INTRODUCTION

In course of our study of the pharmacological possibilities of different dichloroacetomido compounds, it was thought desirable to extend the programme to the preparation of some dichloroacetyl aromatic compounds by a suitable reaction. The search of literature revealed that these compounds (which are not many) are prepared in varied yields, by the direct halogenation of the appropriate acetophenones. Kravets, V. P., G. I., Chervenyuk and G. V., Grinev, Zh. Organ. Khim., 2 (7), 1244 (1966).

A critical study of the existing method brought out the following points which preclude the application of the method in some cases and as such the method loses its general applicability.

On halogenation, at first the w-haloacetophenone results; this product has decreased electron density on the end carbon atom, thus making it open for the replacement of the second hydrogen atom by another halogen atom, the product being w,w-dihalo acetophenone. The electron density of the end carbon atom experiences three inductive forces due to chlorine and oxygen, and as such the electron-density is further decreased. This results in the formation of a trihalogen
derivative; that is, it is difficult to check the reaction at the desired stage. In the case of alkyl substituted aceto-phenones, there is chance of the side chain being halogenated under a slight variation of the conditions of reaction. Nuclear halogenation of those acetophenones which bear aromatic hydroxy or alkoxy groups is also not unlikely.

In consideration of the above demerits of the halogenation process, a simple method had been sought which could introduce directly the group - COCHCl₂ into the aromatic nucleus at a single step of reaction. Friedel Crafts reaction was considered highly feasible and dichloro-acetyl chloride was selected for the purpose. In this connection, a short review of the Friedel Crafts reaction its scope, conditions and applicability is given.

Friedel and Crafts (Compt. rend., 84, 1392, 1450 (1877)) showed that anhydrous aluminium chloride catalyses the condensation of alkyl and acyl halides with various aromatic compounds to effect electrophillic substitution of alkyl or acyl group for one or more hydrogen atoms of the aromatic compound. Since then this reaction has been largely utilised with various alkylating or acetylating agents using different catalysts. The catalysts largely used are AlCl₃, FeCl₃, SnCl₄, ZnCl₂, H₃PO₄, BF₃, SbCl₅ and H.F. The aromatic compounds include hydrocarbons, mono or polyhydric
phenols, their ethers etc.


A variety of solvents has been employed in the Friedel-Crafts Ketone synthesis. Nitrobenzene and CS₂ are the most commonly used solvents which at the same time govern the types of acylation reactions.

In practice, the use of the calculated amount of catalyst generally gives the maximum total yield of Ketone. A deficiency of catalyst lowers the overall yield because of incomplete utilization of the acyl compound. An excess of catalyst, on the other hand, often gives appreciable amount of tar. Although many other catalysts have been increasingly employed recently, the preeminence of anhydrous aluminium chloride remains unchallenged even to-day. It combines the virtues of high catalytic efficiency and cheapness. The purity of AlCl₃ exerts a considerable influence on the yield of product. Boswell, M.C. and R.R. Mchaughlin, Can. J. Research, 1, 40 (1929); and also Riddell, W.A., and
Trace amounts of FeCl₃ have been reported to cause an increase in overall yield, or to exert an accelerating effect on the reaction.

Instead of reviewing the voluminous work on Friedel-Crafts reaction, the earlier work using halogen substituted fatty acid halides is being reviewed.

Benzene was condensed with both chloroacetyl chloride and bromoacetyl chloride in presence of anhydrous aluminium chloride giving respectively a good yield of w-chloroacetophenone (I) and w-bromoacetophenone (II).

\[
\begin{align*}
\text{CH}_3 \\
\text{COC} \text{H}_2 \text{Cl}
\end{align*}
\]

(III)

A good yield of 2,4-dimethyl w-chloroacetophenone (IV) was obtained by the condensation of m-xylene with chloroacetyl chloride, Jorlander H., Ber., 50, 1457 (1917) and Kunckell F., Ber. 30, 577 (1897). Bromoacetyl bromide was condensed with m-xylene by Jacobs et al. giving a moderate yield of 2,4-dimethyl-w-bromoacetophenone (V) Jacobs W.A., and M. Heidelberger, J. Biol. Chem., 21, 455 (1915).

\[
\begin{align*}
\text{CH}_3 \\
\text{CH}_3 \\
\text{COC} \text{H}_2 \text{Cl} \\
\text{CH}_3 \\
\text{CH}_3 \\
\text{COCH}_2 \text{Br}
\end{align*}
\]

