

I, THE SYNTHESIS OF 2-METHYL-S-PHENYL PENTANE AND 2-METHYL-S-PARA HYDROXY PHENYL PENTANE II. THE PREPARATION OF SOME TERTIARY ALCOHOLS BY THE ADDITION OF ORGANIC ACIDS TO GRIGNARD REAGENTS

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I. THE SYNTHESIS OF 2-HETHYL-3-PHENYL PENTANE AND 2-METHYL-3-PARA HYDROXY PHENYL PENTANE

II. THE PREPARATION OF SOME TERTIARY ALCOHOLS BY THE ADUITION OF ORGANIC ACIDS TO GRIGNARD REAGENTS

by

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CONTENTS

	Page
SYNTHESIS OF 2-METHYL-3-PHENYL PENTANE AND 2-METHYL-3-PARA HYDROXY PHENYL PENTANE	
Introduction	1
Historical	2
Experimental	3
Discussion	19
Summery	21
Bibliography	22

II. PREPARATION OF TERTIARY ALCOHOLS

I.

Introduction	25
Historical	26
Theoretical	29
Experimental	32
Discussion	41
Summary	43
Bibliography	44

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I. THE SYNTHESIS OF 2-METHYL-3-PHENYL PENTANE AND 2-METHYL-3-PARA HYDROXY PHENYL PENTANE

INTRODUCTION

In the year of 1941 Huston and Curtis (1) reported the condensation of the six possible secondary hexyl alcohols with phenol in the presence of anhydrous aluminum chloride. However, mixtures or rearrangement products were obtained instead of the normal condensation products.

The following year, 1942, Huston and Kaye (2) reported the condensation of the six secondary hexyl alcohols with benzene as well as the secondary propyl, butyl, amyl, and heptyl alcohols, using aluminum chloride as the condensing agent. Here again, with the exception of pinacolyl, mixtures or rearrangement products were obtained.

The purpose of the present investigation is to prepare the secondary hexyl phenol and secondary hexyl benzene which could not be prepared by direct condensation because of rearrangements and which, up to now, have not been prepared by independent synthesis.

HISTORICAL

The methods of preparing alkyl benzenes and alkyl phenols are many and varied. Of these, direct alkylation of benzene and phenol in the presence of various catalysts has gained a wide popularity and prominence in the literature. However, the products are not always well defined, thus making it necessary to employ other synthetic procedures.

Since this paper concerns itself primarily with syntheses other than those of condensation, only these types of syntheses will be discussed in detail.

It should be mentioned briefly at this time that the condensation of alcohols with aromatic nuclei in the presence of aluminum chloride has been a subject of investigation in this laboratory since 1916 when Huston and Friedeman (3) condensed benzyl alcohol with benzene to obtain diphenyl methane. Also, other investigators have condensed alcohols with benzene and phenols using such catalysts as sulfuric acid (4), phosphoric acid (5), perchloric acid (6), zinc chloride (7), magnesium chloride (8), ferric chloride (9), boron fluoride (10), hydrochloric acid (11), and many other substances.

Alkylbenzenes have been prepared by the polymerization of alkyl acetylenes (12), the reduction of phenols by means of zine dust (13), and the dry distillation of an aromatic acid with soda lime (14). Sabatier has prepared cumene by passing the vapors of various terpenes with hydrogen over nickel at 350-360 degrees centigrade (15). The reaction of zinc alkyls with benzyl chlorides has been used to prepare other alkylbenzenes (16). The Wurtz reaction and some of its modifications also have been used to prepare cumene (17),

secondary butyl benzene (18), and normal phenyl hexane (19). A very good yield of normal propyl benzene has been obtained from the reaction of benzyl magnesium chloride and diethyl sulfate (20). J

One of the most important methods of preparing alkyl benzenes in pure form was used by Klages to prepare a number of compounds (21). It involved the use of the Grignard reagent. A ketone, such as acetophenone, was treated with the proper elkyl magnesium halide to form a tertiary alcohol which split off water easily to yield an olefin. Upon reduction with sodium and alcohol, the olefin gave the saturated alkyl benzene in good yield. Klages also found that unsaturated compounds of the types



were not reducible with sodium and alcohol (22) and was unable to prepare the corresponding alkyl benzene.

A method of preparing alkyl phenols was discovered in 1867 by Kekule and Wurtz, independently. It consisted of sulfonating the alkyl benzene and then fusing the sulfonic acid with potassium hydroxide (23). Another method developed by Malherbe (24) involves the nitration of the alkyl benzene, reduction of the nitre compound to the amino compound, the diazotization of the amino compound, and hydrolysis to the phenol. This method was used by the author to prove the structure of 2-methyl-3-para hydroxy phenyl pentane.

Pyman and coworkers (25) reported the preparation of a number of alkyl phenols in 1930. They prepared acyl phenol from the corresponding phenyl esters by means of the Fries rearrangement. The alkyl phenol itself was obtained by the Clemmensen reduction of the acyl phenol. Johnson and students (26) prepared some of the higher phenols using the Nencki condensation and Clemmensen reduction. An acyl phenol was prepared by the condensation of an aliphatic acid and phenol in the presence of zinc chloride. The acyl phenol was then reduced to the corresponding alkyl phenol by the Clemmensen reduction.

Alkyl phenols also have been prepared by the rearrangement of phenol ethers using heat (27), sulfuric and glacial acetic acids (23), zinc chloride (29), aluminum chloride (30), and boron fluoride (31), as catalysts.

EXPERIMENTAL

I. Materials

Phenol was obtained from the stockroom and redistilled. B.P. = 180-181°C at 745 mm.

Anisole was prepared by the action of dimethyl sulfate on phenol according to the procedure described in <u>Organic Syntheses</u> (32). It was fractionated collecting the fraction distilling from 152-154°C at 742 mm. as the pure anisole. Dimethyl sulfate was used as received from the stockroom.

Isobutyric acid as obtained from the stockroom was redistilled. B.P. = 153-155°C at 737 mm.

Isobutyryl chloride was prepared by reacting thionyl chloride with isobutyric acid (33). The fraction boiling from 91-93°C at 745 mm. was collected. Thionyl chloride could be obtained in pure form.

Ethyl bromide could be obtained chemically pure from the stockroom and was dried over calcium chloride.

The secondary alcohol, 4-methyl pentanol-2, was received from the stockroom and redistilled collecting the fraction boiling from 129-130°C at 745 mm.

