THE ACTION OF SULFURIC ACID

ON

"D.D.T." AND SOME RELATED COMPOUNDS

and

THE SYNTHESIS AND DERIVATIVES OF

1-4 CHLOROPHENYL 2,2,2-TRICHLOROETHANOL

Submitted
by
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TABLE OF CONTENTS

PART I

HISTORICAL SECTION

A BRIEF REVIEW OF SOME MOLECULAR REARRANGEMENTS OF ONE-TWO CARBON-CARBON SHIFTS, OF ALKYL OR ARYL GROUPS CATALYZED BY ELECTROPHILIC REAGENTS

(1) Introduction

The term "rearrangement" refers to an irreversible reaction which produces a change in the structural arrangement of a molecule. "Essentially[1] the processes of rearrangement are basically in every case accompanied by intramolecular oxidation and reduction. This oxidation reduction mechanism involves electron transfers within the molecule and consequently is best explained on the basis of an electronic mechanism. This concept was first advanced by Jones[2] and later expressed by Stieglitz[3], Robinson[4] and Ingold[5]."

Molecular transformations are relatively rare[6] because simple adjustments that can occur within a single molecule have usually been accomplished in the process of synthesis. However, molecules may, under the influence of some reagent, enter a chemical reaction in which the electron density of the carbon atom containing the reactive group is greatly increased or decreased. To compensate for this electronic displacement electrons or groups migrate to the low electron density carbon atom and reestablish equilibrium. Often these shifts are the result of degradation reactions such as the elimination of water or hydrogen halide. Yet addition reactions to olefins, replacement reactions - as in the transformation of amines to alcohols - as well as

reactions involving no change of total molecular formula, can also be accompanied by intramolecular rearrangements.

Intramolecular rearrangements are usually looked upon with suspicion by the organic chemist; as a result of this, organic chemists have attempted to use all manner of mechanisms to avoid admitting the possibility of carbon-carbon bond rupture with a one-two shift of an alkyl or aryl group. Though many examples of rearrangements have accumulated, it has not been until relatively recently that chemists have realized that all these intramolecular transformations have a common basis and are not each in themselves a separate phenomenon.

F. C. Whitmore[7] has advanced the concept that all rearrangements involving change in the carbon skeleton may be accounted for on the hypothesis that a carbonium ion is formed and an alkyl group, together with its bonding pair of electrons, shifts from a neighbouring carbon atom to the carbonium carbon. The direction of the shift is usually such that the new carbonium carbon carries a greater number of alkyl or aryl groups than the old one. Thus in a system $:\overset{..}{A}:\overset{..}{B}:X$, the probability of rearrangement of the molecule by removal of X is greatest when A has a tertiary attachment. The products formed by the removal of X may be (a) normal, (b) abnormal, (c) olefinic. The olefinic product may be a normal or abnormal one.

In this review examples are shown of rearrangements brought about in a variety of different compounds, through the influence of various electrophilic reagents. Not all known rearrangements have been included which involve one-two, carbon-carbon, shifts of alkyl or aryl groups. Such rearrangements as occur in terpenes, heterocycles,

steroids, etc., have been excluded, as well as acyl wanderings, many ring expansions and contractions. A separate treatment of the transformation of substituted ethylene oxides has not been reported in this outline because it is believed that their rearrangement is essentially the same as the "pinacol-pinacolone" or glycol conversion.

It is thought that the number of examples, enumerated in this review, are sufficient to give support as evidence to an intramolecular transformation which occurred in the work to be described. In this outline are given only rearrangements which have been catalyzed by electrophilic reagents (reagents which are electron seeking in order to fill their electron shells). Such electrophilic reagents are sulfuric acid, acetic acid, phosphorus pentoxide, aluminum chloride, zinc chloride and others. A few examples of transformations brought about by heat alone are also described.

In general all rearrangements go through a carbonium ion mechanism and in many cases it is possible to postulate reasonable intermediate transformation steps. However, in the Jacobsen and Friedel Crafts reactions, which involve inter and intramolecular migrations of alkyl or aryl groups, the intermediate steps are not as yet understood and a general mechanism cannot be advanced.

Of the many rearrangements that exist it is essential that some classification be adopted for simplification. The "pinacol-pinacolone" and alcoholic dedydrations are probably the most studied reactions in the field of rearrangements. Because of this extensive study it is possible to break down the above rearrangements into subdivisions.

Intramolecular rearrangements are less numerous in other fields of
chemistry and can usually be classified under a simple single heading.
The following table demonstrates the classification adopted for this
review.

(2) General Historical Review of Rearrangements

Class I   Pinacol-Pinacolone Rearrangements

(A) One-Two Glycols

1) True Pinacol $R_2C(OH)(HO)CR_2 \longrightarrow R_3C-COR$

2) Semipinacol $R_2C(OH)(HO)CHR \longrightarrow R_2CH-COR$

3) Semihydrobenzoin $R_2C(OH)(HO)CHR \longrightarrow R_3C-CHO$

4) Hydrobenzoin $RHC(OH)(HO)CHR \longrightarrow R_2CH-CHO$

(B) One-Two, Amino Alcohols

(C) Halohydrins

(D) Substituted Ethylene Oxides (no examples included)

Class II   Compounds Containing a Carbonyl Group

(A)
1) 2,2,2-Tri substituted aryl aldehydes

2) 2,2-Di substituted aryl aldehydes

3) 2,2-Di substituted aryl-2-hydroxy aldehydes

(B) Keto alcohols

(C) Ketones

Class III   Dehydration of Alcohols

(A) Primary Alcohols

(B) Secondary Alcohols

(C) Tertiary Alcohols

Class IV   -   Amines

Class V   -   Halogen Compounds

Class VI   -   Olefins

Class VII   -   Aromatic Compounds

(a) Jacobsen Reaction
(b) Friedel and Craft Reaction
(c) Naphthalene

Class I   PINACOL-PINACOLONE REARRANGEMENTS

(A) The Dehydration of One-Two, Glycols

1) True Pinacol

The dehydration of one,two-glycols of the type $R_2C(OH)(HO)CR_2$ where R is an alkyl or aryl group leads to rearrangement of the carbon skeleton. This type of intramolecular conversion was first observed by Fittig[8] in 1859 when he converted 2,3-dimethyl butanediol-2,3 into 3,3-dimethyl butanone-2 (I) by the use of sulfuric acid.

$$(CH_3)_2\text{-}C(OH)(HO)C(CH_3)_2 \xrightarrow[H_2SO_4]{\Delta T} (CH_3)_3C\text{-}COCH_3 \qquad I$$
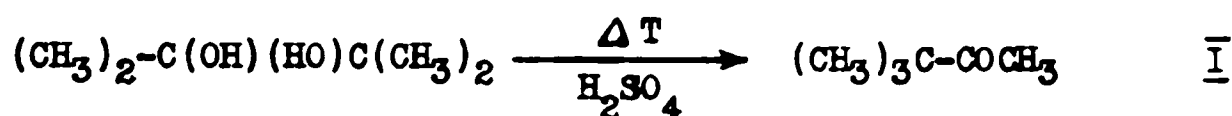
Fittig named the glycol "pinacol" and the product obtained from the dehydration "pinacolone". The generality of the reaction soon became apparent to other workers and numerous similar conversions of one-two, glycols were reported with varying alkyl or aryl groups. Thus the reaction has become known as the "pinacol-pinacolone" rearrangement.

Montagne[9] converted 1,1,2,2-tetra p chlorophenyl ethanediol-1,2 into 1,2,2,2-tetra p chlorophenyl ethanone (II) by the use of sulfuric acid.

$$(pClC_6H_4)_2C(OH)(HO)C(C_6H_4Clp)_2 \xrightarrow{H_2SO_4} pClC_6H_4CO\text{-}C(C_6H_4Clp)_3 \qquad II$$

Montagne's conversion of this glycol to the rearranged ketone was of fundamental importance to the mechanism of the transformation, as only para substituted products were obtained from the para substituted glycol. Conversions of other substituted aryl glycols always resulted in the emergence of products with similarly substituted groups.

It is also of interest to note that both the nature and concentration of the dehydrating agent can affect the direction of the rearrangement. For example, Ramart-Lucas[10] reported the conversion of 1,1-diphenyl-3-methyl propanediol-1, 2 into 3,3-diphenyl butanone-2, (<u>III-A</u>), with concentrated sulfuric acid and into 2-methyl-1, 2-diphenyl propanone (<u>III-B</u>) with acetic anhydride and a trace of sulfuric acid.

$$\underline{\underline{III\text{-}A}}$$

$$\underline{\underline{III\text{-}A}} \quad \xrightarrow[\text{H}_2\text{SO}_4]{\text{conc.}} \quad CH_3\text{-}C(C_6H_5)_2 \text{-}COCH_3 \quad \underline{\underline{III\text{-}A}}$$

$$(C_6H_5)_2C(OH)\text{-}(HO)\text{-}C(CH_3)_2$$

$$\underline{\underline{III\text{-}B}}$$

$$\underline{\underline{III\text{-}B}} \quad \xrightarrow[\substack{\text{trace}\\ \text{H}_2\text{SO}_4}]{\text{Ac}_2\text{O}} \quad (CH_3)_2C(C_6H_5)\text{-}COC_6H_5 \quad \underline{\underline{III\text{-}B}}$$
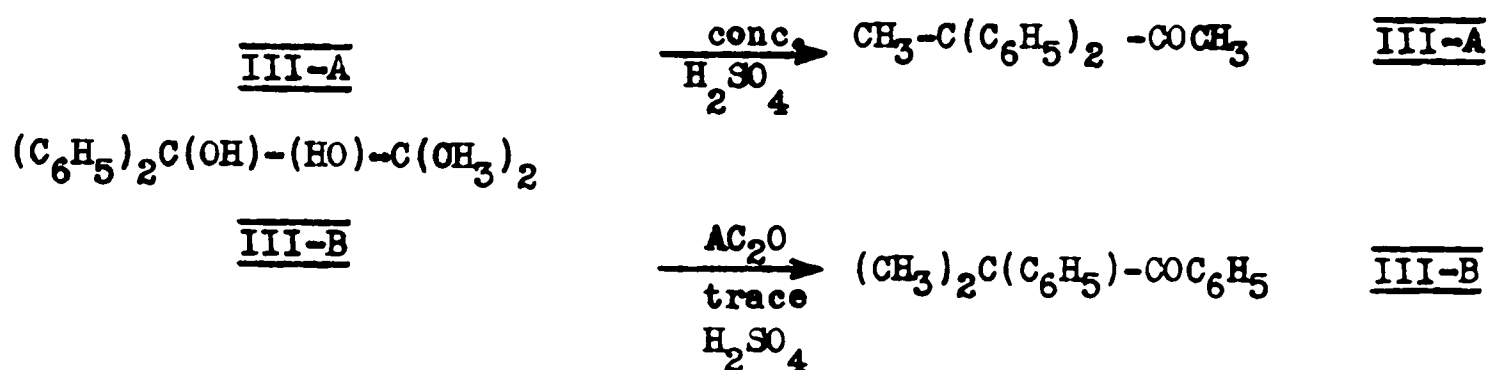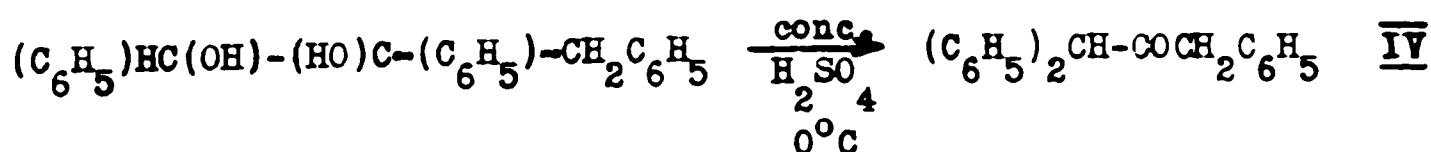
2) Semipinacol

The intramolecular rearrangement of one,two-glycols which have a secondary and tertiary carbon attachment may proceed by two paths. Thus molecules of the following structure - $R_2C(OH)\text{-}(HO)C(H)R$ may (a) lose water without including an alkyl or aryl migration, or (b) involve a hydrogen shift. However, examples of aryl or alkyl group migration in preference to hydrogen do exist. A. Orékoff[11] converted 1,2,3-triphenyl propanediol-1,2 into 1,1,3-triphenyl propanone-2 (<u>IV</u>) by using concentrated sulfuric on the glycol at $0^\circ C$.

$$(C_6H_5)HC(OH)\text{-}(HO)C\text{-}(C_6H_5)\text{-}CH_2C_6H_5 \quad \xrightarrow[\substack{\text{H}_2\text{SO}_4\\ 0^\circ C}]{\text{conc.}} \quad (C_6H_5)_2CH\text{-}COCH_2C_6H_5 \quad \underline{\underline{IV}}$$

Orékoff[11] also converted 1,3-diphenyl-2-benzyl-propanediol-1,2 into 1,3,4-triphenyl butanone-2 (<u>V</u>) with the same reagent.

$$(C_6H_5CH_2)_2C(OH)(HO)CH(C_6H_5) \xrightarrow[\substack{H_2SO_4 \\ 0^oC}]{conc} C_6H_5CH_2\text{-}CO\text{-}CH(C_6H_5)CH_2C_6H_5 \quad \underline{\overline{V}}$$
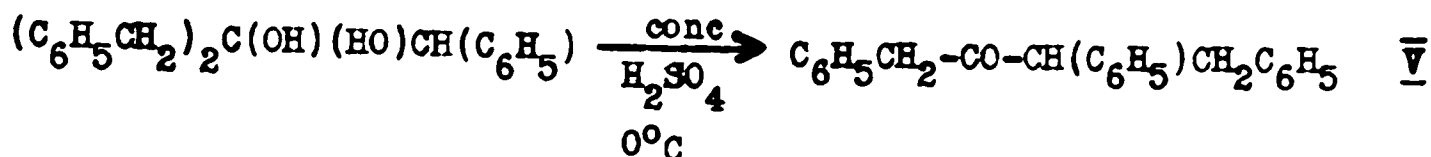
3) Semihydrobenzoin

The semihydrobenzoin rearrangement includes one,two-glycols which have a carbon skeleton similar to those that undergo a semipinacol rearrangement. Thus, these glycols have secondary and tertiary carbon attachments with a general formula $R_2C(OH)(HO)\text{-}C(H)R$. The products obtained in these transformations are aldehydes and not ketones as are obtained in semipinacolinic conversions.

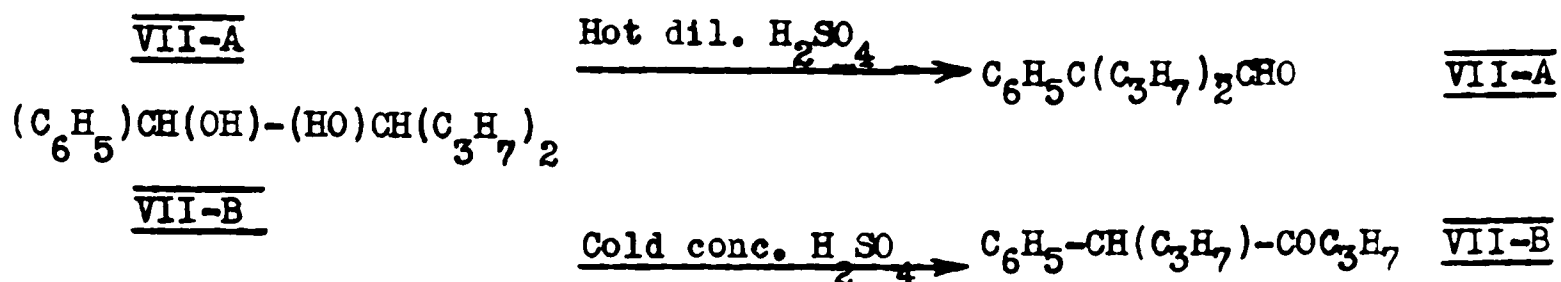This conversion has been shown to take place[12] in the rearrangement of 1,1,2-triphenyl ethanediol-1,2 into triphenyl ethanal ($\underline{\overline{VI}}$) with hot dilute sulfuric acid.

$$(C_6H_5)_2C(OH)(HO)CH(C_6H_5) \xrightarrow[H_2SO_4]{\Delta T} (C_6H_5)_3C\text{-}CHO \qquad \underline{\overline{VI}}$$

The versatility of these intramolecular conversions is indicated by the variety of reagents and conditions which can bring them about. Quite frequently variation of conditions as by increasing or decreasing acid strength or temperature can result in the production of different rearrangements. Thus Tiffeneau[13] has shown that 1-phenyl, 2-propyl pentanediol-1,2 can be made to undergo a semihydrobenzoin rearrangement with hot dilute sulfuric acid and a semipinacol rearrangement with cold concentrated sulfuric acid. Thus was obtained 2-phenyl, 2-propyl pentanal ($\underline{\overline{VII\text{-}A}}$) and 5-phenyl octanone-4 ($\underline{\overline{VII\text{-}B}}$) respectively.

$$\underline{VII\text{-}A}$$

$$(C_6H_5)CH(OH)\text{-}(HO)CH(C_3H_7)_2 \qquad \xrightarrow{\text{Hot dil. } H_2SO_4} \quad C_6H_5C(C_3H_7)_2CHO \qquad \underline{VII\text{-}A}$$

$$\underline{VII\text{-}B}$$

$$\xrightarrow{\text{Cold conc. } H_2SO_4} \quad C_6H_5\text{-}CH(C_3H_7)\text{-}COC_3H_7 \qquad \underline{VII\text{-}B}$$

4) Hydrobenzoin

Rearrangements of the hydrobenzoin type in the one,two-glycols include molecules which have two secondary carbon attachments. Dehydration of these glycols of general formula R(H)C(OH)-(HO)C(H)R need not lead to an intramolecular rearrangement with alkyl or aryl group migration. If an alkyl or aryl group does migrate the products obtained are aldehydes.

The dehydration of "hydrobenzoin"[13,14] itself offers a good illustration of the rearrangement. Thus 1,2-diphenyl ethanediol-1,2 is converted to diphenyl ethanal (VIII) by hot sulfuric acid.

$$(C_6H_5)CH(OH)\text{-}(HO)CH(C_6H_5) \quad \xrightarrow[H_2SO_4]{\Delta\ T} \quad (C_6H_5)_2CH\text{-}CHO \qquad \underline{VIII}$$
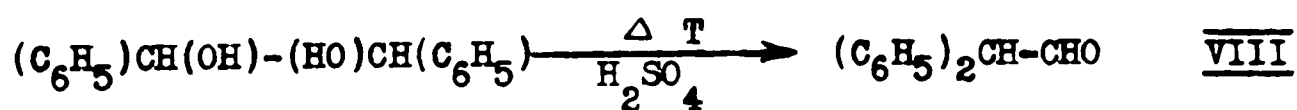
Discussion

The "pinacol-pinacolone" rearrangement of one, two-glycols, which is brought about upon dehydration, is a general one, and can be made to react in two ways, when there are secondary and tertiary carbon attachments. The direction which such a rearrangement takes is unpredictable and subject to the experimental conditions. Even though the "pinacol" rearrangement is general, not all "pinacols", glycols, are converted with equal ease. Aromatic compounds require treatment with more concentrated acid than is required for the aliphatic.

The symmetrical nature of the one, two-glycols, with tertiary carbon attachments, has encouraged a great amount of experimentation to determine the relative migration tendencies of groups. These relative migration tendencies would thus reflect the relative unsaturation of these groups with respect to each other. Extensive work along these lines has been carried out by Tiffeneau[15], Bachman[16] and others.

However, it has been found difficult to evaluate absolutely the relative migration tendencies of groups because many factors, other than inherent group unsaturation, operate in these intramolecular conversions.[15] Qualitatively, para tolyl and para anisyl migrate preferentially to phenyl. Phenyl migrates in preference to para halo phenyl, methyl, ethyl or propyl groups. This preferential scale holds true only in symmetrical glycols. An entirely new scale must be determined for an unsymmetrical glycol series. Bachman[17] has further shown that para substituted phenyl groups migrate preferentially to meta substituted, and meta preferentially to ortho. However, this latter generalization was advanced from observa-
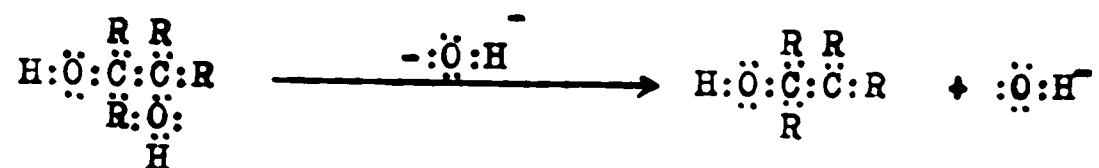
tions on only a few symmetrical glycols and may not apply generally upon further investigation. Thus hard and fast rules for relative migration tendencies cannot be made as there are too many unknowns involved.

Mechanism

The mechanism of this rearrangement has been the subject of much controversy. At this stage it would be fruitless to present the historical sequence of mechanism forms which have been advanced to explain the rearrangement. However, one of the most popular mechanisms has been the ethylene oxide intermediate proposed by Tiffeneau[15]. The exclusion of the oxide intermediate, as the mechanism route, depends upon the relatively greater stability of the oxide to conversion than the corresponding glycol under similar experimental conditions. The substituted ethylene oxides usually give the same products as the corresponding glycol upon rearrangement, notwithstanding slightly modified conditions.

It seems highly probable that glycols on dehydration, as well as ethylene oxides, go through the same type of mechanism in rearrangement. The mechanism as interpreted according to present theory is an electronic one. "The more reactive hydroxyl.....is removed in the course of the reaction, leaving an open sextet which is completed by rearrangement[18]." The steps involved in the conversion are illustrated as follows.

(1)

$$H:\ddot{O}:\ddot{C}:\ddot{C}:R \xrightarrow{-:\ddot{O}:H^{-}} H:\ddot{O}:\ddot{C}:\ddot{C}:R \quad + \quad :\ddot{O}:H^{-}$$

(with R, R substituents on carbons, R:Ö: and H below in left structure)

(2)

$$H:\ddot{O}:\ddot{C}:\ddot{C}:R \xrightarrow[\text{shift}]{R} H:\ddot{O}:\ddot{C}:\ddot{C}:R$$

(3)

$$H:\ddot{O}:\ddot{C}:\ddot{C}:R \xrightarrow{+ :\ddot{O}:H^{-}} H:\ddot{O}:\ddot{C}:\ddot{C}:R$$

(with :O:R and H below right structure)

(4)

$$H:\ddot{O}:\ddot{C}:\ddot{C}:R \xrightarrow{- H_2O} R:C:\ddot{C}:R \quad + \quad H_2O$$

(with :O:R and H below left structure; Ö R below right structure)
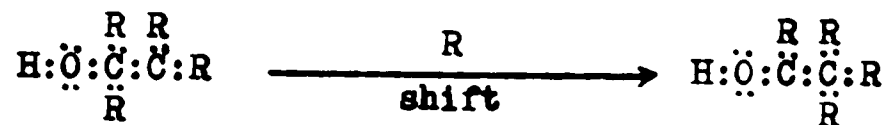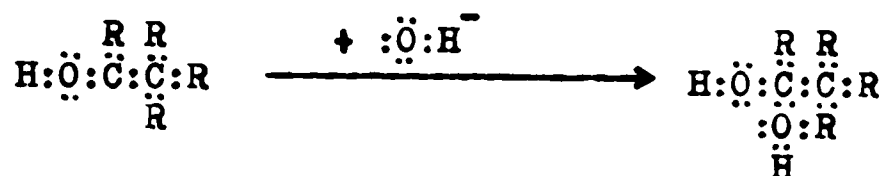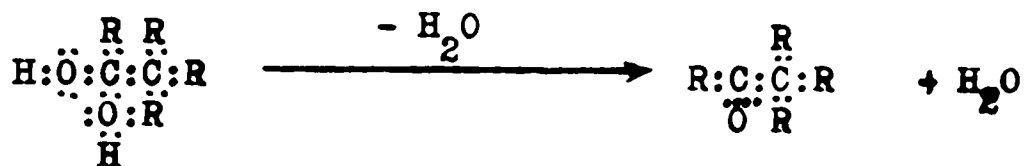
Thus the first step involves the loss of hydroxyl from the molecule with a complete octet of electrons. The resultant carbonium ion can now rearrange itself. This rearrangement is followed by the readdition of a hydroxyl ion which possesses an octet of electrons. Finally water is eliminated and the rearranged product is now stabilized.

In postulating an open sextet one must keep in mind as pointed out by Whitmore and Wallis[18] and by Bartlett and Pockel[19,20] that this open sextet never actually exists as such, for the removal of the hydroxyl group with its electron pair and the rearrangement of the radical R, occur simultaneously. The migrating group is considered to attach itself to the carbon atom on the opposite side to that of the hydroxyl,

thus inverting the carbon configuration. In 1, 2-di methyl cyclohexane-diol-1, 2 the cis compound in 20% sulfuric gives as sole product 2, 2-dimethyl cyclohexanone (IX-A)
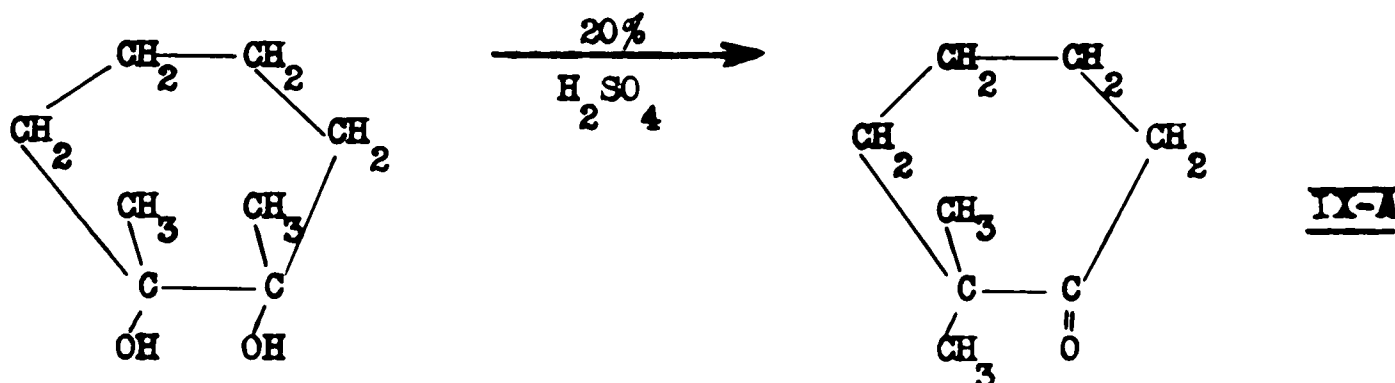
The trans form gives 1-methyl-1-acetyl cyclopentane (IX-B) under similar conditions.
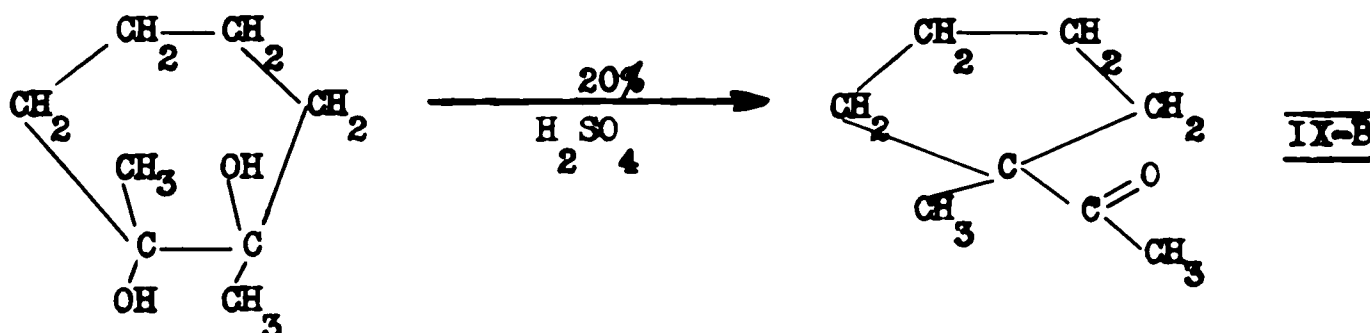
In the first case the methyl migrates because it is in a position to fall in on the side of the carbonium carbon opposite to that from which the hydroxyl is being removed. In the second case a ring carbon is in a similar situation and its migration converts the cyclohexane ring to a cyclopentane.

Further proof of the rearward attack of the migrating group has been given by Bartlett[21] and Brown in the conversion of cis and trans 7, 8-di phenylacenaphthenediol-7, 8. The "pinacol" conversion of the

cis and trans isomers yields the same rearranged product 8,8-diphenylace-
naphthane-7. From a study of the rates of conversion of the cis and trans
forms in dilute acid, it was shown that the cis form converted very much
more rapidly than the trans. The trans form in dilute acid solution was
more slowly converted because it first had to be transformed to the cis
isomer before it could further react in a "pinacol" rearrangement. The
separation of the cis form in the conversion of trans 7,8-diphenylace-
naphthenediol-7, 8 was proof of the preliminary trans-cis conversion.
It was also shown that in strong acid solutions the trans-cis conversion
was rapid and consequently the conversion to the ketone for the two
isomers had the same rate. This necessity of trans conversion to cis,
before rearrangement, is fundamental evidence for the rearward attack of
the migrating carbon atom. The reaction conversion is as illustrated in
equation $\overline{X}$.
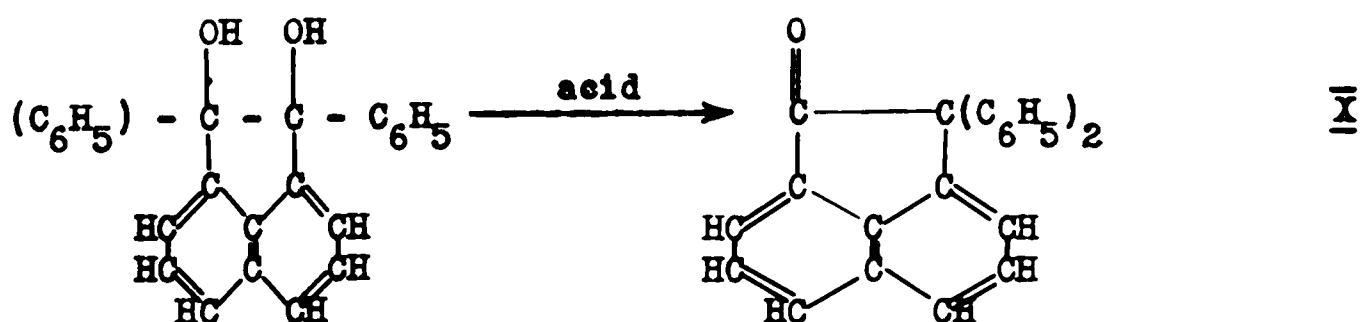
Pinacol rearrangements can be said to occur when a silver ion
attacks a bromohydrin[22] or by the action of nitrous acid on 1,2-amino
alcohols[23]. In any case, the intermediate is a carbonium ion.

(B) One,Two-Amino Alcohols

There are many examples of conversion of one,two-amino alcohols to one,two-glycols which result in rearrangement. The first step is the removal of the amino group with an octet of electrons, thus leaving a carbon atom with an open sextet. This allows the carbon skeleton to rearrange. Tiffeneau[24] converted 1-phenyl, 1-anisyl, 2-amino propanol-1 to 1-phenyl, 2-anisyl propanone-1 with nitrous acid ($\overline{\overline{XI}}$).

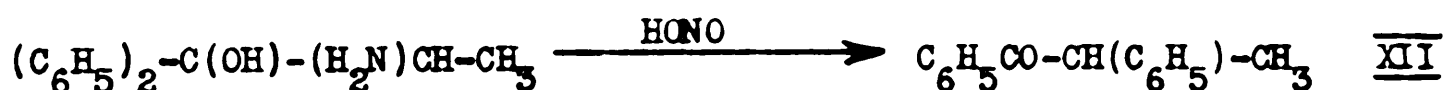$$(pCH_3O \ C_6H_4)-C_6H_5-C(OH)-(H_2N)-CH-CH_3$$

$$\xrightarrow[\text{10\% NaNO}_2]{\text{glacial HOAC}}$$

$$C_6H_5CO-CH(CH_3)(C_6H_4OCH_3p) \qquad \overline{\overline{XI}}$$
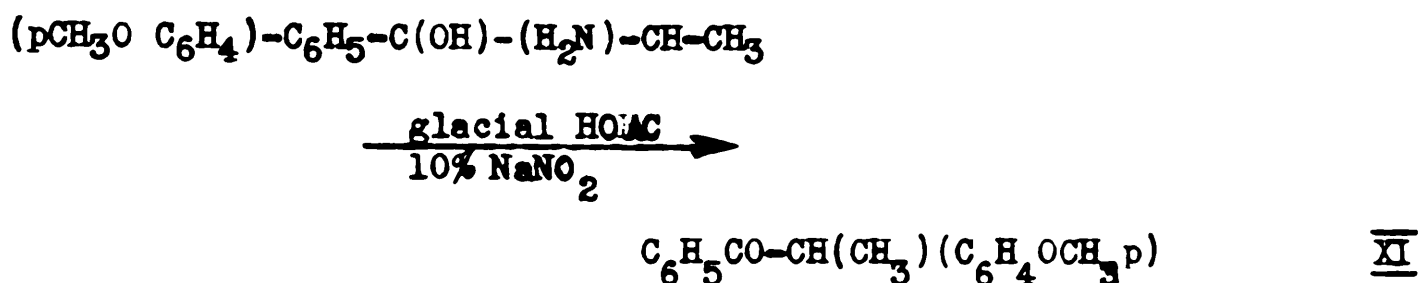
McKenzie[25] converted an optically active laevo compound into the dextro derivative. Thus laevo, 1,1-diphenyl-2-amino propanol-1 becomes dextro, 1,2-diphenyl propanone-1. ($\overline{\overline{XII}}$)

$$(C_6H_5)_2-C(OH)-(H_2N)CH-CH_3 \xrightarrow{\text{HONO}} C_6H_5CO-CH(C_6H_5)-CH_3 \qquad \overline{\overline{XII}}$$

(C) Halohydrins

The action of silver nitrate, sodium thiosulfate, acids, etc., on halohydrins can effect a "pinacol-pinacolone" rearrangement. The mechanism is similar to that previously outlined, the first step being the removal of the halo group with an octet of electrons, thus allowing for rearrangement of the carbonium ion.

