CONDENSATION OF TERT-BUTYL AND TERT AMYL ALCOHOLS WITH PARA-CRESOL IN THE PRESENCE OF ALUMINUM CHLORIDE

Thesis for the Degree of M. S.

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Richard I. Jackson

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Thesis

Submitted to the Faculty of Michigan State College in partial fulfillment of the requirements for the degree of Master of Science

by

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Acknowledgment

To Dr. R. C. Huston, The author wishes to express his thanks for his invaluable aid and advice in the accomplishment of this work.

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I INTRODUCTION

In 1916, Huston and Friedeman (1) condensed benzyl alcohol and benzene with the use of anhydrous aluminum chloride as condensing agent.

In 1920, Huston (2) condensed benzyl alcohol and phenol.

In 1929, Huston and Lewis (3) condensed benzyl alcohol with para-cresol.

In 1934, Huston and Fox (4) condensed tert-butyl and tert-amyl alcohols with benzene.

In 1936, Huston and Hsieh (5) condensed tert-butyl and tert-amyl alcohols with phenol.

To investigate further the use of anhydrous aluminum chloride as a condensing agent, the author has condensed tert-butyl and tert-amyl alcohols with para-cresol.

II HISTORICAL

The first mention of the use of anhydrous aluminum chloride as an agent for the condensation of alcohols and aromatic compounds was by Nef (6) who, in 1897, mentioned the formation of diphenyl methane from the condensation of benzyl alcohol and benzene.

This condensation was repeated in 1916 by Huston and Friedeman (1). Since that time, Huston and co-workers (7), using aluminum chloride as a condensing agent, have condensed primary and secondary aromatic alcohols with benzene, anisole, phenetole, phenols, and cresols, and tert. aliphatic alcohols with benzene, phenol, cresols, and halogenated phenols.

Similar work on the condensation of tert. aliphatic alcohols with phenol in the presence of aluminum chloride has been reported by Tzukervanik and Nazarova (8).

Anhydrous aluminum chloride was used as a catalyst for the rearrangement of phenyl and cresyl ethers by Smith (9)(10) and by Perkins, Dietzler, and Lundquist (11) to condense tert aliphatic halides with phenol and cresols.

Of the other condensing agents which have been used to condense tert. aliphatic alcohols with phenols, the following may be mentioned:

Sulphuric acid (70 to 80%) was used by Meyer and Bernhauer (12), Zinc chloride by Liebmann (13), Senkowski (14), and Baur (15), and use was made of phosphoric acid by Tchitchibabine (16).

Tert-butyl and tert-amyl phenyl ethers were rearranged by heat alone by Smith (17) and Natelson (18).

The preparation of 2 tert-butyl 4 methyl phenol was mentioned by Baur (15) from the condensation of isobutyl alcohol and p-cresol with the use of zinc chloride as condensing agent. It was definitely prepared by Tchitchibabine (16) from tert-butyl alcohol, p-cresol, and phosphoric acid. He did not prove its structure.

Other substituted p-cresols which have been reported are: 2 ethyl 4 methyl phenol (19), 2 propyl 4 methyl phenol (19), 2 butyl 4 methyl phenol (20), 2 amyl 4 methyl phenol (20), 2 hexyl 4 methyl phenol (20), 2 isopropyl 4 methyl phenol (19)(21)(22)(23)(24), 2 iso-butyl 4 methyl phenol (25), 2 sec-butyl 4 methyl phenol (10), 2 cyclopentyl 4 methyl phenol (26)(27), 2 allyl 4 methyl phenol (28)(29), 2 methylallyl 4 methyl phenol (25), 2 pentenyl 4 methyl phenol (30), 2 phenylallyl 4 methyl phenol (31), 2 benzyl 4 methyl phenol (30)(3), 2 cinnamyl 4 methyl phenol (29)(30), and 3 methyl 6 hydroxy triphenyl methane.

III THEORETICAL

Alkylation of Para Substituted Phenols.

The low yields resulting from the condensations of tert-butyl and tert-amyl alcohols with para-cresol in the presence of aluminum chloride are in accord with the results from practically all of the attempts at condensation of para substituted phenols with tert-aliphatic alcohols or halides.

In this laboratory, with the use of aluminum chloride as condensing agent, several para substituted phenols were condensed with tert-butyl alcohol. In Table I the results are tabulated along with results from the condensation of the isomeric ortho substituted phenols placed there for the purpose of comparison.

Meyer and Bernhauer (12) attempted to alkylate para-cresol without success. The condensing agent used was sulphuric acid. (70-80%).

