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BENZYLATION OF M-CHESOL

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PENZYLATION OF M-CRESOL

Thesis

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

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June 4, 1928

## Acknowledgment

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#### BENZYLATION OF M-CRESOL

#### 1. Organic Condensations.

Condensations of organic compounds have been effected since about 1870. The variety of compounds used is very wide but those in which we are most interested are the aromatic compounds, and especially the phenols. Likewise, a great many different catalysts have been used, some of the earlier ones being sulfuric and acetic acids, zinc chloride, hydrochloric acid, phosphoric anhydride, and aluminum chloride. In most condensations either a halogen acid or water is split off, so in some cases the catalyzer acts also in the role of dehydrating agent.

A mixture of sulfuric and acetic acids was used in 1873 by Meyer and Wurster (Ber. 6, 963) in condensing benzyl alcohol with benzene to form diphenylmethane. Two years later the same catalytic mixture was used by Patuno and Fileti (Gazz. Chim. ital. 5,381) in condensing benzyl alcohol with phenol to form a benzyl phenol. Still another use of this catalyst was in 1899 when "ohlan and Klopfer (Ber. 32,2147) condensed benzhydrols with paraquinone and its derivatives. In 1881 Liebmann (Ber. 14, 1842) prepared p-benzylphenol from benzyl alsohol and phenol by using zinc chloride as catalyst. He also prepared butyl phenol, condensing isobutyl alcohol and phenol with molten zinc chloride. Propyl and amyl phenols were similarly prepared.

The action of Zinc chloride on Phenol alone to form diphenylether was investigated in the same year by Merz and Weith (Ber. 14,187 seq.). Auer (Ber. 17,669; 1884) prepared ethylphenol from absolute alcohol and phenol in the presence of zinc chloride. This was also prepared by Dennstedt in 1890 using zinc dust (Eer. 23,2569). Eaur, four years later, (Ber. 27,1614) condensed isobutyl alcohol with o-cresol in the presence of zinc chloride.

Phosphoric anhydride was used in 1886 by Hemilian (Ber. 16,2360) in forming diphenyl-p-xylylmethone from benzhydrol and p-xylene.

Hydrochloric acid was used, in condensing phenols with camphorquinone, by Dey and Sen-Grysta (Proc. chem. Soc. 29,155). It was also used by Diqnin (J. Russ. Chem. Soc. 46,1310; 1914) in condensing phenols with unsaturated ketones, such as mesityl oxide.

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Small quantities of iodine were used as catalyst by Knoll and Co. (Ger. 250,236,Apr. 23, 1911) in condensing organic compounds with alcohols or ketones. It was found to act also as dehydrating agent.

Phosphorus pentachloride was used by Hahn (J. Am. Chem. Soc. 43,175;1921) in condensing 4-methylbenzophenone chloride with phenol.

Magnesium chloride was shown by Mozzara (Gazz. 12,505; 1882) to have catalytic effect in condensing m-cresol with propylalcohol.

#### 2. Aluminum Chloride as Catalyst.

One of the most important catalysts in present-day chemistry is aluminum chloride. One of its earliest uses was by Friedel and Crofts in 1876 (Compt. rend. 84,1392) when they condensed amyl alcohol with hydrocarbons forming amyl-hydrocarbons. They confined their work to aliphatic compounds and even stated that aluminum chloride would not dondense aromatic compounds. Gustamson (Ber. 13,157;1880 and Bull. Soc. Chem. 42,325;1884) believed an unstable aluminum-organic compound to be formed, which breaks down again giving aluminum chloride. This theory was recently confirmed by Schiechen, and by Buttgenbach (J. prokt. chem. 105,355;1923) although it has been denied by others.

In 1881 Merz and Weith (Ber.14,187 seq) prepared a diphenyl ether from phenol, using aluminum chloride. In 1914, Frankforter and helpers (J. Am. Chem. Soc. 36,1511, 1529; 37,385) condensed chloral, chloral hydrate, bromal, and trioxymethylene with various organic compounds, with the elimination of water. He believed that aluminum chloride, while a catalyst, acts at the same time as a dehydrating agent, a theory which is now generally accepted.

Jaubert (compt. rend. 132,841; 1901) prepared aniline and p-toluidine from hydroxylamine hydrochloride and the hydrocarbon in the presence of aluminum chloride or zinc chloride. This was definitely a dehydration reaction.

#### 3. The Work of Huston

Aluminum chloride had not been used to condense aromatic alcohols with aromatic compounds until Huston began a series of investigations in 1916. Huston and Friedemann (J. Am. Chem. Soc. 33,2527) condensed benzene and benzyl alcohol, forming diphenylmethane and a little p-dibenzyl benzene with a trace of the ortho. Anthracene was formed as a by-product. The proportion of the reagents used and the temperature of the reaction influenced the relative yields of the different products.