A typical example is shown by McKenzie[23] in which 2,3-dimethyl-3-bromobutanol-2 is converted into 3,3-dimethyl butanone-2 ($\overline{\overline{XIII}}$) by the action of acid with heating in an open tube to $110°C$.

$$(CH_3)_2C(OH)-(Br)C(CH_3)_2 \xrightarrow[110°C]{\text{acid}} (CH_3)_3C-COCH_3 \qquad \overline{\overline{XIII}}$$

Class $\overline{\overline{\text{II}}}$ <u>COMPOUNDS CONTAINING A CARBONYL GROUP</u>

<u>(A) ALDEHYDES</u>

<u>(1) 2,2,2-Tri Substituted Aryl Aldehydes</u>

The conversion of 2,2,2-tri substituted aryl or alkyl aldehydes to ketones was first reported by Danilov[26] in 1917. Thus 2,2,2-triphenyl ethanal was rearranged to 1,2,2-triphenyl ethanone with sulfuric acid (<u>XIV</u>).

$$(C_6H_5)_3C\cdot CHO \xrightarrow{\text{H}_2\text{SO}_4} (C_6H_5)_2CH\cdot COC_6H_5 \qquad \overline{\overline{\text{XIV}}}$$
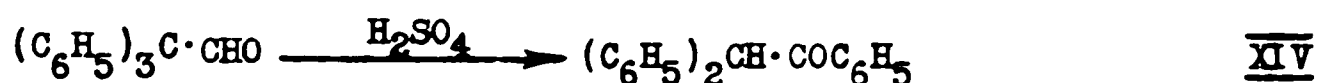
Many examples exist of this type of intramolecular rearrangement of aldehydes to ketones. Orékoff[27] converted 2,2-diphenyl propanal into 1,2-diphenyl propanone (<u>XV</u>) and 2-methyl, 2-phenyl propanal into 3-phenyl butanone-2 (<u>XVI</u>) by using concentrated sulfuric acid at 0°C.

$$CH_3(C_6H_5)_2\cdot C - CHO \xrightarrow[\text{H}_2\text{SO}_4]{\text{conc.}} CH_3(C_6H_5)\cdot CH\cdot COC_6H_5 \qquad \overline{\overline{\text{XV}}}$$

$$C_6H_5(CH_3)_2\cdot C - CHO \xrightarrow[\text{H}_2\text{SO}_4]{\text{conc.}} CH_3(C_6H_5)\cdot CH\cdot COCH_3 \qquad \overline{\overline{\text{XVI}}}$$
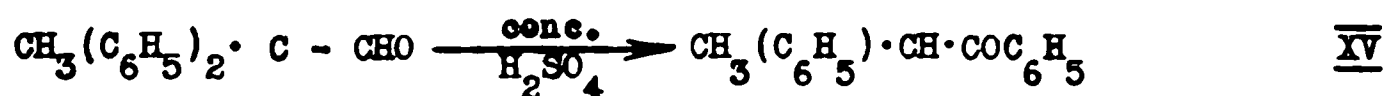
This reaction is a general one and can be made to go with 2,2,2-tri alkyl aldehydes[28]. Thus 2,2-dimethyl propanal is converted into 3-methyl butanone-2 with hot sulfuric acid. (<u>XVII</u>)

$$(CH_3)_3C\cdot CHO \xrightarrow[\substack{\text{H}_2\text{SO}_4 \\ \Delta T}]{70\%} (CH_3)_2\cdot CH\cdot COCH_3 \qquad \overline{\overline{\text{XVII}}}$$
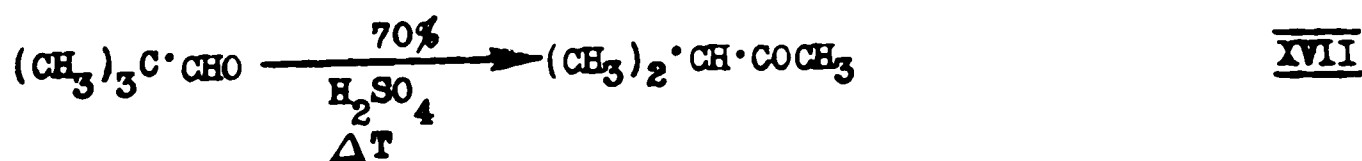
The conversions in equations <u>XIV</u> and <u>XVII</u> can also be carried out by heating the aldehydes to 350°C and passing the vapours over aluminum sulfate at low pressure[29].

2) 2,2-Di Substituted Aryl Aldehydes

In a few instances it has been demonstrated that certain 2,2-di substituted aldehydes can be made to undergo intramolecular rearrangement to ketones. The transformations were accomplished either by using concentrated sulfuric acid at low temperatures or by heating with more dilute acid solutions under reflux. Danilov[30] converted 2,2-diphenyl ethanal into 1,2-diphenyl ethanone (XVIII).

$$(C_6H_5)_2CH \cdot CHO \xrightarrow{H_2SO_4} C_6H_5 \cdot CH_2 - COC_6H_5 \qquad \text{XVIII}$$

It has also been shown possible to convert 2,2-ditolyl ethanal into 1,2-ditolyl ethanone (XIX) by using either method.

$$(pCH_3C_6H_4)_2CH \cdot CHO \xrightarrow{H_2SO_4} pCH_3C_6H_4CH_2 \cdot COC_6H_4CH_3p \qquad \text{XIX}$$

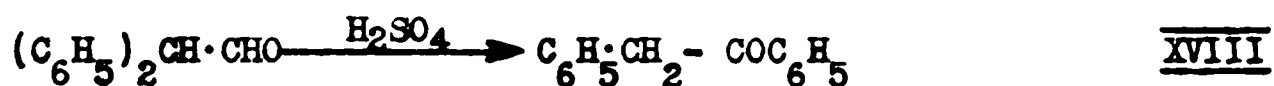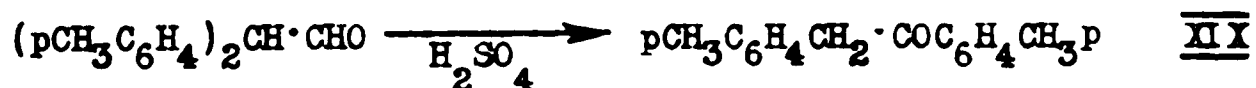## 3) 2-Hydroxy-2,2-Di Substituted Aryl Aldehydes

Conversion of 2-hydroxy-2,2-diaryl or alkyl aldehydes to ketones was first demonstrated ~~by~~ by Danilov[31]. Thus 2-hydroxy-2, 2-diphenyl ethanal was converted into 1,2-diphenyl-2-hydroxy ethanone (XX) by the use of 90% ethanol and a trace of sulfuric acid at 135°C. Danilov[32] also converted 2-hydroxy-2,2-dicyclo hexyl ethanal to 1,2-dicyclo hexyl-2-hydroxy ethanone (XXI) by the same method.

$$(C_6H_5)_2C(OH) \cdot CHO \xrightarrow[\substack{H_2SO_4 \\ ETOH}]{135^{\circ}C} (C_6H_5)CH(OH) \cdot COC_6H_5 \qquad \underline{\underline{XX}}$$

$$(C_6H_{11})_2C(OH) \cdot CHO \longrightarrow (C_6H_{11}) CH(OH) COC_6H_{11} \qquad \underline{\underline{XXI}}$$
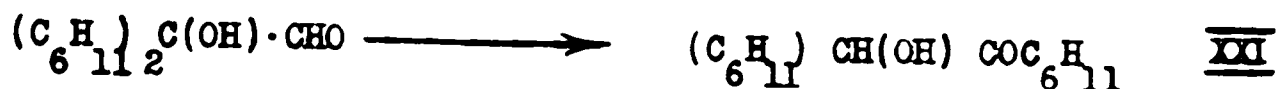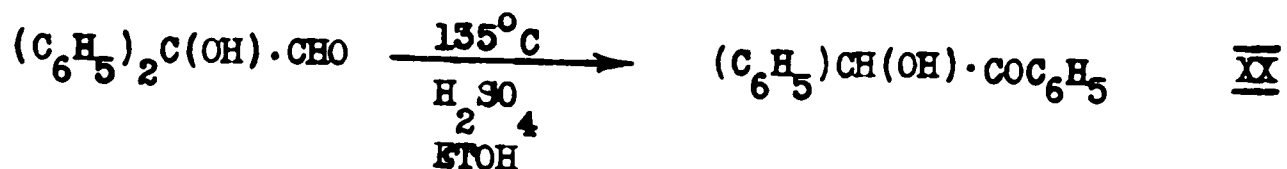
(B) KETO ALCOHOLS

Hydroxy ketones can under favourable circumstances be made to under-go intramolecular rearrangement. Lachman[33] first reported the conversion of "Benzoin" 1,2-di phenyl-1-hydroxy-ethanone to diphenyl acetic acid (XXII) This transformation could be brought about by heating the keto-alcohol with phosphoric or sulfuric acids in sealed tubes.

$$C_6H_5 - \overset{\overset{\displaystyle OH}{|}}{CH} - \overset{\overset{\displaystyle O}{\|}}{C} - C_6H_5 \xrightarrow[3MH_2SO_4]{230^{\circ}C} (C_6H_5)_2 \cdot CH \cdot COOH \qquad \underline{\underline{XXII}}$$
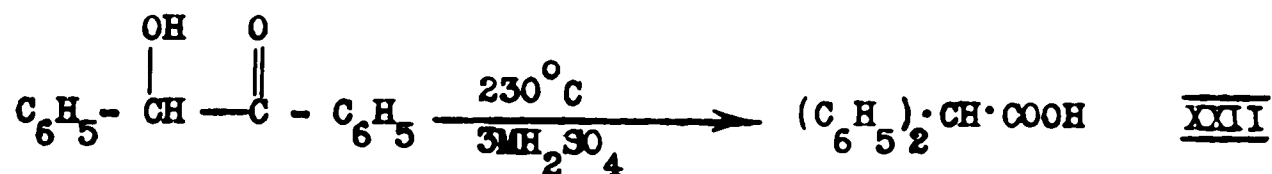
James and Lyons[34] in a later paper reported 50% conversion by the use of silica gel and 60% phosphoric acid and heating for twenty-four hours under pressure. They were unsuccessful in converting other keto alcohols by the same method.

(C) KETONE REARRANGEMENTS

Substituted ketones can give rearranged products when heated with zinc or aluminum chlorides. Examples of such transformations exist for ketones which have secondary and tertiary carbon attachments.

The mechanism is more complicated than in a simple "pinacol-pinacolone" transformation because in these ketonic rearrangements two shifts appear to have taken place.

Al Favorski[35] converted 1-phenyl-2-methyl propanone-1 into 3-phenyl butanone-2 (XXIII).

$$(CH_3)_2CH \ COC_6H_5 \xrightarrow[320°C]{ZnCl_2} \ (CH_3) \ C_6H_5-CH \ COCH_3 \qquad \underline{\underline{XXIII}}$$
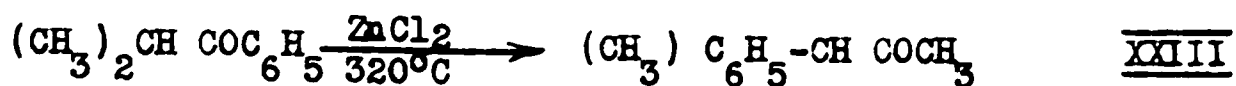
In a later paper[36] the conversion of 1-phenyl-2, 2-dimethyl propanone-1 into 3-phenyl-3-methyl butanone-2 (XXIV) and of 1-phenyl-2, 2-dimethyl butanone into 3-phenyl-3-methyl pentanone-2 (XXV) was reported.

$$(CH_3)_3C-COC_6H_5 \xrightarrow{ZnCl_2} \ (CH_3)_2-C(C_6H_5) \ - \ COCH_3 \qquad \underline{\underline{XXIV}}$$

$$(CH_3CH_2C(CH_3)_2-COC_6H_5 \xrightarrow{ZnCl_2} \ CH_3CH_2-C(CH_3)(C_6H_5)COCH_3 \qquad \underline{\underline{XXV}}$$
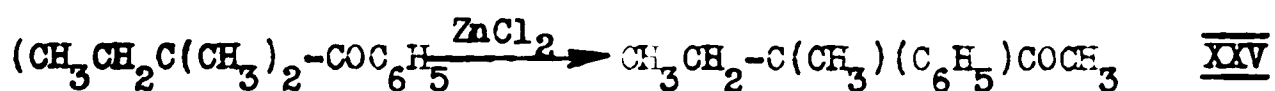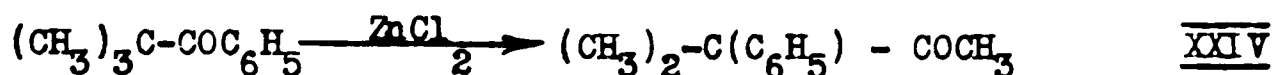
More recently, it has been shown by Baddeley[37] that poly substituted phenyl ketones can also be made to rearrange under the influence of aluminum chloride. Thus 2,5-dimethyl acetophenone was converted into 3,5-dimethyl acetophenone (XXVI), and 2,4,6-trimethyl acetophenone into 3,4,5-trimethyl acetophenone (XXVII).
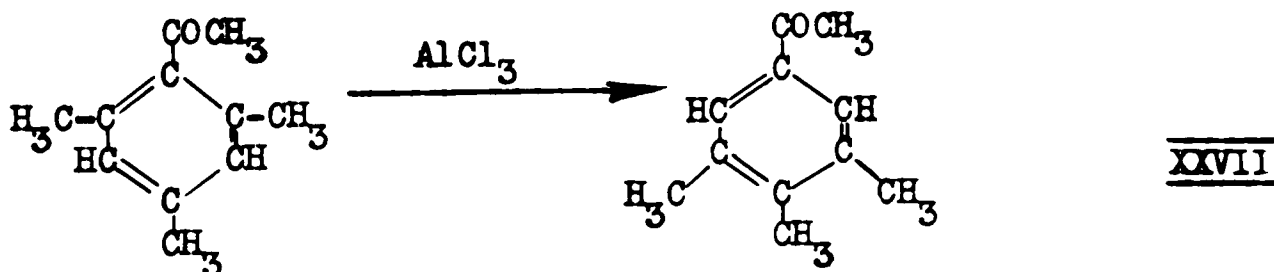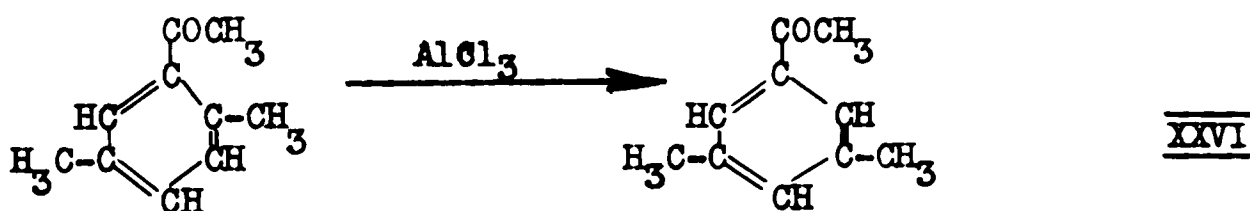
Mechanism

In this outline of rearrangements in carbonyl containing compounds, examples have been given which have an increasingly ―― complex rearrangement mechanism.

The mechanism of the tri, di and hydroxy aryl substituted aldehydes is in essence similar. The first step is an addition of a proton to the carbonyl, thus producing a carbonium with an open sextet which can rearrange. The general mechanism is as follows:

(1)

$$R:\overset{R}{\underset{R}{\ddot{C}}}:\overset{H}{\ddot{C}}:O: \xrightarrow{H^+} R:\overset{R}{\underset{R}{\ddot{C}}}:\overset{H}{\ddot{C}}:\ddot{O}:H$$

(2)

$$R:\overset{R}{\underset{R}{\ddot{C}}}:\overset{H}{\ddot{C}}:\ddot{O}:H \xrightarrow{R\ shift} R:\overset{R}{\ddot{C}}:\overset{H}{\underset{R}{\ddot{C}}}:\ddot{O}:H$$

(3)

$$R:\overset{R}{\underset{R}{\ddot{C}}}:\overset{H}{\ddot{C}}:\ddot{O}:H \xrightarrow[shift]{H} R:\overset{H}{\underset{R}{\ddot{C}}}:\overset{}{\underset{R}{C}}:\ddot{O}:H$$

(4)

$$R:\overset{H}{\underset{R}{\ddot{C}}}:\overset{}{\underset{R}{C}}:\ddot{O}:H \xrightarrow{OH^-} R:\overset{H}{\underset{R}{\ddot{C}}}:\overset{\overset{H:\ddot{O}:}{}}{\underset{R}{C}}:\ddot{O}:H \xrightarrow{-H_2O} R:\overset{H}{\underset{R}{\ddot{C}}}:\overset{}{\underset{R}{C}}:O$$
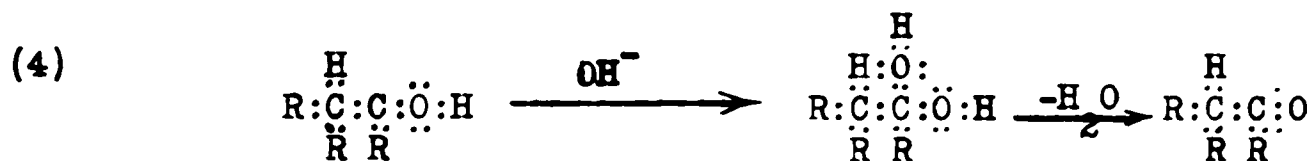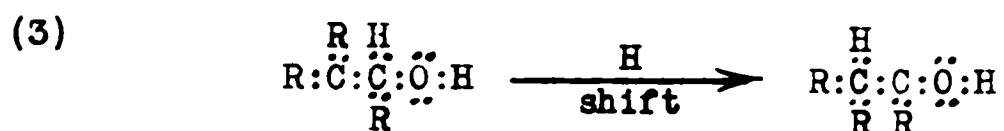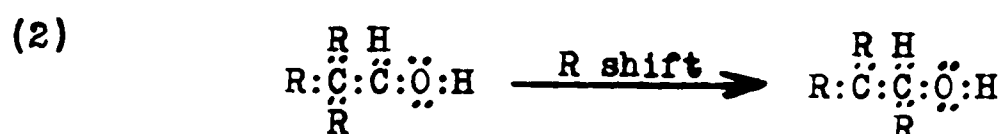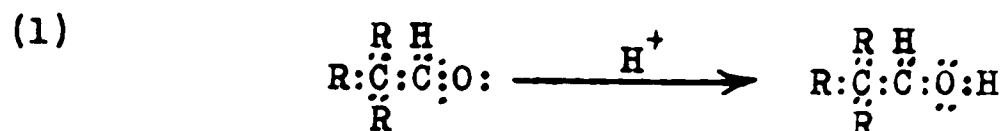
The mechanisms of the ketone rearrangements using aluminum chloride or zinc chloride are more complicated than in the case of the acid catalyzed aldehyde or keto alcohol conversions. However,[38] both aluminum chloride and zinc chloride are powerful electrophilic reagents and the driving force in this rearrangement is the tendency of both these metallic atoms to make up an octet of shared electrons by attacking the unshared pairs on the oxygen atom. The electronic displacement in this case would then be similar to that condition where a proton attaches itself to a carbonyl group. Thus the formation of the complex can allow for intramolecular rearrangement because the carbonyl carbon has an open sextet.

The action of aluminum chloride in the above rearrangement is similar to that taking place in a Friedel and Crafts reaction, and its role will be further discussed under "Rearrangements in Aromatic Compounds."

Class $\overline{\overline{III}}$

ALCOHOL DEHYDRATION

Several alcohols upon dehydration to olefins result in rearranged products. These structural modifications of the carbon skeleton that sometimes occur when a monohydric alcohol is dehydrated are known as the Wagner rearrangement. Wagner first noticed this type of rearrangement upon heating tertiary alcohols. However, many examples of rearrangement from the dehydration of alcohols have now accumulated and indicate that both primary and secondary alcohols can undergo structural transformations.

The nomenclature of alcohols primary, secondary and tertiary is not a sufficiently clear designation of the molecule if we wish to discuss intramolecular rearrangements. The nature of the adjacent carbon attachment must be considered to understand completely the probability of rearrangement in various alcohols. Dehydration of an alcohol to an olefin requires the attachment of a hydrogen atom to the carbon atom which is adjacent to the hydroxyl containing carbon. Thus, it is readily seen that primary alcohols with tertiary carbon attachments $(R_3C \cdot CH_2OH)$ must lead to the formation of rearranged products upon dehydration. In general, the factor determining whether a rearranged olefin is produced upon dehydration would be the availability of a hydrogen atom. Thus in primary alcohols with secondary carbon attachments (R_2CH-CH_2OH), rearrangement can theoretically not take place. However, from experiment the adjacent hydrogen atom is not readily available and this type

of alcohol affords several examples of rearrangement upon dehydration. Secondary alcohols with tertiary carbon attachments ($R_3C \cdot CHR'OH$) usually lead to rearrangement upon dehydration. Tertiary alcohols with tertiary carbon attachments ($R_3C-CR_2'OH$) could also lead to rearrangement. Nevertheless, it is obvious that if intramolecular rearrangements are to occur in both the secondary and tertiary alcohols with either secondary or tertiary carbon attachments, the determining factor is the availability of hydrogen in the adjacent R' group.

(A) REARRANGEMENT IN PRIMARY ALCOHOLS

(a)
Generally, primary alcohols with a primary carbon attachment (RCH_2-CH_2OH) do not lead to rearrangement upon dehydration. However, Senderens[40] has reported that butanol-1 can be forced to rearrange to 2-methyl propene (XXVIII) if a catalyzed dehydration is carried out at high temperature.

$$CH_3CH_2 \cdot CH_2 \cdot CH_2OH \xrightarrow[\text{High Temp.}]{- H_2O} H_3C \cdot CH(CH_3) : CH_2 \quad \underline{\underline{XXVIII}}$$
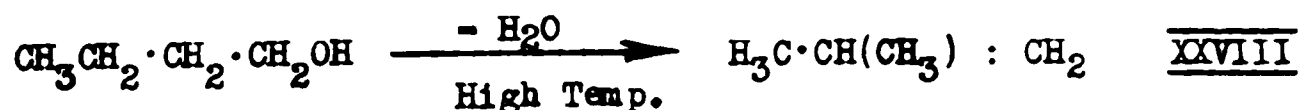
Whitmore[41] has accounted for this product on the basis of the following carbonium ion mechanism.

1) $CH_3CH_2CH \cdot CH_2OH \xrightarrow{\;-OH\;} CH_3CH_2 \cdot CH_2CH_2 + OH^-$

2) $CH_3CH_2CH_2CH_2 + \xrightarrow{\;1,2-H \; shift\;} CH_3 \cdot CH_2 \cdot \overset{+}{CH} \cdot CH_3$

3) $CH_3CH_2\overset{+}{CH} CH_3 \xrightarrow{\;CH_3 \; shift\;} CH_2 \cdot \overset{+}{CH} \cdot CH_3$
$$ CH_3$$

4) $CH_2\overset{+}{CH}(CH_3) \cdot CH_3 \xrightarrow{\;- \; H^+\;} CH_2 = C(CH_3)_2 + H^+$
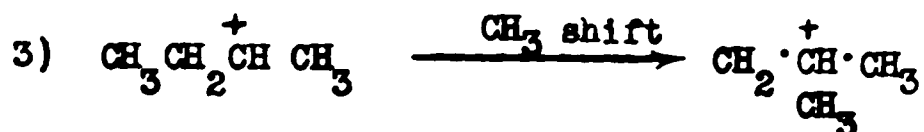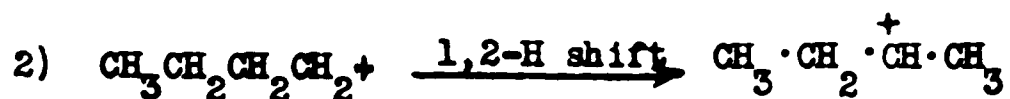
(b) Dehydration of primary alcohols with secondary carbon attachments ($R_2CH \cdot CH_2OH$) may lead to rearranged products. Nevole[45] and Le Bel[46] obtained butene-2 (__XXIX__) upon dehydration of 2-methyl propanol-1.

$$CH_3CH(CH_3) \cdot CH_2OH \xrightarrow{} CH_3CH = CH \cdot CH_3 \qquad \underline{\underline{XXIX}}$$

Ramart[47] showed that 2,2-diphenyl ethanol gave 1,2-diphenyl ethylene (__XXX__) and that 2-phenyl-2-ptolyl ethanol (__XXXI__) upon dehydration with phosphorus pentoxide, gave 1-phenyl-2-p tolyl ethylene.

$$(C_6H_5)_2CH \cdot CH_2OH \xrightarrow{\;P_2O_5\;} C_6H_5CH: CH C_6H_5 \qquad \underline{\underline{XXX}}$$

$$pCH_3C_6H_4 \cdot CH(C_6H_5) \cdot CH_2OH \xrightarrow{\;P_2O_5\;} C_6H_5CH : CHC_6H_4CH_3p \qquad \underline{\underline{XXXI}}$$
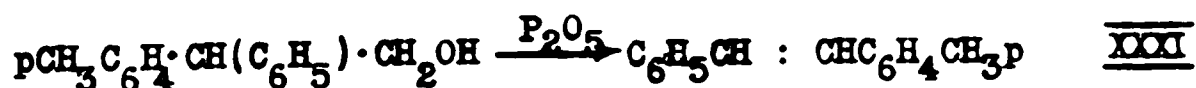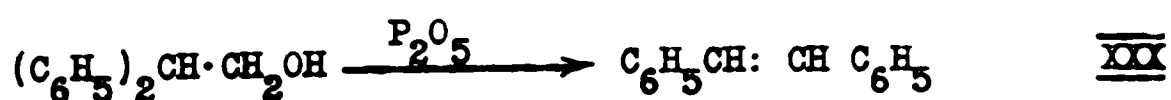
(c) Dehydration of primary alcohols with a tertiary carbon attachment ($R_3C \cdot CH_2OH$) must lead to rearrangement upon dehydration. Haller[42] reported the conversion of 2-phenyl-2-methyl propanol-1 to 2-phenyl butene-2 by passing the alcoholic vapours over infusorial earth at red heat (__XXXII__) and of 2-phenyl-2-benzyl butanol-1 into 1-phenyl-2-benzyl butene-1 by the same method (__XXXIII__).

$$(CH_3)_2 \cdot C(C_6H_5) \cdot CH_2OH \longrightarrow CH_3 \cdot C(C_6H_5) \ ; \ CH \cdot CH_3 \qquad \underline{\underline{XXXI}}$$

$$CH_3CH_2 \cdot C(C_6H_5)(CH_2C_6H_5) \cdot CH_2OH \longrightarrow CH_3CH_2C(CH_2C_6H_5) = CH \cdot C_6H_5 \quad \underline{\underline{XXXII}}$$
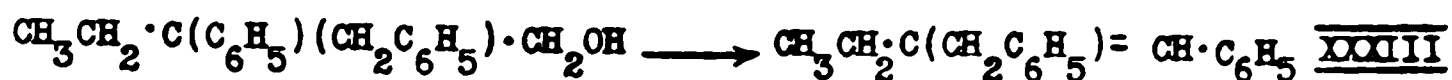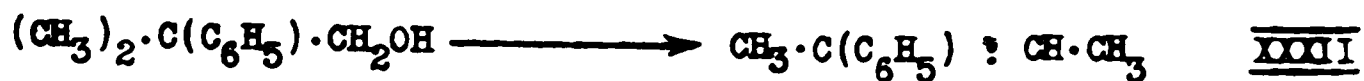
Other examples of rearrangement from the dehydration of primary alcohols with tertiary carbon attachments have been shown by Ramart[43] and Bateman[44] in the conversions of 2,2,3-triphenyl propanol-1 into 1,2,3-triphenyl propene-1 ($\underline{\underline{XXXIV}}$) and of 2,2-dimethyl propanol-1 into 2-methyl butene-2 ($\underline{\underline{XXXV}}$), respectively.

$$(C_6H_5)_2 \cdot C(CH_2C_6H_5) \cdot CH_2OH \xrightarrow{P_2O_5} C_6H \cdot CH \cdot C(C_6H_5) = CHC_6H \qquad \underline{\underline{XXXIV}}$$

$$(CH_3)_3C \cdot CH_2OH \xrightarrow{\quad P_2O_5 \quad} CH_3 \cdot CH_2 \cdot C(CH_3) = CH_2 \qquad \underline{\underline{XXXV}}$$
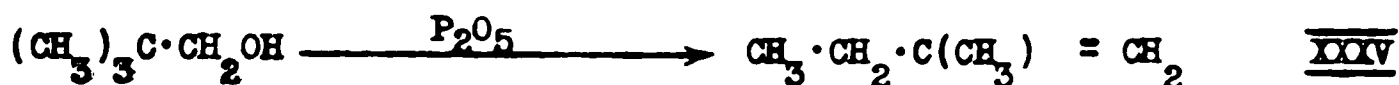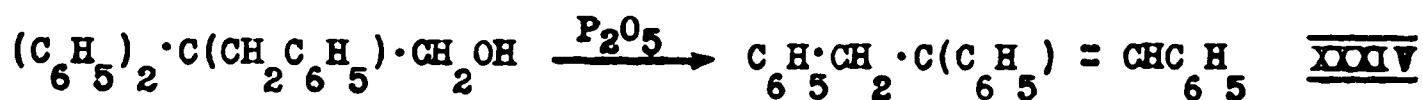
(B) REARRANGEMENT IN SECONDARY ALCOHOLS

Upon dehydration secondary alcohols with a tertiary carbon attachment ($R_3C \cdot HCR'(OH)$) must undergo rearrangement if no available hydrogen atom exists on the adjacent carbon or R' group.

Favorski[48] dehydrated 1-phenyl-2-methyl-2-ethyl butanol-1 and obtained 3-methyl-4-phenyl hexene-2 ($\underline{\underline{XXXVI}}$) by using potassium acid sulfate.

$$(C_2H_5)_2C(CH_3) - (C_6H_5) \ CHOH \xrightarrow{KHSO_4} CH_3CH = C(CH_3) \cdot (C_2H_5)CHC_6H_5 \qquad \underline{\underline{XXXVI}}$$

Both Whitmore[49] and Delacre[50] have shown that "pinacolyl alcohol"- 3,3-dimethyl butanol-2 upon dehydration gives mainly 2,3-dimethy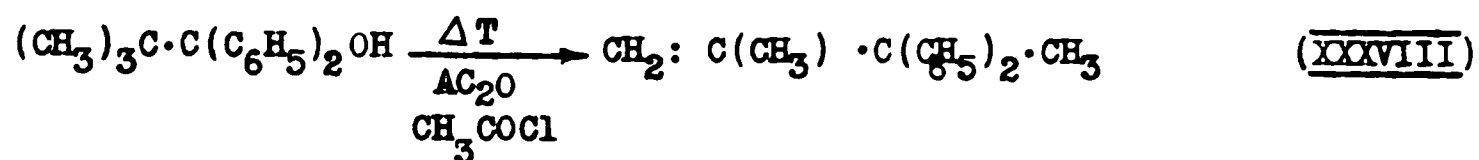l butene-2 ($\underline{\underline{XXXVII}}$) by either oxalic acid[50] or by heating with iodine in a sealed tube to $140^{\circ}C$ [49].

$$CH_3C(CH_3)_2 \cdot C(CH_3) \cdot HOH \xrightarrow{\text{oxalic}} (CH_3)_2C : C(CH_3)_2 \qquad \underline{\underline{XXXVII}}$$

(C) REARRANGEMENTS IN TERTIARY ALCOHOLS

Alcohols which are tertiary and have tertiary carbon attachments $(R_3C \cdot CR_2'OH)$ can rearrange upon dehydration if no available hydrogen atom exists in the R' group adjacent to the hydroxyl containing carbon.

Lucas[51] and Marvel[52] have shown that 1,1-diphenyl-2, 2-dimethyl propanol-1 can be converted into 2-methyl-3, 3-diphenylbutene-1 with acetic anhydride and acetyl chloride by heating under reflux ($\underline{\underline{XXXVIII}}$).

$$(CH_3)_3C \cdot C(C_6H_5)_2 OH \xrightarrow[\substack{AC_2O \\ CH_3COCl}]{\Delta T} CH_2: C(CH_3) \cdot C(C_6H_5)_2 \cdot CH_3 \qquad (\underline{\underline{XXXVIII}})$$

Mechanism

All alcoholic rearrangements which occur as a result of dehydration are explicable by the Whitmore[41] mechanism. The first step in the dehydration is the removal of the hydroxyl group to produce a carbonium carbon. The second step involves the actual rearrangement or shift which is finally concluded by the expulsion of a proton to give an olefin. The ease or probability of rearrangement is greatest in primary alcohols with tertiary carbon attachments and in primary alcohols with secondary carbon attachments. The probability of rearrangement of primary alcohols with a primary carbon attachment is small and is only likely to take place under rather drastic conditions. Secondary alcohols with tertiary carbon attachments can also easily give rearranged products upon dehydration. The probability of secondary alcohols with secondary carbon attachments giving rearranged products upon dehydration is greatly

reduced. This probability is reduced if the R group making the alcohol secondary (-C · CHR-OH) possesses an available hydrogen. The condition
　　　　　　　　H
for a maximum rearrangement probability for these secondary alcohols with secondary carbon attachments is greatest when R is itself tertiary. Finally, tertiary alcohols with a tertiary carbon attachment, having no hydrogen atoms available on any of the adjacent carbon atoms, have a rearrangement probability of unity if dehydrated.

Furthermore, it has been shown by Wallis[53] and Bowman that an optically active primary alcohol can give rise to an optically active rearranged product. Thus, laevo-2-methyl-2-phenyl butanol-1 was converted into 1-phenyl-2-methyl butene-1 and dextro-1-phenyl-2-methyl-2-chloro butane (XXXIX) by the action of sulfuryl chloride.

$$CH_3CH_2 \cdot C(CH_3) \, C_6H_5 \cdot CH_2OH \xrightarrow{\;SOCl_2\;} CH_3CH_2C(CH_3) : CH(C_6H_5) +$$
$$CH_3CH_2C(Cl) \cdot CH_3CH_2(C_6H_5)$$

　　　　laevo　　　　　　　　　　　　dextro　　　　　XXXIX
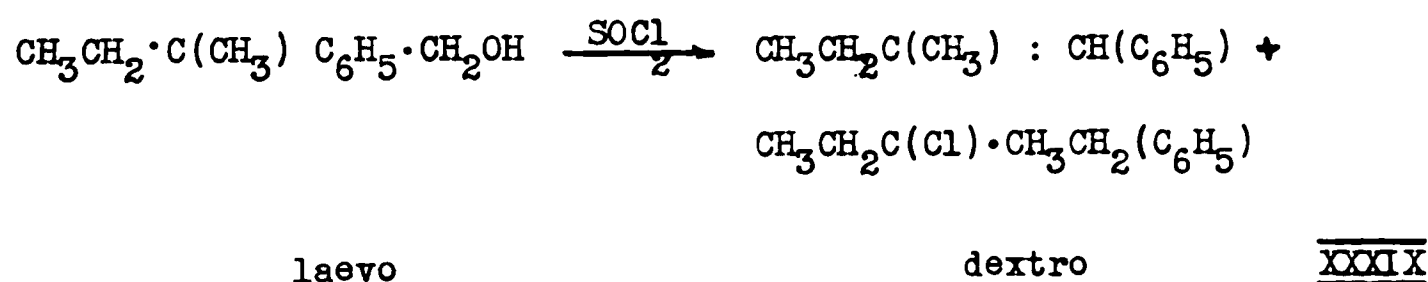
This conversion is important with regard to the reaction mechanism. The optical inversion of the laevo carbon configuration to a dextro configuration is of fundamental importance to the conception of an open sextet. The products obtained from the above reaction contained some of the racemic modification as well as the dextro chloride. The mechanism of the rearrangement must thus follow such a path that an open sextet never actually exists as such,[18,19,20] but that the removal of the hydroxyl and the shift of phenyl occur simultaneously. The migrating phenyl group is at the moment of migration being replaced by the chlorine which attaches to the

carbon atom on the opposite side of the phenyl group, thus inverting the carbon configuration. The elimination, shift and addition reactions all occur as a continuous process. The fact that some racemization takes place favours the conception of ionization of the molecule and the existence of a free open sextet. However, the appearance of the dextro compound implies that the rearrangement takes place intramolecularly without any complete ionization and thus disallows the completely free existence of an open sextet. It is convenient to refer to these reactions as involving a carbonium ion intermediate, but this must not be interpreted to mean that it is a completely free intermediate or even that the re-combination of the ion is not simultaneous with its formation.

Class IV

REARRANGEMENT OF AMINES UPON DEAMINATION

Many primary amines upon deamination lead to the formation of re-arranged products. These amines when decomposed by nitrous acid result either in the production of olefins or of hydroxylated products in which the position of the hydroxyl group is attached to a carbon atom other than that which previously held the amino group. The olefins obtained from these reactions arise from the dehydration of the alcohol formed from the deamination.

The same factors for rearrangement are operating with amines as with alcohols. The more branched the adjoining carbon attachments, the greater the probability of rearrangement taking place upon deamination. Similar nomenclature difficulties exist to explain rearrangement probabilities of amines as with alcohols. Thus a primary amine with primary-primary car-bon attachment $(R-CH_2-CH_2-NH_2)$ would, in general, not be expected to lead to a rearranged or abnormal product upon deamination. However, the pro-babilities of intramolecular transformations are greatly increased when primary amines with primary-secondary carbon attachments $(R_2-CH-CH_2NH_2)$ and primary amines of primary-tertiary carbon attachments $(R_3C-CH_2NH_2)$ are deaminated. The rearrangement probability should reach a maximum with primary amines which have tertiary-secondary $(R_2CH-CR_2-NH_2)$ and tertiary-tertiary carbon attachments $(R_3C-CR_2-NH_2)$.

