

SOME BROMO DERIVATIVES OF
ORTHO AND PARA BENZYLPHENOLS

THESIS FOR THE DEGREE OF M. S.

Arthur House Neeley

1933

THESIS

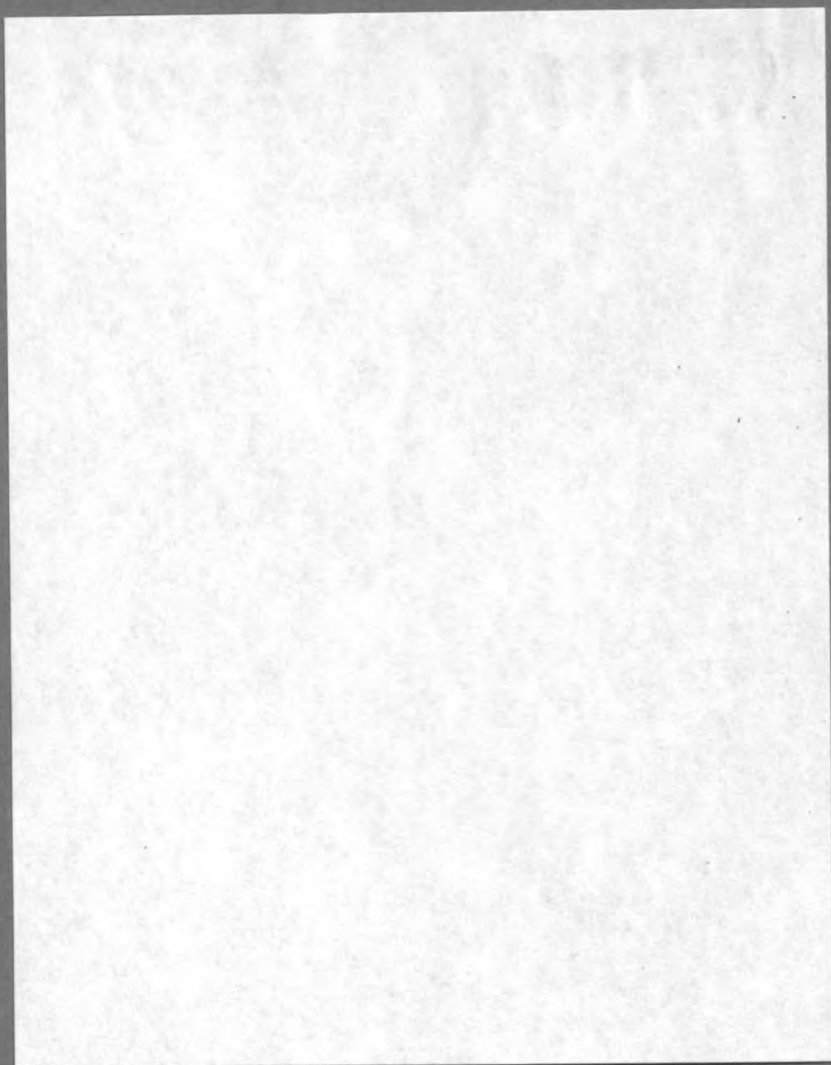
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AND PARA BENZYLPHENOLS

By

Arthur House Neeley

Thesis

Submitted to the faculty of Michigan
State College of Agriculture and Ap-
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HISTORICAL DATA

Historical Data

Benzylphenol was first synthesized by E. Paterno (Gazz. chim. ital., 2, 1-6; 1872) by gently heating a mixture of benzylchloride and phenol in the presence of zinc dust. Silky white needles (m.p. $84^{\circ}\text{C}.$) were isolated which were soluble in ethylether, alcohol, benzene or chloroform. They were also soluble in alkaline solutions but reprecipitated upon acidification. When the substance was treated with nitric acid, substitution products were formed. With sulphuric acid, it produced a sulphonic acid, the barium salt of which was soluble in water. It was also found that when benzylated anisole was treated with hydriodic acid and boiled for eight hours at 170° the above mentioned benzylphenol and methyl iodide were obtained.

Two years later further derivatives of benzylphenol were prepared by Paterno and Jileti. (Gazz. chim. ital., 3, 121, 251; 1874). These were benzylphenol acetate, prepared from acetylchloride in the cold; benzylphenylbenzoate, from benzoylchloride; and a "dibromo" derivative which was later questioned by some investigators. (Zincke and Walter, Ann., 354, 367; 1904) The benzylphenylbenzoate crystallized from alcohol in glistening needles which melted at $86^{\circ}\text{C}.$

In 1875, Paterno and Fileti (Gazz. chim. ital., 5, 381) published an article in which they described the condensation of phenol and benzylalcohol, using a mixture of acetic and sulphuric acids as a dehydrating agent. A mass of crystal was obtained which proved to be benzylated phenol and a fluorescent oil which appeared to be an isomeric benzylphenol.

Perkin and Hodgkinson (J. chem. soc., 1880, 724; 1880) obtained a fluorescent liquid (b.p. $310-320^{\circ}$) by heating a mixture of phenylacetate and benzylchloride. By analysis it was shown to have the formula $\text{C}_{25}\text{H}_{24}\text{O}_3$. This was readily saponified with alcoholic KOH yielding an oil which rose to the surface. This oil, upon further purification, gave crystals (m.p. 39°) which analysis showed to have the formula $\text{C}_{10}\text{H}_{10}\text{O}$. Upon acidification and purification of the

remaining alkaline solution a crystalline compound was obtained (m.p. 80-81°) which had the formula $C_{15}H_{12}O$. This compound was thought to be the same one that was prepared by Paterno using benzylchloride and phenol with zinc dust, the difference in melting point being due to impurities.

Using molten $ZnCl_2$ as a dehydrating agent, Liebmann (Ber., 15, 152; 1882) (Ber., 14, 1842; 1881) succeeded in condensing phenol and benzylalcohol. They obtained a crystalline product which melted at 84°C.

In 1882, Rennie (J. chem. Soc., 33, 220) was able to show that the compound melting at 84° was the parabenzylphenol and the oil obtained by Paterno and Filati was the orthobenzylphenol.

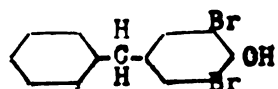
Bakunin (Gazz. chim. ital., 33, 495; 1903) prepared benzyl derivatives of alpha and beta naphthol using zinc as a catalyst.

J. V. Braun (Ber., 43, 1350; 1910) prepared benzylmethylether, benzylethylether, o-xylylethylether and benzylallylether by boiling the corresponding aromatic bromine derivatives (as benzylbromide) with the respective alcohols in the presence of sulphuric acid.

