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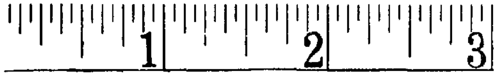

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THE CONDENSATION OF THE METHYL DIPROPYL CARBINOLS WITH PHENOL IN THE PRESENCE OF ALUMINUM CHLORIDE

by

CARL RIDGE MELOY

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INTRODUCTION

In previous papers from this laboratory (1) the condensations of tertiary butyl, tertiary amyl, tertiary hexyl, and tertiary heptyl alcohols with phenol in the presence of anhydrous aluminum chloride have been described. Of the seventeen possible tertiary octyl alcohols, all (2) but the methyl dipropyl carbinols have been condensed with phenol by using aluminum chloride as the condensing agent. The purpose of this paper is to describe the condensation of these remaining tertiary octyl alcohols.

HISTORICAL

Condensation may be defined as the union of two or more organic molecules or parts of the same molecule (with or without the elimination of component atoms) in which the new combination is effected between carbon atoms. It is a process closely associated with the history of synthetic organic chemistry. Internal condensation, the linking of carbon atoms within a molecule, leads to the formation of cyclic compounds, whereas external condensation is the union of two or more different molecules to produce a molecule of greater complexity and, generally, of greater molecular weight.

The union between molecules or parts of the same molecule is usually promoted by unsaturation and by the tendency exhibited by unsaturated atoms to saturate themselves. Whether the combining molecules are already unsaturated or are rendered unsaturated by the withdrawal of certain elements, a catalyst is required to bring about the condensation, serving either as a dehydrating agent, as an activator, or both.

Condensations involving dehydration are very numerous. Among the dehydration catalysts that have been used may be mentioned the following: sulfuric acid, phosphoric acid, phosphorus pentoxide, magnesium chloride, zinc chloride, phosphorus pentachloride, aluminum chloride, ferric chloride,(both the anhydrous salt and in the form of the hexahydrate), stannic chloride, acetic acid, sulfuric and acetic acid mixture, boron trifluoride, hydrogen chloride, hydrogen fluoride, antimony trichloride, and titanium tetrachloride. Of these condensation catalysts the ones listed below have been shown to be more efficient and of greater applicability, so an example of each is listed:

Zinc chloride was the catalyst used by Fischer and Roser (3) in the preparation of aminotriphenylmethane by condensing benzhydrol with aniline hydrochloride.

Sulfuric acid was employed as a catalyst by Becker (4) in 1882 when he condensed m-nitrobenzyl alcohol and benzene to yield m-nitrodiphenylmethane.

Mixtures of acetic and sulfuric acids were used by Meyer and Wurster (5) in condensing benzyl alcohol and benzene to give diphenylmethane.

Stannic chloride was the condensing agent used by Michael and Jeanpretre (6) in preparing phenyltrimethylphenylacetonitrile from mesitylene and phenylhydroxyacetonitrile.

Phosphorus pentoxide was employed by Hemilian (7) as a catalyst in the condensation of benzhydrol with p-xylene to form diphenyl-p-xylylmethane.

Magnesium chloride was the catalyst used by Mazzara (8) in condensing propyl alcohol with m-cresol to give propyl-m-cresol.

Hydrogen chloride was employed by Noelting (9) in preparing p-nitrodimethyldiaminodiphenyltolylmethane from p-nirtodimethylaminobenzhydrol and m-toluidine.

Zincke (10) announced the reaction of aromatic hydrocarbons with halogen compounds in the presence of zinc dust:

$$C_6H_5H + ClCH_2C_6H_5 \xrightarrow{Zn} C_6H_5CH_2C_6H_5 + HCl \qquad I$$

Since aluminum chloride catalyzes the same reaction, zinc chloride may be formed as an intermediate.

Because of its powerful dehydrating action aluminum chloride has engaged the attention of workers in this laboratory, both in studies of its uses and in attempts to determine the possible mechanisms by which it acts.

Friedel and Crafts (11) first introduced aluminum chloride as a catalyst in condensation reactions among aliphatic compounds. They at first observed that aluminum chloride acts in the cold on amyl chloride to produce hydrogen chloride, hydrocarbons of the composition C_nH_{2n+2}, and highly condensed hydrocarbons. Later they found that treatment of mixtures of organic chlorides and aromatic hydrocarbons with aluminum chloride led to the formation of such alkylation products as toluene, ethylbenzene, or amylbenzene, and acylation products like benzophenone. A possible mechanism for the Friedel-Crafts reaction would be the combination of the catalyst with the benzene derivative:

$$C_6R_5H + AlCl_3 \longrightarrow HCl + Al\begin{matrix}\nearrow Cl_2\\ \searrow C_6R_5\end{matrix} \qquad II$$

this intermediate would then react with the halide:

$$Al\begin{matrix}\nearrow Cl_2\\ \searrow C_6R_5\end{matrix} + R'Cl \longrightarrow AlCl_3 + R'C_6R_5. \qquad III$$

Merz and Weith (12) condensed two molecules of phenol to produce diphenyl ether by using aluminum chloride, while Wass (13) used this catalyst in condensing dichloroethylene oxide with benzene to give triphenylethane. These reactions indicated that the aluminum chloride may serve as a dehydrating agent as well as a catalyst. This was still further shown when Graebe (14) succeeded in producing small amounts of aniline by treating benzene with hydroxylamine in the presence of aluminum chloride.

The condensation of chloral, chloral hydrate, bromal, and trioxymethylene with various organic compounds in which an elimination of water occurred was reported by Frankforter and co-workers (15) who showed that, since sulfuric acid did not bring about the same reactions in some cases, the aluminum chloride was acting not only as a dehydrating agent but also as a catalyst.

The first reported condensation of alcohols with aromatic compounds was the work of Auer (16) who, in 1884, condensed ethyl alcohol with phenol using zinc chloride as a catalyst. A mixture of ethylphenol and ethylphenetole resulted. Anisole was obtained when methyl alcohol was substituted for ethyl alcohol.