(IV) (V)
Malinovskii et al. condensed p-cymene with chloro-acetyl chloride in presence of anhydrous aluminium chloride using carboxdisulphide as the solvent. These workers obtained a poor yield of 2-methyl-5-isopropyl-2-chloro-acetophenone (VI) \( \text{Malinovskii, M.S. and K.K.Baralashova, Zh. obsheh. Khim., 12, 559 (1949); Chem. Abstr. 44, 3939 (1950)} \)

\[
\begin{align*}
\text{CH}_3 & \quad \text{CoCH}_2\text{Cl} \\
\text{CH} & \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

(VI)

Chlorobenzene was condensed with both chloro and bromo acetyl chloride by Collet \( \text{Collet A., Compt. rend. 125, 717 (1897)} \) and good yields of the corresponding acetophenones, 4-chloro-2-chloroacetophenone (VII) and 4-chloro-2-bromo acetophenone (VIII) were obtained. Trifluoro acetyl chloride was, however

\[
\begin{align*}
\text{Cl} & \quad \text{CoCH}_2\text{Cl} \\
\text{Cl} & \\
\text{Cl} & \quad \text{CoCH}_2\text{Br}
\end{align*}
\]

(VII) (VIII)

\[
\begin{align*}
\text{Cl} & \quad \text{CoC} \text{F}_3
\end{align*}
\]

(IX)

Bromobenzene was likewise found to condense smoothly with chloro and bromo acetyl chloride under usual conditions, producing 4-bromo-2-chloro acetophenone and 4-bromo-2-bromo acetophenone in fairly good yield.

Kunckell (Ber. 41, 2648 (1908)) obtained a good yield of 2-methyl-4-chloro-2-chloroacetophenone (X) by condensing 3-chlorotoluene with chloroacetyl chloride.

\[
\begin{align*}
\text{Cl} & \quad \text{CH}_3 & & \quad \text{Cl} & \quad \text{CH}_3 \\
& \quad \rightarrow & & \quad \text{Cl} & \quad \text{CH}_3 \\
& & & \quad \text{Cl} & \quad \text{CH}_2 \text{Cl}
\end{align*}
\]

(X)

Extension of haloacetylation to phenolic ethers met with some remarkable abnormalities. While condensing anisole with chloroacetyl chloride at 0° Anwers et al (Ber., 52, 2899(1926)) obtained some 2-methoxy-2-chloro acetophenones (XI) besides
4-methoxy-derivative (XII) which is the normal product.

\[
\begin{align*}
\text{(XI)} & \quad \text{(XII)} \\
\end{align*}
\]

Chloroacetylation at the reflux condition (Nagano T., J. Am. Chem. Soc., 77, 1691 (1955)) produced the demethylated ketone, 4-hydroxy-\(\beta\)-chloroacetophenone (XIII). A case of over acylation was also reported by Tutin (J. Chem. Soc., 97, 2500 (1910)) who condensed anisole at 90° with chloroacetyl chloride in presence of two moles of anhydrous aluminium chloride, yielding the diacylated product (XIV)

\[
\begin{align*}
\text{(XIII)} & \quad \text{(XIV)} \\
\end{align*}
\]
Anwells also condensed p-tolyl methyl ether with excess chloroacetyl chloride in presence of excess catalyst when a mixture of 2-hydroxy-5-methyl-w-chloroacetophenone (XV) and 2,6-di-(chloroacetyl) - 4-methyl phenol (XVI) was produced, the latter having a low yield.

The first report of haloacylation of a nitrogenous compound was the condensations of acetanilide and 2-methyl acetanilide with chloroacetyl chloride in carbon di sulphide as solvent, the product being 4-acetamido-w-chloroacetophenone (XVII) and 3-methyl-4-acetamido-w-chloroacetophenone (XVIII) respectively. The
condensation of bromoacetyl bromide resulted in the corresponding \( \omega \)-bromoacetophenones \( \text{Jacobs, W. A., and M. Heidelberger, J. Biol. Chem., 21, 455 (1915)} \).  

An interesting reaction occurs between benzene and \( \alpha \)-bromo-isobutyryl bromide. \( \text{Kishner, N., Zh. Russ. Fiz.-Khim. Obshchestva, 46, 1411 (1914)} \). The \( \omega \)-bromo-acetophenone derivative (XIX) formed in the first stage loses hydrogen bromide giving isopropenyl phenylketone (XX) and indanone (XXI)

\[
\text{Mesitylene reacts with } \beta \text{-chloropropionyl chloride to give mesityl vinyl ketone (XXII) formed by elimination of hydrogen chloride. } \text{Fuson, R.C. and C.H. McKeever, J. Am. Chem. Soc.,}
\]
Thus $\beta$-halo substituted halides are potentially $\alpha,\beta$-unsaturated.