Johnson and Hodges (J. Am. Chem. Soc., 35, 1014; 1913) prepared substituted phenols and ethers by reducing mixed ketones containing hydroxyl or ether radicals in the benzene nucleus, by means of zinc amalgam and hydrochloric acid. A great many alkyl derivatives were obtained, among which are methylether of 4 ethylphenol by reduction of p-acetylanisole, ethylhydroquinone by reduction of ethylquinone and ethylresorcinol by reduction of acetylresorcinol.

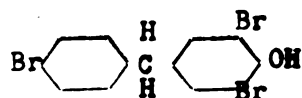
In an article published in 1904, Zincke and Walter (Ann., 334, 367-385) describe their work on bromine substitution in phenols. Using the same method as E. Paterno had used, they condensed benzylchloride and phenol, obtaining a product of silky white needles which melted at 84°C. When this compound was heated by the gradual addition of the calculated amount of bromine in the cold in chloroform, two products were obtained; one formed colorless needles and melted at 44°, while the other consisted of rhombic crystals which melted at 57°.

The former crystals were unstable and changed readily into the latter at room temperature. They attributed the following formula to this compound;

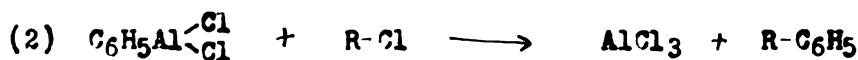
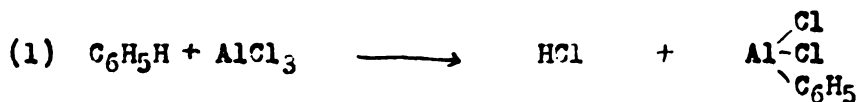


As was noted above, this compound did not compare in properties with the dibromo compound obtained by Paterno.

By agitating the parabenzylphenol with a calculated excess of bromine, Zincke and Walter were also able to prepare a tribromo derivative. It was a solid crystalline substance which formed needles melting at 88°C. It was assigned the following formula;



In 1876, the condensation of amyl alcohol and various hydrocarbons was accomplished by Friedel and Crafts by means of anhydrous aluminum chloride (Compt. rend., 84, 1392). They worked only with aliphatic compounds and were of the opinion that aromatic substances would not condense by this means. They explained the reaction according to the following mechanism.



Gustavson (Ber., 13, 157; 1880) and Buttgenbach (J. Prakt. Chem., 150, 355; 1923) supported the view of the formation of an instable aluminum-organic compound as an intermediate product which subsequently breaks down, regenerating the $AlCl_3$.

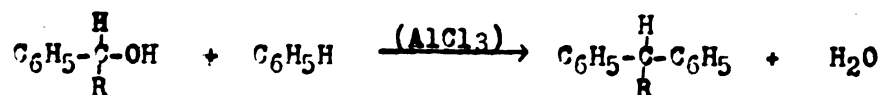
The preparation of aniline and p-toluidine by Jaubert (Compt. rend., 132, 841; 1901) from the action of $H_2NOH \cdot HCl$ with the hydrocarbon in the presence of $AlCl_3$, indicates a dehydration reaction.

The addition product of o-chlorophenol and aluminum chloride was isolated by Perrier (Compt. rend., 122, 195; 1896). It was a white crystalline powder, melting at 207-210° and was given the formula, $\text{Al}_2\text{Cl}_4(\text{OC}_6\text{H}_4\text{Cl})_2$.

The condensation of benzene and benzyl alcohol was carried out by Huston and Friedman (J. Am. Chem. Soc., 38, 2527; 1916) by the use of AlCl_3 as a catalyst. They obtained diphenylmethane, some p-benzylbenzene and anthracene as by-products. In this reaction the AlCl_3 appeared to act as a dehydrating agent. When the reaction was carried out at a low temperature and a large excess of benzene was used, the yield of diphenylmethane was high and the yield of anthracene was much lower.

Later in 1918, the same investigators published an account of the condensation of benzene with various secondary alcohols (J. Am. Chem. Soc., 40, 785; 1918). They found that the reaction proceeded smoothly and with good yield in the case of diphenylcarbinol while in the cases of ethylphenylcarbinol and methylphenylcarbinol the yields were less, the retarding effect of the ethyl group being greater than that of the methyl group.

The mechanism for the reaction was given as follows;

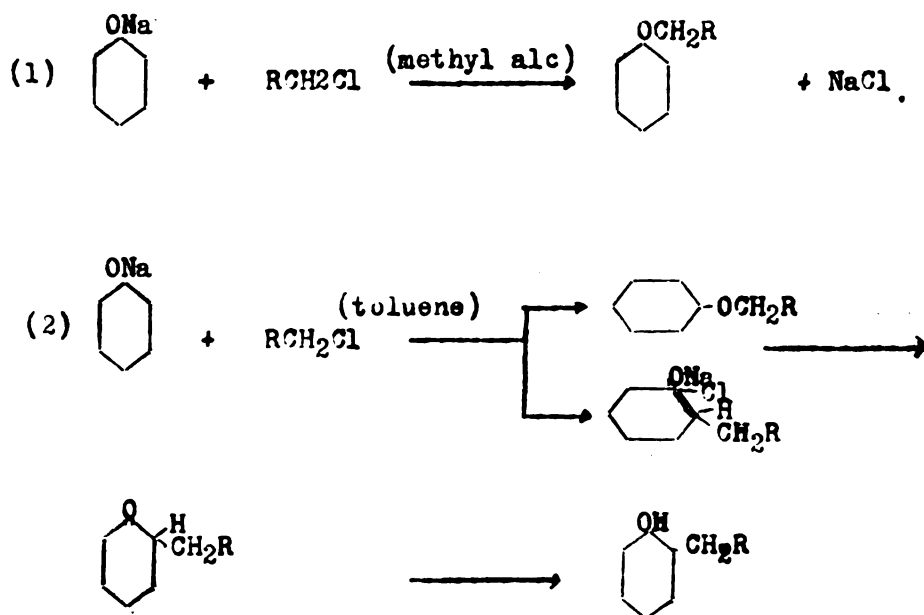


R being a phenyl, ethyl or methyl group.

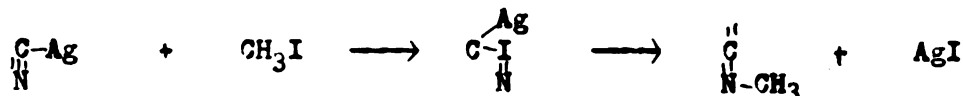
Huston (Sci., 52, 206; 1920) condensed benzyl alcohol and phenol in the presence of AlCl_3 and obtained p-benzylphenol. Later he studied the action of phenol with benzyl alcohol, phenylmethylether, phenylethylether and benzylchloride. (J. Am. Chem. Soc., 46, 2775; 1924). With benzyl alcohol he obtained a 45% yield of p-benzylphenol; with phenylmethylether a 46% yield of p-benzylphenylmethylether and a 57% yield of p-benzylphenylethylether was obtained. The results, together with the fact that a 36% yield of p-benzylphenol was obtained with benzylchloride, bars the possibility that the benzyl alcohol is first converted into benzylchloride.

