

# PLACE IN RETURN BOX to remove this checkout from your record. TO AVOID FINES return on or before date due. MAY BE RECALLED with earlier due date if requested.

DATE DUE	DATE DUE	DATE DUE
-		
	<u> </u>	

6/01 c:/CIRC/DateDue.p65-p.15

Some Chlore Derivatives

of

the Benzylphenols

## Some Chloro Derivatives of Benzylphenols

Ву

Wayne Noel Headley

Thesis

Submitted to the Faculty of Michigan State

College of Agriculture and Applied Science in Partial

Fulfillment of the Requirements for the Degree of Master

of Science.

## Acknowledgment

The writer wishes to express to Dr. R. C. Huston his sincere appreciation for assistance and inspiration received during this work.

## Contents

	Page
Historical	6-
(1) The Work of Claisen ,	1
(2) The Work of Friedel and Crafts,	5
(3) Theory of Action of Aluminum Chloride,	7
(4) The Work of Huston,	11
(5) Chlorination of Benzene Derivatives,	13
(6) Chloro Derivatives of the Benzylphenol	
Ethers,	17
The Problem Defined,	18
Experimental,	19
Summary,	32
Photographs, 33-	·36
Scheme of Condensation	37

Some Chloro Derivatives of the Benzylphenols

#### 1. The Work of Claisen

claisen (Ber., 20, 646-650; Claisen and Low-man, Ber., 20, 651-654) in 1877 published his first work on the effect of sodium, sodium ethoxide, sodamide, or similar agents in effecting condensations between carboxy-lic esters with a ketone or carboxylic esters. His theory of the mechanism of this reaction as applied to the synthesis of acetoacetic ester may be illustrated as follows:

The importance of this work to the present problem is in Claisen's (Ann. 442,212) application of this method to the preparation of benzylated phenols. In this method, sodium phenolate is first prepared and dissolved, or suspended in a suitable medium and treated with the benzyl halide. The resulting product is a mixture of the possible mono or di-benzyl phenols, and an ether which may be removed by shaking the methyl alcoholic potassium hydroxide solution of the phenols with petroleum ether.

--• • •

·--

Claisen states that while the ether is the product one would expect to be formed, the benzyl phenol formed is the result of ring alkylation, when one would naturally expect the benzyl group to take the place of the metal atom displaced. His discussion of the ortho substitution is based on Michael's Theory (J. pr. 31, 486; 46, 189) of the reaction between silver cyanide and methyl iodide. This as applied to the reaction of a sodium phenolate and an alkyl halide may be illustrated as follows:

The most important factor in this reaction is the medium in which the reaction occurs. A dissociating medium yields mainly the ether, while a non-dissociating medium yields mainly the ring alkylation product.

That the nature of the medium is the main factor in determining oxygen or carbon alkylation is further supported by Claisen and Tietze (Ber., 58B, 275,1925) who showed that when alkali phenolates were treated in non-dissociating media with unsaturated alkyl halides, such as allyl, there is obtained almost entirely carbon alkylation. Also by Ulaisen, Kremers, Rath and Tietze (Ann. 442, 210) who found from the condensation of sodium p-cresylate and allyl bromide in methyl alcohol, 90% oxygen alkylation while with benzene

•

sing pital in the sile in the contract of the sile of This will be a sum of A . The A is the A in A is the A in A is the A in 

as the medium, 30% oxygen and 60% carbon alkylation.

K. von Auwers, G. Wegener, and Th. Bohr (Chem. Z entr. 1, 2347-8, 1926) explain the formation of carbon substituents from salts of keto-enols and alkyl halides. They discuss the following hypotheses:

- (1) "The initial formation of addition products with subsequent splitting" (Michael).
- (2) "The initial formation of normal oxygen derivatives, with rearrangement of these into carbon derivatives".
- (3) "The separation of the metal as a metallic halide, formation of free alkyl and enol 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 radical. (Wislicinus)

depends upon its character and upon the alkyl ation agent. Saturated alkyl halides promote the formation of oxygen derivatives, and allyl or benzyl halides promote the formation of carbon derivatives. These facts are well explained by the first hypothesis, which is also used by Claisen as the basis of his theories. The second hypothesis is inadequate, for it is not comprehensible why an oxygen derivative should

•

 $\mathcal{L}_{i,j} = \mathcal{L}_{i,j} = \{\mathbf{e}_i, \mathbf{e}_j\} \in \mathcal{L}_{i,j} = \{\mathbf{e}_i, \mathbf{e}_j\} \in \mathcal{L}_{i,j}$ 

 $(A_{ij} + A_{ij} +$ 

. Programme to the control of the co

**:** 

be transformed into a carbon derivative in benzene more easily than in alcohol. The third hypothesis, states that the oxygen derivatives should be formed with allyl and benzyl radicals because of their great reactivity. It is assumed that great reactivity indicates a large requirement for valence, while the opposite view is just as probable and is upheld by the facts that allyl and benzyl groups are distinguished by their slight valence requirements and so carbon substitution may be expected. Claisen's views also confirm this, for he states that unsaturation in the allyl and benzyl radicals result in a comparatively loosely held halogen, and furthermore that reaction mediums such as toluene exert a loosening effect on the valence bonds between the alkyl or benzyl radical and the halogen.

M. Busch (Z. Angew Chem. 38, 1145-6, 1925) states that the tendency of benzyl radicals toward carbon alkyletion of phenols increases with the increasing substitution of the methane carbon.