Magnesium turnings used were especially prepared for Grignard reactions.

Diethyl ether for Grignard reactions was anhydrous. Benzene was thiophene free and of C.P. grade.

A good grade of petroleum ether was used. The ether, benzene, and petroleum ether were dried over freshly cut sodium before use.

Aluminum chloride was Baker's analyzed, anhydrous, sublimed reagent.

Other commonly used reagents, such as drying agents, were to be found on the side shelf, in the proper degree of purity.

II. Preparation of 2-methyl-3-phenyl pentane

A. Phenyl isopropyl ketone

This ketone was prepared by a modification of the method used by Schmidt (34).

One mole of isobutyryl chloride and eight moles of thiophene free, anhydrous benzene were placed in a dry, two liter, three-necked flask equipped with reflux condenser, thermometer, and motor-driven stirrer. The solution was cooled to 10°C and one mole of anhydrous aluminum chloride was added in small portions during the course of two hours. The temperature was maintained at 10°C throughout the addition. The solution turned a dirty, reddish-brown in color and hydrochloric acid fumes were evolved. Upon standing over-night the reaction mixture was decomposed upon ice and hydrochloric acid. After separation of the benzene and water layers the water layer was extracted once with benzene. The combined benzene extracts were washed with sodium carbonate, dried over calcium chloride, the benzene distilled off, and the ketone fractionally distilled. From two and one-half moles of isobutyryl chloride, 192 grams (52%) of a product boiling from 100-103°C at 15 mm, were obtained.

This product was used as isopropyl phenyl ketone, and was identified by the preparation of a 2,4-dinitrophenylhydrazone which melted at 141°C.

B. Ethyl isopropyl phenyl carbinol

This tertiary alcohol was prepared by addition of isopropyl phenyl ketone to ethyl magnesium bromide by a method much like that used by Klages (35). The Grignard reagent was prepared employing a procedure similar to that used by Whitmore (36).

In a one liter, three-necked flask fitted with an efficient stirrer, reflux condenser, and dropping funnel were placed 36 grams (1.5 moles) of fresh magnesium turnings. 100 ml. of ether were added to the flask. Enough of a mixture of 1.5 moles of ethyl bromide and 200 ml. of ether was added through the dropping funnel to start the reaction. The remainder of the halide-ether solution was diluted with 200 ml. of ether and added through the dropping funnel at the rate of a drop a second. No external cooling was applied, the mixture being allowed to reflux during the addition. After the addition, the mixture was stirred an additional two hours.

A solution of 192 grams (1.3 moles) isopropyl phenyl ketone and 200 ml. of ether was added to the ethyl magnesium bromide at the rate of a drop per second. At the end of the addition a milky precipitate rapidly came out of solution until the reaction mixture appeared to be white.

After standing over-night, the reaction mixture was hydrolyzed on ice and enough concentrated hydrochloric acid was added to dissolve the basic magnesium salts. The ether layer was separated and the water layer extracted with ether. The combined ether extracts were washed with sodium carbonate, dried over sodium sulfate, and the ether distilled off.

Fractionation of the crude tertiary alcohol was carried out under reduced pressure. All of the product distilled from 106-112°C at 8mm. Due to the instability of the tertiary alcohol it was not further fractionated, but used directly as ethyl isopropyl phenyl carbinol.

C. 2-methyl-3-phenyl pentene-2

The tertiary alcohol, ethyl isopropyl phenyl ketone, was converted into the olefin, 2-methyl-3-phenyl pentens-2, by refluxing the alcohol, using a Stark and Dean moisture trap (37), until no more water collected. This usually takes about an hour.

After refractionating several times, the fraction boiling from 83-84°C at 14 mm. was collected as the compound, 2-methyl-3-phenyl pentens-2. The physical constants were as follows:

> $B \cdot P \cdot 745 = 206 - 208 \circ C$ $d_{20} = 0.8870$

4

n₀₂₀

Surface tension at 20°C = 32.20 dynes (DuNuoy)

= 1.5104

Molecular Refraction = 53.98, calculated = 53.66

Parachor = 429.7, calculated = 430.1

D. 2-methyl-3-phenyl pentane

Klages found that the olefin, 2-methyl-3-phenyl pentene-2, could not be reduced to 2-methyl-3-phenyl pentane by means of sodium and alcohol (22). The writer has repeated this work and obtained the same results. Addition of hydriodic acid to the olefin and subsequent reduction of the iodo compound with zinc dust was not successful. The use of a catalytic hydrogenation apparatus similar to that described in <u>Organic Syntheses</u> (38) and using platinum oxide catalyst prepared by the method of Bruce (39) also ended in failure. However, if the platinum oxide catalyst was substituted by palladium, the reduction proceeded quantitatively.

The palladium oxide catalyst was prepared according to the

method of Shriner and Adams (40). In a small casserole, 25 grams of finely ground C.P. sodium nitrate and a solution of 1.0 gram of palladium chloride were thoroughly mixed, evaporated to dryness, and then further heated until fused. At 350-370°C a vigorous evolution of oxides of nitrogen occurred with considerable foaming. After this evolution of gas which lasted for about 5 minutes, the temperature was raised rapidly with the hottest flame of a Meker burner and maintained for about 5 minutes. The melt was permitted to cool, dissolved in 200 cc. of distilled water, and the palladium oxide filtered off. This oxide was washed with 1% sodium nitrate solution, dried in a vacuum desiccator over sulfuric acid, and used in the catalytic reduction.

The catalytic reduction of 2-methyl-3-phenyl pentene-2 to 2-methyl-3-phenyl pentane was carried out using the conditions recommended by Kern, Shriner and Adams (41). A solution of 0.1 mole of the olefin and 150 cc. of alcohol was placed in the reaction bottle of the hydrogenation apparatus and 0.1 gram of palladium oxide catalyst was added. After evacuating the reaction bottle, hydrogen was passed in under pressure (3 atmospheres) and the mixture shaken for two hours. At the end of this time, the theoretical amount of hydrogen had been absorbed. The catalyst was filtered off and the alcohol solution of 2-methyl-3-phenyl pentane was distilled. The fraction containing the alkyl benzene was refractionated, collecting the fraction distilling from 85-86.5°C at 15 mm. The physical constants were:

> B.P.745 = $207-209^{\circ}C$ d $\frac{20}{4}$ = 0.8678 n_p20 = 1.4912

Surface tension at 20°C = 30.96 dynes (DuNuoy) C = 82.78%, H = 11.42% Calculated: C = 88.89%, H = 11.11% Wolecular refraction = 54.08, calculated = 54.05 Parachor = 440.35, calculated = 441.1

III. Preparation of 2-methyl-3-para hydroxy phenyl pentane

A. Isopropyl para methoxy phenyl ketone

This ketone was prepared by a modification of the method used by Auwers (42).

