

SOME BROMO DERIVATIVES OF BENZYLPHENOLS THESIS FOR THE DEGREE OF M. S. Bruce Leeland Fayerweather 1931

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THE BENZYLPHENOLS

OF

SOME BROMO DERIVATIVES

SOME BROND DERIVATIVES OF BENZYLPHENOLS

By

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THESIS

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HISTORICAL DATA

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I. Early work on alkylation of phenols.

Since E. Paterno, in 1872 (Gazz. Chim. ital. 1, 166, (1872) prepared his first benzyl phenol by heating benzyl chloride with zinc dust and phenel, a great number of other experimenters have contributed to the science of chemistry a comprehensive and more or less complete collection of laboratory procedures and theories concerning the preparation of both the benzyl phenols and their related products. The object of this historical review is not to give a complete resume of their work but merely to trace the more important developments along this line of organic condensations which have, innecently enough, brought forth the experimentation covered by this thesis.

Paterno's first work resulted in his isolation of bensyl phenol in the form of white silky meedles (m.p. 84^{θ}.) He prepared various substitution products with HNO, and a sulfonic acid with H₂SO₄.

In 1874, in conjunction with M. Fileti (Gazz. Chim. ital, S. 121--129, 251--254) he prepared further derivatives with acetyl chloride, benzeyl chloride, and bromine. Their di-brem derivative

seems to have been held in some doubt by later experimenters. (Zincke and Walter. Ann. 334, 367--385, (1904))

Again in 1875, Paterno and Fileti (Gazz. Chim. ital. 5, 381) propared benzyl phenol. This time the condensation was effected by using benzyl alcohel and phenol, along with a mixture of H₂SO₄ and assetic acid to remove a molecule of water. Along with their known compound was obtained an eil which did not crystallize but was assumed to be an isomeric benzyl phenol.

It remained for Rennie in 1882 (J. Chem. Soc.41, 220, 1882) to prove the bensyl phenol which melted at 84[®] the para compound. We also owe to him the identification of the cil, im Paterno and Fileti's experiment, as the erthe compound.

Perkins and Hodglinson (J. C.S. 724, 1880) prepared a benzyl phenol, probably the para, from the KOH solution of a mixture of phenyl acetate and benzyl chloride. This compound had a melting point of 80--\$1°.

Further condensations of this same nature were made by Leibmann (Ber. 15, 152, 1882) using zine

chloride, Paterno and Nazzare (Gazz. Chim. ital. 8, 303--305, 1879) using zinc turnings, and Mazarre (Gazz. Chim. ital. 12, 505--511, 1883) using magmesium chloride.

Bakumin (Gazz. Chim. ital. 33, 495--6, 1903) in the presence of zinc prepared benzyl derivatives of alpha and beta maphthol.

Braun (Ber. 43, 1850--52, 1910) prepared ethers by boiling aromatic halogenoids in the presence of H.SOA and alcohol.

Johnson and Hodges prepared substituted phenols and ethers (J. Am. Chem. Soc. 35, 1014, 1913) by reducing the corresponding mixed katones containing the hydroxyl or alkyloxy radicals in the benzene mucleus with zinc amalgam and hydrochloric acid.

II. The work of Claisen.

To Claisen goes credit for the development of the most satisfactory method of condensation of the alkyl halides yet devised. A resume of his work along this line is as follows (L. angew. chem. 36, 478--9, 1923): An alkali phenolate was treated with an alkyl halide in a non dissociating medium, such

as toluene. After heating, a product, principally ring substituted phonol with some alkyl phonyl ether, was obtained. The other was removed by washing with petroleum ether after the mixture had been treated with alcoholic potash solution. The alcoholic petash tied up the phonols present in the form of the petassium salts which were insoluble in petroleum ether and were later broken down by acidifying with HCl. The preduction of a quantity of the ortho phonol dame as a surprise since only the other was expected.

Explanation of this reaction is made by Claisen after the manner of Michael (J. pr. 31, 486; 46, 189) in connection with silver cyanide and methyl iodide. This is illustrated as follows:



Claisen claims unsaturated groups substitute in the ring more readily than do saturated and that once alkylated the ring is more easily substituted

in than previously. Furthermore he states that in dissociating media such as alcohol the entire yield takes the ethereal form while in non-dissociating media such as toluone and benzene yield a proponderance of the phenolic compound.

Claisen does not note the formation of any but the ortho compound in his reaction. Later investigators report traces of the para as well.

The fact that benzyl chloride in toluene forms ethers with phenols while diphenyl chlor methane gives only the carbon alkylated derivatives is held up by H. Busch (L. angew. chem. 38, 1145-6, 1925) to be indicative that the tendency of benzyl radicals toward carbon alkylation in phenols increases with the increasing substitution of the methane carbon atom.

Busch and Knoll (Br. 60 B, 2243--57, 1927) working from phenol instead of the benzyl group state that electro negative groups substituted in the ring of phenols favor the other formation. They also correborate Claisen's statement that the presence of alkyl groups in the phenol ring reduces ether and favors phenol formation in future condensations.