The condensation of benzene with $\gamma$-chlorobutyryl chloride in presence of $\text{AlCl}_3$, gave the expected chloroketone (XXII). Under more strenuous conditions, however, the $\gamma$-halogen atom attacked a second benzene molecule or the $\sigma$-carbon atom to give the ketones (XXIV) and (XXV).
Among the di- and polyhalogen substituted acid halides, di- and trichloro acetyl chloride were only successfully condensed with benzene in presence of aluminium chloride giving \( w_w \)-dichloroacetophenone (XVI) and \( w_w w_w \)-trichloroacetophenone (XVII) in good yields.

\[
\begin{align*}
\text{CH}_2 \text{CO} & \quad \text{Cl} \quad \text{CH} \quad \text{CO} \\
\text{CH}_2 & \quad \text{Cl} \quad \text{CH} \quad \text{CO}
\end{align*}
\]
Dichloroacetyl chloride was also condensed with anisole in carbon-di-sulphide solvent and under the catalytic influence of aluminium chloride. The product was 4-methoxy-\(\text{w,w'-dichloroacetophenone (XXVIII)}\) (Kunckell, F. and F. Johanssen, Ber., 31, 169 (1898)).

\[
\text{OCH}_3
\]

\[
\text{CO}\cdot\text{CHCl}_2
\]

(XXVIII)

Tribromopivaloyl chloride has been reacted with a series of aromatics (Nerdel, F., A. Heymons and H. Gansau, Chem. Ber. 21, 944 (1958)), only the acyl halogen atom reacting in this case.

\[
(\beta_h\cdot\text{CH}_2)_3\cdot\text{C. COCl} \xrightarrow{\text{Ph.H}} \text{AlCl}_3 \rightarrow \text{CO.C(CH}_2\beta_h)_3
\]
Orientation of alkyl and acetyl groups in Friedel-Crafts reaction

As in the case of any other electrophilic substitution, the problem of orientation of the entering group in the aromatic nucleus, is an important one in Friedel-Crafts reaction, particularly when more than one alkyl or acetyl group enter the already substituted aromatic nucleus. Ingold et al., J. Chem. Soc., 1959 (1931); Ingold, ibid., 1938 (1938); Grosse et al., J. Org. Chem., 447 (1937); C. K. Ingold, Structure and Mechanism in Organic Chemistry, Chapter VI, Cornell Univ. Press, New York, 1953.

The relative extent of normal and abnormal orientation depends upon the conditions of the reaction. It has been found that alkylation of benzene with aluminium chloride and alkyl halides gives considerable proportions of m-dialkyl benzenes along with the expected ortho and para isomers. The orientation of the entering alkyl or acetyl group in the aromatic ring depends largely upon the group or groups present already and can be predicted from the existing rules of aromatic substitution. The course of reaction, however, in many cases, appears to be subject to some steric hindrance. In the cases of acylation by large molecules, in most instances the ortho positions are avoided. Thus condensation occurs at the para position preferentially and when the para position is not available, ortho substitution...
takes place without much difficulty. Only one para isomer is formed in the succinoylation of toluene or ethyl benzene \( ^{\text{Krollpfeiffer et al., Ber., 56, 620 (1923); Muhr, Ber., 28, 3215 (1895); Levy, Ann. Chim., 9 (ii), 5 (1938)}} \). In the glutaroylation of toluene and halogenated benzenes, the para positions are exclusively involved \( ^{\text{Carter et al., J. Chem. Soc., 451 (1940); Fieser, J. Am. Chem. Soc., 70, 3174, 3197 (1948); Skraup et al., Ann. 462, 135 (1928); Fieser and Seligman, J. Am. Chem. Soc., 60, 170 (1938)}} \). Para xylene and mesitylene are substituted ortho to a methyl group. Two isomeric acids are obtained in the reaction of succinic anhydride with ortho and meta cresol, but \( p \)-cresol is substituted only at the ortho position to the hydroxyl group \( ^{\text{Raval et al., J. Univ. Bombay, 7, Pt. 3, 184 (1938)}} \).
When methyl ethers of the cresols are the starting substances, the large anhydride molecules always attack the position that corresponds to the stronger directing influence of the methoxyl group. Rosenmund, Arch. Pharm., 272, 313 (1934); Desai and Wali, Proc. Indian Acad. Sci., 6A, 144 (1937). This is also true for higher alkylated derivatives of anisole. Harland et al., J. Chem. Soc., 237 (1939); Soloveva et al., J. Gen. Chem., U.S.S.R., 15, 60 (1945).

