (38, 34) and Ivanov (49) who suggest the mechanism for the reaction of the Grignard addition product formed when carbon dioxide is bubbled into a solution and then further reacted with another mole of Grignard reagent to form a tertiary alcohol:

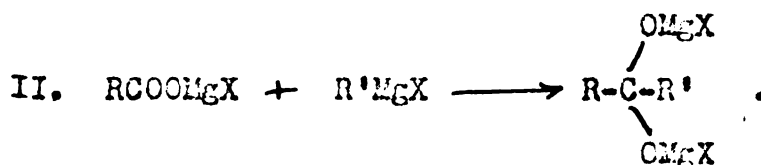


Huston and Bailey suggest that, since the first step of the reaction of the acid with the reagent is undoubtedly:

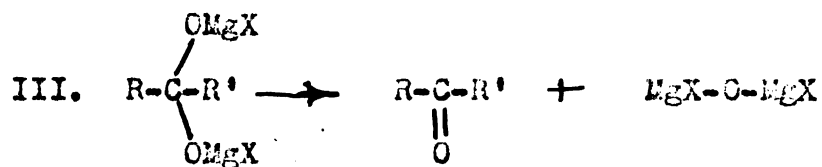


that the same mechanism holds for the remaining reactions:

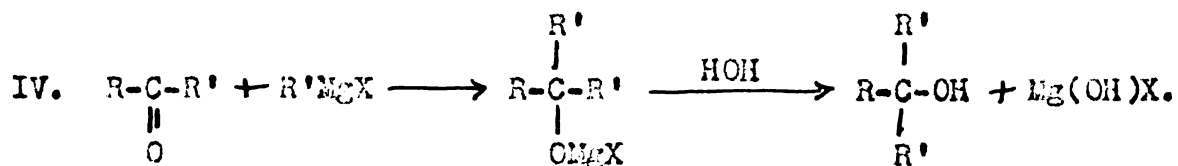
In the second step, a second molecule of the reagent adds across the carbonyl group:



However, this addition product now contains two electro-negative groups in the form of the $-(OMgX)$, on the same carbon atom. The complex is highly unstable $MgX-C-XMg$ is split off leaving a ketone.



The ketone continues the reaction with a third mole of the Grignard reagent and a tertiary alcohol is formed:



PROCEDURE

PREPARATION OF THE GRIGNARD REAGENT:

The reagent was prepared by the method recommended by Gilman (28). Using 105 g. of ethyl bromide (1.50) and 36.4 of Magnesium turnings (1.50) in 6 molecular equivalents of dry ethyl ether. The ethyl bromide was redistilled technical grade and the magnesium had been obtained especially prepared for the Grignard reaction. The ethyl ether was dried as recommended by Fieser and Fieser (22) over sodium wire. The magnesium was weighed and transferred to a 3-necked flask equipped with a glass Hirschberg stirrer, condenser with a calcium chloride drying tube and a 500 ml. dropping funnel. The magnesium was covered with 200 ml. of dry ether and the stirrer started. The ethyl bromide was weighed and transferred with 100 ml. of dry ethyl ether to the dropping funnel, a drying tube being placed over the mouth of the funnel. The time of addition was limited only by the rate of the reaction -- averaging two hours for addition and the whole stirred a half hour following the addition.

ANALYSIS OF THE GRIGNARD REAGENT:

The reagent formed was analyzed as recommended by Gilman (29,30) using water to hydrolyze an aliquot and an excess of standard sulfuric acid was added, heated to 75-80° and then back

titrating with standard sodium hydroxide to a phenolphthalein end point while hot. In all cases, the analysis showed approximately 93% ethyl magnesium bromide (23).

ADDITION OF THE ACID:

All the acids were recrystallized from petroleum ether. They were added to the Grignard reagent over a one hour period. The reaction was vigorous and immediate but care was required due to the rapid evolution of the gas (ethane) formed. After addition of the acid the reaction was stirred three hours. When attempting to force the reaction benzene was added (500 ml.) after addition of the acid and the solution distilled until boiling at 76° C. The reaction mixture was then refluxed at 76° C. for two hours with stirring.

Where possible, the acids were added in ether solution. Benzoic, orthochloro-benzoic, orthocholoro-benzoic, metachloro-benzoic, metabromo-benzoic and orthoiodo-benzoic acids were all added in this wise. The metaiodo-benzoic, parahalo-benzoics, and all the nitro benzoic acids, due to their insolubility in ether and benzene, were added to the dropping funnel dry and covered with 400 cc. of dry ether. They were then washed into the reaction flask at a rate commensurate with the vigor of their reaction. In some cases it was necessary to use a copper wire inserted in a glass rod, to prevent clogging. Addition was complete in all cases. After the first hour of stirring, a white solid was seen to come out of solution.

HYDROLYSIS OF THE ADDITION PRODUCT:

Three forms of hydrolysis were employed in the initial phases when experimenting with benzoic acid. The detrimental effects of strong acid to the anticipated tertiary alcohols (43), (i.e., the tendency of tertiary alcohols to chlorinate or dehydrate in acid solution) suggested that the saturated ammonium chloride method was best (23). But subsequent treatment with acid of the solid formed after ammonium chloride hydrolysis, showed that as much as 20% of the product was absorbed and unremoved through three washings with ether. Hydrolysis with ice water (43) was discontinued due to the long filtration process and the loss of product through absorption. It was finally determined to use the ice and acid method of Fieser and Fieser (23). Thus, 300 ml. of 10% sulfuric acid was poured over 150 g. of ice in the dropping funnel and added to the stirred reaction in an ice bath over a one hour period. Stirring was continued one hour after addition at which time a two-layer system was clearly defined and unreacted particles of acid could be observed.

ISOLATION OF THE ALCOHOL:

The hydrolyzate was filtered free of unreacted acid, if any, and placed in a 2 liter separatory funnel and extracted three times with 150 ml. portions of ether. The ether layer was then washed with water, twice with 5% sodium carbonate solution to remove any acid in the ether layer, and finally water; then dried over anhydrous sodium carbonate.