We are indebted to Claisen for many other Contributions. In 1901 (Ann. 418, 69--120, 1901) he rearranged allyl phenyl ether to e-allyl phenol. Shorigen (Ber. 58 B, 2028, 1925) also worked on analogeus rearrangements. Of particular interest to us is the work of Van Alphen (Rec. Trav. Chim. 46, 799--812) and Short (J. Chem. Sec. 137, 528, 1928). The former heated benzyl phenyl ether with sinc chloride to form the para phenol, the latter prepared both orthe and para benzyl phenol, phenel, and the di benzyl compounds from the same reaction.

In 1925 Claisen (Ann. 442, 210--45, 1925) describes several condensations along the same lines as those of his earlier work. Most important of these is his work on allyl bromide and para cresel.

These most recent works of Claisen are an outgrowth and application of a previous system of condensation employing sodium worked out by him in 1877 (Ber. 20, 646--650, 1877).

K. von Auwers (Chem. Zentr. I, 2347--8, 1926) suggests three methods whereby carbon alkylation may take place. 1. The method as outlined by Claisen.

2. The formation of the ether and later rearrangement.

3. The separation of the metal as a metallic halide with the formation of the free alkyl and enol radicals. The enol rearranges to the kete and the radicals unite. The reaction is as follows.

The first hypothesis is that most generally accepted for this reaction. Its possibility seems much more logical than the existence of free alkyl and enol radicals, or the rearrangement of ether in one media and not in another.

III. The work of Friedel and Crafts and the AlCl3 condensation.

While Friedel and Craft arc generally given credit for being the first to utilize AlCl₃ as a catalytic agent in the condensing of the alkyl halides, alcohols, and aromatic hydrocarbons, the first use of this condensing agent was Kuhlman

(Ann. 33-+34, 97-+204, 1840) who prepared others from mixtures of alcohols thru its use.

Not until 1877 did Friedel and Craft publish their observations on this type of condensation. (Bull. Soc. Chim. 27, 48, 1877; Compt. rend. 84, 1392--5, 1877). Their work at this time was entirely with aliphatic compounds and they go so for as to state that aromatic compounds and especially those containing the OH or O⁺ group can not be satisfactorily condensed by this method. They were very successful in their work with the aliphatice but it remained for later investigation to perfect methods by which the phenols, aromatic alcohols, and benzyl halides might be effeciently combined.

In 1881, Mors and Woith (Ber. 17, 187) reported having prepared di phenyl ether from the action of AlCl₃ on phenol and indicated that AlCl₃ here was acting as a dehydrating agent.

Friedel and Creft (Ann. Chim. Phys. 1, 489, 1854) advanced the following theory of the reaction of Aldle on an alkyl halide and benzene.

CoHoH + AIG -> HCG + HI-CG CHo + RQ -> HICG + HI-CG CHo + RQ -> IIICI3 + CoA5-R

The addition product of e-chlorophenol and aluminum chloride was isolated in 1896 by Perrier (Compt. rend. 122, 195--198, 1896). The product was Al_2Cl_4 ($OC_6H_4Cl_2$ and was a white crystalline powder melting at $20T_{-2}^0$

Huston and Friedeman (J. A. C. S., 38, 2527) in 1916 condensed bensene and benzyl alcohol te obtain di-phenyl methane, some p-dibenzyl benzene. a trace of the corresponding ortho isomer, and anthracene as a by-product. In this reaction the AlCl₃ acted in the capacity of a dehydrating agent. It was found that the proportion of materials used as well as the temperature affected the yields of different products.

These same men published in 1918 (J. A.C.S., 40, 785--93) work on the condensation of benzene with secondary alcohols. They used phenyl methyl carbinel, phenyl ethyl carbinel and di phenyl carbinel for this work. They found that as the

e,

length of the paraffin chain grow, so its retarding effect upon the reaction increased while the presence of the phenyl group did not hinder the progress of the reaction.

Huston (J. A.C.S. 46, 2775--9, 1924) studied the action of AlCl₃ in the condensing of phenol and bensyl alcohol to give p-benzyl phenol.

Benzyl Chloride and phonol in the presence of AlCl₃ gave 36% of p-benzyl phonol. The reaction mixture was carefully regulated as to temperature. It was found that optimum temperature varied with the different compounds being condensed.

Huston and Sager (J. A.C.Sec. 48, 1958, 1928) applied the dehydrating effect of aluminum chloride to saturated and unsaturated aliphatic and arematic alcohols with benzene, to form the fellowing conclusions.

(1) That saturated aliphatic alcohols up to and including amyl alcohol do not react.

(3) That unsaturated aliphatic alcohols, as ally1, do react.

(3) That of the alcoholic derivatives of the aromatic hydrocarbons, only those having the hydrox-

yl group on the carbon atom adjagent to the ring react.

In 1927 Huston, Lowis and Grotomut (J. A.C. Soc. 49, 1365, 1937) extended the series of condensations of secondary alcohols with benzene to include that of secondary alcohols with phenol, in the presence of AlCly. They also observed that substitution is abotted by unsaturation in the substituting molecule.