1.25 moles (135 grams) of anisole were placed in a one liter three-necked flask equipped with thermometer, reflux condenser, and stirrer. 500 ml. of a solution of one mole of isobutyryl chloride dissolved in petroleum ether were then added and the mixture cooled to a temperature of 10°C where it was maintained throughout the reaction. One mole of anhydrous aluminum chloride was added during the course of two hours. The mixture changed to a deep, blood-red color and became so thick that a solid finally settled out of the petroleum ether.

After standing over-night the reaction mixture was decomposed upon ice and hydrochloric acid, extracted with petroleum ether, and the petroleum ether extracts dried over sodium sulfate. Upon distilling off the petroleum ether on the steam bath, the crude ketone was distilled at reduced pressure. After several fractionations, 110 grams of a product boiling from 129-131°C at 3 mm. were collected (62% of the theoretical).

This product was used as the ketone, isopropyl p-methoxy phenyl ketone, and was identified as a ketone by the preparation of a phenyl hydrazone which melted at 92°C. The writer also prepared this ketone by the addition of p-methoxy phenyl magnesium bromide to an ether solution of isobutyrylchloride, but the yield was poor.

B. Ethyl isopropyl p-methoxy phenyl carbinol

This compound was prepared by the addition of isopropyl p-methoxy phenyl ketone to ethyl magnesium bromide in the same manner as that used to prepare ethyl isopropyl phenyl carbinol (see page 6). The alcohol was extremely unstable and split off water upon standing. Therefore, it was not fractionated, but was converted to the olefin directly.

C. 2-methyl-3-p-methoxy phenyl pentene-2

The above olefin was prepared by dehydrating ethyl isopropyl p-methoxy phenyl carbinol in a Stark and Dean moisture trap (see page 8). By refractionating several times a product distilling from 122-124°C at 12 mm. was collected as the unsaturated compound. The physical constants were:

> B.P. $_{739} = 244-247^{\circ}C$ $\frac{d_{20}}{4} = 0.9450$ $n_{D20} = 1.5195$ Surface tension at 20°C = 34.82 dynes (DuNuoy) C = 81.91%, H = 9.49% Calculated: C = 82.11%, H = 9.47% Molecular refraction = 61.09, calculated = 60.03 Parachor = 488.6, calculated = 489.1

D. 2-methyl-3-p-methoxy phenyl pentane

The above saturated ether was prepared by the catalytic reduction of the olefin using palladium oxide as a catalyst in the same manner as that used to reduce 2-methyl-3-phenyl pentens-2 to the alkyl benzene (see page 8). Fractionation of the compound yielded a product boiling from 98-99°C at 3 mm. Physical constants were as follows:

> B.P. $_{739} = 245-247 \circ C$ $d_{20} = 0.9281$ $n_{D}20 = 1.5008$ Surface tension at 20°C = 33.79 dynes (DuNuoy) C = 81.02%, H = 10.52% Calculated: C = 81.25%, H = 10.42% Molecular refraction = 60.99, calculated = 60.43 Parachor = 498.8, calculated = 500.1 E. 2-methyl-3-p-hydroxy phenyl pentane

In order to prepare the above alkyl phenol 10 grams of the saturated ether were hydrolyzed by refluxing with 50 grams of phenol and 100 ml. of 48 per cent hydrobromic acid for four hours (43). The reaction mixture was diluted with several volumes of water and then extracted with ether. Acids were removed from the ether extracts by washing three times with water and the ether was distilled off on the steam bath. The product was vacuum-distilled, discarding the lower boiling phenol and collecting the fraction boiling from 108-110°C at 3 mm. as the compound, 2-methyl-3-para-hydroxy phenyl pentane. After crystallizing the product in the refrigerator and pressing it out on a porous plate, the alkyl phenol was recrystallized from a very small amount of petroleum ether. A satisfactory recrystallization was not obtained. The alkyl phenol melts at 33-35°C.

C = 80.81%, H = 10.18% Calculated: C = 80.90%, H = 10.11%

IV. Derivatives

A. Benzoyl esters

These esters were prepared by a method described in Shriner and Fuson (44). One gram of the alkyl phenol was dissolved in 3 ml. of anhydrous pyridine and 1 ml. of benzoyl chloride was added. After the initial reaction had subsided the mixture was warmed over a low flame for a few minutes and poured with vigorous stirring into 10 ml. of water. The mixture was extracted with ether, the ether solution washed with dilute sulfuric acid to remove the pyridine, with dilute sodium carbonate to remove any acids, and the ether evaporated off on a steam bath. Upon standing for a time in the refrigerator the benzoyl eater crystallized out. It was then pressed out on a porous plate to remove oily impurities and recrystallized from dilute alcohol to constant melting point. The benzoyl ester of 2-methyl-3-para hydroxy phenylpentane melted at 33-34°C.

B. 3,5-Dinitrobenzoyl esters

Preparation of the 3,5-dimitrobenzoyl esters was carried out in a similar manner to that used for preparing benzoyl esters, substituting 3,5-dimitrobenzoyl chloride for benzoyl chloride in the procedure. The 3,5-dimitrobenzoyl ester of 2-methyl-3-p-hydroxy phenyl pentane melted at 118-119°C.

C. Alpha-naphthylurethanes

These were prepared by the following method (45). One gram

of the alkyl phenol was placed in a test tube and one ml. of alphanaphthyl isocyanate was added, the reaction being catalyzed by two drops of a dilute anhydrous other solution of trimethyl amine. Heat was generated by the reaction and the contents of the tube became solid upon standing. The resulting solid was extracted with 40 ml. of boiling ligroin (60-90°C) and all undissolved material filtered out. Upon cooling the alpha-naphthyl urethane crystallized out of the clear filtrate. It was filtered off and recrystallized from ligroin until a constant melting point was obtained. The alpha-naphthyl urethane of 2-methyl-3-p-hydroxy phenyl pentane melted at 124°C.