Agett (33) attempted to condense p-bromo phenol with tert-butyl alcohol using a mixture of zinc and aluminum chlorides ($ZnCl_2$-17g., $AlCl_3$-0.5 to 3.0g.) as condensing agent. A very small yield of a substance, unidentified as yet, resulted. Also, he was unable to condense p-tert-butyl phenol with tert-butyl alcohol by this method.

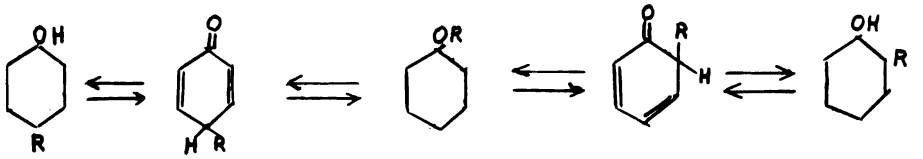
Tchitchibabine (16), using phosphoric acid as condensing agent, condensed p-cresol and tert-butyl alcohol (yield 73%) and o-cresol and tert-butyl alcohol (yield 78%)

To the product from the latter, however, he assigned the structure, 3 methyl, 5 tert-butyl phenol. From evidence described later, there is reason to believe that the correct structure is 3 methyl 4 tert-butyl phenol.

Using phosphoric acid (sp. g. 1.7) as condensing agent, following the procedure used in Tshitschibabine, Arett (13) was unable to condense tert-butyl alcohol with o-bromo phenol or p-tert-butyl phenol.

ALKYL ARYL ETHERS

Concerning the equilibrium between alkyl aryl ethers and substituted alkyl phenols, Watelsen (18) suggested the following mechanism:



He states further, "Equilibrium mixtures of ortho and para substituted phenols are obtained on rearrangement (of alkyl ethers.) In the case of iso-propyl phenyl ethers, the ratio is approximately 33% ortho and 66% para. As the alkyl radical increases in weight or becomes tertiary, the yield of para substituted product is increased so that in the case of tert-amyl phenol, all the phenol obtained is the para substituted product."

Perkins, Dietzler, and Lundquist (11) demonstrated that in the presence of anhydrous aluminum chloride, at 90° to 100°C., tert-butyl chloride and phenol, in equimol-

ecular amounts, give the following equilibrium mixture: (by weight) 10.5% phenol, 70.2% p-tert-butyl phenol, 1.2% o-tert-butyl phenol, and 18.1% 2,4 ditert-butyl phenol. From phenol, tert-amyl chloride, and aluminum chloride at 100°C, they report 0.14% (by weight) o-tert-amyl phenol, 3.0% 2,4 ditert-amyl phenol, the remainder being p-tert-amyl phenol. These last results are strikingly in agreement with those of Natelson (18) from the rearrangement of tert-amyl phenyl ether.

That there is also an almost exclusive formation of the para isomer when tert-alkyl phenols are prepared by other methods has been demonstrated in the following cases.

Using aluminum chloride as condensing agent, Huston and Hsieh (5) and Huston and Hedrick (7) condensed phenol with tert-butyl, tert-amyl, tert-hexyl, and tert-heptyl alcohols. They reported only the p-tert-alkyl phenols.

Using a mixture of zinc and aluminum chlorides as condensing agent, Agett (33) found only a minute yield of o-tert-butyl phenol from the condensation of tert-butyl alcohol and phenol, the principal product being the para isomer.

The tert-amyl phenol prepared by Liebmann (13) with the use of zinc chloride as condensing agent was proved by Anschutz and Beckerhoff (34) to be p-tert-amyl phenol.

Tchitchibabine's Investigations.

Considerable work was done by Tchitchibabine (16) on the condensation of alcohols and phenols with the use of phosphoric acid as condensing agent. Included in this investigations were the following condensations:

tert-butyl alcohol and m-cresol

tert-butyl alcohol and o-cresol

tert-butyl alcohol and p-cresol

He did not report the condensation of tert-butyl alcohol with phenol.

To the tert-butyl m-cresol, he assigned the structure, 3 methyl, 6 tert-butyl phenol, He proved its structure by conversion to the methyl ether and comparison of its dinitro derivative with the dinitro derivative of 3 methyl 6 tert-butyl anisole which had been previously prepared and identified (35). The tert-butyl m-cresol prepared by Tchitchibabine is not appreciable soluble in 20% NaOH solution.

To the tert-butyl o-cresol, by analogy to the tert-butyl m-cresol, he assigned the structure 2 methyl 6 tert-butyl phenol, It is soluble in 20% NaOH solution.

Tchitchibabine stated further that, in the condensations of tert-aliphatic alcohols with phenols in the presence of phosphoric acid (sp. g. 1.7 to 1.87), the principal product, at moderate temperatures, contains the alkyl group in the position ortho to the hydroxyl; only insignificant quantities of the para isomer are produced.