The halogen substituted fatty acid chloride molecules are quite large units and as such acylation with chloro acid chloride follows invariably all the orientation patterns that are followed by big acylating units. Toluene is chloroacetylated exclusively in para position, while p-cymene gives a very poor yield of 2-methyl-5-isopropyl-2-chloroacetophenone. Kunckell, F., Ber., 30, 577 (1897); Moller et al., J. Am. Chem. Soc., 46, 1889 (1924);
Malinovskii et al, Chem. Abstract, 44, 3939 (1950). Halobenzenes are likewise haloacetylated in the para position (Collet, A., Compt. Rend., 125, 717 (1897)).

Meta xylene is chloroacetylated at the position which has the combined directive influence of both the methyl groups, while m-chloro toluene condenses with chloroacetyl chloride at the position para to the chlorine atom having the stronger directive force (Kunckell, F., Ber., 30, 577 (1897); ibid, 41, 2648 (1908)).
Phenol and anisole are exceptional with respect to the orientation pattern it shows during acylation. Many acylations of phenol result in the formation of both ortho and para ketones. When anisole is chloroacetylated at 0° in presence of AlCl₃, some ortho-isomer is formed along with para isomer.

Nature of solvent, to a great extent, actuates the orientation of the incoming group, particularly the acyl groups. A polar solvent, such as nitrobenzene dissolves (and solvates) not only AlCl₃ but also the acyl chloride - AlCl₃ complex, and usually also the AlCl₃ complex of the resulting ketone [Ryvkin, S.M., Zh. Obsch. Khim., 5, 277 (1935)]. So the entering acylating unit becomes large enough and condensations in the ortho positions are essentially avoided. Whereas in the case of a non-polar solvent such as CS₂, CCl₄ etc., the acylhalide - AlCl₃ complex is not solvated and therefore the acylating unit does not become very large and as such both ortho and para condensations take place to a considerable extent. In

The role of catalyst is also significant in the course of Friedel Crafts reaction. In addition to its influence on the total yield of acylated products, the ratio of catalyst to acyl component (herein after termed Q) also exerts a powerful influence on the course of substitution of aromatics, in general, and polycyclic systems, in particular. In the acetylation of naphthalene in ethylene chloride [Baddley, G., J. Chem. Soc., 599 (1949)], a lowering of Q from 1.0 to 0.5 decreases the content of α-isomer from 98% to 60% and the total yield for 93% to 76%. Further, with β-chloropropionyl chloride and Q=1.0, naphthalene is substituted mainly in the β-position, and with Q=2.2, mainly in the α-position.
Summary and discussion

While attempting the synthesis of different dichloroacetyl derivative of aromatic compounds to be tested for their pharmacological possibilities, the Friedel Craft's method of acylation with dichloroacetyl chloride has been developed in this laboratory. Dichloroacetyl chloride has been found to condense smoothly with different aromatic hydrocarbons, their halogenated derivatives, phenolic ethers and some nitrogenous compounds in the presence of anhydrous aluminium chloride, giving the \( \alpha, \beta \)-dichloroacetophenone compounds in high yields. The products are high boiling liquids, some of them being low melting solids. All these compounds are highly irritant to skin and some are lachrimatory. These chloro-ketones are soluble in ether, alcohol and chloroform.

The author describes in this part of the thesis, the condensations of various aromatic hydrocarbons, their halogenated derivatives, anisole, cresol methyl ether, acetanilide and dichloroacetamido benzene with dichloroacetyl chloride under the catalytic influence of anhydrous aluminium chloride. It was found that some reactions took place at 5\(^{\circ}\)-10\(^{\circ}\), while others did not at temperatures below room-temperature. The use of nitrobenzene as solvent was, in certain cases, found to decrease the yield of the desired ketones; in the case of anisole it influenced the course of reaction. The condensations of the anilides were studied in refluxing \( \text{CS}_2 \) solvent.
The dichloroacetylation of aromatic hydrocarbons has served as an excellent method for the preparation of \( w, w \)-dichloroacetophenones some of which have not been previously described in the literature. These dichloroacetophenones are also important starting materials for the preparation of \( \alpha \)-keto aldehydes.