Two years later (J. Am. Chem. Soc. 40,785) they repeated the experiments using secondary alcohols on benzene in the presence of aluminum chloride. The alcohols used were methyl phenyl carbinol, ethyl phenyl carbinol, and diphenyl carbinol, the first two containing alkyl groups and the latter being entirely aromatic. This gives an idea of the effects of the various groups on the reaction. It was found that aliphatic groups have a retarding action on condensation by aluminum chloride, ethyl more than methyl, but that phenyl groups do not retard at all.

In 1920 (Science 52,206) Huston reported the preparation of p-benzyl phenol from benzyl alcohol and phenol in the presence of aluminum chloride. The same compound had been prepared using zinc chloride as catalyst, and also with a mixture of sulfuric and acetic acids, as stated earlier in this paper. Merz and Weith (Ber. 14,189) reported a 10 - 12% yield of diphenyl ether from benzyl alcohol and phenol when heated with aluminum chloride under a reflux condenser, but Huston (J. Am. Chem. Soc. 46,2775; 1924) found scarcely any ether formed if the phenol is suspended in petroleum ether and the temperature kept below

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30°. He also condensed benzyl alcohol with anisol and phenetole, obtaining the methyl and ethyl ethers, respectively of p-benzyl phenol.

Huston and Eartlett, in 1926, condensed phenol and phenyl butyl carbinol in the presence of aluminum chloride to produce p-hydroxy diphenyl butyl methane, and Huston and Strickler, the next year, condensed phenol and phenyl propyl carbinol to form p-hydroxy diphenyl butane, with a little of the ortho product, which was identified by condensing by the Claisen method, in which the ortho is the sole product.

Huston, with Lewis and Grotemut, in 1927 condensed secondary alcohols with phenol. Methyl phenyl carbinol gave a larger yield than ethyl phenyl carbinol and benzhydrol gave a larger yield than either, which corresponds with the results obtained in condensing the same alcohols with benzene, showing that unsaturation on the alpha carbon atom tends to increase the yield of condensation product.

Huston and Sager (J. Am. Chem. Soc. 48,1955; 1926) investigated the effect of unsaturation on the activity of alcoholic hydroxyl and found that only those compounds in which the alpha carbon atom is a member of the benzene ring, or is double bonded, show any appreciable activity. Normal aliphatic alcohols showed no reaction, however, allyl

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alcohol condensed with benzene in the presence of aluminum chloride.

#### 4. The Work of Claisen.

In 1924 L. Glaisen published an article (Ann. 442,212) describing a different method for both the alkylation and benzylation of phenols. In this method the alkali metal salt, usually the sodium salt, if the phenol is first prepared and dissolved or suspended in a suitable medium, such as toluene, and then treated with an alkyl or benzyl halide. The resulting product is a mixture of the possible mono- and di-alkyl or benzyl phenols, and a little either which may be removed by shaking the methyl alcoholic potassium hydroxide solution of the phenols with petroleum ether. This ether is the product which we would expect to be formed, by the simple splitting out of metol halide, but a transformation occurs whereby "anomalous metal substitution", or ring alkylation, takes place.

Claisen believes that only ortho substitution products ere formed by his method. He bases his view on Michael's theory (J. pr. 37,486;216,189) of the reaction between silver cyanide and methyl iodide. According to this Claisen's reaction would take place as follows:

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OH H HO CL HR - C - F R CL C C C

O H R OH R C C C C C C C

This is brought about in a "non-dissociating" medium which seems to promote the splitting apart of the alkyl and halogen radicals. In a dissociating medium, as Methyl alcohol, the ether is the main product.

Claisen and Tietze (Ber. 58B,275; 1925) showed that when alkali phenolates were treated in non-dissociating media with halides of unsaturated alkyls, such as allyl, there is obtained a great deal of, and often almost entirely, ortho alkylphenols instead of the ethers. The same year Claisen, with Kremers, Rath and Tietze (Ann. 442,210) reports the formation, from sodium p-cresylate and allyl bromide, of 90% ether with methyl alcohol as solvent, and of 30% ether and 60% carbon alk/lation with benzene as solvent, showing the effect of a non-dissociating medium in lowering the amount of ether formed.