Even at high temperatures the para isomer is never obtained in very great quantities.

The author wishes to present proof that the above statement by Tchitchibabine is at least in part erroneous. The author wishes to present also very good indications, but not proof, that the structure of the tert-butyl o-cresol prepared by the use of phosphoric acid is 2 methyl 4 tert-butyl phenol, not 2 methyl, 6 tert-butyl phenol.

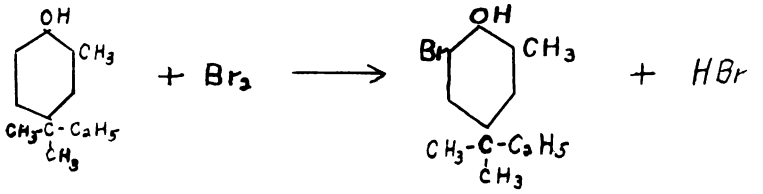
Agett (33) prepared tert-butyl phenol from phenol, tert-butyl alcohol, and phosphoric acid following the methods used by Tchitchibabine. The principal product (yield, 70 to 80% of the theoretical) boiled at 122°-125° /14mm. and melted at 95°. By mixed melting points it was proved to be p-tert-butyl phenol. Less than 5% of the theoretical yield boiled within the range reported for o-tert-butyl phenol by Perkins, Dietzler, and Lundquist (11). He thus demonstrated that where both of the ortho postions and the para position are open, the tert-butyl group exhibits a decided preference for the position para to the hydroxyl.

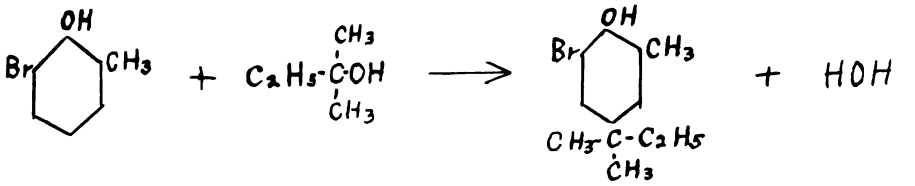
Concerning the structure of the tert-butyl o-cresol prepared with the use of phosphoric acid, the following evidence is presented.

Considering the fact that p-tert-butyl phenol and 2 methyl, 4 tert-amyl phenol are soluble in alkali solution and that o-tert-butyl phenol, 2,4 ditert-butyl phenol, and

2 tert-butyl 4 methyl phenol are not, it would seem that insolubility in alkali solution is characteristic of tert alkyl phenols only when the alkyl group is ortho to the hydroxyl. It is therfore significant that the tert-butyl o-cresol prepared by Tchitchibabine is soluble in 20% NaOH solution.

Huston and Petty (7), using aluminum chloride, condensed tert-butyl and tert-amyl alcohols with o-cresol. The tert-amyl o-cresol was proved to have the structure 2 methyl 4 tert-amyl phenol by comparison of its bromination product with the product from the condensation of tert-amyl alcohol and 2 methyl, 6 bromo phenol.





The two bromo tert-amyl o-cresols were proved to identical by the mixed metling point of their diphenyl urethanes.

The author prepared tert-amyl o-cresol by the procedure of Tchitchibabine. By the melting point of its aryloxy acetic acid, it was proved to be identical with the 2 methyl 4 tert-amyl phenol prepared by Huston and Petty.

In conclusion, it may be safely stated that, in general, the introduction of a tert. alkyl group into the ring of a para substituted phenol is accomplished with more difficulty than the corresponding alkylation of the isomeric ortho substituted phenol.

It may also be stated that, with a few exceptions, in the introduction of a tert. alkyl group into a phenol in which both ortho and para positions are not substituted, the position para to the hydroxyl is strongly favored.

TABLE 1*

PHENOL	ALCOHOL	PRODUCT	%YIELD	INVESTIGATOR
p-cresol	tert-butyl	2 tert-butyl 4 methyl phenol	15%	
o-cresol	tert-butyl	2methyl 4 tert butyl phenol	35%	Petty (7)
p-chloro phenol	tert-butyl	No condensation	---	Coleman (7)
o-chloro phenol	tert-butyl	2 chloro 4 tert-butyl phenol	24%	Coleman (7)
p-bromo phenol	tert-butyl	No condensation	---	Agett (33)
o-bromo phenol	tert-butyl	2 bromo 4 tert-butyl phenol	22%	Swayze (36)
p-tert-butyl phenol	tert-butyl	No condensation	---	Agett (33)

*Condensation with aluminum chloride.