In 1897 Nef (17) obtained diphenylmethane by the reaction between benzene and benzyl alcohol in the presence of aluminum chloride. In repeating this work Huston and Friedemann (18) found that this reaction gave a thirty per-cent. yield of diphenylmethane as well as smaller amounts of o- and p-dibenzylbenzene, a hydrocarbon having the formula

$C_{27}H_{24}$, and anthracene. The yields were found to be a function of the temperature and the amounts of reagents used. In continuing this work Huston and Friedemann (19) condensed methyl phenyl carbinol, ethyl phenyl carbinol, and diphenyl carbinol with benzene to obtain the corresponding substituted benzenes. It was found that both methyl and ethyl groups had a retarding effect upon the condensation while a second phenyl group did not.

In 1924 Huston (20) found that benzyl alcohol would also condense with phenol, anisole, and phenetole in the presence of aluminum chloride to give yields of 45, 46, and 57 percent. respectively. In trying to condense primary alcohols with benzene, Huston and Sager (21) reported negative results for methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, isoamyl, phenylethyl, and phenylpropyl alcohols. Allyl alcohol, however, condensed to give a 16 percent. yield of allylbenzene. This, together with the results obtained by Huston and Bartlet (22) in condensing phenyl butyl carbinol with phenol, led to the hypothesis that only those alcohols in which the alpha carbon atom was a member of a benzene ring or held a double bond would condense under the action of aluminum chloride. This conclusion was favored by the work of Huston, Lewis, and Grotemut (23) on the condensation of methyl phenyl, ethyl phenyl, and diphenyl carbinols with phenol since the latter gave the highest yield of condensate. It is interesting to note that the attempt by Huston and Davis (24) to condense triphenyl carbinol with benzene gave triphenylmethane rather than tetraphenylmethane as the product.

Other papers followed in which Huston and co-workers (25) reported the condensations of benzyl or halogenated benzyl alcohols with phenol or halogenated phenols, cresols, or halogenated cresols.

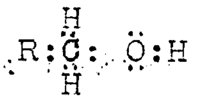
A study of the condensation of cyclohexyl, cyclopentyl, and cyclobutyl carbinols with benzene by Huston and Goodemoot (26) showed an increasing activity with smaller rings.

Although earlier attempts by Huston and co-workers (27) showed dehydration rather than condensation of various diaryl alkyl and dialkyl aryl carbinols, several of these compounds have recently been condensed with phenol by Welsh and Drake (28), Huston and Hughes (29), and Huston and Jackson (30). They modified the usual condensation procedure by adding a solution of the carbinol and phenol in petroleum ether to anhydrous aluminum chloride suspended in petroleum ether. Considerable amounts of p-benzylphenol were obtained as a by-product.

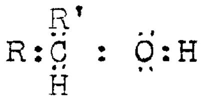
It was the work of Huston and Hsieh (1) which opened up a new field of investigation when they found that it was possible to condense saturated aliphatic alcohols with benzene and with phenol by using anhydrous aluminum chloride. The temperature of the condensations was controlled by regulating the rate of addition of the alcohols to a stirred mixture of aluminum chloride and benzene. Although they were unable to bring about the condensation of aliphatic primary alcohols with benzene or with phenol, they succeeded in condensing isopropyl alcohol, sec-butyl alcohol, methyl n-propyl carbinol, and methyl isopropyl carbinol with benzene to give the mono-substituted derivatives in yields of from 25 to 28 percent. The tertiary butyl, tertiary amyl, and tertiary hexyl alcohols condensed with both benzene and phenol to give good yields of mono-alkyl derivatives. The yields of the p-t-alkyl phenols were from 40 to 56 percent. of the theoretical. Many other investigations (31) in which the alkylation of aromatic nuclei was the object followed. The condensation of the tertiary heptyl alcohols with phenol was accomplished by Huston and Hedrick (1), while Huston and Guile (2) accounted for the condensation of eight of the seventeen tertiary octyl alcohols with phenol. Of the remaining nine, only the methyl dipropyl carbinols have not been condensed with phenol in this laboratory, and, to the writer's knowledge, the condensations described herein have not been previously reported in the literature.

THEORETICAL

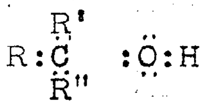
In the course of investigations on the condensation reactions between various alcohols and aromatic hydrocarbons in the presence of aluminum chloride it has been observed by Huston and his co-workers that the alpha carbon atom of the alcohol must be under strain in order to create an active hydroxyl group. This activation is due primarily to the fact that the electron pair which holds the hydroxyl oxygen to the alpha carbon is drawn closer to the hydroxyl group, resulting in a relatively unstable carbon-oxygen bond. The progressively greater reactivity of the alcohols in passing from the primary to the tertiary is accounted for on this basis and may be represented as follows:



$R:\overset{H}{\underset{H}{\ddot{C}}}:\;\ddot{O}:H$



$R:\overset{R'}{\underset{H}{C}}\;:\;\ddot{O}:H$



$R:\overset{R'}{\underset{R''}{C}}\;\;:\ddot{O}:H$

The distance of the electron pair from the carbon atom increases as the reactivity of the alcoholic hydroxyl group increases. This greater reactivity of the tertiary alcohols is reflected in their greater tendency to condense. The fact that the primary alcohols have not been condensed by the methods employed in this laboratory further emphasizes the low reactivity of this class. Ease of condensation parallels the ease with which the hydroxyl group is replaced by the halogen of hydro-halogen acids as well as the ease with which dehydration occurs.

The mechanisms which have been advanced for the condensation of tertiary aliphatic alcohols with aromatic hydrocarbons in the presence of anhydrous aluminum chloride may be divided into three types:

1. The formation of an alkyl halide by the action of aluminum chloride on the alcohol, followed by alkylation through a Friedel-Crafts reaction;
2. Dehydration of the alcohol to form an alkene which then condenses with the aromatic compound;
3. A preliminary action of the aluminum chloride to form an ether-like substance which then rearranges to produce the alkyl substituted aromatic compound.