Found: Nitrogen = 4.02%

Calculated: Nitrogen = 4.04%

V. Proof of Structure

In order to establish its structure, the hexyl phenol, 2-methyl-3-p-hydroxy phenyl pentane, was synthesized in another way, namely, that of nitrating the corresponding alkyl benzene, reducing the p-nitro derivative thus formed, diazotizing the p-amino compound and hydrolyzing to the hexyl phenol. The process will be described in detail.

A. Nitration of the hexyl benzene

Malherbe's procedure (24) was used. One-tenth mole of the alkyl benzene was treated with an equal weight of fuming nitric acid, scoling on an ice bath during the addition to keep the temperature down. After the reaction had subsided the mixture was heated on a steam bath for one hour. It was then poured onto ice and the resulting solution extracted three times with ether. These ether extracts were washed with water and dried over calcium chloride. Upon removing the ether on a steam bath, the p-nitro compound was distilled under reduced pressure. The fraction distilling from 130-140°C at 4 mm. was collected as the nitro compound, and was not further purified. The para position of the entering nitro group has been established by previous workers in this laboratory (46, 47).

B. Reduction of the para nitro hexyl benzene

Catalytic reduction of the nitro compound was carried out using platinum oxide catalyst. A procedure recommended by Adams, Cohen, and Rees (48) was employed as follows.

A solution of 0.1 mole of 2-methyl-3-p-nitro phenyl pentane dissolved in 150 ml. of alcohol was placed in the reaction bottle of a hydrogenation apparatus and 0.1 gram of platinum oxide catalyst was added. The theoretical amount of hydrogen was absorbed after shaking for thirty minutes in the apparatus. Upon filtering off the catalyst and distilling the alcohol from the product at atmospheric pressure, the crude amino compound was distilled under reduced pressure. Several fractionations gave a fraction boiling at 101-103°C at 3 mm. which was collected as the amine.

Found: Nitrogen = 7.84%

Calculated: Nitrogen = 7.91%

An acetylamino derivative was prepared from the amine, 2-methyl-3-p-amino phenyl pentane, by adding one ml. of acetic anhydride to one gram of the amine in a test tube (49). The solid which crystallized immediately was recrystallized from alcohol. Melting point of 2-methyl-3-p-acetylamino phenyl pentane = 134°C.

> Found: Nitrogen = 6.41% Calculated: Nitrogen = 6.39%

C. Conversion of the Amine to the Phenol

Difficulties have been encountered in diazotizing the amino derivatives of alkyl benzenes by previous workers in this laboratory, due to the insolubility of the sulfate salt of the amine, and the yields obtained were very poor. In the following procedure, which is a modification of the methods used by Guile (50) and Kaye (51), an attempt has been made to increase the solubility of the amine salt by the addition of alcohol to the diazotizing mixture.

The amine was treated with 1.5 ml. concentrated sulfuric acid dissolved in 10 ml. of water for each 2 grams of amine. The solid salt thus formed was quite insoluble in the mixture, but it was partially dissolved by adding 10 ml. of alcohol for every 2 grams of amine. After colling the solution down below zero degrees centigrade in an ice-salt mixture. a twenty-five per cent solution of sodium nitrite was added dropwise with stirring over the period of several hours until the theoretical amount had been added. When all the sodium nitrite had been added. the solution was stirred until most of the amine sulfate dissolved, maintaining the temperature of the mixture at or below zero degrees centigrade throughout the diazotization. At this point 0.25 grams of urea (for every two grams of compound) dissolved in a small amount of water were slowly added. The solution was permitted to stand ten minutes and then hydrolyzed by pouring it into two liters of water and heating on the steam bath for two hours. The mixture of phenol and water was extracted with ether. the ether distilled off, and the product steam distilled. After another other extraction, the crude hexyl phenol was distilled, collecting the fraction boiling from 103-110°C at 3 mm.

D. Derivatives

An alpha-naphthylurethane was prepared using 0.5 grams of the

phenol obtained. The alpha-naphthyl urethane of 2-methyl-3-p-hydroxy phenyl pentane melts at 124-124.5°C. A mixed melting point showed no depression. Thus, the structure of 2-methyl-3-p-hydroxy phenyl has been established.

VI. Condensation of 4-methyl pentanol-2 with Phenol

This condensation was carried out in order to establish the identity of the main product or products obtained. Since this condensation has been studied previously by Curtis (1) his conditions of reaction were followed.

A quarter mole of the alcohol and one-half mole of phenol were placed in a dry 500 ml. three-necked flask equipped with stirrer, thermometer, and reflux condenser. 0.18 moles of anhydrous aluminum chloride were then added over a period of two hours, cooling the flask if the temperature exceeded 35°C. As the reaction mixture became viscous and deep orange in color, hydrochloric acid fumes were evolved. After standing over-night the mixture was poured ento ice and hydrochloric acid, extracted with ether, and the ether extract washed with water. The ether was removed on the steam bath and the residue fractionated at reduced pressure. When the lower boiling material had been distilled off two fractions were collected boiling from 0-110°C at 3 mm. and 110-130°C at 3 mm. Further fractionation gave as the main product a fraction distilling from 113-115°C at 2 mm. The yield was 52% of the theoretical.

After standing in the refrigerator the main product crystallized as a white solid. It was pressed out on a porous plate and recrystallized from petroleum ether. The crystals thus obtained melted at 36-37°C and were identified as the compound, 2-methy1-2-p-hydroxy phenyl pentane, by the preparation of an alpha-naphthyl urethane (M.P. = 127-128°C) and a 3,5-dinitrobenzoyl ester (M.P. = 120-121°C). Mixed melting points of these derivatives with the corresponding derivatives prepared from 2-methyl-2-p-hydroxy phenyl pentane (obtained from Curtis) showed no depression.

It is to be noted at this time that the writer has obtained the following melting points for various derivatives of 2-methyl-2-phydroxy phenyl pentane:

Bennoyl ester = 37-38°C

3.5-dinitrobenzoyl ester = 122-123°C

Alpha-naphthylurethane = 129-130°C

After careful refractionation of the lower boiling fractions from the condensation a small amount (3-4%) of a fraction distilling from 98-101°C at 2 mm. was isolated. Attempts to prepare a solid derivative from this fraction were unsuccessful, but the material was undoubtedly a phenol since it was soluble in dilute sodium hydroxide. The physical constants were:

$$\frac{d_{20}}{4} = 0.9585$$

 $n_{D}20 = 1.5133$

DISCUSSION

The writer has been successful in preparing the two compounds, 2-methyl-3-phenyl pentane and 2-methyl-3-p-hydroxy phenyl, and establishing their structure. The procedure used differs from that used by Klages (22) in that catalytic reduction was employed in reducing the unsaturated compound instead of the usual method of sodium and absolute alcohol. Apparently, such a change was necessitated by the fact that the steric hindrance of the groups attached to the carbons of the double bond was great enough to make reduction of the olefin difficult. However, after reading the literature the writer is not able to understand why platinum oxide catalyst cannot be employed as successfully as palladium oxide. Perhaps the palladium catalyst is more specific in the reduction of this type of compound.