In 1923, L. Claisen (Z. Angew. Chem., 36, 478) published an account of the carbon alkylation of phenols. He found that when the sodium derivative of monohydriphenols was heated with an alkyl halide in a "non-dissociating" medium such as toluene, carbon alkylation took place mainly in the position ortho to the hydroxyl group. When a "dissociating" medium such as methyl alcohol or ethyl alcohol was used the alkylation took place on the oxygen, forming the corresponding ether.

The reactions as represented by Claisen are as follows:



The mechanism of the reaction was based by Claisen on Michaels theory (J. pr., 37, 486; 46,189) for the reaction between silver cyanide and methyl iodide:



Three possibilities for this reaction are given by K. von Auwers, Wegener and Behr (Chem. Zentr. 1, 2347; 1926)

- The initial formation of addition products with subsequent splitting.
- The initial formation of normal oxygen derivatives with subsequent rearrangement into the o-derivative.
- Separation of metal as metallic halide forming free enol and keto

radicals and with the slight reactivity of the alkyl group, partial or complete rearrangement of the enol to keto radical, and finally union of the radicals. The first hypothesis, formulated by Claisen is the one that is most generally accepted.

Claisen listed the factors which effect the reaction as follows;

1. The kind of phenol; The condensation of complex phenols was carried out with greater difficulty than the more simple ones.

2. The kind of radical attached to halogen; Unsaturated, saturated, aliphatic or aromatic. It was found that saturated alkyl halides promoted the formation of o-derivatives, while unsaturated alkyl halides promoted the formation of o-derivatives.

3. The kind of halogen.

4. The kind of metal in the metal phenolate.

5. The temperature.

6. The reaction medium.

The rearrangement of phenylbenzylether to give benzylated phenol has been studied by J. Von Alphen (Rec. trav. chim., Vol. 46, 799; 1927).

Benzylphenylether was heated with zinc chloride to 160° for one hour, yielding 4 hydroxydiphenylmethane (m.p. 84°) and a dyestuff.

Closely related to the investigation to be outlined in this thesis is the work done in this laboratory by D'Arcy (Master's Thesis, 1930) and Fayerweather (Master's Thesis, 1931).

D'Arcy carried out the condensation of p-bromobenzylchloride and phenol by both the AlCl₃ method and the Claisen method. By the former method he prepared and identified 4 hydroxy 4'-bromodiphenylmethane and by the latter 2 hydroxy 4'-bromodiphenylmethane. He failed to isolate any 2 hydroxy 4'-bromodiphenylmethane in the products of the AlCl₃ condensation. He also found, as had Maxfield (Master's Thesis, 1929), that bromination took place only in the unoccupied ortho and para positions of the phenolic ring.

Fayerweather prepared and identified 4'-hydroxy 2'-bromodiphenylmethane and 2 hydroxy 2'-bromodiphenylmethane by the AlCl_3 and Claisen methods respectively. He was able to isolate 2 hydroxy 2'-bromodiphenylmethane from the AlCl_3 condensation products and also found that bromination took place only in the unoccupied ortho and para positions of the phenolic ring.

EXPERIMENTAL DATA

The Problem Defined

2 hydroxy 5'-bromodiphenylmethane and
4 hydroxy 5'-bromodiphenylmethane are
to be prepared by the Claisen and
 AlCl_3 methods respectively. The
structures are to be determined by
the comparison of physical constants
of products obtained by the direct
bromination of these compounds with
2 hydroxy 3,5,3'-tribromodiphenylmethane
and 4 hydroxy 3,5,3'-tribromodiphenylmethane.

Experimental Data

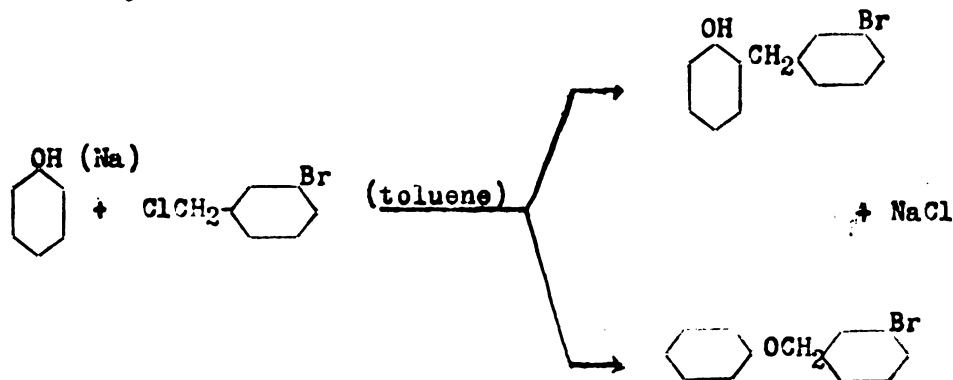
I - Preliminary Work.

m-bromotoluene was prepared according to the method described on pages 106 and 128, volume I, of Organic Syntheses - Gilman. m-bromobenzyl chloride was prepared by a modification of the method of Jacobs and Heidelberger (J. Biol. Chem., 20, 659; 1915) as follows: A weighed amount of m-bromotoluene was placed in a round bottomed three neck flask, fitted with a reflux condenser and a tube for the introduction of chlorine. After having been washed in concentrated sulphuric acid, chlorine was passed slowly through the tube and allowed to bubble through the liquid. A small piece of phosphorous pentochloride was added as a catalyst. The flask was weighed at intervals to determine the weight of chlorine added and to insure under-chlorination. When about 75% of the theoretical amount of chlorine had reacted, the contents of the flask were subjected to fractional distillation. The unchlorinated m-bromotoluene was recovered in the fraction coming over from 70-75°C/15 m.m., while the m-bromobenzyl chloride was found to distill at 115-125°C/15 m.m. The intermediate fraction which contained a mixture of the chlorinated and unchlorinated product was returned to the flask with fresh m-bromotoluene for further chlorination. Three hundred c.c. of m-bromotoluene was found to be a convenient quantity for chlorination in a 500 c.c. flask.

The 2-6 dibromophenol was prepared by the following method, adopted from the method of M. Tanaka and K. Kutani (C. A., 21, 2255) for the preparation of 2-6 dichlorophenol: 1.3 moles of phenol was treated with 220 grams of concentrated sulphuric acid in a 3 neck three liter flask equipped with a mechanical stirrer and dropping funnel for addition of bromine. The mixture was heated for three hours with stirring to insure complete sulphonation and made alkaline with 50% sodium hydroxide. 500 c.c. of water was

added to the resulting crystalline mass and the mixture cooled. A calculated amount of bromine was then added through the funnel with stirring. A light yellow mass was obtained which was divided into two portions each of which was subjected to steam distillation to remove the tribromophenol. After it had stopped coming over, 500 c.c. of concentrated sulphuric acid was added and the steam distillation continued. During the last steam distillation the flask was heated to 200-210°C in an oil bath. An oily substance with a strong odor of SO₂ came over first, followed by the crystals of 2-6 dibromophenol.