(a)

1) An early example of rearrangement in primary amines with a primary-primary carbon attachment is given by Linnemann.[54] Thus n-butylamine is converted into 2-methyl propanol-1 ($\overline{\underline{XL}}$) by nitrous acid.

$$CH_3CH_2-CH_2-CH_2-NH_2 \xrightarrow{HONO} CH_3CH(CH_3)-CH_2OH \quad \overline{\underline{XL}}$$
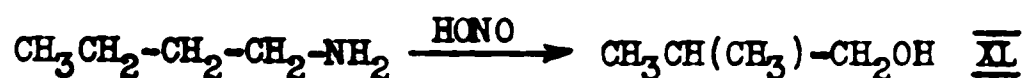
2) More recently Levene[55] converted a primary amine with a primary-secondary carbon into a transformed alcohol. Thus 1-amino-2-phenylpropane was transformed into 1-phenyl-1-chloropropane with nitrosyl chloride ($\overline{\underline{XLI}}$). A similar result was obtained with 1-amino-2-phenyl butane; only here either the ethyl or phenyl group could have shifted to give the rearranged chloride.

$$CH_3-CH(C_6H_5)-CH_2NH_2 \xrightarrow{NOCl} C_6H_5-CHCl-CH_2CH_3 \qquad \overline{\underline{XLI}}$$

3) Freund[56] has shown that a primary amine with a primary-tertiary carbon attachment can also undergo rearrangement. Thus "neopentyl amine", 1-amino-2, 2-dimethyl propane gives 2-methyl-butanol-2 ($\overline{\underline{XLII}}$) upon deamination with nitrous acid.

$$(CH_3)_3C-CH_2NH_2 \xrightarrow{HONO} (CH_3)_2C(OH)CH_2CH_3 \qquad \overline{\underline{XLII}}$$
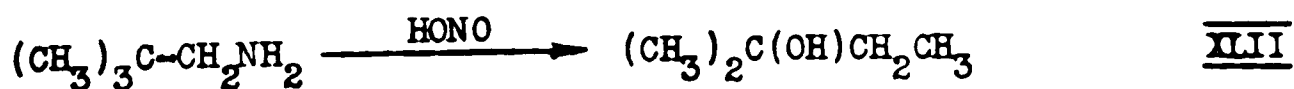
(B)

Jeanne Levy[57] converted a primary amine with a secondary-secondary carbon attachment into a rearranged olefin. Thus 2-amino-3-phenyl-3-anisyl propane gave 1-anisyl-2-phenyl propene ($\overline{\underline{XLIII}}$).

$$C_6H_5-CH(C_6H_4OCH_3)-CH(CH_3)NH_2 \xrightarrow{HONO} CH_3OC_6H_4-CH:C(C_6H_5)CH_3 \quad \underline{\underline{XLIII}}$$
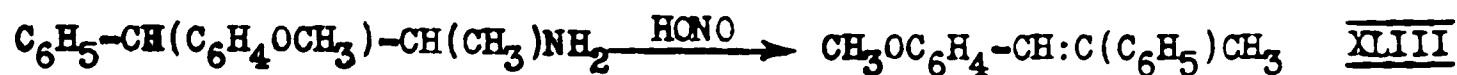
Mechanism

The general reaction mechanism is similar to that used for alcoholic dehydration. The attack of nitrous acid or nitrosyl chloride on the amino group causes its removal, thus forming a carbonium carbon which can undergo rearrangement. Once the rearrangement has taken place the reaction is completed by hydroxyl or chlorine addition or by proton elimination. An example of the steps in the mechanism is shown by Whitmore[41] in conversion (XLII) above.

(1) $(CH_3)_3C-CH_2NH_2 \xrightarrow{HONO} (CH_3)_3C\cdot\overset{+}{C}H_2 + N_2 + H_2O + OH^-$

(2) $CH_3\underset{CH_3}{\overset{}{C}}(CH_3)-\overset{+}{C}H_2 \xrightarrow[shift]{1,2} CH_3-\overset{+}{C}(CH_3)-\underset{CH_3}{\overset{}{C}}H_2 \longrightarrow$

(3) $CH_3\overset{+}{C}(CH_3)-\underset{CH_3}{\overset{}{C}}H_2 \xrightarrow{+ OH^-} CH_3-\underset{OH}{\overset{}{C}}(CH_3)-\underset{CH_3}{\overset{}{C}}H_2$
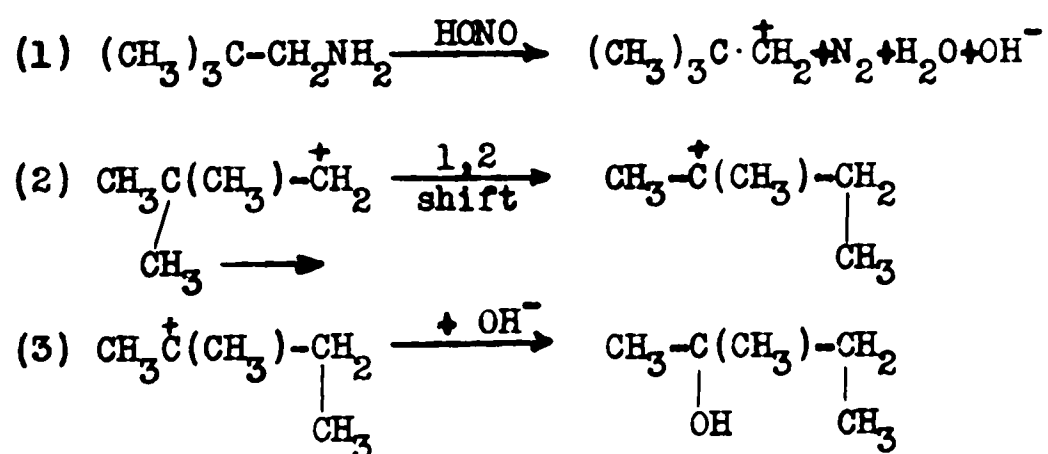
Class $\underline{V}$ <u>HALOGEN COMPOUNDS</u>

Certain halogen-containing compounds can undergo intramolecular rearrangement in either substitution or elimination reactions. The ease or probability of rearrangement depends upon the complexity of the adjacent carbon attachments. The "neopentyl system", 1-iodo-2, 2-dimethyl propane readily undergoes rearrangement when attacked by such electrophilic reagents as silver acetate, silver nitrate or mercuric nitrate[58] to give 2-methyl butanol-2 as product ($\overline{\underline{XLIV}}$).
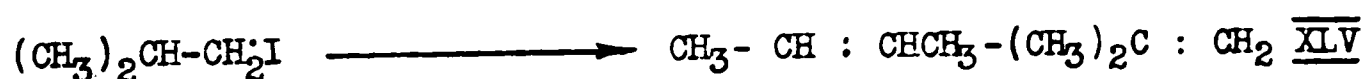
$$(CH_3)_3-C-CH_2\cdot I \longrightarrow (CH_3)_2C(OH)-CH_2CH_3 \qquad \overline{\underline{XLIV}}$$

Many instances of rearrangements occur in elimination reactions of halo-hydrocarbons in their conversion to defins.

Eltekov[59] converted 1-iodo-2-methyl propane to butene-2 and 2-methyl propene by heating with lead dioxide ($\overline{\underline{XLV}}$).

$$(CH_3)_2CH-CH_2I \longrightarrow CH_3-CH : CHCH_3-(CH_3)_2C : CH_2 \quad \overline{\underline{XLV}}$$

Upon dry distillation of several 1-chloro-2, 2-diphenyl ethanes, rearrangement into 1,2-diphenyl ethylenes takes place. Hepp[60] pointed out that in these conversions the unrearranged olefin was the intermediate, because the expected olefin that would result from the dehalogenation can itself be rearranged upon heating. Thus, 1-chloro-2,2-diphenylethane was converted to 1,2-diphenylethylene ($\overline{\underline{XLVI}}$).

$$(C_6H_5)_2CH-CH_2Cl \xrightarrow{-HCl} (C_6H_5)_2C : CH_2 \xrightarrow{1,2 \text{ phenyl}} C_6H_5CH : CHC_6H_5 \quad \overline{\underline{XLVI}}$$
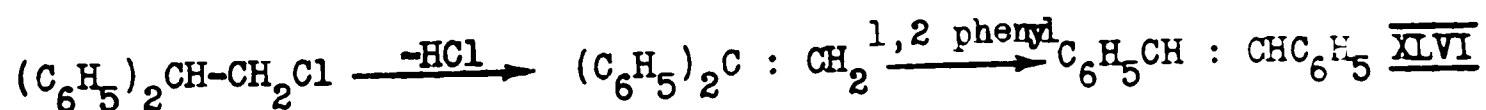
Hepp[60] also reported rearranged products from ditolyl, dixylyl and dinaphthyl substituted ethane derivatives.

More recently Schmidlin[61] converted 1,1,1,2-tetra phenyl-2-bromo ethane into tetra phenyl ethylene (XLVII).

$$(C_6H_5)_2C \cdot CH(C_6H_5) \text{ Br} \longrightarrow (C_6H_5)_2C : C(C_6H_5)_2 \qquad \text{XLVII}$$

Class $\overline{VI}$ OLEFINS

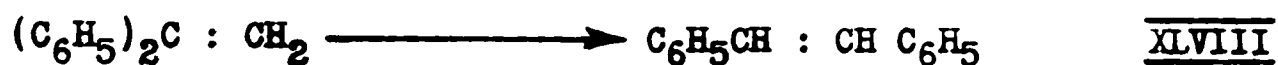It has been shown possible to make certain unsymmetrical di substituted aromatic olefins undergo rearrangement.

Hepp[60] in the "dry distillation" of 1,1-diphenyl ethylene obtained 1,2-diphenyl ethylene ($\overline{XLVIII}$). Other substituted aromatic diphenyl ethylenes could go through the same rearrangement.

$$(C_6H_5)_2C : CH_2 \longrightarrow C_6H_5CH : CH\ C_6H_5 \qquad \overline{XLVIII}$$

Redsko[62] reported that upon reduction of 1,1-diphenyl-2-2-dichloro ethylene with red phosphorus and iodine were obtained both 1,2-diphenyl ethane and 1,1-diphenyl ethane ($\overline{XLIX}$).

$$CCl_2 : C(C_6H_5)_2 \xrightarrow{\text{RED P+I}_2} C_6H_5CH_2-CH_2C_6H+(C_6H_5)_2CH-CH_3 \qquad \overline{XLIX}$$
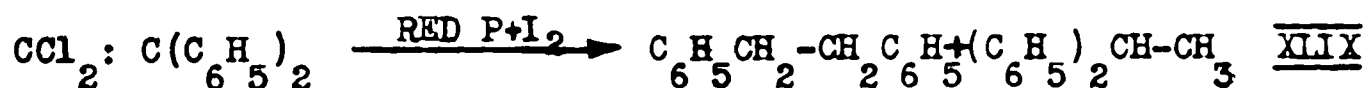
Mechanism

The mechanism through which an olefin may rearrange upon reduction can best be explained on the basis that hydrogen does not add as a molecule but that the reduction follows in two steps. Thus the addition of a proton to the double bond can produce a carbonium carbon which may undergo rearrangement. The second addition of hydrogen to the ion then completes the reduction to give the stable rearranged product[41].

Class $\overline{VII}$ <u>AROMATIC COMPOUNDS</u>

Rearrangements involving alkyl or aryl shifts can be made to take place with highly substituted aromatic compounds. These rearrangements are catalysed by strong electrophilic reagents, like sulfuric acid, aluminum chloride and aluminum bromide.

The rearrangement of poly alkyl benzenes induced by sulfuric acid is known as the "Jacobsen Reaction" after the discoverer Oscar Jacobsen[63].

Rearrangements of poly alkyl or poly aryl aromatic compounds induced by aluminum chloride or aluminum bromide are better known as Friedel and Crafts Reactions.

(A) JACOBSEN REACTION

The "Jacobsen reaction[64] involves halogen, methyl or ethyl shifts on the benzene ring, when that ring is highly substituted, by the use of concentrated sulfuric acid. The mechanism of this reaction appears to be complicated and as yet has no adequate explanation."

A "Jacobsen rearrangement" can follow either one of two paths.

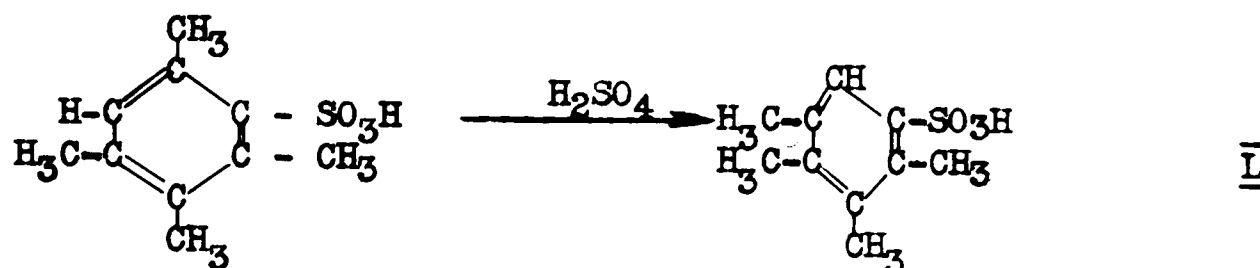(1) <u>Intramolecular Rearrangement</u>:

The halo, methyl or ethyl group migrates from one position to another within the molecule. The shifts are 1,2 or 1,3 carbon-carbon migrations.

(2) <u>Intermolecular Rearrangement</u>:

The halo, methyl, ethyl group or groups migrate from one molecule to another, forming a more highly substituted and a less highly substituted aromatic compound as products.

An example of rearrangement involving the intramolecular type is that afforded by the conversion of 2,3,4,6-tetra methyl[65] (or tetra ethyl) benzene sulfonic acid into 2,3,4,5-tetra methyl (or tetra ethyl) benzene sulfonic acid ($\underline{L}$).

As intermolecular rearrangements are beyond the scope of this outline, they will not be discussed further.

(B) FRIEDEL AND CRAFTS REACTION

The "Friedel and Crafts Reaction" was first discovered in 1884 by Friedel and Crafts.[66,67] Initially, the process involved only the reaction between benzene and some mono halogenated alkane which, under the influence of aluminum chloride, splits out hydrogen chloride giving rise to alkylated benzenes.

Today, however, several classes of chemical reactions come under the Friedel and Crafts Heading. Such reactions include condensations of anhydrides with aromatics, olefin additions to benzene, carbon monoxide additions to benzene, aliphatic reactions, rearrangements, etc. Besides involving different classes of reaction, the Friedel and Crafts reaction can also be carried out by different chemical reagents other than aluminum chloride, such as aluminum bromide, boron trifluoride, zinc

chloride, etc. The common feature of these reagents is the fact that they are all strongly electrophilic.

The only class of Friedel and Crafts reaction discussed here will be that involving rearrangements.

Rearrangements induced by aluminum chloride can follow two paths. In this respect the rearrangement resembles the "Jacobsen reaction".

(1) Intramolecular Rearrangement:

A methyl, ethyl, propyl or phenyl group migrates from one position to another within the molecule. These shifts can be 1,2, or 1,3 or 1,4 carbon-carbon migrations.

(2) Intermolecular Rearrangement:

Rearrangements involving migration of alkyl groups from one molecule to another also take place and give rise to two or more products. In any case the products include more highly substituted and less substituted molecules than the starting material.

It may be of interest to note that Baddeley[68] in a recent paper noted that intramolecular rearrangements take precedence at low temperature and that intermolecular rearrangements are favoured at more elevated temperatures.

An example of intramolecular rearrangement is shown by Baddeley[69]. Thus 1,4-di-n-propyl benzene is converted to 1,3-di-n-propyl benzene with aluminum chloride (II) in 65% yield.

$$\text{(structure: 1,4-di-n-propylbenzene)} \xrightarrow{AlCl_3} \text{(structure: 1,2-di-n-propylbenzene)} \quad (\underline{LI})$$
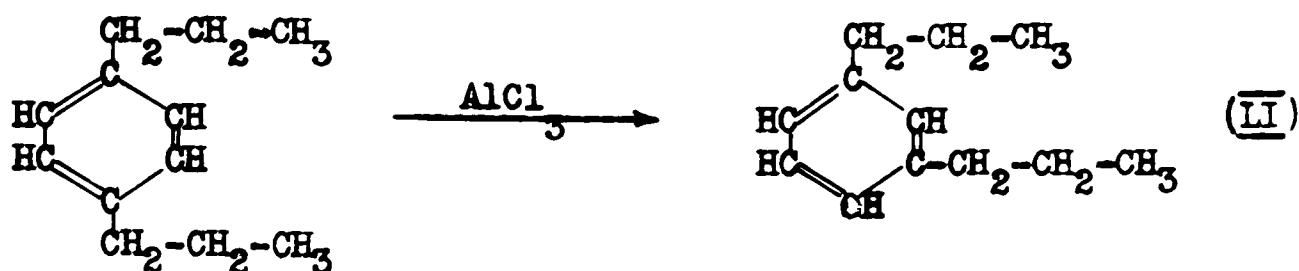
No isopropyl derivatives were obtained in this rearrangement. Aluminum chloride readily rearranges n-propyl chloride to isopropyl chloride (2-chloropropane). Thus the mechanism must have been a 1,2-carbon-carbon shift which did not involve an elimination of $CH_2CH_2CH_3$ ion with subsequent readdition.

More recently Allen[70] has shown an interesting rearrangement to take place with o-terphenyl by the use of traces of aluminum chloride. Upon heating the o-terphenyl to 130°C was first obtained m-diphenyl benzene, and finally p-diphenyl benzene. ($\underline{LII}$)

$$\text{(o-terphenyl)} \xrightarrow[\substack{Quant \\ 130°C}]{AlCl_3} \text{(m-diphenyl benzene)} \xrightarrow{AlCl_3} \text{(p-diphenyl benzene)} \quad \underline{LII}$$
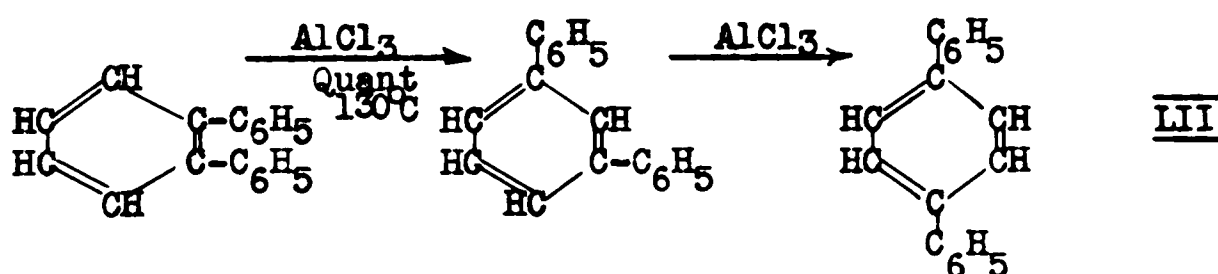
The reaction may be interrupted at the m-diphenyl stage. After eleven days heating the m-diphenyl benzene is nearly completely converted to the p-diphenyl benzene.

Mechanism

The mechanism of the rearrangements that take place in both the Friedel Crafts and Jacobsen reactions is complicated and as yet not fully understood. It is believed possible by the author that both these reactions have a very similar mechanism.

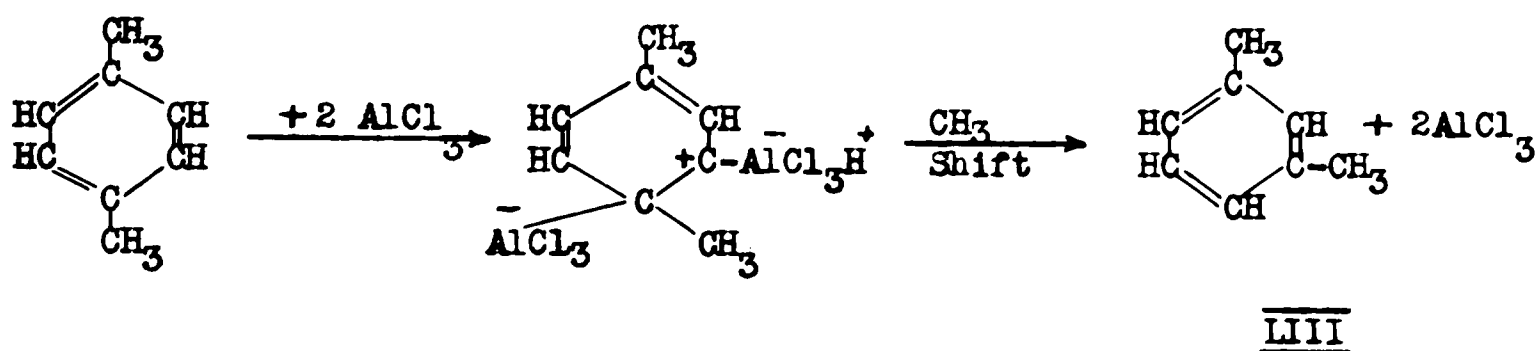G. Baddeley[71] has advanced a possible explanation for the Friedel and Crafts reaction. This mechanism involves the addition of two moles of aluminum chloride to two adjacent carbon atoms in the benzene ring, one of which has the migrating group attached. The essential conditions for a Meerwein Shift are now present and the alkyl group can undergo a 1,2-carbon-carbon rearrangement. The reaction is explained as follows for the conversion of p-dimethyl benzene into m-dimethyl benzene ($\overline{\underline{LIII}}$).

$$\text{p-dimethyl benzene} \xrightarrow{+2\ AlCl_3} \text{intermediate (} -AlCl_3,\ +C-AlCl_3H^+ \text{)} \xrightarrow[\text{Shift}]{CH_3} \text{m-dimethyl benzene} + 2AlCl_3$$

$$\overline{\underline{LIII}}$$

It is considered by Baddeley from atomic model construction that both the alkyl and aluminum chloride groups cannot exist on the same side of the ring. This, therefore, results in a displacement of the two groups and gives rise to polarizations which permit a second molecule of aluminum chloride to attach itself to the carbon holding the alkyl group. Thus the molecule would have the following stereo structure ($\overline{\underline{LIV}}$), which can then rearrange with a methyl shift.

$$\overline{\underline{LIV}}$$

(C)

Other Aromatic Rearrangements

Rearrangement of aromatic ketones has been discussed under ketones and the Friedel and Craft reaction.

However, Mayer[72] has reported that it is possible to rearrange 1-naphthalene derivatives into 2-naphthalenes by heating them to $350^{\circ}C$, using silica gel as catalyst. Thus 1-phenyl naphthalene gives 2-phenyl-naphthalene ($\underline{LV}$)

$$\text{(structure)} \xrightarrow[350^{\circ}C]{SiO_2} \text{(structure)} \qquad (\underline{LV})$$

Similar results were also obtained by heating 1-methyl and ethyl derivatives respectively. The mechanism is unknown.

CONCLUSION

In this outline rearrangements have been shown to take place in a large variety of compounds under the proper conditions. These transformations have been explained on a carbonium ion mechanism. In the more elementary examples it was relatively easy to write simple, logical intermediate steps. However, the more complex rearrangement mechanisms that occur in the Jacobsen and Friedel and Crafts reactions are not clear as to detailed steps. These more complex transformations probably involve the formation of carbonium ions as precursors to the rearrangement as in the more elementary cases.

Again it must be pointed out that intramolecular transformations can take place with more complex molecules than those mentioned in this historical outline. For instance, many rearrangements have been reported to take place in terpenes and heterocyles. The many examples in these series of one-two and one-three carbon-carbon shifts of alkyl or aryl groups follow the same general principles as outlined for the simpler cases.

Terpene and heterocyclic rearrangements are effected in the processes of dehydration, dehydrohalogenation, addition and by heating. In all examples, the essential feature is the formation of a carbonium ion which rearranges. The rearrangement is then followed by either an elimination of some group to give an unsaturated product, or by an addition of some group to the new carbonium carbon produced as a result of the rearrangement.

Many investigators have studied rearrangements in these two fields. Such workers include Meerwein[73], Komppa[74], Bartlett[75], Kharasch[76], etc., in the terpene series, and Wibaut[77], Brunner[78], Knorr[79], Wolff[80], Baeyer[81], Biltz[82], etc., in the heterocyclic series.

HISTORICAL

PART II

HISTORICAL REVIEW OF THE PREPARATIONS OF THE "CARBINOL" 1-4-CHLOROPHENYL-2,2,2-TRICHLOROETHANOL
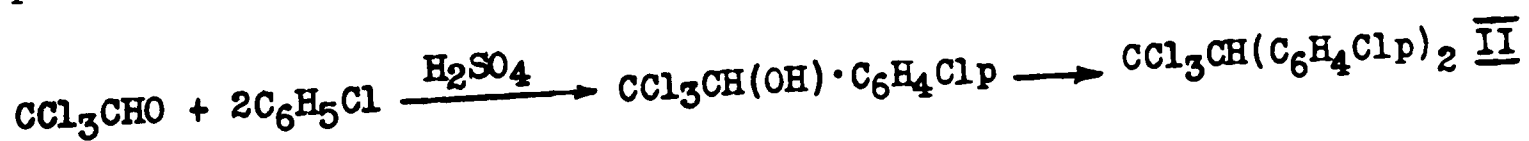
The compound 1-4-chlorophenyl-2,2,2-trichloroethanol can be prepared in many ways.

Howard and Castle[131] prepared the compound by condensing 4-chlorobenzaldehyde and chloroform, using potassium hydroxide as catalyst (I). This preparative method was first used by Jozitsch[132] in the preparation of 1-phenyl-2,2,2-trichloroethanol.

$$pCl\ C_6H_4 \cdot CHO + CHCl_3 \xrightarrow{KOH} pCl\ C_6H_4 \cdot CH(OH)CCl_3 \qquad I$$
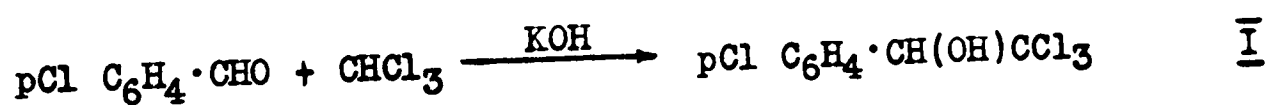
The above method is an easy synthesis, but the yields are low.

The carbinol has also been obtained[133] in about 5% yield from the reaction of chloral and chlorobenzene to give 1,1,1-trichloro-2,2-bis p chlorophenylethane with sulfuric acid (II).

$$CCl_3CHO + 2C_6H_5Cl \xrightarrow{H_2SO_4} CCl_3CH(OH) \cdot C_6H_4Clp \longrightarrow CCl_3CH(C_6H_4Clp)_2 \qquad II$$

More recently the synthesis has been accomplished through a Gringard reaction. Thus, chloral and p-chlorophenylmagnesiumbromide gave the carbinol in 65% yield (III). This method was first used by Jozitsch[134] to prepare 1-phenyl-2,2,2-trichloroethanol.

$$CCl_3CHO + Mg\ Br\ C_6H_4Cl \longrightarrow CCl_3CH(OH) \cdot C_6H_4Clp \qquad III$$
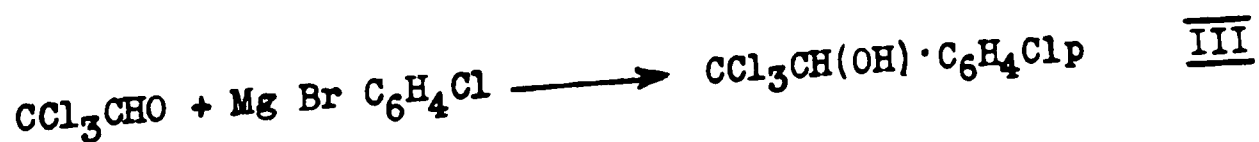
Meerwein[135] and Schmidt were able to reduce 1-phenyl-2,2,2-trichloro ethanone to 1-phenyl-2,2,2-trichloroethanol by the use of aluminum iso-propoxide. This method was successfully applied in this laboratory to prepare 1-4-chlorophenyl-2,2,2-trichloroethanol and by Bartlett[136] to prepare 1-4-chlorophenyl-2,2-dichloroethanol.

HISTORICAL

PART III

ATTEMPTED HISTORICAL PREPARATIONS OF "DIORTHO D.D.T."
1,1,1-TRICHLORO-2,2-BIS 2 CHLOROPHENYL ETHANE
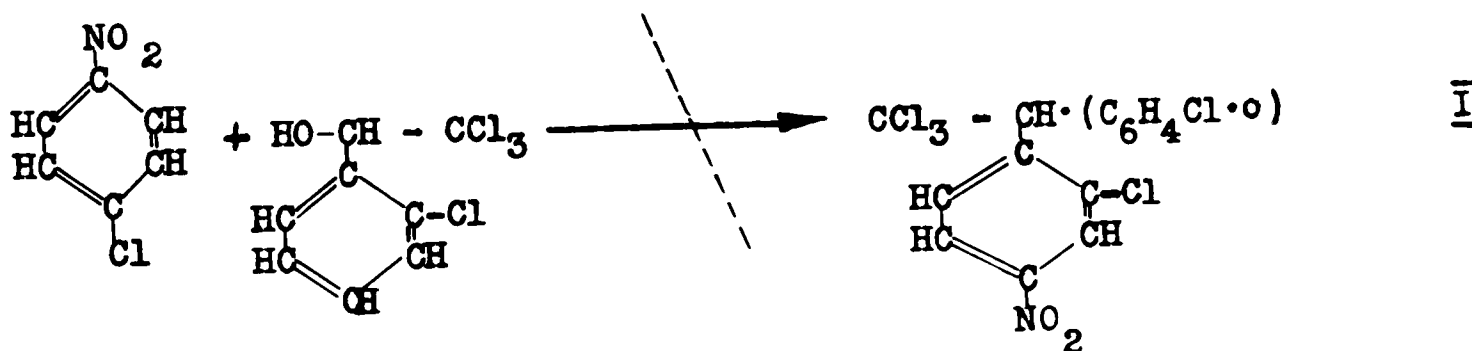
There have been several unsuccessful attempts made to synthesize 1,1,1-trichloro-2, 2-bis 2 chlorophenyl ethane.

Thus, 1-2-chlorophenyl-2,2,2-trichloroethanol and 4-chloro, nitro-benzene[137] were caused to react using sulfuric acid as the condensing agent ($\underline{I}$). The substitution of 3-chloroaniline[137] for 4-chloro, nitro-benzene was also without result.

The nitro group was to be eliminated by reduction to an amino which was to be converted to the diazonium compound. The diazonium was then to be decomposed by ethanol to give the "diortho D.D.T."

Another method attempted for synthesis was the nitration of 1,1,1-trichloro-2,2-bis phenyl ethane to 1,1,1-trichloro-2,2-bis 4 nitrophenyl ethane ($\underline{II}$). The nitration was to be followed by a chlorination into the 2,2'- positions on the ring. The nitro groups were to be eliminated as shown above in trial ($\underline{I}$). However, in the nitration of the 1,1,1-trichloro-2,2-bis phenyl ethane was obtained 1,1,1-trichloro-2-4 nitro-phenyl-2-3' nitrophenylethane[137] ($\underline{II}$) and not the 4',4 dinitro derivative.

$$CCl_3CH(C_6H_5)_2 \xrightarrow[H_2SO_4]{HNO_3}$$
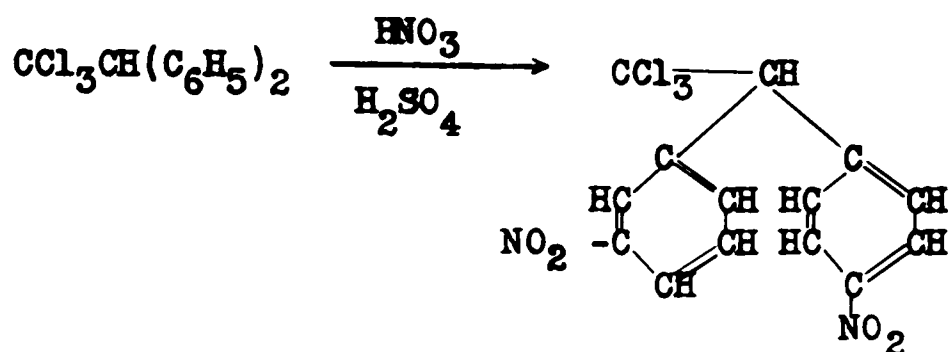
Bartlett[136] reported the attempted addition of o-chlorophenyl-magnesiumbromide to 1-2 chlorophenyl-2,2,2-trichloroethanone which was also unsuccessful (III).

$$CCl_3-CO\ C_6H_4Cl-o + Mg\ Br \longrightarrow CCl_3C(OH)(C_6H_4Cl\cdot o)_2 \quad \underline{\underline{III}}$$
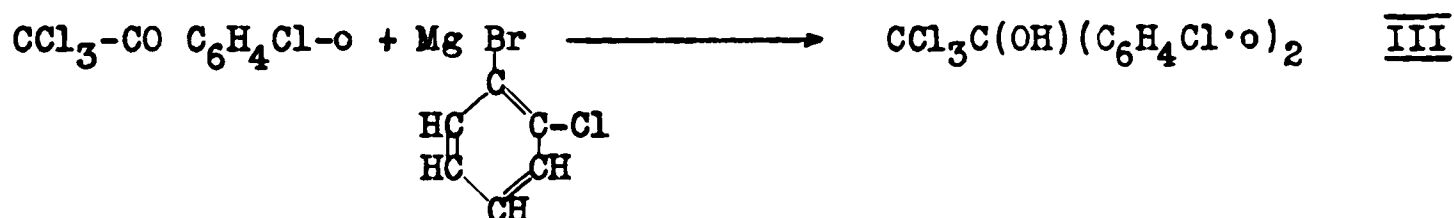
The condensation of 4 chloroiodobenzene[136] with 1-2 chlorophenyl-2,2,2-trichloroethanol was also without result (IV)

$$CCl_3CH(OH)\cdot C_6H_4Cl\cdot o + I\ C_6H_4Cl \xrightarrow{H_2SO_4} CCl_3CH\cdot(C_6H_4Cl\cdot o) \quad \underline{\underline{IV}}$$
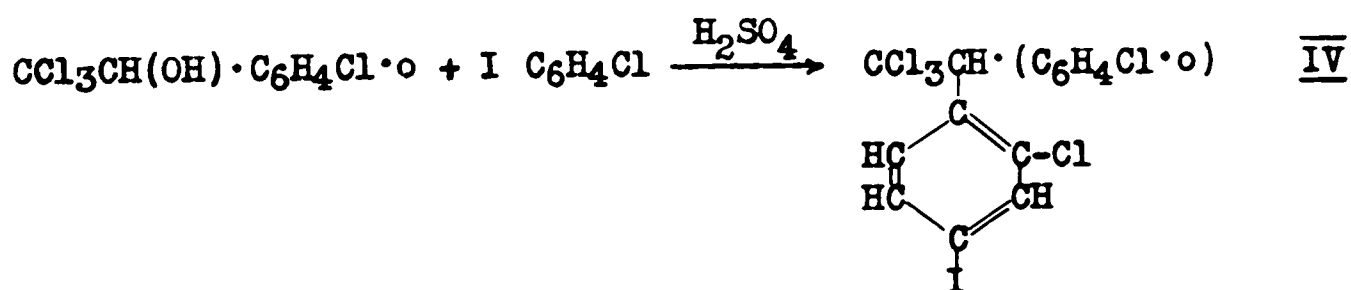
Bartlett[136] also reported the failure to convert bis 4 chlorophenyl acetic acid to 1,1,1-trichloro-2,2-bis 2 chlorophenylethane with phosphorus pentachloride (V).

$$(o\cdot Cl\ C_6H_4)_2\ CHCOOH \xrightarrow{PCl_5} (o\cdot Cl\ C_6H_4)_2\cdot CH\ CCl_3 \quad \underline{\underline{V}}$$
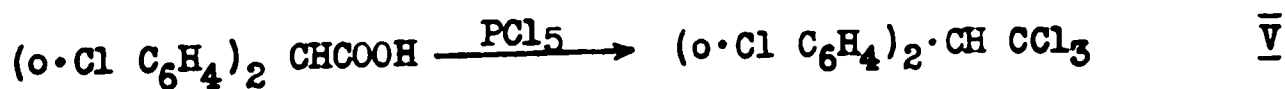
This method was also attempted by the author without success.