In 1929, Huston and Maxfield (Master's thesis) determined the proportions of phenel, benzyl chleride and AlCl₃ from which maximum yield was to be obtained in AlCl₃ condensation. This was found to be 3 molar quantities phenol, 1 molar quantities benzyl chloride, and $\frac{1}{2}$ molar quantities AlCl₂.

Eldridge (Master's thesis 1930) reports that the presence of two chlorine atoms on the phenol eauses the formation of the other in the AlCl₃ condensation. He isolates and identifies the other from such a run for the first time. He suggests that perhaps the other is formed first in all AlCl₃ condensations and that rearrangement follows. He believed that the presence of the halogen on the phenol ring upset the valence equilibrium of the ring causing a greater residual valence to be contralized in the oxygen methyl ()/ union of the other thus tending toward a more stable compound.

The mature of the way in which AlCl₃ brings about the many condensations of which it is able remains somewhat of a mystery. Three possibilities are allowed by the theorists on the subject.

- (1) Catalytic action.
- (2) Intermediate compounds.
- (3) Dehydration.

The intermediate compounds of AlCl₃ have been isolated. In some condensations results prove it to be merely a catalyst or a dehydrating agent.

IV. Work with brominated phenols, and benzyl halegeneids and alcohols.

The first work on the bremination of benzyl phenol took place in 1874 when Paterno and Fileti (Gazz. Chim. ital. 3, 121--129; 351--254, 1874) prepared a di brem derivative of the p-phenol by treating with an excess of bremine in CS, solution They obtained an amorphous material m.p. 175. This compound has been questioned by Zincke and Walter, of whom more later.

Sintenie (Ann 161, 345) reports the preparation of bensyl breme phenyl other by passing bremine into an alcoholic solution of the other to which some EgO has been added as a catalyst.

Remnie (J. Chem. Sec. 49, 405) in 1886, propared 2, 4, di brom 6 benzyl phenol altho he did not knew it. A white compound unidentified by him has been proven by Maxfield (1928 of this laboratery) to be the above mentioned compound, m.p. 91.

Auwers (Ann 357, 85--94, 1907) prepared tribrom phenyl benzyl ether and two di-brom derivatives. In these experiments the tri or di brom phenel was disselved in alcohol and treated with the benzyl compound and sedium ethexide.

The most notable contribution to this field was made in 1909 by Zincke and Walters (Ann 334, 367--385, 1909). They prepared and identified di and tri brome derivatives of p bensyl phenol. The method followed was that of adding the calculated amount of bromine to a cold chloroform solution of the phenol and stirring until all bromine was in solution. They isolated an unstable compound of colorless needles m.p. 42 which changed to the stable form of rhombic crystals m.p. 57. They gave this the formula:



The results here do not check with the work of Paterno.

The tri brem compound was given the following formula:



In 1920 Powell and Adams (J.Am. Chem.Sec. 42, 646--58, 1920) prepared p brem phenyl benzyl ether by refluxing benzyl chloride, para brom phenel and potassium carbonate in acctone solution.

Van Alphen (Rec. Trav. Chem. 46, 799--812, 1921) breminated 4, hydroxy tri phenyl methane and obtained the di brem derivative.



Waxfield (Master's thesis 1929) reports that bromination of phenel takes place in the phenol ring rather than in the benzyl radical. He identified the two forms of 2--6 di brem 4 benzyl phenol found by Zincke and Walters.

Darcy. (Master's thesis 1930) failed to isolate the ortho substitution product when pbrom benzyl chloride was condensed with phenol in presence of AlCl₃. He also checked and identified the structure of 4 hydroxy, 2--6--4' tri brom di phenyl methane as prepared by Zincke and Valtere (Ann 334, 367--385, 1904) His resulting compound did not agree in physical characteristics with that obtained by these men.

The Problem Defined.

Analysis and identification are to be made of all mono-benzyl compounds resulting from the AlCl₃ and Claison condensations of orthe brom benzyl chloride and phenol.

As one step in the identification of the monobenzyl phenols, a study is to be made of the pesitions taken by the substituting groups in the tri brem mono-hydrexyl di phenyl methanes which will be prepared. EXPERIMENTAL DATA

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I. Proliminary Work

Chlorination of O-Brom Teluene

C_H_BFCH3-Cl2---C_H_BFCH2Cl-HCl

The method here followed is a medification of that reported by Jacobs and Heidelberger (J. Biel. Chem. 20, 659--83 (1915).) They state that they passed chlerine (no amount stated) thru beiling e-brom toluone and distilled.

This method was attempted with indifferent success. It was found that while a small yield was obtained the chlorination had a tendency to go too far and introduce a second and a third chlorine atom into the methyl group thus spoiling the reclaimed compound for future use.

By a slight modification of this method we were able to reclaim all of the original compound which was not halogenated, for a future run.

A weighed amount of e-brem toluene was placed in a weighed flask fitted with a reflux condenser and a chlorinating tube. A few crystals of PCl₅ were added as a catalyst. This flask was heated to 150°--160° C. and chlorine bubbled slewly thru the breme telúene. The flask and contents were weighed from time to time until the increase in weight was just short of the calculated increase due to the replacement of the hydrogen in the methyl group by the chlerine. The resulting mixture was distilled under reduced pressure. The e-brem toluene beiling 110° --115° at 15 mm. is a clear celorless compound which, however, becomes cloudy on standing in sunlight. Care must be taken to keep even vapors of it from coming in contact with the eyes.