From the results reported herein it has been shown that in the presence of anhydrous aluminum chloride the condensation of 4-methyl pentanol-2 with phenol gives as the main product the compound, 2-methyl-2-p-hydroxy phenyl pentane. This is not unreasonable since alcohols with branching on the carbon atom adjacent to the carbinol group, when condensed with phenol, invariably rearrange to give the tertiary alkyl phenol. Using the cationoid theory of condensation discussed in a review by Price (52) the following explanation may be plausible.

2.
$$CH_3 - C - CH_2 - CH - CH_3 \longrightarrow (CH_3 - C - CH_2 - CH - CH_3)$$

H OH H
 $C1 - A1 - C1$ $(OH - A1C1_3) - C1$

3.
$$CH_3 - C - CH_2 - CH - CH_3 \xrightarrow{CH_3} CH_3 - C - CH - CH_2 - CH_3$$

H + H + H +

4.
$$CH_3 - CH_2 - CH_2 - CH_3 \xrightarrow{(H_3)}{(H_3 - C - CH_2 - CH_2 - CH_3)} CH_3 - C - CH_2 - CH_2 - CH_3$$

H + + +

.

Undoubtedly a similar explanation of the rearrangement could be offered by use of the mechanism of an intermediate alkyl chloride proposed by Tzukervanik and Nazarova (53) or that of an olefin intermediate proposed by McKenna and Sowa (54).

SUMMARY

1. The compounds, 2-methyl-3-phenyl pentane and 2-methyl-3p-hydroxy phenyl pentane have been prepared synthetically for the first time.

2. The structures of the above two compounds have been established.

3. Derivatives of the above compounds have been prepared.

4. The main product of the condensation of 4-methyl pentanol-2 with phenol has been identified.

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II. THE PREPARATION OF SOME TERTIARY ALCOHULS BY THE ADDITION OF ORGANIC ACIDS TO GRIGNARD REAGENTS ~ •

INTRODUCTION

In the year of 1906 a patent was issued to Bayer and Company for the preparation of some tertiary alcohols by means of the addition of organic acids to Grignard reagents. However, no mention was made of the yields obtained or the possibilities of such a reaction, and since that time little has been published in the literature on this subject.

The purposes of the present investigation are to discover the merits of the above reaction, to study its mechanism, and to extend its usefulness into a general procedure for the preparation of aliphatic tertiary alcohols of the type

$$\begin{array}{c}
\mathbf{R}^{\mathbf{R}} = \mathbf{C} = \mathbf{OH} \\
l \\
\mathbf{R}
\end{array}$$

-

where R and R' are alkyl groups.

HISTORICAL

Tertiary alcohols have been prepared synthetically by various methods and chemical agents. They also are found quite widely in natural products. However, since the scope of this thesis does not permit the enumeration of all methods used to prepare tertiary alcohols, only those syntheses which have to do with the preparation of this class of compounds as a group will be mentioned herein.

One of the oldest methods of preparing tertiary alcohols was described by Butlerow in 1863 (2). He prepared trimethyl carbinol from phosgen and dimethyl zinc. In the following year Butlerow reported that acid chlorides could be added to the zinc alkyl compounds to give tertiary alcohols (3).

In the year of 1865, again Butlerow reported the preparation of trimethyl carbinol from isobutylene and fifty per cent sulfuric acid (4). Since isobutylene, as well as other alkenes, is found in petroleum this method has commercial importance.

Butlerow also has studied the reaction between isobutyl iodide and silver oxide in acetic acid to form trimethyl carbinol and isobutylene (5). This work was further investigated by Linnemann (6) who obtained similar results.

Dobbin has reported that he obtained trimethyl carbinol by boiling the iodide with water (7) and Pogorshelski prepared the alcohol from isobutylene and a mixture of iodide and potassium iodide (8). Baratjew (9) and Sokolow (10) have reported preparing tertiary alcohols from the reaction of a ketone with an alkyl iodide and zinc. The discovery of the Grignard reagent in 1900 led to some of the most important methods of obtaining tertiary alcohols in pure form. In this year Grignard prepared dimethyl phenyl carbinol and dimethyl benzyl carbinol by adding a ketone to the reagent named after him (11). In the following year Grignard prepared some tertiary alcohols (12) by the addition of esters to the Grignard reagent and Tissier and Grignard (13) reported obtaining tertiary alcohols from acid chlorides or acid anhydrides and the reagent.

Ketones and tertiary alcohols were found to be the by-products when carbon dioxide gas was bubbled through a Grignard reagent to form an organic acid. Bodroux (14) has reported obtaining 4,4°-dibromo diphenyl ketone from carbon dioxide and p-bromo phenyl magnesium bromide. In a study of the reaction between phenyl magnesium bromide and carbon dioxide Schroeter (15) found triphenyl carbinol as a by-product. This reaction also was studied by Meyer and Togel (16) who found the same by-products. They attributed the formation of triphenyl carbinol to the presence of water in the reaction, but Schroeter later showed that the formation of triphenyl carbinol was due to the temperature, rate of addition of the carbon dioxide, and the time of standing of the reaction (17). Ferrario and Fagetti (18) have reported obtaining a seventy-five per cent yield of trimethyl carbinol from carbon dioxide and methyl magnesium bromide.

Grignard (19) prepared diethyl isoamyl carbinol by passing carbon dioxide into isoamyl magnesium bromide and adding ethyl magnesium bromide to the reaction mixture. He prepared isobutyl diisoamyl carbinol in a similar manner and offered an explanation of the reaction mechanism. Iwanow (20), in his studies of the reaction between butyl magnesium bromide and carbon dioxide, has offered a similar mechanism for the reaction. Henry (21) has reported the preparation of dimethyl isopropyl carbinol by the addition of trimethyl ethylene oxide to methyl magnesium bromide.