DISCUSSION

P A R T I

Introduction

The historical section of this thesis has been devoted to describing in outline the many compounds that may undergo intramolecular rearrangement. These carbon skeleton transformations are all catalyzed by electrophilic reagents. The examples shown comprised only those rearrangements that involved a one-two, carbon-carbon shift of an alkyl or aryl group. Even though this review only includes carbon-carbon, one-two shifts, it is believed by the author that the examples shown adequately support the rearrangement discussed below.

The present work includes rearrangement of a few polyhalogen compounds, under the influence of sulfuric acid, resulting from degradation of the molecules. Thus, in attempting to hydrolyze the tertiary aliphatic chlorine in 1,1,1,2-tetrachloro-2, 2-di p chlorophenylethane to 1,1,1-trichloro-2-hydroxy-2, 2-di p chlorophenylethane with sulfuric acid, a product was obtained which appears to be 4,4'-dichlorobenzil. The reaction is schematically pictured below:
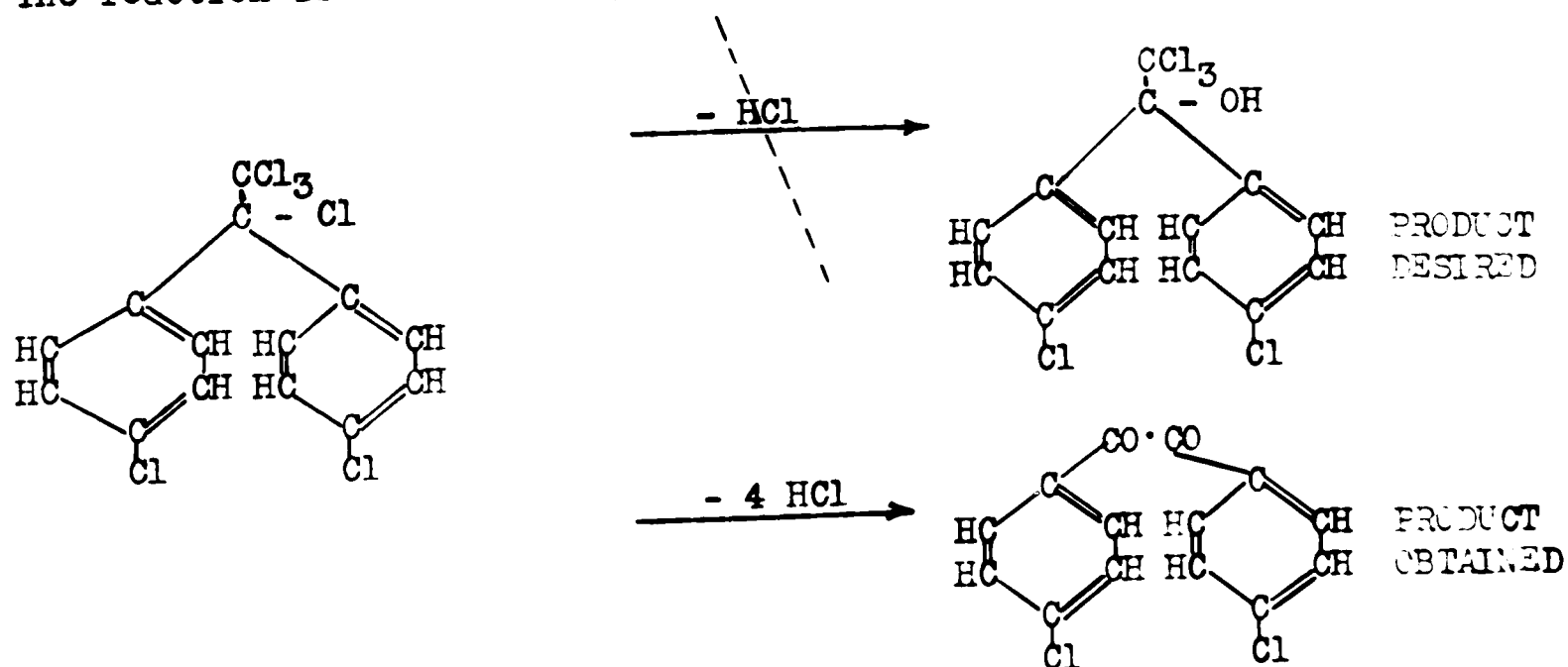
The product obtained, 4,4'-dichloro benzil, was first reported
by Montagne[84], who prepared it by oxidizing the corresponding 4,4'-di-
chlorobenzoin compound with nitric acid.

Commentary

The extent of the rearrangement of 1,1,1,2-tetrachloro-2, 2-di p
chlorophenyl ethane seems to be limited by experimental conditions.
For instance, the transformation is quite slow at 90°C, using 96% sul-
furic acid and does not seem to take place at all with acid concentra-
tions greater than 100%, with which no water insoluble products are
obtainable after dilution of the reaction mixture with water. If the
rearrangement does take place under conditions of high acid concentra-
tions, then it is conceivable that the product is sulfonated. Further-
more, this rearrangement does not appear to be a general reaction for
poly halogen compounds. In the many attempted conversions of di aryl
substituted trichloro ethanes, only two gave rise to rearranged pro-
ducts. It is believed that the failure of some of these compounds to
rearrange may be due either to their greater ease of sulfonation or to
their lower solubility in concentrated sulfuric acid. Nevertheless,
the two successful examples are of interest because they throw some
light on the possible decomposition products of "D.D.T", 1,1,1-trichloro-2,
2-bis p chlorophenyl ethane, in strong acid solutions under slightly
elevated temperatures. Both 1,1,1,2-tetrachloro-2, 2-bis p chlorophenyl
ethane and 1,1,1-trichloro-2, 2-bis p chlorophenyl ethane undergo this
intramolecular transformation to 4,4'-dichlorobenzil - the former with

98% sulfuric acid and the latter with 100% sulfuric acid, respectively.
It is of interest to note that kinetic studies on the rate of formation
of "D.D.T." from chloral and chlorobenzene at 70°C indicate that the
amount of pure p,p-D.D.T. produced falls even though the crude yield
rises.[140] This decreased yield indicates that D.D.T. is converted to some
other products which may in part consist of 4,4' dichloro benzil.

Structure Proof of the 4,4'-Dichloro Benzil

The product obtained from the hydrolysis of 1,1,1,2-tetra chloro-2,
2-bis p chloro phenyl ethane and 1,1,1-tri chloro-2, 2-bis p chloro
phenyl ethane with sulfuric acid was subjected to the following tests
to establish its structure.

The material had a m.p. 195°-196°C which did not correspond to
any product which might have been expected from the reaction. A total
analysis of the material established that the empirical formula was
$(C_{14}H_8O_2Cl_2)_X$. Several molecular weight determinations in acetone
by the ebullioscopic method of Menzies-Wright[123] gave values for the
product 289, 290 and 281. The molecular weight of the starting material
is 389. The mean value of the molecular weight (286) established that
the material was not an associated molecule and indicated that X in the
empirical formula was unity.

The material formed several derivatives, such as an oxime with
hydroxylamine, a mono phenylhydrazone with phenyl hydrazine and a quin-
oxaline with o-phenylene diamine.

The oxime was analysed for chlorine and the result obtained showed
that only a mono oxime derivative had been formed. The phenylhydrazone

and quinoxaline were not analysed.

The unknown material was oxidized with a chromic acid-acetic acid mixture and 4-chlorobenzoic acid was obtained in 30% yield. (This yield is based on 4,4'-dichlorobenzil.) No other product could be obtained from this oxidation.

Another oxidation with alkaline hydrogen peroxide[85] gave 4-chlorobenzoic acid in 61% yield (also based on 4,4'-dichloro benzil).

A control oxidation on 4,4'-dichlorobenzil synthesized by another method[89,90,95], using alkaline hydrogen peroxide gave 4-chlorobenzoic acid in 71% yield.

From these results the unknown compound must possess a structure such that two molecules of 4-chlorobenzoic acid could be obtained upon decomposition.

The experimental evidence obtained for the structure of the unknown material can be compared with the known properties of 4,4'-dichlorobenzil.

Properties	4,4'-Dichlorobenzil	Unknown Compound Obtained from the Hydrolysis
1) Molecular Formula	$C_{14}H_8O_2Cl_2$	$C_{14}H_8O_2Cl_2$
2) Molecular Weight	279	286 (mean value)
3) Oxidation Product	4-chloro benzoic acid	4-chloro benzoic acid
4) Melting Point	lit. 193°C[118] and 200°C[84] this lab. 194-195°C	195-196°C
5) Phenyl Hydrazone	lit. 178°C (84)	178°C
6) Colour	yellow	yellow

Apparently the product obtained from the hydrolysis of 1,1,1,2-tetrachloro-2, 2-bis p chlorophenyl ethane is 4,4'-dichloro benzil.

4,4'-Dichloro benzil was synthesized by condensing two molecules of 4-chloro benzaldehyde to 4,4'-dichloro benzoin and oxidizing the latter to 4,4'-dichloro benzil with nitric acid.[89],[90],[95] Even though the melting point of 4,4'-dichloro benzil, prepared by this method, was reported by Montagne[84] to be 200°C, and by Kenner[118] to be 193°C, the material prepared in this laboratory possessed an m.p. of 194-195°C after two recrystallizations from ethanol. Further recrystallization did not raise the m.p.

The final proof of the structure of the unknown material is shown by the melting point taken of the mixture of 4,4'-dichloro benzil and the product obtained in the hydrolysis of 1,1,1,2-tetrachloro-2, 2-bis p chloro phenyl ethane which showed no depression.

Mechanism

It has been shown that from 1,1,1-trichloro-2,2-bis 4 chlorophenyl ethane and 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane was obtained 4,4'-dichlorobenzil by the hydrolytic action of sulfuric acid. However, no substituted benzil derivatives could be obtained from 1,1,1-tri-chloro-2,2-bis 4 tolylethane; 1,1,1-trichloro-2,2-diphenylethane; 1,1,1-trichloro-2-phenyl-2-4 chlorophenylethane; 1,1,1-trichloro-2,2-bis 4 bromophenylethane; 1,1,1-trichloro-2,2-bis 4,4'-dichloro-3,3'-dinitro-phenylethane; 1,1-dichloro-2,2-di 4 chlorophenyl ethylene; 1,1-bis 4 chlorophenyl ethylene and 1,1-di 4 tolylethane by the use of 96%, 98% or 100% sulfuric acid. Many of these compounds were subjected to other acid concentrations with different durations of heating, but no re-arranged acid insoluble products were obtained. The action of 98%

sulfuric acid on 1,1,1-trichloro-2,2-bis 4,4'-dichloro-3,3'-dinitro-phenylethane gave a material from which no crystalline product has been obtained.

The rearrangement of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane to 4,4'-dichloro-benzil encourages speculation as to the mechanism. The close relation-ship between the rearrangement of these compounds and the "pinacol-pinacolone" transformation is apparent. To postulate any reasonable mechanism for the observed conversions is more difficult than for a "pinacol" transformation, because of the loss of four groups from the molecule as compared with one for the "pinacol-pinacolone" transforma-tion. On paper, many mechanisms can be devised but none is completely satisfactory.

The postulation of any rearrangement mechanism must include the formation of some kind of intermediate carbonium ion which can allow the shift to take place. Thus, to consider a mechanism, it is first necessary to decide the point of attack on the molecule; thus the skeleton of the two molecules is as follows:-

$$\overset{\alpha}{CH} \cdot \overset{\beta}{C} \ Cl_3 \qquad and \qquad \overset{\alpha}{CCl} \cdot \overset{\beta}{C} Cl_3$$
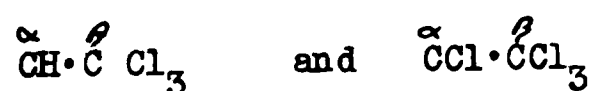
The unsymmetrical nature of the molecules makes this decision rather difficult.

Any mechanism must take into account that the conversion of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane proceeds only when 100% sulfuric

acid is employed, whereas the conversion of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane can be brought about with 96% sulfuric acid. Two comparatively simple mechanisms will be suggested, which would not be contrary to the observed behaviour; other mechanisms, somewhat less attractive, could also be outlined, but there seems little point in doing so in the absence of more complete experimental basis for differentiation between various possible mechanisms.

Mechanism A

If it is assumed that the initial attack is on the carbon atom , then the mechanism could be represented as follows for 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane, respectively.

<u>STEP I</u>

$$(pClC_6H_4)_2CH \cdot CCl_3 \xrightarrow[\text{oxid'n}]{+H_2SO_4} (pClC_6H_4)_2C(OH) \cdot CCl_3 + H_2O + SO_2 \uparrow$$

$$(pClC_6H_4)_2CCl \cdot CCl_3 \xrightarrow{\text{hydrolysis}} (pClC_6H_4)_2C(OH) \cdot CCl_3 + HCl$$

<u>STEP II</u>

$$(pClC_6H_4)_2 \cdot C(OH) \cdot CCl_3 \xrightarrow{2H_2SO_4} (pClC_6H_4)_2 \cdot \overset{+}{C} \cdot CCl_3 + \overset{+}{OH_3} + 2HSO_4^-$$

<u>STEP III</u>

$$(pClC_6H_4)_2 \cdot \overset{+}{C} \cdot CCl_3 \xrightarrow[\substack{\text{1,2-4 chlorophenyl} \\ \text{shift}}]{\text{1,2-chloro shift}} pClC_6H_4 \cdot \overset{+}{C}Cl \cdot CCl_2C_6H_4Clp$$

<u>STEP IV</u>

$$pClC_6H_4 \cdot \overset{+}{C}Cl \cdot CCl_2C_6H_4Clp \xrightarrow{+ OH^-} pClC_6H_4\overset{OH}{C}Cl \cdot CCl_2 \cdot C_6H_4Clp$$

$$\downarrow -HCl$$

$$pClC_6H_4CO \cdot CCl_2C_6H_4Clp$$

STEP V

$$pClC_6H_4CO \cdot CCl_2C_6H_4Clp \xrightarrow[- Cl^-]{+ HO^-} pClC_6H_4CO \cdot \overset{OH}{CCl} \cdot C_6H_4Clp$$

$$\downarrow -HCl$$

$$pCl\ C_6H_4 \cdot CCCO \cdot C_6H_4Clp$$
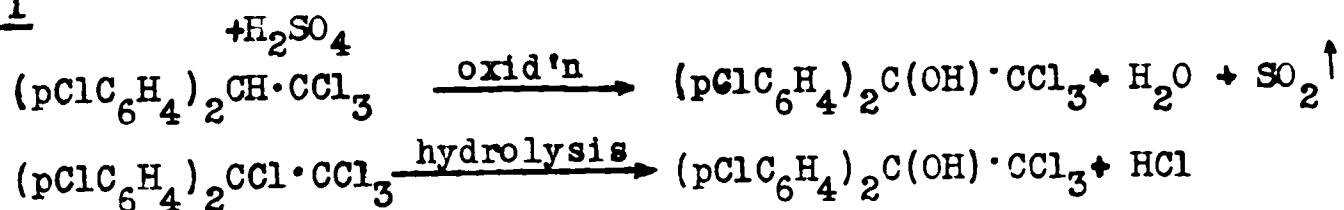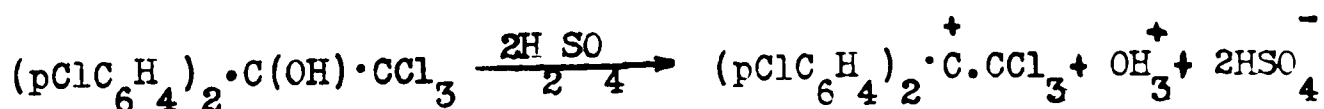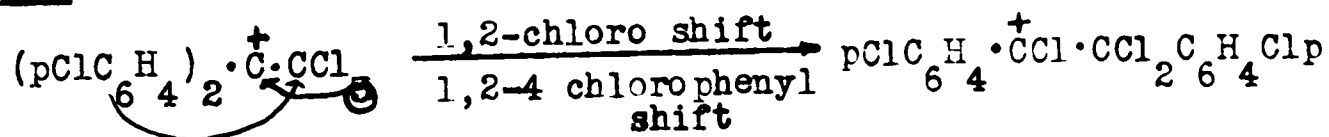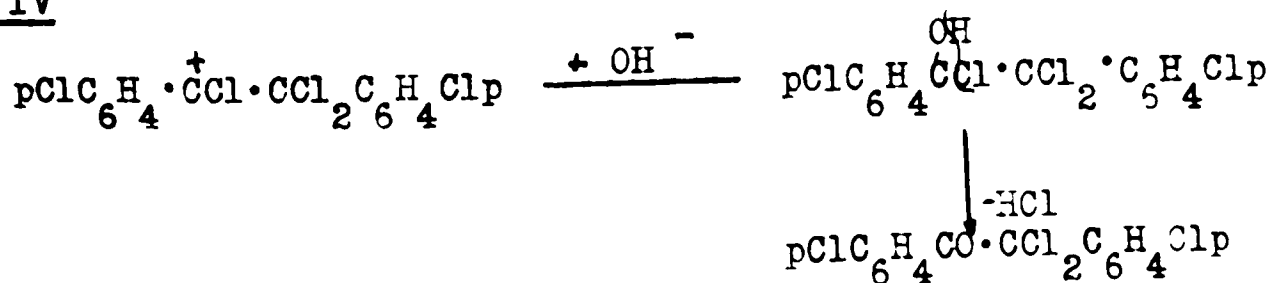
The oxidation of the tertiary hydrogen in Step I is a questionable point[#], because it would be expected that some conversion could take place with 96% sulfuric acid. However, if this reaction is analogous to the decomposition of formic acid to carbon monoxide and water[143] ($\underline{I}$) where the rate with 95% sulfuric acid is one hundred times less than with 100% acid, then this conversion must be considered to be an acid catalyzed reaction which is inhibited by the base water. As the conversion of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane to 4,4'-dichlorobenzil is slow, even with 100% sulfuric acid, it is conceivable that if the rate were decreased one hundred times for 96% sulfuric acid, no product would have been detected.
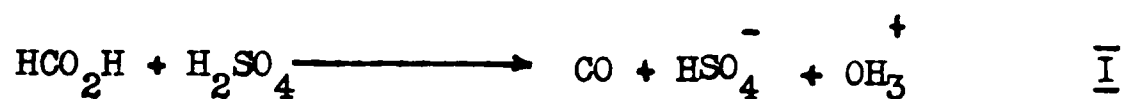
$$HCO_2H + H_2SO_4 \longrightarrow CO + HSO_4^- + OH_3^+ \qquad \underline{I}$$

On the basis of the electronic theory, the trichloromethyl group is an "electron sink", that is, the grouping is very strongly electron attracting. This condition is observable in chloral[130] and trichloroacetic acid. Phenyl groups can act either as electron "donors" or
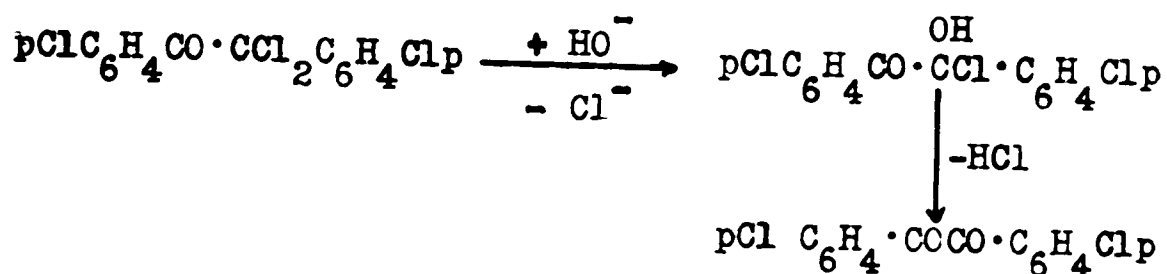

[#] Experiments carried out after this thesis was written showed that by the use of mercuric sulfate or ferric sulfate as catalysts, the transformation of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane to 4,4'-dichlorobenzil can take place with 96% sulfuric acid. This may be accepted as evidence for mechanism A as both mercuric and ferric sulfate are considered to be oxidation catalysts.

"sinks" as the conditions require. Thus, 1,1,1-trichloro-2,2-bis 4 chlorophenylethane would have electronic displacements as follows:-

$$pClC_6H_4 \rightarrow \leftarrow C \xrightarrow{} \underset{Cl}{\overset{Cl}{\underset{|}{\overset{|}{C}}}} \rightarrow Cl$$

Therefore, it would be reasonable to postulate that the hydrogen atom is loosely bound and could easily be displaced. The fact that chlorine can easily displace this tertiary hydrogen at moderate temperature is in accord with such a postulate.

It has been reported that the tertiary hydrogen in such compounds as 2-phenyl propionic acid can be easily oxidized to 2-hydroxy-2-phenyl propionic acid ($\overline{\overline{II}}$) with alkaline permanganate under controlled conditions.[144] In this molecule a somewhat analogous electronic picture exists as in 1,1,1-trichloro-2,2-bis 4 chlorophenylethane.

$$C_6H_5CH \cdot (CH_3) \cdot COOH \xrightarrow{\text{oxid'n}} C_6H_5 \cdot C(OH)CH_3 \cdot COOH \qquad \overline{\overline{II}}$$

The carboxyl group is an "electron sink" which deactivates. The phenyl group can operate as a "donor" or as a "sink". The tertiary hydrogen is thus loosely bound ($\overline{\overline{III}}$) but must be considered to be more firmly held than in 1,1,1-trichloro-2,2-bis 4 chlorophenylethane.

$$C_6H_5 \rightarrow \leftarrow \underset{H}{\overset{CH_3}{\underset{|}{\overset{|}{C}}}} \rightarrow C \xrightarrow{\overset{O}{\parallel}} OH \qquad \overline{\overline{III}}$$

Triphenylmethane and tri 4 nitrophenylmethane can also be easily oxidized to the corresponding carbinols by chromic acid and acetic acid.[145]

The hydrolysis or ionization of the tertiary chlorine in 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane should proceed without much difficulty. Triphenyl methyl chloride readily hydrolyses to triphenylcarbinol, even with water. Tertiary chlorines are generally considered to be easily hydrolysable.

The formation of a carbonium ion in Step II is considered to be a reasonable postulate. This is known to take place with triphenyl carbinol in concentrated sulfuric acid.[146] ($\overline{\overline{IV}}$)

$$(C_6H_5)_3C-OH + 2H_2SO_4 \longrightarrow (C_6H_5)_2C+ + OH_3^+ + 2HSO_4^- \qquad \overline{\overline{IV}}$$
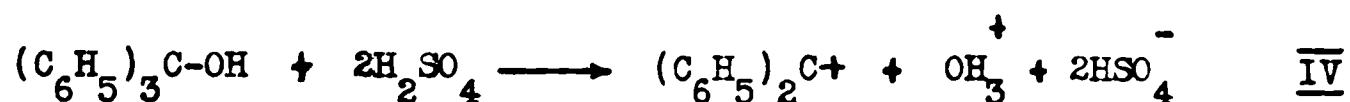
The rearrangement which takes place in Step III appears complicated but, in fact, need merely represent the emergence of products from the activated complex in which the identity of atomic grouping must become vague indeed. It will be recalled that Al Favorski[35,36] reported a double shift in the rearrangement of some ketones with zinc chloride ($\overline{\overline{V}}$).

$$(CH_3)_3CCO \cdot C_6H_5 \xrightarrow{\ ZnCl_2\ } (CH_3)_2(C_6H_5)C \cdot COCH_3 \qquad \overline{\overline{V}}$$
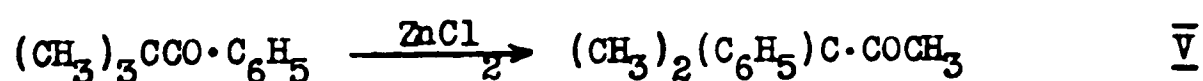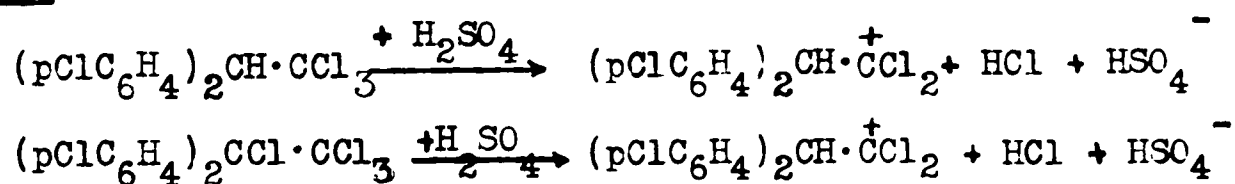
Both Steps IV and V are considered to be quite reasonable and possible with the experimental conditions used. The hydrolysis of the aliphatic chlorines in 1,2-di 4 chlorophenyl-2,2-dichloroethanone is considered to proceed quite easily, since a 40/10 mixture of glacial acetic acid and water has been shown to convert 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane to 4,4'-dichlorobenzil by heating to 170°C for six hours.[118] It has also been shown possible to convert 1,1,2,2-tetrachloro-1,2-diphenylethane to benzil by heating with sulfuric acid to 165°C.[119] Zinin[128] converted 1,2-diphenyl-2,2-dichloroethanone into
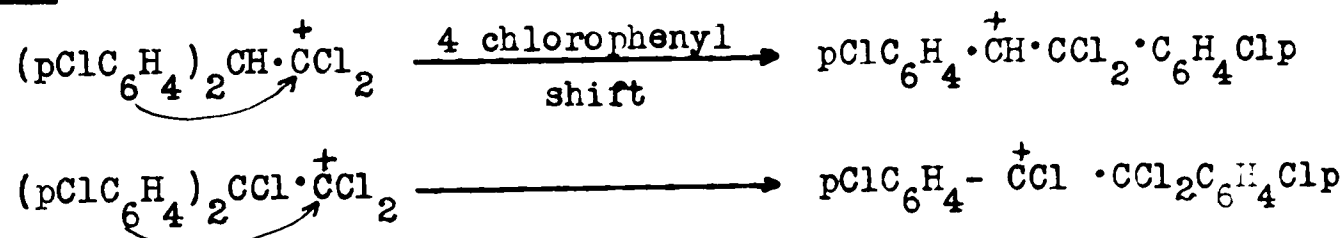
bénzil by heating with water in a sealed tube to 180°C.

Mechanism B

A second suggested mechanism assumes that the β carbon atom is initially attacked. This mechanism can be represented as follows, for the conversion of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane, respectively.
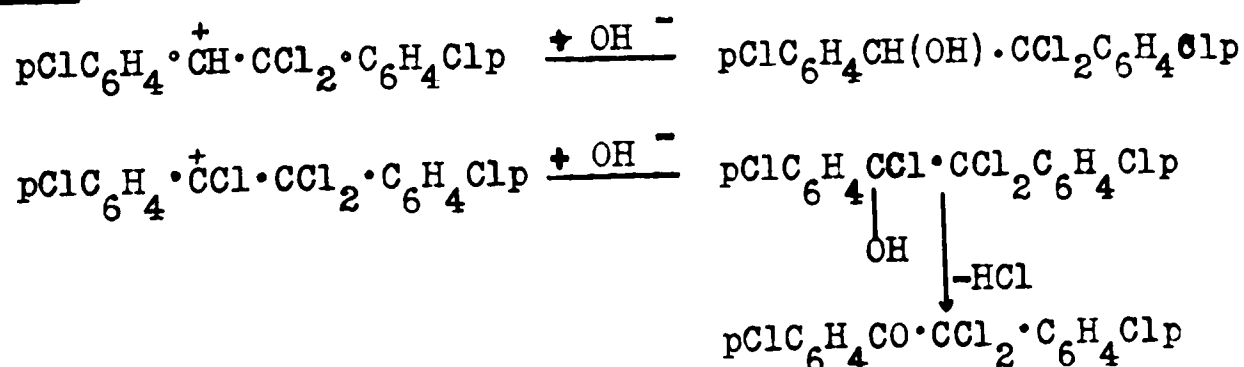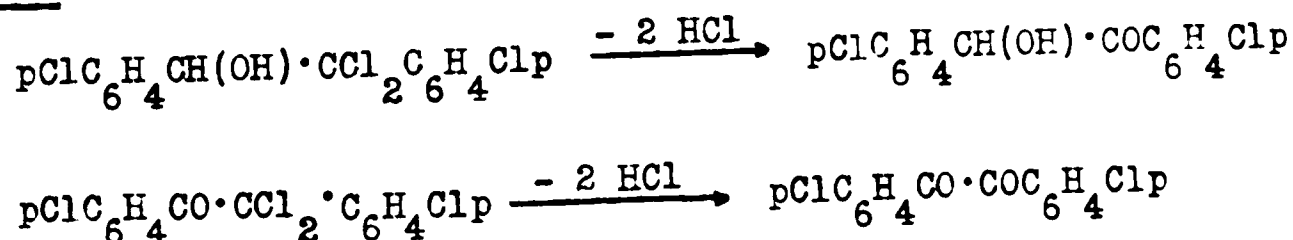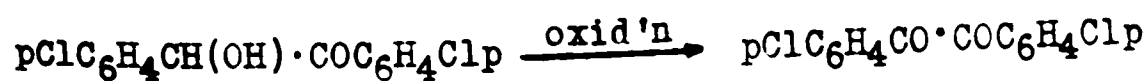
STEP I'

$$(pClC_6H_4)_2CH \cdot CCl_3 \xrightarrow{+ H_2SO_4} (pClC_6H_4)_2CH \cdot \overset{+}{C}Cl_2 + HCl + HSO_4^-$$

$$(pClC_6H_4)_2CCl \cdot CCl_3 \xrightarrow{+ H_2SO_4} (pClC_6H_4)_2CH \cdot \overset{+}{C}Cl_2 + HCl + HSO_4^-$$

STEP II'

$$(pClC_6H_4)_2CH \cdot \overset{+}{C}Cl_2 \xrightarrow[\text{shift}]{\text{4 chlorophenyl}} pClC_6H_4 \cdot \overset{+}{C}H \cdot CCl_2 \cdot C_6H_4Clp$$

$$(pClC_6H_4)_2CCl \cdot \overset{+}{C}Cl_2 \xrightarrow{\hspace{2cm}} pClC_6H_4 - \overset{+}{C}Cl \cdot CCl_2 C_6H_4Clp$$

STEP III'

$$pClC_6H_4 \cdot \overset{+}{C}H \cdot CCl_2 \cdot C_6H_4Clp \xrightarrow{+ OH^-} pClC_6H_4CH(OH) \cdot CCl_2 C_6H_4Clp$$

$$pClC_6H_4 \cdot \overset{+}{C}Cl \cdot CCl_2 \cdot C_6H_4Clp \xrightarrow{+ OH^-} pClC_6H_4 \underset{\underset{OH}{|}}{CCl} \cdot CCl_2 C_6H_4Clp$$

$$\downarrow {-HCl}$$

$$pClC_6H_4CO \cdot CCl_2 \cdot C_6H_4Clp$$

STEP IV'

$$pClC_6H_4CH(OH) \cdot CCl_2 C_6H_4Clp \xrightarrow{- 2 HCl} pClC_6H_4CH(OH) \cdot COC_6H_4Clp$$

$$pClC_6H_4CO \cdot CCl_2 \cdot C_6H_4Clp \xrightarrow{- 2 HCl} pClC_6H_4CO \cdot COC_6H_4Clp$$

STEP V'

$$pClC_6H_4CH(OH) \cdot COC_6H_4Clp \xrightarrow{oxid'n} pClC_6H_4CO \cdot COC_6H_4Clp$$

This mechanism depends upon ionization of a chlorine from the tri-
chloromethyl group. On the basis of the electronic picture, the tertiary
chlorine in the â,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane, because
of its $(+I_s)$ inductive effect, should tend to deactivate the chlorines
in the trichloromethyl group with respect to the trichloromethyl group
in 1,1,1-trichloro-2,2-bis 4 chlorophenylethane $(\overline{\overline{VI}})$.
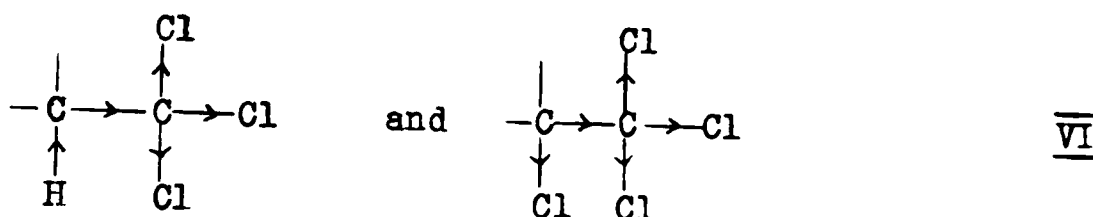
However, as stated previously, 1,1,1,2-tetrachloro-2,2-bis 4
chlorophenylethane is more readily converted than 1,1,1-trichloro-2,2-
bis 4 chlorophenylethane to 4,4'-dichlorobenzil and this is not in
agreement with deactivation of the trichloromethyl group in the former
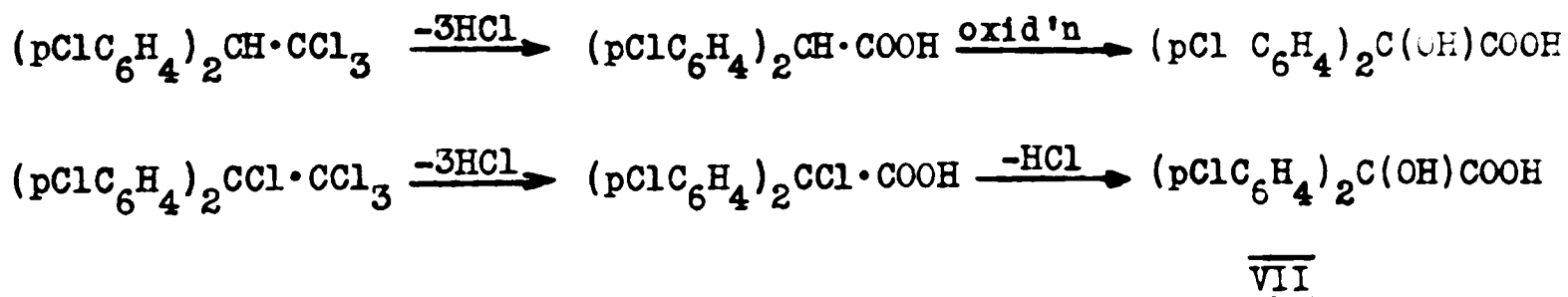molecule in accordance with electronic considerations.

The objection to a hydrolysis of a chlorine in the trichloro-
methyl group of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane on
the basis of electronic concepts may not be valid. "It is evident
that there are certain special types of organic reactions which cannot
be dealt adequately on the basis of the four electronic concepts......"
(electromeric, mesomeric, inductive and inductomeric). "When a re-
action involves redistribution of atomic nuclei among themselves
(tautomerism, and intramolecular rearrangements), the introduction of
additional special principles is required.[142] "

If StepI' can be accepted, the ensuing steps are all reasonable.
The 4 chlorophenyl shift in Step II', the hydroxyl group addition in
Step III' and the aliphatic chlorine hydrolysis of Step IV' should all

proceed without serious difficulty. Step V'which involves the oxidation of 4,4'-dichlorobenzoin to 4,4'-dichlorobenzil is not considered to be impossible, even though none of this material has been isolated from the reaction mixture.

The main weakness in mechanism B is the assumption that a chlorine in the trichloromethyl group ionizes to form the intermediate carbonium ion.

Other possible mechanisms may be mentioned briefly. It is possible to assume that all the chlorines in the trichloromethyl groups are hydrolyzed before the rearrangement takes place. Thus, bis 4,4'-dichlorophenyl-acetic acid and bis 4,4'-dichlorophenyl benzilic acid would be obtained from 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane, respectively ($\overline{VII}$).

$$(pClC_6H_4)_2CH \cdot CCl_3 \xrightarrow{-3HCl} (pClC_6H_4)_2CH \cdot COOH \xrightarrow{oxid'n} (pCl\ C_6H_4)_2C(OH)COOH$$

$$(pClC_6H_4)_2CCl \cdot CCl_3 \xrightarrow{-3HCl} (pClC_6H_4)_2CCl \cdot COOH \xrightarrow{-HCl} (pClC_6H_4)_2C(OH)COOH$$
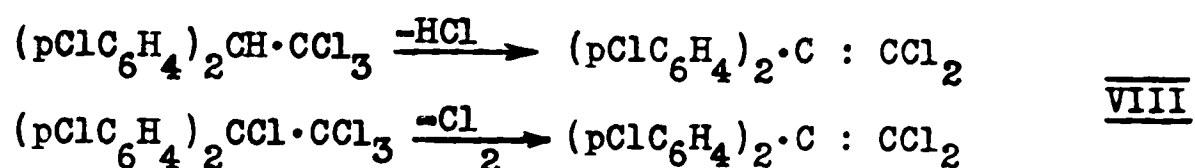
$$\overline{VII}$$

It is readily seen that it is possible to obtain 2-hydroxy-2,2-di 4 chlorophenyl acetic acid derivative. If this were the reaction mechanism, then it should be possible to convert the above acid into 4,4'-dichlorobenzil with sulfuric acid.