M. Busch and B. Knoll (Ber., 60 B, 2243-57, 1927) found that diphenylbrommethane with phenol, with or without a solvent in the presence of heat, gives the para hydroxy carbon derivative, while sodium phenolate under similar conditions gives the corresponding ortho derivative.

K. von Auwers and Th. Bohr (Ber. 61B, 408-16, 1928) state that the halides of such radicals as are characterized by a small affinity consumption, such as allyl and benzyl, yield chiefly carbon derivatives; while true alkyls like ethyl and propyl, favor the formation of oxygen derivatives.

## 2. The Work of Friedel and Crafts

The synthesis of organic compounds received an impetus in 1876 when Friedel and Crafts (Compt. rend., 84, 1392-95) in a study of the action of aluminum and its salts on organic substances, discovered the remarkable condensing powers of the aluminum halides. They investigated the condensation of alkyl halides and aromatic hydrocarbons in the presence of aluminum chloride. Further work has shown that aluminum chloride may be put to the most diverse applications and consequently the reaction has been used very extensively.

The mechanism of the Friedel-Crafts reaction deserves some attention here on account of its general application to aluminum chloride condensations.

Boeseken (Rec. trav. chim., (a) 19, 19-26, 1900; (b) 20, 102-106, 1901; (c) 22, 301-314, 1903; (d) 23, 98, 1904, (e) 30, 148-150, 1911) has put forward the view that the reactions take place according to the following scheme:

 $R C O Cl + AlCl_{\bullet} = R C O Cl, AlCl_{\bullet}$ 

R C O Cl,  $AlCl_8 + R'H = R C O R'$ ,  $AlCl_8 + HCl$ 

R C O R',  $AlCl_8 + xH_2O = R C O R' + AlCl_8 + xH_2O$ where R'H represents an aromatic hydrocarbon or one of its

derivatives.

Schaarschmidt (Z. Angew. Chem. 37, 286-8, 1924) bases his explanation on the activation of the aromatic hydrocarbon (by the aluminum chloride) effecting a loosening of the bonds of the organic halogen compound. A primary complex is formed consisting of metallic chloride, hydrocarbon, and addend, in which the metallic chloride is held by auxiliary valences

1 W ...

•

•

•

The second control of the secon

The second second

grand and grand the control of the state of Berlin and the state of the sta

• •

and the addend by ordinary valences. The stability of this complex depends upon the division of the inner valences and may pursue one of two courses, - the "mol course" or the "catalytic course".

Several other theories have been advanced, but all are based on the formation of an addition compound between aluminum chloride and the organic material. The reality of these intermediate addition products of aluminum chloride has been established by Gustavson (Ber., 11, 2151, 1878) who isolated an addition product of benzene, AlCla, 3CeHe; benzene and ethyl chloride, AlCla.(CeHe)2.3CeHe, (Comp. rend. 136, 1065, 1903; 140, 940, 1905). The work of Gustavson has been confirmed by Schleichen (J. pr. Chem., 11, 105, 355, 1922).

Other workers who have shown the presence of addition compounds with aluminum chloride are Boeseken, (Rec. trav. chim., 20, 102-106, 1901; 23, 98-109, 1904). Kronberg, (J. pr. chem. ii, 61, 494-496, 1900) and Menschutkin (J. Ruso. P Nys. Chem. Soc., 41, 1053, 1089; 1909).

stated that their reaction is usually impossible in the presence of compounds containing the group OH or OR.

.

e de la companya de l La companya de la companya de

•

## 3. Theory of Action of Aluminum Chloride

Agents commonly used in effecting condensations are: - zinc chloride, sulphuric acid, sulphuric and acetic acids, hydrochloric acid, ferric chloride, and aluminum chloride.

Condensation processes are usually divided into two classes (Cohen-Part I, P 196):

- (1) Those in which the combining molecules are induced to unite by being rendered artifically unsaturated as the result of withdrawing certain elements.
- (2) Those already unsaturated which combine either spontaneously or with help of a catalyst.

The exact nature of the effect of aluminum chloride in condensations is not definitely known. The possible action may be one or a combination of all of the following general theories:

- (1) catalytic action
- (2) intermediate compounds
- (3) dehydration

explained by Sabatier (catalysis in organic chemistry, p 794). His theory is the temporary production of a combination between the chloride and the organic substance. The latter would react immediately on the halogen derivative, yielding the product and regenerating the chloride. The use of large amounts of aluminum chloride in effecting condensations has caused some

**:** 

•

doubt to the catalytic action of aluminum chloride. This, however, is due to the tardiness of the reaction in some cases and the desire to hasten it by formation of large amounts of the required intermediate compound, or in other cases, to the fact that aluminum chloride is withdrawn from the reaction by the formation of stable compounds.

J. Boeseken (Rec. trav. chim. 30, 148-50) describes the catalytic action of aluminum chloride as one made possible by the loss of free energy.

Norris (Ind. Eng. Chem., 16, 184,1924) has studied the catalytic action of aluminum chloride between triphenyl methyl chloride and ethyl ether and other similar reactions.

The action of aluminum chloride informing intermediate addition compounds has been previously discussed in the work of Gustavson, Boeseken and Menschutkin.

The dehydrating action of aluminum chloride is illustrated by the work of Merz and Weith (Ber., 14, 187,1881) who prepared di-phenyl ether by the action of zinc or aluminum chloride on phenols.