Regardless of the path the reaction may take, an atom of hydrogen must be split off the ring to combine with the alcoholic hydroxyl group as follows:

$$R_3COH + HC_6H_4OH \xrightarrow{AlCl_3} R_3C\text{-}C_6H_4OH + H_2O \qquad \text{IV}$$

Much evidence has accumulated to show that the above simple representation cannot fully explain the condensation. A brief discussion of each of the three mechanisms suggested above will be given.

The Alkyl Halide Intermediate Mechanism

Perrier and Pouget (32) and Mpetse (33) showed that the action of anhydrous aluminum chloride on a primary alcohol proceeds in two directions: with an excess of the alcohol, in the cold, are formed compounds of the type $Al_2Cl_6(ROH)_n$, while with an excess of aluminum chloride, on heating, hydrogen chloride is liberated and there are formed addition products such as $Al_2Cl_4(OR)_2$ together with simple ethers:

$$AlCl_2OR + ROH \longrightarrow AlCl_2OH + ROR \qquad V$$

Tzukervanic (34) found that in the beginning of the reaction between a tertiary aliphatic alcohol and sufficient aluminum chloride there are formed the above addition products, but with the addition of an excess of aluminum chloride and heat the corresponding olefins and alkyl halides are formed. In his suggested scheme of reaction it will be observed that all the required components for a Friedel-Crafts synthesis are present:

$$C_5H_{11}OH + AlCl_3 \longrightarrow AlCl_2(OC_5H_{11}) + HCl \qquad VI$$
$$AlCl_2(OC_5H_{11}) \longrightarrow C_5H_{10} + AlCl_2OH \qquad VII$$
$$C_5H_{10} + HCl \longrightarrow C_5H_{11}Cl \qquad VIII$$

A later study by Tzukervanic and Nazarova (35) showed that secondary alcohols and phenol in the presence of aluminum chloride give only insignificant amounts of alkyl phenols. This has since been disproved by the work of Huston and Curtis (36) on the condensation of the secondary hexyl alcohols with phenol to give secondary hexyl phenols in good yields. Tzukervanic and Nazarova stated that in general, the mechanism of condensation of secondary and tertiary alcohols with phenol is different. They found the main product to be a phenolic ether of the type RC_6H_4OR. Since the secondary alcohols, in distinction from the tertiary, do not give considerable amounts of olefins and alkyl halides, they proposed a scheme of reaction which did not involve the Friedel-Crafts mechanism:

$$ROH + AlCl_3 \longrightarrow AlCl_2OR + HCl \qquad IX$$

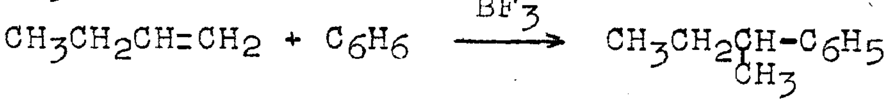
$$C_6H_5OH + 2\ AlCl_2OR \longrightarrow RC_6H_4OR + 2\ AlCl_2OH \qquad X$$

One objection to the mechanism suggested in steps VI-VIII is the difficulty always encountered in replacing the hydroxyl hydrogen atom of a tertiary alcohol even when a metal as active as sodium is employed. The evolution of hydrogen chloride and heat was observed by Huston and Hedrick (37) on adding a solution of n-butyl dimethyl carbinol in petroleum ether to a suspension of aluminum chloride in the same solvent. Although hydrogen chloride is evolved in step VI, it must be again introduced in step VIII if the alkyl halide is to be an intermediate in the reaction. Further, upon adding phenol to this mixture of carbinol and aluminum chloride in petroleum ether, a much smaller yield of alkyl phenol was obtained than had been produced by the usual procedure.

The Dehydration Mechanism

McKenna and Sowa (38) proposed that the alkene formed by dehydration of the alcohol was the intermediate in the condensation of alcohols with benzene using boron trifluoride as the catalyst:

$$CH_3CH_2CH_2CH_2OH \xrightarrow{BF_3} CH_3CH_2CH{=}CH_2 + H_2O \qquad XI$$



$$CH_3CH_2CH{=}CH_2 + C_6H_6 \xrightarrow{BF_3} CH_3CH_2\underset{CH_3}{\underset{|}{C}}H{-}C_6H_5 \qquad XII$$

This reaction was found to apply to primary, secondary, and tertiary alcohols. A similar mechanism has been proposed by McGreal and Niederl (39) using zinc chloride as catalyst, and by **Welsh** and Drake (28) for the condensation of aryl carbinols with phenol in the presence of aluminum chloride. Where the elimination of water from the carbinol is impossible, as in the cases of benzyl alcohol, benzhydrol, and triphenyl carbinol, Welsh and Drake assumed the elimination of the hydroxyl group along with a nuclear hydrogen. This explanation was advanced to account for the reaction between triphenyl carbinol and phenol at high temperatures in the absence of a catalyst.

It cannot be denied that olefins will condense with aromatic hydrocarbons in the presence of aluminum chloride as this has been shown by several papers (40). Nevertheless, the fact that primary alcohols will not condense with benzene under ordinary conditions (21) leads to the conclusion that this mechanism does not fully explain all condensations between alcohols and aromatic compounds.

The Ether Intermediate Mechanism

In 1892 Hartmann and Gattermann (41) reported that p-butylphenol could be produced by treating iso-butyl phenyl ether with aluminum chloride. Other similar rearrangements of alkyl-aryl ethers were reported from time to time, and in 1933 Smith (42) discovered that tert-alkyl phenyl ethers can rearrange into the corresponding p-tert-alkyl phenols upon the application of heat. He also reported the rearrangement of some alkyl phenyl ethers by means of aluminum chloride.

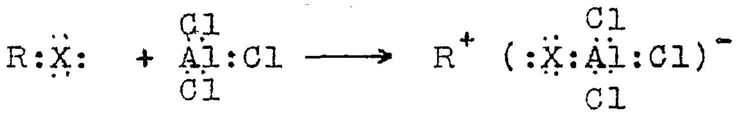
That such ethers may be intermediates in the condensation reaction is indicated in the work of Huston and Eldridge (43) who found a benzyl phenyl ether among the products obtained in the benzylation of 2,6-dichlorophenol with benzyl alcohol in the presence of aluminum chloride.