The benzilic acid derivative was prepared and it was not found possible to convert it to 4,4'-dichlorobenzil with 96% sulfuric acid.

Alternately, it may be assumed that the reaction route lies in

the initial loss of hydrogen chloride from 1,1,1-trichloro-2,2-bis 4 chlorophenylethane or of chlorine from 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane to give the unsymmetrical olefin ($\overline{VIII}$). However, this is not considered to be a likely reaction, since 1,1-di 4 chlorophenyl-2-2-dichloroethylene, the intermediate in such a re-arrangement, is not converted to 4,4' dichlorobenzil with either 98% or 100% sulfuric acid; the 1,1-di 4 chlorophenyl-2,2-dichloroethylene was recovered unchanged.

$$(pClC_6H_4)_2CH \cdot CCl_3 \xrightarrow{-HCl} (pClC_6H_4)_2 \cdot C : CCl_2$$
$$(pClC_6H_4)_2CCl \cdot CCl_3 \xrightarrow{-Cl_2} (pClC_6H_4)_2 \cdot C : CCl_2$$
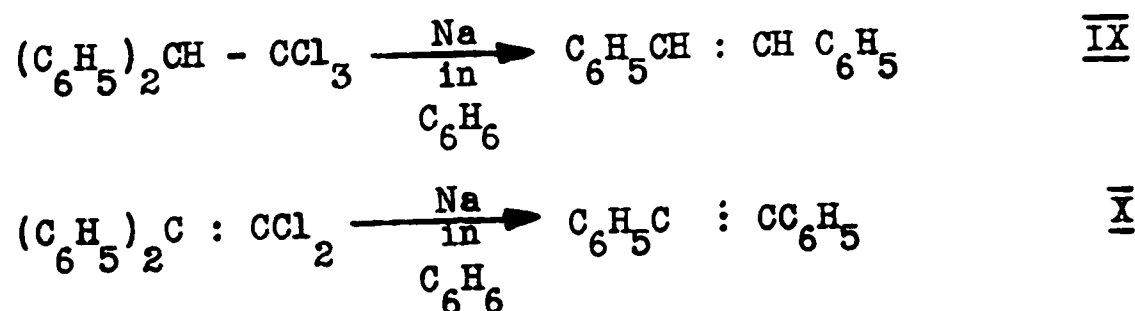
$$\overline{VIII}$$

Any mechanism involving the rupture of the molecule into a benzoyl fragment which could couple to give 4,4'-dichlorobenzil is also excluded. The yield of 4,4'-dichlorobenzil obtained from the rearrangement of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane was 56%. For two benzoyl groups to couple, the yield could not exceed 50%.

Conclusions

The above rearrangement appears to take place only with 1,1,1,2-tetrachloro-2-2-bis 4 chlorophenylethane and 1,1,1-trichloro-2,2-bis 4 chlorophenylethane. This fact is not disturbing, perhaps, when it is considered that only "benzoin", 1,2-diphenyl-1-hydroxy-ethanone can be made to undergo rearrangement to diphenyl acetic acid as shown by Lachmann,[33] James and Lyons.[34] James and Lyons[34] were unable to convert other closely related substituted hydroxy diphenyl ethanones to cor-responding substituted diphenyl acetic acid derivatives. Furthermore,

only a few ketones can be rearranged by zinc chloride as reported by

Favorski.[35] Even though Favorski[35] attempted to convert a large number

of ketones to rearranged products, he was successful in only three

cases. It is thought possible that if lower acid concentrations with

higher temperatures and pressures were employed for the conversions

of these poly halogen compounds, many more might have given rearranged

products. The conversion of the 1,1,1,2-tetrachloro-2,2-bis 4 chloro-

phenylethane is more easily accomplished than the conversion of the

1,1,1-trichloro-2,2-bis 4 chlorophenylethane. Consequently, future

attempted conversions of poly halogen compounds should consider these

two points.

It may be of interest to note that Harris[125] and Frankfurter were

able to convert a few polyhalogen compounds to rearranged olefins by

the use of sodium. These conversions probably follow a free radical

mechanism[141]. Thus the conversions of 1,1,1-trichloro-2,2-bis phenyl-

ethane to 1,2-diphenylethylene ($\overline{\overline{IX}}$) and of 1,1-dichloro-2,2-diphenyl-

ethylene to 1,2-diphenylethyne ($\overline{\overline{X}}$)were reported by the use of sodium.

$$(C_6H_5)_2CH - CCl_3 \xrightarrow[C_6H_6]{Na \atop in} C_6H_5CH : CH\ C_6H_5 \qquad \overline{\overline{IX}}$$

$$(C_6H_5)_2C : CCl_2 \xrightarrow[C_6H_6]{Na \atop in} C_6H_5C : CC_6H_5 \qquad \overline{\overline{X}}$$

The conversion of 1,1-dichloro-2,2-di 4 methoxyphenylethylene to

1,2-di 4 methoxyphenylethyne ($\overline{\overline{XI}}$) was also reported to take place with

sodiumethylate.

$$(pCH_3OC_6H_4)_2C : CCl_2 \xrightarrow[180^\circ C]{NaOET} CH_3O \; C_6H_4\text{-}C : C\text{-}C_6H_4OCH_3 \qquad \overline{XI}$$

They attempted to convert other polyhalogen compounds to rearranged products with sodium ethylate, but only succeeded in the example shown.

In a later paper, Harris[125] reported the conversion of 1,1,1-tri-chloro-2,2-bis 4 methylphenyl ethane to 1,2-di 4 methylphenylethylene and 1,2-di 4 methylphenylethyne by sodium ($\overline{XII}$). This conversion had to be catalyzed by a trace of water.

$$2(pCH_3C_6H_4)_2CH \cdot CCl_3 \xrightarrow[\substack{trace \\ H_2O}]{Na} pCH_3C_6H_4CH : CHC_6H_4CH_3 p \; +$$

$$pCH_3C_6H_4C : CC_6H_4CH_3 p \qquad \overline{XII}$$
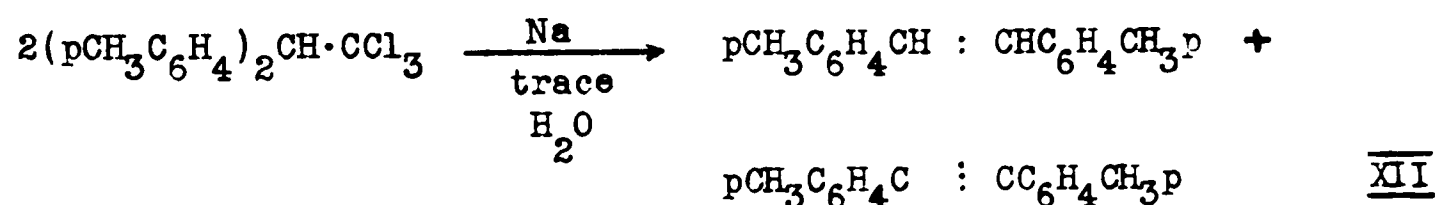
DISCUSSION

PART II

Introduction

In the experimental part of this thesis there are recorded several synthetic preparations of compounds which were submitted for biological testing as insecticides. Generally, insecticides can be classified into two main types - (a) those that are poisonous if ingested by the insect, known as stomach poisons, and (b) those that kill insects by physical contact, known as contact insecticides. An insecticide must not be confused with a repellent. A repellent such as dimethyl phthalate or pyrethrum does not kill the insect. The latter, when applied as a spray, dazes the insect but it recovers after a short period. There are many other methods available to kill insects besides direct poisoning. These methods are of varying efficiency and usefulness. A novel and interesting method to kill insects is by spraying very fine hard dust particles, (such as diamond) which act as an abrasive on the insect's body, producing large tears or openings which allow evaporation of the insect's fluid, causing partial dessication and resulting in death.

However, the most useful kind of insecticide is the contact type. The range of a contact insecticide is far greater than that of stomach poisons. Many insects, such as the mosquito, do not eat the solid parts of the plants or animals but suck the sap or blood. These insects are equipped with long, sharp proboscis to penetrate the surface of the

plant or skin of the animal to the fluid beneath. Thus an insecticide of the stomach poison type would be useless against these insects, as the exposed parts of the plant or animal on which the poison lies are not ingested.

The most effective contact insecticides known are "D.D.T." and "666" which are 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and hexachlorocyclohexane, respectively. The biological killing mechanism of these insecticides is unknown. It is believed that the nervous system of the insect is attacked first, causing violent tremors and finally paralysis.

An ideal contact insecticide would be one that is poisonous to insect pests but harmless to the desirable insects and to all mammals. Such an ideal may well never be attained by a single insecticide but it is possible that a series of insecticides could be developed which would act specifically against only one or two classes or orders of insects. Both "D.D.T." and "666" are very toxic to a large variety of insects. ".D.D.T." is quite toxic to the mouse but much less poisonous to the dog and to man. However, sufficiently large doses can be lethal to man.

"D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenylethane, has a very low water solubility. A contact insecticide with a greater water solubility than "D.D.T." would be a desirable development. The work in this laboratory had three main objectives in view while attempting to synthesize new insecticides. These objectives were to prepare a water soluble insecticide, selective insecticides, which would be toxic to certain orders or groups of insects and to further chemical knowledge of "D.D.T." itself. However, a limitation of this work was encountered in the

biological testing. Drosophila melanogaster (fruit fly) was the only insect used for testing the potency of the potential insecticides submitted for examination. Thus some of the chemical derivatives tested on this insect might show a higher potency if tested on other kinds of insects. Many of these compounds are to be sent to the Suffield experimental testing station at Saskatchewan, Canada for further trials.

Chemical Killing Mechanism

There has been a great deal of controversy about the mechanism by which "D.D.T." acts as an insecticide. From the biological viewpoint, it is known that the insect's nervous system is attacked. The question that arises is: how is the nervous system attacked? What chemical reaction takes place which upsets the nervous system? If the insecticide possesses some specific property essential for lethal action, then this might be indicated in the chemical and physical properties of the molecule. If some chemical property could be isolated as the lethal factor when present in the insect's body, the task of synthesizing new active reagents would be greatly facilitated.

Many attempts have been made to identify certain chemical properties with toxic activity. Lauger[121] et al., assumed that the chlorobenzene fragment of the "D.D.T." molecule was the potent factor and that the trichloromethyl group acted as a fat solvent to allow the introduction of the chemical into the insect's system. Once in the system the chlorobenzene fragment could then act lethally. This theory, however, cannot

explain why certain nearly similarly constituted molecules are inactive. For instance the ortho, para isomer of "D.D.T.", 1,1,1-trichloro-2-O chlorophenyl-2-p chlorophenylethane is totally inactive as an insecticide yet a trichloromethyl and two chlorobenzene groups are present in the molecule.

Another theory advanced by several English workers[122] considers that the ease with which hydrogen chloride is lost is the important factor for insecticidal activity. This factor is coupled with the fat solubility of the molecule as a whole. Thus, qualitatively, the ortho, para isomer of "D.D.T." is ineffective because its rate of hydrogen chloride loss is only 1/67[123] of that of the para, para isomer. It has been shown that such compounds as 1,2-bis 4 chlorophenylcyclopropane[121] have strong insecticidal activity, yet they cannot lose hydrogen chloride. Again, 1,1,1-trichloro-2,2-bis tolylethane can lose hydrogen chloride more rapidly than "D.D.T."[123] but has a lower toxicity. Perhaps the latter molecule has a lower fat solubility factor than "D.D.T."

Other theories consider that some enzymetic reaction takes place with "D.D.T.", or that the calcium metabolism of the insect is upset to produce hypocalcemia. However, these theories are supported by little or no chemical evidence.

It must be recognized that no theory adequately summarizes the essential characteristics for an insecticide. Furthermore, it is not inconceivable that there are several paths by which an insecticide may act to cause death. Thus, several different single properties, if present in a molecule, may lead to the same toxic result for the insect. A combination of these factors in one molecule should achieve the maximum

result. Until more is known about insecticides, it will be difficult to synthesize molecules to desired toxicity values. In general, it appears that a good working hypothesis for the synthesis of insecticides is to have several chlorine groups present in the molecule.

The compounds submitted as potential insecticides by the present author, together with the many hundreds which have already been tested by other workers, may some day aid in determining the essential characteristics for an insecticide. After thousands of compounds have been prepared and tested as insecticides, some specific property may emerge from the mass of comparative data which will give the chemist a clue for the preparation of selective insecticides.

COMMENTARY AND DISCUSSION OF SYNTHETIC APPROACH

"D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenylethane is prepared

commercially by condensation of chlorobenzene and chloral, using sulfuric

acid as the condensing agent. Zeidler[93] first reported its preparation

in 1874. The reaction is assumed to proceed as follows ($\underline{\text{I}}$).

| chloral | chlorobenzene | Carbinol (1-p chlorophenyl-2,2,2-trichloro-ethanol) | D.D.T. |
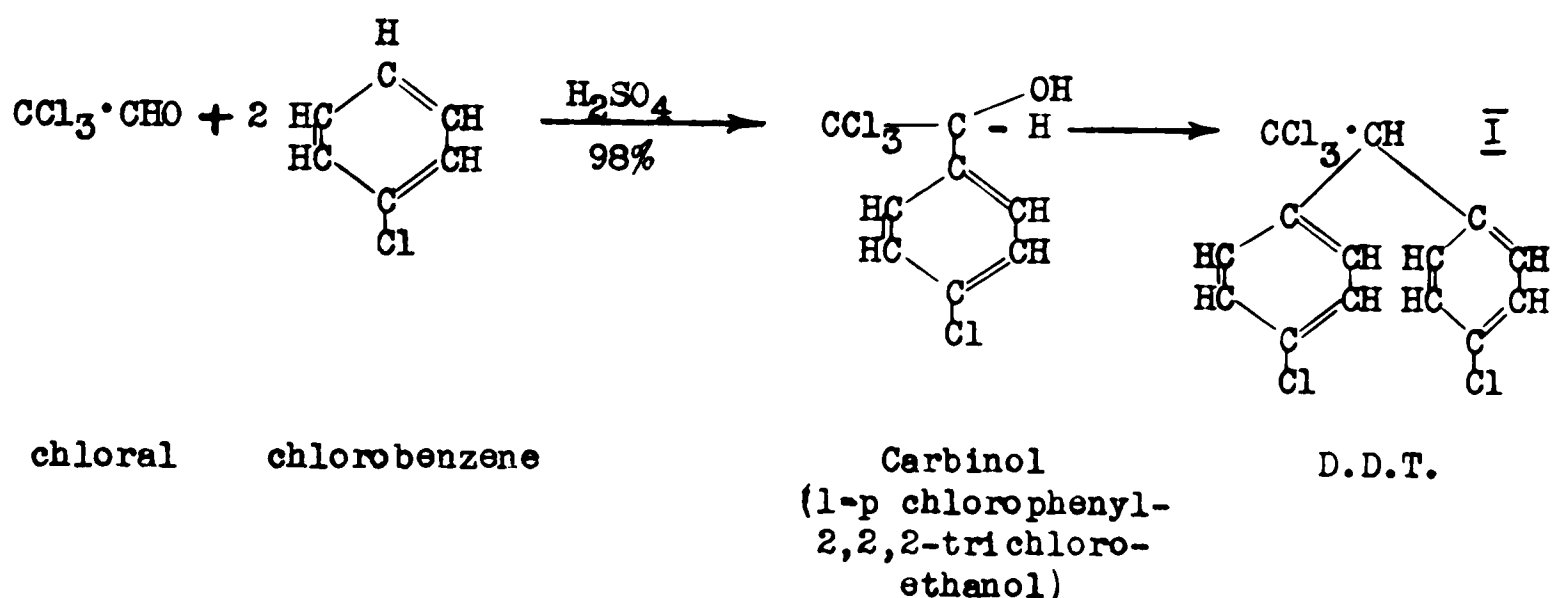
The carbinol intermediate, 1-4 chlorophenyl-2,2,2-trichloroethanol,

can be isolated in small amounts from the reaction mixture.[134] By this

method many homologues of "D.D.T." have been prepared containing different

substituents on the ring. Thus p bromo, p fluro, p iodo, p methyl,

p hydroxy, p methoxy, etc. compounds have been synthesized, which, besides

having different ring substituents, have the trichloromethyl replaced by

tribromomethyl, trifluromethyl, dichloromethyl, monochloromethyl, methyl,

etc. Many other materials have been synthesized which have little in

common with the "D.D.T." structure. However, the majority of the "D.D.T."

homologues have little or no insecticidal activity. None of the homo-

logues are superior to "D.D.T.". Several mixed homologues have also been

prepared, one of the more important being 1,1,1-trichloro-2-phenyl-2-4

chlorophenylethane which is quite toxic. It is to be noted that to prepare pure mixed homologues it is necessary to obtain the 1-4 chloro-phneyl-2,2,2-trichloroethanol intermediate in a pure state. Some work has been done to prepare these pure mixed homologues, but no work has been done to test such derivatives of the 1-4 chlorophenyl-2,2,2-trichloroethanol as esters, ethers, etc. The "carbinol" has been shown to be 25-50 times less active than "D.D.T.". Its use as an insecticide would be unlikely unless it were found to be highly specific against some insect pest. It was thought that some other chemical attachment to the carbinol might raise its reactivity and thus produce a new insecticide with different properties.

It was first necessary to find a reasonably good method to prepare pure "carbinol", 1-4 chlorophenyl-2,2,2-trichloroethanol in large yield. The method adopted was a three-step reaction. The first stage was the preparation of 4-chloroacetophenone by the condensation of acetic anhydride and chlorobenzene with aluminum chloride[106] ($\overline{\underline{II}}$). The second step was the chlorination of 4 chloroacetophenone to 1-4 chlorophenyl-2,2,2-trichloroethanone[100] ($\overline{\underline{III}}$).
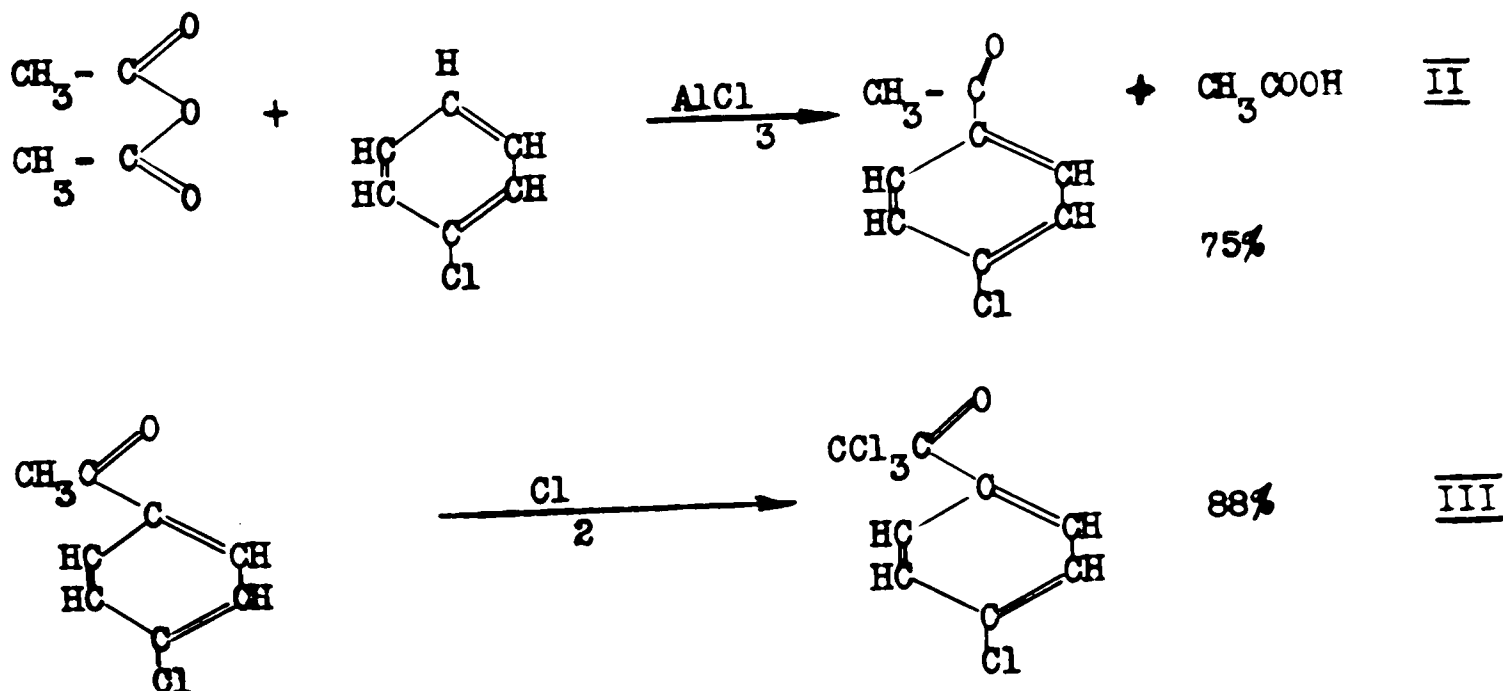
The final step was the reduction of the ketone with aluminum isopropoxide to the "carbinol", 1-4 chlorophenyl-2,2,2-trichloroethanol[101] ($\overline{\underline{IV}}$).
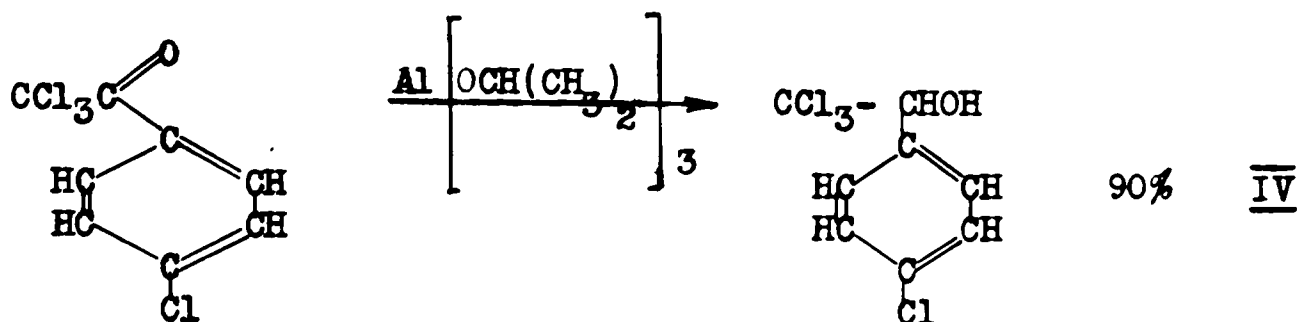

The accomplishment of this synthesis opened the way for the preparation of several carbinol derivatives.

Derivatives

(A) Esters

The carbinol has a hydroxyl group which can be made to react to form derivatives. It is of interest to note that the hydroxyl group is relatively unreactive and usually requires long periods of heating under reflux with acid anhydrides or acid chlorides to obtain ester derivatives.

The first derivative prepared was 1-4 chlorophenyl-1-acetoxy-2,2,2-trichloroethane which was obtained from acetic anhydride and the carbinol[102] ($\overline{\underline{V}}$).
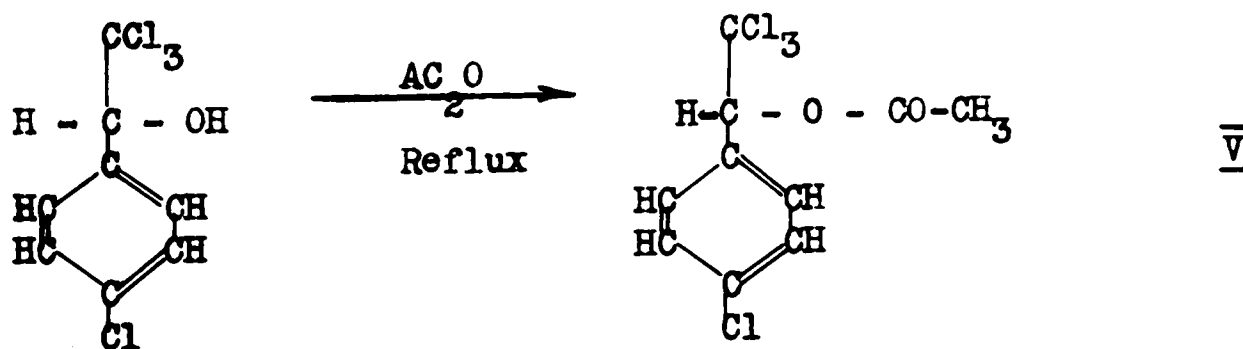

The acetate was found to have a greater insecticidal activity than the carbinol - about one tenth that of "D.D.T." However encouraging

this result, the preparation of the propionate[102] from propionicanhydride and the butyrate[102] from butyryl chloride yielded esters with a lower insecticidal activity than the carbinol.

If trichloromethyl groups are of advantage to an insecticide, then the trichloroacetate derivative should have been interesting. Thus, carbinol and trichloroacetyl chloride were reacted to yield the 1-4 chlorophenyl-1-trichloroacetoxy-2,2,2-trichloroethane ($\overline{VI}$)
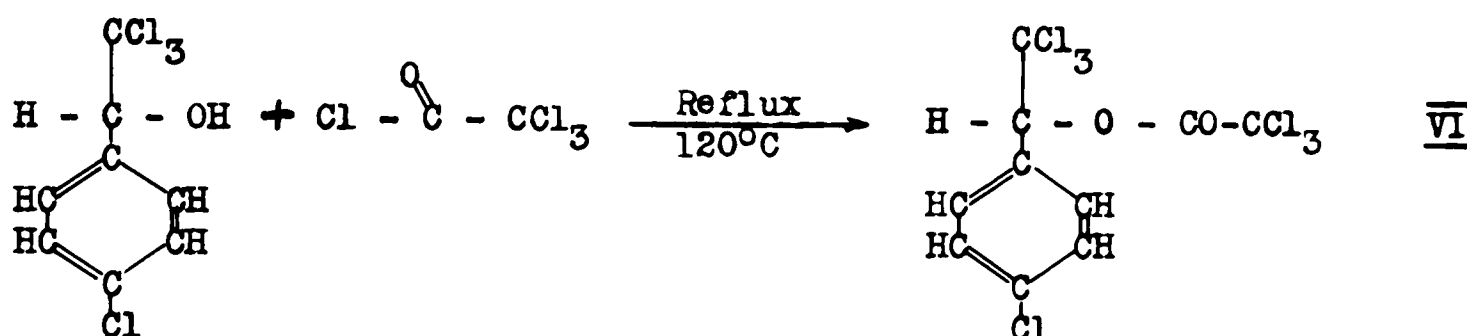
The trichloro acetate proved to be completely inactive as a contact insecticide.

It was thought that an ester of a dibasic acid might show interesting properties. Succinyl chloride[104] methyl ester was refluxed with the carbinol to yield a diester methyl, carbinol succinate or 1-4 chlorophenyl-2,2,2-trichloroethyl, methyl succinate. ($\overline{VII}$)
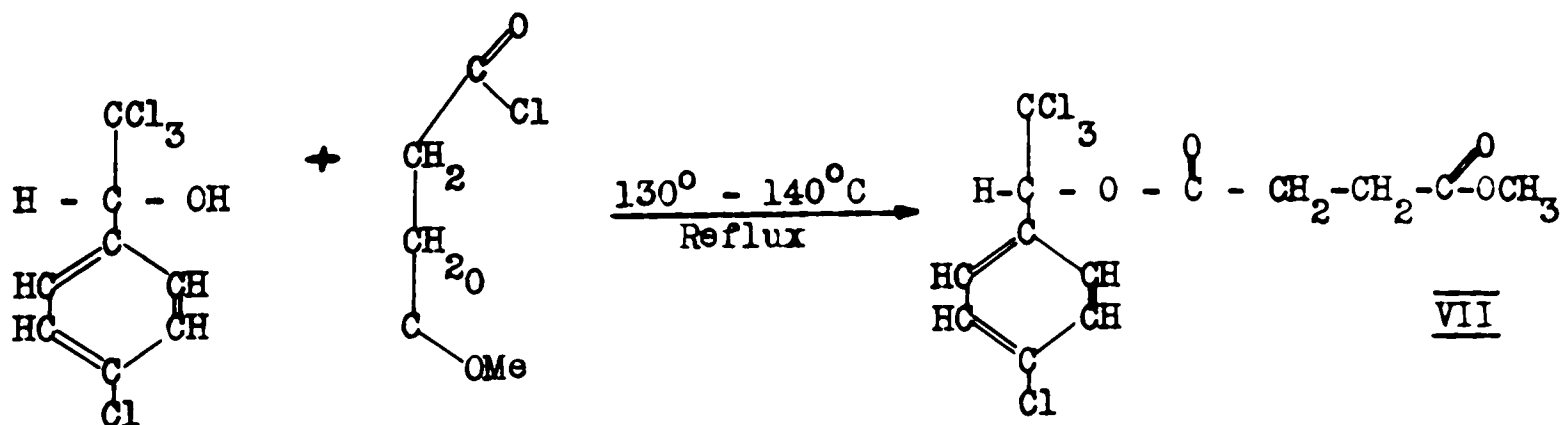

This diester was shown to have no insecticidal activity.

From the results obtained, it appears that ester derivatives were not a particularly fruitful line of research. With one exception, the acetate, all the esters showed a lower insecticidal activity than the carbinol.

(B) Ethers

Ether groups attached to the carbinol should increase its fat solubility and allow easier penetration of the fatty layers of the insect's body. Both a methyl and ethyl ether derivative were prepared from the respective methyl and ethyl iodides with silver oxide and the carbinol ($\overline{\text{VIII}}$).
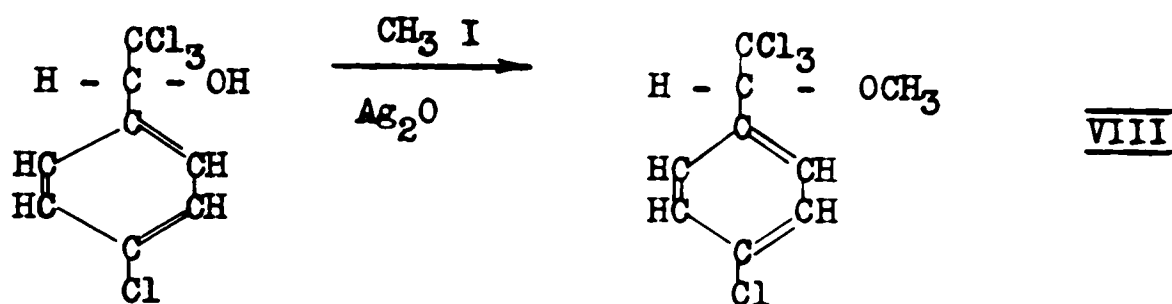
Though both the ether derivatives were rather active as insecticides, neither was more active than the carbinol. The methyl ether was more active than the ethyl derivative. The failure in the preparation of the propoxy derivative is not unusual for, with propyl iodide and higher iodides, the ease of olefin formation takes precedence over ether formation.

Other Compounds

A few compounds were also prepared which did not bear any direct relation to the "carbinol", 1-4,chlorophenyl-2,2,2-trichloroethanol.

The attempted synthesis of several of these compounds did not result in the isolation of pure crystalline products.

One of the first failures was an attempt to prepare 1-4 chloro-phenyl-2,2,2-trichloroethyl mono maleate (IX) and 1-4 chlorophenyl-2,2,2-trichloroethyl mono succinate (X).

The purpose of this synthesis was to increase the water solubility of the carbinol.

$$IX$$

$$X$$

These anhydrides resisted their transformation to ester products even when heated to 175-200°C. The failure of this reaction to take place is due to the inactivity of the hydroxyl group in the carbinol. It was necessary to form first the mono methyl ester of succinic acid and then convert this mono acid to mono methyl succinyl chloride to obtain the ester derivative (XI).

As the product 1-4 chlorophenyl-2,2,2-trichloroethyl, methyl succinate was inactive as an insecticide, no further derivatives were prepared.
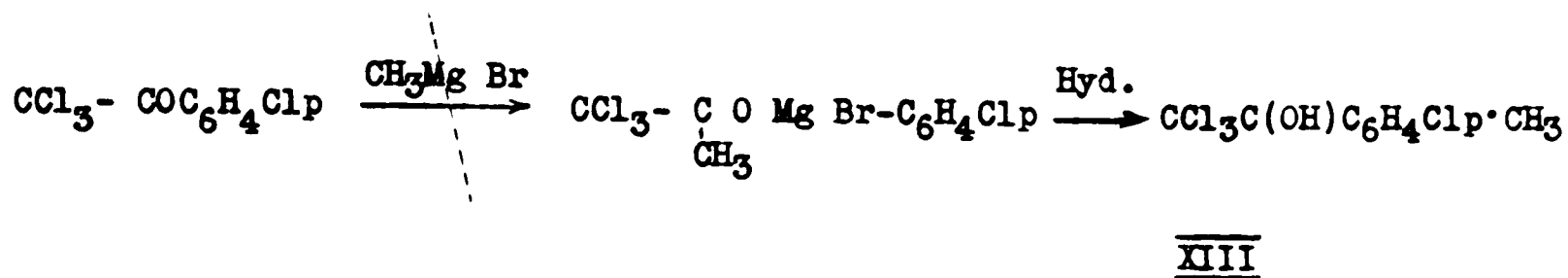
A similar attempt, made with the objective of increasing water solubility of the carbinol was the condensation of α -aceto bromoglucose tetraacetate[105] and 1-4 chlorophenyl-2,2,2-trichloroethanol ($\overline{\overline{XII}}$).
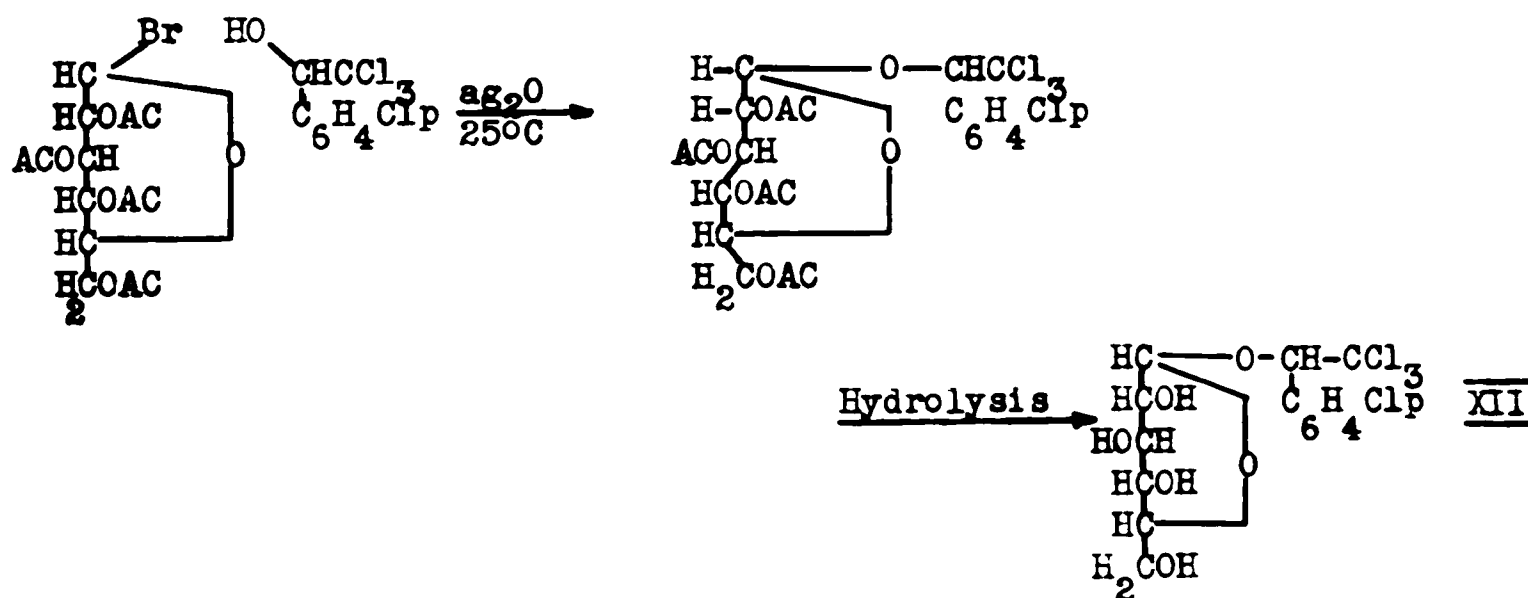
This reaction did not yield a readily crystalline tetraacetate.

