IPSO AROMATIC
SUBSTITUTION

A thesis

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of

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ABSTRACT

In the first part of this thesis the conformation and stereochemistry of a number of polychlorocyclohex-3-enones, formed by the reaction of chlorine in acetic acid and hydrochloric acid with polysubstituted phenols (or anilines), are discussed. Those polychlorocyclohex-3-enones with the H(Cl)C5 or the Me(Cl)C5 structural features were shown to exist in a twist-boat conformation with the C5-Cl bond in the flagpole orientation. In contrast, two polychlorocyclohex-3-enones with *gem*-dichloro substituents at C5, were shown to be conformationally mobile in solution. The alicyclic ring of two 4,4,5-trichlorocyclohex-2-enones were also shown to exist in twist-boat conformations, but with the C5-Cl bond in the equatorial orientation. A satisfactory correlation between the ^1H n.m.r. and infrared spectroscopic data and the known structures in the solid state indicates that these polychlorocyclohex-3-enones and polychlorocyclohex-2-enones adopt conformations in solution close to those observed in the solid state.

Extensive use of single-crystal X-ray structure analysis was made in the above structural studies; some thirteen structure analyses are reported in this thesis.

In the second part of this thesis are discussed the reactions of polysubstituted 2-methylphenols with chlorine in carbon tetrachloride in the presence of pyridine to give 6-chloro-6-methylcyclohexa-2,4-dienones. These 6-chloro-6-methylcyclohexa-2,4-dienones arise from *ipso* chlorine attack on the phenol *ortho* to the hydroxy function. It was shown that attack *ipso* to a methyl group occurred in preference to attack *ipso* to a chlorine atom. Where both *ortho* positions of the phenolic substrate are methyl substituted, the site of *ipso* chlorine attack is affected by the *meta* substituents.

In the third part of this thesis the additions of chlorine to 6-chloro-6-methylcyclohexa-2,4-dienones to give polychlorocyclohex-3-enones and polychlorocyclohex-2-enones are discussed. These addition reactions proceed by three distinct reaction mechanisms, 2,3-, 4,5- and 2,5-chlorine addition. The 2,3-chlorine addition reaction was shown to be powerfully acid-catalysed. In contrast, the 4,5- and 2,5-chlorine additions were shown to be only mildly acid-catalysed. Reaction mechanisms which accommodate these observations are discussed.

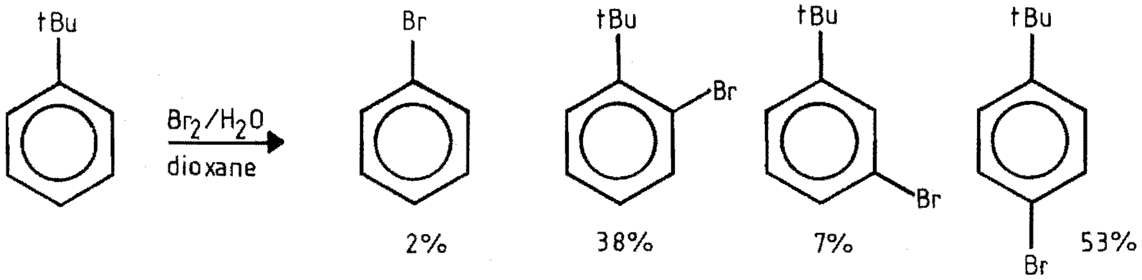
Finally, the formation of an acyclic pentachloro hex-3-enoic acid by the chlorination of 4-chloro-2-methyl-6-nitrophenol (130) in acetic acid and hydrochloric acid is described and a probable mode of formation suggested.

CHAPTER 1

GENERAL INTRODUCTION

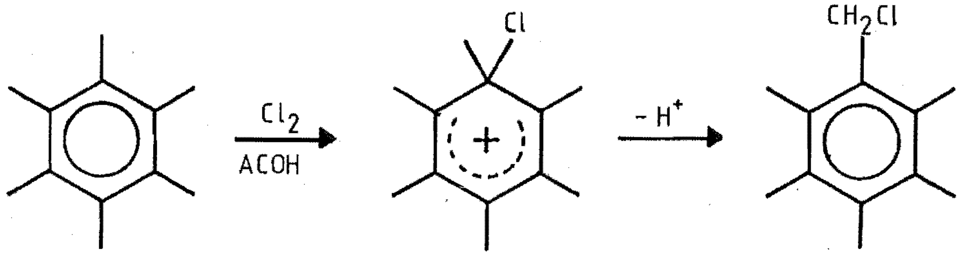
1.1 Electrophilic Aromatic Halogenation

Conventional electrophilic substitution reactions of aromatic compounds involving the halogens F, Cl, Br, I are now generally well understood and a number of good reviews have been written on this topic.[1,2,3,4] Less well understood are reactions, often observed alongside electrophilic substitution reactions, in which the product is unexpected in terms of conventional substitution. Many such reactions, previously termed anomalous or non-conventional, have been reported. For instance, the bromination of *t*-butylbenzene yields bromobenzene in addition to the expected products; *ortho-*, *meta-* and *para-* bromo-t-butylbenzene.[5]



It is probable that the bromobenzene is formed by electrophilic attack of bromine on the carbon bearing the *t*-butyl group, followed by loss of the comparatively stable *t*-butyl carbocation.

Other non-conventional reactions, such as side-chain modification have been reported. For instance, the chlorination of hexamethylbenzene has been shown to give the side-chain chlorinated chloromethylpentamethyl benzene as the product.[6]

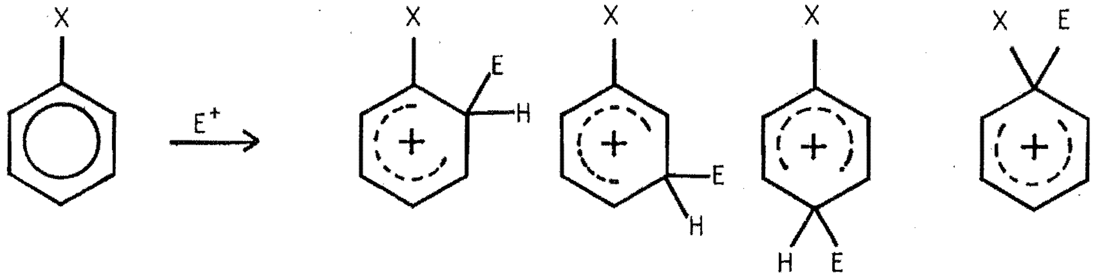


The initial step in this reaction is attributable to electrophilic attack of chlorine at a carbon bearing a methyl group.

The term *ipso* was introduced by Perrin and Skinner[7] to denote attack by a reagent at a substituted nuclear position. Subsequently many of the previously observed, anomalous or non-conventional reactions could be described in terms of the consequences of *ipso* aromatic attack.

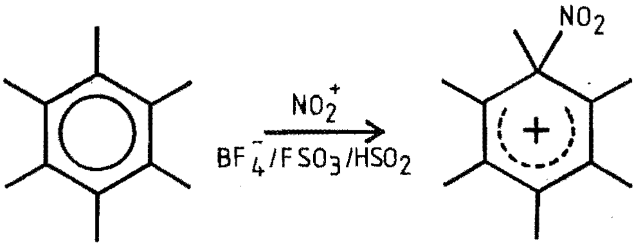
1.2 Consequences of *Ipso*-Attack

The Wheland intermediates (*W's*) from a mono-substituted benzene are of two kinds, those (W_o, W_p, W_m) in which the electrophile is attached to an unsubstituted position, and that W_i^X in which it is attached to the position at which the substituent X is attached.

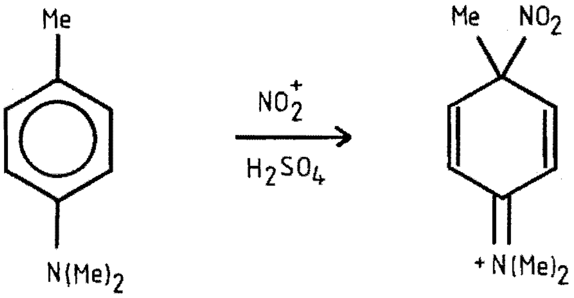


W_i^X

Observation of the intermediates W_o, W_m, W_p is rare since generally the chemistry associated with these forms is simple, rapid proton loss. However, direct observation of W_i^X has proved possible under exceptional circumstances. For instance, the reaction between hexamethylbenzene and NO_2^+, under conditions in which bases and nucleophiles are absent, has been shown to give the W_i^{Me} below, by ^{13}C n.m.r.[8]



Other stable W_i^X's are obtained when a stabilising group is situated *para* to the position of *ipso* attack. For instance the reaction of N,N-dimethyltoluidine with NO_2^+ gives the stabilised W_i^{Me} below.[9]

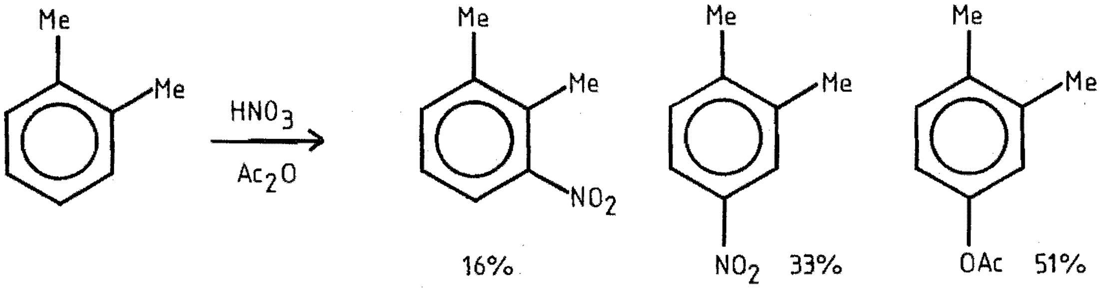


The W_i^X can undergo a variety of reactions, for example, return to reactants, migration of the *ipso* group, side-chain modification, capture of a nucleophile or *ipso* substitution. These reactions are considered in the next section.

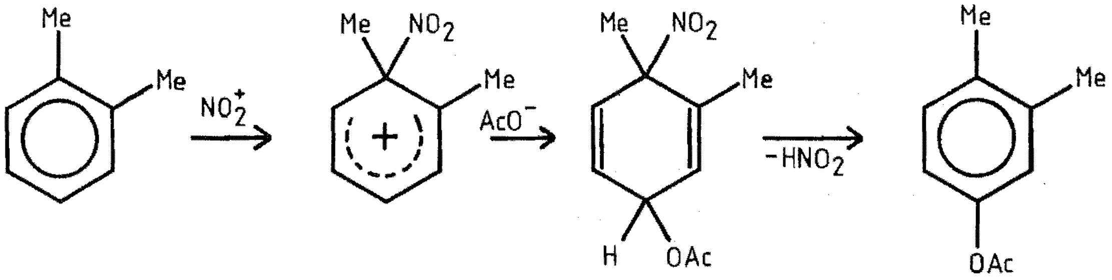
1.3 Reactions of the Wheland Intermediates

(a) Nucleophilic Capture of W_i^X

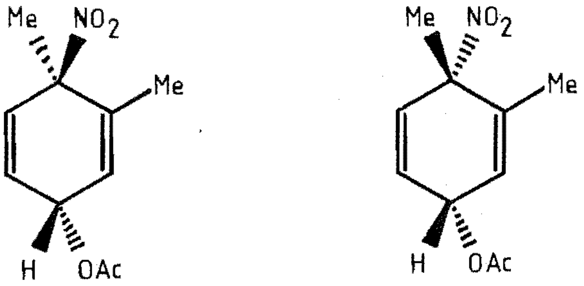
The Wheland intermediate, with its cationic character, is susceptible to nucleophilic attack. Many examples have been reported in the field of electrophilic nitration of aromatic compounds. One in particular, the nitration of *o*-xylene in acetic anhydride, was important in attracting attention to *ipso* attack in nitration.[10]



The major product was found to be the acetoxy-*o*-xylene (51%) along with the expected nitro-*o*-xylenes. Further studies carried out on a number of methyl benzenes showed that the ratio of nitration to acetoxylation was dependent upon the nature of the substrate but independent of its concentration.[10,11] It was suggested that the mechanism involved capture of the W_i^{Me} by acetate followed by elimination of nitrous acid to give the aryl acetate product.

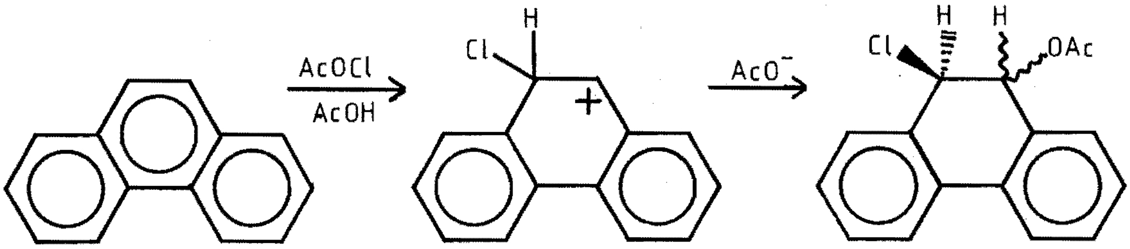


This mechanism was confirmed by the isolation of the stereoisomeric adducts,



formed during the nitration of *o*-xylene.[10,11] Similar products were obtained for a large number of aromatic substrates, mainly by Fischer and co-workers.[12]

Another example, the chlorination of phenanthrene by chlorine acetate in acetic acid, while not involving *ipso* attack as such, does illustrate the nucleophilic capture of the Wheland intermediate formed from electrophilic halogen attack.[13]

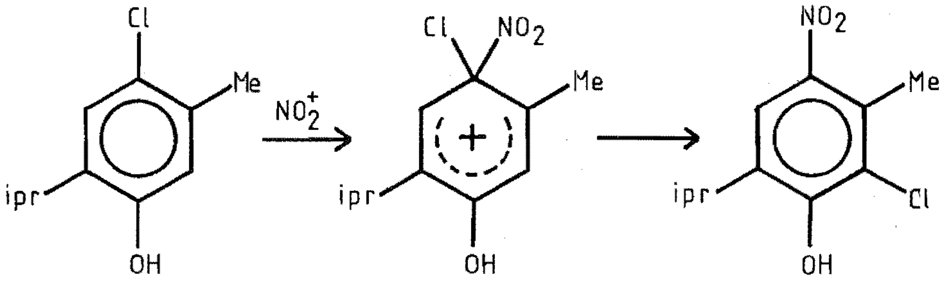


The reaction of phenanthrene with chlorine acetate gave the *cis*- 9-chloro-10-acetoxyphenanthrene (30%), *trans*-9-chloro-10-acetoxyphenanthrene (30%) and the substitution product, 9-chlorophenanthrene (40%). The product ratios are unaffected by added sodium acetate.

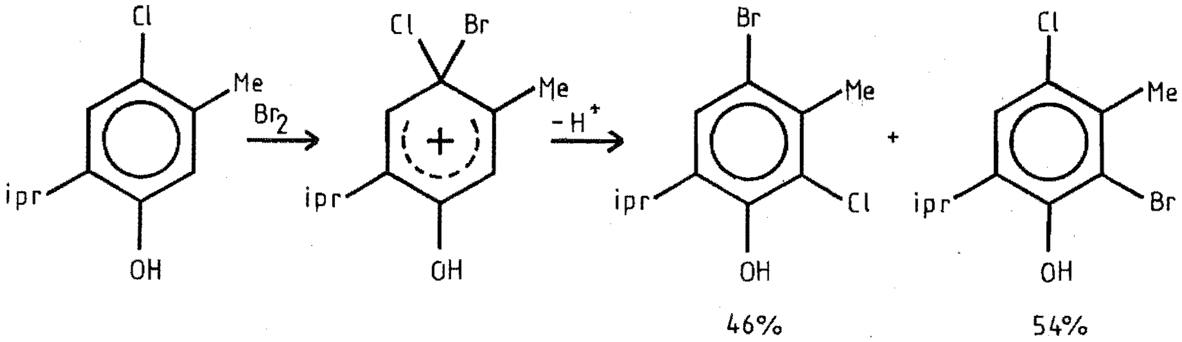
Since the *cis* and *trans* isomers are formed in equal quantities and the reaction is unaffected by added nucleophile, it seems reasonable to suggest that the carbocationic Wheland intermediate is formed directly from Cl^+ attack and subsequently reacts indiscriminately with solvent to give *cis* or *trans* products.