However, it must be remembered that Huston has reported good yields of the alkylation product resulting from the condensation of tertiary alcohols and benzene, anisole, and m-cresylmethyl ether (1) as well as in the condensation of benzyl alcohol with anisole and phenetole (20). In all these reactions ether formation is an impossibility. No ethers have been isolated from reactions between tertiary aliphatic alcohols and phenol as carried out in this laboratory (1).

An attempt has been made by Huston and Hedrick (37) to explain the color changes that always accompany the condensation of phenol with tertiary aliphatic alcohols. It is well known that ferric chloride forms colored compounds with phenols. It is conceivable that similar compounds may be formed between phenol and aluminum chloride. An hydro-aluminum phenolic acid of the type $H_3(Al(OC_6H_5)_6)$ was suggested. This, then, would react with the alcohol to form an intermediate addition complex which would rearrange to give the alkyl phenol and aluminum phenolate, the latter undergoing hydrolysis to phenol and aluminum chloride.

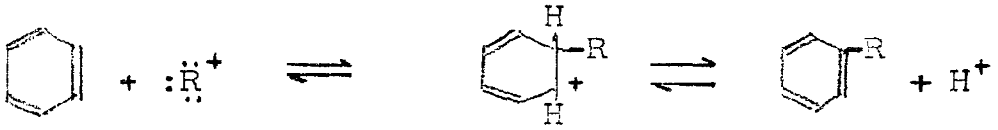
In reviewing studies on the mechanism of the Friedel-

Crafts type of reaction, Price (44) points out that Wertyporoch and Firla (45) have clearly demonstrated by conductance studies the formation of an ionic complex between aluminum chloride and an alkyl halide:



$$R:\underset{\cdot\cdot}{\ddot{X}}: \; + \; \overset{Cl}{\underset{Cl}{\dot{A}l}}:Cl \longrightarrow R^{+}\;(:\underset{\cdot\cdot}{\ddot{X}}:\overset{Cl}{\underset{Cl}{\dot{A}l}}:Cl)^{-} \qquad XIII$$

Ulich and Heyne (46), in studying the equilibrium for the formation of some catalyst-alkyl halide complexes, found that the rate of alkylation of benzene was directly proportional to the concentration of the complex. Price assumes that the electron-deficient carbonium ion, R^{+}, reacts, just as does the bromine cation Br^{+} during bromination, to complete its octet by association with a pair of electrons from a double bond of the aromatic nucleus:

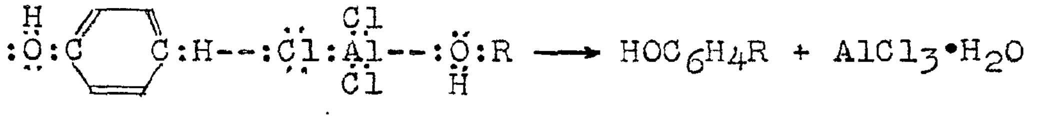


XIV

This is supported by evidence of the reversibility of the alkylation reaction uncovered by Ipatieff and Corson (47) in a study of the reaction of p-di-tert-butylbenzene with benzene in the presence of ferric chloride, sulfuric acid, or phosphoric acid to yield tert-butylbenzene:

$$(CH_3)_3C\text{-}C_6H_4\text{-}C(CH_3)_3 + C_6H_6 \xrightarrow{FeCl_3} 2\ C_6H_5\text{-}C(CH_3)_3 \qquad XV$$

Perhaps the mechanism showing the most promise at the present **time** is based upon the formation of addition products of alcohol and phenol with aluminum chloride. Such a theory has also been proposed for the catalytic action of several other catalysts. In the case of aluminum chloride, the complex or "polymolecule" is linked together by the outer electrons of the aluminum or chlorine atoms. Since the new arrangement of atoms and electrons is unstable under the conditions of the reaction, rearrangement occurs, resulting in the formation of a more stable system:



XVI

Such a mechanism is further suggested by the fact that aluminum chloride is such a powerful electrophilic reagent. The aluminum atom exhibits a great tendency to make up an octet of shared electrons. Also, the chlorine atom exerts a stronger pull upon the nuclear hydrogen than does the less electronegative ring carbon atom.

Two experimental observations lead to the conclusion that a different mechanism exists for the condensation of tertiary aliphatic alcohols with phenol as compared to their condensation with benzene. First, lowering the temperature decreases the yield of alkylphenol but increases the yield of alkylbenzene. Second, no fragmentaion of the alcohol appears during the phenol condensation; whereas the degree of fragmentation is found to be very high when benzene is condensed.

EXPERIMENTAL PROCEDURES

Materials Used

Magnesiun turnings especially prepared for Grignard reactions were used after drying in an oven at 45° C. for several days.

Benzene was thiophene-free, C. P. grade.

Petroleum ether, B. p. 30-65° C., was dried over freshly cut sodium.

Phenol was Mallinckrodt's (crystals) and was redistilled before use.

Aluminum chloride was Baker's Analyzed, special for condensations, C. P. anhydrous.

Diethyl ether was C. P. anhydrous, and was dried over freshly cut sodium before use.

Diisopropyl ketone was obtained from Eastman's.

Methyl iso-propyl ketone was prepared by brominating tertiary amyl alcohol and hydrolyzing (48).

Ethyl acetate was Baker's U. S. P., redistilled before using.

n-Propyl bromide was prepared by adding 48% hydrobromic acid to n-propyl alcohol in the presence of concentrated sulfuric acid and refluxing for several hours (49).

Preparation of the Tertiary Octyl Alcohols

4-Methylheptanol-4

By adding methyl iodide to di-n-propyl ketone in the presence of zinc, Gortalow and Saytzeff (50) first prepared methyl di-n-propyl carbinol in 1886. They reported a yield of 30 percent. Halse (51), in 1914, prepared the same alcohol by the reaction between n-propyl magnesium bromide and ethyl acetate. Stadnikow (52) modified the procedure of Halse by substituting benzhydryl acetate for the ethyl ester to obtain a yield of 40 percent.