A typical run.

Weight of flask & teluene	349.	fgms.	
Weight of empty flash	24 9.	Zgms.	
Weight of toluene	100.	gms.	
Calculated increase	20.	gms.	
Flask weight at end of chlorin	na tien	367	gn s .
Amount of e-brom benzyl chlori	lde		
b.p. 110 ⁹ 115 ⁹ 15 mm.	93.1	Sema.	

Yield 77.08% theoretical

II. Preparation of Stbrom 2 hydroxy di phenyl

nothene by Claison's method.

Equimelar quantities of e-brom bensyl chleride, sodium, and phenol were used in this proparation. The sodium was cleaned of all corresive and exidized matter and beaded in dry teluene ever an oil bath. This was done by placing the sodium and toluene in a three neck flask fitted with reflux condenser and stirring the mixture very rapidly just as the toluene began to beil. The sodium immediately broke up into tiny globules which hardened as the flask was allowed to cool and stirring continued. The phenol was added ever a period of two hours with constant stirring. It was found that the phenol and sodium would react more completely with one another if the phenol was added in the form of a toluene solution. In either case a white cheesy mass of sodium phenolate was formed. This was heated to 180° for one hour with stirring and allowed to stand over night.

The freshly distilled e-brem benzyl chleride

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was then added all at once thru the condenser and the reaction mixture was heated to 150°--160° with stirring on the oil bath for eight hours and again allewed to stand over night.

The NaCl formed, was removed by washing with water, which in turn was removed thru a separatory funnel. All remaining water and toluene was driven eff by heating to 125° in a distilling flask.

If all the teluene is not driven off, a complete separation between the ether and phenolic products can not be effected in the following step.

The toluene free mixture was treated with an excess of Claisen's alcoholic potash solution (the amount varied with the size of the run frem_100 to 500 cc.) which tied up all free hydroxyl groups present and rendered them insoluble in the petroleum ether which was now used to remove the ethers present. Three washings with petroleum ether were made and this extract reserved for further treatment.

The heavy oil remaining was acidified with a mixture of concentrated HCl and ice and extracted with ethyl ether. The ether was driven off as far as possible on a water bath after which the extract 20.

was transferred to a Claisen's flash and heated to 185° to remove what other and water might still be present.

The residual material was distilled under Vacuum. It was found that results obtained at 3 mm. using a meter were much better than those obtained at 15mm, with a water pump. The distillates in the case were found to be much purer and to show less signs of decomposition than in the latter.

Several runs using small amounts were made with comparatively unsatisfactory results. Different molar quantities of phenol and time of heating were experimented with but the above precess was found to be the most satisfactory. Per cent yield was not calculated for these first four runs. Results of the first four Claisen's and amounts of compounds used are below:

t

30	gms.	e-brem	ben zy l	chloride
3.	.6 •	sedium.		
13	.6 *	phenel		
7\$	80.	toluene	I	
	heated	for seven heur	*	

Products from distilling ethyl ether extract 180* 1.3 gms. up te 180[°]-210[°] 6.0 * 210° - up 4.1 . 4. * residue Second condensation 30 gms. e-brem benzyl chloride phonol 18 . sodium 4.6 * 75 ... tolueme heated for six hours. Products from distilling ethyl ether extract 180 4.4 gms. up to 180-210 5.9 " 210 - up 5. * 6. " residue Third condensation. 30 gms. e-brom benzyl chloride sodium 3.3 * 13.6 * phenol 75 ec. teluene heated for eight hours.

Products from distilling othyl other extract

180 3.0 gms. up te 180°-210° 6.2 * 210 - up 5.9 . residue 3. * Fourth condensation 30 gms. e-brom benzyl chloride 3.3 * sodium 13.6 * phenel toluene 75 ...

heated for eight hours.

Products from distilling ethyl ether extract

u p	to	180 ⁰	6.2	gms.
		180 ⁰ -210 ⁰	7.	•
		210 [°] - up	4.4	•
		residue	2.	

It was found that in most cases the fraction from 180°--210° either solidified or became very viscous in nature. This was assumed to be the fraction desired. The four fractions were united and redistilled giving about 18 grams of a colorless compound boiling between 193°--300° which selidified in the ice bex but returned to liquid form at reem temperature. An attempt was made to purify by crystallization but crystals obtained from ligroin in the cold passed back into the liquid state at room temperature. The compound was returned to the bex and allowed to stand.

The various fractions up to 180° were found to be mostly phonol, while those above 210° were assumed to be the di benzyl compound. The residue was a high boiling tarlike compound which solidified on standing, into a brittle cakelike slag.

From the results of the above runs, it was decided that eight ho irs was the optimum time of heating and that equi molecular quantities were to be preferred to excesses of any of the reacting substances.