As 1,1,1-trichloropropanol-2 has some physiological reactivity, it was thought that a methyl substituent replacing the hydrogen in the 1-4 chlorophenyl-2,2,2-trichloroethanol might show interesting results. Thus it was attempted to add methyl magnesium bromide to 1-4 chloro-

phenyl-2,2,2-trichloroethanone to obtain 1,1,1-trichloro-2-4 chlorophenyl-2-hydroxypropane ($\overline{XIII}$).

$$CCl_3- COC_6H_4Clp \xrightarrow{CH_3Mg\ Br} CCl_3- \underset{\underset{CH_3}{|}}{C}\ O\ Mg\ Br-C_6H_4Clp \xrightarrow{Hyd.} CCl_3C(OH)C_6H_4Clp \cdot CH_3$$
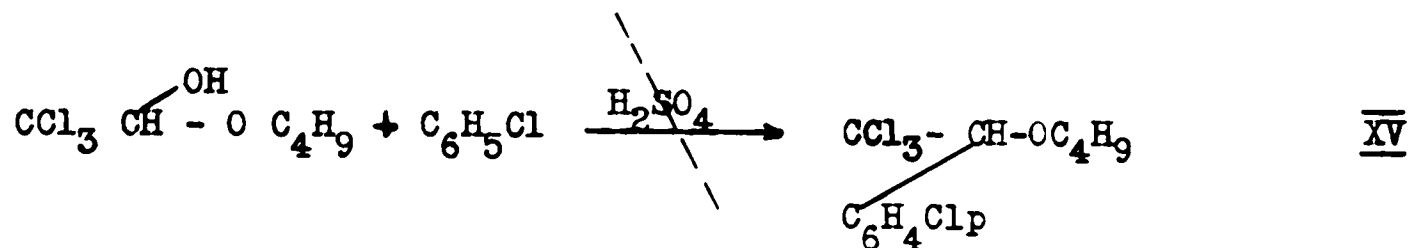
$$\overline{XIII}$$

This synthesis failed and the attempts were abandoned after a few trials. Its failure is probably due to the attack of the Gringard reagent on the trichloromethyl group. Avy,[127] attempting to synthesize 1,1-dichloro-2-hydroxy-2,2-diphenylethane from dichloroethyl acetate by the use of phenyl magnesium bromide, reported very low yields of the desired product. Other workers have reported similar difficulties with dichloro- and trichloromethyl groups in a Gringard synthesis. However, the Gringard reagent adds to chloral to give a fair yield of the normal product. Thus, p-chlorophenylmagnesiumbromide gives a 65% yield of carbinol and methylmagnesiumbromide also adds[128] to chloral in good yield.

The preparation of 1,1,1-trichloro-2-phenyl-2-hydroxy propane was attempted by addition of chloroform to acetophenone, using potassium hydroxide as catalyst. ($\overline{XIV}$) This reaction has been reported to take place with benzaldehyde[102] and substituted benzaldehydes and with chloral.[129] The extension of the reaction to include ketones failed in this instance.

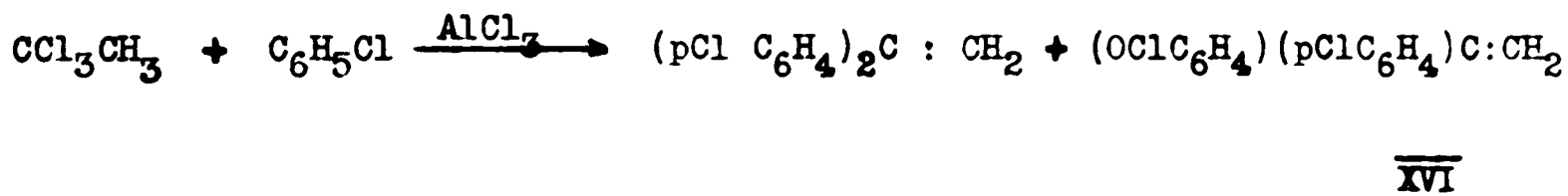$$CH_3- COC_6H_5+ HCCl_3 \xrightarrow{KOH} CH_3C(OH)C_6H_5- CCl_3 \qquad \overline{XIV}$$
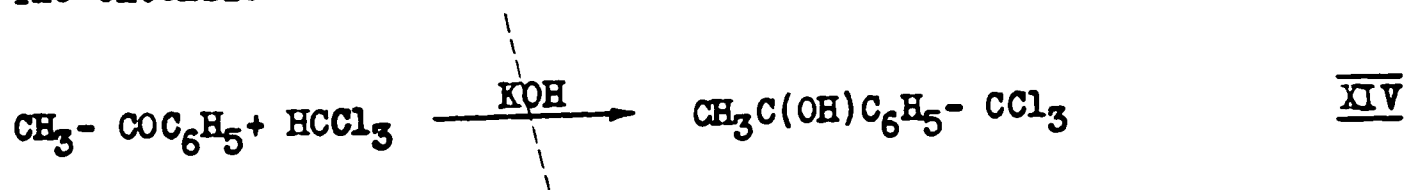
The failure to form 1-4 chlorophenyl-1-butoxy-2,2,2-trichloroethane ($\overline{XV}$) from chloral butyl alcoholate and chlorobenzene can be attributed to the breakdown of the alcoholate even with cold sulfuric. Though some

evidence exists to show that the higher alcoholates are more stable than the lower members,[139] the stability was not great enough to give any condensation in the desired direction.

$$CCl_3 \; \overset{OH}{\underset{}{CH}} - O \; C_4H_9 \; + \; C_6H_5Cl \; \xrightarrow{\;H_2SO_4\;} \; CCl_3 - \underset{C_6H_4Clp}{CH-OC_4H_9} \qquad\qquad \underline{\overline{XV}}$$

Lauger and Martin[121] had advanced the theory that fat solubilizing groups attached to a chlorobenzene ring increases the insecticidal toxicity of the substance. Consequently, a molecule such as 1,1-di 4 chlorophenylethylene might show interesting properties. This molecule was prepared from 1,1,1-trichloroethane and chlorobenzene by a Friedel and Craft reaction ($\underline{\overline{XVI}}$) using aluminum chloride.

$$CCl_3CH_3 \; + \; C_6H_5Cl \; \xrightarrow{\;AlCl_3\;} \; (pCl \; C_6H_4)_2C \; : \; CH_2 \; + \; (OClC_6H_4)(pClC_6H_4)C{:}CH_2$$

$$\underline{\overline{XVI}}$$

The yields of the 1,1-di 4 chlorophenylethylene and 1-4 chlorophenyl-1-2 chlorophenylethylene were not large but afforded a convenient method of quick preparation. The residue after distillation of the product did not yield any other crystalline products. If any of the 1,1,1-tri 4 chlorophenylethane was formed, it was not readily isolated. The structure proof of 1,1-di 4 chlorophenylethylene and 1-2 chlorophenyl-1-4 chlorophenylethylene was obtained by oxidation with chromic acid, and acetic acid to 4 chlorobenzoic. Molecular weight determinations and chlorine analysis confirmed the structure. Both these materials showed fair

activity as insecticides. However, the toxicity, though greater than the carbinol, is less than "D.D.T."

Attempted Hydrolysis of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane

Many unsuccessful attempts to hydrolyze selectively the tertiary chlorine in 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane lead to the conclusion that this molecule possesses one of the most unreactive tertiary chlorines known to organic chemistry. The molecule is unaffected by dilute acids and relatively strong acids at low temperatures. Strong acid hydrolyzes all the aliphatic chlorines to give 4,4'-dichlorobenzil as the principal product. Unsuccessful attempts were made to use strong sulfuric acid and steam to effect hydrolysis, as both these reagents are effective in hydrolyzing the chlorines in benzotrichloride and in dichlorodiphenylmethane, respectively. Alkaline reagents such as alcoholic sodium hydroxide, sodium ethylate, potassium acetate, silver oxide, etc., either do not affect the molecule or lead to the formation of 1,1-dichloro-2,2-bis 4 chlorophenylethylene as the only isolable product. It would seem, therefore, that selective hydrolysis of the tertiary chlorine without affecting the trichloromethyl group is not possible because of the reactivity of the chlorine atoms in the latter group. This non-reactivity of the tertiary chlorine may be partially accounted for on the basis of the electronic theory. The trichloromethyl group is an electron "sink", that is, it is highly electron attracting. This effect is shown in chloral[130] and from ionization studies made of

trichloroacetic acid. A strong ($+I_s$) inductive effect towards the trichloromethyl group arises from the chlorine demand on the carbon.
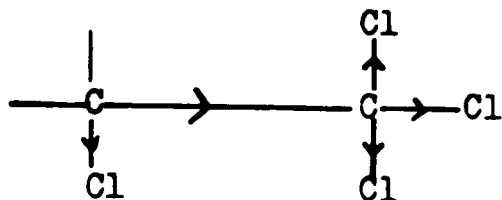
The inductive ($+I_s$) influence is always large for bonded atoms or radicals which are electrically non -equivalent. Thus the tertiary chlorine on the carbon containing the two 4 chlorophenyl groups is deactivated because it is competing unfavourably for the available electron supply on the carbon. However, its presence should also serve to deactivate partially the trichloromethyl group in 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane relative to the trichloromethyl group in "D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenylethane.
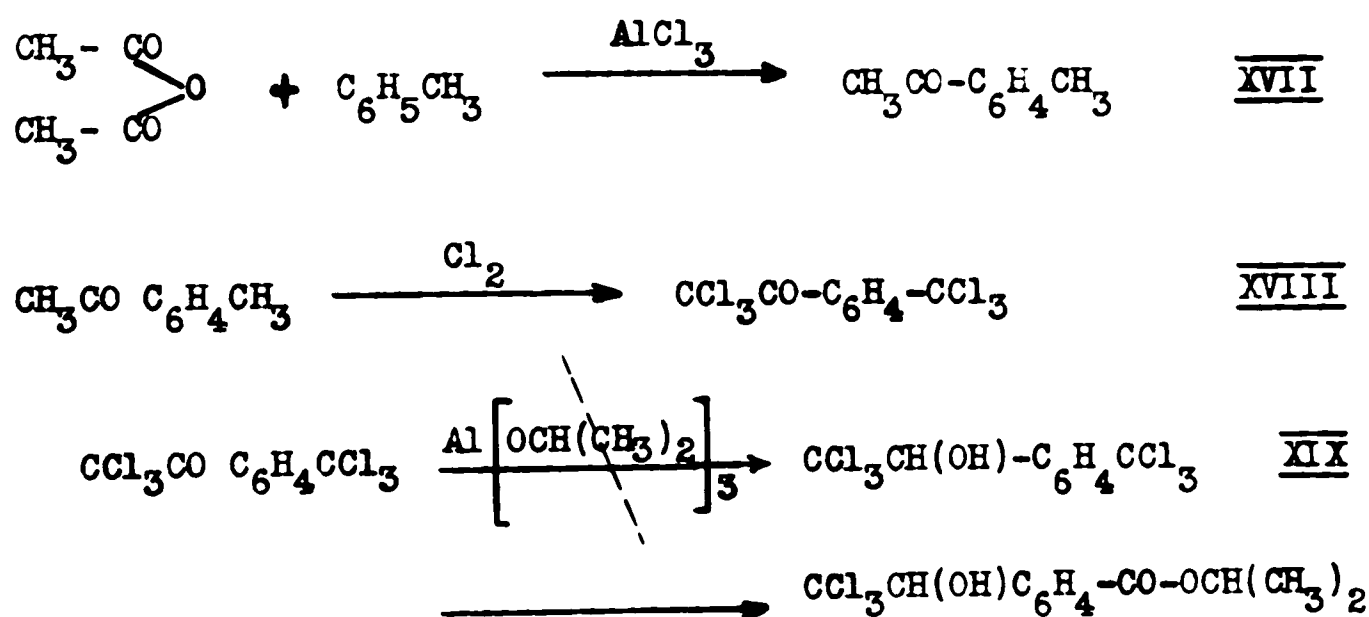
This lowered reactivity of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane is indicated by being more difficult to hydrolyze to the olefinic compound than "D.D.T."

The relative difference in reactivity of the tertiary chlorine and a chlorine in the trichloromethyl group does not appear to be very great. In alkaline media, the appearance of 1,1-dichloro-2,2-bis 4 chlorophenylethylene as the only isolable product seems to substantiate this small reactivity difference between these two chlorines. In acid media rather drastic conditions are necessary to obtain any reaction.

It was thought that if a strong "electron sink" were attached to the phenyl group in the carbinol, then the hydrogen atom in the side chain of 1-4 trichloromethyl phenyl-2,2,2-trichloroethanol would be
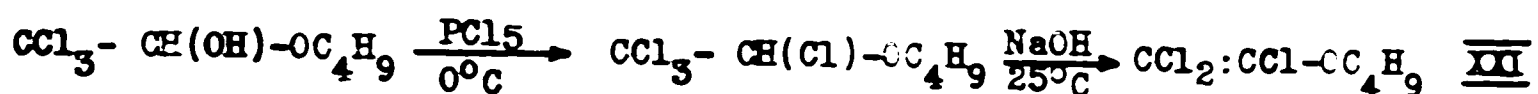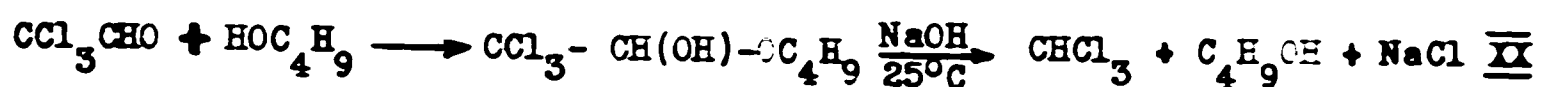
greatly activated and the elimination of hydrogen chloride would be encouraged. Thus, the synthesis of 1-4 trichloromethylphenyl-2,2,2-trichloroethanol was attempted by the following steps: the preparation of 4 methylacetophenone by a Friedel and Crafts reaction with aluminum chloride, toluene and acetic anhydride[106] ($\overline{\overline{XVII}}$), the chlorination of the 4 methyl acetophenone to 1-4 trichloromethyl phenyl-2,2,2-trichloroethanone[100] ($\overline{\overline{XVIII}}$) and the reduction of the ketone to 1-4 trichloromethylphenyl-2,2,2-trichloroethanol with aluminium isopropoxide[101] ($\overline{\overline{XIX}}$). The final step failed and the product obtained was 4 - (1-hydroxy-2,2,2-trichloroethyl) isopropylbenzoate.

$$CH_3-CO\diagdown_{CH_3-CO}O \quad + \quad C_6H_5CH_3 \quad \xrightarrow{AlCl_3} \quad CH_3CO-C_6H_4CH_3 \qquad \overline{\overline{XVII}}$$

$$CH_3CO\ C_6H_4CH_3 \quad \xrightarrow{Cl_2} \quad CCl_3CO-C_6H_4-CCl_3 \qquad \overline{\overline{XVIII}}$$

$$CCl_3CO\ C_6H_4CCl_3 \quad \xrightarrow{Al[OCH(CH_3)_2]_3} \quad CCl_3CH(OH)-C_6H_4CCl_3 \qquad \overline{\overline{XIX}}$$

$$\xrightarrow{\qquad} CCl_3CH(OH)C_6H_4-CO-OCH(CH_3)_2$$

The 4-methyl acetophenone was inactive but the 1-4 trichloromethyl phenyl-2,2,2-trichloroethanone had an activity equal to that of "carbinol", 1-4 chlorophenyl-2,2,2-trichloroethanol, and was ten times more active than the corresponding 1-4 chlorophenyl-2,2,2-trichloroethanone. The 4- (1-hydroxy.-2,2,2-trichloroethyl)-isopropyl benzoate was inactive.

It is, therefore, of interest to note that aluminum isopropoxide here fails to reduce selectively a carbonyl group if chlorines are attached to a carbon atom adjacent to the benzene ring.

Another compound, 1,1,1,2-tetrachloroethyl, butyl ether, was prepared and was shown to be inactive. This compound was prepared from chloral butyl alcoholate[110] and phosphorus pentachloride. ($\overline{XX}$ and $\overline{XXI}$)

$$CCl_3CHO + HOC_4H_9 \longrightarrow CCl_3- CH(OH)-OC_4H_9 \xrightarrow{\text{NaOH}}_{25°C} CHCl_3 + C_4H_9OH + NaCl \; \overline{\underline{XX}}$$

$$CCl_3- CH(OH)-OC_4H_9 \xrightarrow{\text{PCl5}}_{0°C} CCl_3- CH(Cl)-OC_4H_9 \xrightarrow{\text{NaOH}}_{25°C} CCl_2:CCl-OC_4H_9 \; \overline{\underline{XXI}}$$
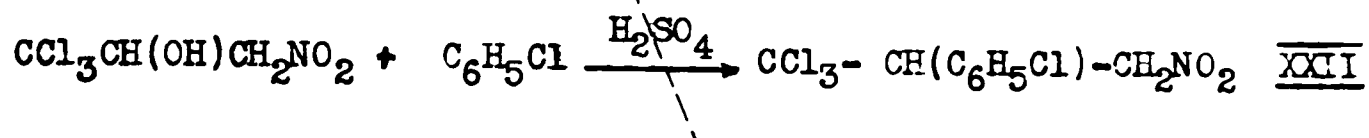
Paterno[112] showed that 1,1,1,2-tetrachloroethyl, ethyl ether gave 1,1,2-trichloroethylene, ethyl ether by the action of alkali. Thus, it is believed probable that 1,1,1,2-tetrachloroethyl, butyl ether gave 1,1,2-trichloroethylene, butyl ether when reacted with alcoholic alkali. The 1,1,2-trichloroethylene, butyl ether is sweet-smelling oil of high boiling point. The chloral butyl alcoholate gave only chloroform, butanol and sodium chloride when reacted with alcoholic alkali. The chlorine analyses on these compounds, though low, are indicative of the reactions that have taken place.

In attempting to prepare 1,1-bis 4 chlorophenyl-2,2,2-trichloro-ethanol by the hydrolysis of the tertiary chlorine in 1,1,1,2-tetra-chloro-2,2-bis 4 chlorophenylethane only 4,4'-dichlorobenzil was obtained by the action of strong acid. The 4,4'-dichlorobenzil had no insecticidal activity. Alkaline hydrolysis of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane gave 1,1-dichloro-2,2-bis 4 chlorophenyl

ethylene which was also inactive as an insecticide.

An attempt was also made to prepare 1,1,1-trichloro-2-4 chlorophenyl-3-nitropropane by causing to react 1,1,1-trichloro-2-hydroxy-3-nitro-propane[113] and chlorobenzene. ($\overline{\overline{XXII}}$)

$$CCl_3CH(OH)CH_2NO_2 + C_6H_5Cl \xrightarrow{H_2SO_4} CCl_3- CH(C_6H_5Cl)-CH_2NO_2 \quad \overline{\overline{XXII}}$$

The reaction was attempted by using various strengths of sulfuric acid, all of which resulted in failure. The unchanged 1,1,1-trichloro-2-hydroxy-3-nitropropane was recovered even from 98% sulfuric acid. The possible alternative reaction of water elimination from 1,1,1-trichloro-2-hydroxy-3-nitropeopane to give 1,1,1-trichloro-3-nitropropylene ($\overline{\overline{XXIII}}$), is, therefore, excluded.

$$CCl_3CH(OH)-CH_2NO_2 \xrightarrow[98\%]{H_2SO_4} CCl_3CH:CHNO_2 \quad \overline{\overline{XXIII}}$$
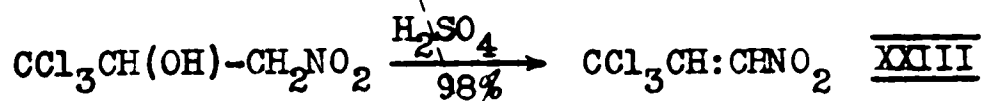
The reason for preparing the derivative in $\overline{\overline{XXII}}$ is because the following material, 1,1,1,3,3,3-hexachloro-2-4 chlorophenyl propane[129] ($\overline{\overline{XXIV}}$) prepared from 1,1,1,3,3,3-hexachloro-2-hydroxypropane and chlorobenzene was quite toxic.

$$CCl_3CH(OH)CCl_3 + C_6H_5Cl \longrightarrow CCl_3CH(C_6H_5Cl)-CCl_3 \quad \overline{\overline{XXIV}}$$
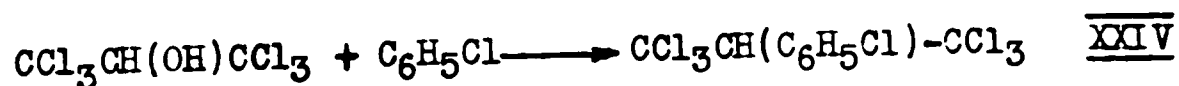
DISCUSSION

P A R T III

The author of this thesis was first presented with the problem of suggesting an alternate synthesis for "D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenylethane. The development of the problem soon indicated that this aim could not be realized by the proposed synthetic method chosen. Consequently, the objective was changed in favour of preparing candidate insecticides and to studying the chemistry of "D.D.T."

The reasons for finding an alternate synthesis were numerous. In Canada, chloral was not being manufactured commercially. All chloral for home consumption was imported from the United States. Furthermore, American manufacturers did not desire to sell chloral to the home government for "D.D.T." production. The preparation of "D.D.T." from chloral and chlorobenzene is a method which is extensively protected by foreign patents and this extra limitation would increase production costs and would hinder widespread postwar use of the insecticide for agricultural purposes. The usual commercial process of "D.D.T." yields only 70% of the pure para, para isomer which is the active ingredient. Thus a process which could increase the yield would also be of value. However, yields of "D.D.T." have lately been improved in the chloral, chlorobenzene process. In the past, twenty moles of 98% sulfuric acid were needed to bring about the conversion of one mole of chloral to "D.D.T." The use of such large amounts of acid was a troublesome factor for production, because of the large reactors needed for the process.

Recently, the use of one mole of chloro- or fluro sulfonic acid per mole of chloral gave yields which were larger than when the twenty mole volume of 98% sulfuric acid was employed. The use of excess chlorobenzene can also increase the yield to almost 100% "D.D.T." if based on chloral.[140]

In this laboratory an alternative method of preparing "D.D.T." was attempted by trying to cause pentachloroethane and chlorobenzene to react in the proper manner ($\overline{\underline{I}}$). There are no experimental data to indicate that pentachloroethane would react in this manner, though it was thought possible that the chlorines in the dichloromethyl fragment might be more reactive than the chlorines in the trichloromethyl part.

$$CCl_3-CCl_2H + 2C_6H_5-Cl \xrightarrow{AlCl_3} CCl_3-CH-(C_6H_4Cl)_2 \qquad \overline{\underline{I}}$$
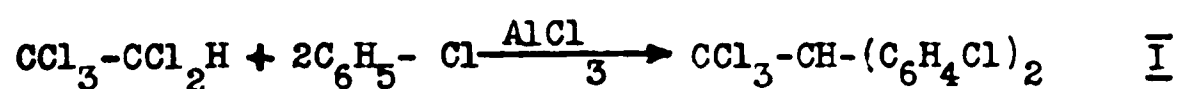
The choice of this method for investigation was prompted by the fact that the Canadian government possesses a plant to prepare hexachlorethane. Pentachloroethane is easily and economically prepared from trichloroethylene, a precursor to hexachloroethane. However, all attempts to prepare "D.D.T." from pentachloroethane and chlorobenzene have resulted in failure. Only highly substituted and high melting or oily products were obtained. These products were not further investigated as is the custom with war problems of this nature. It was also shown that "D.D.T." was unstable to aluminum chloride, it being converted to some other products which were insecticidally inactive. The action of ferric chloride on "D.D.T." converted it to 1,1-dichloro-2,2-bis 4 chloroethylene when chlorobenzene was used as solvent. In this

decomposition a small amount of a high melting product was also obtained which was not investigated further. This destruction of "D.D.T." by aluminum chloride is in agreement with results reported by other workers.[117]

Theoretically, the condensation of chloral and chlorobenzene should yield three isomeric products. The para,para; ortho,para; and ortho,ortho; 1,1,1-trichloro-2,2 bis chlorophenylethane derivatives. Thus the three possible isomeric products are written as follows. (II)

p,p   p,o   o,o

II
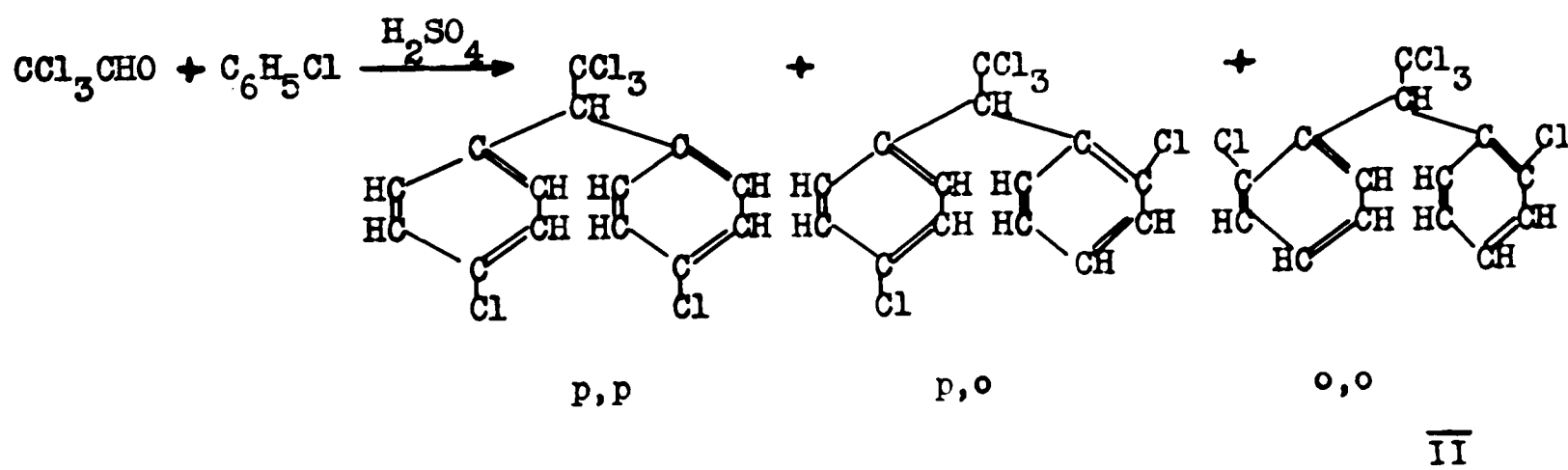
Several investigators have attempted to isolate the ortho-ortho isomer from the reaction products but have been unsuccessful. Other attempts of synthesis of this material have also resulted in complete failure. A method attempted in this laboratory was also without result. The method consisted in attempting to convert 2,2-bis 2 chlorophenyl acetic acid to 1,1,1-tri chloro-2,2-bis 2 chlorophenylethane with phosphorus pentachloride. (III)

III
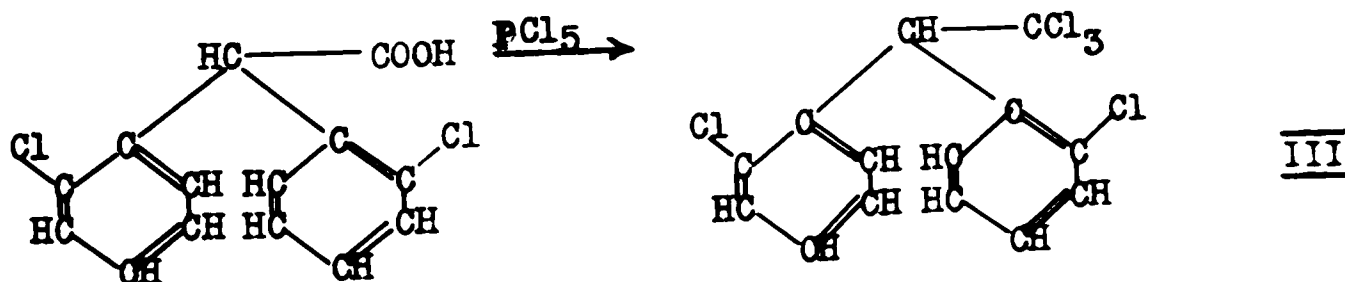
The above type of reaction could not be accomplished in the con-
version of benzoylchloride and acetylchloride to benzotrichloride and
1,1,1-trichloroethane, respectively, and was thus abandoned. It is
of interest to note that Schischkow,[114] Limprecht,[115] and Anshutz[116] have
reported conversion of a carboxyl group (-COOH) to a trichloromethyl
(-CCl$_3$) with phosphorus pentachloride. More recently, Bartlett[137] has
also reported failure to convert the carboxyl group of 2,2-bis 2 chloro-
phenyl acetic acid to a trichloromethyl group.

EXPERIMENTAL

PART I

(A)

(1) <u>Preparation of 1,1,1,2-Tetrachloro-2,2-bis 4 Chlorophenyl Ethane</u>[83]

To a 2 litre, three necked round bottom flask, were added 154 g. (1 mole) of carbon tetrachloride, 35.4 g. (0.1 mole) of 1,1,1-trichloro-2,2-bis 4 chlorophenyl ethane and 1 g. of phosphorus trichloride which acted as a catalyst in the chlorination. A water cooled reflux condenser and a chlorine gas inlet tube were attached to the three necked flask. The chlorine tube was connected by rubber tubing to two Erlenmeyer flasks connected in series. One of the flasks contained concentrated sulfuric acid and the other water. Thus the chlorine gas was washed and dried as it was emitted from the storage tank. To the top of the reflux condenser was attached a drying tube filled with calcium chloride. The reaction flask was heated by a small electric heater placed three inches below the flask. The reaction mixture was also illuminated by a 500 watt light bulb placed horizontally six inches away from the flask. The chlorine gas was bubbled into the reaction flask for five hours at a fairly brisk rate. The solution was cooled and the carbon tetrachloride was evaporated off under moderate vacuum. The residue was washed with 200 c.c. of water and was separated. The water layer was extracted with 75 c.c. of ether. The ether extract was added to the oil. The combined either oil solution was heated to evaporate off the ether. The residue crystallized m.p. 89°C. The product was recrystallized from 95% ethanol m.p. 91-92.5°C. The

melting point of the mixture of the product and an authentic sample of 1,1,1,2-tetra chloro-2, 2-bis 4 chlorophenyl ethane showed no depression. The yield was 35 g. or 90% of the theoretical value.

2) Action of Acid on 1,1,1,2-Tetrachloro-2, 2-bis 4 Chlorophenyl Ethane

To a 200 c.c. round bottom flask were added eleven grams of 98% sulfuric acid and 2.0 g. (0.005 mole) of 1,1,1,2-tetrachloro-2, 2-bis 4 chlorophenyl ethane. The flask and contents were thoroughly shaken. The reaction mixture was heated on the steam bath for fourteen hours at $90^{\circ}C$. The dark acid solution was cooled and was diluted with 50 c.c. of distilled water. The precipitated greenish product was collected on a filter. The solid was dissolved in 95% ethanol and small yellow crystals were obtained m.p. 194-195°C. The product was recrystallized from 95% ethanol m.p. 195-196°C. Further recrystallization from either ethanol, acetic acid or chloroform did not raise the m.p. The weight of the product was 0.8 g. This was a 56% yield of 4,4'dichlorobenzil.

Anal. calcd. for $C_{14}H_8O_2Cl_2$: C,60.21; H, 2.86; O,11.49; Cl,25.44.

Found: C,60.6; 60.6; H,3.00; 2.78; Cl,25.25; 25.35; 25.45.

Mol. wt. in acetone - Calcd: 279 - Found: 289, 290, 281.

The melting point of the mixture of the product taken with 4,4' dichlorobenzil[89,90] synthesized by another method showed no depression.

3) Action of Acid on 1,1,1-trichloro-2, 2-bis 4 Chlorophenyl Ethane

a) To a 200 c.c. round bottom flask were added 3.54 g. (0.01 mole) of

1,1,1-trichloro-2, 2-bis 4 chlorophenyl ethane and 50 g. of 100% sulfuric acid. The mixture was shaken thoroughly and was heated on the steam bath at 90°C for seven hours. The reaction mixture was cooled and was diluted with approximately 150 c.c. of distilled water. The precipitated product was collected on a filter and was dissolved in 95% ethanol. From the ethanol solution on partial cooling were precipitated some small yellow crystals. The solution was filtered warm before the unchanged starting material could crystallize out of the ethanol. The yellow crystals had an m.p. 180°-190°C. The product on recrystallization from 95% ethanol raised the m.p. 193°C.

The melting point of the mixture of the product taken with the material obtained from the action of 98% sulfuric acid on 1,1,1,2-tetra chloro-2, 2-bis 4 chlorophenyl ethane showed no depression. The yield of the 4,4'-dichlorobenzil was quite small.

b) To a 200 c.c. round bottom flask were added 3.54 g. (0.01 mole) of 1,1,1-trichloro-2, 2-bis p chlorophenyl ethane and 35 g. of 98% sulfuric acid. The mixture was thoroughly shaken and was heated on the steam bath for twenty-four hours at 90°C. The solution was cooled and was diluted with water. The precipitate was collected on a filter. The product was recrystallized from 95% ethanol m.p. 107°C. The melting point of the mixture of the product taken with the starting material showed no depression.

(B) <u>Investigation of the structure of the product obtained from the Reaction of acid on 1,1,1,2-tetrachloro-2, 2-bis p chlorophenyl ethane and from 1,1,1-trichloro-2, 2-bis p chlorophenyl ethane</u>

1) <u>Oxidation</u>

a) <u>Chromic Acid</u>

To a 20 c.c. beaker were added 3 c.c. of oxidation mixture[#] and 340 mg. of the product obtained by the reaction of sulfuric acid on 1,1,1,2-tetrachloro-2, 2-bis p chlorophenyl ethane (4, 4'-dichloro benzil). The solution was heated for thirty minutes on the edge of the steam bath. The reaction mixture was diluted and the product was collected on a tared sintered glass crucible. The crucible and contents were dried in the oven at $110^{\circ}C$ for one hour. The crucible was weighed. The weight of the product was 12 mg. and had a m.p. $240^{\circ}C$. The melting point of the mixture of the product and 4-chlorobenzoic acid showed no depression. The yield of 4-chlorobenzoic acid was 30% of the theoretical based on 4,4'-dichloro benzil.

b) <u>Alkaline Hydrogen Peroxide</u>[85]

To a 250 c.c. Erlenmeyer flask were added 7 c.c. of 5% sodium hydroxide solution and 20 c.c. of 3% hydrogen peroxide. The solution was warmed on the steam bath to 65-70$^{\circ}C$ and 0.105 g. of the product obtained from the reaction of sulfuric acid on 1,1,1,2-tetrachloro-2, 2-bis p chlorophenyl ethane were added to the reaction mixture. About 30 c.c. of 95% alcohol were added to make the solution homogeneous. An additional 10 c.c. of 3%

[#] Oxidation mixture was prepared by adding 35 g. of chromic oxide to 35 c.c. of glacial acetic acid and 35 c.c. of distilled water.

90

hydrogen peroxide were added and the mixture was warmed for about fifteen
minutes on the steam bath. The yellow solution soon became colourless,
which indicated that the oxidation was completed. The solution was made
acid to Congo Red Paper by the addition of dilute hydrochloric acid. The
4 chloro benzoic acid was precipitated from the solution and was collected
on a tared sintered glass crucible. The product was dried in the oven at
100°C for one hour and was weighed. The weight of the product was 0.0726
g., giving a 61.5% yield m.p. 240°C of the 4 chloro benzoic acid.

A similar experiment was repeated in the oxidation of 4,4'-dichloro
benzil which had been prepared by a different method. The yield of 4-
chlorobenzoic acid obtained was 71% of the theoretical value.