K. von Auwers, with Wegener and Bahr (Chem. Zentr. 1926, I, 2347) performed experiments to explain the formation of carbon substituents from salts of keto-enols and alkyl halides. They sum up the three possibilities as:

1. "The initial formation of addition products with subsequent splitting" (Michael)

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- 2. "The initial formation of normal O-derivatives with rearrangement into C-derivatives"
- 3. "Separation of metal as metallic halide, formation of free alkyl and enol radicals.

$$\begin{array}{ccc} -c = c < & -c - c < \\ 1 & - - - & - & - \\ 0 - & 0 \end{array}$$

and with the slight reactivity of the alkyl group, partial or complete rearrangement of the enol to keto radical, and finally untion of the radicals". (Wislicenus)

The course of alkylization depends on the nature of the enol-keto and on the alkylization egent, as well as on the type of medium used. Saturated alkyl halides promote the formation of O-derivatives while unsaturated halides, as allyl or benzyl, promote the formation of C-derivatives. These facts are best explained by the first hypothesis, which also agrees with the theories of Claisen. According to the second hypothesis it is not comprehensible why an ether should be transformed into a carbon derivative more easily in benzene than in alcohol, and according to the third hypothesis ethers should be formed from allyl and benzyl radicals because of their greater reactivity, which is not the case. Allyl and benzyl radicals are characterized by their slight valence requirements, so they hold oxygen only loosely and form a more stable combination with carbon.

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# Shorigin (Ber. 58B, 2028; 1928) found that benzyl ethers reamange to form carbinols under the influence of sodium, according to the equation:

 $C_6H_5CH_2OR \longrightarrow C_6H_5CH(OF)R$ 

This is true when  $\mathbb{R}$  is p-tolyl, cyclohexyl, or benzyl, but with o-cresyl benzyl ether the phenol, instead of carbinol, was formed. The phenyl and ethyl ethers of o-cresol also gave no rearrangement but formed toluene and the alcohol, showing that the ability to rearrange depends upon the presence of a benzyl group. Shorigin also found (Der. 59B,2502;1926) that when condensing carbinols with o-cresol, the migrating group enters the side chain to form, in the case of triphenyl carbinol,  $(C_{6}H_{5})_{3}COH_{2}C_{6}H_{4}OH$  instead of  $(C_{6}H_{5})_{3}CO_{6}H_{3}(OH)OH_{3}$  as assigned to it by the experiments of Baeyer, Claisen and Eusch.

M. Busch (Z. Angew. Chem. 38,1145;1925) showed that the tendency of benzyl radicals toward carbon alkylation increases with the increasing substitution of the methane carbon. It is possible, in non-dissociating media, to obtain ethers from benzyl chloride, but diphenylchlormethane will give only carbon derivatives.

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Euch and Knoll (Ber.60B,2243;1927) found that diphenylbrommethane with phenol, with or without a solvent, gives the p-hydroxy product, and with sodium phenolate gives the o-hydroxy product. Shorigin obtained mostly ethers but he used the phenolates in a large excess of phenol, which is a dissociating solvent and, according to Claisen, promotes ether production. Busch and Knoll also found that the introduction of electro-negative groups causes a pronounced loosening of the nuclear hydrogen atoms. Phenols and cresols show a slight tendency toward formation of disubstitution products, while with p-nitrophenol, hydroquinone, and p-hydroxybenzaldehyde the disubstitution product is formed almost exclusively.

J. Von Alphen (Rec. trav. chim. 46,799;1927) heated phenyl benzyl ether with zinc chloride for one hour at 160° and obtained 4-hydroxy diphenylmethane, showing a migration of the benzyl group. He prepared the same compound by heating phenol with diphenyl chlormethane. He also prepared (Rec. TBON. chim. 46,287;1927), from potassium phenolate and triphenylmethyl chloride, a triphenylmethyl phenyl ether, which on heating with zinc chloride or hydrochloric acid was converted into p-hydroxytetrophenylmethane.

Shorigin (Ber. 60B,2373;1927), in the reaction between sodium-o-cresylate and triphenylmethyl chloride and also between o-cresol and triphenylcarbinol, found the triphenylmethyl group to enter the side chain. M-cresol, under the

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same conditions, yields a cryptophenol which is believed to be a tetrophenylmethane derivative. P-cresol gave triphenylmethane almost quantitatively in the presence of sulfuric acid. A little amorphous crimson powder which is probably a highly polymerized quinomethane was also obtained.

#### 5. Benzylation of Cresols.

As early as 1888 Paterno and Mazzara (Gazz.5,381) condensed benzyl chloride and cresol in the presence of zinc. Aluminum chloride was not used as condensing agent until recently, when Muston and Lewis condensed p-cresol with benzyl alcohol. One monobenzyl and one dibenzyl derivative were all that could be formed. These ortho derivatives were also formed by the Claisen method.

Huston and Swartout condensed o-cresol and benzyl alcohol, both by usming aluminum chloride and by the Claisen method. In this case the para position is open, so a larger number of derivatives would be possible.

The position taken by any entering group depends upon the nature of the group or groups already present in the ring. The relative directive strengths of the saturated groups have been investigated by Hollemann (Chem. Rev. July, 1924, 187 seq.). He found that the hydroxyl group has the greatest, and the methyl group the least influence toward the ortho and para positions. Therefore in cresol the hydroxyl would so greatly predominate that the effect of the methyl would be practically nil and the entering groups would go or the and para to the hydroxyl.