(b) Migration of an *Ipso* Group

The Wheland intermediate W_i^X can formally rearrange in two ways, by migration of the substituent X or by migration of the electrophile. Examples of the former, where any distinction can be made, are rarely observed. One example, the nitration of 6-chlorothymol, was shown to give the product arising from the formation of the W_i^{Cl} followed by 1,3 migration of the chlorine atom.

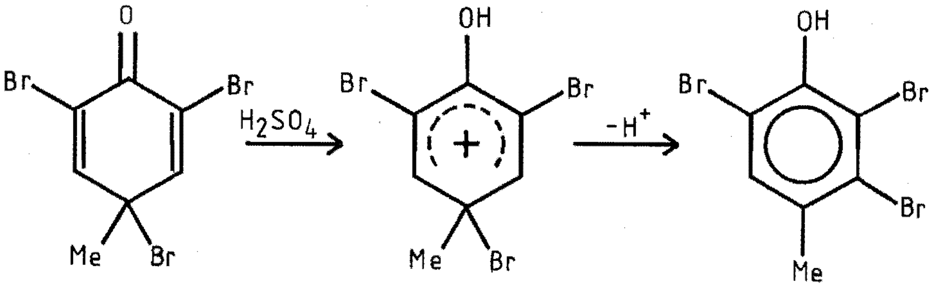


Bromination of 6-chlorothymol gave a 46% yield of the product arising from 1,3 chlorine migration from the W_i^{Cl}.[14]



It is unlikely that the 2-bromo-6-chlorothymol (54%) is formed totally from migration of bromine from the W_i^{Cl} (since chlorination of 6-bromothymol shows only 17% of the product of bromine migration from the W_i^{Br},[14]) and is probably mainly formed by direct bromination at the activated position *ortho* to the OH function.

Migration of the electrophile is more commonly reported, especially in nitration studies. Examples in halogenation are less common but have been reported for the rearrangement of dienones formed by *ipso* attack on phenol derivatives. For instance, the rearrangement of the bromo dienone below in sulphuric acid has been shown to give the tribromo phenol in nearly quantitative yield.[15]



The reaction is strongly acid-catalysed and is thought to proceed through the W_i^{Me} intermediate.

There are three distinct mechanisms for migration, (i) intramolecular, (ii) extramolecular and (iii) intermolecular. Intramolecular migration is characterised in that the migrating group never becomes sufficiently free of the carbon structure to do other than move to a position adjacent to the *ipso* position *i.e.* a(1,2 migration).

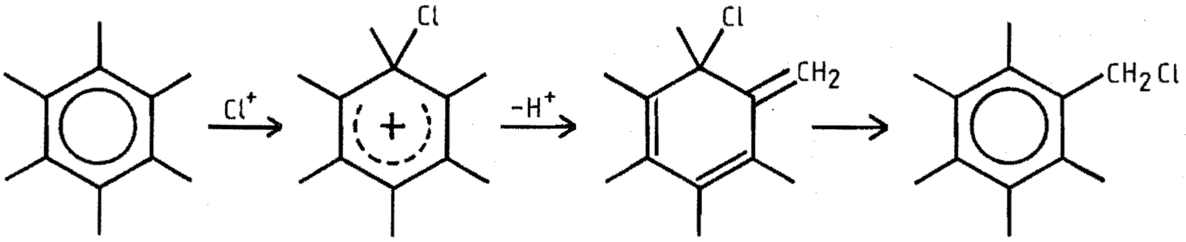
Extramolecular migration differs from intramolecular migration in that the migrating group becomes free enough to be able to distinguish and select amongst the positions in the carbon structure, but does not leave the "encounter-pair".

In intermolecular migration the *ipso* group leaves the carbon-structure and diffuses into the solvent, it may then react with carbon structures other than the one it left.

The mode of migration depends largely upon the rate of formation of the W_i^X which, if it proceeds at the encounter rate favours extramolecular migration or, if it proceeds slower than the encounter rate, intermolecular migration is dominant.

(c) Substituent Modification

The driving force behind the reaction of a W_i^X is often the collapse back to aromaticity. Modification of the substituent by the *ipso* attacking species is one way of achieving this. For example, the reaction of hexamethylbenzene with chlorine in acetic acid gives predominantly the chloromethylpentamethylbenzene as product.[6]

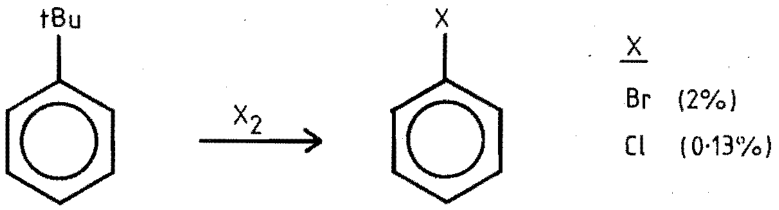


Illuminati and co-workers have shown that the reaction exhibits first-order kinetics in both substrate and molecular chlorine and is electrophilic in character. While it is reasonable to suggest that the W_i^{Me} is the intermediate initially formed the precise mechanism of the formation of the chloromethyl compound is not known. It is possible that the rearrangement proceeds by loss of H^+ from a methyl group adjacent to the *ipso* site, followed by migration of the *ipso* chlorine to the reactive methylene carbon.

An alternative mechanism suggested was the formation of a cyclic transition state, from the W_i^{Me} involving the *ipso* chlorine atom and a neighbouring methyl carbon atom, followed by loss of H^+ and rearrangement to the chloromethyl compound.

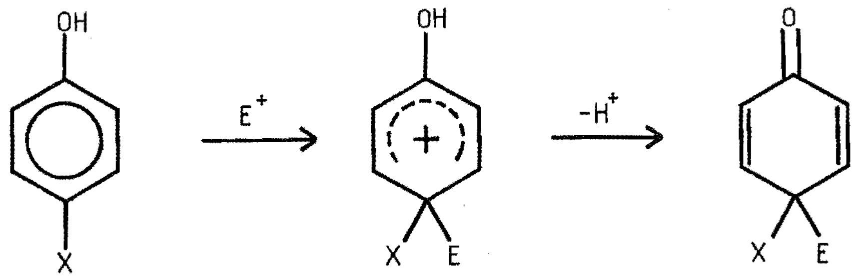
(d) *Ipso* Substitution

Bromination and chlorination of *t*-butylbenzene have both been shown to give products arising from *ipso* substitution along with the expected *ortho*, *meta* and *para* electrophilic substitution products.[5,17] A partial rate factor of 1 has been derived for the chloro-de-*t*-butylation of *t*-butylbenzene in 99% aqueous acetic acid, and for the bromination of *t*-butylbenzene with hydrobromous acid in 50% aqueous dioxane a partial rate factor of 1.4 can be deduced for the bromo-de-*t*-butylation reaction. The replacement of *t*-butyl occurs therefore at approximately the same rate as the replacement of a hydrogen in benzene. *Ipso*-substitution can become the predominant reaction under favourable conditions. For example, the bromination of 1,3,5-tri-*t*-butylbenzene gives 71% of the product of *ipso* substitutions - 3,5-dibromo-1-*t*-butylbenzene. In this case it was proposed that the *t*-butyl groups provided steric hindrance to the ring positions bearing hydrogen.



There are many other examples of *ipso* halogen substitution where the *ipso* substituent is $B(OH)_2$, SiR_3, CHO, COOH, or *t*-alkyl.[18]

Of more importance, at least to this present work, is the consideration of the consequences of *ipso* attack when the substrate is a substituted phenol. It has long been known that one of the direct consequences of *ipso* attack is the loss of the phenolic proton to give a cyclic ketone.



Many of these dienones arising from *ipso* halogen attack have been prepared and a few stable examples isolated. This substitution reaction has been designated a SE_2' reaction mechanism since it exhibits bimolecular kinetics and is electrophilic in character. The prime indicates that some rearrangement of the double bonds has occurred.

Substituted aromatics bearing OAc, OR or NH_2 substituents have also been shown to undergo *ipso*-substitution reactions to give cyclohexadienones.

1.4 The Chlorination of Polysubstituted Phenols with Chlorine

The chlorination of pentachlorophenol has been shown to give, as products of *ipso* chlorine attack, the 2,4-dienone (1) and the 2,5-dienone (2)[19] (refer Block A)*. Formation of the 2,4-dienone (1) is favoured in non-polar solvents and good yields are obtained if pyridine or some other compound is present, which is able to remove hydrogen chloride. Formation

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* (Block A as fold-out at end of General Introduction)

of the thermodynamically more stable 2,5-dienone (2) occurs when the 2,4-dienone (1) is treated with iodine, or when the chlorination is carried out in the presence of iodine or some catalyst such as aluminium trichloride.

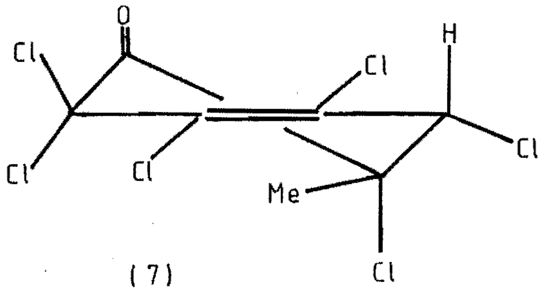
In acetic acid, and with excess chlorine, the reaction proceeds through to the octachlorocyclohex-3-enone (3) and the octachlorocyclohex-2-enone (4). It was proposed that the cyclohex-3-enone (3) was formed by capture of the 2,4-dienone (1) by further 2,5-addition of chlorine and that the cyclohex-2-enone (4) was formed by 1,2-addition to the 2,5-dienone (2).[19] However, it should be noted that the cyclohex-2-enone (4) could also be formed by 4,5 addition to the 2,4-dienone (1).

As the 2,4-dienone (1) is formed more rapidly than the thermodynamically stable 2,5-dienone and since pentachlorophenol is almost as strong an acid as acetic acid, it has been suggested that the substrate attacked by the electrophile is the phenoxide ion; such a phenoxide ion is more strongly *ortho* directing than the corresponding phenol.[20] However, no kinetic investigations are reported which resolve this question.

In 1969, Morita and Dietrich reported the chlorination of a number of *ortho* and *meta* cresols (and toluidines) to give polychlorocylohexenones.[21] Also prepared were a number of cyclohexa-2,4-dienones from the chlorination of polysubstituted phenols in carbon tetrachloride in the presence of pyridine. It was proposed, although not proved by experiment, that the 2,4-dienones were the intermediate species formed during the exhaustive chlorination of polysubstituted phenols to give the polychlorocyclohexenones.

For example, the chlorination of 3-chloro-6-methylaniline (6) (refer Block A) was reported to give the two hexachlorocyclohex-3-enones (7) and (8). The reaction was proposed to proceed first, by electrophilic substitution at the *ortho* and *para* vacant ring positions (Scheme 1), then chlorination *ipso* to the C6-methyl group to give the 2,4-dienone (9). Subsequent 2,5-addition of Cl_2 would then give the observed hexachlorocyclohex-3-enones (7) and (8). The 2,4-dienone (9) was prepared in admixture with another compound (*c.* 3:1), but was not isolated in a pure state. No attempt to prepare the hexachlorocyclohex-3-enones (7) and (8) by further chlorine addition to the dienone was reported.

The structures of these polychlorocyclohex-3-enones were assigned on the basis of u.v., infrared and ^1H n.m.r. spectroscopic data. It was assumed that the conformation of the cyclohex-3-enone ring structure was a modified half-chair.



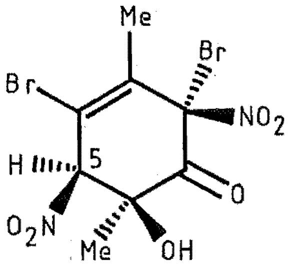
(7)

It was also assumed that the C5-hydrogen was in the *pseudoaxial* position and that the C5-Cl bond was therefore *pseudoequatorial*. Compound (7) was then assigned the *cis* stereochemistry and compound (8) the *trans* stereochemistry.

While, on first inspection, these stereochemical assignments appeared reasonable, consideration of the spectroscopic data for a series of polychlorocyclohex-3-enones formed by the exhaustive chlorination of 2,4-dichloro-6-methylphenol (10), 2,3-dimethylaniline (13)[22] and 3-chloro-2-methylaniline (16)[21] showed a number of inconsistencies between the stereochemical assignments and spectroscopic data (refer Block B). For example, the observed ^1H n.m.r. chemical shifts for the C2-methyl protons in (14) (δ 1.89) and (15) (δ 2.06) are apparently reversed from the observed methyl shifts for (11) (δ 2.07) and (12) (δ 1.89) and for (17) (δ 2.17) and (18) (δ 2.01), for the same variation in stereochemistry. On the assumed basis that the cyclohex-3-enone ring structure is in the same conformation in each case, it might be expected that a consistent pattern of ^1H n.m.r. methyl shifts would be found.

Also of concern was the apparent reversal in trend for the infrared carbonyl stretching frequencies observed for the compound pairs (14) (ν 1752) and (15) (ν 1770) and compounds (17) (ν 1758) and (18) (ν 1768) for the stereochemical reassignment for (14) and (15) on the basis of the ^1H n.m.r. methyl proton chemical shifts. This disparity could not be resolved by comparison with (11) and (12) since the infrared data recorded was for a (*c.* 1:1) mixture of the two isomers.

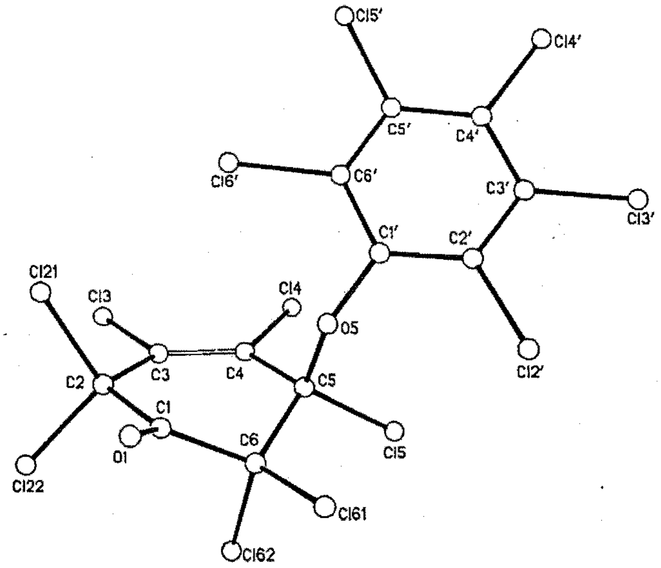
Finally, the assumption made in the stereochemical assignments by Morita and Dietrich that the cyclohex-3-enone ring structure was in a modified half-chair conformation with the C5-H bond pseudoaxial also seemed questionable. This concern rested upon firstly, the known ring conformation of the 5-nitrocyclohex-3-enone (19) (skew-boat) with the C5-NO_2 bond pseudoaxial![23]



(19)

It was appreciated from the outset that the analogy between the polychlorocyclohex-3-enones and the 5-nitrocyclohex-3-enone (19) was somewhat distant, particularly because intramolecular hydroxy-carbonyl hydrogen bonding was probably present in the nitro ketone (19). Nonetheless, it remained conceivable that the C5-Cl bond in the polychlorocyclohex-3-enones adopted the pseudoaxial position also.