2) The Preparation of Derivatives of the Product Obtained from the Reaction
   of Sulfuric Acid on 1,1,1,2-Tetrachloro-2, 2-bis p Chlorophenyl Ethane

a) Mono-Oxime[86]

To a 250 c.c. Erlenmeyer flask were added 1.5 c.c. of 5 M hydroxyla-
mine hydrochloride and 1.5 c.c. of 5 M sodium acetate. About 0.1 g. of
the product obtained from the reaction of sulfuric acid on 1,1,1,2-tetra
chloro-2, 2-bis p chlorophenyl ethane and 10 c.c. of 95% ethanol were
added to the solution. The reaction mixture was heated on the steam bath
under reflux for three hours. The solution was cooled and water was
added until the solution became turbid. A white precipitate was formed
and this was collected on a sintered glass filter m.p. 133°C. The product
was recrystallized from 95% ethanol and water m.p. 142°C. Further re-
crystallization did not raise the melting point.

Anal. Calc. for $C_{14}H_9O_2NCl_2$: Cl, 24.13

      Found. Cl, 24.04; 24.07

b) Phenyl Hydrazone[87]

To a 250 c.c. Erlenmeyer flask were added 0.554 g. (0.038 mole) of phenyl hydrazine hydrochloride and 1.5 c.c. of 5 M sodium acetate solution. To this solution were added 0.27 g. (0.01 mole) of the product obtained from the reaction of sulfuric acid on 1,1,1,2-tetra chloro-2, 2-bis p chloro phenyl ethane dissolved in 10 c.c. of 95% ethanol. The homogeneous solution was heated under reflux for three hours on the steam bath. The reaction flask was cooled and the sides of the container were rubbed with a rubber policeman until crystallization took place. The crystallized product was collected on a filter and was washed with water m.p. 178°C. The product was recrystallized from 95% ethanol and showed no rise in melting point. The melting point of the mixture of the product and of the starting material gave a large depression. The phenyl hydrazone was coloured a deep mustard yellow. The weight of the product was 0.35 g. or a yield of 90% of the theoretical. The melting point of the product corresponds to the m.p. of the mono phenyl hydrazone of 4,4' dichloro benzil, as reported in the literature by Montagne[84] as 178°C.

c) Quinoxaline[88]

To a 125 c.c. Erlenmeyer flask were added 150 mg. of the product obtained from the reaction of sulfuric acid on 1,1,1,2-tetrachloro-2, 2-bis p chloro phenyl ethane and 5 c.c. of glacial acetic acid. To this solution were added 50 mg. of O-phenylenediamine. The reaction mixture was heated under reflux for five hours on the steam bath. The solution was cooled and precipitation was induced by the addition of water until

the solution showed incipient cloudiness. A heavy white precipitate was formed which was collected on a sintered glass filter crucible. The precipitate was dried for a few hours by the water aspirator, m.p. 185°C. No rise of melting point was obtained upon recrystallization from 95% ethanol. The weight of the product after recrystallization was 48 mg. This was 25% of the theoretical yield for the quinoxaline.

3) Synthesis of 4,4'-dichlorobenzil[89,90]

a) Preparation of 4,4'-dichloro benzoin[89]

To a 250 c.c. Erlenmeyer flask were added 14 c.c. of 95% ethanol, 6 c.c. of water, 0.5 g. of sodium cyanide and 7 g. (0.05 mole) of 4-chloro-benzaldehyde. The solution was heated under reflux for one half hour on the steam bath. The reaction mixture was cooled and the 4-chlorobenzoin separated out as a reddish oil. The supernatant mother liquor was decanted off and was diluted with water which caused more benzoin to be precipitated as an oil. The oily benzoin was dissolved in 20 c.c. of 95% ethanol. The benzoin persisted in precipitating as an oil and consequently the ethanol was evaporated off on the steam bath. The weight of the oil was 8 g.

b) Preparation of 4,4'-dichloro benzil[90]

The crude benzoin oil as obtained above was placed into a 250 c.c. beaker and 21 c.c. of nitric acid (Spg. 1.42) were added to the oil. The mixture was heated on the steam bath for one hour until no more oxides of nitrogen were evolved. The solution was diluted with water and the crude 4,4'-dichloro benzil was precipitated from the reaction mixture. The precipitate was collected on a filter and was washed with water.

The weight of the crude product was 5.6 g. or a theoretical yield of 80%. About 0.5 g. of this crude 4,4' dichlorobenzil were recrystallized from 95% ethanol m.p. 194-195°C. Further recrystallization did not raise the melting point.

(C) THE ACTION OF SULFURIC ACID ON OTHER 1,1,1-TRICHLORO-2,2-DI
SUBSTITUTED PHENYL ETHANES AND RELATED COMPOUNDS

(1) The reaction of sulfuric acid on 1,1,1-trichloro-2,2-diphenylethane

(a) Preparation of the 1,1,1-trichloro-2,2-diphenylethane.

This material was prepared in the manner as reported in the litera-
ture.[91] Into a 2,000 c.c. round bottom flask were added 1000 g.(20 moles)
of 98% sulfuric acid and 165 g. (1 mole) of chloral hydrate. To this
acid solution were added 142 g. (2 moles) of benzene. The solution was
stirred for four hours at 0°C in an ice bath, after which it was diluted
with ice and the solid product collected on a filter. The product was
recrystallized from 95% ethanol, m.p. 62-63°C.

(b) 1) In a 50 c.c. round bottom flask was thoroughly shaken a
mixture of 2.86 g. (0.01 mole) of 1,1,1-trichloro-2, 2-diphenylethane and
50 g. of 96% sulfuric acid (sp. g. 1.84). The mixture was then heated on
the steam bath for eighteen hours and the resulting solution cooled and
diluted with water. The solid product was collected on a filter, washed
with water and dried, m.p. 55-56°C. The melting point of the mixture of
the product with the starting material showed no depression.

2) The above procedure was repeated using 98% sulfuric acid.
Very little reaction occurred, since most of the reactant was recovered
unchanged.

3) Into a 50 c.c. round bottom flask were added 2.86 g. (0.01
mole) of 1,1,1-trichloro-2, 2-diphenylethane and 50 g. of 100% sulfuric
acid. After the contents had been heated on the steam bath for thirty-
one and a half hours, the reaction mixture was cooled, poured over ice,

and filtered through a sintered glass crucible. There was a small amount of solid on the filter which was unchanged reactant. No high melting water insoluble products were obtained. The diluted acid filtrate was not investigated further.

4) Similar experiments were made using 96% sulfuric acid and heating to 130-140°C and 160-165°C for various lengths of time. No benzil was obtained from any of these reactions.

(2) <u>Action of acid on 1,1,1-trichloro-2,2-bis 4 tolylethane</u>

The 1,1,1-trichloro-2,2-bis 4 tolylethane was at hand in this laboratory. The material had been prepared by D. L. Garmaise according to the procedure outlined in the literature.[92]

1) Into a 50 c.c. round bottom flask were added 3.13 g. (0.01 mole) of 1,1,1-trichloro-2,2-bis 4 tolylethane and 50 g. of 100% sulfuric acid. The mixture was heated on the steam bath for fifteen hours at 90°C. Hydrogen chloride gas rather rapidly evolved during the initial part of the heating. The reaction mixture was cooled and diluted with water, but no water insoluble precipitate was obtained. The diluted acid solution was not investigated further.

2) The above experiment was repeated by heating 1.57 g. (0.005 mole) of 1,1,1-trichloro-2,2-bis 4 tolyl ethane and 35 g. of 96% sulfuric acid for twenty-one hours on the steam bath. The reactant was recovered unchanged. The experiment was again repeated by heating 1.57 g. (0.005 mole) of 1,1,1-trichloro-2,2-bis 4 tolylmethane and 30 g. sulfuric acid for ten and one half hours on the steam bath. The reaction mixture was diluted with water and 0.5 g. of reactant was recovered unchanged.

3) Other experiments in which 1,1,1-trichloro-2,2-bis 4 tolyl-ethane was heated with 96% sulfuric acid to 120°C and to 140°C did not yield any water insoluble rearranged products after the reaction mixture was diluted with water.

(3) <u>Action of acid on 1,1,1-trichloro-2,2-bis 4 bromophenylethane</u>

(a) Preparation of the 1,1,1-trichloro-2,2-bis 4 bromophenylethane.

The 1,1,1-trichloro-2,2-bis 4 bromophenylethane was prepared in the manner reported in the literature.[93] To 500 g. of 98% sulfuric acid contained in a 1000 c.c. round bottom flask were added 42 g. (0.25 mole) of chloral hydrate and 79 g. (0.5 mole) of bromobenzene. The mixture was vigorously stirred at room temperature for six hours, after which the reaction mixture was poured over ice and the precipitated product collected on a filter. The solid was recrystallized from 95% ethanol m.p. 141-142°C. The weight of the 1,1,1-trichloro-2,2-bis 4 bromophenylethane was 24 g. This was a yield of 21% of the theoretical value.

(b) 1) Into a 50 c.c. round bottom flask were added 2.22 g. (0.005 mole) of 1,1,1-trichloro-2,2-bis 4 bromophenylethane and 30 g. of 100% sulfuric acid. The mixture was heated on the steam bath for sixteen hours. The resulting solution was cooled and diluted with water and the precipitate collected on a filter and washed with water. After one recrystallization from 95% ethanol, the material gave m.p. 140°C.

2) The above procedure was repeated, using a higher temperature 160-170°C., and heating for six hours. The starting material was recovered unchanged.

3) A mixture of 1.1 g. (0.0025 mole) of 1,1,1-trichloro-2,2-bis 4 bromophenylethane and 20 g. of 101% sulfuric acid contained in a 50 c.c. round bottom flask was heated with stirring on the steam bath for four and one half hours. The reaction mixture was cooled and diluted with water, but no water insoluble products were obtained. The diluted acid solution was not investigated further.

4) Both 96% and 98% sulfuric acid failed to convert 1,1,1-trichloro-2, 2-bis 4 bromophenylethane by long heating on the steam bath.

(4) <u>The Action of acid on 1,1,1-trichloro-2,2-bis 2', 4 dichlorophenyl-
ethane</u>.

The 1,1,1-trichloro-2,2-bis 2', 4 dichlorophenylethane was obtained from H. White in this laboratory. It was prepared by condensing 2,2,2-trichloro-1-o chlorophenylethanol with chlorobenzene, using 98% sulfuric acid with stirring at room temperature.

1) A mixture of 30 g. of 99% sulfuric acid and 1.2 g. (0.0033 mole) of 1,1,1-trichloro-2,2-bis 2', 4-dichlorophenylethane contained in a 50 c.c. round bottom flask was heated on the steam bath at 90°C. for thirty-nine hours. The solution was cooled and diluted with water. The precipitate consisted of unchanged starting material.

2) In a 50 c.c. round bottom flask were mixed 40 g. of 101% sulfuric acid and 1.2 g. (0.0033 mole) of 1,1,1-trichloro-2,2-bis 2', 4 dichloro-phenylethane, and the mixture heated on the steam bath for five and one

quarter hours. The solution was cooled and poured into water, but no water insoluble products separated. The acid was neutralized by addition of calcium oxide, the excess calcium sulfate collected on a filter and the filtrate evaporated to dryness. About 150 c.c. of 95% ethanol were added to the solid from the filtrate evaporation and this was heated to boiling. The solution was filtered free of the insoluble material; the ethanol soluble products were obtained by evaporation of the filtrate. A reddish salt was obtained which could be recrystallized from 95% ethanol. The solid showed a negative test[96] for a trichloromethyl group with pyridine and 20% sodium hydroxide. The product was not investigated further.

(5) The action of acid on 1,1,1-trichloro-2,2-bis 4,4'-dichloro-3,3'-dinitrophenylethane[92]

(a) Preparation of the 1,1,1-trichloro-2,2-bis 4,4'-dichloro-3,3'-dinitrophenylethane.

Into a 50 c.c. beaker were placed 1.2 g. of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane, 22 g. of 96% sulfuric acid (sp.g. 1.84) and 3 g. of 70% nitric acid (sp.g. 1.42). The mixture was heated on the steam bath for half an hour, cooled and diluted with water. The precipitate was collected on a filter and recrystallized from 95% ethanol; m.p. 142-144°C. The melting point of the mixture of the product taken with an authentic sample of 1,1,1-trichloro-2,2-bis 4,4'-dichloro-3,3'-dinitrophenylethane showed no depression. The weight of the product was 1.0 g., or 67% of the theoretical yield.

(b) 1) A mixture of 30 g. of 100% sulfuric acid and 1.0 g. (0.0025

mole) of 1,1,1-trichloro-2,2-bis 4,4'-dichloro-3,3'-dinitrophenylethane

contained in a 50 c.c. round bottom flask was heated on the steam bath

for thirteen hours, after which the solution was cooled and diluted with

water. The precipitate was collected on a filter and washed with water.

The material was quite soluble in acetone and 95% ethanol, but was

obtained as an oil rather than crystals from these solvents.

2) The above procedure was repeated, using 98%, 97% and 96%

sulfuric acid and heating on the steam bath for various lengths of time.

The only products obtained were ethanol soluble oils which refused to

give crystalline products.

(6) The action of acid on 1,1,1-trichloro-2-phenyl-2-4-chlorophenyl-
    ethane.

(a) Preparation of the 1,1,1-trichloro-2-phenyl-2-4-chlorophenyl-

ethane.

A mixture of 10.2 g. of 96% sulfuric acid, 2.6 g. (0.01 mole) of

1-4-chlorophenyl-2,2,2-trichloroethanol and 0.94 g. (0.01 mole) of ben-

zene was placed in a 50 c.c. Florence flask and stirred for four hours

at room temperature during which time the product precipitated from the

solution. The acid was decanted, and the product washed with water by

decantation. The solid was recrystallized from 95% ethanol; m.p. 75-

76°C. The weight of the product was 1.4 g. which is 43% of the theo-

retical yield.

(b) 1) Into a 50 c.c. round bottom flask were placed 0.80 g. (0.0025 mole) of 1,1,1-trichloro-2-phenyl-2-4-chlorophenylethane and 30 g. of 99% sulfuric acid. The reaction mixture was heated on the steam bath at 90°C. for fifteen hours, then cooled and the contents filtered free of any unchanged material. The reaction mixture was diluted with water without precipitation of any product. There was very little unchanged material.

2) The above experiment was repeated by heating 0.50 g. (0.0015 mole) of 1,1,1-trichloro-2-phenyl-2-4 chlorophenylethane and 20 g. of 96% sulfuric acid for forty-two hours on the steam bath. The reactant was recovered unchanged.

3) A further experiment was attempted by heating 0.4 g. (0.00135 mole) of 1,1,1-trichloro-2-phenyl-2-4 chlorophenylethane with 15 g. of 98% sulfuric acid for ten hours. The reaction mixture was diluted with water but no water insoluble products were obtained.

(7) The action of acid on 1,1-dichloro-2,2-bis 4 chlorophenylethylene.

(a) Preparation of the 1,1-dichloro-2,2-bis 4 chlorophenylethylene.

The 1,1-dichloro-2,2-bis 4 chlorophenylethylene was prepared as indicated in the literature.[94] Thus, an alcoholic potassium hydroxide solution of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane was heated under reflux for two hours, the solution cooled, filtered free of potassium chloride and the product precipitated by evaporation of the filtrate.

(b) 1) Into a 50 c.c. round bottom flask were placed 25 g. of 98% sulfuric acid and 1.59 g. (0.005 mole) of 1,1-dichloro-2,2-bis 4 chlorophenylethylene, the mixture heated on the steam bath for fifteen hours, cooled, diluted with water, the precipitate collected on a filter and washed with water; m.p. 88-89°C. The melting point of the mixture of the product taken with the starting material showed no depression.

2) A repetition of this experiment with 100% sulfuric acid and heating on the steam bath for forty-six hours at 90°C. resulted in the recovery of the reactant unchanged.

(8) <u>The attempted conversion of 2-hydroxy-2,2-bis 4 chlorophenyl acetic acid to 4,4'-dichlorobenzil.</u>

(a) <u>Preparation</u>

The 2-hydroxy-2,2-bis 4 chlorophenyl acetic (4 chlorobenzilic) acid was prepared as outlined in the literature.[95] The 4,4'-dichlorobenzil was heated with alcoholic potassium hydroxide for ten minutes on the steam bath, then allowed to remain overnight in a porcelain dish. The 4,4'-dichloropotassiumbenzilate was precipitated as an oil which, after acidification, would not recrystallize from ethanol.

(b) One gram of the oily 2-hydroxy-2,2-bis 4 chlorophenyl acetic acid was mixed in a 50 c.c. round bottom flask with 10 g. of 96% sulfuric acid. The solution was heated on the steam bath for ten hours, after which time the reaction mixture was cooled and diluted with water. The solid, collected on a filter, was found to be quite soluble in ethanol. No 4,4'-dichlorobenzil was obtained upon recrystallization from the ethanol solution.

(9) <u>The action of oleum on 1,1,1-trichloro-2,2-bis 4 chlorophenylethane.</u>

Into a 100 c.c. beaker were placed 25 g. of 106% sulfuric acid and 3.54 g. (0.01 mole) of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane. The mixture was heated on the steam bath until complete solution had taken place (ten minutes). The solution was cooled, diluted with water, and calcium oxide added to neutralize the acid. The excess calcium sulfate was collected on a filter and the filtrate evaporated to dryness. About 50 c.c. of 95% ethanol were added to the solid which was heated to boiling. The solution was filtered free of insoluble material and the filtrate evaporated to dryness. The residue was quite soluble in ethanol and methanol, but insoluble in ether. The product was subjected to the following tests.

<u>Examination of the product:</u>

(a) <u>Test for a trichloromethyl group.</u>

A sample of the material was heated with 2 c.c. of 20% sodium hydroxide and 1 c.c. of pyridine. The pyridine remained colourless. A red discoloration would have indicated the presence of a trichloromethyl group.[96]

(b) <u>Test for a sulfonic acid group.</u>[97]

The product (0.25 g.) was fused with sodium hydroxide (about 0.25 g.) in an eight inch test tube, after which the tube was cooled and the excess alkali neutralized with hydrochloric acid. A piece of filter paper, saturated with freshly prepared nickel hydroxide, was placed over the mouth of the tube. When the tube was gently warmed in hot water, the nickel hydroxide paper became quite black, indicating that a sulfonic acid group was present.

A control test made with calcium sulfate gave negative results.

(c) <u>Preparation of the 4 toluidine sulfonamide derivative.</u>[98]

To one gram of the product in a 50 c.c. beaker was added enough water to effect complete solution. The solution was brought to the boiling point, 0.5 g. of 4 toluidine and 2 c.c. of concentrated hydrochloric acid were added, and the solution boiled for two minutes. The reaction mixture was cooled and after standing for a few days at room temperature, crystals were precipitated from the solution; m.p. $316°C.$, with decomposition. The mother liquor was concentrated and more crystals were obtained; m.p. $325°C.$, with discolouration. These crystals were recrystallized from water; m.p. $325°C.$ The crystals were needle shaped.

(10) <u>Action of acid on 1,1-bis 4 chlorophenylethylene.</u>

In a 50 c.c. round bottom flask was thoroughly shaken a mixture of 3.0 g. (0.012 mole) of 1,1-bis 4 chlorophenylethylene and 40 g. of 97% sulfuric acid. The mixture was then heated on the steam bath for fourteen hours. The reaction product was cooled, the solution diluted with water and the residue collected on a sintered glass filter. The product was dissolved in 95% ethanol. (The acid filtrate on standing yielded some crystals; m.p. $135°C.$ These crystals were recrystallized from 95% ethanol; m.p. $144-145°C.$ The melting point of the mixture of this material taken with 4,4'-dichlorobenzophenone showed no depression. A solution of the precipitate in ethanol gave crystals on standing which were collected on a sintered glass crucible; m.p. $195-196°C.$ These crystals were salmon coloured and, upon recrystallization from 95%

ethanol, showed no rise in melting point. The crystals were recrystal-
lized from acetone and gave colourless needles; m.p. 195-197°C. The
melting point of the mixture of this material taken with 4,4'-dichloro-
benzil gave a large depression. The yield of this product was quite
small. This high melting point material was not investigated further.

(11) <u>Action of acid on 1,1-4 tolylethane.</u>

Into a 50 c.c. round bottom flask were placed 2.1 g. (0.01 mole)
of 1,1-ditolylethane and 30 g. of 98% sulfuric acid. The mixture was
shaken thoroughly and heated on the steam bath at 90°C. for fifteen
hours. The acid solution became very dark during the heating. The re-
action mixture was cooled and diluted with water, but no solid product
was precipitated, while some of the reactant was recovered unchanged.
The diluted acid solution was not investigated further.

<u>EXPERIMENTAL</u>

P A R T $\overline{\text{II}}$

(A)   PREPARATION OF 1-4 CHLOROPHENYL-2,2,2-TRICHLOROETHANOL
        AND 1-4 CHLOROPHENYL-2,2-DICHLOROETHANONE

(1)   <u>Preparation of 4-chloroacetophenone</u>

The preparation of 4-chloroacetophenone was performed by condensing

acetic anhydride and chlorobenzene by the use of aluminum chloride.[99]

(2)   <u>Preparation of 1-4-chlorophenyl-2,2,2-trichloroethanone</u>

The procedure as originally used by Gautier[100] was modified and the

preparation was carried out as outlined below.

To a 500 c.c. three necked, round bottom flask were added 154 g. (1

mole) of 4-chloroacetophenone and 1 g. of phosphorus trichloride as a

catalyst for the chlorination. To the three necked flask were attached

a water cooled reflux condenser, chlorine inlet tube and a 250°C thermo-

meter. The chlorine inlet tube was attached in series to two 250 c.c.

Erlenmeyer flasks which contained water and 96% sulfuric acid, respec-

tively. The water and acid solutions served to wash and dry the chlorine

gas as it evolved from the storage cylinder. The reaction was heated by

an electric hot plate which was placed underneath the flask. The hot

plate was adjustable so that the contents of the flask could be heated from

50°C at three inches to 210°C at about one inch distance below the flask.

The reaction was illuminated by a 500 watt light bulb which was placed

on the same level as the flask, six inches away. Dry chlorine gas was passed into the solution for twelve hours. The gain in weight after nine hours was 96.5 g. At the end of twelve hours the total gain in weight was 98 g. (theoretical 103 g.) The chlorination was initially carried out at room temperature. The heat was gradually increased, until at the end of about six hours the temperature was 200-210°C. At the termination of the chlorination the reaction flask was cooled and dry air was passed through the viscous liquid to drive out the dissolved chlorine gas. The viscous oil was placed in a 500 c.c. Claisen flask and was distilled under reduced pressure. The product was distilled at 140-143°C under 7 m.m. The yield was 226 g. or 88% of the theoretical value, m.p. 28°C.

(3) Reduction of 1-4 chlorophenyl-2,2,2-trichloroethanone to 1-4 chlorophenyl-2,2,2-trichloroethanol with aluminum isopropoxide

a) The aluminum isopropoxide was prepared as outlined in the literature[101].

b) To a 500 c.c. round bottom flask were added 25.8 g. (0.1 mole) of 1-4 chlorophenyl-2,2,2-trichloroethanone, 40 g. (0.2 mole) of aluminium isopropoxide-and 200 c.c. of dry isopropyl alcohol. To the flask was attached a short 30 cm. reflux condenser. The top of the reflux condenser was attached to another condenser which was set for distillation. The second condenser was connected to a 250 c.c. suction flask. A drying tube which was filled with calcium chloride was attached to the arm of the suction flask. Cold water was only allowed to circulate through the second condenser which was set for distillation. The reaction

flask was heated on the steam bath so that only about 5-10 drops of distillate per minute distilled into the receiver. The distillate was periodically tested for acetone by the use of an acetone test reagent (2,4 dinitrophenyl hydrazine) which was prepared as shown in the literature.[101]

The test was considered negative when three drops of distillate would not turn cloudy three c.c. of the clear test reagent within five seconds. When the acetone test became negative, water was then allowed to circulate through the reflux condenser and the reaction mixture was heated under vigorous reflux for ten minutes. The apparatus was reset for distillation. This procedure of distillation, reflux, then redistillation was carried out three times before a permanent negative acetone test was obtained and the reaction was then considered to be completed. The reduction had taken nine hours for completion. The excess isopropyl alcohol was distilled off, and the contents of the flask were poured into 420 c.c. of a cold acid solution containing 70 c.c. of concentrated hydrochloric acid. The water solution was extracted twice with 100 c.c. and 50 c.c. portions of ether respectively. The ether extracts were combined and were dried over 20 g. of anhydrous sodium sulfate. The dried ether solution was poured into a 250 c.c. modified Claisen flask and the ether was distilled off. The oily residue was distilled under reduced pressure and the product was collected between 147-154°C, at 15 mm. The weight of the product was 29.7 g. The yield of the 1-4 chlorophenyl-2,2,2-trichloroethanol was over 90% of the theoretical value. (This yield was based on the consideration that the oil was

converted to the acetate in 91% yield.) The product was coloured yellow, which became darker on standing. Several weeks later, the product crystallized; m.p. 43°C. The product was recrystallized from n-heptane; m.p. 47°C.

(4) Identification of the 1-4 chlorophenyl-2,2,2-trichloroethanol by conversion to known derivatives.

(a) Conversion of 1-4 chlorophenyl-2,2,2-trichloroethanol to 1-4 chlorophenyl-1-acetoxy-2,2,2-trichloroethane[102]

Into a 50 c.c. round bottom flask were placed 1.358 g. (0.0052 mole) of the 1-4 chlorophenyl-2,2,2-trichloroethanol oil and 2.04 g. (0.01 mole) of acetic anhydride. The flask was heated in an oil bath, under reflux, for four hours at 140-150°C. The reaction mixture was cooled first in air, then in a dry ice acetone bath. After much scratching, the product was precipitated from the reaction mixture. The solid was collected on a filter and was recrystallized from the minimum amount of glacial acetic acid which just dissolved the precipitate at the boiling point. The re-crystallized product was collected on a filter; m.p. 124-125°C. The melting point of the mixture of the product taken with an authentic sample of 1-4 chlorophenyl-1-acetoxy-2,2,2-trichloroethane showed no depression. The product was dried in the oven at 70°C. for twelve hours. The product was weighed 1.434 g. The yield of the 1-4 chlorophenyl-1-acetoxy-2,2,2-trichloroacetate was thus 91% of the theoretical value.

In a similar manner, 1-4 chlorophenyl-2,2,2-trichloroethylpropionate[102] and 1-4 chlorophenyl-2,2,2-trichloroethyl butyrate[102] were prepared from propionic anhydride and butyrylchloride, respectively.

Both these esters were submitted for testing as insecticides.

(b) Conversion of the 1-4 chlorophenyl-2,2,2-trichloroethanol to 1,1,1-trichloro-2,2-bis 4 chlorophenylethane.

To a 200 c.c. round bottom flask were added 20 g. of 98% sulfuric acid. The flask was surrounded by an ice bath and was cooled to $10^\circ C$. The acid was stirred while a solution containing 2.47 g. (0.02 mole) of chlorobenzene and 5.34 g. (0.02 mole) of 1-4 chlorophenyl-2,2,2-trichloro ethanol was slowly dripped into the acid over a two hour period. The reaction mixture was stirred for an additional four hours, after the final addition of the reactants. To the stirred reaction mixture were added 50 c.c. of chloroform. The chloroform and acid mixture was poured into a 250 c.c. separatory funnel. The chloroform layer was separated and the solvent was evaporated by heating on the steam bath. The product was crystallized from the residue. The weight of the crude product was 6.07 g. The crude yield was thus 83% of the theoretical. The product was recrystallized from 95% ethanol saturated with pp' DDT at $0^\circ C$ m.p. 105-106°C. The melting point of the mixture containing the product taken with 1,1,1-trichloro-2,2-bis 4 chlorophenylethane showed no depression. The yield of the recrystallized product was 42% of the theoretical value.

(5) Preparation of 1-4 chlorophenyl-2,2-dichloroethanone

To a 1000 c.c. round bottom, three necked flask were added 116 g. (0.75 mole) of 1-4 chlorophenyl ethanone, 225 g. (2 moles) of chlorobenzene

and 2 g. phosphorus trichloride. To the three necked flask were connected

a reflux condenser with a calcium chloride drying tube attached, a

thermometer and a chlorine gas inlet tube. The chlorine gas was washed by

conducting it through a water solution and dried by bubbling it through

concentrated sulfuric acid. The reaction flask was heated by an electric

hot plate placed underneath the flask at a distance such that the contents

were gently refluxed. The flask was irradiated by a 500 watt light bulb

placed six inches away from the reaction flask. The solution temperature

was 140-143°C throughout the eleven hour chlorination. The reaction product

was added to a 1000 c.c. separatory funnel and was washed with 500 c.c. of

10% sodium bicarbonate solution. The product was washed twice with two

separate 250 c.c. portions of water. The washed product was dried over

calcium chloride. The dried solution was poured into a 500 c.c. Claisen

flask and was distilled under reduced pressure. The product was collected

under 7.5 cm. at 140-150°C. The product crystallized in the receiver m.p.

58°C. The product was obtained in good yield and did not give a positive

trichloromethyl test[96] with pyridine and 20% alkali.

The above procedure is a modification of Gautier's[100] and results in

a purer product being obtained uncontaminated with any mono- or trichloro

derivatives.

(B)   NEW DERIVATIVES OF 1-4 CHLOROPHENYL-2,2,2-TRICHLOROETHANOL

(1)   Preparation of 1-4 chlorophenyl-1-trichloroacetoxy-2,2,2 trichloro-
       ethane.

(a)   Preparation of 1,1,1-trichloroacetyl chloride.

To a 500 c.c. round bottom flask were added 82 g. (0.5 mole) trichloro-
acetic acid and 23 g. (0.16 mole) of phosphorus trichloride. The flask was
heated under reflux at 50°C for five hours. The reaction mixture was dis-
tilled and the product was collected under atmospheric pressure between
114°C-118°C. The weight of the product was 32.5 g. or 35% of the theo-
retical yield.

(b)

To a 50 c.c. round bottom flask were added 3.9 g. (0.015 mole) of 1-4
chlorophenyl-2,2,2-trichloroethanol and 5.46 g. (0.03 mole) of trichloro-
acetyl chloride. The reaction mixture was heated under reflux by an oil
bath for eighteen hours at 150-160°C. To the top of the reflux condenser
was attached a calcium chloride drying tube. The flask was cooled and
10 c.c. of water were added to the reaction mixture. The flask was heated
to about 50-60°C for ten minutes to hasten hydrolysis of the unreacted
acid chloride. The flask was cooled and the water layer was pipetted off.
The residue was taken up in 10 c.c. of ether and cooled in a dry ice
acetone bath. After much shaking, a heavy precipitate was formed which
was collected on a filter m.p. 67-68°C. The product, upon recrystalli-
zation from acetone, showed an m.p. 71°C. The crystals were needle
shaped. The yield was over 80%.

Anal. calcd. for $C_{10}H_5O_2Cl_7$: Cl; 61.25

found.   Cl; 61.00; 60.85;

Molec. weight in acetone calcd. 405.5;

found. 393; 399

(2) Preparation of 1-4 chlorophenyl-1-methoxy-2,2,2-trichloroethane

To a 50 c.c. round bottom flask were added 3.9 g. (0.015 mole) of 1-4 chlorophenyl-2,2,2-trichloroethanol, 8.6 g. (0.06 mole) of methyl-iodide and 3 g. of silver oxide. (A further 3.9 g. of silver oxide were added after the initial reaction had subsided. This totalled 6.9 g. (0.03 mole).) To the reaction flask was connected a reflux condenser with a calcium chloride drying tube attached. The flask was gently heated on the steam bath and after the reaction had started, it was immersed in cold water. After ten minutes the balance of the silver oxide was added and the flask heated under reflux for six hours. The reaction flask was cooled and the contents were extracted with two 20 c.c. portions of ether respectively. The ether extract was filtered to remove the insoluble silver oxide. The ether solution was poured into a 50 c.c. distilling flask and was distilled under reduced pressure. The product was distilled at 86-88°C under 1.1 mm. The oily distillate was cooled to -20°C and left for several hours - crystals formed m.p. 28-29°C. The crystals, on standing at room temperature, slowly melted to an oil. The weight of the product was 2.7 g. or 65% of the theoretical yield.

Anal. calcd. for $C_9H_8OCl_4$: Cl; 51.79

found. Cl; 51.76; 51.66;

Molec. weight in acetone calcd. 274; found. 269; 271.

(3) <u>Preparation of 1-4 chlorophenyl-1-ethoxy-2,2,2-trichloroethane</u>

To a 50 c.c. round bottom flask were added 3.9 g. (0.015 mole) of ethyl-iodide and 6.9 g. (0.03 mole) of silver oxide. The mixture was heated under reflux on the steam bath for six hours. The flask was cooled and the contents were extracted with two 20 c.c. portions of ether respectively. The ether extract was filtered free of insoluble silver oxide and the solvent was evaporated. The yellow oil obtained from the evaporation was poured into a 10 c.c. Claisen distilling flask and was distilled under reduced pressure. The product distilled at 90-94°C. under 0.4 mm. The oil, on standing for several days at room temperature, gave crystals which after drying on porous plate gave an m.p. 46-46.7°C. The product was recrystallized from glacial acetic acid m.p. 48°C. The melting point of the mixture of the product taken with the starting material gave a large depression. The product was quite soluble in low boiling petroleum ether, heptane, dioxane, nitromethane, ethanol, methyl alcohol, dibutyl ether, isoamyl alcohol and benzene. The product was obtained in 37% yield. The crystals were square shaped.

Anal. calcd. for $C_{10}H_{10}O\ Cl_4$: Cl; 49.27

found Cl: 49.02; 49.25;

Molec. weight calcd. 288; found. 284; 303.

(4) Preparation of 1-4 chlorophenyl-2,2,2-trichloroethyl, methyl succinate.

(a) Preparation of mono methyl succinate.

To a 200 c.c. round bottom flask were added 30 g. (0.3) mole of suc-cinic anhydride and 9.6 g. (0.3 mole) of methanol. The flask was heated on the steam bath under reflux for two hours. The reaction mixture was cooled and the product precipitated from the solution. The solid preci-pitate was collected on a filter m.p. 50-55°C. The product was dissolved in ether and was allowed to stand in the refrigerator for two days. A solid had precipitated from the cooled ether solution which was collected on a filter m.p. 160-165°C. The melting point of the mixture of this solid taken with succinic acid showed no depression. To the filtrate were added a few c.c. of high boiling petroleum ether. The solution, upon standing for two more days in the refrigerator, yielded a second crop of crystals. This product was collected on a filter and was dried by air suction m.p. 58°C. The weight of the product was 15 g. This is a 38% yield of the theoretical value.

(b) Preparation of the mono methyl succinyl chloride.[103]

To a 100 c.c. round bottom flask were added 15 g. (0.038 mole) of mono methyl succinate and 50 c.c. of thionyl chloride. The solution was heated under reflux for five hours. The excess thionyl chloride was distilled off under atmospheric pressure. The oily residue was transferred to a 250 c.c. Claisen flask and was distilled under reduced pressure. The distillate was collected between 70-76°C at 0.5 mm. The weight of the distillate was 14 g. or a yield of 82% of the theoretical. The oily distillate on standing in a dry ice-acetone bath yielded crystals which melted below room temperature.

(c) Preparation of 1-4 chlorophenyl-2,2,2-trichloroethyl, methyl

succinate.

To a 50 c.c. round bottom flask were added 3.9 g. (0.015 mole) of

1-4 chlorophenyl-2,2,2-trichloroethanol and 3.02 g. (0.03 mole) of mono

methyl succinyl chloride. The flask was heated by an oil bath under

reflux for eighteen hours at 120-140°C. The reaction was cooled and

was diluted with 20 c.c. of water. The water oil solution was allowed

to stand for four hours with occasional shaking. The water was decanted

off and a fresh 20 c.c. portion was added. The product and water was

poured into a separatory funnel and was extracted with 20 c.c. of ether.

The mixture was shaken and after the layers had separated, the ether

layer was run into a 50 c.c. Erlenmeyer flask and was dried by the addi-

tion of 2 g. of sodium sulfate. The dried ether solution was poured

into a 25 c.c. distilling flask and the ether was distilled off. The

residue remaining from the evaporation of the ether was distilled under

reduced pressure. The product distilled at 183-186°C under 0.25 mm.