In 1906 Bayer and Company obtained patents (1) for the preparation of tertiary alcohols from organic acids and Grignard reagents as well as their preparation from the potassium salt of the acid and Grignard reagents. These methods have gained little importance in the literature, however, and have never been fully studied.

THEORETICAL

To the writer's knowledge, no one has offered an explanation of the reaction mechanism involved in the direct addition of an acid to a Grignard reagent to form the tertiary alcohol. However, since the first step in the mechanism is the reaction between the acidic hydrogen of the acid and the reagent in the following manner

$$R + MgX + R - C + OH \longrightarrow R - C - OMgX + RH$$

it is quite obvious that the succeeding steps of the reaction mechanism are identical with those present in the reaction between carbon dioxide and a Grignard reagent.

Grignard (19) and Iwanow (20) have both proposed the same mechanism for the reaction between carbon dioxide and a Grignard reagent. It consists of a normal addition of one mole of the reagent to one of the carbonyl groups of carbon dioxide forming the magnesium addition product. The reaction is rapid and complete. A second mole of the reagent then adds to the second carbonyl group, but this reaction takes place much more slowly. The addition product now contains two electronegative groups (-OMgX) on the same carbon atom and therefore is unstable. It splits off the salt, MgX-O-MgX, and forms the ketone which rapidly and completely reacts with the third mole of reagent to give the tertiary alcohol. The mechanism may be expressed by the following equations:

1. R - MgX + C
$$\stackrel{0}{\sim}$$
 rapid R - C - OMgX



4.
$$R - C' - R + R - MgX$$
 rapid $R - C' - OldgX$

The above mechanism also explains why the reaction cannot be stopped at the ketone.

Applying the mechanism proposed by Grignard and Iwanow to the reaction between an organic acid and the Grignard reagent, the following was obtained.

$$\begin{array}{c} 0 & 0 \\ 1. R - MgX + R - C - OH \underline{rapid} & R - C - OMgX + RH \end{array}$$

2.
$$R - C \xrightarrow{0} + R - MgX \xrightarrow{\text{slow}} R \xrightarrow{0} OMgX$$

3.
$$R \xrightarrow{OMgX} R \xrightarrow{O} R + MgX \xrightarrow{O} R$$

5.
$$R = \begin{pmatrix} R \\ C \\ R \end{pmatrix} = 0 \xrightarrow{R} R = \begin{pmatrix} R \\ C \\ R \end{pmatrix} = 0 \xrightarrow{R} R = \begin{pmatrix} R \\ C \\ R \end{pmatrix} = 0 \xrightarrow{R} R = \begin{pmatrix} 0 \\ R \\ R \end{pmatrix} = \begin{pmatrix} 0 \\ R \\ R \end{pmatrix}$$

The writer will attempt to investigate such a mechanism by studying some of the intermediates formed in the reaction.

EXPERIMENTAL

I. Materials

Normal butyl, normal amyl, and secondary butyl bromides were prepared from the corresponding alcohols (Eastman technical and redistilled) by the action of sulfuric acid and hydrobromic acid (22).

Tertiary butyl bromide was prepared by refluxing tertiary butyl alcohol (Eastman B.P. = $82-83^{\circ}$ C) with an excess of 48 per cent hydrobromic acid for several hours.

Methyl bromide was obtained by the action of concentrated sulfuric acid upon a mixture of methyl alcohol, sodium bromide, and water, using a procedure described in detail by Barrett (23).

Ethyl bromide was obtained in the pure form from the stockroom.

Glacial acetic acid was received from the stockroom in the chemically pure form. It was dried over anhydrous sodium sulfate.

Propionic, butyric, isobutyric, valeric, isovaleric, and caproic acids were obtained from the stockroom. They were Eastman's tehenical grade and were carefully fractionated until a two degree range in boiling point was obtained.

Magnesium turnings used were especially prepared for Grignard reactions.

Ether for Grignard reactions was anhydrous. It was dried over freshly cut sodium before use.

Other reagents, such as drying agents, were to be found on the side shelf in the proper degree of purity and were ready for use.

II. Preliminary

The writer first attempted to find out what the best condi-

tions for the reaction between an organic acid and a Grignard reagent actually were to obtain an optimum yield of the tertiary alcohol. Ethyl magnesium bromide and butyric acid were used for the study since the former is conveniently made and butyric acid gives a tertiary alcohol which seems rather easily purified and was obtained in good yield.

It was found that the reaction proceeded best at the boiling point of ether and that the yield is increased by refluxing the reaction mixture several hours after the addition of the organic acid. Allowing the reaction to stand over-night also gave a slight increase in yield. The following results were obtained when the amount of Grignard reagent was varied:

Butyric Acid	Ethyl Magn esium Bromide	Yield of diethyl prop yl carbinol	Yield of ethyl propyl ketone
0.5 moles	1.35 moles	55.4%	10%
0.5 moles	1.5 moles	58.4%	12%
0.5 moles	1.75 moles	64.6%	10Z

From the above it has been shown that an excess of Grignard reagent is important in obtaining a high yield of the tertiary alcohol. Also, the yield of ketone is apparently independent of the amount of the reagent present. This was further borne out by the fact that attempts to prepare the ketone by adding two moles of Grignard reagent to an ether solution of one mole of the acid have ended in failure, since the tertiary alcohol was the main product obtained.

III. Preparation of the Tertiary Alcohols

Since the procedure used for preparing tertiary alcohols was the same in all cases it will be described in detail. The Grignard reagent was prepared employing a procedure similar to that used by Whitmore (24).

In a one liter, three-necked flask fitted with an efficient stirrer, reflux condenser, and dropping funnel, were placed 42.5 grams (1.75 moles) of fresh magnesium turnings. The reaction flask was protected from molsture and carbon dioxide in the air by means of soda lime tubes in the usual manner. 100 ml. of anhydrous ether were added to the flask (at this point in the preparation of tertiary butyl mangesium bromide several crystals of iodine were added as catalyst). Enough of a mixture of 1.75 moles of the alkyl halide used and 200 ml. of ether was added through the dropping funnel to start the reaction. The remainder of the halide-ether solution was diluted with 200 ml. of ether and added through the dropping funnel at the rate of a drop a second. No external cooling was applied, the mixture being allowed to reflux during the addition. After the addition, the mixture was stirred an additional two hours. The reagent was then titrated with standard acid and the actual amount of the reagent determined.