II - Preparation of 2 hydroxy 3-bromodiphenylmethane by the Claisen condensation;



One-half mol of freshly chipped sodium was suspended in 200-250 c.c. of toluene in a three neck one liter round bottomed flask, equipped with a reflux condenser and an efficient mercury sealed stirrer. The contents of the flask was heated until the toluene reached its boiling point at which time the melted sodium rose to the surface of the liquid, and stirred vigorously until all the sodium was finely divided. During the first condensation the suspension was allowed to cool before the addition of one-half mol of phenol in small quantities, but the reaction between the sodium and phenol was often retarded so that in later condensations it was found desirable to very cautiously add the phenol dissolved in chloroform to the hot suspension in small quantities, making sure that no open flames were

present in the vicinity of the apparatus. A vigorous reaction occurred between the sodium and phenol in the hot solution with an active evolution of hydrogen which resulted in the formation of a white mass of sodium phenolate. After the addition of the entire quantity of phenol the reaction mixture was heated with stirring, on an oil bath at 100°C for several hours to insure complete reaction and allowed to cool. One-half mol of m-bromobenzyl chloride was slowly and cautiously added through the reflux condenser to the cool mixture and the contents of the flask were slowly heated on the oil bath until a temperature of $150\text{--}155^{\circ}\text{C}$ was reached. The heating was continued at this temperature with stirring over a period of six to eight hours.

After cooling the mixture was washed twice with water to remove the NaCl and distilled under atmospheric pressure to 125°C to remove water and toluene. The resulting oil was treated with 300 c.c. of Claisen's reagent (350 grams of KOH dissolved in 400 c.c. of water and made up to one liter with methyl alcohol) to form the potassium salt of the phenol derivative which is insoluble in petroleum ether. The mixture was then extracted with three separate 100 c.c. portions of petroleum ether to remove any 3-bromobenzylphenyl ether formed. 200 grams of ice were added to the residue which was neutralized with concentrated hydrochloric acid. After cooling the phenol derivative was removed by extraction with three 100 c.c. portions of diethylether.

The diethylether and water were removed by distilling the mixture to 125°C at atmospheric pressure and the resulting mixture subjected to distillation *invacuo* to purify the phenol derivative.

The same procedure was followed for the petroleum ether extracts. The distillations were carried out under a pressure of 3 m.m., the product showing no signs of decomposition.

Four condensations were made according to the above procedure which resulted in the formation of very small yields (about 4%) of 2 hydroxy 3'bromodiphenylmethane. The results are as follows;

First Condensation;

Ethyl ether extract.

13 grams	phenol	below 70°C/3 m.m.
7 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.
15 grams	tar	above 180°C/3 m.m.

Petroleum ether extract

15 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
12 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
No tar		

Second Condensation;

Ethyl ether extract

10 grams	phenol	below 70°C/3 m.m.
5 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.
7 grams	tar	above 180°C/3 m.m.

Petroleum ether extract

50 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
14.5 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
7 grams	tar	above 180°C/3 m.m.

Third Condensation;

Ethyl ether extract

8 grams	phenol	below 70°C/3 m.m.
7.3 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.
2 grams	tar	above 180°C/3 m.m.

Petroleum ether extract

27.5 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
15.2 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
10 grams	tar	above 180°C/3 m.m.

Fourth Condensation:

Ethyl ether extract

5 grams	phenol m	below 170°C/3 m.m.
5 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.
2 grams	tar	above 180°C/3 m.m.

Petroleum ether extract

18 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
20 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
10 grams	tar	above 180°C/3 m.m.

The four 150-180°C fractions of 2 hydroxy 3'bromodiphenylmethane were combined and re-distilled twice at 3 m.m. pressure and during the second distillation came over quite constantly at a temperature of 167-169°C. A total yield of 23 grams of the purified product was obtained for the four runs making a 3.7% average based on the phenol used. It remained a liquid at room temperature.

Upon re-distillation the 3 bromobenzylphenylether came over at a constant temperature of 145°C at 3 m.m. pressure, the average yield being 11.9% based on the phenol. It crystallized upon standing and was found to have a constant melting point of 36-37°C after several re-crystallizations. It formed flakey white leaflets in alcohol. In order to determine whether or not any equilibrium exists in the formation of the 2 hydroxy 3'bromo-diphenylmethane and the 3 bromobenzylphenylether, four runs were made in the manner described above with the exception that in three cases, 3 bromobenzylphenylether was added to the reaction mixture. The results obtained are as follows;

Fifth Condensation - (15 grams 3 bromobenzylphenylether added)

Ethyl ether extract

6.5 grams	phenol	below 70°C/3 m.m.
16 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.

Petroleum ether extract

20 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
11 + 15 grams	3 bromobenzylphenylether	140-150°C/3 m.m.

Sixth Condensation - (15 grams 3 bromobenzylphenylether added)

Ethyl ether extract

4 grams	phenol	below 70°C/3 m.m.
15 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.

Petroleum ether extract

25 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
16 + 15 grams	3 bromobenzylphenylether	140-150°C/3 m.m.

Seventh Condensation - (25 grams 3 bromobenzylphenylether added)

Ethyl ether extract

4 grams	phenol	below 70°C/3 m.m.
12 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.

Petroleum ether extract

25 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
25 + 6 grams	3 bromobenzylphenylether	140-150°C/3 m.m.

Eighth Condensation - (No 3 bromobenzylphenylether added)

Ethyl ether extract

5 grams	phenol	below 70°C/3 m.m.
8 grams	2 hydroxy 3'bromodiphenylmethane	150-180°C/3 m.m.

Petroleum ether extract

30 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
15 grams	3 bromobenzylphenylether	140-150°C/3 m.m.

It will be noted that in the first two runs (5th and 6th condensations) the addition of 15 grams of 3 bromobenzylphenylether resulted in the formation of approximately three times greater yield of 2 hydroxy 3'bromodiphenylmethane than the average for the first four condensations where no 3 bromobenzylphenylether was added.

In the 7th condensation, 25 grams of 3 bromobenzylphenylether was added and contrary to expectations only 11 grams of 2 hydroxy 3'bromodiphenylmethane was obtained although this yield was considerably greater than those obtained in the first four condensations and the 8th condensation where none of the ether was added.