The distillate was cooled in a dry ice acetone bath and after a short

time crystallized m.p. 38-39°C. The product was dissolved in 4 c.c. of

95% ethanol heated to the boiling point and a few drops of formamide

was added until the solution became cloudy. The solution was cooled

first in air then in the refrigerator. After standing for a few days,

the product crystallized from the solution. The product was collected

on a filter and dried by air suction m.p. 41°C. The weight of the

product was 4.7 g. or 84% of the theoretical yield.

Anal. calcd. for $C_{13}H_{12}O_4Cl_4$: Cl; 37.94;

found. Cl; 37.75; 38.01;

Molec. weight in acetone calcd. 374; found 372; 369.

ATTEMPTED PREPARATIONS

1) **Attempt to prepare 1-4 chlorophenyl-2,2,2-trichloroethyl mono-maleate.**

Into an eight inch test tube which was attached to a reflux condenser were placed 3.9 g. (0.015 mole) of 1-4 chlorophenyl-2,2,2-trichloroethanol and 1.96 g. (0.03 mole) of maleic anhydride. The reaction tube was heated for seven hours at 170-180°C, after which the contents were cooled and poured into 25 c.c. of water. The water-oil solution was extracted with 25 c.c. of ether, the ether layer dried over sodium sulfate, and the ether evaporated. The oily product was distilled under reduced pressure and an oil collected between 83-87°C. at 0.25 mm. The oily distillate was seeded with a crystal of 1-4 chlorophenyl-2,2,2-trichloroethanol, to yield crystals, m.p. 47°C. The residue in the distilling flask was dissolved in acetone and the acetone evaporated to an oily residue which crystallized; m.p. 72°C. The melting point of the mixture of the crystallized products taken with maleic anhydride gave no depression.

The reaction was attempted with succinic anhydride instead of maleic, but no reaction would take place.

2) **Attempted preparation of 1-4 chlorophenyl-1-propoxy, 2,2,2-trichloroethane.**

A mixture of 3.9 g. (0.015 mole) of 1-4 chlorophenyl-2,2,2-trichloroethanol, 10.2 g. (0.06 mole) propyliodide, 6.9 g. (0.03 mole) silver oxide and 1 g. of calcium sulfate was heated under reflux for eight hours at 100°C. The reaction product was cooled and was filtered

through a sintered glass crucible. The filtrate was extracted with 20 c.c. of ether, the extract dried over sodium sulfate, and the ether removed by distillation from a 50 c.c. distilling flask. The residue was distilled between 88-92°C at 1.1 mm.

3) Attempted preparation of 1-4 chlorophenyl-1-butoxy-2,2,2-trichloro-ethane.

Into a 500 c.c. round bottom flask, equipped with a stirrer, were placed 384.0 g. (4 mole) 99% sulfuric acid which was cooled by an ice bath to 0°C.

Into the stirred solution, over a twenty minute period, were added 22.5 g. (0.30 mole) of chlorobenzene containing 22 g. (0.20 mole) of chloralbutyl alcoholate. After the final addition, the solution was stirred for an additional three hours. The acid solution was filtered and the precipitate was washed with water and dried; m.p. 99-100°C. The product was recrystallized from 95% ethanol; m.p. 105-106°C. The melting point of the mixture taken with the product and "D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenylethane showed no depression. An oil separated upon dilution of the filtrate which was dissolved in 95% ethanol and gave crystals; m.p. 85°C. A recrystallization from 95% ethanol gave m.p. 104°C. The melting point of the mixture taken of the product with "D.D.T." showed no depression. The desired reaction to give 1-4 chlorophenyl-1-butoxy-2,2,2-trichloroethane had not taken place.

4) Attempted preparation of 1-4 chlorophenyl-2,2,2-trichloroethyl glucose tetraacetate.

1) The   acetobromoglucose tetraacetate was prepared as outlined in the literature[104] by Robertson.

2) Into a 250 c.c. Erlenmeyer flask were placed 3.9 g. (0.015 mole) of 1-4 chlorophenyl-2,2,2-trichloroethanol, 6.17 g. (0.015 mole) of bromoglucose tetra acetate, 6.9 g. (0.03 mole) of silver oxide and 50 c.c. of dry ether, which was allowed to stand for twenty-four hours with occasional shaking. The solution was filtered free of silver oxide and the ether evaporated to an oily residue which resisted all attempts at crystallization. An attempt was made to distill the product under reduced pressure but this resulted in decomposition. The oily product was not investigated further.

(C) Miscellaneous preparations and attempted preparations.

1) Attempted preparation of 1,1,1-trichloro-2-4 chlorophenyl propanol-2.

Into a 250 c.c. Gringard flask, equipped with a mercury seal stirrer, gas inlet tube, reflux condenser and separatory funnel were added 3.1 g. (0.13 mole) of magnesium strips and a crystal of iodine. The flask was gently heated with a luminous flame while dry nitrogen gas was swept through the system for fifteen minutes. The nitrogen gas was dried by bubbling it through two traps, each containing concentrated sulfuric acid. The flame was removed and a little dry ether (dried over sodium) was added to cover the magnesium. The methyl bromide container was connected to the inlet tube and a stream of gas was directed to the

spot where the iodine and magnesium were lying together. (A stream of methyl bromide was produced by warming the container with the hand.) The magnesium was rubbed against the side of the flask by gently moving the stirrer and after several minutes of rubbing, the reaction commenced. The stirring motor was set in motion and within forty-five minutes most of the magnesium had dissolved, giving a grayish liquid. The methyl bromide stream and stirrer were stopped and dry nitrogen was swept through the system. The stirring was resumed and a solution containing 25.8 g. (0.1 mole) of 1-4 chlorophenyl-2,2,2-trichloroethanone in 50 c.c. of dry ether was slowly added by portions over a half hour period, after which stirring continued for an additional four and a half hours. The product was poured into 250 c.c. of water and ice, which contained 10 c.c. of concentrated hydrochloric acid. After a half hour, the oily hydrolyzed product was extracted from the water solution with two portions of ether, 10 c.c. and 75 c.c., respectively. The ether extracts were combined and dried over sodium sulfate. The dried solution was filtered into a 250 c.c. Claisen flask, the ether was distilled off and the residue was distilled between 110-115°C. at 8.3 cm. The distillate was cooled in a dry ice acetone bath and some crystallization took place. The crystals were collected on a filter; m.p. 175-222°C. with charring. The filtrate was washed with 10 c.c. of 10% sodium thiosulfate solution to eliminate some iodine which had distilled over during distillation. The washed oil was dissolved in 50 c.c. of ether and dried over sodium sulfate. The product redistilled between 115-118°C. at 9.3 cm. The distillate was crystallized by cooling in a dry ice acetone bath; m.p. 28°C. The

melting point of the mixture of the product taken with the starting material showed no depression. Little of the desired reaction could have taken place.

The reaction was repeated, using dry toluene as solvent and heating for seven hours between 80-100°C. after the addition of the 1-4 chlorophenyl-2,2,2-trichloroethanone. Only unchanged reactant was obtained after working up the product. These failures indicate an attack of the trichloromethyl group.

2) Attempt to prepare 1,1,1-trichloro-2-phenyl propanol-2.

A solution containing 60 g. (0.5 mole) of dry chloroform and 36 g. (0.33 mole) of acetophenone was placed in a 250 c.c. round bottom, three necked flask. The contents of the flask were vigorously stirred at room temperature. To the reaction over a one hour period, were added by portions 4 g. (0.07 mole) of powdered potassium hydroxide. The reaction mixture was allowed to stand overnight. The solution was diluted with 50 c.c. of ether and was filtered free of potassium hydroxide. The ether was evaporated on the steam bath and the residue was steam distilled which yielded unchanged acetophenone.

3) Preparation of 1,1-di 4 chlorophenylethylene.

Into a 500 c.c. round bottom, three necked flask, equipped with a mercury seal stirrer, water cooled reflux condenser and separatory funnel, were placed 40.5 g. (0.3 mole) of aluminum chloride and 67.2 g. (0.6 mole) of chlorobenzene. To the top of the condenser was attached rubber tubing which led to the sink. A solution of 26.7 g. (0.2 mole)

of 1,1,1-trichloroethane dissolved in 22.4 g. (0.2 mole) of chloro-benzene was slowly dripped into the stirred reaction mixture over a forty-five minute period. The addition was accompanied by a copious evolution of hydrogen chloride gas. The reaction was started at room temperature, then cooled to 5-10°C. with an ice bath. The reaction mixture was stirred for seven hours after the addition of the 1,1,1-trichloroethane. The product was hydrolyzed by pouring it over ice to which had been added 20 c.c. of concentrated hydrochloric acid, and allowed to stand for three hours. The water-oil solution was poured into a 1000 c.c. separatory funnel and the oil layer separated. The water layer was extracted three times with 75,50 and 50 c.c. portions of ether, respectively. The combined ether extracts and oil were steam distilled. To the non-steam distillable portion were added 75 c.c. of ether. The ether layer was separated and dried over calcium chloride. The dried solution was poured into a 250 c.c. Claisen flask and the ether distilled. The oily residue was distilled between 150°-160°C. at 11 mm. The weight of the product was 22 g. which partly crystallized upon cooling. The crystals were collected on a filter and weighed 10 g.; m.p. 80-81°C. The filtrate oil was set aside for further examination. After two recrystallizations from 95% ethanol the melting point rose to 86°C. - further recrystallizations did not raise the melting point (literature[131] gave an m.p. 91°C.) This was a 20% yield of 1,1-di 4 chlorophenylethy-lene.

Anal. Calcd. for $C_{14}H_{10}Cl_2$: Cl; 28.45;

found: Cl; 28.25; 28.20;

Molec. weight in acetone, calcd. 249; found: 246; 250; 241.

The uncrystallized filtrate oil was redistilled and was collected in three fractions. The first fraction distilled between 137-139°C. at 5-8 mm. and weighed 0.9 g.; the second between 136-139°C. at 5.0 mm. and weighed 3 g.; the third between 137-142°C. at 5.8 mm. and weighed 3 g. (approximately). The last fraction was slightly coloured. The combined weight of distillates was 7 g.

Anal. calcd. for $C_{14}H_{10}Cl_2$; Cl; 28.45;
found: Cl; 28.10; 28.35

Molec. weight in acetone calcd: 249; found: 251; 258;

Proof of the structure of the crystalline and oily products from oxidation.

(a) The Crystalline Solid

Into a 20 c.c. beaker were placed 0.2 g. of the crystals and 3 c.c. of a chromic acid-acetic acid oxidation mixture. The beaker was heated for thirty minutes on the edge of the steam bath and was diluted with water which precipitated the product. The solid was collected on a filter and dried by suction; m.p. 144-145°C. The melting point of the mixture of the product taken with 4,4'-dichlorobenzophenone, synthesized by another method, showed no depression.

(b) The Oil

Into a 20 c.c. beaker were placed five drops of the oil and 3 c.c. of the chromic acid-acetic acid oxidation mixture. The beaker was heated for thirty minutes on the edge of the steam bath, then cooled, and 15 c.c. of water were added. The precipitated product was collected on a filter and was recrystallized from 95% ethanol; m.p. 144°C. The melting point of the mixture of this material, taken with 4,4'-dichloro-benzophenone, showed no depression. The filtrate, upon cooling, gave a second crop of crystals which were collected on a filter and were recrystallized from 95% ethanol; m.p. 58°C. The melting point of the mixture of the product taken with 2,4'-dichlorobenzophenone, synthe-sized by another method, showed no depression.

It was, therefore, concluded that the crystals were 1,1-di 4 chlorophenylethylene and that the oil was a mixture of 1,1-di 4 chloro-phenylethylene and 1-2 chlorophenyl-1-4 chlorophenylethylene but con-sisted mostly of the latter.

4) Attempted preparation of 1-nitro-2-4 chlorophenyl-3,3,3-trichloro-propane.

(a) Preparation of 1,1,1-trichloro-3-nitropropanol-2

This material was prepared as outlined in the literature.[113]

(b) Into a 250 c.c., round bottom, three necked flask were placed 46g. of 99% sulfuric acid, 4.16 g. (0.02 mole) of 1,1,1-trichloro-3-nitropropanol-2 and 4.0 g. (0.034 mole) of chlorobenzene. The solu-tion was stirred at room temperature for eight and one half hours, then cooled, and diluted with ice and water. The diluted solution

was poured into a 250 c.c. separatory funnel and 50 c.c. of ether were added. The ether layer was separated and the water layer was extracted with two 25 c.c. portions of ether, respectively. The ether extracts were combined and the ether evaporated by heating on the steam bath to an oily residue which crystallized; m.p. 44°C. The melting point of the mixture of the product taken with the starting material showed no depression.

The above reaction was repeated using 96% and 98% sulfuric acid. However, only unchanged 1,1,1-trichloro-3-nitropropanol-2 was obtained.

(D) **The attempted preparation of 1-4 trichloromethylphenyl-2,2,2-trichloroethanol.**

The synthesis of this compound was attempted through a three-step process.

1) Preparation of 4-methyl acetophenone.

This was prepared by the process as outlined in the literature, Organic Syntheses.[106] The yield was 75%.

2) Preparation of 1-4 trichloromethylphenyl-2,2,2-trichloroethanone[107]

Into a 500 c.c., three necked, round bottom flask were placed 134 g. (1 mole) of 4 methylacetophenone and 3 g. phosphorus trichloride. A water cooled reflux condenser, thermometer and chlorine gas inlet tube were connected to the flask. The reaction was heated by an electric hot plate and illuminated by a 500 watt light bulb placed horizontally six inches away from the flask. Chlorine gas was passed into the solution, after first being washed with water and dried by concentrated

sulfuric acid. The flask was slowly heated to 140°C. and, after four hours, showed a gain in weight of 76 g. The temperature was raised to 175°C. and the chlorination resumed for an additional five hours. The total gain in weight for the nine hour chlorination was 166 g. The chlorination was continued for an additional seven hours at 190-210°C. (The chlorine inlet tube burst and a back flow resulted in a loss of some of the chlorinated product.) The product was distilled between 210-220°C. at 6 cm. On redistillation, the distillate was collected at 150-155°C. under 0.25 mm. and weighed 201.5 g.

Into a 500 c.c., three necked flask were placed 154 g. of the above oil and 1.5 g. of phosphorus trichloride. The solution was further chlorinated in the manner just described for sixteen hours at 200-210°C. The gain in weight was 8 g. The product was transferred to a 500 c.c. Claisen flask, was distilled at 143oC. under 1.25 mm., and weighed 136.5 g. The yield of 1-4 trichloromethylphenyl-2,2,2-trichloroethanone was 40% of the theoretical value.

Proof of the structure of 1-4 trichloromethylphenyl-2,2,2-trichloro-ethanone.[107]

A mixture of 1.119 g. (0.0338 mole) of the 1-4 trichloromethyl-phenyl-2,2,2-trichloroethanone and 10 c.c. of 96% sulfuric acid was heated on the water bath for one and a half hours. The solution was cooled, diluted with water and a flocculant precipitate was obtained which was collected on a filter. The solid was washed and dried; m.p. 182°C. The product weighed 0.78 g. and was soluble in 5% sodium bicarbonate solution, which indicated a carboxyl group. A positive test for a

trichloromethyl group was obtained when the solid was heated with pyridine and 20% alkali.[96] The product was 4 trichloromethyl benzoic acid and was first reported by F. Feist[107]. The yield was 89% of the theoretical; m.p. 182°C.

3) Attempt to reduce 1-(4-trichloromethylphenyl),2,2,2-trichloroethanone.

(a) Aluminum isopropoxide was prepared as outlined in "Organic Reactions".[108]

(b) Into a 500 c.c., round bottom flask were placed 113.7 g. (0.33 mole) of 1-(4 trichloromethylphenyl)-2,2,2-trichloroethanone, 300 c.c. of dry isopropyl alcohol and 70 g. (0.34 mole) of aluminum isopropoxide. To the flask was attached a short reflux condenser and to the top of the reflux condenser was connected a second condenser set for distillation. A suction flask with a calcium chloride tube on the side arm was connected to the second condenser. Water was circulated only in the condenser set for distillation. The reaction mixture was heated on the steam bath under reflux at a rate such that 5-10 drops of distillate were obtained per minute in the receiver. Acetone distilled over into the receiver and was detected by the acetone test reagent[108] (2,4 dinitrophenylhydrazone). After a few hours distillation, the acetone test was negative. Water was circulated in the reflux condenser and the reaction was refluxed vigorously for five minutes. The water was removed from the reflux condenser and distillation was resumed as previously. The distillate gave a negative acetone test and the distillation was discontinued. The reflux condenser was removed and the excess isopropyl alcohol was distilled and collected. The reaction mixture was poured into 475 c.c. of a solution containing 175 c.c. of concentrated hydrochloric acid. The solution was stirred for a half

hour for complete hydrolysis of any unreacted aluminum isopropoxide.
The water oil solution was extracted with three portions of ether,
250, 150 and 100 c.c. portions, respectively. The combined ether
extracts were dried over sodium sulfate. The dried ether solution
was poured into a 250 c.c. Claisen flask and the ether was distilled
off under atmospheric pressure. The oily residue would not distill
under reduced pressure, as the material decomposed quite rapidly.
The oily mass was transferred to a 500 c.c. round bottom flask which
had a side arm attached at the point where the bulb and neck of the
flask joined. The material was distilled at 135-150°C., under 1 mm.
with decomposition and was a heavy viscous oil which weighed 24.1 g.
A portion of the product was crystallized by cooling and by rubbing
in petroleum ether. A seed was added to the mass of the product which
caused it to crystallize. The product was recrystallized from petrol-
eum ether and collected on a filter; m.p. 88°C. A portion of the pro-
duct was recrystallized several times from petroleum ether and finally
gave a constant m.p. 95-96°C. The material gave a positive qualitative
test for an ester[109] This test indicated that the trichloromethyl
group on the benzene ring had been attacked by the aluminum isopropoxide.

Anal. calcd. for $C_{12}H_{13}O_3Cl_3$ C: 46.30; H: 4.17; Cl: 34.18

Found. C; 46.16; 46.13; H; 4.25; 4.04; Cl; 33.90; 33.78

#Procedure: A drop of the ether solution of the ester was put into a
porcelain micro crucible with a drop of alcohol saturated with hydroxy-
lamine hydrochloride. A drop of saturated alcoholic potassium hydroxide
was added. The solution was heated till bubbling commenced. The alkali
was neutralized with 0.5N hydrochloric acid and one drop of 1% ferric
chloride solution was added. A violet colour was obtained, which is a
positive test for an ester.

E) Preparation of 1,1,1,2-tetrachloroethyl, butyl ether.

1) To 68.5 g. (0.46 mole) of freshly distilled chloral contained in a 250 c.c. Erlenmeyer flask were added 34.5 g. (0.46 mole) of dry butanol. The solution crystallized on cooling; m.p. 49°C. The weight of the product was 103 g. of chloral butyl alcoholate.[110]

2) Into a 500 c.c. Erlenmeyer flask surrounded by an ice bath were placed 78 g. (0.39 mole) of phosphorus pentachloride and 50 c.c. of dry ether (dried over sodium). A solution containing 81 g. (0.36 mole) chloralbutylalcoholate and 75 c.c. dry ether was added to the reaction at a rate such that the temperature remained between 10-20°C. After the addition, the solution was allowed to stand for two and one half hours and was then diluted with 2:1 sodium hydroxide until just basic to litmus. The oily layer was separated and was steam distilled. A clear oil was obtained from the steam distillation which was separated and dried over calcium chloride. The dried solution was poured into a 250 c.c. Claisen flask and was distilled. The first fraction included all material which distilled below 100°C at atmospheric pressure. The second fraction was collected between 67-95°C. (mostly 86°C.) at 14 cm. The weight of the product was 35 g. which was redistilled and collected in four fractions as tabulated below. The yield of the 1,1,1,2-tetra-chloroethyl, butyl ether[111,112] was 46% of the theoretical value.

Fraction No.	1	2	3	4
Pressure cm.	7.5	7.4	7.2	6.9
Temperature ^{o}C.	64-67	64-67	60-71	70-95
Bath Temp. ^{o}C.	105-107	100-110	100-117	128-137
Weight in grams	4.4	7.10	7.4	6.6

Fraction No. 2

This fraction was considered to be the purest and was submitted to a few tests. A molecular weight determination by the Menzies-Wright ebulloscopic method, using acetone as the solvent, was attempted. No results could be obtained, however, because the vapour pressure of the 1,1,1,2-tetrachloroethyl, butyl ether is great enough at 57°C to offset the readings.

Anal. calcd. for $C_6H_{10}O\ Cl_4$: Cl; 59.14;

found: Cl; 57.9; 57.8;

3) The effect of alcoholic potassium hydroxide on 1,1,1,2-tetrachloro-ethylbutyl ether[112].

Into a 250 c.c. Erlenmeyer flask were placed 6.14 g. (0.0256 mole) of the 1,1,1,2-tetrachloroethyl, butyl ether and 10 c.c. of 95% ethanol. To this solution were added 40 c.c. of 95% ethanol containing 3.36 g. (0.06 mole) of potassium hydroxide. After standing for ten minutes at room temperature (24°C.), the solution was filtered and 1.99 g. of potassium chloride were collected on the filter. The filtrate was diluted with 300 c.c. of water and an oil was precipitated from the solution which

was extracted from the water with three separate 25 c.c. portions of ether.
The ether extracts were combined and were dried over calcium chloride.
The dried ether solution was poured into a 125 c.c. distilling flask and
the ether was distilled off and collected. The residue was distilled
under normal pressure and a colourless oil was obtained;3.pt. 199-204°C.
The weight of this product was 1.7 g., or a theoretical yield of 33% of
1,1,2-trichloroethylene butyl ether. The product possessed a sweet small,
and was redistilled between 60-61°C. at 14 cm.

Anal. calcd. for C_6H_9O Cl_3 ; Cl; 52.82;

found. Cl; 48.6; 48.8

4) Effect of alcoholic potassium hydroxide on chloral butyl alcoholate.

In a 250 c.c. Erlenmeyer flask were placed 6.63 g. (0.03 mole) of
chloral butyl alcoholate and 10 c.c. of 95% ethanol. A solution contain-
ing 3.36 g. (0.06 mole) of potassium hydroxide dissolved in 40 c.c. of
95% ethanol was added and the flask allowed to stand at room temperature
(25°C.) for thirty minutes. The solution was filtered and 2.05 g. of
potassium chloride were collected on the filter. The excess alkali was
neutralized with dilute nitric acid and the solution was distilled under
atmospheric pressure. The first fraction to 81°C. contained mostly
chloroform which was redistilled. The weight of the redistilled chloro-
form was 1.3 g. The second fraction distilled between 86°C-109°C and
contained mostly alcohol and water which smelled of butanol. No high
boiling products were obtained from the distillation.

(F) <u>Hydrolysis experiments on 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenyl-</u>
<u>ethane.</u>

A) Alkali

1) Into a 250 c.c. Erlenmeyer flask were placed 8 c.c. of 95% ethanol,

1.2 g. (0.02 mole) of potassium hydroxide and 1.94g.(0.005 mole) of 1,1,1,2-

tetrachloro-2,2-bis 4 chlorophenylethane. The solution was heated under

reflux on the steam bath for three hours, cooled, and was filtered free of

impurities. The filtrate was diluted with water and the excess alkali

neutralized with dilute nitric acid. The water-oil solution was extracted

with three separate portions of ether - 25 c.c., 15 c.c. and 15 c.c.,

respectively. The ether extracts were combined, the ether evaporated,

and the oily residue was crystallized from 95% ethanol; m.p. 77°C. The

melting point of the mixture of the product taken with the starting

material showed no depression. The filtrate was further concentrated,

but only unchanged reactant was obtained.

2) <u>Use of 1% sodium ethoxide.</u>

Into a 50 c.c., round bottom flask were placed 1.94 g. (0.005 mole)

of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane and 15 c.c. of dry

alcohol, containing 0.34 g. (0.005 mole) of sodium ethoxide. The solu-

tion was heated under reflux for fifteen hours on the steam bath, cooled,

and filtered free of alcohol insoluble impurities. Upon dilution of the

filtrate with water, an oil separated, which was extracted with two 25

c.c. portions of ether, respectively. The ether extracts were combined,

the ether evaporated and the oily residue recrystallized from 95% ethanol;

m.p. 91-92°C. The melting point of the mixture of the product taken with

the starting material showed no depression.

3) Miscellaneous Reagents

Similar experiments carried out with other alkaline reagents, such as magnesium butoxide, 10% sodium methylate, potassium acetate, silver oxide, etc., were used without success in the attempted hydrolysis of the tertiary chlorine contained in 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane. For example, an alcoholic sodium hydroxide solution containing 1.94 g. (0.005 mole) of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane which was heated on the steam bath under reflux for ten hours, gave 1,1-dichloro-2,2-bis 4 chlorophenylethylene in fair yield, as well as some unchanged starting material. In all trials, either the unchanged reactant or 1,1-bis 4 chlorophenyl-2,2-dichloroethylene were obtained as products.

(B) Acid

Into a 50 c.c. round bottom flask were placed 3.89 g. (0.01 mole) of 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane and 25 c.c. of 48% sulfuric acid. The solution was heated on the steam bath for fifteen hours at 90°C., cooled and diluted with water. The precipitated product was collected on a sintered glass filter and was recrystallized from 95% ethanol; m.p. 91-92°C. The melting point of the mixture of the product taken with the starting material showed no depression.

The above procedure was repeated using higher acid concentrations. For sulfuric acid concentrations of 72%, 80% and 85%, only the starting material was recovered unchanged. When 96% sulfuric acid was used, there resulted a complete hydrolysis of all the aliphatic chlorines and

the product was identified as 4,4'-dichlorobenzil.

The use of acetic anhydride sulfuric acid mixtures was also unsuccessful in the hydrolysis of the tertiary chlorine.

EXPERIMENTAL

PART III

(A) ATTEMPTS TO FIND AN ALTERNATE SIMPLE SYNTHESIS FOR "D.D.T."

(1) Friedel and Crafts reaction of pentachloroethane and chlorobenzene, using aluminum chloride.

Into a 1000 c.c. round bottom, three necked flask were placed 53.2 g. (0.4 mole) of aluminum chloride and 40.2 g. (0.2 mole) of pentachloroethane. To the reaction flask were attached a separatory funnel, thermometer and Mercury seal stirrer. The reaction mixture was vigorously stirred and maintained at 40-45°C while 44.8 g. (0.4 mole) of chlorobenzene were slowly added over a half hour period. After the addition the mixture was stirred for an additional hour. The product was hydrolyzed by pouring it over a mixture of ice and 75 c.c. of concentrated hydrochloric acid, all contained in a 3 l. beaker. The hydrolyzed product was heated to 100°C, cooled and a gummy mass settled to the bottom of the beaker. The product was quite soluble in acetone, ether, ethanol, etc., from which no crystalline solids were obtained. The product was non-toxic to insects and was not investigated further. Several similar unsuccessful attempts were made with chlorobenzene and pentachloroethane, using zinc chloride, boron trifluoride, aluminum chloride and ferric chloride as catalysts. With aluminum chloride under various reaction conditions, only high melting point or gummy products were obtained. The products from these runs were not investigated further.

Boron trifluoride under reaction temperatures from 0° to 125°C. did not catalyze the desired reaction.between pentachloroethane and chlorobenzene. In these runs most of the chlorobenzene and pentachloroethane was recovered unchanged.

(2) **Action of aluminum chloride on "D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenylethane.**

Into a 500 c.c. round bottom flask were placed 17.7 g. (0.05 mole) of "D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and 24 g. (0.6 mole) of aluminum chloride. To this mixture were added 25 g. (0.25 mole) of chlorobenzene which resulted in a violent reaction taking place with copious evolution of hydrogen chloride. In a half hour after the main reaction had subsided, the solution was stirred for one day at room temperature and the gummy product poured over a mixture of ice and 10 c.c. of concentrated hydrochloric acid, all contained in a 3 litre beaker. The hydrolyzed product was poured into a 1 litre separatory funnel and 500 c.c. of ether was added. The ether extract was separated, the ether evaporated and the residue was steam distilled. The non-steam distillable residue was dissolved in chloroform, separated and evaporated to a gummy product. This product was submitted for insecticidal testing and showed no activity. The "D.D.T." was thus destroyed by the aluminum chloride.

(3) **Action of ferric chloride on "D.D.T.", 1,1,1-trichloro-2,2-bis 4 chlorophenyl ethane.**

Into a 500 c.c. round bottom, three necked flask were placed 17.7 g.

(0.05 mole) of commercial "D.D.T." (containing o,p and p,p isomers),
1,1,1-trichloro-2,2-bis 4 chlorophenylethane, 3.36 g. (0.02 mole) of
ferric chloride and 28 g. (0.25 mole) of chlorobenzene. To the flask
were attached a mercury seal stirrer, reflux condenser with a calcium
chloride drying tube attached, and a thermometer. The reaction mix-
ture was stirred for two days at 25°C., while a slow steady stream of
hydrochloric acid gas was evolved. The product was poured over ice
and 10 c.c. of concentrated hydrochloric acid, all contained in a 3
litre beaker. The oil layer was separated from the water by decanta-
tion and was steam distilled. The oily residue was dissolved in 95%
ethanol and a small yield of yellow coloured crystals was obtained;
m.p. 150°C. The crystals were recrystallized from 95% ethanol; m.p.
156°C. The filtrate, on standing for several days in the refrigerator,
yielded more crystals; m.p. 82°C. Upon recrystallization from 95%
ethanol, the product showed an m.p. 86-87°C. The melting point of the
mixture of this product, taken with 1,1-dichloro-2,2-bis 4 chloro-
phenylethylene showed no depression.

(B) Attempted conversion of a carboxyl to a trichloromethyl group.[114,115,116]

a) Into a 150 c.c. bomb tube were placed 8.73 g. (0.05 mole) of
benzoyl chloride and 10.5 g. (0.05 mole) of phosphorus pentachloride.
The tube was heated to 170-215°C. for thirty-four hours, cooled and
was opened with accompaniment of an outrush of gas. The product was
transferred to a 50 c.c. distilling flask and was distilled and col-
lected in three fractions under normal pressure.

The first fraction was a water white distillate, collected between 25°C-130°C., which solidified to a gummy mass and was not investigated further.

The second fraction, which fumed in air, was collected between 130°C.-160°C.

The third fraction should have contained the benzotrichloride as it boils at 245°C. It was collected between 170°-235°C., but the bulk distilled between 220°C-235°C. The weight of the distillate was 8.5 g. and excess water was added to hydrolyze any benzoyl chloride. The whole distillate crystallized out into a solid and was collected on a filter; m.p. 238°C. The melting point of the mixture taken with 4 chlorobenzoic acid showed no depression. The reaction had failed to yield any trichloromethyl benzene.

The above reaction was repeated, using higher temperatures, but only negative results were obtained.

b) Attempt to convert acetyl chloride to 1,1,1-trichloroethane.

In a 150 c.c. bomb tube were placed 1.6 g. (0.02 mole) of acetyl chloride and 4.1 g. (0.02 mole) of phosphorus pentachloride. The reaction tube was heated to 100°C. for twenty hours, cooled, opened and 10 c.c. of water were added. The entire tube contents dissolved, leaving no water insoluble products.

The above reaction was repeated by heating the bomb tube and contents to 160-170°C for twenty-four hours and to 200-220°C for forty-eight hours. In the first case, some charring had taken place, but no water insoluble oil product was obtained after dilution of the tube contents with water. In the second attempt, the entire tube contents

had been destroyed and only a charred mass remained.

The conversion of a carboxyl group to a trichloromethyl group does not appear to be feasible under the conditions employed. The results obtained are in contradiction to those reported by earlier workers.[114,115,116.]

SUMMARY

An investigation was made of the decomposition products of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane when treated with 96%, 98% and 100% sulfuric acid for various lengths of time and temperatures. The only decomposition product which was positively identified was 4,4'-dichlorobenzil. Other trichlorodiarylethanes were also investigated but these did not yield any water or acid insoluble products after treatment with sulfuric acid.

Mechanisms have been advanced to explain the formation of 4,4'-dichlorobenzil in the decomposition of these two polyhalogen compounds. The mechanisms are based on the formation of intermediate carbonium ions which allow the rearrangement to take place.

An alternate synthesis of the "carbinol", 1-4 chlorophenyl-2,2,2-trichloroethanol was developed. This method was an adaptation of the Meerwein and Schmidt reduction of 1-phenyl-2,2,2-trichloroethanone to 1-phenyl-2,2,2-trichloroethanol with aluminum isopropoxide. In addition to the synthesis, several new derivatives of this "carbinol" were prepared. Such new compounds included 1-4 chlorophenyl-1-methoxy-2,2,2-trichloroethane, 1-4 chlorophenyl-1-ethoxy-2,2,2-trichloroethane, 1-4 chlorophenyl-1-trichloroacetoxy-2,2,2-trichloroethane and 1-4 chlorophenyl-2,2,2-trichloroethyl, methyl succinate. These new compounds, as well as several others, including pentachlorethane, chloralid, 4-bromobenzenesulfonic acid, 4 bromobenzenesulfone, 1-4 chlorophenyl-2,2,2-trichloroethyl, acetate, propionate and butyrate, 4 chloroacetophenone, 1-4 chlorophenyl-2,2,2-trichloroethanone, 1-4 chlorophenyl-2,2,2-trichloroethanol, bis 2 chlorophenylacetic acid,

chloral butyl alcoholate, 1,1,1,2-tetrachloroethyl,butyl ether, 1-4 trichloromethylphenyl-2,2,2-trichloroethanone, 4 methylacetophenone, 4-(2,2,2-trichloro-1-hydroxyethane) isopropylbenzoate, 1-1-di 4 chlorophenyl-2,2-dichloroethylene;1,1-di 2',4 chlorophenyl-2,2-dichloroethylene, 1,1,1-trichloro-2-hydroxy-3 nitropropane etc., were submitted for testing as insecticides. However, none of the above compounds were found to be superior to "D.D.T." and from the results of these tests no conclusion could be advanced as to the essential physical or chemical properties needed for an insecticide. Among the more active of these compounds which have a toxicity which approximates that of the "carbinol", are 1,1-di 4 chlorophenyl-2,2-dichloroethylene, 1,1-di 2',4 dichlorophenyl-2,2-dichloroethylene, 1-4 chlorophenyl-1-methoxy-2,2,2-trichloroethane, 1-4 trichloromethylphenyl-2,2,2-trichloroethanone and 1-4 chlorophenyl-1-ethoxy-2,2,2-trichloroethane. The most active compound was 1-4 chlorophenyl-2,2,2-trichloroethyl acetate, which has an activity of one-tenth that of "D.D.T." itself.

An alternate synthesis of "D.D.T." was attempted from pentachloroethane and chlorobenzene, using one of the following as the condensing agent; aluminum chloride, zinc chloride, ferric chloride and boron trifluoride. All these attempts were failures; the products from these reactions were not fully investigated on account of the war urgency of this problem and because they possessed no insecticidal toxicity.

One attempt was made to synthesize "Di ortho D.D.T.", 1,1,1-trichloro-2,2-bis 2 chlorophenylethane from bis 2 chlorophenylacetic acid and phosphorus pentachloride. However, the conversion of a carboxyl group to a trichloromethyl group with benzoyl chloride and

acetyl chloride was without success and this approach was, therefore,

abandoned.

CLAIMS TO ORIGINAL RESEARCH

(1) A study was made of the action of sulfuric acid on several 1,1,1-trichloro-2,2-bis aryl ethanes. The experiments were made by heating the compounds with the acid for various lengths of time and at different temperatures.

(2) A new rearrangement was observed to take place in the conversion of 1,1,1-trichloro-2,2-bis 4 chlorophenylethane and 1,1,1,2-tetrachloro-2,2-bis 4 chlorophenylethane to 4,4'-dichlorobenzil with sulfuric acid.

(3) Mechanisms have been advanced which can, in part, account for the product obtained from the rearrangements.

(4) A new synthesis of "the carbinol", 1-4 chlorophenyl-2,2,2-trichloroethanol was accomplished by the reduction 1-4 chlorophenyl-2,2,2-trichloroethanone with aluminum isopropoxide.

(5) Syntheses of several new derivatives of 1-4 chlorophenyl-2,2,2-trichloroethanol were accomplished with the objective of finding a more powerful insecticide than "D.D.T."

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