The ether was distilled off and the residue placed in a distilling pot and fractionated over a two-and one-half foot glass Helix - packed column under vacuum using a nitrogen atmosphere. The alcohol would come over without traces of dehydration.

Unfortunately, all the alcohol fractions contained minute traces of ketone and unsaturates as determined by use of 2,4-dinitrophenyl-hydrazine (41) and bromine in chloroform. Yields were based upon these slightly impure fractions.

The pure alcohols were obtained only upon redistilling the alcohol fractions three times under the same conditions. Once distilled, the alcohols had no tendency to dehydrate under vacuum so long as no air was present. Thus all fractions were redistilled using a pine splinter to prevent bumping.

DERIVATIVES OF THE ALCOHOLS:

Tertiary alcohols dehydrate when treated with phenyl-isocyanate and chlorinate when treated directly with acid chlorides. The pyridine variation of the method of Schotten and Baumann was found to give low yields of the solid paranitro benzoates:

One milliliter of the alcohol was placed in 5 ml. of dry pyridine (prepared by redistillation from barium oxide and collected over potassium hydroxide sticks). One gram of p-nitrobenzoyl chloride was added. The mixture was refluxed

in a 50 ml. flask for one hour and poured hot over 15 g. of ice. The solid was then filtered and allowed to stand over night in a large excess of 5% sodium carbonate. The oil was then extracted with ether and washed with water, dilute HCl, water again and then dried over sodium carbonate. The ether was then evaporated off and a thick oil obtained. The oil was taken into solution in alcohol and water added dropwise just to the cloud point. The paranitro benzoate crystallized out upon cooling and standing and was readily recrystallized from alcohol.

INDEPENDENT SYNTHESIS OF THE ALCOHOLS:

Although the phenyl diethyl carbinol had been prepared previously (40, 34, 81), no solid derivative is reported. The other tertiary alcohols appear nowhere in the literature.

SYNTHESIS OF DIETHYL PHENYL CARBINOL:

1). By reacting one mole 80.1 g. of diethyl ketone with one mole of phenyl magnesium bromide, 25.0 g. of a clear colorless oil was obtained which contained no trace of a carbonyl group and reacted positively with the Lucas reagent. With paranitrobenzoyl chloride it formed a solid ester M.P. 80° C. Mixed M.P. 80° C. Refractive index, $n_D^{25} = 1.5145$. B.P. $75^{\circ}/5\text{mm}$.

2). Using the recent method of Swain and Boyles (84) to insure large yields of tertiary alcohols, 63.6 g. (0.40M) of Bromine were added slowly and with continuous stirring to 9.1 g. of magnesium (0.40M) in 100 ml. of dry ethyl ether and stirred until the bromine color had disappeared. Then 20 g. (0.15M) of propiophenone were added over a period of one hour with stirring. 0.5M of ethyl magnesium bromide in 100 ml. of ether were added slowly to the mixture and stirred one half hour thereafter. The reaction mixture was hydrolyzed by adding it to 500 cc. of 10% sodium carbonate at 0° C. A yield of 16.5 g. (70% yield) of phenyl diethyl carbinol was obtained. Refractive index $n_D^{25} = 1.5142$. Paranito benzoate M.P. 80° C.

SYNTHESIS OF PARABROMO PHENYL DIETHYL CARBINOL:

One mole of diethyl ketone was added to 1.2 mole of parabromo-phenyl magnesium bromide and 40 g. of a heavy colorless oil obtained. B.P. $110^{\circ}/2$ mm. P-nitrobenzoate M.P. 142° C.

Obviously the procedure used in the above two cases was limited by the availability of the correctly substituted halogen aromatics. Since the method of Swain and Boyles worked so well with propiophenone, and most of the intermediate ketones were known, the product from the addition of ethyl Grignard to the correctly substituted propiophenones could be considered a valid proof of structure coupled with the melting points of the derivatives and the results of dehalogenation.

SYNTHESIS OF PARA CHLORO- AND PARA BROMO-PROPIOPHENONE:

The para-chloro- and parabromo-propiophenone were readily synthesized using the Friedel Crafts reaction of Collet (12, 13). One mole of the halobenzene and one mole of propionyl chloride (made using phosphorus trichloride and propionic acid on the water bath) (1, 42) in an excess of carbon disulfide were stirred while one mole of anhydrous aluminum chloride was added over a 2 hour period. The whole was then refluxed 6 hours on the steam bath, then poured over one kilo of ice. The CS_2 layer was removed and washed with 10% sodium hydroxide solution, dried and evaporated. The para-halo propiophenones crystallized out very nicely with cooling and were recrystallized

from alcohol. Para-chloro-propiophenone M.P. 35-6° C., Oxime M.P. 63° C. (10). P-bromo-propiophenone M.P. 44° C. Acetoxime M.P. 90-1° (10). The respective yields were 60% and 72%.

The above ketones were reacted with magnesium bromide and ethyl magnesium bromide in the manner of Swain and Loyles (24) as previously described. The alcohols produced: P-chloro phenyl diethyl carbinol B.P. 129-30°/1 mm. P-bromophenyl diethyl carbinol B.P. 114°/2 mm.

SYNTHESIS OF THE META HALO PROPIONPHENONES:

The preparation of the ortho and meta halo-propionphenone was undertaken following the method of Elson, Gibson et al (19) as modified by Keneford and Simpson (54).

Propiophenone was prepared using the method of Shriner and Turner (30) as modified by Raddley and Kenner (5) by reacting 2M of propionyl chloride (195.0 g.) and 154 g. (3M) of benzene with 3.5 M of anhydrous aluminum chloride in an excess of carbon disulfide. However, upon working up and distilling, only 50% yield was obtained (reported 28.5%) (5) and this appeared impure. The distillation residue was totally polymerized. Redistillation only lost more propiophenone and another run was necessary. And this run too yielded impure propiophenone. The propiophenone was used in that impure condition (traces of unsaturation).