Preparation of n-Propyl Magnesium Bromide.

To a mixture of 50 grams (2.06 moles) of dry magnesium turnings and 100 ml. of anhydrous ethyl ether contained in a three-liter, three-necked, round-bottomed flask, a solution of 246 grams (2 moles) of n-propyl bromide in 500 ml. of anhydrous ethyl ether was added dropwise through a dropping funnel. The mixture was stirred continuously during the addition of the halide by means of a glycerine-sealed stirrer. A long reflux condenser having a calcium chloride drying tube at its upper end served to condense the ether vapors.

Preparation of the Carbinol.

To the Grignard reagent thus prepared was added 88 grams (1 mole) of freshly distilled ethyl acetate. The rate of addition was so regulated that the ether refluxed gently.

After the ester had all been added the stirring was continued for a period of at least two hours.

Hydrolysis of the mixture, after it had been allowed to stand overnight, was brought about by pouring the contents of the flask onto ice in a three-liter beaker. The cold mass was then treated with 1:1 hydrochloric acid while the whole was vigorously stirred until the magnesium hydroxide was completely dissolved as shown by the clearing of the water layer.

The ether layer was separated from the water layer by means of a large separatory funnel. The water layer was next extracted three times with fresh portions of ether. The ether extracts were combined and dried overnight by standing over anhydrous sodium sulfate.

The ether was distilled off by use of a water bath and the residual liquid subjected to a distillation under reduced pressure. The methyl di-n-propyl carbinol was collected between 58° and 60° C. under a pressure of 7 mm. of mercury.

2,3-Dimethylhexanol-3

By adding 2-methylbutanone-3 to n-propyl magnesium bromide, Clarke (53), in 1911, obtained a 45 percent. yield of methyl n-propyl iso-propyl carbinol. He prepared the ketone by converting ethyl acetoacetate to ethyl dimethylacetoacetate and hydrolyzing with aqueous potassium hydroxide.

The methyl iso-propyl ketone was prepared (48) by the action of bromine on tertiary amyl alcohol at 50-60° C. forming trimethylethylene dibromide which was then hydrolyzed to the ketone. A 70 percent. yield of ketone boiling at 93-96° C. at 750 mm. pressure was obtained.

To a 2 mole theoretical of n-propyl magnesium bromide, prepared as described under 4-methylheptanol-4, was added 172 grams (2 moles) of methyl iso-propyl ketone. The rate of addition was such that the ether refluxed gently. The stirring was continued for two hours after the last of the ketone had been added. The resultant product was hydrolyzed in the usual manner with ice and 1:1 hydrochloric acid. Methyl n-propyl iso-propyl carbinol was collected between 46° and 47° C. at a pressure of 3 mm. of mercury.

2,3,4-Trimethylpentanol-3

A 76 percent. yield of methyl di-iso-propyl carbinol was reported by Whitmore and Laughlin (54) in 1932 from the action of di-iso-propyl ketone on methyl magnesium chloride.

Preparation of Methyl Magnesium Bromide.

The methyl bromide generator, by a modification of the procedure given for methyl chloride (55), consists of a three-liter, round-bottomed flask resting on a sand bath. The flask is fitted with a reflux condenser which has a delivery tube running from its upper end to a train of wash bottles. This train is made up of three bottles containing saturated sodium hydroxide solution, three containing concentrated sulfuric acid, and three safety bottles, one at each end of the train and one between the alkali and the acid bottles.

In the flask was placed 53 grams of water and 586 grams (320 ml.) of concentrated sulfuric acid. The addition of 370 grams (470 ml.) of methyl alcohol was carried out, with cooling, at such a rate that the temperature did not rise above 70° C. After adding 1130 grams of sodium bromide the apparatus was tightly connected and the flask heated on the sand bath so that the gas was evolved at a fairly rapid rate. The washed methyl bromide was passed into a three-liter, three-necked, round-bottomed flask which contained 75 grams (3.09 moles) of magnesium, a few iodine crystals and some ethyl bromide to start the reaction, and 600 ml. of anhydrous ethyl ether. The reaction was carried out under the hood because of the poisonous nature of the methyl bromide fumes. About two hours were required to use up all the magnesium.

Preparation of the Carbinol.

To the methyl magnesium bromide was added 296 grams (370 ml.) of di-iso-propyl ketone in 400 ml. of anhydrous ethyl ether. It was added at such a rate that the ether refluxed gently. The resulting product, after standing overnight, was hydrolyzed in the same manner as the 4-methylheptanol-4. Methyl di-iso-propyl carbinol was distilled under diminished pressure. The fraction boiling between 53° and 54° C. at 13 mm. pressure was collected.

CONDENSATIONS

Each of the tertiary octyl alcohols whose preparation has been described was condensed with phenol. Since the procedure was the same in every case, only a typical run will be described.

A 500 ml. three-necked, round-bottomed flask was fitted with a short reflux condenser, a thermometer, and a glycerine-sealed mechanical stirrer. In the flask was placed 32.5 grams (one-fourth mole) of the carbinol and 35 grams (three-eighths mole) of freshly distilled phenol. The stirring motor was started and stirring continued until the phenol was completely dissolved to form a colorless solution in the alcohol. The addition of 17 grams (one-eighth mole) of aluminum chloride was carried out by introducing small portions at frequent intervals during a two hour period. The stirring was continued vigorously for another hour and the mixture was then allowed to stand overnight before hydrolysis was carried out. The temperature was not at any time allowed to rise above 30° C. It was always observed that the first addition of the aluminum chloride caused the mixture of carbinol and phenol to undergo a series of color changes beginning with a yellow, going through a purple, and ending with a final condensation product which was uniformly a deep maroon color.

The condensate was hydrolysed by pouring the thick mixture onto ice in a three liter beaker. While stirring constantly, 1:1 hydrochloric acid was added until the plastic mass rose to the top. The hydrolysate was then extracted three times ether. The ether extracts were combined and the ether removed on a water bath. The residue was then subjected to a distillation under reduced pressure. The fraction obtained between 45° and 60° C., at a pressure of 6 mm. of mercury, consisted of uncombined carbinol. From 60° to 90° C. the uncombined phenol distilled over. The octyl phenol itself was obtained in the range between 140° and 160° C. at the low pressure. The octyl phenol fraction was then redistilled and collected over a two degree range of temperature. The product usually crystallized in the receiving flask, or, if not, crystallization was induced by cooling the distillate in the icebox overnight.