Secondly, and perhaps more compelling, was the reported single-crystal X-ray structure of a hexachloro-5-pentachlorophenoxycyclohex-3-enone (20), formed as a by-product in the technical production of pentachlorophenol.[24]



The cyclohex-3-enone ring is in a twist-boat conformation as shown by the appropriate torsion angles C(6)-C(5)-C(4)-C(3) (-26.2°)* and C(4)-C(3)-C(2)-C(1) (6.9°).* That the bulky pentachlorophenoxy group is *pseudoaxial* is shown by the torsion angle C(3)-C(4)-C(5)-O(5) (88.4°).

In all these structures 1,3-diaxial non-bonded interactions between pseudoaxial C5-substituents and substituents at C3 and C1 (both sp^2 carbons) are absent.

Since elucidation of the mechanism of the formation of these polychlorocyclohex-3-enones was the prime objective of this present work, the stereochemistry of the compounds was of considerable importance because the stereochemistry of these and related compounds might yield information about the chlorination process. Because we were not convinced of the total accuracy of the available data, it was considered that a reinvestigation of these polychlorocyclohex-3-enones, with full characterisation and determination of their stereochemistry, was warranted. In particular, we sought a clear relationship between the observed spectroscopic properties and the stereochemistry of *any* polychlorocyclohex-3-enone.

The method adopted was one of preparation, isolation of the compounds (by a variety of chromatographic techniques), spectroscopic characterisation, identification and use of single crystal X-ray analysis as an *a priori* method of determining the stereochemistry of selected key compounds.

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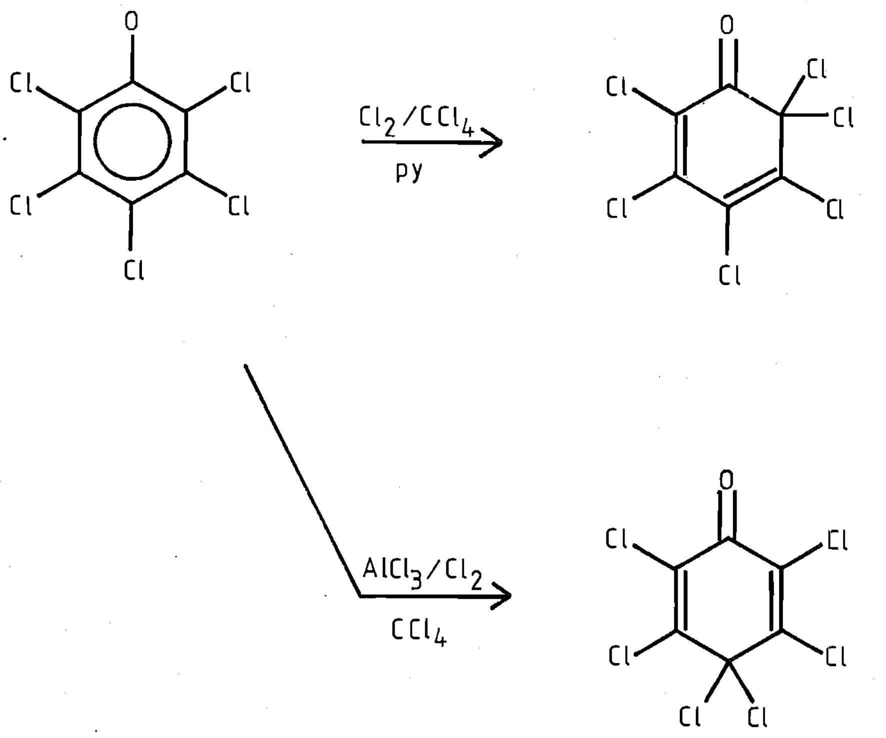
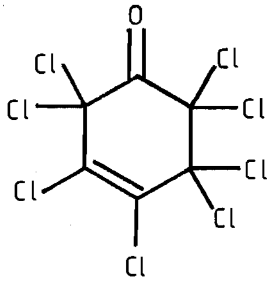
* (For the enantiomer of the compound structure determined)

BLOCK A



(1)

(2)



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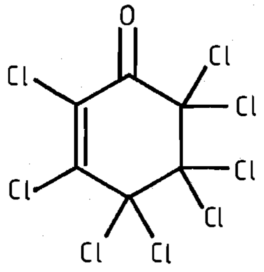

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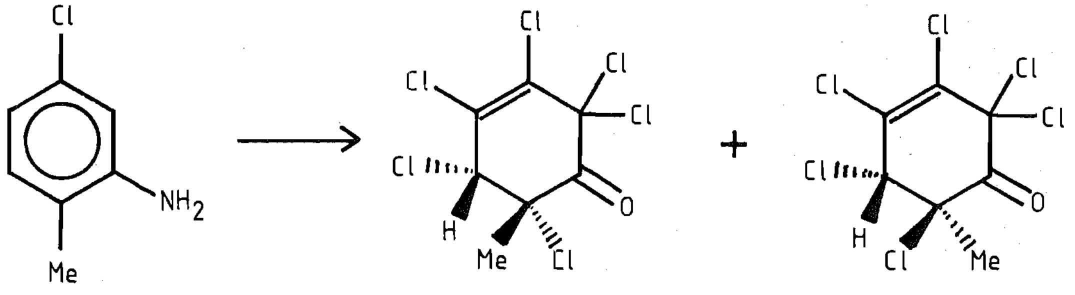
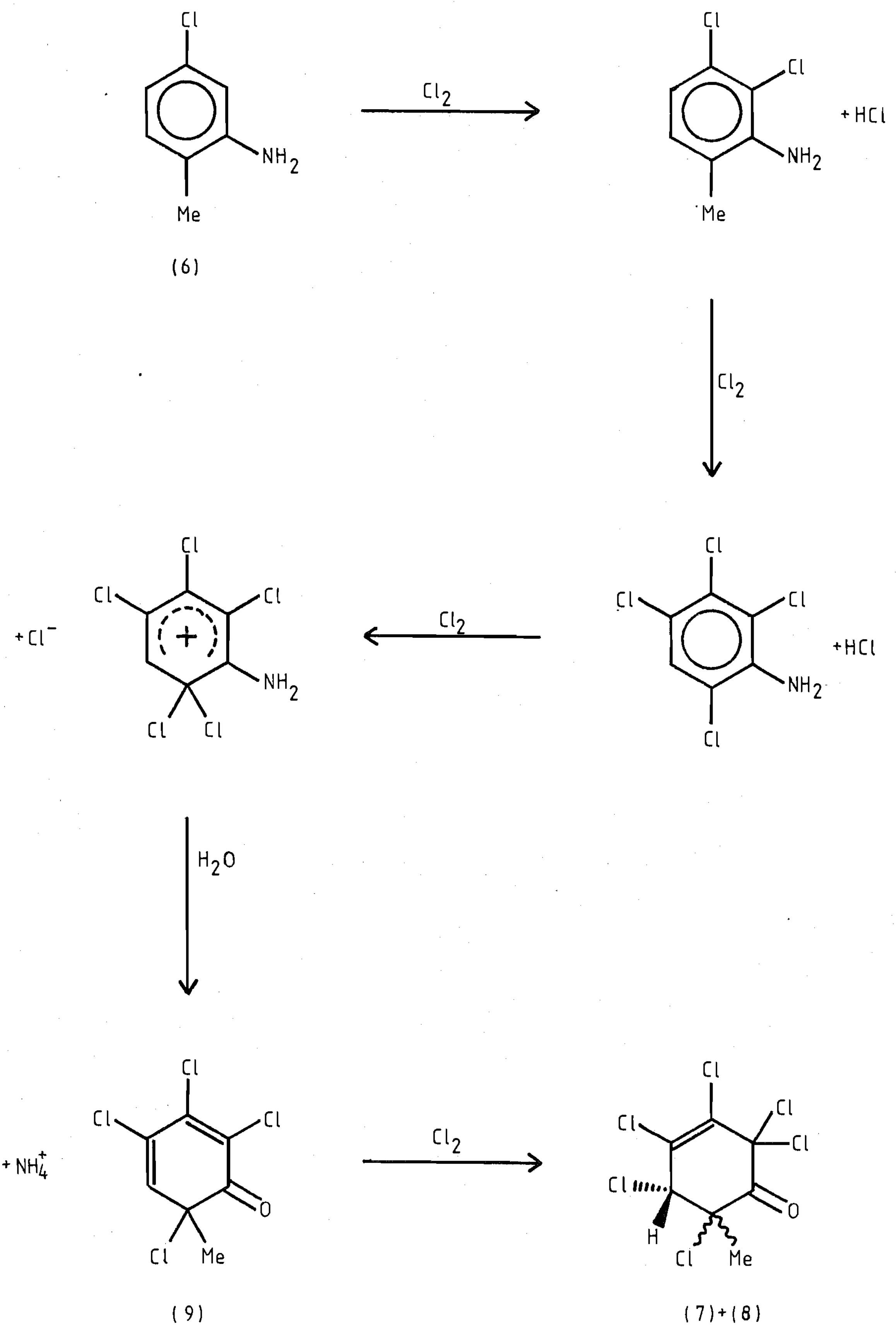


(6)

(7)

(8)

SCHEME 1


Cl
NH2
Me
(6)
Cl2
Cl
Cl
+HCl
NH2
Me
Cl2
+Cl⁻
Cl
Cl
Cl
NH2
Cl
Cl
Cl2
Cl
Cl
Cl
+HCl
NH2
Cl
H2O
+NH4+
Cl
Cl
Cl
O
Cl
Me
(9)
Cl2
Cl
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Cl
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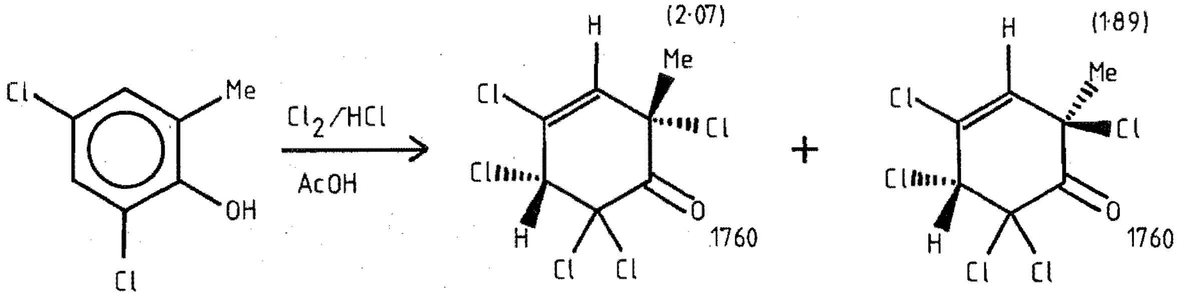
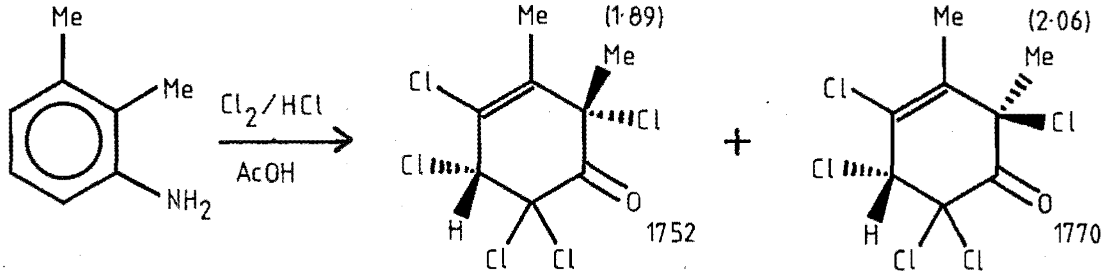
Cl
Me
(7)+(8)

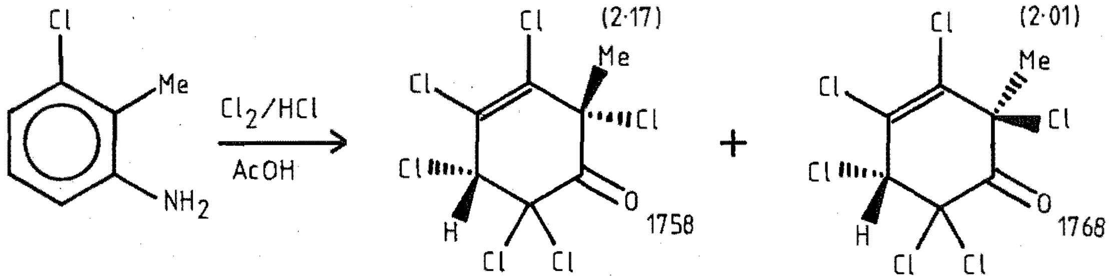
BLOCK B



(10) (11) (12)



(13) (14) (15)



(16) (17) (18)

CHAPTER TWO

Chlorination of Phenols and Anilines in Acetic Acid and Hydrochloric Acid: A Structural Study

Introduction

The chlorination of all the phenols and anilines were carried out under the same reaction conditions. The phenol (or aniline) was dissolved as a 10% solution in glacial acetic acid and concentrated hydrochloric acid 5% v/v. Chlorine gas was then bubbled slowly through the stirred solution until the reaction was complete. Reactions were carried out at 20°, the reaction mixture being cooled when necessary to maintain this reaction temperature. All reactions were carried out in the dark to eliminate free-radical side-chain chlorination. For detailed reaction conditions refer to the experimental section relating to Chapter 2.

The following chlorination reactions are discussed in sections. Each section contains a group of polychlorocyclohex-3-enones, which have some structural feature(s) in common.

2.1 Chlorination of 3-Chloro-6-methylaniline and 2,5-Dimethylaniline

2.1.1 Chlorination of 3-Chloro-6-methylaniline (21)

Chlorination of (21), as above, followed by crystallization of the crude product from pentane gave a mixture (*c.* 1:1) of the hexachlorocyclohex-3-enones (22) and (23) (refer Block C)*. Separation was achieved on a

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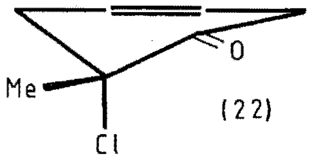
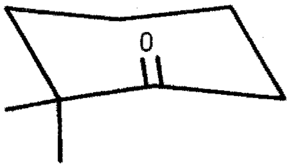
* (As fold-outs at the end of the experimental section).

Chromatotron* equipped with a silica gel plate. First eluted was the *trans* isomer (22), $C_7H_4Cl_6O$, m.p. 109.5-110.5°, the structure of which was established by single-crystal X-ray analysis. A perspective drawing of this structure (22) is presented in Figure 1 and the corresponding atomic co-ordinates are given in Table 1[#].