One hundred grams of propiophenone (0.75M) in 30 g. of glacial acetic acid were added to 400 ml. of fuming nitric acid (density 1.5) at minus 10° over a two hour period. Only m-nitro propiophenone (70%) could be isolated upon pouring upon ice, filtering and making the filtrate basic and extracting with ether. This reaction was attempted three times and only m-nitro propiophenone could be isolated since the redistillation of the propiophenone still yielded a product impure enough to break the delicate temperature balance required for the ortho nitration. The m-nitro propiophenone was recrystallized from alcohol, M.P. 102° C. and reduced in SnCl_2 and concentrated HCl (6). The reaction was made basic and extracted with ether. The boiling point of the m-amino propiophenone was 145°/10 mm, M.P. 42° C. from alcohol. Senicarbazone M.P. 196° C. dec. The yield upon reduction was 90%.

Three Sandmeyer reactions were run to get the three orthohalo-propiophenones. Since the methods used are the same as those used with the ortho-amino propiophenone, they will be given now:

PREPARATION OF M-BROMO PROPIOPHENONE:

Using the modified conditions of Leonard and Loya (64), 30 g. (0.20M) of m-amino propiophenone were dissolved in 80 g. of HBr(33%) and 100 cc. of water. 20 g. of NaNO_2 in 350 cc.

water were added at 0° C. A solution of cuprous bromide (made by treating 54 g. of CuSO_4 in 60 cc. of water and 30 g. KBr with 50 g. NaHSO_3 and 20 g. NaOH) was added and stirred one half hour. The whole was then warmed on the steam bath for four hours and then steam distilled and the oil collected was extracted with ether. The ethereal layer was treated with dilute NaOH, then dilute HCl, water and then dried and distilled. The yield was 31.0 g. of m-Bromo propiophenone; B.P. 135°C/14 mm. Recrystallized from ligroin M.P. 41-2° C. Semi-carbazone M.P. 180° dec.

PREPARATION OF m-CHLORO PROPIONPHENONE:

Thirty grams (0.20M) of m-aminopropiophenone were dissolved in 30 cc. of concentrated HCl and 80 cc. of water. The amine was diazotized using 20% aqueous NaNO_2 at 5° C. The slush was added to a solution of cuprous chloride in 60 cc. of HCl and 30 cc. of water. After one hour at room temperature the mixture was kept at 50-60° for 20 minutes. The ketone was collected from ether and distilled at 124°/14 mm. and crystallized upon cooling: M.P. 48-9° C.

ATTEMPT TO REVERSE THE m-IODO PROPIONPHENONE (69):

Thirty two grams (0.22M) of m-amino propiophenone were placed in 110 g. concentrated HCl and 100 cc. of water and cooled to 5° C. in an ice bath with stirring. Sixteen grams

of NaNO_3 (0.23M) in 80 cc. of ice water were added from a separatory funnel with the stem below the surface and the whole stirred 10 minutes.

An aqueous solution of KI (36.0 g. (0.22M) in 100 ml. of water) was added directly to the diazo-compound and the reaction allowed to stand overnight. The flask was then heated on a steam bath until the frothing stopped. A heavy organic layer settled out. The aqueous layer was decanted and the residue made alkaline with NaOH pellets. It was then extracted with 150 cc. of ether and dried. A heavy oil (crude wt 42 g.) was obtained upon distilling off the ether. It refused to crystallize from alcohol, alcohol and water, petroleum ether, or upon freezing and recourse was made to vacuum distillation. At 160°C . decomposition began and continued even when the heat source was removed until a temperature of 218°C . was reached. The pot contained only charcoal.

A second attempt to make the m-iodopropiophenone in the same manner failed even though much more care was taken to wash all trace of base from the ether layer and nitrogen passed during distillation.

PREPARATION OF THE m-HALO PHENYL DIETHYL CARBINOLS:

Tertiary alcohols were prepared from the two available m-halo-propiophenones using the methods of Swain and Boyles (op. cit.). The alcohols formed: m-Chlorophenyl diethyl

carbinol and m-bromophenyl diethyl carbinol boiled at 128° C./14 mm. and 113-14° C./14 mm. respectively and yielded the p-nitro benzoates M.P.'s 86° C. and 137° C.

SYNTHESIS OF ortho-AMINO PROPIONPHENONE:

Ortho-amino propiophenone was made according to the method of Claessen and Shadwell (11) as modified by Auwers and Duesberg (4).

Ortho-nitro benzoic acid was made in 80% yield by alkaline permanganate oxidation of o-nitrotoluene by the method of Reimer and Gatewood, (77).

The acid chloride was made by reaction of 200 g. of the acid with a large excess of thionyl chloride. The thionyl chloride was distilled off as well as possible on the steam bath. Although Auwers claims the o-nitrobenzoyl chloride was purified by vacuum distillation, the acid chloride tends to decompose when heated and no attempt was made to distill it. The crude acid chloride was added to the sodium salt of ethyl-methylacetoacetate in ether.

The ethyl methyl acetoacetate was made according to the method of Geuther (26) by adding 1.5M of ethyl acetoacetate (195 g.) to 1.5M of NaOEt in excess alcohol and then adding 1.6M (232 g.) of methyl iodide and heating the reaction to 160-170° C. for six hours. The reaction was then cooled and

the NaI filtered off. The ethyl methylacetoacetate distilled over at 30-30.5° C./14 mm. The yield was 90%.

One mole of ethyl methyl aceto acetate was added to one mole of sodium ethylate in alcohol and 1.1M of ortho-nitrobenzoyl chloride in 100 cc. of ether was slowly added to the sodium salt. The alcohol and ether were distilled off as formed and the reaction stirred and heated to 100° C. for 6 hours. The reaction was then cooled and the NaCl filtered off, then the filtrate was distilled. The ethyl- α -(o-nitro benzoyl)- α -methyl acetoacetate came over a brilliant red at 210° C./20 mm. The yield was 85% (237 g.).