Scholl and See's (Ann. 394, 111-177, 1912) found that, by means of anhydrous aluminum chloride, aromatic nuclei can be satisfactorily united, particularly in case of letones where elimination of hydrogen is accompanied by formation of new rings. By heating phenyl alpha naphthyl ke tone and anhydrous aluminum chloride at 150° for two and one-half hours they obtained benzathrone.

•

:

•

In 1901 Jaubert (compt. rend. 132, 841-842) and Graebe (Ber., 34, 1778-1781) independently prepared aniline by the action of hydroxylanine on benzene in the presence of aluminum chloride.

Frankforter and Kritchevosky (J. Am. Chem. Soc. 36, 1614-29, 1914) condensed pentane, benzene, resorcinol, etc., with chloral. Frankforter and Kokatnur (J. Am. Chem. Soc. 36, 1529, 1914) worked on the action of trioxymethylene on various hydrocarbons. This work was also extended by Frankforter (J. Am. Chem. Soc. 37, 385, 1915 to include polycyclic hydrocarbons. Nametkin and Kursanov (J. Russ. Phys.-Chem. Soc., Chem. Pt. 60, 917-20,1928) have prepared diphenylmethane and di-benzyl-benzene by the dehydrating action of phosphorus pentaoxide on benzyl-alcohol in the presence of benzene.

Other workers have used various condensating agents to split off hydrogen chloride. The earliest of them was probably E. Paterno (Gazz. Chim. ital. 1, 589; ii, 1-6) who, in 1872 prepared benzylphenol and benzyl anisol respectively by the action of benzyl chloride on phenol and anisol in the presence of zinc. In the following year Paterno, in connection with Fileti, (Gazz. Chim. ital. 5, 381-833) prepared benzyl phenol by means of acetic and sulphuric acids, also in 1879, in connection with Mazzara (Gazz. Chim. ital. 8, 303-305) he prepared benzylated cresol in the presence of zinc turnings.

Perkins and Hodgkenson (J.C.S. 37, 721,1880) prepared benzyl phenyl acetate by the condensation of benzyl chloride and phenyl acetate in the presence of aluminum chloride.

:

•

:

• •

¢

Peratoner and Vitali (Gazz. chim. ital. 28, 197-240, 1898) treated benzylphenol prepared by Paterno's method with sulphamyl chloride and obtained a chlor-benzylphenol. They were working with Nef's views on the addition of halogen and subsequent elimination of hydrogen chloride, according to which the chlorine atom entered the hydroxypheny ring probably in the ortho position.

J. Bueseken (Rec. trav. chim. 27, 10-15) condensed dihalogen derivatives of benzene with acetyl and benzoyl chlorides in the presence of aluminum chloride.

## 4. The Work of Huston

In 1916 Huston and Friedmann (J.A.C. Soc. 38, 2527) applied the dehydrating action of aluminum chloride to the condensation of aromatic compounds. They prepared diphenylmethane by condensing benzyl alcohol with benzene in the presence of aluminum chloride. They state that the yield of the product is greatly influenced by the amounts of the reagents and the temperature. As to the mechanism of the reaction, they observed the formation of an intermediate product resembling the intermediate product of Friedel and Crafts reaction.

Two years later Huston and Friedmann ( J. A. C. Soc. 40, 785) extended this reaction to include secondary alcohols. They also studied the effect of aryl and alkyl groups upon the reaction and concluded that alkyl groups have a depressing effect (ethyl—methyl) while aryl groups, such as phenyl, have a stimulating effect.

Huston (Science 52, 206-7) applied this reaction to the condensation of aromatic alcohols and phenols, preparing benzylphenol as follows:

 $C_6H_5CH_2OH + C_6H_5OH$  Alcle  $C_6H_5CH_2C_6H_4OH + H_2O$ 

This condensation had previously been accomplished by Paterno (Gazz. chim. ital. 2, 2; Ber. 5, 288) using zinc as a catalyst; Paterno and Mazzura (ibid 8, 303) in the presence of a mixture of sulphuric and acetic acids; Paterno and Fileti (ibid 5, 381); with zinc chloride by Liebman (Ber. 15,

•

• • • •

• • •

• •

: 

fix z 

 $(1.11, 2.11) \times (1.11) \times (1.1$ 

Huston (J. A. C. Soc. 46, 2775, 1924) condensed benzyl alcohol with phenol, anisol and phenetol in the presence of aluminum chloride. He also condensed benzyl chloride with phenol in presence of aluminum chloride and states that no definite data (c. f. Millers Chem., 5th Edition, revised by Armstrong and Groves, Part III, P 772) on this condensation is found in the literature.

Huston and Sager (J. A. C. Soc. 48, 1955, 1926) applied the dehydrating effect of aluminum chloride to saturated and unsaturated aliphatic and aromatic alcohols with benzene, and concluded:

- (1) that saturated aliphatic alcohols up to and including amyl alcohol do not react.
- (2) that unsaturated aliphatic alcohols, as allyl, do react.
- (3) that of the alcoholic derivatives of the aromatic hydrocarbons, only those having the hydroxyl group on the carbon atom adjacent to the ring react.

Huston, Lewis and Grotemut (J. A. C. Soc. 49, 1365, 1927) extended the series of condensation of secondary alcohols with benzene to include that of secondary alcohols with phenol, in the presence of aluminum chloride. They also found additional evidence of the tendency of unsaturation on the alpha carbon atom to increase the yield of the product.