The petroleum other extracts from these four condensations were combined, the other driven off on a water bath and the remaining heavy amber eil distilled at 15 mm. The following fractions resulted.

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75 [°] - 125 [°]	18 gms.	
125 [°] - 170 [°]	9.8 *	
170 [°] - 195 [°]	20.2 *	
195 ⁰ - up	8.3 •	

The fraction from 75°- 125° was found to be o-brom benzyl chloride, that from 125° to 170° was a mixture of the benzyl chloride and the ether. The fraction from 170° - 195° was redistilled, the fraction from 175° - 179°, some 12 gms., coming ever as a light yellow oil and solidifying in the receiver. This solid was pressed between filter papers and then washed with cold alcohol. The solid diminished by half in mass but became colorless and crystalline in nature. When recrystallized from hot alcohol, the white fluffy crystals were obtained which melted at 34° to 36.°

This was assumed to be the other and analysis by the Parr sulphur bomb method gave the following result.

Eght. of sample Wght. of bromine % Br.Theoretical
% Br..2368.0744831.0230.4.2104.0596029.3330.4This is compound Number One (I) or 2-brem

benzyl phenyl other.

Two more Claison's were run in order to obtain sufficient of the orthe compound to prepare derivatives and esters. In these runs half melar quantities were used with the following results.

Fifth condensation

Ethyl ether extract at 15 mm.

90 ⁰ - 125 ⁰	10 gms.
125[°] - 180 [°]	.7 •
180 ⁰ - 195 ⁰	5.2 •
195 ⁰ - 203 ⁰	18.4 *
203 ⁰ - up	10. *
residue	13. •

Petrolaum other extract at 15 mm.

\$0 [®]	•	1250	23	gms.
125*	-	170*	8	•
170 ⁰	-	195*	24	•
195*	-	up	4	

Again we found in the phenelic fractionation phenol coming over from 90-125°, a mixture from 125°--180°, and 180°--195° and the orthe, orthe brom benzyl phenol from 195°--203° The fraction from 203° up appeared to be di benzyl compound. This time, however, the fraction from 195°-

203⁹ came down as a crystalline selid which re-

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mained fairly solid at room temperature. In an attempt to further purify it it was redistilled with the corresponding fraction from the next condensation.

There were no solid products from the petroleum other extract distillation and it also was laid aside to be combined with corresponding fractions in the following condensation.

Sixth condensation

Ethyl other extract

$90^{\bullet} - 125^{\bullet}$	13.2 gms.
125° - 180°	2. "
180 ⁰ - 195 ⁰	3.6 *
195 ⁰ - 203 ⁰	14. •
residue	20.7 •

Petroleum ether extrast

90 ⁴	-	125*	18	gms.
125°	•	170 ⁰	3	•
170*	•	195*	81.	.4•
195		H D	7.	.3.*

The results here were very analogeus to these of the preceding condensation, the same fractions solidifying. A larger amount of charred material

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was obtained, probably, the result of a small amount of morcury from the mechanical stirrer having worked down into the reaction mixture of the flask. The presence of morcury seems to retard the reactive ability of the sedium phenolate. Whether this is a catalytic or chemical reaction is not known but the fact remains that the yield of phenol in the presence of morcury is greatly reduced.

The four phenolic fractions 125° - 180°, and 180° - 195° from the last two condensations were combined and distilled at 15 mm. The distillate up to 195° was taken off and then the fractions from 195° - 203° were added. The majority of the compound came over from 196° - 198° and solidified when seeded with a crystal from the original 198°-803° fraction. Thirty grams of a white crystalline phenol were obtained which recrystallised from high test gasoline in small thick celerless plates having a melting peint of 47° - 43°. This yield represents 16% theoretical for the fifth condensation and 12% for the sixth.

Analysis for bromine content was as follows:

Weight of Sample	Weight of bromine	Z bromine by analysis	theoretical
.2439	.0752	30.7	30.4
.1378	.07264	30.58	30.4
		ave 30.64	

This is compound number two (II) and represents a 15% yield. It is 2° brom 2 hydroxy diphonyl methane.

The phenolic compound from the earlier condensations was placed in solution in petroleum ether and seeded with a crystal of the phenol just obtained. The resulting white flaky plates were filtered in the cold and dried between filter papers in the ice box. A yield of 12.2 grams was obtained with a m.p. of 44° to 45°. Five grams of this compound was recrystallized slowly from gaseline and gave practically a quantitative yield of heavy crystalline white plates melting at 45° to 47°. It would appear that these two forms are interchangeable and result from a difference in crystallizing media and speed of crystallization.

The petroleum ether extract fractions from 180° to 195° were combined and distilled at 15 mm. with 42 grame coming over between 184° - 190°

This refused to solidify even when seeded with erthe brem benzyl phenyl ether srystals. It was then redistilled at 3 mm. pressure. Thirty seven grams came over at 155° --188° and solidified in the receiver as distilled. This material was recrystallized twice out of hot ethyl alcohel, to give a yield of 30 grams of the same ether obtained in a previous run. (m.p. 34° -- 36°)

III Aluminum chloride condensation.