Condensation of dichloroacetyl chloride with aromatic hydrocarbons, their halogen derivatives, phenolic ethers and acetanilides.

In condensing toluene with dichloroacetyl chloride, \( p \)-methyl \( w, w \)-dichloroacetophenone (1) is obtained in good yield.

Both ortho-xylene and meta-xylene have smoothly condensed with dichloroacetyl chloride giving \( 3,4 \)-dimethyl \( w, w \)-dichloroacetophenone (2) and \( 2,4 \)-dimethyl \( w, w \)-dichloroacetophenone (3) respectively in quantity.
Para-cymene gives a poor yield of 2-methyl 5-isopropyl \( w, w \)-dichloroacetophenone (4) on being condensed with dichloroacetyl chloride.

Similarly, chlorobenzene and bromobenzene have undergone ready condensation with dichloroacetyl chloride yielding respectively \( p \)-chloro-\( w, w \)-dichloroacetophenone (5) and \( p \)-bromo-\( w, w \)-dichloroacetophenone (6).
The phenolic ethers anisole and ortho-cresol methyl ether were likewise condensed with dichloroacetyl chloride in nitrobenzene solvent leading to the formation of p-methoxy w, w-dichloroacetophenone (7) and 3-methyl 4-methoxy - w,w-dichloroacetophenone (8) respectively.

When dichloroacetyl chloride was condensed with an excess of anisole (and in absence of nitrobenzene), the product was probably a high molecular wt. triketone, sym.tri-\(\alpha\)-chloro - \(\alpha\)-{(p-anisoyl) \(J\) acetyl anisole (9) in good yield.
In condensing meta-chloro toluene with dichloroacetyl chloride, 2-methyl-4-chloro-\(\alpha,\alpha\)-dichloroacetophenone (10) was obtained in good yield.

\[
\begin{array}{c}
\text{Cl} \\
\text{CH}_3 \\
\text{COCHCl}_2 \\
\end{array}
\]

(10)

Both acetamidobenzene and dichlroacetamido benzene condensed with dichloroacetyl chloride in refluxing \(\text{CS}_2\) solvent forming \(p\)-dichloroacetylacetanilide (11) and \(p\)-dichloroacetyl \(\alpha,\alpha\)-dichloroacetanilide (12)

\[
\begin{array}{c}
\text{NHCOCH}_3 \\
\text{COCHCl}_2 \\
\end{array}
\]

(11)

\[
\begin{array}{c}
\text{NHCOCHCl}_2 \\
\text{COCHCl}_2 \\
\end{array}
\]

(12)
EXPERIMENTAL
p-Methyl-\(\text{w, w}^-\) dichloroacetophenone:

Toluene (15.0 g.) was taken in a 250 ml. three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (8.0 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetylchloride (7.3 g.) in toluene (7 g.) was added through the dropping funnel over a period of 2 hours. The stirring was continued for a further period of 4 hours at a temperature of 0°-5°. It was then decomposed with ice and hydrochloric acid and distilled with steam to remove unreacted toluene. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was then dried over anhydrous sodium sulphate. The ether was then removed by distillation and the resulting p-methyl-\(\text{w, w}^-\) dichloroacetophenone (9.6 g.) was distilled under reduced pressure, b.p. 110°/10 mm.

\[\begin{align*}
\text{Found: } & \text{C, 53.45; H, 4.1; } \text{C}_9\text{H}_9\text{OCl}_2 \text{ requires } \\
& \text{C, 53.2; H, 3.94%} \\
\text{I.R. Spectra: } & \text{\(\nu\) (Thin film) 2950, 1680, 1600, 1440, 1400, 1270, 1220, 1200, 1170, 1120, 1040, 995, 840, 795, 745, \text{cm}^{-1}\)} \\
\text{The 2,4-D.I.P. crystallised from alcohol as orange-yellow needles, } & \text{p.p. 186°} \\
\text{Found: } & \text{N, 14.6; } \text{C}_{15}\text{H}_{12}\text{O}_4\text{Cl}_2\text{N}_4 \text{ requires N, 14.62%} 
\end{align*}\]
PLATE - 1