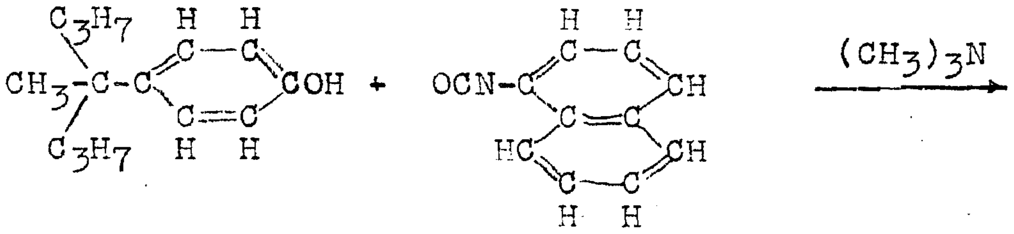
Purification of the product presented some difficulty because of the extremely high solubility of the alkylated phenol in all of the common solvents. The slight color of the product was removed by pressing the crystals on an unglazed porcelain plate. Further purification was attained by recrystallization from petroleum ether.

DERIVATIVES

The α-naphthyl urethanes and the 3,5-dinitrobenzoyl esters were prepared as derivatives of the p-tert-octyl phenols.

α-Naphthyl Urethanes

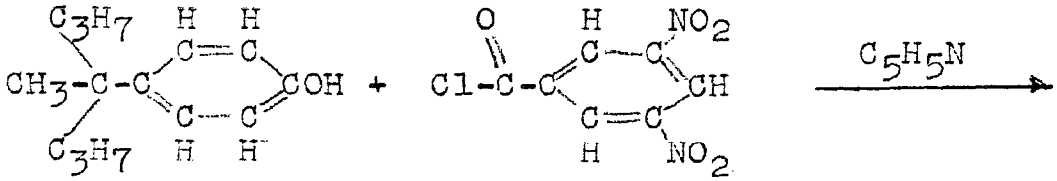
The method of French and Wirtel (56) was employed in the preparation of the urethanes. One gram of the crystalline phenol was placed in a test tube and 0.5 ml. of α-naphthyl isocyanate added. It has been found that, if the reaction is not spontaneous, addition of a few drops of a solution of trimethylamine in absolute ether will readily catalyze it. During the reaction the contents of the tube must be protected against moisture by means of a calcium chloride drying tube. The solution was warmed on a steam bath for thirty minutes, cooled in a beaker of ice, and the sides of the tube scratched with a stirring rod in order to induce crystallization. The urethane was purified by repeated recrystallizations from petroleum ether until a constant melting point was obtained.



$C_8H_{17}C_6H_4\text{-O-CO-NH-}C_{10}H_7$ XVII

3,5-Dinitrobenzoyl Esters

A modification of the method described by Shriner and Fuson (57) was used in the preparation of the 3,5-dinitrobenzoyl esters of the three p-tert-octylphenols. In a 50 ml. Erlenmeyer flask were placed three grams of the phenol and an equal weight of 3,5-dinitrobenzoyl chloride dissolved in four ml. of pyridine. After the initial reaction had subsided the mixture was refluxed over a small flame for one hour, cooled, poured on ice, and the oily layer extracted with ether. The ether extract was washed with cold dilute sulfuric acid to remove the pyridine and then with cold dilute sodium carbonate solution to remove excess acid. The ether was removed on a water bath and the ester then recrystallized from a water-alcohol mixture until a constant melting point was obtained.



$C_8H_{17}-C_6H_4-O-CO-C_6H_3(NO_2)_2$ + HCl XVIII

PROOF OF STRUCTURE

To prove the structure of the octyl phenols the corresponding octyl benzenes were prepared, nitrated to the p-nitro derivative, reduced to the p-amino compound, diazotized, and the diazonium salt finally hydrolyzed to form the octyl phenol.

The three methyl di-propyl phenyl methanes had been previously prepared in this laboratory (58) and their physical constants determined. The method employed in the preparation of these octyl benzenes was to condense the three methyl di-propyl carbinols with benzene in the presence of aluminum chloride.

The methyl di-n-propyl carbinol and the methyl n-propyl iso-propyl carbinol were condensed with benzene in the same manner so that a general description of the procedure will suffice. The condensation of the methyl di-iso-propyl carbinol, however, required special treatment because of its great tendency to undergo fragmentation during the reaction.

Preparation of the Octylbenzenes

A one-liter, three-necked, round-bottomed flask was provided with a glycerine-sealed mechanical stirrer, a reflux condenser, and a separatory funnel. A calcium chloride drying tube was inserted in the upper end of the reflux condenser to exclude moisture. In the flask was placed 195 grams (two and one-half moles) of benzene and 33 grams (one-fourth mole) of anhydrous aluminum chloride. The mixture was then stirred until the aluminum chloride was uniformly suspended in the benzene. Next, 65 grams (one-half mole) of carbinol was added through the dropping funnel at the rate of one drop per second. The stirring was continued for four or five hours after the last of the carbinol had been added. At no time during the addition of the carbinol was the temperature allowed to rise above 30° C., external cooling being applied if needed. The evolution of considerable amounts of hydrogen chloride gas was noted as the reaction proceeded. After standing overnight the mixture was hydrolyzed by pouring into ice and 1:1 hydrochloric acid. The benzene layer was separated and the water layer extracted three times with ether. The benzene-ether solution was washed with sodium carbonate solution in order to remove any excess acid and then dried overnight over anhydrous sodium sulfate. After removing the ether and benzene on a water bath the residue was distilled under reduced pressure.