#### 5. Chlorination of Benzene Derivatives

chim. ital. 4, 305, 446, 1874) Hubner, (Ber. 8, 873, 1875) and Nolting (Ber. 9, 1797, 1876) concluded that acid groups direct a new substance to the meta positions, while the halogens, the hydroxyl group, and basic groups direct to the ortho-para positions. This hypothesis has been extended by Armstrong (J. C. Soc. 51, 258, 1887); Crum-Brown and Gibson, (J. C. Soc. 61, 367, 1892); Vorlander (Ann. 320, 122, 1902) and Holleman.

For the purpose of this paper the work of Halleman ("Die directe Einfuhrung von substituenten in der Benjolkern" 1910) is sufficient. He states that the rule of Beilstein (Handbuch der organischen chemie, II, 10; 3 edition) can hardly be described as very helpful. "If a substituent C enters into a compound CoHaB, both A and B exert an influence, but the group (A or B) whose influence predominates directs C to the place it will occupy". He has suggested that if we knew the velocities of the two reactions -

 $C_{e}H_{b}A + C = C_{e}H_{4}AC$ 

andi

 $C_6H_5B + C = C_6H_4BC$ 

we might be able to predict the course of the reaction.

 $C_6H_4AB + C = C_6H_3ABC$ 

and the ratio of the isomerides formed. He assumes in this postulate that A and B keep their "directing influence" when the second substituent is introduced or that the "directing influence" of each is changed proportionally. He has shown

and the second of the second o

that the introduction of a third substituent into a disubstituted benzene derivative reveals for ortho-para directing substituents the following diminishing series:

 $OH > NH_R > I > Br > C1 > CH_S$ 

and similarly for the meta directing substituents:

COOH>SOgOH>NOg

With this knowledge and the quantitative ratio in which the isomerides are formed, it is possible to predict the action of C on a compound CoH4AB.

A partial list of workers in this field follows:

#### 1. Directive influence

- a. Helleman Ber. 44,725, 2504, 3556, 1911; J. Am. Chem. Soc. 36, 2495, 1914; Chem. Rev. 1, 187, 1924.
- b. Fry J. Am. C. Soc. 36, 1035-47; ibid 37, 855.
- c. Prins Chem. Weckblod 15, 571-80, 1918.
- d. Fraser and Humphries Chem. News 126, 161-8, 241-5, 257-61, 1923.
- e. Pastak Rev. glu. sci. 36, 70-6, 1925.
- f. Blanksma Rev. trav. chim. 21, 282, 1902.
- g. Pfeiffer and Wiezimer Ann. 461, 132-34, 1928.

•

· Sureman in the second second

## 2. Mechanism

- a. Boeseken
  Proc. Acad. Wetenschappen 14, 1066-81.
- b. Barnett and Cook Rec. trav. chim. 43, 262-5; 897-8, 1924.
- c. Prins
  Rec. trav. chim. 44, 166-72, 1925.
- d. von Alphen Rec. trav. chim. 46, 799, 1927; ibid 47, 169-73, 1928.
- e. Blanksma Rec. trav. chim. 23, 200, 1904.
- f. Vorlander Ber. 58, 1893, 1925.

A careful review of literature has shown no very definite data regarding the chlorination of

(c.f. Peratoner and Vitali, Gazz. chim. ital. 28, 197-240, 1898). However, Zinche and Wilhelm (Ann. 1904, 334, 367, 385) have brominated 4-hydroxydiphenyl methane yielding 3:5 dibrom-4-hydroxy diphenylmethane,

$$CH_2 \bigcirc B_r$$

but they do not state any proof of this structure. Also van Alphen (Rec. trav. chim. 46, 799-812, 1927) has brominated 4-hydroxy triphenylmethane yielding

•

•

to 🚅 🛬 🛬

e was the second of the second

which he gives the name of 2:6 - dibrom 4-hydroxytriphenylmethane. His designation of the position of the bromine
atoms as 2:6 is misleading and evidently a mistake, for
with the hydroxyl group in the 4 position the bromine atoms
as illustrated would occupy the 3:5 positions. His proof
of this structure is that a similar brominated product could
not be obtained from bromine and 2:4:6 tri (diphenylmethyl) - phenol, so it must be assumed that bromine is
introduced into these positions.

The above work lends confirmation to the hypothesis that in halogenation of groups of this nature the halogenation enters first into the group containing the hydroxyl group, but no definite proof has been given. An attempt to determine the correctness of this theory will be part of the object of this paper.

6. Chloro Derivatives of the Benzyl-Phenyl Ethers

A careful review of literature reveals only a few preparations of such derivatives. Sintenis (Ann. 161, 345) prepared benzylchlorophenyl ether by adding chlorine to an alcoholic solution of the ether in which freshly precipitated mercuric oxide was suspended. The bromoderivative was also similarly prepared.

Auvers (Ann. 1907, 357, 85-94) has prepared 2, 4, 6 tri-chlorphenyl benzyl ether by boiling the substituted phenol with benzyl chloride and sodium ethoxide in an alcoholic solution. He has also prepared the corresponding tri-bromo derivative and two di-brom derivatives by the same method.