I.R. Spectra of para- methyl - w, w - dichloroacetophenone.
3,4-dimethyl-w, w-dichloroacetophenone:

o-xylene (12 g.) was taken in a 250 ml. three necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (7.8 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetyl chloride (7.3 g.) in o-xylene (6 g.) was added through the dropping funnel over a period of two hours. The stirring was continued for a further period of 4 hours at a temperature of 15°-20°. It was then decomposed with ice and hydrochloric acid. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was dried over anhydrous Na₂SO₄. The solvent was distilled off and the residual liquid was subjected to fractional distillation at reduced pressure when 3,4-dimethyl-w, w-dichloroacetophenone (8.6 g.) distilled out, b.p. 150°-20°/13 mm.

\[
\text{Found: C, 55.44; H, 4.79; C}_{10}\text{H}_{10}\text{OCl}_2 \text{ requires C, 55.29; H, 4.60 %} \]

The 2,4-D.N.P. crystallised from methanol, bright yellow needles, m.p. 181°.

\[
\text{Found: N, 14.32; C}_{16}\text{H}_{14}\text{OCl}_2\text{N}_4 \text{ requires N, 14.10 %} \]
2,4 - dimethyl - w, w-dichloroacetophenone:

m-Xylene (22 g.) was taken in a 250 ml. three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (15 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetyl chloride (14.6 g.) in m-xylene (12 g.) was added through the dropping funnel over a period of 2 hours. After the addition of the dichloroacetyl chloride was over, the reaction mixture was kept at room temperature for 8 hours. It was then decomposed with ice and hydrochloric acid. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was kept over anhydrous sodium sulphate for 24 hours. The solvent was distilled off and the residual liquid was subjected to fractional distillation at reduced pressure when 2,4-dimethyl - w, w-dichloroacetophenone (19.5 g.) distilled out, b.p. 139-144°/10 mm.

Found: C, 55.48; H, 4.78; \( \text{C}_{10}\text{H}_{10}\text{OCl}_2 \) requires C, 55.29; H, 4.60 %

The 2,4 - D.N.P.* crystallised from alcohol as yellow needles, m.p. 175°.

Found: N, 14.32; \( \text{C}_{16}\text{H}_{14}\text{O}_4\text{Cl}_2\text{N}_4 \) requires N, 14.10 %
2-Methyl-5-isopropyl-\(w,w\)-dichloroacetophenone:

A solution of dry \(p\)-cymene (13.4 g.) in 15 ml. nitrobenzene was taken in a 250 ml. three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (15 g.) was added to the solution maintained at \(0^\circ\text{C}-5^\circ\text{C}\). A solution of dichloroacetyl chloride (14.6 g.) in 15 ml. nitrobenzene was added through the dropping funnel over a period of 2 hours. The stirring was continued for a further period of 6 hours at room temperature. It was then decomposed with ice and hydrochloric acid and distilled with steam to remove nitrobenzene. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was then kept over anhydrous sodium sulphate for 24 hours. The ether was then removed by distillation and the resulting 2-methyl-5-isopropyl-\(w,w\)-dichloroacetophenone (6.6 g.) was distilled under reduced pressure, \(\text{b.p.} \ 170-5^\circ\text{C}/10\ \text{mm}\).

\[
\begin{align*}
\text{Found:} & \quad C, \ 58.11\% ; \ H, \ 5.66\% ; \ C_{12}H_{14}OCl_2 \text{ requires} \\
& \quad C, \ 58.77\% ; \ H, \ 5.71\% \\
\end{align*}
\]

The compound did not form 2,4-D.N.P. and oxime derivatives.
Chlorobenzene (20 g.) was taken in a 250 ml. three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (11 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetyl chloride (11.1 g.) in chlorobenzene (7 g.) was added through the dropping funnel over a period of 2 hours. The stirring was continued for a further period of 5 hours at room temperature. It was then decomposed with ice and hydrochloric acid. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was dried over anhydrous sodium sulphate. The solvent was distilled off and the residual liquid was subjected to fractional distillation at reduced pressure when p-chloro-w,w-dichloroacetophenone (12.55 g.) distilled out, b.p. 128°/10 mm. The liquid, on standing, solidified; the solid could be crystallised from alcohol, white crystalline needles, m.p. 66-7°.

Found: C, 42.86; H, 2.35; \( \text{C}_9\text{H}_5\text{OCl}_2 \) requires C, 43.04; H, 2.24 %.

The 2,4-D.N.P. crystallised from alcohol, Vermillion red needles, m.p. above 260°.