In the following condensation molar quantities of benzyl chloride and three molar quantities of phenel were placed in solution in petroleum ether and treated with $\frac{1}{2}$ molar quantities of Alcla.

Freshly distilled ortho brom benzyl chloride and phenol were placed in solution in dry petreleum ether in a jar. The AlCl₃ was added ever a period of two hours with efficient stirring. Care was exercised to keep the temperature of the reaction mixture down. This was accomplished, not by artificial cooling, but by a gradual addition of the AlCl₃. Itwas found that too efficient cooling was apt to speil the run. An attempt was made to carry on a condensation at 5° to 10° C. Nost of the phenol and benzyl chloride was recovered in this run and very little of the preduct ebtained. A temperature from 20° - 30° seemed to give the maximum yield. After adding the AlCl₃ the reaction mixture was stirred vigorously for two hours. Clouds of HCl were given off as the reaction took place. The mixture was then allowed to stand over might.

The AlCl₃ complex molecule was then decomposed with a mixture of concentrated HCl and ice, and the resulting mixture treated with an excess of Claisen's alcoholic potash solution. This, as in the Claisen condensation, rendered the phenolic compounds insoluble in petroleum ether and allewed the extraction of any ether compounds present with this solvent. This extract was handled in the same fashion as that in the Claisen reaction. The ether was driven off on a water bath and the remaining oil fractionated under vacuum.

After extracting with petroleum ether, the mixture was acidified with ice and concentrated HCl. washed with water to remove the salt that was formed, and extracted with ethyl ether. The ethyl ether solution of the ortho and para phenols was fractionated under vacuum, the ether having first been removed on water bath.

Amounts used-

In the work of this experiment it was possible to separate the ortho from the para by pressing the mixture of oil and crystals resulting from fractionation, between filter papers. The para being crystalline was obtained in a fairly pure form and redrystallized. The oil was extracted from the filter papers used in pressing, and upon redistillation also crystallized out and was later shown to be the orthe compound.

Two runs using 1 melar quantities of e-brem benzyl chleride were made with the following results.

phenol 141 grams • brom bensyl chloride 102 33 A101. Results of fractionation of first run. Ethyl ether extract - at 15 mm. up to 185 75 grams 185°- 194° 10 194⁰ - 205⁰ 20 205° - 215° 14 . 215 - 235 12

Charred material 32.6 *

Petroleum ether extract - at 15 mm.

up to 165	27.5 grams
165 ⁰ - 185 ⁰	24.6 *
185 [°] - 195 [°]	2.9 *
195 [°] - up	10.1 •

Results of fractionation of second run. Ethyl ether extract - at 15 mm.

up to 185 ⁰	87,2	grams
185 [°] - 194 [°]	7.2	
194° - 205°	17.7	
205° - 215°	15.6	٠
215 ⁰ - 235 ⁰	10.0	
charred material	41.9	

Petroleum ether extract - 15 mm.

up to 165 [°]	30.3 grams
165° - 185 ⁰	11.1 "
188 [°] - 195 [°]	6.3 *
195 ⁰ - up	2.1 *

Purification and separation of fractions from AlCl₂ condensation.

The phopolic fractions in and around 200[®] became semi solids but it was considered best to purify further by distillation. Accordingly the fractions were redistilled as fellows:

The fractions from both condensations from 185° to 194° were distilled at 15 mm. and fractions taken off up to 198°.

The 194° to 205° fractions were then added and the following fractions made; 195° to 200° and 200° to 204°

The 205° to 215° fractions were then added to the distilling flask and fractions made from $204^{\circ} - 207^{\circ}$ and $207^{\circ} - 212^{\circ}$.

The final result of the fractionation is as follows:

18 5°	•	195				6.1	grams
1950	-	200 ⁰				10.7	•
2 00 [°]	-	204*				15.6	•
204 ⁰	•	207 ⁰				15.7	₽
207	-	212				10.5	•
212 ⁰	•	up	at	16	n n -	24.2	•

All of the above solidified except 185°-195° fraction which remained an eil and that fraction above 212° which was an amber somiresineus eil, assumed to be the di bensyl compound. The various solidified fractions were pressed between chilled filter papers and the eil removed from them, then recrystallized. The result was $37\frac{1}{2}$ grams of the para phonol. This was white in color, long meedles in form, had a b.p. of 304° to 206° at 15 mm. and a m. p. of $71^{\circ} - 73^{\circ}$.

Parr bemb analysis of para sompound is as fellews:

Weight of sample Weight of bromine [Bromine Theoretical by analysis

.1169	•04970	31.0	30.4
. 2 3 4 3	•07008	31.0	80.4

This is compound number three (III) and represents 15 % yield. This compound is 2° brom 4 hydroxy diphenyl methane.

The filter papers used in the removal of the oil were extracted with ethyl ether, added to the fraction from 188° - 195° and fractionated. This gave us about 10 grams of a white solid boiling at 194° - 198°. This was recrystallised from gaseline and petroleum ether to give a compound very similar in appearance to our orthe compound. This compound had a molting point of 43° - 45° when crystallised from ether and 48° - 46° from gaseline as compared to that of 44° - 45° and 47° - 45° respectively shown by the orthe compound prepared

by Claisen's mothed. The yield here is 5% of theoretical and is later proved to be compound number II.