Barv (Quant. J. Indian Chem. Soc. 3, 101-4, 1926) prepared by the means of leucotrope, the following ethers:

- (1) Benzyl o-chlorophenyl ether
- (2) Benzyl m-chlorophenyl ether
- (3) Benzyl p-chlorophenyl ether
- (4) Benzyl, 2, 4 di-chlorphenyl ether

Raiford and Colbert (Proc. Iowa Acad. Sci. 31, 287-8, 1924) have worked on the activating and retarding influence of groups in rings on the formation and reduction of ethers.

#### The Problem Defined

The object of this work may be briefly outlined as follows:

- (1) To determine the influence of chlorine in the benzyl and phenyl rings in regard to condensations of their derivatives.
- (2) To establish definitely that o-substitution accompanies the p-substitution in condensations with aluminum chloride and the ratio of such substitution.
- (3) To establish the position of halogens entering into the groups;

#### Experimental

experiments was prepared by first making para chlorotoluene according to the method of Marvel and Mc. Elvain
(Org. Syn. Vol. 3, pp. 33, (1923)). This was then
chlorinated according to the procedure used by Jack son
and Field (Ber. 11, 904, (1878)). The product formed
compared exactly in properties with those given in the
literature.

The first condensation attempted was that of chlorobenzyl chloride and phenol in the presence of aluminum chloride. The method used was similar to that of Huston's (J. A. C. Soc., 46, 2775, 1924) preparation of benzyl phenol, which procedure is quoted from the Journal. "Fifty grams of benzyl chloride and fifty grams of phenol were added to 100 cc. of petroleum ether in which they completely dissolved; thirty grams of aluminum chloride was then added in small portions. The reaction was quite vigorous and was retarded by placing the vessel in cracked ice. The temperature rose to 350. Two layers were formed, the lower one of which was dark red and rather viscous.

After twenty-four hours, the entire mixture was decomposed;

"The third refraction gave 28.4 g. at 150-2000; 26 g. at 120-1800 (4 m); 10.2 g. at 180-2300 (4 m); and 21.2 g. of residue. The fraction obtained at 120-1800 was para benzyl phenol".

In the condensations carried out the reactants were of the following proportions:

•

• 5 5 6 6 6 6

are the second of the second o

 $(1-\epsilon)^{-1} = (1-\epsilon)^{-1} = (1-$ 

•

•

	Mol.Eq.	Grams
Chloro-benzyl chloride	1	50
Phenol	3	87
Aluminum chloride	•5	21
Petroleum ether		200 cc.

The reaction proceded similarly to the one quoted above with the exception that the temperature remained at 18 - 20° without controlling by means of ice.

The crude condensation product was allowed to stand overnight and decomposed with ice and hydrochleric acid (1; 1).

This yielded a dark red oil which was extracted with ether and the ether extract was dried over anhydrous potassium carbonate for twenty-four hours.

The ether was distilled off and the remaining residue fractionally distilled.

#### First Fractionation

70-1500	14 m.m.	45.3 g
80-1900	6 7 11	3.5 *
180-2500	5 n n.	33.5 ×
250-320°	5-19 m.m.	16.0 *
Residue		5.7 "

•

the state of the s

 $\bullet = \{ e^{-i\theta} \mid e^{-i\theta} = e^{-i\theta} \}$ 

• •

•

Fourth Fractionation (another condensation)

60-1400	14	m.	m.	phe <b>nol</b>	47.0	g
140-1610	3	Ħ	Ħ		4.2	#
161-169°	3	11	Ħ		2.8	17
169-1900	3	11	11		24.1	**
190-2500	3	77	11		1.3	Ħ
230-2650	3	**	77		4.7	Ħ
Residue (tot	al)				16.0	**

The fraction 140-1610 and 169-1900 gave evidence of being different compounds. It was thought one fraction might be a para derivative while the other might be an orthoderivative. The fraction 140-1610 we will call compound A and the fraction 169-1900 compound B.

A condensation of chloro-benzyl chloride and phenol by Claisen's method was next carried out.

### The amounts used were:

Phen ol	14.6 g.
Chloro benzylchlorid	e 25.0 g.
Sodium	3 <b>.5 "</b>
Toluene	50 cc.

The sodium was added to a solution of the phenol in toluene, forming sodium phenolate, a white cheesy mass. This mixture was allowed to stand over night. To this was added the chloro benzylchloride and the resulting mixture heated at 150° (thermometer in oil bath) for eight hours while connected to a reflux condenser. This product was shaken out with two portions of water to remove the salt and the toluene distilled off. The residue was treated with Claisen's alcoholic potash which dissolves any free

• •

•

- · ·

•

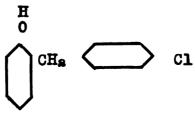
to the second se

hydroxyl groups. This mixture was shaken out with petroleum ether to remove any possible ethers and the remainder acidified. A dark red oil separated out which was taken up with ether and the ether extract dried over anhydrous potassium carbonate for twenty-four hours. The ether was then distilled off and the residue fractionated.

#### Third Fractionation

80 <b>-</b> 150o	18 m.m. phenol	5 g,
160-1760	5 m m	9 m
176-2500	5 m m	1.5 *
Residue		8 *

The fraction 160-176° was pressed between filter papers and recrystallized from petroleum ether, high test gasoline, or ligroin. The compound had a melting point of 60-61° and a boiling point of 157-158° at 3 m.m. The yield of the product in this condensation was \$5% of the theoretical. The yield, however, was increased considerably in subsequent condensations. For the appearance and characteristic growth of the crystals consult photographs, - Figures 3, 4 and 5. This compound must be:



2-hydroxy 4' chloro di-phenyl methane.