Found: N, 14.02; \( \text{C}_{14}\text{H}_9\text{O}_4\text{Cl}_3\text{N}_4 \) requires N, 13.89 %.
**p - Bromo - w, w - dichloroacetophenone :**

Bromobenzene (20 g.) was taken in a 250 ml, three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (10 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetyl chloride (7.3 g.) in bromobenzene (7 g.) was added through the dropping funnel over a period of 2 hours. The stirring was continued for a further period of 4 hours at room temperature. It was then decomposed with ice and hydrochloric acid. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was then kept over anhydrous sodium sulphate for 24 hours. The solvent was distilled off and the residual liquid was subjected to fractional distillation at reduced pressure when p-bromo-w,w-dichloroacetophenone (11.4 g.) distilled out, b.p. 150°/10 mm.

\[
\text{Found: C, } 36.12; \text{ H, } 2.12; \text{ C}_8\text{H}_8\text{OCl}_2\text{Br requires C, } 35.82; \text{ H, } 1.86\%\]

The 2,4-D.N.P. crystallised from alcohol as red needles, m.p. 240° (d)

\[
\text{Found: N, } 12.41; \text{ C}_{14}\text{H}_9\text{OCl}_2\text{BrN}_4 \text{ requires N, } 12.50\%\]
A solution of dry anisole (10.8 g.) in 20 ml. nitrobenzene was taken in a 250 ml. three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (15.0 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetyl chloride (14.6 g.) in 15 ml. nitrobenzene was added through the dropping funnel over a period of 2 hours, the reaction mixture being heated on a steam bath at a temperature of 70°-80° with stirring. The stirring was continued for a further period of 2 hours at room temperature. It was then decomposed with ice and hydrochloric acid and distilled with steam to remove nitrobenzene. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was then kept over anhydrous sodium sulphate for 24 hours. The ether was then removed by distillation and the resulting p-methoxy- w, w-dichloroacetophenone (12.05 g.) was distilled under reduced pressure, b.p. 160-5°/10 mm.

The yellow viscous liquid, on standing, solidified. The solid could be crystallised from alcohol, white shining needles, m.p. 82-3°.

Kunckell et al. Kunckell, F. and F. Johannssen, Ber., 31, 169 (1898) reported m.p. 76-7°.
The above experiment was carried out in a similar way in the absence of nitrobenzene, using excess anisole and AlCl₃ (25.0 g.). Dichloroacetyl chloride (14.6 g.) was added over a period of 2 hours at room temperature. The stirring was continued for a further period of 4 hours at room temperature. It was then decomposed with ice and hydrochloric acid when a semi-solid mass was isolated. This was then crystallised from alcohol, white shining needles, m.p. 115°. The compound did not form any derivative of the carbonyl function and did not undergo hydrolysis with aqueous alkali (10% NaOH or 15% Na₂CO₃). Molecular weight determination (Rast's) revealed that it was a high mol. wt. Compound (625-675):

Found: C, 62.4; H, 4.6; C₃₄H₂₉.7Cl₃ requires C, 62.29; H, 4.43 %.

I.R. Spectra: \( \gamma_{\text{max}} \) (nujol) 2885, 1600, 1500, 1460, 1370, 1300, 1250, 1170, 1030, 965, 855, 830, 810 cm⁻¹.
PLATE - 2

I.R. Spectra of abnormal chloroketone of anisole
3-Methyl-4-methoxy-\(\mathbf{w},\mathbf{w}\)-dichloroacetophenone

A solution of dry \(\alpha\)-cresol-methylether (6.1 g.) in 15 ml. nitrobenzene was taken in a 250 ml. three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium chloride (8.0 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetyl chloride (7.3 g.) in 10 ml. nitrobenzene was added through the dropping funnel over a period of 2 hours. The stirring was continued for a further period of 4 hours at room temperature. It was then decomposed with ice and hydrochloric acid and distilled with steam to remove nitrobenzene. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was then kept over anhydrous sodium sulphate for 24 hours. The ether was then removed by distillation and the resulting 3-methyl-4-methoxy-\(\mathbf{w},\mathbf{w}\)-dichloroacetophenone (6.0 g.) was distilled under reduced pressure, b.p. 145°-50°/10 mm.