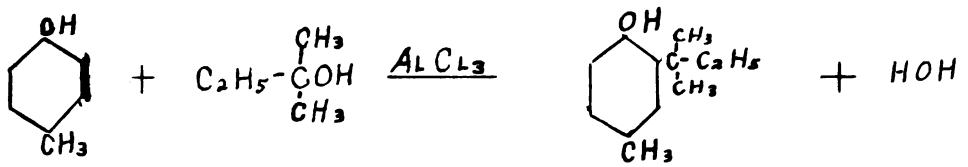
TABLE II

Condensations with zinc and aluminum chorides				
p-bromo phenol	tert-butyl alcohol	compound unidentified	5%	Agett (33)
p-tert-butyl phenol	tert-butyl alcohol	2,4 ditert-butyl phenol	0%	Agett (33)
	Condensations	with phosphoric acid		
p-bromo phenol	tert-butyl alcohol	no condensations	---	Agett (33)
p-cresol	tert-butyl alcohol	2 tert-butyl 4 methyl phenol	73%	Tchitchibabine (16
o-cresol	tert-butyl alcohol	?tert-butyl 2 methyl phenol	78%	Tchitchibabine (16
o-cresol	tert-amyl alcohol	2 methyl 4 tert-butyl phenol	62%	
phenol	tert-butyl alcohol	p-tert-butyl phenol	80%	Agett (33)
phenol	tert-butyl alcohol	o-tert-butyl phenol	2%	Agett (33)

IV DISCUSSION

I Tert-amyl alcohol and para cresol.

The condensation of tert-amyl alcohol and p-cresol, which results in the formation of 2 tert-amyl 4 methyl phenol, may be represented by the equation:



Two different procedures were used for this condensation.

By the first procedure, anhydrous aluminum chloride was suspended with stirring in petroleum ether and a solution of the alcohol and cresol was added dropwise. In each case, by this procedure, the yield of 2 tert-amyl 4 methyl phenol was small (not exceeding 7% of the theoretical) and a large amount of tarry residue was formed. Where an excess of the alcohol or aluminum chloride or both was used, a larger percentage of the tarry residue and a smaller percentage of the product resulted. No differences in yields were noticed when the reaction was carried out at 5° to 10° or at 30° to 35°.

By the second procedure, the cresol and alcohol were placed in a flask and dry aluminum chloride was added over a period of 30 minutes to 2 hours. By this procedure, higher yields of the product were obtained. (maximum yield 12.5%) It was found that by increasing the molecular equivalent of the p-cresol from 1 to 1½, a noticeable increase in

yield resulted. A further increase in the amount of p-cresol resulted in but slight increase in yield.

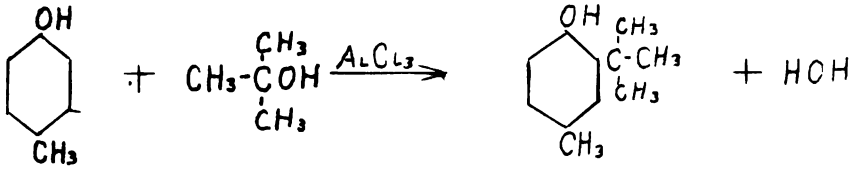
In two condensations, the reaction mixture, during the addition of the aluminum chloride, solidified, forming a pale blue jelly-like mass, the nature of which was not investigated. In the first condensation, there was practically no yield. In the second, the mass was broken up and more petroleum ether and aluminum chloride were added. The yield was considerably reduced.

2 tert-amyl 4 methyl phenol is a clear viscuous oil of a phenolic, but comparatively pleasant, odor, which failed to crystallize when placed in an ice-salt mixture or when left in the refrigerator for more than a month. It boils at 128° to 130°/14mm. and at 245° to 247°/739.5mm.

Analysed by combustion, it was found to have the following composition: C=80.07%, H=10.31%, O=9.72%
The theoretical, based upon the formula $C_{13}H_{18}O$ is:

C=80.76%, H=10.17%, O=8.96%

II <u>Tert-butyl alcohol and para cresol.</u>



Condensations of tert-butyl alcohol and p-cresol were, with the following exception, run by a procedure analogous to the second procedure used for tert-amyl alcohol and p-cresol.

Due to the tendency of the condensation mixtures to solidify, they were cooled in an ice-water bath which allowed more rapid addition of the aluminum chloride. This procedure seemed to assist in the prevention of solidification and the lowering of the yield which accompanied it. The molar proportions of the alcohol and cresol which produced the maximum yields were found to be the same as in the condensations with tert-amyl alcohol, namely: p-cresol $1\frac{1}{2}$ to 2, alcohol 1.