The ethyl- α -(o-nitrobenzoyl)- α -methylacetoacetate was placed in 600 ml. of 1:1 sulfuric acid and refluxed for 10 hours. The reaction was then cooled and diluted to 2 liters and then extracted with ethyl ether. The ether layer was washed with water. The ether was distilled off and the yellow oil distilled at 145°/1 mm. The yield upon hydrolysis was 35% (60 g). The solid crystallized from petroleum ether and was recrystallized, M.P. 47°. The semicarbazone M.P. 185° C. dec.

The o-nitropropiophenone was reduced (68) by addition in glacial acetic acid to tin and concentrated HCl and refluxing for 2 hours. After being made basic, steam was passed until no more oil was delivered. The oil was extracted in ether and dried over potassium carbonate. The ether was distilled at 140°C./14 mm. when it slowly crystallized into pale yellow crystals M.P. 46° C.

SYNTHESIS OF o-CHLOROPROPIOPHENONE: & o-BromOPROPIOPHENONE:

The ortho chloropropiophenone B.P. $65^{\circ}/1$ mm. refractive index 1.5219 2,4-dinitro phenylhydrazone M.P. 205° C. and the ortho-bromopropiophenone: B.P. $127^{\circ}/14$ mm., semicarbazone M.P. 132° C. were made by the Sandmeyer reaction previously described in yields of 70% and 72% respectively.

ATTEMPTED SYNTHESIS OF O-IODOPROPIOPHENONE:

The synthesis was attempted in the same manner as that for the m-iodopropiophenone. Again, the oil decomposed upon attempted distillation.

SYNTHESIS OF p-iodopropiophenone:

Para-amino propiophenone was made in the same manner as the o-amino propiophenone (4): 1.2M (224 g.) of p-nitrobenzoyl chloride were added in dry ether to one mole of ethyl-methyl acetoacetate in one mole of NaOEt and heated to 100° C. for 6 hours. In attempting to distill the resulting oil, decomposition occurred at 170° C. and, upon cooling, a solid was obtained. The solid was recrystallized from alcohol M.P. 57° C. and was added immediately to 1:1 sulfuric acid and refluxed 12 hours. P-nitro propiophenone was extracted from the diluted reaction mixture in ether. The ether was distilled off and the yellow solid recrystallized from alcohol. M.P. 114° C. Yield 40 g. (total yield 28%).

The p-nitropropiophenone (0.25M) was reduced using tin and concentrated HCl (3). The p-amino propiophenone was recovered from a sodium hydroxide solution of the hydrochloride salt. M.P. 140° C. Yield 32.2 g.

The attempt to make the p-iodopropiophenone by the Diazo method as previously described failed again at the distillation step. Decomposition occurred at 170° C. and only charcoal remained in the pot. A solid derivative of the oil was obtained: 2,4-dinitrophenylhydrazone M.P. 139° C. dec.

Para-iodopropiophenone was finally made using Kimura's (58) anhydrous aluminum chloride preparation of p-iodoacetophenone as a guide. One hundred and ten grams (0.83M) of anhydrous aluminum chloride were covered with 300 cc. of carbon disulfide in a three-necked flask cooled to 20° C. in a water bath. 168 g. (0.83M) of iodobenzene were added to the cooled and stirred mixture and then 76.4 g. (0.83M) of propionyl chloride were added and the whole stirred one half hour in the water bath while stirring. The mixture was then placed on the steam bath and very slowly heated until the carbon disulfide refluxed. The reaction was allowed to continue until the evolution of HCl was hardly visible (thirty minutes). Then the solvent was distilled off and the oily residue was poured slowly into one kilo of ice while stirring vigorously. The solid formed was filtered off and taken up in ether. The ether layer was then

washed with dilute K_2CO_3 and water, and then dried over K_2CO_3 . The ether was then distilled off and the solid recrystallized three times from alcohol. By the third recrystallization all trace of free iodine had disappeared. A faintly brown plate-like crystal resulted. M.P. $198^\circ C.$, 2,4-dinitrophenylhydrazone M.P. $199^\circ C.$ dec. The yield was 50%.

SYNTHESIS OF p-IODOPHENYL DIETHYL CARBINOL:

The p-iodophenyl diethyl carbinol was prepared in 30% yield in the manner of Swain and Boyles (cit. pre.). B.P. $125^\circ C./4 \text{ mm.}$, refractive index $n_D^{22} = 1.5735$. M.P. of p-nitro benzoate $134^\circ C.$

A FURTHER PROOF OF STRUCTURE:

Since diethylphenyl carbinol is a known compound and has been made previously by an independent method which yields a solid derivative, dehalogenation of the ring of its halo-derivatives ought to be an acceptable proof of the structure, if the p-nitrobenzoate has the same mixed melting point as that of the known compound.

Using the method of Schwenk, Papa and Ginsberg (71, 72, 73), 2 g. of each of the alleged alcohols were placed in a 300 cc. Ehrlenmeyer flask in 20 ml. of ethanol and 4 g. of Raney Nickel alloy added. The Ehrlenmeyer was fitted to a reflux condenser and immersed in an ice bath. 150 cc. of

chilled 10% NaOH were added through the reflux condenser and, when the initial reaction had subsided, a low flame was placed under the Thrlenmayer. When the reaction ceased after approximately 2 hours, the flask was heated on the steam bath until the solution was clear and colorless. The solution was then decanted hot and, when cool, extracted with ether. The ether layer was washed with water and dried over Na_2CO_3 . The ether was then distilled off and the resulting oil was treated with p-nitrobenzoyl chloride and pyridine and refluxed one hour and the ester worked up. In each case, the p-nitrobenzoate formed had the M.P. 80°C. , the mixed M.P. 80°C.