The fractions from petroleum ether extract were redistilled in the same manuer with the fellowing results.

up to 140	552 grams.		
140 [°] - 155 [°]	10.7 •		
155 [°] - 158 [°]	29 .9 •		
158 ⁰ - 180 ⁰	15.3 *		
160° - up	4.4 •		

The fractions 185° - 158° and 158° - 160° solidified when seeded with a crystal of the known other and upon recrystallization from hot alcohol some 23 grams of the other molting at 34° - 86° were obtained. This is compound number one (I) and is a yield of 10%. IV. Proof of identity of the 2 brom benzyl phenyl other.

As a check on the 2 brom benzyl phenyl other, a condensation in alcohol between the o brom benzyl chloride and phenol was made. Quantities used are equi molar. OH $Pr = \begin{pmatrix} H \\ H \end{pmatrix} + \begin{pmatrix} C \\ H \\ N \\ H \end{pmatrix} = \begin{pmatrix} C \\ H \\ N \\ H \end{pmatrix} = \begin{pmatrix} C \\ H \\ T \\ H \\ T \\ H \end{pmatrix}$

The phenol was put in solution in methyl alcohol and finally divided sodium was added slewly. This gave a clear syrupy mixture which was heated and stirred one hour at 130° and allowed to stand over night. The benzyl chloride was then added thru the condenser and the mixture was stirred and heated to 130° for four hours. The remaining alcohol was then driven off on a water bath and the mixture then washed with water to remove the salt. It was then fractionated under vacuum.

Quantities used in run.

12 grams	phenol
25.7 *	o brom benzyl chleride
3. *	sodium
Results of fractionation.	3 mm.
up ts 125⁰	15 grams

125 - 152	4 grams
152° - 156°	4 •
155° - 158°	7 •
158 [°] - 160 [°]	5 *
160 [°] - up	decomposition

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The fractions from $152^{\circ} - 156^{\circ}$, $156^{\circ} - 158^{\circ}$, and $158^{\circ} - 150^{\circ}$ solidified and were crystallized twice out of hot alcohol. The result was 13 grams of the other, white and crystalline in form, having molting point of $34^{\circ} - 36^{\circ}$. This is compound number one (I) and represents a yield of 42°_{2} . V. Proof of identity of the 2' brom 2 hydroxy diphenyl methane (Compound II).

The quantities used were as follows.

50 g	rams	2	•4• d:	i brom	phenol
42	•	0	brom	benzyl	chleride
4.6	•	8	odium		

This condensation was run in the usual manner with the following results.

Ethyl other extract at 3 mm.

up to 200	33	grams
200 [°] - 220 [°]	8	•
220 ^{°°} - 250 [°]	6	•
250 [°] - up (Cl	narred) 15	•

The fraction up to 200° was found to be the unreacted phenol and the fraction 220° - 250° was mostly decomposition products.

The fraction 200° - 220° was redistilled at 3 mm. to give 4 grams of the 2, 4 di brom. 6 erthe brom benzyl phenol with a boiling point of 204° - 206° This did not solidify on long standing. In an attempt to produce crystallisation, this phenel was seeded with a small crystal of 2, 4, 4° tri brem 6 hydroxy di phenyl methane. It was heped that the similarity of the compounds might cause crystallisation. Such was the case, for the $\frac{3}{4}$, $\frac{3}{4}$. 2° tri brom $\frac{3}{4}$ hydroxy di phenyl methane solidified over night. This compound was recrystallized to give a yield of $3\frac{1}{4}$ grams of fine white crystalline phenol. m.p. $41\frac{1}{4}^{\circ} - 42\frac{1}{2}^{\circ}$.

Perr sulphur bomb analysis.

Wght. of	Wght. of	Z Brom by	Z Brom by
Sample	bromine	analysis	calculation
.2007	.11431	56.9	\$7.1

This is compound number four (IV).

Petroleum ether extract. 3 mm.

up to 125	30.2	grams
125 - 180	2.7	•
180 [°] - 200 [°]	8.4	•
200 ⁰ - up	2.3	•

The fraction up to 125° was assumed to be principally e-brom bensyl chloride. That from 125° - 180° was found to be a mixture of e-brom benzyl chloride and 2 brom benzyl 2, 4, di brom phonyl ether. That from 180° - 200° selidified in the flask and was assumed to be the other. This fraction was redistilled and gave us six grams boiling at $173^{\circ} - 195^{\circ}$ at 3 mm. On the third crystallisation from hot ethyl alcohol this gave $4\frac{1}{2}$ grams of white meedles with a m.p. of $60^{\circ} - 64^{\circ}$.

Parr analysis follows.

Wght. of Wght. of % Br. by % Br. by Sample bromine analysis calculation .2133 .1215 57.3 57.1 This is compound number five (V).

Direct bromination of 2° brom 2 hydrexy diphenyl methane.