2 tert-butyl 4 methyl phenol, upon purification, crystallizes readily. When crystallized from petroleum ether by very slow evaporation of the ether, the crystals closely resemble those of menthol in general appearance. The odor is indistinguishable from that of 2 tert-amyl 4 methyl phenol. 2 tert-butyl 4 methyl phenol melts at 50.0-50.4°C?,, boils at 117° to 119°/13.5mm. and at 232° to 234°/740.2mm.

It was found by combustion to have the following composition: C=80.29%, H=9.87%, O=9.84%
The theoretical, based upon the formula $C_{11}H_{16}O$, is:

C=80.46%, H=9.81%, O=9.73%.

Separation of the p-cresol and the alkylated cresol was accomplished by fractional distillation. However,

advantage may be taken of the insolubility of the two alkylated cresols in 10% NaOH solution in their separation.

The reported yield from the condensation of tert-butyl alcohol and p-cresol by Tchitchibabine (16) by the use of phosphoric acid as condensing agent, was 73% and the melting point (of the unrecrystallized product (?)) was reported to be 44°C.

To compare the two products and to investigate the differences in melting points, the condensation was repeated by use of phosphoric acid (sp. g. 1.7). The yield was 75%, m.p. 50.0°-50.4°C.

Tert-amyl alcohol and p-cresol were also condensed by use of phosphoric acid. The yield of 2 tert-amyl 4 methyl phenol was 65%.

From the high boiling fractions from the condensations of tert-butyl alcohol and p-cresol, were separated 10.5g. of material boiling at 124° to 132°/14mm., about two thirds of which crystallized at room temperature when seeded with crystals of 2 tert-butyl 4 methyl phenol.

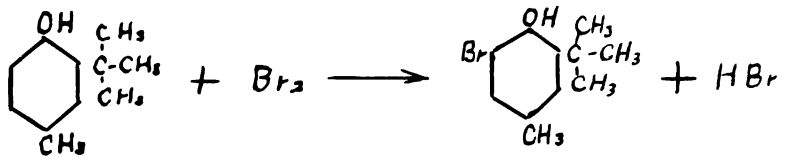
An attempt was made to condense 2 tert-butyl 4 methyl phenol with tert-butyl alcohol by use of phosphoric acid, No condensation resulted.

Therefore it was concluded that tert-butyl alcohol and 2 tert-butyl 4 methyl phenol do not condense in the presence of either phosphoric acid or aluminum chloride.

III 2 bromo 4 methyl phenol and tert-butyl alcohol.

As a further investigation of the directing influence of the hydroxyl group and of the use of aluminum chloride as a condensing agent, attempts were made to condense 2 bromo 4 methyl phenol with tert-butyl alcohol. No condensation resulted. Moreover, no condensation resulted from using phosphoric acid as the condensing agent.

For purposes of comparison, 2 tert-butyl 4 methyl phenol was brominated, chlororform being used as the medium.



The theoretical amount of bromine reacted readily, but a few drops in excess produced a distinctly red color.

2 tert-butyl 4 methyl 6 bromo phenol is a colorless viscuous liquid boiling at 133° to 134°/14.5mm. At atmospheric pressure (741.8mm.), it boils at 255° to 257°with slight decomposition. Analysis for bromine by the Carius method gave 33.05%. The theoretical is 32.92%.

IV Preparation of derivatives.

The aryloxy acetic acids were prepared from 2 tert-butyl 4 methyl phenol and 2 tert- amyl 4 methyl phenol by the method of Koelsch (37). This method was modified somewhat due to the slight solubility of the two compounds in 33% NaOH solution. Due to the slight solubility of the aryloxy acetic acids in hot water, they were crystallized from 50% ethyl alcohol.

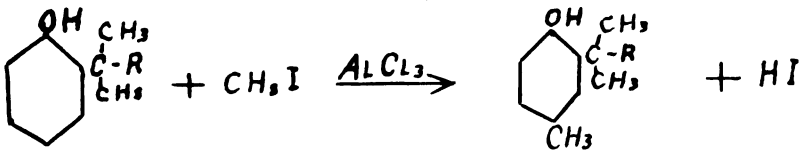
2 tert-butyl 4 methyl phenoxy acetic acid melts at 129.0°-129.5°C. Neutralization equivalent calculated 222.14. Found 227.6.

2 tert-amyl 4 methyl phenoxy acetic acid melts at 125.5°-126.0°. Neutralization equivalent calculated 236.16. Found 238.0.

The p-toluene sulphonic esters, 3,5 dinitro benzoyl esters, and diphenyl urethanes were formed in very small yields, if any, and could not be separated from the original compounds. Phenyl iso-cyanate gave no evidence of reaction with either of the compounds.

V Proof of structure.