RESULTS

TABLE NO. 1

-Benzoin Acid	Grams Acid	Moles Acid	Moles Grn.	H Gr./ M Acid	Grams Alc.	Moles Alc.	% Yld. Alc.*	Ave. % Yld.	Moles Ketone	% Yld. Ketone	Ave. % Yld.
Benzoin	57.3	0.47	1.5	3.2	22.3	0.136	29.0%	29.0%	0.019	4.0%	4.6%
(forced)	57.3	0.47	1.5	3.2	22.3	0.136	29.0%	29.0%	0.024	5.2%	5.2%
(forced)	57.3	0.47	1.5	3.2	21.5	0.131	28.0%	28.5%	0.043	9.2%	8.1%
	57.3	0.47	1.5	3.2	22.3	0.136	29.0%	29.0%	0.033	7.0%	7.0%
	42.8	0.35	1.5	4.2	29.6	0.180	50.0%	49.2%	--	--	--
	42.8	0.35	1.5	4.2	28.6	0.174	48.4%	65.0%	--	--	--
	36.6	0.30	1.5	5.0	32.1	0.195	65.0%	94.4%	--	--	--
	30.6	0.25	1.5	6.0	38.6	0.235	94.2%	94.4%	--	--	--
	30.6	0.25	1.5	6.0	38.8	0.236	94.6%	95.0%	--	--	--
	26.9	0.22	1.5	7.0	34.3	0.209	95.0%	95.0%	--	--	--
O-chloro-	73.5	0.47	1.5	3.2	39.8	0.200	42.5%	41.4%	0.038	8.0%	7.4%
(forced)	73.5	0.47	1.5	3.2	37.8	0.190	40.3%	29.4%	0.032	6.8%	6.8%
(forced)	73.5	0.47	1.5	3.2	28.1	0.141	31.1%	48.1%	0.037	7.8%	9.0%
	73.5	0.47	1.5	3.2	27.1	0.136	28.3%	67.5%	0.052	11.2%	11.2%
	58.7	0.38	1.5	4.0	35.6	0.179	47.8%	--	--	--	--
	58.7	0.38	1.5	4.0	36.2	0.182	48.4%	--	--	--	--
	39.2	0.25	1.5	6.0	33.4	0.168	67.5%	--	--	--	--
m-chloro-	58.7	0.38	1.5	4.0	50.5	0.254	67.8%	66.3%	--	--	--
	58.7	0.38	1.5	4.0	48.9	0.246	64.8%	--	--	--	--
p-chloro-	73.5	0.47	1.5	3.2	47.6	0.240	52.1%	51.3%	--	--	1.1%
(forced)	73.5	0.47	1.5	3.2	47.1	0.237	50.5%	47.7%	0.011	2.2%	2.1%
(forced)	73.5	0.47	1.5	3.2	45.3	0.228	48.5%	71.4%	0.005	1.2%	2.1%
	73.5	0.47	1.5	3.2	43.7	0.220	46.9%	93.1%	0.014	3.0%	3.0%
	52.1	0.33	1.5	4.5	50.0	0.251	75.5%	--	--	--	--
	52.1	0.33	1.5	4.5	44.3	0.223	66.9%	--	--	--	--
	39.2	0.25	1.5	6.0	46.9	0.236	94.2%	--	--	--	--
	39.2	0.25	1.5	6.0	45.7	0.230	92.0%	--	--	--	--

TABLE NO. 1. (Contd.)

-Benzoinic Acid	Grams Acid	Moles Acid	Moles Grp./ H. Acid	Grams Alc.	Moles Alc.	%Yld. Alc.#	Ave. % Yld. Ketone	Moles Ketone	% Yld. Ketone	Ave. % Yld. Ketone
O-bromo-	94.5	0.47	1.5	39.9	0.164	35.0%	34.6%	0.015	3.1%	3.8%
(forced)	94.5	0.47	1.5	38.9	0.160	34.2%		0.021	4.5%	
(forced)	94.5	0.47	1.5	31.9	0.131	27.3%	23.4%	0.028	5.9%	5.4%
	94.5	0.47	1.5	22.3	0.092	19.5%		0.023	4.9%	
	67.4	0.33	1.5	31.9	0.131	39.2%	38.6%	--	--	
	67.4	0.33	1.5	30.7	0.126	38.0%		--	--	
	50.2	0.25	1.5	54.3	0.223	89.3%	89.0%	--	--	
	50.2	0.25	1.5	54.0	0.221	88.7%		--	--	
m-bromo-	75.4	0.38	1.5	59.4	0.244	65.2%	64.0%	--	--	
	75.4	0.38	1.5	57.4	0.236	62.3%		--	--	
	50.2	0.25	1.5	55.0	0.226	90.5%	91.0%	--	--	
	50.2	0.25	1.5	55.7	0.229	91.5%		--	--	
p-bromo-	94.5	0.47	1.5	39.9	0.164	35.0%	34.2%	--	--	
(forced)	94.5	0.47	1.5	38.0	0.156	33.2%		--	--	
(forced)	94.5	0.47	1.5	38.7	0.159	34.0%	32.6%	0.002	0.4%	1.0%
	94.5	0.47	1.5	35.4	0.146	31.2%		0.008	1.6%	
	70.4	0.35	1.5	65.1	0.268	79.8%	76.6%	--	--	
	70.4	0.35	1.5	62.5	0.257	73.4%		--	--	
	50.2	0.25	1.5	58.6	0.241	96.1%	95.0%	--	--	
	50.2	0.25	1.5	57.2	0.235	93.9%		--	--	
o-nitro-	63.5	0.38	1.5	--	--	--	--	--	--	
	63.5	0.38	1.5	--	--	--	--	--	--	

TABLE NO. 1 (Contd.)

Benzole Acid	Grams Acid	Moles Acid	Moles Grign.	M Gr./ H Acid	Grams Alc.	Moles Alc.	% Yld. Alc.*	Ave. % Yld.	Moles Ketone	% Yld. Ketone	Ave. % Yld.
m-nitro	63.5	0.38	1.5	4.0	--	--	--	--	--	--	--
	63.5	0.38	1.5	4.0	--	--	--	--	--	--	--
p-nitro-	63.5	0.38	1.5	4.0	--	--	--	--	--	--	--
	63.5	0.38	1.5	4.0	--	--	--	--	--	--	--
o-Iodo-	62.0	0.25	1.0	4.0				**			**
	62.0	0.25	1.0	4.0				**			**
m-Iodo-	62.0	0.25	1.0	4.0				**			**
	62.0	0.25	1.0	4.0				**			**
p-Iodo-	62.0	0.25	1.0	4.0				**			**
	62.0	0.25	1.0	4.0				**			**

*All yields based upon the first distillation.