In the crystalline state, structure (22) exists with its cyclohex-3-enone ring structure in a twist-boat conformation as shown by the relevant torsion angles C(3)-C(4)-C(5)-C(6) -29.0(5)° and C(1)-C(2)-C(3)-C(4) 9.6(5)°. Previously, it had been assumed that the ring conformation was a modified half-chair.[22] The C5-Cl bond is in the flagpole orientation, C(3)-C(4)-C(5)-Cl(5) 90.5(4)°, notably different from the previously assumed orientation.[22] The C6-Cl and C6-Me bond orientations, with respect to the carbonyl function, are closely similar to the α-axial and α-equatorial bond orientations in a cyclohexanone in the chair conformation, as shown by the torsion angles



(22)



O(1)-C(1)-C(6)-Cl(6) -107.5(4)° and O(1)-C(1)-C(6)-C(7) 12.2(5)° respectively. This structural feature is reflected in the infrared carbonyl stretching frequencies of these compounds. It is known that an equatorial chlorine atom of an α-chlorocyclohexanone will shift the infrared carbonyl stretching frequency by approximately 20 cm^{-1} to higher wave

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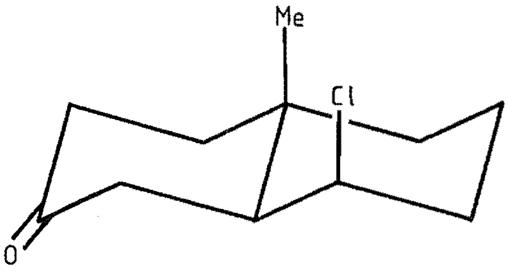
* (Refer to experimental section; Apparatus, Materials and Instrumentation)

\# (Refer to experimental X-ray section, Appendix 1) number,[25,26] due to increased dipole-dipole interaction of the equatorial chlorine with the carbonyl function. An axial chlorine atom however, has little or no effect upon the carbonyl stretching frequency.

In contrast, and as a consequence of the cyclohex-3-enone ring conformation, the magnitude of the torsion angles between the C2-substituents and the carbonyl functional group are much more similar, O(1)-C(1)-C(2)-Cl(21) -47.0(4)° and O(1)-C(1)-C(2)-Cl(22) 68.6(4)°.

Eluted subsequent to (22) was an isomeric compound (23) $C_7H_4Cl_6O$, m.p. 122.5-123°. With the structure of ketone (22) determined as above, the structure of the C6-epimeric compound (23) is defined by exclusion. The infrared carbonyl stretching frequencies of (22) (ν 1760 cm^{-1}) and (23) (ν 1778 cm^{-1}) (Nujol mulls) are markedly different. Assuming that the ring conformations of (22) and (23) are similar in the solid state, this difference (18 cm^{-1}) is consistent with the known effects of axial and equatorial chlorine atoms on the infrared carbonyl stretching frequencies of α-chlorocyclohexanones.[25,26] The assumption that the ring conformations of (22) and (23) are similar seems reasonable since the X-ray crystal structures of cyclohex-3-enones (22),(28),(38),(46),(48),(49),(57),(58) and (59) all exhibit similar ring conformations (refer Table 16: Selected Torsion Angles for Polychlorocyclohex-3-enones). Furthermore, if the assumption is made that the conformations of (22) and (23) in solution are similar to those in the solid state, then the observed ^1H n.m.r. C6-methyl resonances may be rationalised in terms of the now-established structures. It is known from the ^1H n.m.r. spectra of 5α-steroids that the angular $(H19)_3$ methyl protons are deshielded by (δ 0.32) by a 1,3-*syn*-axial 6-β-chloro substituent.[27]



In compound (23), the geometry of the molecule is such that the C(7)-Cl(2) *syn* distance is greater than in the steroid model. The observed differences in the C6-methyl ^1H n.m.r. chemical shifts between ketones (22) and (23) is correspondingly reduced (δ 0.13). Similar effects were observed in other C2 and C6 epimeric ketones, considered later in this chapter.

On the above grounds, the second isomer (23) was assigned the *cis* stereochemistry, *i.e.* simply epimeric at C6 with ketone (22).

Morita and Dietrich reported the inverted stereochemistry at C6 for ketones (22) and (23).[22]

2.1.2 Chlorination of 2,5-Dimethylaniline (24)

Chlorination of (24), as above, gave a mixture (*c.* 2:1) of the pentachlorocyclohex-3-enones (25) and (26) (refer Block C). Crystallization of the crude material from pentane gave a mixture of the two isomers, which were separated on a Chromatotron silica gel plate. The major component (25), $C_8H_7Cl_5O$, m.p. 129-130° was assigned the *trans* stereochemistry and the minor component, $C_8H_7Cl_5O$, m.p. 116-118°, (26) assigned the *cis* stereochemistry on the basis of their spectroscopic properties, by analogy to ketones (22) and (23).

The C2-methyl ^{1}H n.m.r. chemical shifts (25) (δ 1.94) and (26) (δ 2.08), follow closely those observed for ketones (22) (δ 1.97) and (23) (δ 2.10). The infrared carbonyl stretching frequencies for isomers (25) (ν 1758 cm^{-1}) and (26) (ν 1772 cm^{-1}) show a difference of (14 cm^{-1}), comparable to that observed between ketones (22) and (23) (18 cm^{-1}), consistent with the isomers (25) and (26) being epimeric at C6.

Morita and Dietrich reported the inverted stereochemistry at C6 for ketones (25) and (26).[21]

2.2 Chlorination of 2,4-Dichloro-6-methylphenol, 2,3-Dimethylaniline and 3-Chloro-2-methylaniline

2.2.1 Chlorination of 2,4-Dichloro-6-methylphenol (27)

Chlorination of (27), as above, gave a mixture (*c.* 3:1) of the pentachlorocyclohex-3-enones (28) and (29) (refer Block D). Crystallization of the crude material from pentane gave a mixture of the two isomers, which were separated on a Chromatotron silica gel plate. Compound (29), eluted first, was obtained in admixture with an impurity (*c.* 20%) formed during the chromatographic separation of (28) and (29). The structure of the major component (28), $C_7H_5Cl_5O$, m.p. 52-53°, was established by single-crystal X-ray analysis. A perspective drawing of this structure (28) is presented in Figure 2, with corresponding atomic co-ordinates given in Table 2. The cyclohex-3-enone ring is in a twist-boat conformation and closely resembles the ring structure for ketone (22), as shown by the torsion angles C(3)-C(4)-C(5)-C(6) -27.9(8)° and C(1)-C(2)-C(3)-C(4) 6.7(8)°. The C5-Cl bond is in the flagpole orientation C(3)-C(4)-C(5)-Cl(5) 92.2(6)°, a feature also observed in the structure of ketone (22).

The C6-*gem*-dichloro substituents assume the axial and equatorial positions, as shown by their torsion angles relative to the carbonyl functional group, O(1)-C(1)-C(6)-Cl(61) -104.4(5)° and O(1)-C(1)-C(6)-Cl(62) 12.3(7)°. These torsion angles are, again, close to those expected for the axial and equatorial bonds of an α-substituted cyclohexanone. The C2-substituents however, exhibit much more similar torsion angles relative to the carbonyl functional group, O(1)-C(1)-C(2)-C(7) 65.2(7)° and O(1)-C(1)-C(2)-Cl(2) -50.5(6)°. The consequence of this similarity in torsion angles is that the C2-Cl2/C1=O1 dipole interaction would not be dramatically different for C2-epimers, for example, (28) and (29). Consequently differences in the infrared carbonyl stretching frequencies would be less marked than for C6-epimers, for example, ketones (22) and (23). In fact, compound (29) (ν 1761 cm^{-1}) has an infrared carbonyl stretching frequency very close to that observed for its isomer (28) (ν 1766 cm^{-1}), suggesting that the cyclohex-3-enones (28) and (29), are epimeric at C2. Furthermore, the ^1H n.m.r. resonance of the C2-methyl group in (28) (δ 2.07) shows deshielding of the methyl protons by the *syn*-axial C6-chlorine atom. The ^1H n.m.r. methyl resonance of (29) (δ 1.89), which is not deshielded by an axial C6-Cl atom, is correspondingly upfield of that position observed for (28). On the above basis the second isomer was assigned structure (29), *i.e.* the C2-epimer of (28).

Morita and Dietrich reported the correct stereochemistry for ketones (28) and (29), but their argument was based on incorrect conformations for the two compounds.[22]

2.2.2 Chlorination of 2,3-Dimethylaniline (30)

Chlorination of (30) as above, gave a mixture (*c.* 1:3) of the pentachlorocyclohex-3-enones (31) and (32), (refer Block D), which were separated on a Chromatotron silica gel plate. Eluted first was the major component (32), $C_8H_7Cl_5O$, m.p. 84-85°, assigned the *trans* stereochemistry. Eluted subsequently was compound (31), $C_8H_7Cl_5O$, m.p. 128.5-129.5°, assigned the *cis* stereochemistry.

The structures were assigned to (31) and (32) by analogy with ketones (28) and (29) on the basis of the ^1H n.m.r. and infrared spectroscopic data.

The C2-methyl ^1H n.m.r. resonances of (31) (δ 2.06) and (32) (δ 1.89), follow closely those observed for cyclohex-3-enones (28) (δ 2.07) and (29) (δ 1.89). The infrared carbonyl stretching frequencies of ketones (31) (ν 1770 cm^{-1}) and (32) (ν 1767 cm^{-1}) are similar in frequency and in magnitude of difference to those observed for ketones (28) (ν 1766 cm^{-1}) and (29) (ν 1761 cm^{-1}). On the above basis the two isomers (31) and (32) are simply epimeric at C2.

Morita and Dietrich reported the inverted stereochemistry at C2 for the ketones (31) and (32).[21]

2.2.3 Chlorination of 3-Chloro-2-methylaniline (33)

Chlorination of (33) as above, gave a mixture (*c.* 2:3) of the hexachlorocyclohex-3-enones (34) and (35), (refer Block D), which were separated on a Chromatotron silica gel plate.

Eluted first was compound (35), $C_7H_4Cl_6O$, m.p. 60-61°, assigned the *trans* stereochemistry. Eluted subsequently was the isomeric compound (34), m.p. 111.5-112°, assigned the *cis* stereochemistry. The structures were assigned by analogy to ketones (31) and (32) and to ketones (28) and (29), on the basis of the spectroscopic data. The C2-methyl ^1H n.m.r. resonances of ketones (31) (δ 2.17) and (32) (δ 1.99) follow the trend observed for ketone pairs (28) (δ 2.07) and (29) (δ 1.89) and for (31) (δ 2.06) and (32) (δ 1.89). The larger difference in chemical shift between ketones (34) and (35) is most probably attributable to the C3-chlorine substituent.

The infrared carbonyl stretching frequencies of ketones (34) (ν 1770 cm^{-1}) and (35) (ν 1765 cm^{-1}) parallel those observed for ketone pairs (28) and (29) and for (31) and (32). The small difference in the infrared carbonyl stretching frequencies between ketones (34) and (35) (5 cm^{-1}) indicates that these ketones are C2-epimers.

Morita and Dietrich reported the inverted stereochemistry at C2 for the ketones (34) and (35).

2.3 Chlorination of 2,3,6-Trimethylphenol, 2,6-Dimethylaniline and 2,6-Dimethylphenol

2.3.1 Chlorination of 2,3,6-Trimethylphenol (36)

Chlorination of (36), as above, followed by crystallization of the crude product from pentane, gave a mixture (*c.* 3:1) of the tetrachlorocyclohex-3-enones (37) and (38) (refer Block E), the components of which were separated on a Chromatotron silica gel plate.

The structure of the first eluted compound (38), $C_9H_{10}Cl_4O$, m.p. 106-107°, was determined by single-crystal X-ray analysis. A perspective drawing is presented in Figure 3, with the corresponding atomic co-ordinates given in Table 3. The ring structure of the cyclohex-3-enone (38), in the solid state, (twist-boat), is almost identical to that observed for the cyclohex-3-enone (22) above, and similar to other cyclohex-3-enones, as shown by the relevant torsion angles C(3)-C(4)-C(5)-C(6) -31(1)° and C(1)-C(2)-C(3)-C(4) 11(1)° (refer Table 16).

The C5-Cl bond is in a flagpole orientation as shown by the torsion angle C(3)-C(4)-C(5)-Cl(5) 89(1)°, similar to cyclohex-3-enones (22) and (28) above. The C6-substituents adopt the axial and equatorial bond orientations, as shown by the torsion angles relative to the carbonyl function, O(1)-C(1)-C(6)-Cl(6) -108.5(9)° and O(1)-C(1)-C(6)-C(9) 9(1)°. In contrast, the C2-substituents exhibit torsion angles, relative to the carbonyl function, much more similar in magnitude, O(1)-C(1)-C(2)-Cl(2) 73(1)° and O(1)-C(1)-C(2)-C(7) -44(1)°.

Comparison of the spectroscopic data for ketone (38) with that of the isomer (37), allows assignment of the stereochemistry to the latter compound. The close similarity of the infrared carbonyl stretching frequencies for (37) (ν 1742 cm^{-1}) and (38) (ν 1740 cm^{-1}) indicates a common C6-Cl bond orientation for the two isomers. The ^1H n.m.r. spectrum of ketone (37) (δ 2.02) shows the C2-methyl-protons to be deshielded (δ 0.20) relative to the C2-methyl resonance for ketone (38) (δ 1.82). This indicates that the *syn*-axial C6-Cl/C2-methyl relationship is present in ketone (37). On the above basis the compounds (37) and (38) are simply C2-epimers.

Morita and Dietrich reported the inverted stereochemistry at C2 for the ketones (37) and (38).[22]

2.3.2 Chlorination of 2,6-Dimethylaniline (39)

Chlorination of (39), as above, gave a mixture (*c.* 2:3) of the tetrachlorocyclohex-3-enones (40) and (41) (refer Block E), which were separated on a Chromatotron silica gel plate. The structures of the isomers (40) and (41) were assigned by analogy with the trimethyl ketones (37) and (38) on the basis of their spectroscopic data, which parallel closely those observed for the ketones (37) and (38). The C2-methyl ^1H n.m.r. resonances for ketones (40) (δ 2.02) and (41) (δ 1.82) are identical to those observed for ketones (37) and (38) respectively, indicating a 1,3-*syn*-axial relationship in compound (40). The infrared carbonyl stretching frequencies for ketones (40) (ν 1748 cm^{-1}) and (41) (ν 1745 cm^{-1}) differ by only 3 cm^{-1}, indicating a common C6-Cl bond orientation for the two isomers. On the above basis the isomeric ketones (40) and (41) are simply C2-epimers.

Morita and Dietrich reported the inverted stereochemistry at C2 for the ketones (40) and (41).[22]

2.3.3 Chlorination of 2,6-Dimethylphenol (42)

Chlorination of (42), as above, gave a mixture (*c.* 3:2) of the pentachlorocyclohex-3-enones (43) and (44) (refer Block E). Crystallization of the crude material from pentane gave the isomer (43). The second isomer (44) was separated from the crude mixture on a Chromatotron silica gel plate.

Chlorination of 2,6-dimethylphenol (42) has been reported by Vollbracht *et.al.*[28] to yield only one pentachlorocyclohex-3-enone. On the basis of its infrared spectrum and ^{1}H n.m.r. spectrum and a consideration of Dreiding and Stuart-Courtauld models, these authors suggested that the cyclohex-3-enone ring existed in a conformation intermediate between a half-chair form and one of two extreme boat-forms.[28] In this conformation it was proposed that the C6-Cl bond was axial, the C5-H bond was close to planar with the alkene system, and the C5-Cl bond was close to perpendicular to that plane. This conformation described, corresponds closely to that expected for compound (43) on the basis of the crystal structures for cyclohex-3-enones (22) (28) and (38), considered above.

Taking into account the downfield chemical shift of the C2-methyl ^{1}H n.m.r. signal, due to the proximal C3-Cl atom (an effect also observed in ketones (34) and (35) above), the structures of ketones (43) and (44) can be assigned by analogy to ketones (37) and (38) and to ketones (40) and (41) above. The difference in the C2-methyl ^{1}H n.m.r. resonances between ketones (43) (δ 2.11) and (44) (δ 1.88) indicates that a *syn*-axial C2-methyl/C6-Cl relationship is present in ketone (43). The similarity of the infrared carbonyl stretching frequencies for ketones (43) (ν 1750 cm^{-1}) and (44) (ν 1750 cm^{-1}) indicate a common C6-Cl bond orientation for the two isomers. On the above grounds the pentachlorocyclohex-3-enones are simply C2-epimers.