# 

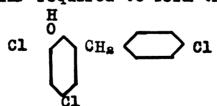
The mother liquor of the recrystallization of the 2-hydroxy 4' chlor diphenyl methane yielded a few crystals (rhombohedronal plates) having a melting point of 86.5-87.5°. There was not a sufficient amount of these for further recrystallization.

A Parr Bomb determination for chlorine carried out on the 2-hydroxy 4' chloro diphenyl methane gave the following results:

Sample	% Cl. detn.	%Cl calc.
0,2045	16.3 <b>6</b>	16.22
0.2794	16.27	16,22

The theoretical was calculated for one atom of chlorine and the experimental results bear out this statement.

The 2-hydroxy 4' chloro diphenyl me thane was chlorinated by dissolving in chloroform and passing into this solution a ten percent excess of the theoretical amount of chlorine required to form the compound.



f

The resulting compound on purification melted at 68.5 - 69.50.

The amount was to small to recrystallize further.

A condensation of 2: 4 di chloro phenol and chloro benzyl chloride was carried out by Claisen's me thod.

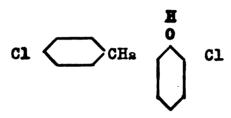
The procedure was similar to the preparation of the 2-

•

•

 $\dot{\mathcal{L}}$ 

hydroxy 4' chloro diphenyl methane previously described. The condensation yielded, as usual for this type of reaction, a petroleum ether extract containing possible ethers and the main product which when recrystallized from high test gasoline or ligroin, melted at 69.5 - 70.50. The compound from its method of preparation must have the following formula:



2-hydroxy 3:5:4' chloro diphenyl methane.

For the appearance and the manner of crystal growth consult the photograph, Figure 2.

A small amount of a compound melting at 200-210° was also obtained by fractional crystallization. This product was not identified.

A Parr Bomb determination for chloring carried out on the 2-hydroxy 3:5:4' tri chloride phenyl methane gave the following results:

Sample	s detn.	% calc.	
0.1826	37.02	37.01	
0.1939	36.85	37.01	

The theoretical percent of chlorine was calculated for three atoms of chlorine and the experimental data verifies this statement.

The melting point of the 2-hydroxy 5:5:4' tri chloro diphenyl methane of 69.5 - 70.50 checks within one degree with that obtained by chlorinating 2-hydroxy

the state of the s

•

4° chloro diphenyl methane. This is further evidence that the compound resulting from Claisen's condensation of phenol and chloro benzyl chloride is 2-hydroxy 4° chloro diphenylmethane.

We have now proven that the substitution derivative formed by a condensation of chloro benzyl chloride and phenol by the Claisem method is 2-hydroxy 4' chloro diphenyl methane having a melting point of 60-61° and a boiling point of 157-1580 at 3 m.m.

In the condensation of chloro benzyl chloride and phenol with aluminum chloride, we stated that we found evidence of two compounds; - compound A, fraction 140-161 and compound B, fraction 169-1900. The properties of 2-hydroxy 4' chlorodiphenylmethane suggest that compound A may be the ortho derivative. Therefore, compound B would be the para derivative or 4 chloro 4' hydroxy diphenyl methane.

Compound B was pressed between filter paper and recrystallized from high test gasoline or ligroin, yielding a compound having a melting point of 87 - 87.50 and a boiling point of 169-1700 at 2 m.m. For the appearance and nature of the crystal growth, consult photographs, Figure

Compound B was analyzed for chlorine by the Parr Bomb method with the following results:

sample	% Cla detn.	% Cla calc.
0.2317	15,97	16,22
0.2419	16.15	16,22

The theoretical percentage of chlorine was calculated for the compound 4 chloro 4' hydroxy diphenyl methans. The experimental results verify this assumption.

compound B was chlorinated by dissolving in chloroform and passing in a ten percent excess of the theoretical amount of chlorine required to form the compound.

The resulting oil crystallized immediately upon seeding with a crystal of 3:5:4' tri chloro 4-hydroxy methane. The crude compound was pressed between filter paper and recrystallized from petroleum ether.

Upon repeated recrystallization it melted at 55.5-580 and with the amount available could not be purified further.

A condensation of 2:6 di chloro phenol and chloro benzyl chloride in the presence of aluminum chloride was carried out in a similar manner to the condensation of phenol and chloro benzyl chloride previously described. This condensation yielded a product melting at 61.5 - 62.5°. The yield obtained was approximately 35%. The appearance, nature of crystal growth, and occurrence of the crystals in two forms may be seen by consulting the photographs, Figures 7 and 8.

•

•

•

• 

•

The method of preparation of this compound allows only one possible formula:

3:5:4' tri chloro 4-hydroxy diphenyl methane

A Parr Bomb determination for chlorine on

3:5:4' tri chloro 4-hydroxy diphenyl methane supports
the above statement by showing that three atoms of chlorine
are present.

Sample .	% Cl detn.	% Cl. calc.
0.2100	<b>3</b> 6 <b>.90</b>	37.01
0.2539	3 <b>7</b> .08	37.01

compound B on chlorination gave a product whose solubility, crystal growth, crystal structure, and melting point showed it to be crude 3:5:4' trichloro 4-hydroxy diphenyl methane. Therefore we assign the following formula to compound B.