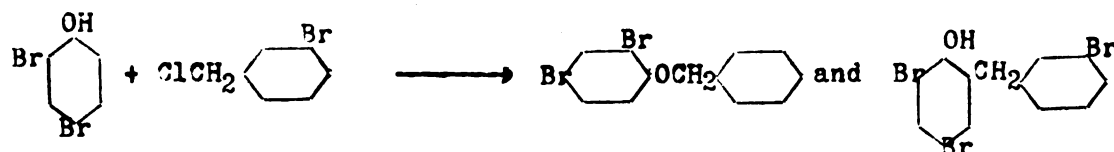
It is apparent from the above data that the addition of 3 bromobenzylphenyl ether to the reaction mixture substantially increased the amount of 2 hydroxy 3'bromodiphenylmethane formed. These facts seem to indicate that there is some sort of an equilibrium established between the substituted phenol and the corresponding ether formed as a result of the reaction.

A condensation of phenol and 3 bromobenzyl chloride was run in methyl alcohol as an additional means of checking on the ether formed in the previous condensations which were carried out in toluene, one-eighth mol quantities being used. A calculated amount of freshly chipped sodium was carefully added in small amounts to 200 c.c. of methyl alcohol in the same apparatus used for the Claisen condensations described above. To this the phenol was added, followed by a careful addition of the m-bromobenzyl chloride. The mixture was heated for eight hours to a temperature of 100-110°C. As no carbon-alkylated compound was formed in a dissociating medium such as methyl alcohol it was unnecessary to treat with Claisen's alcoholic potash. The mixture was heated on a steam bath to evaporate the alcohol, treated with water to dissolve the NaCl formed and extracted with three 50 c.c. portions of ethylether. After evaporation of the ether the resulting oil was subjected to distillation. 18 grams (55.0%) of 3 bromobenzyl-
was obtained in the fraction coming over at 140-150° c/3 m.m.

After several re-crystallizations it melted at a constant temperature of 36-37°C as had that obtained in the toluene condensations.

III - Proof of Structure of 2 hydroxy 3,5,3'-tribromodiphenylmethane.

As a means of proving the structure of 2 hydroxy 3,5,3'-tribromodiphenylmethane, another Claisen condensation of 3 bromobenzyl chloride and 2,4 dibromophenol was carried out in the same manner as outlined for the first four condensations described above. The reaction was considered to place as follows:



One-fourth mol quantities were used and the following yield was obtained;

9th Condensation:

Ethyl ether extract

16.5 grams	2,4 dibromophenol	100-105°C/3 m.m.
12 grams	2 hydroxy 3,5,3'-tribromodiphenylmethane	195-205°C/3 m.m.
7½ grams	tar	above 205°C/3 m.m.

Petroleum ether extract

20 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
10 grams	3 bromobenzyl, 2,4 dibromophenylether	180-200°C/3 m.m.
8 grams	tar	above 200°C/3 m.m.

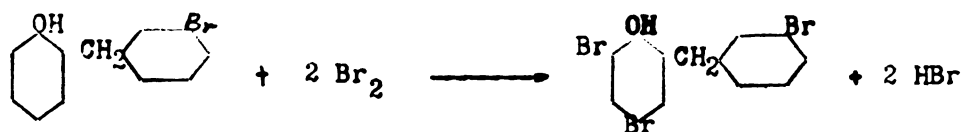
The 2 hydroxy 3,5,3'-tribromodiphenylmethane immediately crystallized and after several re-crystallizations from petroleum ether was obtained as fine white needles which melted at a constant temperature of 76-77°C. The 3 bromobenzyl 2,4 dibromophenylether isolated from this condensation was re-crystallized several times from alcohol, forming fine white needles which melted at 49-50°C.

A condensation in methyl alcohol similar to the one described above for 3 bromobenzylphenylether was made using 1/20 mol quantities of 2,4 dibromophenol and benzyl chloride.

A yield of 12.5 grams of 3 bromobenzyl 2,4 dibromophenylether was obtained which also melted at 49-50°C when re-crystallized from alcohol. None of the corresponding 2 hydroxy 3,5,3'tribromodiphenylmethane was isolated.

As the next step in the identification of the 2 hydroxy 3'bromodiphenylmethane, five grams of the product was dissolved in 20 c.c. of chloroform, contained in an erlenmeyer flask and placed in an ice salt water bath. A ten per cent excess of the calculated amount of bromine was dissolved in chloroform which was allowed to drop slowly into the solution of the phenol derivative from a funnel. The contents of the erlenmeyer flask was subjected to continual agitation during the bromination while the flask was kept partially submerged in the ice salt water bath. After all the bromine had been added the flask was allowed to remain in the bath for one hour or more to insure complete reaction. A vigorous evolution of hydrobromic acid took place throughout the entire bromination. The reaction mixture was then poured into a beaker and the chloroform evaporated off on a steam bath. The resulting oil immediately crystallized upon cooling.

Since Maxfield, D'Arcy, and Fayerweather had been unable to introduce bromine into any position other than the unoccupied ortho and para positions of the phenolic ring the reaction was considered to take place as follows:



The crystals thus secured were pressed between filter papers to remove impurities and re-crystallized from petroleum ether. Difficulty was encountered in the purification of the compound. After repeated re-crystallizations a melting point, 4 degrees lower than that found for 2 hydroxy 3,5,3'-tribromodiphenylmethane was procured. Accordingly, 10 grams of the product were brominated and after fifteen subsequent re-crystallizations from petroleum ether fine white needles similar to those prepared in the Claisen condensation were obtained which melted at 73-75°C. This difference in melting point was explained by assuming the presence of a small quantity of 4 hydroxy 3'-bromodiphenylmethane in the 2 hydroxy 3'-bromodiphenylmethane which could not be removed by fractional distillation as the two compounds have practically the same boiling point.

To further prove the 2 hydroxy 3,5,3'-tribromodiphenylmethane obtained in the Claisen condensation of 2,4 dibromophenol and *m*-bromobenzyl chloride, to the same compound as the product isolated from the direct bromination of 2 hydroxy 3'-bromodiphenylmethane, the benzoyl derivative of each compound was prepared by the method of Einhorn and Holland (A., 301, 95; 1898) (Method of Organic Chem.; Porter, Stewart, and Branch; page 181-182) as follows: 2 grams of the substance was dissolved in 5 grams of dry pyridine and a 10% excess of the calculated amount of benzoyl chloride added. After standing over night an equal volume of water was slowly added and the mixture shaken until no odor of benzoyl chloride could be detected. The mixture was poured into cold dilute sulphuric acid and extracted with ether. After being washed with cold dilute sodium carbonate the ether was distilled off. In both cases white needle like crystals were obtained. The benzoyl derivative of the 2 hydroxy 3,5,3'-tribromodiphenylmethane, obtained by the Claisen condensation of 2,4 dibromophenol and *m*-bromobenzyl chloride, melted at 90-91°C while those obtained from the product isolated from the direct bromination of 2 hydroxy 3'-bromodiphenylmethane melted at 89.5-91°C. In

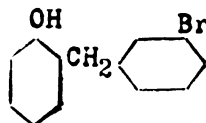
each case the compounds were re-crystallized from petroleum ether.