An attempt was made to prove the structure of the compounds, 2 tert-butyl 4 methyl phenol and 2 tert-amyl 4 methyl phenol by the reaction:

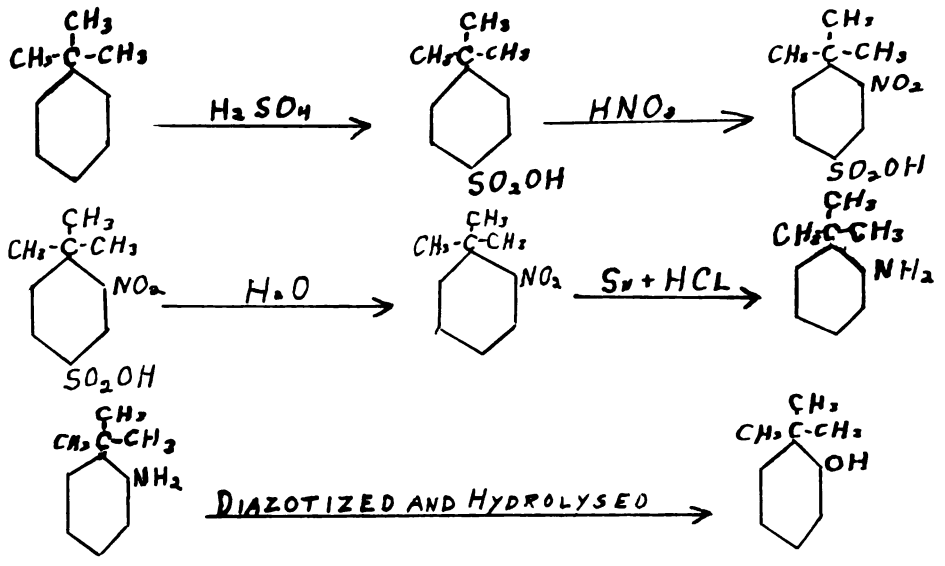


25g. o-tert-butyl phenol were prepared as a by-product of the preparation of p-tert-butyl phenol and allowed to react with methyl iodide and anhydrous aluminum chloride. The result was an almost quantitative rearrangement of the o-tert-butyl phenol to p-tert-butyl phenol.

Previously, several attempts were made to prepare o-tert-butyl and o-tert-amyl phenols in larger quantities.

(1) By the Claisen method (20), unsaturated aliphatic halides may be condensed with sodium phenolate to form the ortho substituted phenols. However, it was found that when tert-butyl bromide and sodium phenolate in toluene are allowed to react, p-tert-butyl phenol is the principal product.

(2) An attempt was made to prepare the two o-tert-alkyl phenols by the following scheme of reaction:



Tert-amyl and tert-butyl benzenes were prepared by the method of Huston and Fox (4) and barely dissolved, with cooling, in sulphuric acid (65% fuming). Nitric acid was added with cooling and, after the reaction was complete, the mixtures were poured into water, the water distilled off, and the mixture steam distilled with superheated steam (160° to 175°). The resulting nitro-alkyl benzenes were oxidized by the method of Malherve (38). The resulting nitro benzoic acids were found to melt at 241° to 245°, a melting point which corresponds to that of p-nitro benzoic acid. Thus it was demonstrated that the nitro group had replaced the sulphonic acid group in the position para to the tert. alkyl group.

(3) According to Niederl and Natelson (23), phenyl iso-propyl ether, in the presence of a mixture of sulphuric and acetic acids, rearranges to o-iso-propyl phenol. According to Sowa, Hinton, and Nieuwland (24), iso-propyl and

sec-butyl phenyl ethers are rearranged by boron trifluride to o-iso-propyl phenol and o-sec-butyl phenol.

An attempt to prepare tert-butyl phenyl ether by the method of Niederl and Natelson (23) resulted in a 40% yield of p-tert-butyl phenol. Tert-amyl phenyl ether was prepared by the modified method of Sowa, Hinton and Nieuwland (24) and an attempt was made to rearrange it by the method of Niederl and Natelson (23). A small yield of gummy, high boiling material resulted. Further work on this method was discontinued when the rearrangement of o-tert-butyl phenol, in the presence of aluminum chloride, was observed.

The structure, of 2 tert-amyl 4 methyl phenol was proved by the rearrangement of tert-amyl o-cresyl ether. The ether was prepared by the method of Sowa, Hinton, and Nieuwland (24), washed with 10% NaOH solution and distilled at 14mm. pressure. A fraction, boiling at 125° to 130° was separated. This fraction had the odor of 2 tert-amyl 4 methyl phenol and was proved to be identical with it by the melting point of its aryloxy acetic acid.

It was not determined whether the ether rearranged during the reaction for its preparation or during its subsequent distillation.