In order to complete the evidence of the formation of compound A, several more condensations of chlorobenzylchloride and phenol were carried out in the presence of aluminum chloride. The fractions were collected after four distillations at 140-161°, 161-169° and 169-190°. These at 140-161° (compound A) were combined and upon standing a short time in the ice chest solidified. This product was pressed between filter papers and recrystallized from petroleum ether yielding a compound having a melting point of 87-87.5°.

•

We therefore gave the compound A the same formula as compound B, 4 chloro 4' hydroxy diphenyl methane, and conclude
that no ortho substitution occurred in the condensation
of phenol and chloro benzyl chloride by aluminum chloride.
The yield for 4 chloro 4' hydroxy diphenyl methane as represented by the fractions from 140 - 1900 after four distillations is forty-six percent of the theoretical.

In the preparation of the ortho derivative, 2-hydroxy 4' chloro diphenyl methane, by Claisen's method, we obtained a few crystals, rhombohderonal plates, c.f. Figure 6. These melted at 86.5 - 87.5° and we concluded that they are the para derivative, 4 chloro 4' hydroxy diphenyl methane. Para substitution with Claisen's method has previously been ortho observed by Huston and Houk who obtained a trace of para.dibenzyl cresol where only the ortho dibenzyl cresol was expected. The occurrence of 4 chloro 4' hydroxy diphenyl methane in two forms can be seen by consulting the photographs, Figures 1 and 6.

The petroleum ether extract of the condensation of phenol and chloro benzylchloride by Claisen's method was concentrated and fractionally distilled. The fraction 100-1650 at 6 m.m. of 3.9 g. solidified and when recrystallized from alcohol gave a compound melting at 85.5-86.50. This was expected from Claisen's theories to be

4 chloro-benzyl phenylether.

In order to obtain further evidence of the structure of this compound a condensation of chloro benzyl chloride and sodium phenolate was carried out in a dissociating medium, methyl alcohol. The resulting compound was found to be identical with that obtained as a by-product in Claisen's condensation.

A Parr Bomb determination for chlorine on this compound gave the following results:

Sample .	% Cl detn.	% Cl calc.
0.2153	15.80	16.22
0.2514	15.87	16.22

The low percentage of the experimental is probably due to the difficulty of obtaining the crystals in a pure state. The theoretical was calculated for the compound 4 chlorobenzyl phenyl ether and the experimental confirms the formula as containing one atom of chlorine.

With the evidence offered by the two methods of preparation and the analysis, the formula of the compound may be given as.

## 4 chlero-benzylphenylether.

The petroleum ether extract of the condensation of 2:4 di chlorophenol and chloro-benzylchloride by Claisen's method was concentrated and fractionally distilled. The fraction 120 - 210° at 5 m.m. of 2.4g. solidified in the ice chest and on recrystallization yielded a compound melting at 64.5 - 65.5°. This was expected from Claisen's theory to be.

• • • •

•

 $(\mathcal{M}_{\mathcal{A}}, \mathcal{M}_{\mathcal{A}}, \mathcal{$ 

•

:

$$C1$$
  $CH_{8}-0 C1$   $C1$ 

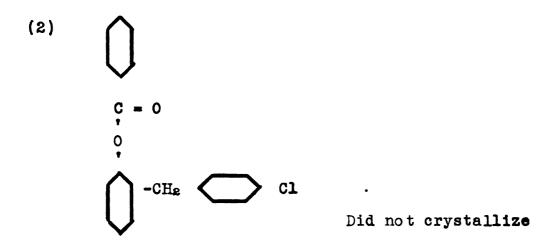
4 chlorobenzyl 2: 4 dichlorophenylether.

The compound 4 chloro-benzyl 2: 4 di chloro-phenylether was also prepared by condensing the sodium salt of 2: 4 dichlorophenol and chloro benzyl chloride in a dissociating solvent, methyl alcohol. The melting point was 64.5 - 65.5°, showing that two methods yield identical compounds.

A Parr Bomb determination for chlorine on 4 chlorobenzyl 2: 4 dichlorophenylether, gave the following results:

This was the total sample of sufficient purity for analysis, and while the experimental is low, there can be no doubt to the amount of chlorine present in the compound.

The benzoyl derivatives of (1) 4 chloro 4'
hydroxy di phenylmethane, (2) 2-hydroxy 4' chloro di phenyl
methane, (3) 3:5:4' tri chloro 4-hydroxy di phenyl methane,
and (4) 2-hydroxy 3:5:4' tri-chloro-diphenylmethane were
prepared by dissolving 2 g, of the phenols in pyridine and
adding a ten percent excess of the calculated amount of benzoyl
chloride. The following formulas indicate the compounds respectively formed:



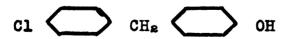
m.p. 116-117°

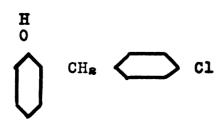
#### Summary

- (1) A comparison of the yields of 4 chlor4' hydroxy diphenyl methane and 4 hydroxy di phenyl methane
  (Huston, J.A.C. Soc. 46, 2775) shows that the introduction
  of a chlorine atom increases the activity of the benzyl
  group. A ten percent larger yield being obtained.
- (2) Were not able to establish the presence of ortho substitution in the aluminum chloride condensations.
- (3) Prepared and identified the following compounds:
  - a. 4 chlor-4' hydroxy diphenyl methane
  - b. 2 hydroxy 4' chlor diphenyl methane
  - c. 4 chlor benzyl phenyl ether
  - d. 2 hydroxy 3:5:4' tri chlor diphenyl me thane
  - e. 4 chlor benzyl 2 : 4 di chlor phenyl ether
  - f. 4 hydroxy 3:5:4' tri chlor di phenyl methane

A careful review of literature has not shown the previous preparation of any of these compounds. For their formulas consult "Scheme of Condensation".