By the same method the benzoyl ester of 2 hydroxy 3'-bromodiphenylmethane was prepared. It gave white plate like crystals when recrystallized from petroleum ether which had a constant melting point of 69-70°C.

Further verification of the identity of 2 hydroxy 3'-bromodiphenylmethane and its derivatives was accomplished by means of the Parr Bomb analysis for bromine content described by J. Lemp and H. Broderson (J. Am. Chem. Soc., 39, 2069; 1917). Following is a tabulation of the analysis of the various compounds together with their proposed structural formulae and physical constants:

1. 2 hydroxy 3'-bromodiphenylmethane

Structural formula:



Crystalline form: Liquid at room temperature

Boiling point: 167-169°C/3 m.m.

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N AgNO ₃	% Bromine found	% Br. Calcd.
1	.2307	9.00	31.21	30.39
2	.2303	8.90	<u>30.91</u>	
		Ave.	31.06	

2. 3 bromobenzylphenylether

Structural formula



Crystalline form: Leaflets from alcohol

Boiling Point : 145°C/3 m.m.

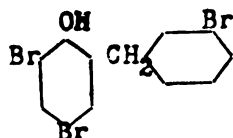
Melting point: 36-37°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO ₃	% Bromine Found	% Bromine Calcd.
1	.2577	9.90	30.73	30.39
2	.2734	10.6	<u>31.01</u>	
Ave.			30.87	

3. 2 hydroxy 3,5,3'tribromodiphenylmethane.

Structural formula



From Claisen condensation of
2,4 dibromophenol and m-bromo-
benzylchloride.

Crystalline form: Fine white needles from petroleum ether.

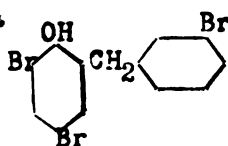
Melting point: 76-77°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO ₃	% Bromine Found	% Bromine Calcd.
1	.1610	11.50	57.14	57.01
2	.1895	13.45	<u>56.78</u>	
Ave			56.96	

4. 2 hydroxy 3,5,3'tribromodiphenylmethane.

Structural formula



From direct bromination of
2 hydroxy 3'bromodiphenyl-
methane.

Crystalline form: Fine white needles from petroleum ether.

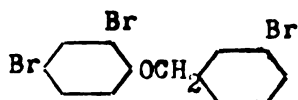
Melting point: 73-75°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO ₃	% Bromine Found	% Bromine Calcd.
1	.1807	13.00	57.55	57.01
2	.2112	15.00	<u>56.82</u>	
Ave.			57.18	

5. 3 benzyl 2,4 dibromophenylether.

Structural formula:



Crystalline form: Needles from alcohol

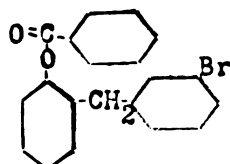
Melting point: 49-50°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO ₃	% Bromine Found	% Bromine Calcd.
1	.2454	17.46	56.92	57.01
2	.3413	24.45	<u>57.19</u>	
		Ave.	57.06	

6. Benzoyl ester of 2 hydroxy 3-bromodiphenylmethane.

Structural formula:



Crystalline form: Small white leaflets from petroleum ether.

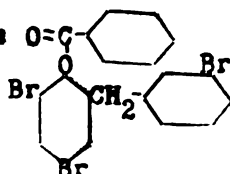
Melting point: 69-70°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO ₃	% Bromine Found	% Bromine Calcd.
1	.1964	5.40	21.99	21.77

7. Benzoyl ester of 2 hydroxy 3,5,3'-tribromodiphenylmethane.

Structural formula:



From a mixture of two samples described above.

Crystalline form: White needles from petroleum ether.

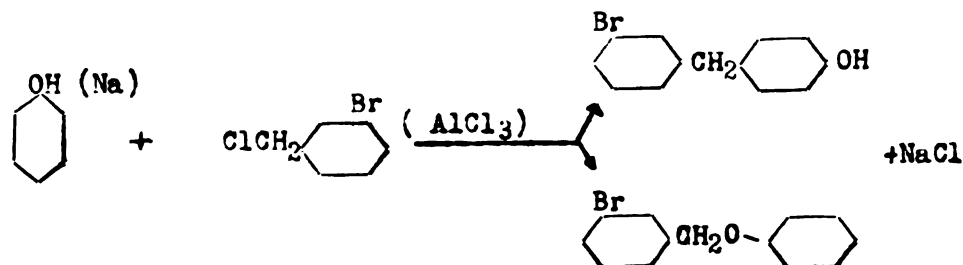
Melting point: 90-91°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO ₃	% Bromine Found	% Bromine Calcd.
1	.1373	7.95	46.32	45.85

IV - Preparation of 4 hydroxy 3'-bromodiphenylmethane by the AlCl_3 Method.

A. Preparation:



One and one-half mols of phenol were suspended in 400 cc. of petroleum ether in a condensation jar partially submerged in a water bath and fitted with an efficient mechanical stirrer. To this suspension one-half mol of m-bromobenzyl chloride was added followed by one-fourth mol of anhydrous AlCl_3 added in small portions at regular intervals over a period of from one and one-half to two hours time. Vigorous stirring took place during the addition of the AlCl_3 and was continued for two hours after the last portion of AlCl_3 had been added. The reaction mixture was allowed to stand over night to complete the reaction. During the addition of AlCl_3 and for a time afterwards, large volumes of HBr were evolved.

The complex mixture was then poured with constant stirring into a mixture of 500 grams of ice and 500 cc. of concentrated hydrochloric acid to accomplish decomposition after which it was extracted three times with 100 cc. portions of ethylether. The extraction solution was heated to 125°C . to drive off the ether and water and the residue was treated with Claisen's reagent and extracted three times with 100 cc. portions of petroleum to remove oxygen-alkylated products.

The alkaline mixture was neutralized with concentrated HCl (in the same manner given for the Claisen condensation) and extracted three times with 100 cc. portions of ethylether. Both extractions were distilled under reduced pressure after removal of the extraction solvents by evaporation.

Four condensations were carried out at various temperatures to determine the effect of the temperature on the yield of the phenol derivative and 3 bromobenzylphenylether.

The results are as follows:

First Condensation: Temperature, 25°C

Ethyl ether extract

96 grams	phenol	below 70°C/3 m.m.
7 grams	4 hydroxy 3'-bromodiphenylmethane	150-180°C/3 m.m.
15 grams	tar	above 180°C/3 m.m.

Petroleum ether extract

68 grams	m-bromobenzyl chloride	95-105°C/3 m.m.
10 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
6 grams	residue	above 160°C/3 m.m.

Second Condensation Temperature, 25°C

Ethyl ether extract

100 grams	phenol	below 70°C/3 m.m.
3½ grams	4 hydroxy 3'-bromodiphenylmethane	150-180°C/3 m.m.
10 grams	residue	above 180°C/3 m.m.

Petroleum ether extract

56 grams	m-bromobenzyl chloride	90-105°C/3 m.m.
27 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
15 grams	residue	above 160°C/3 m.m.