The benzylation of m-cresol should proceed similarly to that of o-cresol and p-cresol except that in m-cresol all of the ortho and para positions are open, so a greater number of derivatives would be possible. Benzylation by the Huston method should give a mixture of para and ortho compounds, with the para somewhat in predominance. The Claisen method should give only ortho compounds. The compounds which are theoretically possible are two ortho and one para monobenzyl cresols and three dibenzyl cresols. The properties of the compound, ease of esterification, etc., are considered in determining with which of these possibilities each product conforms.

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#### Experimental

1. Condensation by the Huston Method.

a. In the first trial the following amounts were used:

The mixture of m-cresol and benzyl alcohol in petroleum ether was stirred constantly and the aluminum chloride added in small amounts over a period of about two hours. The temperature was kept at about 35°. Additional petroleum ether was added occasionally. HCl was given off copiously and the substance became a light brown viscous mixture. The layers first formed disappeared. It was dtirred an hour after final addition of aluminum chloride, and then let stand over night. The next day it was decomposed with ice, extracted with ether, and distilled.

It was divided into the following fractions, distilling under 4 mm. pressure:

		1250 - 1	40 <b>0</b>			
		$140^{\circ} - 1$	65 <b>0</b>			
		· 165° - 1	85 <b>°</b>			
		185° - 2	50 <b>0</b>			
b.	In	the second tri	al the	emounts	were	doubled:
		M-Gresol			<b>L</b> 20 gr	n <b>.</b>
		Penzyl Alcoh	01		<b>L00</b> gr	<b>a.</b>
		Fatroleum St	hor	•	150 0	n

Aluminum Chloride ..... 60 gr.

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Aluminum chloride was added over a period of one hour. The resulting brown, thick mixture was treated as in the first trial. The following fractions were obtained, using 4mm. pressure:

To 225° (at. press.)	54.0 gr	1.
100° - 165°	38.0 gn	1.
165° - 185°	41.0 gr	1.
185° - 250°	48.5 ga	1.
Residue	15.0 gr	1.

After give distillations the fractions were as follows:

140 <sup>0</sup>	-	160°	40 gm.
160 <sup>0</sup>	-	185	33 gm.
185°	-	2500	44 gm.

c. In the third trial the smaller amounts were used as in #1. This was stirred in a closed container fitted with reflux condenser, addition ' tube, and thermometer. It was allowed to stand 48 hours before decomposing. The following fractions were obtained, all at 4 mm. pressure:

To 125	5 <b>0</b>		13.0 g	n.
1250	-	140 <sup>0</sup>	4.0	n.
140 <sup>0</sup>	-	165 <b>0</b>	21.0 g	11.
1650	-	185°	18.0 g	11.
185°	-	250°	24.0 8	m.

d. In the fourth condensation the double amounts
 were again used. Treatment was the same as in the
 third trial. The fractions obtained were:

125°	- 1400	6.0 gu	<b>n</b> .
140°	- 165°	38.0 ga	1
165°	- 185	33.0 g	ŋ
185°	- 250°	46.3 g	1

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The fraction  $140^{\circ}$  -  $165^{\circ}$  in each case boiled mostly at  $153^{\circ} - 157^{\circ}$  (4 mm). It was a thick yellow oil and solidified after standing for some time in the refrigerator. Crystallization was carried out in petroleum ether out-of-doors in freezing weather. The substance came out in a mass of soft, white, felted, meedle-like crystals, melting after several crystallizations at  $46^{\circ} - 47^{\circ}$  and boiling at  $153^{\circ} - 155^{\circ}$  (4 mm). This compound will be discussed more fully under the Claisen reaction.

The fraction  $165^{\circ} - 185^{\circ}$  solidified in the receiver and was crystallized from petroleum ether in colorless prisms, melting at  $93^{\circ} - 94^{\circ}$  and boiling at  $168^{\circ} - 170^{\circ}$  (5 mm). The factors causing a relatively higher melting point are compactness of structure and symmetry. A para derivative is, in general, more symmetrical than an ortho derivative, so would tend to melt higher. Hence, since we would expect one para derivative by this method of condensation and since this compound melts much higher than the first one mentioned, we assign to this the pera structure:

Ι.			m. 1 b. 1	)t. )t.	93°_94° 168°-170 (5 mm.	)
3 :	$c_{H_2}c_6 H$ as thy 1 4 1	s Denzyl phenol				
Analysis	C14 <sup>H</sup> 14	4 <sup>0</sup>				
. 21	154 gra. gr	ave .6680 gm.	00 <sub>2</sub> a	nd	.1381 gm	, H <sub>2</sub> 0
Ce Fo	alc. Dund	C 84.80 C 84.57			H 7.12 H 7.17	