**No reportable yields due to decomposition upon distillation.

PHYSICAL PROPERTIES OF THE ALCOHOLS

Diethyl phenyl carbinol:

B.P. 117° @ 19 mm.

n_D^{22} 1.5142

p-nitrobenzoate M.P. 80° C.

Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>
calculated	80.44	9.82
found		

p-chlorophenyl diethyl carbinol:

B.P. $129-30^{\circ}$ @ 14 mm.

n_D^{22} 1.5472

p-nitrobenzoate M.P. 122° C.

Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Chlorine</u>
calculated	66.49	7.62	17.85
found			

m-chlorophenyl diethyl carbinol:

B.P. 128° @ 14 mm.

n_D^{22} 1.5308

p-nitrobenzoate M.P. 86° C.

Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Chlorine</u>
calculated	66.49	7.62	17.85
found			

o-chlorophenyl diethyl carbinol:

B.P. 140-1° @ 26 mm.

 n_D^{22} 1.5298

p-nitrobenzoate M.P. 122° C.

Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Chlorine</u>
Calculated	66.49	7.62	17.25
Found			

p-bromophenyl diethyl carbinol:

B.P. 115-16° @ 3 mm.

 n_D^{22} 1.5472

p-nitrobenzoate M.P. 142° C.

Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Bromine</u>
Calculated	54.11	6.20	32.86
Found			

m-bromophenyl diethyl carbinol:

B.P. 113-14° @ 14 mm.

 n_D^{22} 1.5470

p-nitrobenzoate M.P. 137° C.

Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Bromine</u>
Calculated	54.11	6.20	32.86
Found			

o-bromophenyl diethyl carbinol:

B.P. 138-40° @ 13 mm.

 n_D^{22} 1.5490

p-nitrobenzoate M.P. 133° C.

Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Bromine</u>
Calculated	54.11	6.20	32.86
Found			

p-Iodophenyl diethyl carbinol:

B.P. 125° @ 4 mm.

 n_D^{22} 1.5735 n_D^{22}
p-nitrobenzoate M.P. 134° C.Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Bromine</u>
Calculated	45.54	5.21	43.64
Found			

m-Iodophenyl diethyl carbinol:

B.P. 127° @ 1 mm.

 n_D^{22} 1.5812 n_D^{22}
p-nitrobenzoate M.P. 116° C.Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Bromine</u>
Calculated	45.54	5.21	43.64
Found			

o-Iodophenyl diethyl carbinol:

B.P. 118° @ 2 mm.

 n_D^{22} 1.5750 n_D^{22}
p-nitrobenzoate M.P. 93° C.Analysis:

	<u>Carbon</u>	<u>Hydrogen</u>	<u>Iodine</u>
Calculated	45.54	5.21	43.64
Found			

DISCUSSION OF RESULTS

Since benzoic acid is both inexpensive and plentiful, it was used to determine the proper conditions under which the other acids were to be reacted. The first reactions were with one mole of the acid added to 3.2 moles of the Grignard reagent. (See Table 1) Only 29% of the tertiary alcohol was obtained in this manner and 4.6% ketone. The unreacted acid was recovered and found to make up for the percentage difference. This was the expected yield. However it was decided to force the reaction by increasing its temperature to see if the yield could be increased. The reaction was forced and the diethyl phenyl carbinol was obtained in 28.5% yield and the yield of ketone rose to 8.1%. This showed little improvement in yields of the desired product. Forcing the reaction in some manner increased the rate of the ketone formation step (III see THEORY) and had no effect upon the rate of addition of the Grignard reagent to the intermediate ketone, since the total yield of product is greater than that of the unforced total yield.

Since solvents sometimes affect rates of reactions, the presence of a preponderance of benzene may account for the altered yields -- rather than the temperature increase. When the reactions with the other acids were forced in the same proportions, the yield of ketone was generally increased

(except in the cases of *m*-chlorobenzoic acid and *m*-bromobenzoic acid which produced only traces of the ketones in both cases) and the yields of the alcohols would remain the same or diminish. Thus, when *o*-chlorobenzoic acid was reacted with 3.2 moles of ethyl Grignard 41.4% tertiary alcohol and 7.4% ketone were obtained. When the same reaction was forced, the yield of the alcohol decreased decidedly to 29.4% and the yield of ketone increased to 9%. When *o*-bromobenzoic acid reacted with 3.2 moles of Grignard reagent 34.6% tertiary alcohol was obtained and 3.8% ketone, when forced the same reaction yielded only 23.4% alcohol and 5.4% ketone. The *p*-bromobenzoic acid reacted with 3.2 moles of Grignard reagent produced no ketone fraction and 34.2% tertiary alcohol while the forced reaction yielded 1% ketone and 32.6% tertiary alcohol.

Thus it appears that the unforced reaction gives better yields of tertiary alcohols (although traces of ketone appear in every case) than the forced reaction--or, at any event, less by-products are obtained.

Since relatively low yields of tertiary alcohols were obtained as compared with ester and acid chloride and ketone reactions with Grignard reagents and benzoic acids were recovered intact after hydrolysis, it was decided that the use of a greater excess of the Grignard reagent might induce more of the acid to react:

When benzoic acid was reacted with 4.2 moles of Grignard reagent, 49.2% tertiary alcohol was produced and only a trace of the ketone. This appeared to be a sufficient excess (44) to permit all the benzoic acid to react--at least stoichiometrically. Thus all the acids were reacted in the ratio of 1:4 to 1:4.5 moles of Grignard reagent (See Table II):

Ortho-chlorobenzoic acid now gave a yield of 48.1% tertiary alcohol reacting with 4 moles of the reagent; m-chlorobenzoic acid yielded 66.3% alcohol with 4 moles of reagent; p-chlorobenzoic acid reacting with 4.5 moles of ethyl Grignard yielded 71.4% alcohol and no isolatable ketone.