(4) Chlorine entering into the following groups,





first substitutes in the ring containing the hydroxyl.

• • • •

•

•

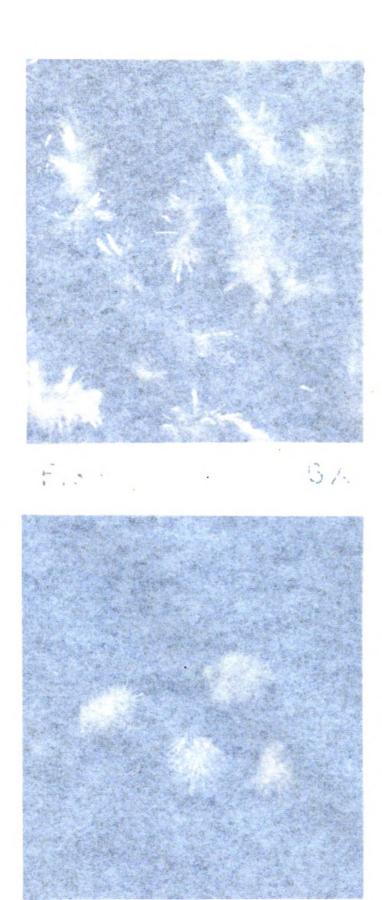


Fig. 2

101



Fig.1

6 X



Fig. 2

10 X

•



Fig. 3

4 X

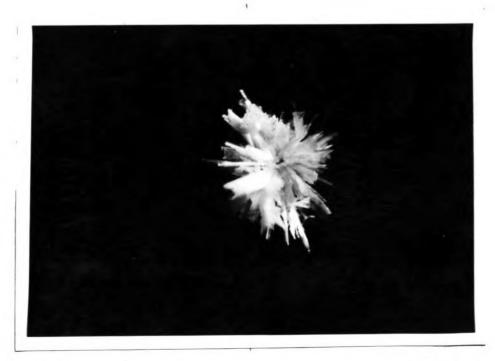


Fig. 4

4 X

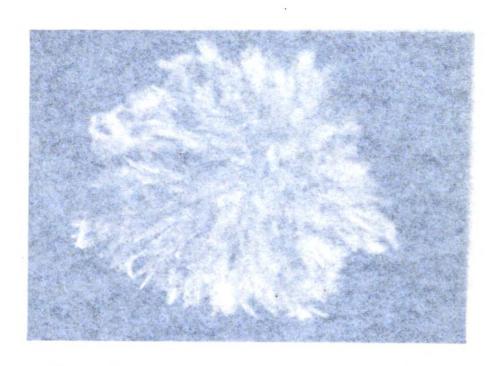


Fig. 5



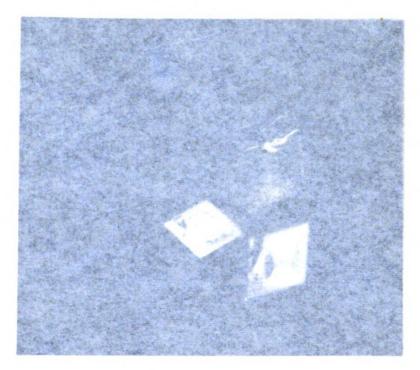


Fig.6

TX



Fig. 5





Fig.6

4 X

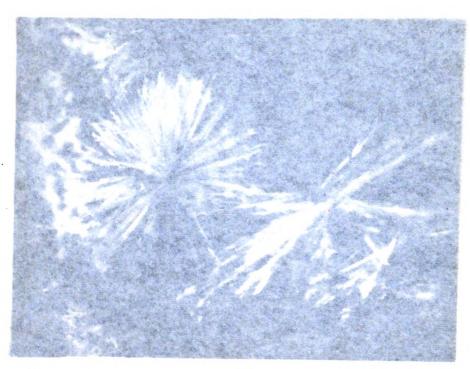
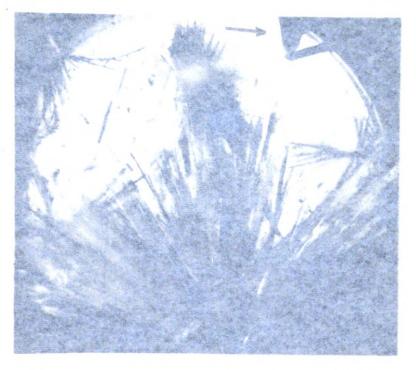


Fig. 7



Fige

9 X



Fig. 7

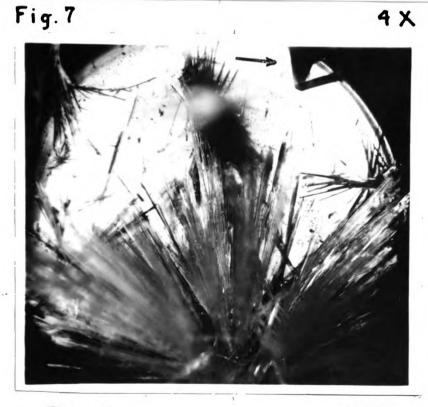


Fig.8

4 X

# Scheme of Condensation