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The fraction  $185^{\circ} - 250^{\circ}$  nearly all came over at  $220^{\circ} - 230^{\circ}$  and solidified to form an oily mass which, after several crystallizations, came down as a very soft, felted, white mass, melting at  $106^{\circ} - 107^{\circ}$  and boiling at  $230^{\circ} - 232^{\circ}$  (5 mm.). This compound we assumed to be a dibenzyl derivative, which assumption was verified by analysis. The two benzyl groups would be in the same positions as those in the two mono-benzyl derivatives. It is apparently very difficult, by this method of condensation, to introduce a group between the hydrogyl and methyl groups. This compound we will designate as II, and assist the formula:

II.  $C_{6}H_{5}CH_{2}$   $C_{H_{5}}CH_{2}$   $C_{H_{5}}CH_{2}CH_{2}$  $C_{H_{5}}CH_{2}CH_$  Analysis: C<sub>21</sub>H<sub>20</sub>O

.1902 gr. gave .6074 gr.  $CO_2$  and .1184 gr.  $H_2O$ . .1908 gr. gave .6059 gr.  $OO_2$  and .1194 gr.  $H_2O$ . .1874 gr. gave .5964 gr.  $OO_2$  and .1147 gr.  $H_2O$ . Calc. C 87.45 H 7.00 Found C 87.09; 86.60; 86.79. H 6.96; 7.00; 6.85.

2. Condensation by the Claisen Method.

In the first trial the amounts used were:

 Sodium
 11.4 gm.

 M-Cresol
 54.0 gm.

 Toluene
 125.0 gm.

 Benzyl chloride
 64.0 gm.

The sodium was added to a solution of the cresol in toluene. forming the sodium cresylate, a white, cheesy mass. The action was rapid, the temperature being controlled by immersing the flask in cold water. After the mass had stood over night the freshly distilled benzyl chloride was added and the mixture heated, under reflux condenser, to 110° on an oil bath, when the reaction started. When the cresylate was all dissolves the beth was raised to 150° and the mixture boiled for five hours. It was then cooled, washed twice with water to remove the sodium chloride, and the toluene distilled off. The residue was dissolved in 250 cc Claisen's methyl alcoholic potash (Ann. 442,224). Any derivatives with a free phenolic hydroxyl group would dissolve, leaving the small amount of the ether free to be taken up in petroleum ether, using 200 cc in 50 cc portions.

The potesh solution was then acidified with 6 N. HCl, again freeing the phenolic derivatives. A dark, heavy oil separated out, which was taken up in other. The ether was distilled off and the residue fractionated. After the second distillation, at 4 mm.:

To 1	.40	)	8.5	gn.
1400	-	160 <b>°</b>	34.5	gm.
1600	-	230 <b>°</b>	12.5	gm.

1

Six other trials were made, with results and amounts of various fractions very similar to the above data.

The fraction  $140^{\circ}$  -  $160^{\circ}$  partially solidified in the receiver. As this fraction contained two isomers, one solidifying and the other remaining an oil, the two were separated by pressing the mass between filter papers, which absorbed the oily compound and then could be extracted with ether. The ether, after being distilled off, yielded a heavy, yellow oil boiling at 153° - 155° (4 mm.). This oil solidified after standing in the refrigerator some time. It crystallized from petroleum ether, in the cold, in fluffy, felted needles, melting at 46° - 47°. That this compound was identical with that melting at the same temperature from the Huston reaction was proven by mixing the two and taking the melting point of the mixture. This was the same as that of the separate compounds. This being made by the Claisen reaction, we expect it to be an ortho isomer, and since it has a low melting point we give it the ortho structure which has has the least compactness and symmetry:





3 methyl 6 benzyl phenol Analysis:  $C_{14}H_{14}$ .2797 gm. gave .8638 gm.  $CO_2$  and .1792 gm.  $H_2O$ .3157 gm. gave .9719 gm.  $CO_2$  and .2004 gm.  $H_2O$ Calc. C 84.80 H 7.12 Found C 84.23; 83.96 H 7.17; 7.10

The crystals from the fraction  $140^{\circ} - 160^{\circ}$ , after being pressed between filter papers, were crystallized from petroleum ether. They come out as long, regular needles, melting at  $71^{\circ} - 72^{\circ}$  and boiling at  $157^{\circ} - 159^{\circ}$ (5 mm.). This also must be an ortho isomer, according to Claisen, and since it melts considerably above compound III just described, we assign to it the structure which, on account of its compactness of grouping, and symmetry, tend to cause a higher melting point than that assigned to III. Compound IV. then, we designate as: IV.  $\int_{-\pi}^{0^{H}} c_{\mu_{2}}c_{\mu} \pi_{5}$  m. pt.  $71^{\circ} - 72^{\circ}$ b. pt.  $157^{\circ} - 159^{\circ}$  (5 mm)

2 benzyl 3 methyl phenol Analysis: C<sub>14</sub>H<sub>14</sub>O .1769 gm. gave .5483 gm. CO<sub>2</sub> and .1127 gm. H<sub>2</sub>O .2256 gm. gave .6993 gm. CO<sub>2</sub> and .1408 gm. H<sub>2</sub>O Calc. C 84.80 H.7.12 Found C 84.53; 84.53 H 7.13; 7.08

IV. then we destruct

.