Morita and Dietrich[22] also reported only one isomer from the above reaction. They assigned the same stereochemistry to the ketone (43) as had been proposed by Vollbracht *et.al.*[28], but assumed the incorrect conformation for that compound.[22]

2.4 Chlorination of 2,5-Dimethylphenol, 3,5-Dimethylphenol, 2,3,4,6-Tetrachloro-5-methylphenol, 2,3-Dimethylphenol and 2,3,4,5-Tetrachloro-6-methylphenol

2.4.1 Chlorination of 2,5-Dimethylphenol (45)

Chlorination of (45), as above, gave a mixture (*c.* 5:17:13:9:24:11) of the compounds (46), (47), (48), (49), (25) and (26), which were separated on a Chromatotron silica gel plate. Compounds (25) and (26) were shown to be identical to those formed from the chlorination of 2,5-dimethylaniline (24) (Section 2.1.2).

The structure of ketone (46), $C_8H_6Cl_6O$, m.p. 94.5-95°, eluted subsequent to ketones (25) and (26), was determined by single-crystal X-ray analysis. A perspective drawing is presented in Figure 4 and the corresponding atomic co-ordinates are given in Table 4. The cyclohex-3-enone ring structure of (46) is in a twist-boat conformation as shown by the relevant torsion angles C(3)-C(4)-C(5)-C(6) -28.9(3)° and C(1)-C(2)-C(3)-C(4) 8(1)°. This conformation is similar to that observed for the cyclohex-3-enones (22),(28) and (38) above (refer Table 16). In contrast to those structures, the C5-ring carbon of ketone (46) is fully substituted, bearing a methyl group and a chlorine atom. Despite this difference the C5-Cl bond still adopts the flagpole orientation, as shown by the torsion angle C(3)-C(4)-C(5)-Cl(5) 86.2(8)°. The C6-substituents Cl(61) and Cl(62) occupy the axial and equatorial positions respectively as shown by their torsion angles relative to the carbonyl function, O(1)-C(1)-C(6)-Cl(61) -104.5(8)° and O(1)-C(1)-C(6)-Cl(62) 12(1)°. The C2-substituents however, exhibit torsion angles, relative to the carbonyl function, much more similar in magnitude, O(1)-C(1)-C(2)-Cl(2) -51.2(9)° and O(1)-C(1)-C(2)-C(7) 65.5(9)°. These structural features are also similar to those observed for the structures of ketones (22), (28) and (38) above.

Eluted subsequent to ketone (46) was the 2,5-dienone (47), which crystallized from pentane as pale yellow needles, m.p. 55-56°. The structure assigned to dienone (47) by Morita and Dietrich[22] is in accord with the observed spectroscopic properties.

Eluted subsequent to dienone (47) were two polysubstituted cyclohex-2-enones (48) and (49).

The structures of cyclohex-2-enones (48) and (49) were determined by single-crystal X-ray analysis. A perspective drawing of cyclohex-2-enone (48), $C_8H_9Cl_5O$, m.p. 92.5-93°, is presented in Figure 5 and the corresponding atomic co-ordinates given in Table 5. The cyclohex-2-enone ring structure of ketone (48) is in a twist-boat conformation, as shown by the relevant torsion angles C(2)-C(3)-C(4)-C(5) 18.7(8)° and C(3)-C(4)-C(5)-C(6) -47.8(7)°.

In contrast to the cyclohex-3-enones (22), (28) and (38) the C5-Cl bond of cyclohex-2-enone (48) adopts the equatorial position with the C5-H bond axial. The torsion angles, relative to the carbonyl function, for the "axial" and "equatorial" groups at C6 however, are very much more similar in magnitude, O(1)-C(1)-C(6)-C(8) -76.8(7)° and O(1)-C(1)-C(6)-Cl(6) 40.9(7)°. The olefinic system is essentially coplanar with the ketone function, O(1)-C(1)-

C(2)-Cl(1) 0.0(8)°. The structure determined contains two independent molecules in the asymmetric unit. Least-squares best-fit calculations using the programme XFIT[29] show the two molecules to be essentially non-crystallographic mirror images of each other, with only minor conformational differences.

A perspective drawing of the isomeric compound (49), $C_8H_9Cl_5O$, m.p. 84-85°, is presented in Figure 6 and the corresponding atomic co-ordinates are given in Table 6. The cyclohex-2-enone ring structure of ketone (49) is in a twist-boat conformation, as shown by the relevant torsion angles C(2)-C(3)-C(4)-C(5) 14.0(5)° and C(3)-C(4)-C(5)-C(6) -42.3(4)°. These angles are comparable to those observed for cyclohex-2-enone (48).

The C5-Cl bond adopts the equatorial position and the C5-H5 the axial position. The C6-substituents adopt the axial and equatorial positions, as shown by their torsion angles relative to the carbonyl function, O(1)-C(1)-C(6)-Cl(6) -90.3(4)°* and O(1)-C(1)-C(6)-C(8) 26.1(5)°.*

The infrared carbonyl stretching frequencies (Nujol mulls) for compounds (48) and (49) reflect the differences between the two structures. Ketone (49) (ν 1708 cm^{-1}), has the C6-Cl bond in the axial orientation while ketone (48) (ν 1718 cm^{-1}) has the C6-Cl bond in orientation close to that for an equatorial position. Consequently the infrared carbonyl stretching frequency for ketone (48) is observed at a higher frequency. The difference is not as great in magnitude as that observed for the cyclohex-3-enones (22) and

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* (For enantiomer to structure determined)

(23), because the C6-C15 and C6-C8 bonds are more equally bisected by the carbonyl function in ketone (48) than in the cyclohex-3-enone examples, above.

Vollbracht *et.al.* reported the formation of (25) from the chlorination of 2,5-dimethylphenol.[28] Morita and Dietrich, in contrast, reported the formation of ketones (25) and (26) together with ketone (46), to which they assigned the correct stereochemistry but assumed the incorrect conformation. Cyclohex-2-enone (48) was reported in admixture with 2,5-dienone (47) by Morita and Dietrich,[22] but no attempt was made to assign the stereochemistry.

2.4.2 Chlorination of 3,5-Dimethylphenol (50)

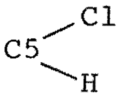
Chlorination of (50), as above, gave a mixture (*c.* 1:9) of the compounds (51) and (52) (refer Block G). Crystallization of the crude product gave the 2,5-dienone (52). Separation of the components of the remaining mixture on a Chromatotron silica gel plate gave the hexachlorocyclohex-3-enone (51). The structure of ketone (51) was determined by consideration of the spectroscopic data and by analogy with other cyclohex-3-enones above, on the assumption that the C5-Cl bond was in the flagpole orientation. This assumption seems reasonable, since the X-ray structure of the cyclohex-3-enone (46) with the C5-Me/C5-Cl structural feature, and the ketones (22), (28) and (38) with the C5-H/C5-Cl structural feature, all have the C5-Cl bond in that orientation. On the above basis, the C5-methyl ^{1}H n.m.r. resonance for ketone (51) (δ 2.20) is close to that observed for the methyl ^{1}H n.m.r. resonance in ketone (46) (δ 2.25), taking into account the known deshielding effect of the C3-Cl atom. The chemical shift of the C3-methyl ^1H n.m.r. resonance of the ketone (51) (δ 2.30) suggests that the methyl group is attached to an olefinic carbon atom. The ketones (25) and (26) exhibit similar C3-methyl resonances for the methyl groups in similar environments to ketone (51).

Morita and Dietrich assigned the same gross structure to ketone (51), but assumed that the C5-methyl bond was pseudoaxial and thus proposed the incorrect conformation for ketone (51).[22]

Vollbracht *et.al.*[28] reported the 2,5-dienone (52) as being the only product from the chlorination of 3,5-dimethylphenol (50). The structure of this 2,5-dienone (52) was assigned on the basis of its spectroscopic data, and was the structure proposed earlier by Auwers *et.al.*,[30] Muller and Linde[31] and Fort.[32]

2.4.3 Chlorination of 2,3,4,6-Tetrachloro-5-methylphenol (53)

Chlorination of (53), as above, gave a mixture (*c.* 3:2) of the compounds (54) and (55), which were separated on a Chromatotron silica gel plate.

The issue in question in this case was the position of the methyl group. It was possible that the methyl group was located at the olefinic C3-ring carbon atom, since the observed ^1H n.m.r. resonance for ketone (54) (δ 2.27) is close to that expected for such a methyl group, *cf.* ketone (51) (δ 2.30). Alternatively the methyl group could be located at the sp^3 C5 site. The ^1H n.m.r. resonance for the C5-methyl in ketone (46) (δ 2.25) is also close to that observed for the compound in question. This issue could be resolved by examination of the infrared C=C stretching frequency of ketone (54) in comparison with other cyclohex-3-enones (refer Table 2.1). It was observed that a difference of approximately 22 cm^{-1} in the infrared C=C stretching frequency occurred betweeen polychlorocyclohex-3-enones differing only in the substituent at C3 (i.e. Cl or methyl). Comparison of the infrared olefinic stretching frequencies for the cyclohex-3-enones in Sections 2.1, 2.2 and 2.3, all having the common  $\mathrm{C5}{<}^{\mathrm{Cl}}_{\mathrm{H}}$ structural feature, shows that the infrared olefinic stretching frequency is largely independent of the nature of the C2- and C6-substituents and of the stereochemistry at these sites. Therefore the dominant factor effecting the infrared olefinic stretching frequency is the nature of the substituent at C3 (since C4 always bears a Cl atom in these structures). Replacement of the C5-H atom by a methyl group (or a chlorine atom as shown in Section 2.4, later) results in a shift in the infrared olefinic stretching frequency by approximately 20 cm^{-1} to lower frequency. This shift is observed for both C3-Cl and C3-methyl as shown by ketones (46) and (51). On the above basis, ketone (54) (ν 1597 cm^{-1}) (C=C) must have a chlorine atom as the C3-substituent, the methyl group is therefore at C5. Assuming that the heptachlorocyclohex-3-enone (54) is in a similar conformation to those cyclohex-3-enone structures discussed above, then the ^{1}H n.m.r. methyl resonance of (54) (δ 2.27) is consistent with the methyl group being in a similar orientation to that found for ketone (46) (δ 2.25).

Morita and Dietrich reported the same gross structure to ketone (54), but assumed a half-chair conformation with

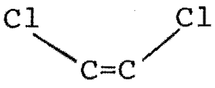
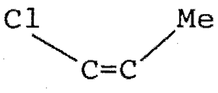
					Δcm^{-1}
2.1	(22)	1622	(25)	1645	23
	(23)	1612	(26)	1640	28
2.2	(34)	1623	(31)	1646	23
	(35)	1620	(32)	1640	20
2.3	(43)	1625	(37)	1643	18
	(44)	1627	(38)	1648	21
2.4	(46)	1607	(51)	1627	20
	*(54)	1597			
	(57)	1603			
	(58)	1596			
	(61)	1598	(59)	1620	22

TABLE 2.1 infrared olefinic stretching frequencies for some cyclohex-3-enones.

the C5-methyl group pseudoaxial.[21]

The structure of the 2,5-dienone (55) was proposed by Crowther and McCombie in 1913 (m.p. 92°)[33] and subsequently by Morita and Dietrich[21] and is in accord with its spectroscopic data.

2.4.4 Chlorination of 2,3-Dimethylphenol (56)

Chlorination of (56), as above, gave a mixture (*c*. 8:2:1) of the compounds (57) (58) and (59) (refer Block H), which were separated on a Chromatotron silica gel plate. Eluted first was the hexachlorocyclohex-3-enone (57), $C_8H_6Cl_6O$, m.p. 87-88°, the structure of which was determined by single-crystal X-ray analysis. A perspective drawing is presented in Figure 7 and corresponding atomic co-ordinates are given in Table 7.

The cyclohex-3-enone ring structure is in a twist-boat conformation, as shown by the torsion angles C(3)-C(4)-C(5)-C(6) -32.8(3)° and C(1)-C(2)-C(3)-C(4) 8.5(4)°. These angles, and hence the conformation, are similar to those observed for other cyclohex-3-enones (refer Table 16). The C5-Cl bond adopts the flagpole orientation, as shown by the torsion angle C(3)-C(4)-C(5)-Cl(5) 80.2(3)°. The C6-substituents Cl(6) and C(8) adopt the axial and equatorial positions respectively, as shown by their torsion angles relative to the carbonyl function, O(1)-C(1)-C(6)-Cl(6) -108.6(2)° and O(1)-C(1)-C(6)-C(8) 8.8(3)°. The C2-substituents adopt positions with torsion angles, relative to the carbonyl function, more similar in magnitude, O(1)-C(1)-C(2)-Cl(21) 71.3(2)° and O(1)-C(1)-C(2)-Cl(22) -44.8(3)°. These structural features are similar to those observed for other polychlorocyclohex-3-enone structures (refer Table 16).

The structure of the C6-epimer (58), $C_8H_6Cl_6O$, m.p. 142-143°, eluted subsequent to compounds (57) and (59), was determined by single-crystal X-ray analysis. A perspective drawing of ketone (58) is presented in Figure 8 and corresponding atomic co-ordinates are given in Table 8. The cyclohex-3-enone ring structure of ketone (58) (twist-boat) is almost identical to that of ketone (57) above, as shown by the relevant torsion angles C(3)-C(4)-C(5)-C(6) -32.6(3)° and C(1)-C(2)-C(3)-C(4) 9.5(3)°. The C5-Cl atom is again in the flagpole orientation as shown by the torsion angle C(3)-C(4)-C(5)-Cl(5) 82.9(2)°. The C6-substituents C(8) and (Cl6) adopt the axial and equatorial positions respectively, as shown by their torsion angles, relative to the carbonyl function, O(1)-C(1)-C(6)-C(8) -106.8(3)° and O(1)-C(1)-C(6)-Cl(6) 10.7(3)°. The C2-substituents Cl(21) and Cl(22) adopt positions with torsion angles, relative to the carbonyl function, more similar in magnitude, O(1)-C(1)-C(2)-Cl(21) 75.7(2)° and O(1)-C(1)-C(2)-Cl(22) -40.4(2)°.

The difference between the two structures (57) and (58) is reflected in the infrared carbonyl stretching frequencies. Ketone (58) (ν 1765 cm^{-1}) has the C6-equatorial chlorine atom, and consequently the infrared carbonyl stretching band occurs at higher frequency than for ketone (57) (ν 1760 cm^{-1}) with the C6-axial chlorine atom. This effect was observed for other C6-epimeric cyclohex-3-enones above, but is of smaller magnitude (5 cm^{-1}) than the examples previously discussed (*cf* 20 cm^{-1}).

The hexachlorocyclohex-3-enone (59), eluted subsequent to ketone (57) above, was of special interest since the

C5-ring carbon has *gem*-dichloro substituents. The issue in this structure was whether the C2-substituents (Cl and methyl) would dictate the conformation of the cyclohex-3-enone ring structure.

At room temperature the ^1H n.m.r. spectrum of ketone (59) showed one sharp resonance (δ 2.19) due to the C3-methyl group and one very broad resonance (δ 1.98, 10Hz at half height), assigned to the C2-methyl group. Repeating this experiment at lower temperature (-12°), the ^1H n.m.r. spectrum of (59) resolved into 3 sharp peaks (δ 2.20) (δ 2.13) (δ 1.89) in an approximate ratio 2:1:1. On the above basis it appeared reasonable to suggest, at least in the solution state, that the ketone (59) exists as an equilibrium mixture of the two conformers (59a) and (59b). The observed ^1H n.m.r. methyl resonances (at -12°) are as expected for such conformational isomers, being similar to the chemical shifts for methyl groups in the isomeric pairs (31) (δ 2.07) and (32) (δ 1.89), and (34) (δ 2.17) and (35) (δ 1.99).