Ortho-bromobenzoic acid yielded 38.6% alcohol and no ketone when reacted with 4.5 moles of the Grignard reagent. Meta-bromobenzoic acid yielded 64.0% with 4 moles of Grignard and the p-bromobenzoic acid gave the enormous yield of 76.6% alcohol with 4.3 moles of Grignard reagent.

The iodo-alcohols would decompose upon working up and no true yields can be reported for their reaction. Part of the iodo product would distill as the dehalogenated alcohol and part as the unsaturate and part would distill as the iodo-alcohol, slowly decomposing upon standing.

TABLE II

YIELDS OF ALCOHOLS FROM REACTION OF THE ACIDS WITH 4.0-4.5 MOLES
GRIGNARD

In Order of Decreasing Yield

Order	Acid	Ratio of Moles of Gr. to Moles of Acid	Yield of Alcohol
1.	p-bromo benzoic	4.3	76.6%
2.	p-chloro benzoic	4.5	71.4%
3.	m-chloro benzoic	4.0	66.3%
4.	m-bromo benzoic	4.0	64.0%
5.	Benzoic	4.2	49.2%
6.	o-chloro benzoic	4.0	48.1%
7.	o-bromo benzoic	4.5	38.6%

The order of reactivity of the acids is therefore:
 p-bromo-, p-chloro-, m-chloro-, m-bromo-, benzoic, o-chloro-,
 o-bromo-, and then presumably followed by the iodocompounds.
 Thus in each of the series of halobenzoic acids, the order of
 reactivity is para meta ortho in a decreasing scale with
 the bromo compounds edging out the ortho compounds in reactivity.

Both the ortho-benzoic acids gave lower yields of
 tertiary alcohols than benzoic acid and the meta- and para-
 benzoic acids gave greater yields than the benzoic acid. This
 reactivity shows some correspondence to the order of solubilities

and ionization constants of the acids -- yet shows no direct correspondence to either. According to Dippy and Watson (16) there is a-- "...connection of roughly linear characteristics (which) exists in a number of cases between the values of log K for the same reaction of a series of m- or p-substituted benzene derivatives and those of log K for the corresponding benzoic acids." (16) According to Jenkins (54), this linear relationship can be extended to the ortho compounds too. In Table III, the ortho, meta and para compounds are listed with their yields and also with the pKa's of the acids. Since the yields can be taken as a function of the k of the reaction, they are divided by the pKa's to see if a somewhat linear relationship can be seen. The same is done with the negative log of the solubilities of the acids in water at 25° C. to see if this is a determining factor too:

TABLE III

<u>Relationship of Yields of Alcohols to pKa and Solubility</u>					
<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>	<u>6</u>
<u>Acid</u>	<u>Yield of Alcohol</u>	<u>pKa</u>	<u>Yield/pKa</u>	<u>-Log Sol'y.</u>	<u>% Yield/-Log Sol'y.</u>
p-bromo	76.6%	3.95	19.3	3.56	21.5
m-bromo	64.0%	3.86	17.0	2.71	23.6
o-bromo	38.6%	2.85	13.5	2.05	19.2
			16.6		21.4 Ave.
p-chloro	71.4%	3.98	18.0	2.92	24.5
m-chloro	66.3%	3.82	17.4	2.65	25.0
o-chloro	48.1%	2.90	17.0	1.87	25.7
			17.5		25.1 Ave.

The bromo compounds could hardly be taken as a proof of the linear relationship of pK_a to reaction rate. Certainly a slope that shows such deviation should be considered a curve. There is a little better correspondence of the solubilities and reaction rate as seen in the last column. However, when we look at the chloro series, we see a marked correlation of slope in both columns 4 and 6. Certainly this is one of the cases where such a relationship as Dippy suggests will hold. In the light of what follows, there would have been greater correspondence of the *p*-chloro compound, if only 4.0 mole ratios had been used instead of 4.5. And that explains the lack of close correlation of the bromo compounds, which were reacted in mole ratios of 4.5, 4.3, and 4.0 rather than all the same. Since, there isn't a definite linear increase of yield with excess Grignard reagent (as will be shown later), no mathematical account can be taken of these differences to obtain the desired slope. The writer believes that there is a linear relationship of rate to pK_a in this reaction for each series of substituted acids and also points out the linear relationship of the solubility with the rate of reaction. This should not be too surprising since water solubility would certainly be affected by the degree of ionization. This relationship would certainly have been more strongly established if the nitro compounds had reacted for, in that series, the order of the pK_a 's is meta, para, ortho (68, 32, 70).

By a fortunate accident, it was found that the yield of alcohol could be increased even further by addition of a greater excess of Grignard reagent. Although the usual 1.5 moles of ethyl Grignard reagent had been prepared, only 42.0 grams (0.25M) of o-chlorobenzoic acid was available. This amount was added to the reagent with the expectation that no further excess of Grignard reagent could affect the yields (enolization (43) did not appear to increase with excess Grignard reagent). When the product was worked up, it was found that the yield of o-chlorophenyl diethyl carbinol had increased to 67.5% in this 6:1 ratio. It was decided that the increase in yields of alcohols with increase in excess Grignard reagent be investigated. Using benzoic acid to determine the best conditions:

TABLE IV

Ratio of EtMgX to Benzoic Acid	Yield of Alcohol	Increase/ Mole Increment
3.2	29.0%	
4.2	49.2%	20.2%
5.0	65.0%	19.8%
6.0	94.4%	29.4%
7.0	95.0%	0.5%

As can be seen in Table IV, the yield of alcohol increased almost linearly from 3 moles to 6 moles. Apparently, little or no increase occurred from 6 to 7 mole ratios.