 $\int_{-\frac{1}{2}}^{0^{H}} \frac{n}{1+2Bn} \frac{C_{H}}{2} \frac{n}{1+2HBn} + 2HBn$

Five grams of the 2° brom 2 hydroxy di-phenyl methane (ortho phenol) was dissolved in 25 ec. of chloroform. To this was slowly added seven grams of bromine in chloroform. The addition was made ever a period of one hour in order that the temperature might not rise. Dense clouds of HBr were given off. This was allowed to stand over night then the excess CHCl₂ and Br₂ was driven off on a

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steam bath. The phenol failedte solidify. The mixture was distilled at 3 mm. and gave $3\frac{1}{2}$ grams of 3, 5, 5° tri brom 2 hydrexy di phenyl methane, having a b. p. of 205° = 207°. Partial decomposition took place during distillation giving the distillate a greenish tinge. This distillate was seeded with a crystal of the 3, 5, 2° tri brom 2 hydrexy di phenyl methane and immediately solidified. Upon recrystallisation this compound showed a melting point of $41\frac{1}{2}$ ° = 43°. This corresponds to the phenol obbined by the Claisen condensation of 2-4, di brom phenol and e-brom bensyl chloride. This is also compound number four (IV) and proves the construction of the orthe substituted phenol.

Comparison of the 2° brom 2 hydroxy diphonyl methane prepared by Claisens with that from the AlCle condensation.

In each case a compound was obtained existing in two forms. The first was a white flaky crystalline material and the second a white thick plate formation. The beiling points of the com-

pounds were the same, the molting points varying by about one degree. It was found that these two forms were dependent upon the media of crystallization and were interchangeable. The light flaky form same down out of petroleum ether. while the heavy plate formation resulted from a gasoline crystallization. VI. Check on identity of the 2° brom 4 hydroxy di phonyl methane. 45

Alcie condensation of 2. 6 di brom phenol and o brom benzyl chloride. $m \int_{m}^{oH} m \int_{cH_{sl}}^{cH_{sl}} m \int_{m}^{oH} + Hcl$

The usual procedure for the AlCl_B condensation was here followed. Quantities used were as follows.

30 gras	Rs	2,		6,	đi	brom	phenel
28.8	•	•	b	rox	ı be	msyl	chloride
8.4		•1		12			

In this run equi melar quantities were used instead of the usual excess of the phenol since there was no possibility of the formation of the di benzyl phenol due to the presence of the twe bremine atoms in the 2, 6, position.

The result of the fractionation of the ethyl ether extract was as follows. 3 mm.

up to 200⁶	18 grams.		
200 ⁰ - 205 ⁰	.7 *		
205° - 209°	6.5 ×		
209 ⁰ - up	4.0 *		
charred material	6.3 *		

. nog søre "x

The fraction up to 200° was mostly the unreacted 2. 6. di brom phenol. From 200° to 208° was a mixture of 2. 6 di brom phenol and 2° 3. 5. tri brom 4 hydroxy di phenyl methane. The fraction from 208° - 209° solidified and was assumed to be the compound desired. This was pressed between filter papers and finally recrystallized twice from ligrein to give 4.2 grams of (2. 8 di) twillows dishary methane brom 4 o-brom benzyl phenol, m.p. 78° - 80°. This

is compound number six (VI).

Parr bomb analysis.

Vght. of sample .2030	Wght. of bromine .11672	% Br.by analysis 57.4	% Br. theoretical 87.1
Theuf	A ficient mate	ve 57.15 rial resulte	d from the

petroleum ether extract to be of value.

Direct bromination of the 2* brom 4 hydroxy

di phenyl methane.

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Five grams of the para compound were disselved in chloroform and treated with seven grams bromine in chloroform. Addition was made over period of an 46

hour, to keep the temperature down, and the mixture was allowed to stand over might. When evolution of the H Br fules had ceased the compound was placed on the water bath and the chloroform driven off. It did not solidify. It was distilled coming over at 208° - 309°. It still did not solidify. It was rebreminated in chloroform and immediately started to form crystals around the edge of the beaker. After the chloroform was again driven off, it came dewn in a solid mass which on the second crystallisation from gasoline gave 3.5 grams of long yellew meedles. m.p. 78° - 80°. This is also compound VI.

VII. Preparation of esters.

The method followed is below (Stewert and Branch, organic analysis).

*Disselve 2 grams of the substance in 5 grams of dry pyridine, add 1 gram benzoyl chloride and allow it to stand over night. Add an equal volume of water slowly, cooling if necessary, and shake the mixture until there is no detectable eder of benzeyl chloride.

Pour the mixture into cold dilute sulphuris acid, extract it with other, wash the other with cold dilute sodium carbonate, and distill off the other. The ester is crystallized out of hot alcohol.*

This procedure was modified to the extent of using 5 grams of the phenol in starting and propertionately larger amounts of pyridine and benzeyl chloride.

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Benzeyl ester of 2' brom 2 hydrexy di phenyl methane.



m. p. . 64° - 65°

Benseyl ester of 2° brom 4 hydroxy di phenyl methane.



m.p. = (did not selidify)

Benzeyl ester of 2° 3, 5, tri brom 4 hydrexy diphenyl methane. Scheme of Condensation.



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