,

The high boiling fraction, which we assumed to contain a dibenzyl derivative in which a benzyl group occupies each ortho position, was very difficult to narrow to a definite boiling point. After many distillations a fraction boiling at  $208^{\circ} - 212^{\circ}$  (4 mm.) was collected. This was a very heavy yellow oil. After some weeks in the refrigerator it began to solidify and a very small amount of fluffy crystalline substance was obtained, melting at  $106^{\circ} - 107^{\circ}$ . This proved to be identical with compound II in which one of the benzyl groups is in the para position. The amount is small but it is interesting in that it apparently contradicts the theory advanced by Claisen that only ortho derivatives can be formed by this method.

The remaining oil was in such small quantity that it was decided to make more from compound IV, by the Claisen meaction:



The quantities used were:

Benzyl cresol	8.0 gm.
Sodium	1.0 gn.
Toluene	50 cc
Benzyl chloride	5.7 gm.

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The sodium reacted to give a brownish yellow solution of the phenolate. This was heated to  $130^{\circ}$ to complete the reaction, the benzyl chloride added, and the mixture treated as in the former Claisen condensations. After four distillations two grams of heavy yellow oil boiling at  $216^{\circ} - 218^{\circ}$  (5 mm.) were obtained. This checks very well with that obtained from the other condensations so we are safe in calling this the o-odibenzyl derivative:

V. CBHSCH2 OH CH3CH2 CBHS

b.pt. 216° - 218° (5 mm.)

3 methyl 2,6 dibenzyl phenol

Analysis:  $C_{21}H_{20}O_{21}H_{20}O_{2145}$  gm. gave 16869 gm. CO<sub>2</sub> and .1335 gm. H<sub>2</sub>O .1969 gm. gave .6268 gm. CO<sub>2</sub> and .1239 gm. H<sub>2</sub>O .2157 gm. gave .6852 gm. CO<sub>2</sub> and .1260 gm. H<sub>2</sub>O Calc. C 87.45 H 7.00 Found C 87.33;86.61; 86.63 H 6.96; 7.04;7.05

#### 3. The Claisen Ethers

The petroleum ether extracts containing the Claisen ethers were distilled. That from the first condensations should give an ether of the structure  $\int_{CH_2CLH_5}^{CCH_2CLH_5}$ 

CH33 methyl phenyl benzyl ether

which has been made by Staedal (Ann. 217,46;1882). The ether was described by him as crystallizing from alcohol in lustrous platelets, melting at  $43^{\circ}$  and boiling without decomposition at  $300^{\circ} - 305^{\circ}$ . The product obtained from our condensations distilled mostly at  $280^{\circ} - 290^{\circ}$  and underwent vigorous decomposition above  $290^{\circ}$ . Distillation was repeated several times with the same result so the work of Staedel was repeated. The reaction proceeded as he described, but the product distilled at  $280^{\circ} - 290^{\circ}$ and decomposed above that temperature. Finally it was distilled under reduced pressure, at which it boiled at  $142^{\circ} - 145^{\circ}$  at 5mm. pressure and solidified into white platelets which, when purified, melted at  $45^{\circ} - 46^{\circ}$ . This is somewhat at variance with Staedel's results but the Claisen ether gave identical results so we conclude that it has the composition of the ether described by Staedel, and has the formula given above.

The petroleum other extract from the last condensation, that of compound IV with benzyl chloride, solidified as soon as the petroleum other had evaporated off. Recrystallized from alcohol in fine yellowish meedles, it melted at  $71^{\circ} - 73^{\circ}$ . This would be the structure:  $CH_2C_LH_S$  $CH_2C_LH_S$ M, pt.  $71^{\circ} - 73^{\circ}$ 

2 benzyl 3 methyl phenyl benzyl ether Analysis: C<sub>21</sub>H<sub>20</sub>O .0804 gm. gave .2568 gm. CO<sub>2</sub> and .0505 gm. H<sub>2</sub>O Calc. C 87.45 H 7.00 Found C 87.10 H 7.03

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#### 4. Bromine Derivatives

Brownine, when added to a phenol, easily substitutes in the ortho and para positions, filling as many of those as are open. The calculated molecular quantities of bromine were added to the chloroform solutions of our benzylated cresols, with vigorous reaction and copious evolution of hydrobromic acid. In most cases the bromine derivative crystallized out on evaporation of the chloroform. Petroleum ether and alcohol were both used as recrystallizing solvents, but the better results were obtained with alcohol.