The structure of 2 tert-butyl 4 methyl phenol was proved to an analogous manner. The fraction isolated was proved to be identical with the product from the direct

alkylation of p-cresol by mixed melting points and by the metling point of its aryloxy acetic acid.

V EXPERIMENTAL

2 tert-butyl 4 methyl phenol.

In a 1 L. 3 neck round bottom flask, fitted with mechanical stirrer and mercury seal, reflux condenser fitted with a thermometer, $CaCl_2$ tube, trap for escaping HCL fumes, and ice-water bath, are placed 168g. (1½ mols) p-cresol, 72g. (1 mol) tert-butyl alcohol, and 200cc. petroleum ether. The stirrer is started and 64g. (½mol) anhydrous aluminum chloride is added in small portions, the temperature being maintained below 30C. Stirring is continued for 2 to 6 hours and the mixture is allowed to stand over night. During the addition of the aluminum chloride, a deep red color is developed. Evolution of HCL fumes does not commence until approximately two thirds of the aluminum chloride has been added. The mixture is then decomposed with ice and hydrochloric acid, separated, and the aqueous layer twice extracted with diethyl ether. The extractions are combined, dried with anhyd. Na_2SO_4, and most of the ether and unreacted tert-butyl alcohol removed on the steam bath. The remaining liquid is fractionated under reduced pressure (14mm.) and the following fractions are collected:

--	85°	alcohol, petroleum ether, etc.
85°--	100°	p-cresol
100°--	130°	
130°--		high boiling,-tarry material.

The fraction, 100°-130° is refractionated several times, the fraction boiling at 117°-118°/14mm. which is 2 tert-

butyl 4 methyl phenol is collected.

2 tert-amyl 4 methyl phenol

An analogous procedure is used for the preparation of 2 tert-amyl 4 methyl phenol except that the fraction 105°-140°/14mm. is separated and refractionated, the fraction 126°-129°/14mm. Which is 2 tert-amyl 4 methyl phenol, being collected. The reaction mixture, during the addition of the aluminum chloride, takes on a dark purple color.

Separation of p-cresol and 2-tert-amyl 4 methyl phenol by the use of 10% NaOH solution.

After the ether has been removed from a condensation mixture, the remaining liquid is distilled, and the fraction boiling at 95°-140°/14mm. is collected. This fraction is poured into an excess of 10% NaOH sol., well mixed, cooled, extracted once with petroleum ether, the ether removed on the steam bath, and the remaining liquid distilled at 14mm. pressure. It distills at 125°-140°, practically free from p-cresol. It may be purified further by fractional distillation. The NaOH sol. is acidified, cooled, and extracted twice with diethyl ether. The ether extractions are dried, the ether is removed on the steam bath. The remaining liquid boils 90°-100°/14mm. and contains very little 2 tert-amyl 4 methyl phenol.

An analogous procedure is used for the separation of p-cresol and 2 tert-butyl 4 methyl phenol.

2 tert-butyl 4 methyl phenol and 2 tert-amyl 4 methyl phenol with the use of phosphoric acid as condensing agent.

A 1 L., 3 neck round bottom flask, fitted with mechanical stirrer and mercury seal, reflux condenser, and separatory funnel, is placed on the steam bath. In it is placed a mixture of 54g. ($\frac{1}{2}$ mol) p-cresol and 100g. H_3PO_4 (sp. g. 1.7). In a separatory funnel is placed mixture of 100g. H_3PO_4 and 0.6 mols tert-butyl or tert-amyl alcohol. (The tert-butyl alcohol-H_3PO_4 mixture solidifies and must be melted on the steam bath before being placed in the separatory funnel.) The mixture is added from the separatory funnel dropwise with stirring. Stirring is continued (90° to 95°) for 8 to 10 hours. The two layers are then separated and the upper layer is treated in the same manner as in the condensations by the use of aluminum chloride. In these condensations no color is developed and there is little or no tarry residue formed.

2 tert-amyl 4 methyl phenoxy acetic acid.

In a small flask, are placed 3 g. 2 tert-amyl 4 methyl phenol, 5 g. NaOH, 8cc. 50% chloroacetic acid, and 20cc. 95% ethyl alcohol. The flask is placed on the steam bath for an hour or more until most of the ethyl alcohol is driven off. The mixture is then diluted, acidified to the end-point of congo red with hydrochloric acid, cooled, and

extracted once with diethyl ether. The ether layer is washed once with water and twice extracted with dilute Na_2CO_3 solution. The Na_2CO_3 solution is acidified, filtered, and the aryloxy acetic acid crystallized from 50% ethyl alcohol.

2 tert-amyl 4 methyl phenol from tert-amyl p-creyl ether.