In the solid state, the infrared carbonyl stretching frequency for compound (59) (Nujol mull) shows a single peak (ν 1761 cm^{-1}).

While this may suggest that the ketone (59) exists as only one conformer in the solid state, the possibility that both conformers (59a) and (59b) exist in the solid state cannot be excluded, since it has been observed that the orientation of C2-substituents (when Cl and methyl) on other cyclohex-3-enones has little or no effect on the infrared carbonyl stretching frequency.

A single-crystal X-ray analysis was performed upon a uniform crystal formed from the crystallization of compound (59) from pentane, $C_8H_6Cl_6O$, m.p. 92-92.5°. A perspective drawing of the structure is presented in Figure 9 and the corresponding atomic co-ordinates are given in Table 9. The cyclohex-3-enone ring structure of ketone (59) is in a twist-boat conformation, as shown by the torsion angles C(3)-C(4)-C(5)-C(6) -26.9(5)° and C(1)-C(2)-C(3)-C(4) 6.6(5)°. The C6-substituents Cl(61) and Cl(62) adopt the equatorial and axial orientations respectively, as shown by their torsion angles relative to the carbonyl function, O(1)-C(1)-C(6)-Cl(61) 7.0(4)° and O(1)-C(1)-C(6)-Cl(62) -111.1(2)°. The C2-substituents Cl(2) and C(7) were found to be non-stoichiometrically disordered about the C2-ring carbon atom. The C2-chlorine atom was found to have a site-occupancy-factor of 0.85 in the position Cl(2), Figure 9a, and 0.15 in the position Cl(2)', Figure 9b, as shown by the torsion angles O(1)-C(1)-C(2)-Cl(2) -44.1(4)° and O(1)-C(1)-C(2)-Cl(2)' 77.3(5)°, respectively. Correspondingly the C2-methyl group was found to have a site-occupany-factor of 0.85 in the position C(7), Figure 9a and 0.15 in the position C(7)', Figure 9b, as shown by the torsion angles, O(1)-C(1)-C(2)-C(7) 70.5(5)° and O(1)-C(1)-C(2)-C(7)' -39.3(9)°, respectively.

Morita and Dietrich[22] reported ketones (57) and (58) as being the products of chlorination of 2,3-dimethylphenol (56). The structures they proposed for these compounds were 5,6-*trans*-dimethyl conformers, *i.e.* for the compound (57), the C5-methyl group equatorial and the C6-methyl group equatorial, and for compound (58), the C5-methyl group axial and the C6-methyl group axial, for the cyclohex-3-enone ring in a half-chair conformation. On this basis the stereochemistry for compound (57) was correct, and that of

(58) incorrect. In both cases the incorrect ring conformation was assumed.

The hexachlorocyclohex-3-enone (59) was not reported as a product in the above reaction.

2.4.5 Chlorination of 2,3,4,5-Tetrachloro-6-methylphenol (60)

Chlorination of (60), as above, gave a mixture (*c.* 3:2) of the compounds (61) and (73) (refer Block I), which were separated on a Chromatotron silica gel plate. The molecular uncertainties for compound (61) were, (i) whether the methyl group was located at C2 or C6 and (ii) whether the C2 (or C6) methyl substituent dictated the ring conformation.

The ^{1}H n.m.r. spectrum of compound (61) at room temperature shows a single very broad resonance (δ 2.10, 7Hz at half height). Repeating the experiment at -10°, the ^{1}H n.m.r. spectrum resolves into two sharp peaks (δ 2.22) and (δ 2.00).

On this basis it seems reasonable to suggest that the ketone (61) exists as a mixture of the C2-conformers, at least in solution. The ^{1}H n.m.r. methyl chemical shifts, observed at -10°, are as expected by analogy with the C2-epimers (34) (δ 2.17) and (35) (δ 1.99).

The infrared spectrum (Nujol mull) of the ketone (61) shows two carbonyl stretching frequencies (ν 1778 cm^{-1}) and (ν 1768 cm^{-1}) of equal intensity. It therefore seems likely that both C2-conformers of ketone (61) exist in the solid state. The small difference between the infrared carbonyl stretching frequencies (10 cm^{-1}) is consistent with the methyl group being at C2.

Morita and Dietrich[21] reported ketone (61) as having a single ^{1}H n.m.r. resonance (δ 2.11), but did not report any conformational mobility for this compound. The structure proposed by Morita and Dietrich for ketone (61) was based on the incorrectly assumed half-chair conformation with the methyl group at C2 in the axial orientation.[21]

The 2,4-dienone (73) formed in this reaction, was assigned the structure on the basis of its spectroscopic properties by Morita and Dietrich.[21] The formation of these 2,4-dienones are discussed in detail in a later chapter.

2.5 Chlorination of 3-Methylphenol (63)

Chlorination of (63), as above, gave >75% of the hexachlorocyclohex-3-enone (64) (refer Block I), which was crystallized from the crude material from pentane/diethylether.

Morita and Dietrich had reported ketone (64) as being the major product of the chlorination of 3-methylphenol (63).[21]

The spectroscopic data for this compound were consistent with that assigned structure in the twist-boat conformation, as seen above for analogous compounds.

CHAPTER 3

FORMATION OF 6-CHLOROCYCLOHEXA-2,4-DIENONES FROM POLYSUBSTITUTED PHENOLS

3.1 Introduction

Denivelle and Fort[19] reported the formation of 6-chlorocyclohexa-2,4-dienones from the chlorination of phenols in the presence of pyridine in carbon tetrachloride. Morita and Dietrich[21] subsequently used a similar method to prepare a number of 6-chlorocyclohexa-2,4-dienones, in the course of their identification of some minor products formed by the reaction of *ortho* and *meta* cresols with chlorine in acetic acid. Our interest was in preparing a number of these 6-chlorocyclohexa-2,4-dienones so that the addition of chlorine in acetic acid to the 2,4-dienone system could be studied.

The reaction conditions employed differed slightly from those used by the above workers. In general, the phenol was dissolved as a 10% solution in carbon tetrachloride and an equimolar amount of pyridine. Chlorine, as a chlorine/carbon tetrachloride solution, was added dropwise, in slight excess, (1.1 mole equivalent) to the rapidly stirred phenolic solution at 0°. The reaction was rapid, as judged by the immediate formation of a pyridine hydrochloride precipitate. A neutral aqueous work-up was used to give the 6-chlorocyclohexa-2,4-dienones in good yield. For detailed reaction conditions refer to the experimental section relating to Chapter 3.

3.2 Reaction of Polysubstituted Phenols with Chlorine in Carbon Tetrachloride and Pyridine

3.2.1 Reaction of 2,4-Dichloro-6-methylphenol (65)

Chlorination of phenol (65), as above, gave the 2,4-dienone (66) (refer Block J), as a pale yellow oil. This oil was shown (^{1}H n.m.r.) to be essentially pure dienone (66). Attempts to chromatograph the oil on silica resulted in decomposition and crystallization from a variety of solvents failed to yield any solid material. The structure was assigned on the basis of its spectroscopic properties.

The infrared spectrum (ν 1698 cm^{-1}, C=O and 1625, 1560 cm^{-1}, C=C) confirms the presence of a conjugated dienone system. The ^{1}H n.m.r. chemical shift of the C6-methyl group (δ 1.83) (refer Table 3.1)* is downfield relative to that expected for a vinylic methyl group adjacent to a carbonyl function (*c.* 2.0-2.1 ppm). This indicates that the C6-ring carbon bears a chlorine atom in addition to the C6-methyl group. This downfield chemical shift of the C6-methyl proton resonance, is observed consistently for all the 6-chloro-6-methylcyclohexa-2,4-dienones prepared (refer Table 3.1).

The C3-H and C5-H proton resonances appear as doublets (J 2.3 Hz), this is consistent with allylic coupling as part of the linear 2,4-dienone π-system. Furthermore, the C6-methyl proton resonance appears as a sharp singlet, coupling between these protons and the adjacent C5-H proton does not occur, again consistent with the proposed structure. The

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* (As a fold-out at the end of Chapter 3)

structure of 2,4-dienone (66) is in agreement with that proposed by Morita and Dietrich,[21] the 2,4-dienone (66) being formed by selective *ipso* chlorine attack at the *ortho* position bearing the methyl group.

3.2.2 Reaction of 2,4-Dichloro-3,6-dimethylphenol (67)

Chlorination of phenol (67), as above, gave the 2,4-dienone (68) (refer Block J), which crystallized from dichloromethane/pentane as pale yellow crystals, m.p. 57-58°. The structure of this compound (68) was assigned on the basis of its spectroscopic data. The infrared spectrum (ν 1695 cm^{-1}, C=O and 1630, 1554 cm^{-1}, C=C) confirms the presence of a conjugated dienone system.

The ^{1}H n.m.r. spectrum, (refer Table 3.1) exhibited a C6-methyl proton resonance (δ 1.81) consistent with that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The C3-methyl resonance (δ 2.40) is consistent with that expected for a vinylic methyl group. The C3-methyl protons and the C5-H proton are coupled ($J \approx 0.5$ Hz), in accord with homoallylic coupling in the linear 2,4-dienone π-system. Coupling between the C6-methyl group protons and the C5-H proton is absent, the C6-methyl peak appearing as a sharp singlet. This structure (68) is in agreement with that proposed by Morita and Dietrich,[22] and the 2,4-dienone (68) is formed by selective *ipso* chlorine attack at the *ortho* position bearing the methyl group.

3.2.3 Reaction of 2,4-Dichloro-5,6-dimethylphenol (69)

Reaction of phenol (69), as above, gave the 2,4-dienone (70) (refer Block J), as a pale yellow oil. This oil was shown (^{1}H n.m.r.) to be essentially pure dienone (70). The structure was determined from its spectroscopic properties. The infrared spectrum (ν 1700 cm^{-1}, C=O and 1625, 1575 cm^{-1}, C=C) confirms the presence of a conjugated dienone system. The ^{1}H n.m.r. spectrum (refer Table 3.1) includes a C6-methyl proton resonance (δ 1.85) similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The structure therefore, is that of 2,4-dienone (70) and is in agreement with that proposed by Morita and Dietrich.[22]

The 2,4-dienone (70) is formed by selective *ipso* chlorine attack at the *ortho* position bearing the methyl group.

3.2.4 Reaction of 2,4-Dichloro-3,5,6-trimethylphenol (71)

Chlorination of phenol (71), as above, gave the 2,4-dienone (72) (refer Block J), as a pale yellow oil. This oil was shown (^{1}H n.m.r.) to be essentially pure dienone (72). The structure was determined from the spectroscopic data. The infrared spectrum (ν 1690 cm^{-1}, C=O and 1620, 1560 cm^{-1}, C=C) confirms the presence of a conjugated dienone system. The ^{1}H n.m.r. spectrum (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.80) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The C3-methyl resonance (δ 2.42) is similar to that observed for dienone (68) (δ 2.40), which is in a similar chemical environment. The C5-methyl resonance (δ 2.20) is similar to that observed in dienone (70) (δ 2.17). The C3-methyl protons and the C5-methyl protons are coupled ($J \approx 0.5$ Hz), consistent with homoallylic coupling in the linear 2,4-dienone π-system. This structure (72), is in agreement with that proposed by Morita and Dietrich,[22] and the

2,4-dienone (72) is formed by selective *ipso* chlorine attack at the *ortho* position bearing the methyl group.

3.2.5 Reaction of 2,3,4,5-Tetrachloro-6-methylphenol (60)

Chlorination of phenol (60), as above, gave the 2,4-dienone (73) (refer Block J), as a pale yellow oil, which crystallized from pentane as pale yellow crystals, m.p. 57-58°. The structure was determined from its spectroscopic properties. The infrared spectrum (ν 1700 cm^{-1}, C=O and 1585, 1532 cm^{-1}, C=C) confirms the presence of the conjugated dienone system. The ^{1}H n.m.r. spectrum (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.97) is similar to that observed in other 6-chloro-6-methylcyclohexa-2,4-dienones, taking into account the deshielding effects of the other chlorine atoms. The uv. spectrum (λ_{max} 239, 363 nm; ε 5570, 3900) confirms the presence of the linear 2,4-dienone structure.

The 2,4-dienone (73) is formed by selective *ipso* chlorine attack at the *ortho* position bearing the methyl group.

3.2.6 Reaction of 4-chloro-2,6-dimethylphenol (74)

Chlorination of phenol (74), as above, gave the 2,4-dienone (75) (refer Block K), as a pale yellow oil. This oil was shown (^{1}H n.m.r.) to be essentially pure dienone (75). The structure was determined from its spectroscopic data. The infrared spectrum (ν 1690 cm^{-1}, C=O and 1643, 1593 cm^{-1}, C=C) confirms the presence of a conjugated dienone system. The ^{1}H n.m.r. spectrum (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.77) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones.

The C3-H proton and the C5-H proton are coupled (J 1.5 Hz), and in addition, the C2-methyl protons are coupled to the C3-H proton (J 0.5 Hz). These couplings are consistent with allylic coupling in the linear 2,4-dienone π-system. This structure (75) is in agreement with that proposed by Morita and Dietrich.[22] The 2,4-dienone (75) is formed by selective *ipso* chlorine attack at the *ortho* positions, both of which bear methyl groups, between which no distinction can be made because the phenolic substrate is symmetrical.

3.2.7 Reaction of 3,5-Dichloro-2,4,6-trimethylphenol (76)

Chlorination of phenol (76), as above, gave the 2,4-dienone (77) (refer Block K), as a pale yellow oil. This oil was shown (^{1}H n.m.r.) to be essentially pure dienone (77). The structure was determined from its spectroscopic properties. The infrared spectrum (ν 1675 cm^{-1}, C=O and 1623, 1568 cm^{-1}, C=C) confirms the presence of a conjugated dienone system. The symmetrical 4-chloro-2,5-dienone isomer can be excluded because the ^{1}H n.m.r. spectrum of compound (77) has three methyl resonances (refer Table 3.1). The ^{1}H n.m.r. C6-methyl proton resonance (δ 1.90) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The structure of this compound is therefore that of the 2,4-dienone (77).

The 2,4-dienone (77) is formed by selective *ipso* chlorine attack at the *ortho* positions, both of which bear methyl groups, between which no distinction can be made because of the symmetry of the phenolic substrate (76).

3.2.8 Reaction of 4-Chloro-2,3,6-trimethylphenol (78)

Chlorination of phenol (78), as above, gave a mixture (*c.* 11:1) of the 2,4-dienones (79) and (79a) (refer Block K), which could not be separated by crystallization or chromatographic techniques. The structure of the major component (79) was assigned from the spectroscopic data of the above mixture. The infrared spectrum (ν 1679 cm^{-1}, C=O and 1640, 1599 cm^{-1}, C=C) confirms the presence of a conjugated dienone system. The uv. spectrum (λ_{max} 246, 344 nm; ε 2670, 3190) indicates that the structure is a linear 2,4-dienone system. The ^1H n.m.r. spectrum (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.77) is similar to that observed for other 2,4-dienones. Double frequency irradiation experiments show that the C3-methyl protons and the C5-H proton are coupled (J 1.5 Hz) and that the C2-methyl protons and the C3-methyl protons are also coupled (J 0.5 Hz). These homoallylic couplings are consistent with the 2,4-dienone structure of (79).

The alternative structure, (79a), proposed by Morita and Dietrich,[22] is inconsistent with the observed decoupling experiments. Irradiation at the C3-H proton resonance, of their structure, should collapse the C2- and C5-methyl resonances to singlets. This is not observed.

The 2,4-dienone (79) is formed by preferential *ipso* chlorine attack at the *ortho* position adjacent to the ring carbon bearing a hydrogen atom, rather than a methyl group. Since both *ortho* sites bear methyl groups, it would seem to be the substituent on the adjacent ring carbon which directs the position of chlorine attack.