2,6 dibrou-3-methyl-4-benzyl phenol Analysis: C<sub>14</sub>H<sub>12</sub>OBr<sub>2</sub> 0.1289 gm. gave 0.0570 gm. Fr<sub>2</sub> 6 9 fm 0./339 0.1609 gm. gave 0.0712 gm. Br<sub>2</sub> 0./673 Calc. 44.913 %; found 44.227, 44.231 %. The brownine derivative of compound II, a dibenzyl cresol, melting at  $106^{\circ} - 107^{\circ}$ , crystallized from both petroleum ether and sloohol in white platelets. The melting point was  $65^{\circ} - 67^{\circ}$ . Analysis showed this to be a monobrom derivative, as expected, the formula being  $c_{b}H_{5}CH_{2}$  GR m. pt.  $65^{\circ} - 67^{\circ}$ 

2 Brom-3-methyl-4,6 dibenzyl phenol

Analysis: C<sub>21</sub>H<sub>19</sub>OBr

0.1643 gm. gave 0.0351 gm. bromine. 478.0.0825 Calc. 21.76%; found 21.38%.

Compound III, formed from both the Huston and Claisen condensations and melting at  $46^{\circ} - 47^{\circ}$ , gave a dibrom derivative which crystallized from both petroleum ether and alcohol in fine, felted form. The melting point was over a range of 99° - 103°. The structure would be:

> $C_{L}H_{5}CH_{2}$   $G_{R}$   $m. pt., 99^{\circ} - 103^{\circ}$  $C_{H_{5}}CH_{2}$   $C_{H_{3}}$   $m. pt., 99^{\circ} - 103^{\circ}$

2.4 dibrom-3-methyl-6-benzyl phenol Analysis: C<sub>14</sub>H<sub>12</sub>OBr<sub>2</sub> 0.1267 gn. gave 0.0568 gm. bromine.

Celc. 44.913%; found 44.813%.

Compound IV, formed from the Claisen reaction and melting at  $71^{\circ} - 72^{\circ}$ , gave a dibrom derivative crystallizing from petroleum ether in light, feathery crystals and from alcohol in white felted crystals, melting at  $106^{\circ} - 107^{\circ}$ . The structure is

 $B_{1}$   $C_{H_{2}}C_{L}H_{5}$  m. pt. 106° - 107°

2 benzyl 3 methyl 4,6 dibrom phenol

Analysis: C<sub>14</sub>H<sub>12</sub>OBr<sub>2</sub>

0.1574 gm. gave .0721 gm. bromine 07 B- . 51694.

Calc. 44.913%; found 44.754%.

Compound V, a dibenzyl cresol from the Claisen method which did not crystallize, gave a bromine derivative which also did not crystallize. A reddish oil formed, the quantity of which was insufficient for distillation, and since the amount of V on hand was small more could not be made up. However, a vigorous reaction having occurred with evolution of HBr, we would not hesitate to say that the monobrom derivative, in the form of an oil, had formed, having the structure of

C6H5CH2CH2C6H5

2,6 dibenzyl 3 methyl 4 brom phenol.

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#### 5. Esterification

The benzoyl esters of the five phenols were formed by the Schotten-Baumann reaction. The ease of solubility in the alkali and formation of the esters further substantiates the structures which we have assigned. When the phenolic hydroxyl is "crowded" between two groups we would expect extreme difficulty in effecting this reaction.

Compound I dissolved very easily in a slight excess of 5% potassium hydroxide. On addition of benzoyl Chloride and shaking a gummy mass separated out. When dissolved in petroleum ether and crystallized in the cold, rosette-like crystalls formed. From alcohol the crystals were thin, flaky plates, melting at 70° - 71°. The structure would be

m. pt. 70° - 71°

# 3 methyl 4 benzyl phenyl benzoate

Analysis: C<sub>21</sub>H<sub>18</sub>O<sub>2</sub>

.2230 gm. gave .6789 gm.  $CO_2$  and .1194 gm.  $H_2O$ 

Found C 83.03 H 5.99		<b>U</b>		46	
	Found	C	83.03	H	5.99

Compound II dissolved in an excess of 40% potassium hydroxide, the less case of dissolving probably being due to the poximity of the rather large benzyl group. With benzoyl chloride it formed a gummay mass which hardened in the refrigerator and crystallized from both petroleum ether and alcohol in very fine, fluffy needles, melting at 88° - 89°. The compound would have the structure:

 $C_{L}H_{5}CH_{2}$   $C_{H_{5}}CH_{2}$   $C_{H_{2}}C_{L}H_{5}$   $C_{H_{2}}C_{L}H_{5}$   $C_{H_{2}}C_{L}H_{5}$   $C_{H_{2}}C_{L}H_{5}$  $C_{H_{2}}C_{L}H_{5}$ 

3 methyl 4,6 dibenzyl phenyl benzoate

Analysis: C<sub>28</sub>H<sub>24</sub>O<sub>2</sub>

.1431 gm. gave .4467 gm. CO<sub>2</sub> and .0753 gm. H<sub>2</sub>O Calc. C 85.67 H 6.17 Found C 85.13 H 5.89