All attempts which have been made to condense methyl di-iso-propyl carbinol with benzene at room temperature have led to fragmentation of the carbinol resulting in the formation of alkyl benzenes of lower molecular weight. This is the subject of an investigation now under way in this laboratory by Huston and Awuapara. In order to avoid this splitting as much as possible, the condensation was run at a temperature of minus 30° C. This temperature was maintained by mixing ether and solid carbon dioxide ("dry ice"). To prevent the freezing of the benzene, an equal weight of petroleum ether was added. The suspension of aluminum chloride, petroleum ether, and benzene was cooled in the icebox overnight, then cooled down to -30° C. and the carbinol added over a period of five hours. The low temperature was maintained while stirring was continued for another five hours after which the mixture was placed in the icebox overnight. The material was allowed to come slowly to room temperature and then treated in the usual manner. Even with all these precautions the yield of the desired product was low as indicated in the table.

Nitration of the Octylbenzenes

The nitration of the alkyl benzenes followed Malherbe's procedure (59). The hydrocarbon was treated with an equal weight of fuming nitric acid (sp. gr. 1.52), cooling during the addition. After the first violent reaction had subsided the mixture was warmed to 90° C. in a water bath for one hour. It was then poured on ice and the resulting solution extracted three times with ether. The ether extracts were dried over calcium chloride, the ether removed, and the liquid nitro compounds subjected to a distillation under reduced pressure.

Oxidation of the Nitrated Octylbenzenes

In order to determine the position taken by the nitro group, the octyl side chain was converted into a carboxyl group and the nitrobenzoic acid identified by melting point.

The oxidation was adapted from a method proposed by Anshütz and Beckerhoff (60). One gram of the nitro compound and 20 ml. of 6 N nitric acid were sealed up in a Carius tube and heated in a Carius furnace at 130° C. until crystals appeared on cooling. The time required was from 10 to 20 hours. The crystals were removed, filtered by suction, washed with petroleum ether, dried, and recrystallized from alcohol until they melted at 238-240° C. and caused no depression of the melting point of a known sample of p-nitrobenzoic acid.

<u>Reduction of the Nitrated Octylbenzenes</u>

Conversion of the nitro derivatives into the corresponding amino compounds was accomplished by the method of Ipatieff and Schmerling (61). For each gram of the nitro compound, contained in a 500 ml. round-bottomed flask equipped with an air condenser, 5 grams of granulated tin and 5 ml. of concentrated hydrochloric acid were added. To this mixture was added sufficient ethyl alcohol to bring nearly all of the material into solution. The flask was shaken until reduction was complete as was shown by the absence of a marked turbidity on pouring a test portion into water. The flask was heated on a steam bath if the reduction was slow. Ten minutes was all that was usually required to complete the process. The aqueous-alcoholic solution was then decanted into about twice its volume of water and the amine extracted with ether after the solution had been made alkaline with 40 percent. sodium hydroxide solution. A purer product was obtained if the amine was steam distilled before the ether extraction. The ether solution was washed with potassium carbonate solution, the ether evaporated, and the amine dried with solid potassium hydroxide.

Replacement of the Amino Group by Hydroxyl

For each two grams of the amine, a solution of 1.5 ml. of concentrated sulfuric acid in 10 ml. of water was added. The insoluble sulfate thus formed was suspended by vigorous stirring in 10 volumes of water. After cooling to 5° C. a 25 percent. solution of sodium nitrite was added dropwise until an excess was shown by a positive starch-potassium iodide test. The solution was tested from time to time with Congo red paper to make sure that the acid concentration did not drop too low. When the diazotization was complete the solution was brought to room temperature with continued stirring and finally heated on the steam bath for an hour to bring about hydrolysis of the diazonium salt. The phenol was extracted with ether, dried with anhydrous sodium sulfate and distilled in vacuo. After isolation of the pure phenol the α-naphthyl urethane was prepared. Melting point and mixed melting point determinations indicated that the phenols obtained by this method were identical with the others.

TABLES

Table I

Condensation of tert-Octyl Alcohols with Phenol

Product:	4-Methyl-4-p-hydroxyphenylheptane	2,3-Dimethyl-3-p-hydroxyphenylhexane	2,3,4-Trimethyl-3-p-hydroxyphenylpentane
Yield:	65.0%	47.0%	59.6%
M. p.	63-63.5° C.	72-73° C.	57-58.5° C.
B. p.	151-152°/6 mm.	122-124°/2 mm.	116-117°/2 mm.
	282-284°/738	279-281°/738	285-287°/738
Analyses:			
%C *	81.17%	80.91%	80.96%
%H *	10.68%	10.77%	10.81%

* Calculated for $C_{14}H_{22}O$: C= 81.50%, H= 10.75%

Table II

3,5-Dinitrobenzoyl Esters

Phenol Esterified	M. p. (°C.)	% N *
4-Methyl-4-p-hydroxyphenylheptane	124.5-126.0	6.97%
2,3-Dimethyl-3-p-hydroxyphenylhexane	97.0-98.0	7.01%
2,3,4-Trimethyl-3-p-hydroxyphenylpentane	103.0-103.5	6.98%

* Calculated for $C_{21}H_{24}O_6N_2$: N = 7.00%

Table III

α-Naphthylurethanes

α-Naphthylurethane of:	M. p. (°C.)	% N *
4-Methyl-4-p-hydroxyphenylheptane	105.0-106.0	3.72%
2,3-Dimethyl-3-p-hydroxyphenylhexane	127.5-128.5	3.69%
2,3,4-Trimethyl-3-p-hydroxyphenylpentane	106.0-107.0	3.70%

* Calculated for $C_{25}H_{29}O_2N$: N= 3.73%

Table IV

Methyl Di-Propyl Carbinols *

Compound:	4-Methyl-heptanol-4	2,3-Dimethyl-hexanol-3	2,3,4-Trimethyl-pentanol-3
B. p. found:	62-63°/12 mm	54-56°/13 mm.	53-54°/13 mm.
	157-9°/748.5	155.5-7.5°/748.5	146-7°/740.5 mm
reported:	61-63°/12mm		75-77°/40 mm.
	159-61°/755	158-58.2°/758 mm	
% Yield:	54.5 %	36 %	80 %
Index of refraction (20° C.):	1.4258	1.4317	1.4342
Surface tension (20° C.):	26.675	27.500	28.325
D_4^{20} :	0.8208	0.8344	0.8457

* Physical constants taken from the M. S. thesis of Kenneth D. Cline (58)

Table IV-A

p-Nitro-tert-octylbenzenes

Nitro Derivative of:	Boiling point:
4-Methyl-4-phenylheptane	137-139°/ 6 mm.
2,3-Dimethyl-3-phenylhexane	140-141°/ 7 mm.
2,3,4-Trimethyl-3-phenylpentane	133-135°/ 6 mm.