Thus a ratio of 6 moles of Grignard reagent to each mole of acid was now reacted with the available acid to see if their yield, too, would increase under these new conditions:

The o-chlorophenyl diethyl carbinol yield increased from 43.1% for 4.0 moles to 67.5% with 6 moles. The yield of p-chlorophenyl diethyl carbinol increased from 71.4% with 4.5 moles to 93.1% with 6.0 moles of Grignard reagent. The yield of m-bromophenyl diethyl carbinol increased from 64.0% for 4.0 moles to 91.0% with 6.0 moles of reagent. O-bromo benzoic acid increased its yield to 89.0% alcohol and p-bromo benzoic acid increased to give 98.0% tertiary alcohol.

In this case, all the acids were reacted in equal mole ratios and Dippy's relationship should get a fairer test. Unfortunately, there was no m-chloro benzoic acid available for this experiment. But its yield could be filled in since the yields of the other two compounds are known and the pKa of m-chlorobenzoic acid is known. The m-chlorobenzoic acid should yield 89.1% tertiary alcohol when reacted with 6 moles of ethyl Grignard.

TABLE VRelationship of Yields of Alcohol to pKa of Acids

Acid	Yield of Alcohol	pKa	% Yield/pKa
p-bromo	95.0%	3.95	24.0
m-bromo	91.5%	3.86	24.3
o-bromo	89.0%	2.85	23.2
—			23.8 average
p-chloro	93.1%	3.98	23.4
m-chloro	(89.1%)	3.82	(23.3)
o-chloro	67.5%	2.90	23.3
			23.3 average

This method of reacting the aromatic acids with 3 moles of excess Grignard reagent in refluxing ethyl ether brings this reaction into the realm of more successful reactions. It is now possible to prepare tertiary alcohols of the form $\text{Ar-C(OH)R}'_2$ in yields which would actually surpass those usually obtained by using the corresponding esters or ketones with less interfering by-products. As a laboratory tool, this method would save the time required for esterification--though admittedly, requiring the use of large excesses of reagent.

The fact that twice the theoretical amounts of reagent are required to produce near molar yields would appear to

indicate that some equilibrium step is being forced in accordance with the Mass Action Law. However, it is equally possible that the excess reagent increases the rate of reaction, making the reaction appear as one of a lesser kinetic order than when molar quantities are used. It is suggested that this reaction is ripe for kinetic studies and would readily lend itself to such an investigation.

SUMMARY

1. The halobenzoic acids react readily with ethyl Grignard reagent to give tertiary alcohols and traces of ketones.
2. The nitrobenzoic acids didn't react with the ethyl Grignard.
3. The yields of tertiary alcohols can be increased to 70-95% by addition to excess Grignard reagent.
4. The rates of reaction of the halobenzoic acids show a linear relationship with the pKa's of the acids.

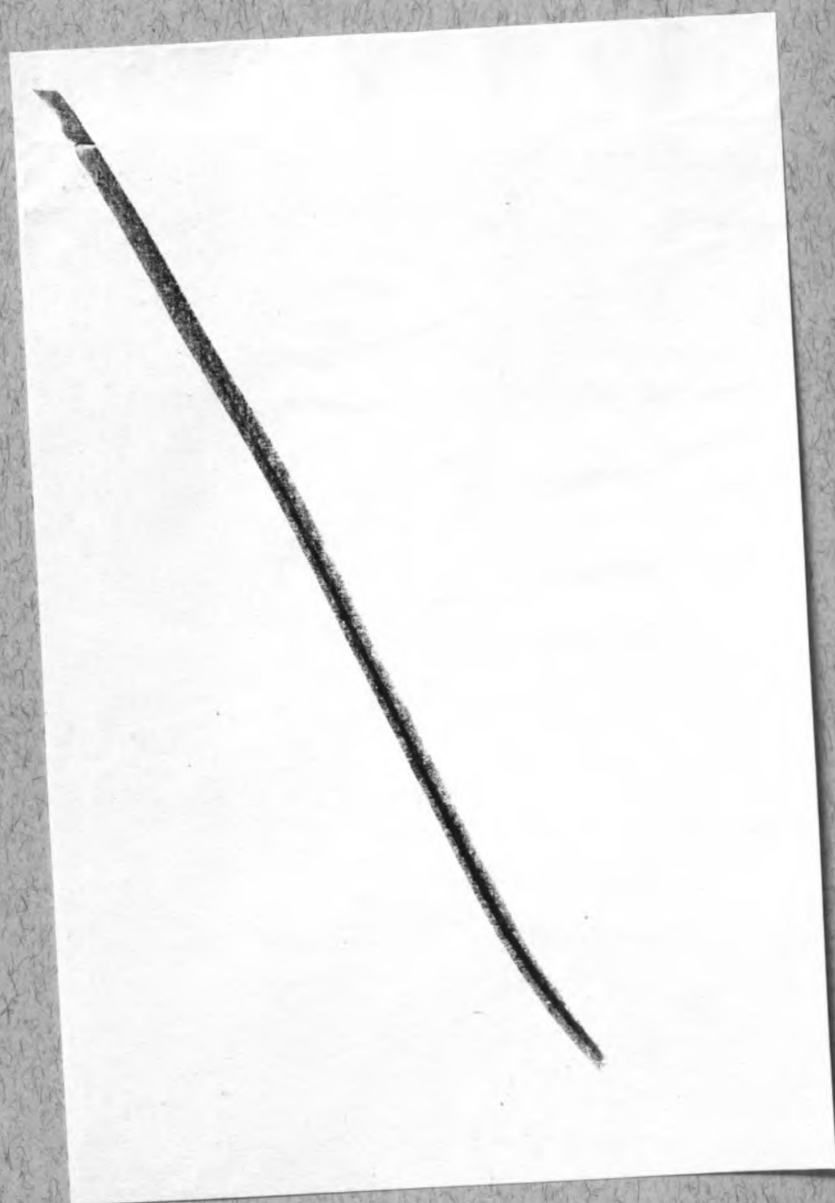
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