A solution of 0.5 moles (or the amount necessary to maintain a 10 per cent excess of the Grignard reagent) of the erganic acid and 200 ml. of ether was added to the alkyl magnesium bromide at the rate of a drop per second. The reaction was quite violent and large amounts of gas were evolved. Thus, it was necessary to control the rate of addition of the acid if the reaction refluxed too fast. Towards the end of the addition a white, crystalline salt settled out of solution on the bottom of the flask. The reaction_mixture was heated to reflux for several hours after the addition by means of a pan of warm water. After standing over-night, the reaction mixture was hydrolyzed on ice and enough concentrated hydrochloric acid was added to dissolve the basic magnesium salts. The ether layer was separated and the water layer extracted three times with ether. The combined ether extracts were washed with dilute sodium hydroxide, dried over sodium sulfate, and the ether distilled off.

Fractionation of the crude tertiary alcohols was carried out under reduced pressure if the boiling point of the alcohol was not under 130°C at atmospheric pressure, since tertiary alcohols tend to split off water at high temperatures. The tertiary alcohols were purified until a two degree range in boiling point was obtained.

The ketone fractions were collected over a ten degree range and were not further purified. They were identified by their boiling points and the fact that they gave the characteristic test for a ketone. Several of the ketones were identified by preparation of a 2,4-dinitrophenylhydrazone.

The data for the above preparations is summarized in Table I.

IV. Analysis of the Intermediate Product

It has been noted that in every case where a tertiary alcohol was formed in the reaction between an organic acid and a Grignard reagent a white, crystalline salt settled out of solution on the bottom of the flask. In reactions where the tertiary alcohol was not formed no crystalline salt was found. Thus, it is indicated that this salt must be involved in the reaction mechanism. The salt from various reaction mixtures was analyzed in the following manner:

The reaction mixture was decanted from the intermediate salt and the salt crystals were washed four or five times with anhydrous ether. They were then dried over sulfuric acid in a vacuum desiccator. Since the intermediate salt is rapidly decomposed by water it was necessary to protect the salt from moisture of the air at all times. Total magnesium was determined by decomposing a weighed sample with a Meker burner (25). The results compared with those obtained by other analytical methods. Total bromine was determined by the use of a Parr bomb fusion cup (26). However, the results were comparable to those obtained by dissolving a weighed sample in dilute nitric acid and determining the bromide ion by the Volhard method (27), so the latter method was used. A rough molecular weight was taken by titrating the salt with standard acid.

Analysis

Magnesium	*	53.9%	10.93%
Bromine	=	10.93%	53.9%
Holecular weight		460 er 4 7	-9 20 ⁻

The intermediate salt was hydrolyzed with water and the solution filtered. After evaporating the filtrate to dryness the residue was analyzed.

Analysis

		Found	MgBr2•6H20
Magnesium	2	8.15%	8.31%
Bromine		54.4%	54.7%

The dried precipitate from the hydrolysis was also analyzed.

		Found	Mg ()H)2
Magnesium	=	35.5 %	41.7%
Bromine	2	9.28%	0.0%
Molecular weight	=	77	58

Analysis

The precipitate may be contaminated with MgBr2.6H20.

A gas was given off when the intermediate salt was hydrolyzed which burned with a blue flame, was soluble in concentrated sulfuric acid, and had an odor characteristic of ether. No other organic products were obtained.

From the above analyses, the intermediate salt may have one of the two following structures:

MgBr - 0 - MgBr	Molecular weight	=	8 89
2 MgBr ₂	Magn esium	=	10.93%
$4 C_{2}H_{5} - 0 - C_{2}H_{5}$	Bromine	×	54.0%

or

мgBrOH	Molecular weight	=	4 5 3
MgBr ₂	Magnesium	=	10.73%
$2 C_2 H_5 - 0 - C_2 H_5$	Bromine	*	52.9%

Either structure could be hydrolyzed to give the compounds, $MgBr_2 \cdot 6H_20$, ether, and $Mg(OH)_2$, which are indicated by the analyses of the hydrolysis products. However, since no water was present in the reaction mixture and since the analyses for bromine and magnesium indicate that the former structure is the correct one, it is felt by the writer that the structure is the following:

$$\begin{bmatrix} MgBr - 0 - MgBr \\ 2 MgBr_2 \\ \Psi C_2H_5 - 0 - C_2H_5 \end{bmatrix}$$

This structure agrees with the mechanism proposed by Grignard (19) and Iwanow (20). The magnesium bromide in the intermediate salt was undoubtedly formed through the Schlenk equilibrium (28).



TABLE I

: •

	UNTING I	MUNA CHURCH	A CULUE ALLA ALLA	N UNANUTAN UN	EAUENIS	1	
llcohol	Boiling Point	Yield	Density ₂₀ D_{a}^{20}	02 04 K	Molecular Refraction Found	Molecular Refraction Calculated	Yield Ketone
Crimethyl Carbinol 2-many 2- Jugunel	80-92 at 735	Less than $1\% - 4$	0332-	1.3873	22.06	22,03	Less then 1%
dethyl diethyl sarbinol 3- huthur 3- bentanol	121-123°C @ 747 mm.	31.5%	.8253	1.4178	31.23	31.24	20.9
Simethy propyl	120 -121°C @ 743 mm.	30% +1.3	5308.	1.4108	31.37	31.24	-13.0% - 2.7, 75
Simethyl butyl	138-141°C @ 743 mm.	42%	.8125	1.4168	35.88	35.84	10.5%
Stethyl propyl	64-65°C @ 14 mm. 161.5°C @ 741 mm.	64.6%	.8417	1.4326	40.06	40 . 45	12.0%
Sethyl isopropyl sarbinol	63-85°C @ 14 mm. 158.5°C @ 741 mm.	53%	• 8323	1.4362	40.86	40.45	11.0%
Sethyl butyl	66-68°C @ 14 mm.	49%	.8414	1.4360	44.75	45.05	6.5%
Sarbinol isobutyl	66-67°C @ 13 mm.	50 . 5%	.8397	1.4355	44.80	45.05	9.5 <i>%</i>
Stethyl amyl " arbinol " alanol	90-91°C @ 14 mm.	54.5%	.8414	1.4388	49.38	49.65	12.0%