In a 1 L. 3 neck round bottom flask fitted with reflux condenser, mechanical stirrer, and separatory funnel are placed 108g. (1 mol) p-cresol, 58g. (1 mol) KOH and sufficient distilled water, without cooling, to make a clear solution. 110g. tert-amyl chloride is added dropwise with stirring (60°to 80°) and stirring is continued for 10 to 12 hours. The contents of the flask are placed in a separatory funnel, separated, and the oily layer washed twice with 10% NaOH. and with water. It is then dried and fractionated at 14mm. pressure, the fraction boiling at 125° to 130° being collected. This fraction is 2 tert-amyl 4 methyl phenol.

2 tert-butyl 4 methyl phenol from tert-butyl p-cresyl ether.

The reaction is carried out by an analogous procedure, The fraction 116° to 120°/14mm. is collected, seeded with crystals of 2 tert-butyl 4 methyl phenol, placed in the ice box over night, and the crystals pressed on filter

papers to remove the oily impurities.

o-tert-butyl phenol, methyl iodode, and anhydrous aluminum chloride.

In a 500 cc. 3 neck round bottom flask fitted with reflux condenser and mechanical stirrer was placed a solution of 25g. (1/6 mol) o-tert-butyl phenol and 25g. (1/5 mol) methyl iodide in petroleum ether. The mixture was cooled on a cold water bath and 12 g. anhydrous aluminum chloride added slowly with stirring. Stirring was continued for 6 hours and the mixture was allowed to stand over night. A light red color was developed and evolution of HCl (or HI) fumes was noticeable. The mixture was decomposed with ice and hydrochloric acid, separated, the aqueous layer extracted twice with diethyl ether, and the ether removed on the steam bath. The remaining liquid was distilled at 14mm. pressure. The main portion (22g.) boiled at 118°to 125°, dissolved completely in 5% KOH and was identified as p-tert-butyl phenol by its melting point.

TABLES OF RESULTS

tert-butyl alcohol and p-cresol

p-cresol	tert-butyl alcohol	$AlCl_3$	2tert-butyl 4 methyl phenol	yield	residue
27g.	18g.	16g.	2g.	4.9%	2-3g.
54g.	36g.	24g.	5g.	6.2%	2-3g.
*108g.	54g.	32g.	1-2g.	1.8%	3g.
#108g.	54g.	48g.	7g.	5.8%	3g.
108g.	54g.	48g.	17g.	14.2%	4g.
162g/	54g.	48g.	18g.	15.0%	5g.
135g.	72g.	64g.	18g.	11.2%	5G
#135g.	72g.	64g.	15g.	9.4%	10g.

*Mixture solidified

Mixture solidified, was broken up, and more petroleum ether and aluminum chloride were added.

Tert-amyl alcohol and p-cresol

p-cresol	tert-amyl alcohol	$AlCl_3$	2 tert-amyl 4 methyl phenol	yield	residud
*27g.	21g.	16g.	2g.	4.5%	2g.
*27g.	21g.	32g.	2g.	4.5%	6-8g.
*81g.	21g.	16g.	2g.	4.5%	2-3g.
*54g.	84g.	64g.	3g.	1.7%	20g.
*54g.	42g.	32g.	2g.	2.2%	8g.
@54g.	42g.	32g.	8g.	9.0%	3-4g.
@54g.	42g.	48g.	7g.	8.0%	5g.
@#54g.	63g.	32g.	3g.	2.3%	3g.
@81g.	42g.	32g.	11g.	12.5%	2g.
@108g.	42g.	32g.	8g.	9.0%	3g.
@#324g.	168g.	96g.	30g.	3.3%	20g.

Mixture solidified

* p-cresol and tert-amyl alcohol added to $AlCl_3$ in pet.ether

@ $AlCl_{\#}$ added to p-cresol and tert-amyl alc. in pet. ether.

VII SUMMARY

(1) Tert-butyl alcohol and para-cresol have been condensed in the presence of aluminum chloride to form 2 tert-butyl 4 methyl phenol.

(2) Tert-amyl alcohol and para-cresol have been condensed in the presence of aluminum chloride to form 2 tert-amyl 4 methyl phenol.

(3) Tert-butyl alcohol and 2 bromo 4 methyl phenol, in the presence of aluminum chloride, did not condense.

(4) From 2 tert-butyl 4 methyl phenol and 2 tert-amyl 4 methyl phenol, 2 tert-butyl 4 methyl phenoxy acetic acid and 2 tert-amyl 4 methyl phenoxy acetic acid have been prepared.

(5) The structures of 2 tert-butyl 4 methyl phenol and 2 tert-amyl 4 methyl phenol have been proved by the rearrangement of tert-butyl and tert-amyl p-cresyl ethers.

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