The minor component of the above product mixture could not be isolated by crystallization or chromatographic techniques. It is probable, but not proved conclusively that this minor component is the alternative 2,4-dienone (79a).

3.2.9 Reaction of 3,4-Dichloro-2,6-dimethylphenol (80)

Chlorination of phenol (80), as above, gave a mixture (*c.* 3:2) of the 2,4-dienones (81) and (82) (refer Block K), as a pale yellow oil. This mixture could not be separated by crystallization or chromatographic techniques. The mixture was shown (^{1}H n.m.r.) to consist essentially of a mixture of the two dienones (81) and (82). The structures of these compounds were determined from the spectroscopic properties of the mixture. The infrared spectrum (ν 1687 cm^{-1}, C=O and 1634, 1575 cm^{-1}, C=C) confirms the presence of the conjugated dienone system.

The ^{1}H n.m.r. spectrum of the major component (81) (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.82) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The C2-methyl protons are coupled to the C3-H proton (J 1.5 Hz). This allylic coupling is consistent with the conjugated 2,4-dienone structure.

The structure of the minor component (82) was assigned on the basis of its spectroscopic data. The ^{1}H n.m.r. spectrum of (82) (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.70) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The observed long-range coupling between the C2-methyl protons and the C5-H proton (J 0.8 Hz) is consistent with the presence of the conjugated 2,4-dienone π-system. These structures (81) and (82) are in agreement with those proposed by Morita and Dietrich.[22] However, the product ratio (*c.* 3:2), obtained consistently in the present work, is the reverse of that reported by those workers.[22]

The 2,4-dienone (81) is formed by *ipso* chlorine attack at the *ortho* position adjacent to the ring carbon bearing a chlorine atom. Attack at the alternative *ortho* position adjacent to the ring carbon bearing a hydrogen atom gives rise to the minor component 2,4-dienone (82). Of note is the fact that the 2,4-dienone (81) is formed in preference to 2,4-dienone (82), suggesting that the directing effect of the substituent on the ring carbon adjacent to the *ortho* position, is not purely steric in origin. On steric grounds alone the 2,4-dienone (82) would be expected to be the preferred product, due to the greater accessibility of the *ortho* site adjacent to the ring carbon bearing a hydrogen atom rather than the alternative ring carbon bearing a chlorine atom.

3.2.10 Reaction of 3,4-Dichloro-2,5,6-trimethylphenol (83)

Chlorination of phenol (83), as above, gave a mixture (*c.* 9:1) of the 2,4-dienones (84) and (85) (refer Block L), as a pale yellow oil. The components of this mixture could not be separated by crystallization or by chromatographic techniques. The structures of these products were assigned from the spectroscopic properties of this mixture. The ^1H n.m.r. spectrum of the major component (84) (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.80) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The C2-methyl resonance (δ 2.15) and the C3-methyl resonance (δ 2.25) are coupled ($J \simeq 0.5$ Hz), consistent with homoallylic coupling in the 2,4-dienone conjugated structure.

The infrared spectrum (ν_{max} 1678 cm^{-1}, C=O and 1613, 1575 cm^{-1}, C=C) confirms the presence of the conjugated dienone structure.

The minor component (85) could not be isolated, but could be detected in the ^1H n.m.r. spectrum of the above mixture. The ^1H n.m.r. spectrum of (85) (refer Table 3.1) shows that the C6-methyl proton resonance (δ 1.90) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones. The C2-methyl resonance (δ 2.04) is close to that observed for dienone (82) (δ 2.05) for a methyl group in a similar chemical environment. The C5-methyl resonance of dienone (85) (δ 2.24) is close to that observed for the C5-methyl resonance of dienone (72) (δ 2.20).

The major product of the above reaction, 2,4-dienone (84), was assigned the structure of the minor component, 2,4-dienone (85), by Morita and Dietrich.[22] These workers reported only a single compound as the product of the above reaction.

3.2.11 Reaction of 2-Chloro-3,4,6-trimethylphenol (86)

Chlorination of phenol (86), as above, gave a mixture (*c.* 2:1) (*c.* 75% total) of the exocyclic methylene compound (87) and the 2,5-dienone (88) (refer Block L), which were separated on a Chromatotron silica gel plate.

Eluted first was the exocyclic methylene compound (87), m.p. 100-101°, $C_9H_9Cl_3O$, the structure of which was assigned on the basis of its spectroscopic data and subsequently proved by single-crystal X-ray analysis.[34] The infrared spectrum (ν 1700 cm^{-1}, C=O and 1570 cm^{-1}, C=C) suggests the presence of a conjugated dienone system, and is confirmed by the uv. spectrum (λ_{max} 294 nm; ε 14,100). The ^{1}H n.m.r. spectrum of compound (87) exhibits only two methyl peaks; (δ 1.87) corresponding to the C6-methyl group and (δ 2.31) corresponding to the C3-vinylic methyl group. The C4-methylene protons appear as a sharp singlet (δ 5.72), without coupling to either each other or the allylic C5-H proton. The C5-H proton (δ 4.88), also a singlet, has a chemical shift consistent with the assigned structure.

The exocyclic methylene compound (87) is formed by further chlorine attack on the 6-chloro-6-methylcyclohexa-2,4-dienone (88a) (refer Scheme 2). Attack by chlorine at the unsubstituted C5-ring carbon of 2,4-dienone (88a) gives the cationic intermediate species (87a) (refer Scheme 2) which can undergo proton loss from the C4-methyl group to give the exocyclic methylene compound (87). The proton loss is likely to be aided by the presence of pyridine in the reaction mixture. Because the 6-chloro-6-methylcyclohexa-2,4-dienone (88a) was not detected in, or isolated from, the above reaction it could not be proved, by experiment, that the exocyclic methylene compound (87) was formed from this 2,4-dienone (88a). However, the above reaction scheme is supported by the analogous reaction discussed in Section 3.2.12 , in which the origin of the exocyclic methylene compound (91) was proved to be the 6-chloro-6-methylcyclohexa-2,4-dienone (90).

The structure of the 2,5-dienone (88), eluted subsequent to compound (87), was determined from its spectroscopic properties. The infrared spectrum (ν 1661 cm^{-1}, C=O and 1608 cm^{-1}, C=C) confirms the presence of the conjugated cyclic ketone. The uv. spectrum (λ_{max} 248 nm; ε 10,000) indicates that the compound has a cross-conjugated 2,5-dienone structure. The ^1H n.m.r. spectrum exhibits the C4-methyl proton resonance (δ 1.82) as a singlet and the C6-methyl resonance (δ 1.98) as a doublet, coupled to the C5-H proton (J 1.5 Hz); these data are consistent with the assigned 2,5-dienone structure. The C3-methyl resonance (δ 2.31) is as expected for a vinylic methyl group.

The 2,5-dienone (88) can be formed from either direct *ipso* chlorine attack at the *para* position or *ipso* attack at the methyl-substituted *ortho* position to give the 6-chloro-2,4-dienone (88a) followed by rearrangement to give the 4-chloro-2,5-dienone (88) (refer Scheme 2). The latter rearrangement process was shown to be the most probable route to the 4-chloro-2,5-dienone (92) for an analogous reaction system (discussed in Section 3.2.12). Therefore, it seems likely that the 4-chloro-2,5-dienone (88), formed in the above reaction, arises by rearrangement of the 6-chloro-2,4-dienone (88a).

3.2.12 Reaction of 2-Chloro-4,6-dimethylphenol (89)

Chlorination of phenol (89), as above, gave a mixture (*c.* 20:1) of the 2,4-dienone (90) and the exocyclic methylene compound (91) (refer Block L). Separation of the above mixture on a Chromatotron silica gel plate gave the exocyclic methylene compound (91), the 4-chloro-2,5-dienone (92) and the 4-hydroxy-2,5-dienone (93), (refer Block L). The structures of these compounds (91), (92) and (93) were determined from their spectroscopic properties.

The exocyclic methylene compound (91), m.p. 65-67.5°, $C_8H_7Cl_3O$, exhibits the infrared peaks (ν 1695(br)cm^{-1}, C=O and 1625, 1579 cm^{-1}, C=C), suggesting the presence of a conjugated dienone system, which was confirmed by the uv. spectrum (λ_{max} 292 nm; 12,000). The ^{1}H n.m.r. spectrum of compound (91), has only one methyl proton resonance (δ 1.92); this chemical shift is similar to that observed for the C6-methyl protons in the analogous compound (87). The peaks at (δ 5.58) and (δ 5.67) correspond to the C4-methylene protons. The C3-H proton (δ 7.20) is coupled to the *syn* C5-methine proton (δ 4.87), both peaks appearing as doublets (J 2.0 Hz). This coupling indicates that the C5-H bond is in a position close to coplanar with the C3-H bond and the ring structure. The C5-Cl bond is therefore axial and the stereochemistry, 5,6-*trans*-dichloro, is indicated by the similar C6-methyl resonance (δ 1.92) to that observed for the analogous compound (87) (δ 1.87). The ^{13}C n.m.r. spectrum is consistent with the structure of the exocyclic methylene compound (91).

The 4-chloro-4-methylcyclohexa-2,5-dienone (92), a lightly coloured oil, $C_8H_8Cl_2O$, was eluted second. The infrared spectrum of the compound (92) (ν 1685 cm^{-1}, C=O and 1667, 1620 cm^{-1}, C=C) suggests the presence of a conjugated dienone system. The uv. spectrum (λ_{max} 246 nm; ε13,600) is consistent with a cross-conjugated 2,5-dienone structure. The ^{1}H n.m.r. spectrum of compound (92) exhibits two methyl proton resonances. The first, a singlet (δ 1.83), is consistent with that expected for the methyl group on the fully substituted C4-carbon atom. The second, (δ 1.93), a doublet, has a chemical shift as expected for a vinylic methyl group adjacent to a carbonyl function, and is coupled to the C5-H proton (δ 6.67) (J 1.5 Hz), consistent with the 2,5-dienone structure. The C3-H proton (δ 7.20) is coupled to the C5-H proton (δ 6.67) (J 3.0 Hz), this "W" coupling is consistent with the 2,5-dienone structure.

The 4-hydroxy-4-methylcyclohexa-2,5-dienone (93), a lightly coloured oil, $C_8H_9Cl\,O_2$, was eluted third. The infrared spectrum of 2,5-dienone (93) (ν 3450 cm^{-1}, OH, 1678 cm^{-1}, C=O and 1660, 1609 cm^{-1}, C=C) suggests the presence of a hydroxy dienone system. The uv. spectrum (λ_{max} 243 nm; ε 10,500) indicates a cross-conjugated 2,5-dienone structure for compound (93). The ^1H n.m.r. spectrum of the 2,5-dienone (93) exhibits a methyl proton resonance (δ 1.48); this chemical shift is consistent with that expected for a methyl group geminal to a hydroxyl group. These two groups therefore constitute the substituents on the C4-ring carbon atom. The C6-methyl protons (δ 1.90) are coupled to the C5-H proton (δ 6.63) (J 1.5 Hz); this allylic coupling is consistent with the 2,5-dienone structure. The C3-H proton (δ 7.00) is coupled to the C5-H proton (δ 6.63) (J 3.0 Hz), this "W" coupling is consistent with the 2,5-dienone structure (93).

The two 2,5-dienones (92) and (93) were not present in the reaction mixture before chromatography. The exocyclic methylene compound (91) was unaltered by the chromatographic process, being neither formed nor destroyed. The 2,5-dienones (92) and (93) are therefore likely to be formed from the 2,4-dienone (90), which constitutes 95% of the reaction mixture before chromatography. The reaction scheme likely to be involved in the formation of the two 2,5-dienones (92) and (93) on chromatography is presented in Scheme 3.

This reaction scheme, is supported by the observed formation of the 4-hydroxy-2,5-dienone (93), from the

4-chloro-2,5-dienone (92), in a non-polar solvent (pentane) in the presence of silica gel and a small quantity of water.

The structure of the 6-chloro-6-methylcyclohexa-2,4-dienone (90) (refer Block L), was assigned on the basis of its reaction chemistry, in conjunction with the spectroscopic data for the reaction mixture (*c.* 20:1) (in admixture with (91), from which the 2,4-dienone (90) could not be isolated. The C6-methyl proton resonance (δ 1.77) is similar to that observed for other 6-chloro-6-methylcyclohexa-2,4-dienones (refer Table 3.1). Double frequency irradiation experiments show that the C3-H proton (δ 7.03), a doublet, is coupled to the C5-H proton (δ 6.08), a multiplet. In addition the C4-methyl protons (δ 1.98), are coupled to the C5-H proton (J 2.0 Hz). These coupling constants are consistent with the 2,4-dienone conjugated π-structure. The 2,4-dienone (90) is formed by selective *ipso* attack at the *ortho* position bearing a methyl group.

The exocyclic methylene compound (91) was shown to be formed from the 6-chloro-2,4-dienone (90). The crude reaction mixture (*c.* 20:1) (in admixture with the compound (91)), obtained from the reaction of the phenol (89) with chlorine in carbon tetrachloride and pyridine, was subjected to further chlorine addition, in carbon tetrachloride and pyridine, at 20°, for 10 minutes. The resultant product was shown (^{1}H n.m.r.) to consist essentially of the exocyclic methylene compound (91). This experiment was repeated using the 4-chloro-2,5-dienone (92), but this substrate remained unchanged under these reaction conditions. The reaction scheme is therefore likely to involve chlorine attack on the 6-chloro-2,4-dienone (90) (refer Scheme 4). Electrophilic chlorine attack at the C5-position on dienone (90) gives the cationic intermediate (95), which then can lose a proton from the C4-methyl group to give the exocyclic methylene compound (91). The proton loss is likely to be assisted by the pyridine, present in the reaction mixture.

3.3 Mechanism of 2,4-Dienone Formation

All of the reactions, discussed above, involve *ipso* chlorine attack at a methyl-substituted *ortho* site on the parent phenol. The reaction mechanism involved in the formation of these 6-chloro-6-methylcyclohexa-2,4-dienones is almost certainly the SE_2' mechanism, as outlined in Chapter 1. However, a number of mechanistic uncertainties exist. For instance, the reaction could proceed by either *ipso* chlorine attack on the phenol molecule or *ipso* chlorine attack on a pre-equilibrium concentration of the phenoxide ion. This question is particularly pertinent under the above reaction conditions. (*i.e.* in the presence of pyridine, a weak base). It has been suggested that chlorine attack on the phenoxide ion is most favourable at the *ortho* positions whereas, under acidic conditions, chlorine attack on the phenol molecule occurs predominantly at the *para* position.[20] Fisher and Henderson[35] have reported the formation of a number of 4-chloro-4-methylcyclohexa-2,5-dienones from the reaction of 4-alkyl phenols with chlorine in acetic anhydride. For example, the chlorination of 2,4-dimethylphenol (96) was reported to give only the 4-chloro-4-methylcyclohexa-2,5-dienone (97). These workers proposed that *ipso* chlorine attack on phenols in the *para* position is competitive with *ipso* attack at a substituted *ortho* position or even with chlorine attack at an unsubstituted *ortho* position. For instance, the chlorination of 4-methylphenol (98) in acetic anhydride was reported to give the 4-chloro-4-methylcyclohexa-2,5-dienone (99) (28%); also formed were a number of chlorophenol(s) which were not identified (68%). Fischer and Henderson[35] reported that no 6-chloro-2,4-dienones were formed by *ortho* attack, even when 2,6-dimethylphenol or 2,4,6-trimethylphenol were the substrates. For example, the chlorination of 2,4,6-trimethylphenol (100) in acetic anhydride was reported to give the 4-chloro-2,5-dienone (101) (90%), (refer Block M). However, these workers could not exclude the possibility that any 6-chloro-2,4-dienone (102) formed might undergo rapid rearrangement to the thermodynamically more stable 4-chloro-2,5-dienone (101) (Scheme 5a). This rearrangement process is of significance, in 2,4-diakyl systems, since it has been recently found that the 2-*t*-butyl-6-chloro-4,6-dimethylcyclohexa-2,4-dienone (104), formed by the reaction of chlorine in carbon tetrachloride and pyridine with the parent phenol (103), undergoes rapid, acid-catalysed rearrangement to give the 2-*t*-butyl-4-chloro-4,6-dimethylcyclohexa-2,5-dienone (105) (refer Scheme 5b), in acetic acid or indeed, in the presence of the trace amount of DCl in deuteriochloroform.[34]

This observation is significant in terms of the experiments of Fischer and Henderson because, under their reaction conditions an equimolar amount of hydrogen chloride is formed during the *ipso* chlorination process and this is available for the rearrangement reaction. If this rearrangement mechanism is invoked, then the general observation that chlorinations of phenols under acidic conditions yield predominantly the products of *para ipso* attack (*ie* 2,5-dienones), is readily explained.