Third Condensation Temperature, below 15°C

Ethyl ether extract

95 grams	phenol	below 70°C/3 m.m.
21 grams	4 hydroxy 3'-bromodiphenylmethane	150-180°C/3 m.m.
15 grams	residue	above 180°C/3 m.m.

Petroleum ether extract

25 grams	m-bromobenzyl chloride	90-105°C/3 m.m.
5 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
10 grams	residue	above 160°C/3 m.m.

Fourth Condensation Temperature, below 12°C

Ethyl ether extract

93 grams	phenol	below 70°C/3 m.m.
24 grams	4 hydroxy 3-bromodiphenylmethane	150-180°C/3 m.m.
13 grams	tar residue	above 180°C/3 m.m.

Petroleum ether extract

27 grams	m-bromobenzyl chloride	90-105°C/3 m.m.
15 grams	3 bromobenzylphenylether	140-150°C/3 m.m.
5 grams	residue	above 160°C/3 m.m.

The four 150-180°C fractions containing the 4 hydroxy 3-bromodiphenylmethane were combined and re-distilled several times under a reduced pressure of 3 m.m. A constant boiling point of 169-171°C was obtained for the product which remained a liquid.

The fractions containing the 3 bromobenzylphenylether which came over at 140-150°C/3 m.m. solidified and gave a constant melting point of 36-37°C when crystallized several times out of alcohol. This compound was identical in crystalline form, boiling point and melting point with the 3 bromobenzylphenylether isolated from the Claisen condensation and was, therefore, assumed to be the same compound.

Observation of the above data will show that the temperature at which the various $AlCl_3$ condensations were run had a very great effect on the yield of 4 hydroxy 3-bromodiphenylmethane and 3 bromobenzylphenylether.

In the first two runs at which the temperature was kept at 25°C the yield of 4 hydroxy 3'-bromodiphenylmethane was low, being 7 grams (5.4%) and 5½ grams (2.7%) respectively while a yield of 3 bromobenzylphenylether was secured being 10 grams (7%) and 27 grams (21%) respectively. In the third and fourth runs where the temperature was kept in the neighborhood of 15°C the yield of 4 hydroxy 3'-bromodiphenylmethane was greatly increased, being 21 grams (17%) and 24 grams (18%). The average yield of 3 bromobenzylphenylether 5 grams (3.8%) and 15 grams (11.3%) was lower than the average yields of the same product in the first two condensations. It appears that a low temperature (below 12°C) favors the production of 4 hydroxy 3'-bromodiphenylmethane and that a higher temperature (near 25°C) retards its production, increasing the yield of the corresponding ether.

V - Proof of Structure of 4 hydroxy 3'-bromodiphenylmethane.

The method adopted for the proof of structure of this phenol derivative was similar to that employed for the compound produced in the Claisen condensation. An AlCl₃ condensation using ¼ mol of 2,6 dibromophenol, 1/8 mol benzyl chloride and 1/16 mol of anhydrous AlCl₃ was run in the same manner as the previous AlCl₃ condensations, the temperature being kept near 15°C. The following yields were obtained:

Fifth Condensation Temperature, 15°C

Ethyl ether extract

30 grams	2,6 dibromophenol	100-115°C/3 m.m.
15 grams	4 hydroxy 3,5,5'-tribromodiphenylmethane	200-210°C/3 m.m.
36 grams	tar residue	above 210°C/3 m.m.

Petroleum ether extract

No product isolated.

The fraction coming over at 200-210°C/5 m.m. immediately crystallized and was assumed to be 4 hydroxy 3,5,3'-tribromodiphenylmethane. It formed white needle like crystals in petroleum ether. After several re-crystallizations it was found to have a melting point of 106-107°C. None of the corresponding ether was isolated in this condensation.

Assuming that upon direct bromination of 4 hydroxy 3'-bromodiphenylmethane bromine would enter the two unoccupied ortho positions of the phenolic ring, a direct bromination was carried out in the cold in chloroform in the same way as described in the previous section. It was expected that 4 hydroxy 3,5,3'-tribromodiphenylmethane, the same compound that was isolated in the AlCl_3 condensation of 2,6 dibromophenol and m-bromobenzyl chloride, would be produced. The product immediately crystallized upon evaporation of the chloroform and was re-crystallized a number of times from petroleum ether. Again a great deal of difficulty was experienced in purifying the compound. After the fourth re-crystallization the product gave a melting point of 100-105°C. Six additional re-crystallizations were made, care being exercised to select the most perfectly formed crystals for each subsequent re-crystallization. A constant melting point of 106-107°C was finally attained. The compound had the same crystalline form and melting point as the 4 hydroxy 3,5,3'-tribromodiphenylmethane prepared in the AlCl_3 condensation and was assumed to be the same substance.

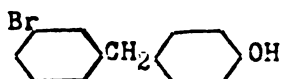
As Fayerweather (Master's Thesis, M.S.C., 1932) and Marfield (Master's Thesis, M.S.C., 1930) had been able to isolate a small amount of the ortho substituted phenol from the para substituted compound in his AlCl_3 condensation, the difficulty encountered in the purification of the 4 hydroxy 3,5,3'-tribromodiphenylmethane was attributed to the presence of a small amount of the ortho

substituted phenol in the 4 hydroxy 3'-bromodiphenylmethane used for bromination. The nearness of the boiling point of the two compounds made their separation by fractional distillation impossible.

As a further check on the identity of the 4 hydroxy 3'-bromodiphenylmethane and its phenolic derivatives the benzoyl esters of these compounds were prepared and analyzed. The method used were the same as those employed for the compounds prepared by the Claisen reaction, i.e. the method of (Zinborn and Holland, A., 501, 95; 1898) methods of (Org. Chem.; Porter, Stewart and Branch; page 181-182) and the Parr Bomb analysis (J. Am. Chem. Soc.; 39, 2069; 1917). The tabulated results are as follows:

1. 4 hydroxy 3'-bromodiphenylmethane.

Structural formula;



Crystalline form: Liquid

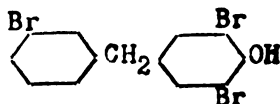
Boiling point: 169-171°C/5 m.m.

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO ₃	% Bromine Found	% Bromine Calcd.
1	.2824	10.95	31.02	30.39
2	.2629	10.12	<u>30.79</u>	
Ave.			30.90	

2. 4 hydroxy 3,5,3'-tribromodiphenylmethane.

Structural formula:



Crystalline form: White needles from petroleum ether.