Compound III dissolved in a slight excess of 5% potassium hydroxide. The mass formed with benzoyl chloride hardened and was crystallized from alcohol, forming fine, slender needles, melting at  $58^{\circ} - 59^{\circ}$ . A second quantity was made up but did not crystallise, so a larger quantity was prepared, taking up in ether, shaken with sodium carbonate, and distilled. The product was a pale yellow oil distilling at  $215^{\circ} - 220^{\circ}$  (5 mm.). The structure of this ester would be:  $c_{0}H_{5}CH_{2}$   $c_{0}H_{5}$   $c_{0}H_{5}$   $c_{0}H_{5}$  (5 mm.)

3 methyl 6 benzyl phenyl benzoate

- 29 -0 Analysis:  $C_{21}H_{18}O_2$ .2135 gm. gave .6508 gm.  $CO_2$  and .1173 gm.  $H_2O$ Calc. C 83.40 H 6.00 Found C 83.13 H 6.14

Compound IV dissolved in excess of 5% potassium hydroxide. The gummy mass formed with benzyl chloride was crystallized from alcohol in shiny platelets, melting at  $71^{\circ} - 73^{\circ}$ , very nearly the same as the original phenol which melted at  $71^{\circ} - 72^{\circ}$ . The structure of the ester would be:  $o^{-c}c_{L}H_{5}$  $e^{-H_{2}}c_{L}H_{5}$ m. pt.  $71^{\circ} - 73^{\circ}$ 

2 benzyl 3 methyl phenyl benzoate

Analysis: C<sub>21</sub>H<sub>18</sub>O<sub>2</sub>

.2207 gm. gave .6733 gm.  $CO_2$  and .1142 gm.  $H_2O$ .2475 gm. gave .7512 gm.  $CO_2$  and .1317 gm.  $H_2O$ Calc. C 83.40 H 6.00 Found C 83.20; 82.77 H 5.78; 5.95

Compound V, having the hydroxyl group between two benzyl groups, we would expect to be very difficult to esterify. The oil was put in an excess of 50% potassium hydroxide and the mixture heated to boiling. The phenol did not dissolve but became very dark colored. The alkali was poured off and the remaining hard mass washed with water. Benzoyl chloride was added and stirred up with the dark mass, causing great evolution of heat. An orange-yellow oil resulted, which was washed with water, taken up in ether, and distilled. Some benzoic acid came over first, then a yellow oil which finally became constant at  $235^{\circ} - 240^{\circ}$  (5mm.). A drop would not crystalize from alcohol. Since the original phenol boils at  $216^{\circ} - 218^{\circ}$  (5 mm.) this product is sufficiently different to justify us in calling it the ester, of the structure:  $c_{i} H_{1} CH_{2}$  (c) H C H

3 methyl 2,6 dibenzyl phenyl benzoate Analysis: C<sub>28</sub>H<sub>24</sub>O<sub>2</sub>

.1914	gm.	gave	.6004	gn.	c0 <sub>2</sub>	and	.1089	gm.	$H_2$ C
Calc. Found	(	C 85.	<b>67</b> 55		H H	6.1 6.1	17 56		

#### 6. Nitro Derivatives

Several of the phenols were treated with concentrated nitric acid. In each case a vigorous reaction was obtained with formation of a reddish yellow gummy mass. The only one, however, which could be obtained in crystalline form was the derivative from compound IV, the Claisen monobenzyl cresol melting at  $71^{\circ} - 72^{\circ}$ . This solidified and was crystallized from alcohol several times, finally giving thin yellow plates, melting at  $111^{\circ} - 113^{\circ}$ . This compound was not analyzed but we assume it to be a dinitro derivative of the structure 0 H m. pt.  $111^{\circ} - 113^{\circ}$ 

 $O_2 N$   $C H_2 C_6 H_3$ 

2 benzyl 3 methyl 4,6 dinitro phenol

The other nitro derivatives remained as heavy reddish oils and time would not permit their purification.

#### 7. Sumary

1. M-cresol was condensed with benzyl alcohol by the Huston method, forming a para and an ortho mono-substitution product and a para-ortho disubstitution product. 2. M-cresol was condensed with benzyl chloride by the Claisen method, forming two ortho monosubstitution products and an ortho-ortho disubstitution product, also a trace of the para-ortho disubstitution product. A small quantity of the corresponding "Claisen ether" was formed.

 2 benzyl 3 methyl phenol was condensed with benzyl chloride to form the same ortho-ortho disubstitution product mentioned above. A little of the ether, 2 benzyl
 3 methyl phenyl benzyl ether, was formed in this reaction
 4. Bromine and benzoyl derivatives and one nitro deriyative were prepared.