Table V

tert-Octylbenzenes *

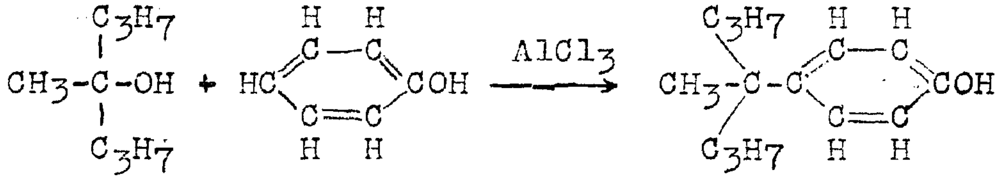
Compound:	4-Methyl-4-phenylheptane	2,3-Dimethyl-3-phenylhexane	2,3,4-Trimethyl-3-phenylpentane
B. p. found:	109-111°/10 mm.	104.5-6.5/11 mm	104-106°/13 mm.
	242-3°/749 mm.	237-8°/748 mm.	234-6°/743 mm.
reported:	120-1°/12 mm.		
Yield:	31.8 %	18.4 %	6.0 %
Refractive Index 20°	1.4930	1.4900	1.4968
Surface tension	31.488	30.80	31.763
D_4^{20}	0.8700	0.8663	0.8808
Analyses % C **	88.34 %	88.43 %	88.55 %
% H **	11.64 %	11.68 %	11.51 %
Mol. Wt. found:	190.88	189.92	189.72
Mol. Refr. calc.:	63.25	63.25	63.25
found:	63.57	63.51	63.18
Parachor calc.:	522.4	519.4	516.4
found:	518.25	517.52	513.0

* Physical constants determined by Cline (58)

** Calculated for $C_{14}H_{22}$: C = 88.33 %, H = 11.67 %

DISCUSSION

The general procedure used to prepare the p-tert-octyl phenols described consisted in the preparation of the three isomeric methyl dipropyl carbinols, followed by their condensation with phenol using anhydrous aluminum chloride as the catalyst:



XIX

The three carbinols, 4-methylheptanol-4, 2,3-dimethylhexanol-3, and 2,3,4-trimethylpentanol-3, have all been previously prepared. The methods involved in their preparation are described in the experimental portion of this thesis, while their physical constants, as determined in this laboratory by Kenneth D. Cline (58), are listed in table IV. Attempts by the writer to prepare 2,3,4-trimethylpentanol-3 by using iso-propyl magnesium bromide and methyl iso-propyl ketone led only to failure. It has been found that such branched Grignard reagents have a tendency to cause enolization and polymerization of the ketone.

In preparing the octylphenols, the phenol was dissolved in the carbinol by rapid stirring and the aluminum chloride added in small portions. This "shaker method" was decided upon following the observation of Curtis (36) that higher yields resulted from this method than when the alcohol was added to phenol and catalyst in petroleum ether. No increase in yield was observed when a temperature of 45 to 50° C. was tried, whereas a temperature of 10° C. was found by Huston and Guile (62) to cause a decrease in yield. For these reasons the temperature was held between 25 and 30° C. After completion of the reaction the condensate appeared as a gummy mass which stuck to the sides of the beaker when water was added. The addition of hydrochloric acid thinned the mass and permitted it to rise to the surface. A deep maroon color was always observed at the final stage in the condensation.

The presence of unchanged phenol in the condensate was shown by its crystallization as long white needles in the receiving flask during the distillation of the products. These needles slowly changed to a purple and finally to a deep blue color, suggesting the color reactions between phenol and ferric chloride.

Separation of the octyl phenols from colored impurities was difficult due to their great solubility in all common organic solvents. The problem was solved by pressing them out on porous porcelain plates which were kept for several days in the icebox. This method was necessary in the case of 2,3-dimethyl-3-p-hydroxyphenylhexane because the impure compound would not crystallize at room temperature.

After purification of the octylphenols, their physical constants were determined, they were analyzed for carbon and hydrogen, and two solid derivatives, the α-naphthyl urethanes and 3,5-dinitrobenzoyl esters, were prepared for identification. The latter were chosen in preference to benzoyl esters because the melting points of the benzoyl esters were not high enough to make them satisfactory derivatives. The percentages of nitrogen and the melting points of these derivatives are shown in tables II and III.

The proof of structure was the same as was used by Huston and Hsieh (1) and by several subsequent investigators in this laboratory. The octyl benzenes were prepared by condensing the same three carbinols with benzene in which the catalyst, aluminum chloride, was suspended. The yields (table V) were found to decrease as the branching of the alcohol increased. Not only alkyl benzenes of lower molecular weight, but also alkyl chlorides appeared in the lower fractions when these condensates were distilled. Although very low temperatures increased the yield of octylbenzene and decreased the yield of the lower alkyl benzenes, it simultaneously increased the amount of alkyl halide.

These tert-octylbenzenes, whose physical constants had been previously determined in this laboratory (58), were nitrated, reduced, diazotized, and the diazonium salt hydrolyzed to the octylphenol. Oxidation of the side chain of the nitrated octylbenzenes showed that the substitution of alkyl group for hydrogen in the phenol occurs in the para position rather than in the ortho or meta positions.

SUMMARY

1. The methyl di-propyl carbinols have been condensed with phenol in the presence of aluminum chloride to give good yields of the corresponding p-tert-octylphenols.

2. The 3,5-dinitrobenzoyl esters and the α-naphthyl urethanes of these p-tert-octylphenols have been prepared.

3. The structures have been established by synthesis.

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