coholBoiling PointYieldthyl diamyl97-99°C @ 6 mm.42%rbinol97-99°C @ 6 mm.42%rbinol84-100°C @ 3 mm.53%rbinol53%53%rbinol98-100°C @ 3 mm.53%rbinol98-100°C @ 2 mm.56.5%rbinol6106-108°C @ 2 mm.48.5%rbinol6106-108°C @ 2 mm.48.5%rbinol6100°C @ 2 mm.49.5%rbinol67100°C @ 2 mm.49.5%	Density 20 4	nD.ser	11-1		
thyl diamyl 97-99°C & 6 mm. 42% rbinol wyl diamyl 98-100°C & 3 mm. 53% rylnol cyl diamyl 98-100°C & 3 mm. 53% rbinol opyl diamyl 106-108°C & 2 mm. 56.5% opyl diamyl 106-108°C & 2 mm. 48.5% rbinol rbinol rbinol tyl diamyl 104-106°C & 2 mm. 48.5% rbinol rbinol tyl diamyl 110-112°C & 2 mm. 49.5% rbinol	.8313 .8381		motecutar Refraction Found	Molecular Refraction Calculated	Yield Ketone
hyl diamyl 98-100°C & 3 mm. 53% rbinol coyl diamyl 106-108°C & 2 mm. 56.5% rbinol - bendeamed propyl diamyl 106-108°C & 2 mm. 48.5% rbinol - bendeamed opropyl diamyl 104-106°C & 2 mm. 48.5% ryl diamyl 104-106°C & 2 mm. 49.5% rbinol - bendeamed tyl diamyl 110-112°C & 2 mm. 49.5%	.8381	1.4394	58.89	58.86	14.5%
opyl diamyl 106-108°C & 2 mm. 56.5% rbinol -6-buddeouch opropyl diamyl 104-106°C © 2 mm. 48.5% rbinol** tyl diamyl 110-112°C © 2 mm. 49.5% tyl diamyl 110-112°C © 2 mm. 49.5%	And in the other statements of the statement of the state	1.4446	63.46	63.46	12.0%
opropyl diamyl 104-106°C © 2 mm. 48.5% rbinol** rttickyr-b-ladened tyl diamyl 110-112°C @ 2 mm. 49.5% rbinol-b-haderad	.8381	1.4458	68.06	68.07	11.0%
tyl diamyl 110-112°C @ 2 mm. 49.5%	. 8425	1.4477	67.96	68.07	7.5%
	.8371	1.4463	72.68	72.67	10.0%
obutyl diamyl 116-118°C 2 3 mm. 50.5% Tbinol*** wertyd-6-turotecomed	.8367	1.4464	72.73	72.67	12.5%
iamyl carbinol 127-129°C @ 2 mm. 58.5%	.8386	1.4489	77.39	77.27	15.0%
ibutyl carbinol 99-101°C © 5 mm. 50.0%	. 8382	1.4443	63.42	63.46	10.5%
Butyl secdibutyl Less than 1%	1% = = = =	8	8 5 8	8 8 8	14.5%
Butyl tert Less than 1%	1%	e e a e	8 9 9 8	1	1-2%

DISCUSSION

The writer has been successful in preparing tertiary alcohols from all of the primary Grignard reagents and acids used with the exception of acetic acid and methyl magnesium bromide. This is not understandable since Ferrario and Fagetti reported obtaining a seventy-five per cent yield of trimethyl carbinol from carbon dioxide and methyl magnesium bromide (18). It is felt that the writer did not use the proper conditions of reaction and the reaction proceeded abnormally. However, it is to be noted that in every case where acetic acid was used a low yield of the tertiary alcohol was obtained.

Tertiary alcohols could not be prepared from either secondary or tertiary magnesium bromide although a small yield of the ketone was obtained from valeric acid and secondary butyl magnesium bromide. This fact is attributed to the steric hindrance of the secondary and tertiary groupings. Thus, the general method of preparing tertiary alcohols from organic acids and Grignard reagents is limited in its use to the primary Grignard reagents.

Study of the intermediate salt which formed during the reaction of an organic acid and a Grignard reagent has led to an idea of what its structure may be. The writer has suggested the following formula for the intermediate salt formed:

$$\begin{bmatrix} MgX - 0 - MgX \\ 2 MgBr_2 \\ 4 C_2H_5 - 0 - C_2H_5 \end{bmatrix}$$

Since the above formula is thought to be the correct one, a reaction



mechanism similar to that proposed by Grignard (19) and Iwanow (20) can now be offered for the addition of acids to Grignard reagents.

1.
$$R - M_E X + R - C - OH$$
 ______ $R - C - OH gX + RH$

2.
$$R = C \xrightarrow{0} + R = MgX \xrightarrow{\text{slow}} R \xrightarrow{0} OmgX$$

3.
$$R \xrightarrow{O!4gX} R \xrightarrow{O} R \xrightarrow{O} R \xrightarrow{O} R \xrightarrow{I} R \xrightarrow{I}$$

4.
$$R - C - R + R - MgX$$
 rapid $R - C - 0MgX$

$$\begin{array}{c} R \\ I \\ \mathbf{5.} R - \begin{array}{c} l \\ \mathbf{C} \\ R \end{array} \\ R \end{array} \xrightarrow{\mathsf{R}} R - \begin{array}{c} 0 \\ \mathbf{H} \\ \mathbf{R} \end{array} \xrightarrow{\mathsf{R}} R - \begin{array}{c} 0 \\ \mathbf{H} \\ \mathbf{R} \end{array} \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{OH}} R \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{OH}} R \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{OH}} R \xrightarrow{\mathsf{R}} \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{R}} \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{R}} \xrightarrow{\mathsf{R}} \xrightarrow{\mathsf{R}} R \xrightarrow{\mathsf{R}} \xrightarrow{\mathsf{R}}$$

The MgX - O - MgX which splits off in the reaction combines with MgBr₂ from the Schlenck equilibrium (28) and ether to form the crystalline, intermediate salt.

SUMMARY

1. Sixteen alighatic tertiary alcohols have been prepared by the addition of organic acids to primary Grignard reagents.

2. Tertiary alcohols could not be prepared by the addition of organic acids to secondary and tertiary Grignard reagents.

3. The tertiary alcohols, isopropyl diamyl carbinol and isobutyl diamyl carbinol, have been prepared for the first time, to the writer's knowledge, but their structures have not been definitely established.

4. A formula for the structure of one of the reaction intermediates has been proposed.

5. A mechanism for the reaction between an organic acid and a Grignard reagent has been proposed.



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