The yellow liquid, on standing, solidified. The solid could be crystallised from alcohol, white shining needles, m.p. 83-4°.

\[
\text{Found: C, 51.72; H, 4.61; C}_{10}\text{H}_{1002}\text{Cl}_2 \text{ requires C, 51.50; H, 4.29%}
\]

The 2,4 - D.N.P. crystallised from alcohol, m.p. above 230°.

\[
\text{Found: N, 13.62; C}_{16}\text{H}_{1405}\text{Cl}_2\text{N}_4 \text{ requires N, 13.55%}
\]
4-Chloro-2-methyl-\(w, w\)-dichloroacetophenone:

\(m\)-Chlorotoluene (16.0 g.) was taken in a 250 ml. three-necked flask fitted with a mechanical stirrer, a dropping funnel and a gas outlet tube. Aluminium Chloride (8.0 g.) was added to the solution maintained at 0°-5°. A solution of dichloroacetyl chloride (7.3 g.) in \(m\)-chlorotoluene (5 g.) was added through the dropping funnel over a period of 2 hours. After the addition of the dichloroacetyl chloride was over, the reaction mixture was kept at room temperature for 16 hours. It was then decomposed with ice and hydrochloric acid. The reaction mixture was then extracted with ether and washed free from acid with water. The ether extract was kept over anhydrous sodium sulphate for 24 hours. The solvent was distilled off and the residual liquid was subjected to fractional distillation at reduced pressure when 4-chloro-2-methyl-\(w, w\)-dichloroacetophenone (10.2 g.) distilled out, b.p. 141-45°/10 mm.

The above reaction did not take place when nitrobenzene was used as solvent (at room temperature).

\[\text{Found: C, 45.89; H, 3.15; C}_9\text{H}_7\text{OCl}_3 \text{ requires C, 45.57; H, 2.95%}\]

The 2,4-\(D.N.P\). crystallised from alcohol as Orange-Yellow needles, m.p. 159°-60°

\[\text{Found: N, 13.62; C}_{15}\text{H}_{11}\text{O}_4\text{Cl}_3\text{N}_4 \text{ requires N, 13.42%}\]
**p - Dichloroacetyl acetanilide:**

In a 250 ml. three necked flask mounted on a steam bath and equipped with a mechanical stirrer and a spiral condenser, was placed 35 g. of carbon disulphide. Through the open neck of the flask 5 g. of acetanilide and 10 g. of dichloroacetyl chloride were introduced. The mixture was vigorously stirred while 15 g. aluminium chloride was added portionwise over a period of 20-30 minutes; the neck of the flask stoppered between additions. After the addition of the last portion of aluminium chloride, the mixture was heated at reflux temperature for 30 minutes while stirring was continued. Heating and stirring was discontinued and the mixture was allowed to stand for 3 hours when it separated into layers. The upper layer of CS₂ was decanted and the lower layer was decomposed with crushed ice and hydrochloric acid. The precipitated solids were collected by filtration, washed well with water and crystallised from alcohol; the p-dichloroacetyl-acetanilide (6.3 g.) was obtained as fine white crystals, m.p. 160°-1°.

\[ \text{Found: C, 48.60; H, 3.44; } C_{10}H_9O_2Cl_2N \text{ requires C, 48.78; H, 3.65%} \]

The 2,4 - D.N.P. crystallised from alcohol as deep yellow needles, m.p. above 260° (d).

\[ \text{Found: N, 16.59; } C_{16}H_{13}O_6Cl_2N_5 \text{ requires N, 16.43%} \]
p-Dichloroacetyl-oc^®-dichloroacetanilide.

In a 250 ml. three-necked flask mounted on a steam bath and equipped with a mechanical stirrer and a spiral condenser, was placed 30 g. of carbon disulphide. Through the open neck of the flask 5 g. of dichloroacetamidobenzene and 6 g. of dichloroacetyl chloride were introduced. The mixture was vigorously stirred while 10 g. of aluminium chloride was added portionwise over a period of 20-30 minutes; the neck of the flask stoppered between additions. After the addition of the last portion of aluminium chloride, the mixture was heated at reflux temperature for 30 minutes while stirring was continued. Heating and stirring was discontinued and the mixture was allowed to stand for 3 hours when it separated into layers. The upper layer of CS₂ was decanted and the lower layer was decomposed with crushed ice and hydrochloric acid. The precipitated solids were collected by filtration, washed well with water and crystallised from alcohol; the p-dichloroacetyl-oc^®-dichloroacetanilide (5. 5 g.) was obtained as fine white crystals, m.p. 115°-16°.

| Found: C, 37.91; H, 4.65; C₁₀H₇O₂Cl₂N requires C, 38.09; H, 4.44% |
The 2,4-D.N.P. crystallised from alcohol as brick red needles, m.p. above 250° (d)

Found: N, 14.32; C_{16}H_{11}OCl_{4}N_{5} requires
N, 14.14%