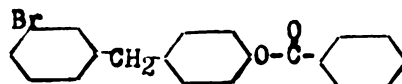
Melting point: 106-107°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO_3	% Bromine Found	% Bromine Calcd.
1	.2902	20.85	57.47	57.01
2	.2419	17.42	<u>57.65</u>	
Ave.			57.56	

3. Benzoyl ester of 4 hydroxy 3-bromodiphenylmethane.

Structural formula:



Crystalline form: Fine white needles from petroleum ether

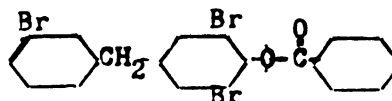
Melting point: 97-98°C

Analysis:

Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO_3	% Bromine Found	% Bromine Calcd.
1	.1680	4.63	22.04	21.77

4. Benzoyl ester of 4 hydroxy 3,5,3'-tribromodiphenylmethane.

Structural formula:



Crystalline form: Elongated leaflets from petroleum ether.

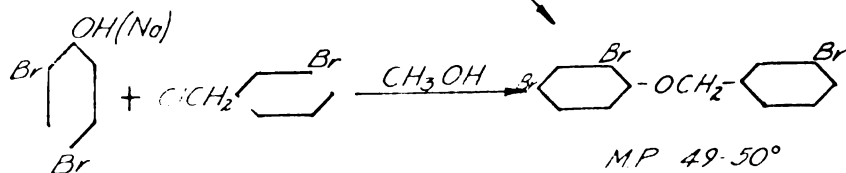
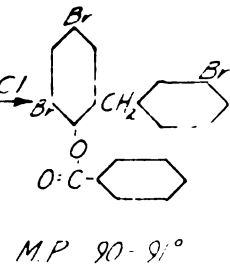
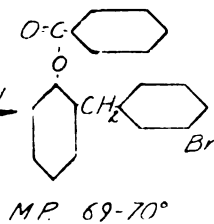
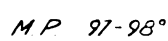
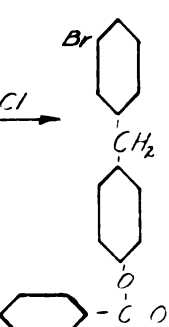
Melting point: 131.5-132.5°C

Analysis:

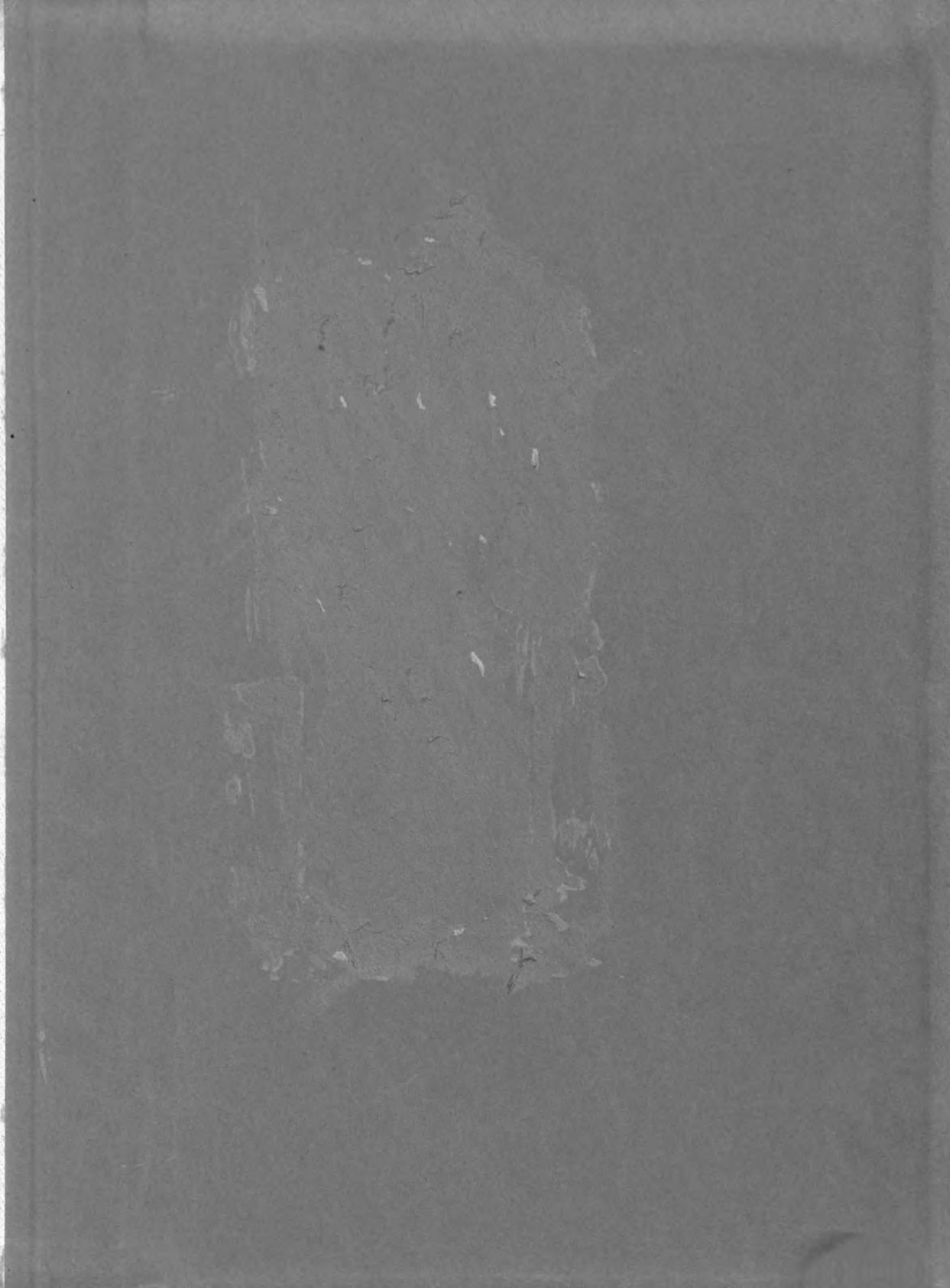
Sample	Wt. of Sample	cc. $\frac{1}{10}$ N. AgNO_3	% Bromine Found	% Bromine Calcd.
1	.2095	12.29	46.93	45.85
2	.1914	11.19	<u>46.68</u>	
Ave.			46.85	

VI - Summary

1. 2 hydroxy 3'bromodiphenylmethane and 4 hydroxy 3'bromo-diphenylmethane and derivatives have been prepared and identified.
2. Bromine was found to enter only the unoccupied ortho and para positions of the phenolic ring of 2 hydroxy 3'bromo-diphenylmethane and 4 hydroxy 3'bromophenylmethane.
3. Evidence of ortho substitution in the aluminum chloride condensation of 3 bromobenzyl chloride and phenol was noted but the compound was not isolated.
4. Equilibrium was found to exist between the 2 hydroxy 3'bromodiphenylmethane and the 3 bromobenzylphenylether during their formation in the Claisen reaction.
5. Temperatures below 12⁰C were found to favor the formation of the phenol derivative by the aluminum chloride method.

c1ccccc1C(=O)Oc2cc(Br)ccc2





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