While the mechanistic details of the formation of the 6-chloro-6-methyl-2,4-dienones, from the reaction of phenols with chlorine in carbon tetrachloride and pyridine, is by no means certain, some comments can be made on the basis of the experiments described in Section 3.2 above. First, the fact that the site of *ipso* attack occurs at the methyl-substituted *ortho* site rather than the chloro-substituted *ortho* site, where such distinction exists, suggests that the *ipso* attacking species is electrophilic in character and is likely to be molecular chlorine. Second, the factors involved in directing the site of *ortho ipso* attack, when both *ortho* positions are methyl-substituted, are not fully understood and are affected, only in part, by steric considerations (*e.g.* reactions in Sections 3.2.8, 3.2.9 and 3.2.10). Third, because polychlorinated phenols are relatively acidic (PK_a ~6-9), as compared with phenol (PK_a 10), it seems probable that the formation of the 6-chloro-6-methyl-2,4-dienones, under the above conditions, involves *ipso* chlorine attack on the phenoxide ion rather than the parent phenol molecule.

2,4-dienone	C6	C2	C3	C5	C4
(65)	1.83(s)Me	-	7.16(d)H	6.45(d)H	-
			J=2.3Hz		
(68)	1.81(s)Me	-	2.40(br)Me	6.52(br)H	-
			J≃0.5Hz		
(70)	1.85(s)Me	-	7.17(s)H	2.17(s)Me	-
(72)	1.80(s)Me	-	2.42(m)Me	2.20(m)Me	-
			J≃0.5		
(73)	1.97(s)Me	-	-	-	-
(75)	1.77(s)Me	2.00(m)Me	6.70(m)H	6.33(d)H	-
		J=0.5Hz	H=1.5Hz		
(77)	1.90(s)Me	2.12(s)Me	-	-	2.29(s)Me
(79)	1.77(s)Me	2.13(m)Me	1.97(m)Me	6.77(q)H	-
		J=0.5Hz	J=1.5Hz		
(81)	1.82(s)Me	1.92(d)Me	6.57(q)H	-	-
		J=1.5Hz			
(82)	1.70(s)Me	2.05(d)Me	-	6.30(q)H	-
			J=0.8Hz		
(84)	1.80(s)Me	2.15(br)Me	2.25(br)Me	-	-
			J≃0.5Hz		
(85)	1.90(s)Me	2.04(s)Me	-	2.24(s)Me	-
(90)	1.77(s)Me	-	7.03(d)H	6.08(m)	1.98(d)Me
			J=2.0Hz		J=2.0Hz

Table 3.1: ^{1}H n.m.r. data for 6-chloro-6-methylcyclohexa-2,4-dienones.

CHAPTER 4

REACTIONS OF 6-CHLORO-6-METHYLCYCLOHEXA-2,4-DIENONES WITH CHLORINE IN ACETIC ACID

4.1 Introduction

6-Chloro-6-methylcyclohexa-2,4-dienones may undergo addition reactions of molecular chlorine to the conjugated diene system in a number of ways. For instance, the three modes of chlorine addition (2,3-, 4,5- and 2,5-) (refer Block N) to the cyclic dienone, can all give rise to polychlorocyclohex-3-enones and polychlorocyclohex-2-enones, of the type discussed in Chapter 2. For each of the above reaction types, the stereochemistry of the addition process must also be determined, not only whether the addition of the two chlorine atoms occurs *cis* or *trans* to each other but also the orientation of such addition relative to the C6 substituents.

The aim of this present work was to investigate some of the factors which dictate the mode of chlorine addition to these 6-chloro-6-methylcyclohexa-2,4-dienones. To this end, a number of 6-chloro-6-methylcyclohexa-2,4-dienones were reacted with chlorine in dry acetic acid, and the products isolated and identified. The 2,4-dienone substrates were chosen, where possible, so that the polychlorocyclohexenones produced were known compounds (*i.e.* they had been characterised in the work discussed previously in Chapter 2). The reactions were all carried out under similar reaction conditions. Generally, the 2,4-dienone substrate was dissolved as a (*c.* 10%) solution in dry acetic acid at 20° in a darkened flask. Chlorine was added (1.2 mole equivalent) as a chlorine/acetic acid solution, and the mixture stirred for one hour. The solvents were removed *in vacuo* at 30° or less, and the resulting crude product mixture separated and the isolated compounds identified. In addition, each 2,4-dienone subjected to the above reaction, was also tested for stability in straight acetic acid at 20° over a period of one hour. For detailed reaction conditions refer to the Experimental Section Relating to Chapter 4.

4.2 Chlorine Addition to 6-Chloro-6-methylcyclohexa-2,4-dienones in Acetic Acid

4.2.1 Reaction of 2,4,6-Trichloro-5,6-dimethylcyclohexa-2,4-dienone (70)

Chlorine addition to the 2,4-dienone (70), as above, gave a mixture (*c*. 3:2) of the two pentachlorocyclohex-3-enones (31) and (32), which were separated on a Chromatotron silica gel plate. These two compounds were found to be identical to the pentachlorocyclohex-3-enones formed in the exhaustive chlorination reaction of 2,3-dimethylaniline (30) in acetic acid and hydrochloric acid (*i.e.* pentachlorocyclohex-3-enones (31) and (32) in a ratio of (*c*. 1:3) discussed earlier in Section 2.2.2).

The 2,4-dienone (70) was shown to be stable in dry acetic acid; no decomposition or isomerisation was observed over the period of one hour, at 20°. The mode of chlorine addition is therefore 2,3-addition, as indicated (refer Block N). The stereochemistry of this 2,3-chlorine addition cannot be determined because the C6-*gem*-dichloro substituents in compounds (31) and (32) are indistinguishable.

4.2.2 Reaction of 2,4-Dibromo-5,6-dimethylphenol (106) with chlorine in acetic acid

In order to ascertain the stereochemistry of the 2,3-chlorine addition to the 2,4-dichloro-2,4-dienone (70) above, an attempt was made to prepare the analogous 2,4-dibromo-2,4-dienone (111) (refer Block N). However, using the experimental method discussed in Chapter 3, (which was used to produce all other 6-chloro-6-methylcyclohexa-2,4-dienones) an unstable mixture of compounds which rapidly decomposed was obtained. To overcome this problem the parent phenol (106) was reacted directly with chlorine (2.2 mole equivalent) in dry acetic acid. This reaction of 2,4-dibromo-5,6-dimethylphenol (106) gave a mixture (*c*. 5:8:2:2) of the dibromo-trichloro-cyclohex-3-enones (107), (108), (109) and (110) (refer Block O), representing all possible stereoisomers. This mixture was separated by repetitive passes on a Chromatotron using either a silica gel plate or a silica gel polyethylene glycol plate, the elution order was (109), (110), (107) and (108).

The structure of these compounds were assigned on the basis of their spectroscopic properties and by comparison with the cyclohex-3-enone (107), the structure of which was confirmed by single-crystal X-ray analysis. A perspective drawing of the dibromo-trichlorocyclohex-3-enone (107), $C_8H_9Br_2Cl_3O$, m.p. 130-131°, is presented in Figure 10* and the corresponding atomic coordinates are given in Table 10*. The cyclohex-3-enone ring structure is in a twist-boat conformation and closely resembles the conformation adopted by the polychlorocyclohex-3-enones (refer Table 16)*, as

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* (refer Appendix 1)

shown by the relevant torsion angles. C(3)-C(4)-C(5)-C(6) 27(1)° and C(1)-C(2)-C(3)-C(4) 7(1)°. The C5-Cl5 bond is in the flagpole orientation, C(3)-C(4)-C(5)-Cl(5) 93(1)°, and the C(6)-substituents Cl(6) and Br(6) adopt the axial and equatorial positions respectively, as shown by their torsion angles, relative to the carbonyl function, O(1)-C(1)-C(6)-Cl(6) 110(1)° and O(1)-C(1)-C(6)-Br(6) 7(1)°. These structural features are also observed for other polychlorocyclohex-3-enones (refer Table 16). By comparison, the C(2) substituents Cl(2) and C(7), adopt orientations with torsion angles, relative to the carbonyl function, much more similar in magnitude O(1)-C(1)-C(2)-Cl(2) -45(1)° and O(1)-C(1)-C(2)-C(7) 69(1)°. The consequence of this similarity in torsion angles is that the C(2)-Cl(2)/C(1)=O(1) dipole-dipole interaction, and hence the infrared carbonyl stretching frequency, would not be dramatically different for C2-epimers, an effect observed in other polychlorocyclohex-3-enones, discussed in Chapter 2.

The structures of the remaining compounds (108) (109) and (110) were assigned on the assumed basis that (i) the cyclohex-3-enone ring systems were all in a conformation similar to that observed for compound (107) (*i.e.* twist-boat) and (ii) that the C5-Cl(5) bond was in the flagpole orientation in all cases. These two assumptions seem reasonable because (i) all of the polychloro-cyclohex-3-enone structures, determined by X-ray analysis, exhibit similar twist-boat conformations (refer Table 16) and (ii) all the polychloro-cyclohex-3-enones discussed previously having the substituents chlorine and hydrogen at C5, have the C5-Cl bond in the flagpole orientation. The similarity of the

C5-H proton ^1H n.m.r. chemical shifts (refer Block O) for these compounds supports this latter assumption.

Making the above assumptions, the structure of the cyclohex-3-enone (108) can be assigned by comparison of the infrared and ^1H n.m.r. data with those observed for compound (107).

The difference in the infrared carbonyl stretching frequencies between compounds (107) (ν 1764 cm^{-1}) and (108) (ν 1754 cm^{-1}), suggests that these compounds differ in stereochemistry at C6. Such a shift in the infrared carbonyl stretching frequency (10 cm^{-1}) is consistent with the difference observed between the infrared carbonyl stretching frequencies of α-bromocyclohexanones and α-chlorocyclohexanones, the halogen being in the equatorial orientation.[25,26] The ^1H n.m.r. C2-methyl proton resonances of compounds (107) (δ 2.05) and (108) (δ 2.13), show that the C2-methyl protons are deshielded by a *syn*-axial C6-chlorine relationship in compound (107) and that the C2-methyl protons are further deshielded in compound (108) ($\Delta\delta$ 0.08) by a *syn*-axial C6-bromine relationship. The compounds (107) and (108) are therefore simply C6-epimers.

The structure of cyclohex-3-enone (110) is readily established by comparison of its spectroscopic data with those observed for compound (108) (δ 2.13), suggesting that a *syn*-axial C6-bromine/C2-methyl relationship is absent in compound (110). The similarity of the infrared carbonyl frequencies of compound (108) (ν 1754 cm^{-1}) and compound (110) (ν 1753 cm^{-1}) indicates a common stereochemistry at C6, for both compounds, and is consistent with the compounds (108) and (110) being simply C2-epimers.

The structure of the compound (109) which was obtained only in admixture with (110) (*c.* 1:1), is determined by exclusion. The upfield position of the ^1H n.m.r. C2-methyl proton resonance of compound (109) (δ 1.88) is similar to that observed for compound (109) (δ 1.88), consistent with a common stereochemistry at C2 for these compounds. The infrared carbonyl stretching frequency of compound (110) (ν 1757 cm^{-1}) (obtained from the mixture (*c.* 1:1) (110) (109)) is shifted to a higher frequency relative to that observed for compound (109) (ν 1753 cm^{-1}), consistent with these two compounds being C6-epimers.

It is evident from the range of stereoisomers formed in this reaction, that both *cis* and *trans* 2,3-chlorine addition to the 2,4-dienone (111) occurs. It is therefore probable that both *cis* and *trans* 2,3-chlorine addition to the analogous 2,4-dienone (70), also occurs (refer Section 4.2.1).

4.2.3 Reaction of 2,4,6-Trichloro-6-methylcyclohexa-2,4-dienone (66)

Chlorine addition to the 2,4-dienone (66), as above, gave a mixture (*c.* 5:5:1) of the pentachlorocyclohex-3-enones (28) and (29) and the pentachlorocyclohex-2-enone (112) (refer Block P) which were separated on a Chromatotron silica gel plate. The two pentachlorocyclohex-3-enones (28) and (29) were found to be identical to the pentachlorocyclohex-3-enones formed in the exhaustive reaction of 2,4-dichloro-6-methylphenol (27) with chlorine in acetic acid and hydrochloric acid (*i.e.* compounds (28) and (29) in a ratio of (*c.* 3:1) as discussed previously in Section 2.2.1).

The structure of the pentachlorocyclohex-2-enone (112) was assigned on the basis of its spectroscopic properties and by comparison with the cyclohex-2-enones (48) and (49), the structures of which were determined by single-crystal X-ray analysis (refer Section 2.4.1, Block F).

The infrared carbonyl stretching frequency of cyclohex-2-enone (112) (ν 1721 cm^{-1}) indicates the presence of a conjugated ketone and is confirmed by the uv. spectrum (λ_{max} 246 nm; ε 11,700). The ^1H n.m.r. spectrum exhibits a signal (δ 7.40) corresponding to the olefinic C3-H proton, a signal (δ 5.02) corresponding to the C5-methine proton and the signal (δ 1.90) corresponding to the C6-methyl proton resonance. This ^1H n.m.r. data corresponds closely to the observed for the 5,6-*trans*-dichloro cyclohex-2-enone (48) (*cf.* (δ 5.12), C5-H and (δ 1.89), C6 methyl), suggesting the same 5,6-*trans*-dichloro stereochemistry for cyclohex-2-enone (112). Furthermore, the infrared carbonyl stretching frequency of cyclohex-2-enone (112) (ν 1721 cm^{-1}) is close to that observed for the cyclohex-2-enone (48) (ν 1718 cm^{-1}). The C6-epimer of cyclohex-2-enone (48), compound (49) exhibits an infrared carbonyl stretching band at lower frequency (ν 1708 cm^{-1}), suggesting that the cyclohex-2-enones (112) and (48) have common stereochemistry at C6 (*i.e.* equatorial chlorine, axial methyl group).

The pentachlorocyclohex-3-enones (28) and (29) arise from 2,3-chlorine addition to the 2,4-dienone (66). The stereochemistry of this 2,3-addition is not determined since no distinction can be made of the C6-*gem*-dichloro-substituents, but it is likely that both *cis* and *trans* addition occurs, by analogy to the reaction of 2,4-dibromo-5,6-dimethyl phenol (106) above. The pentachlorocyclohex-2-enone (112) arises from 4,5-chlorine addition to the 2,4-dienone (66). It is likely that attack occurs at C5, *trans* to the C6-chlorine substituent. No comment can be made as to the stereochemistry of the 4,5-chlorine addition itself, because the C4-*gem*-dichloro substituents are indistinguishable. The 2,4-dienone (66) was shown to be stable in dry acetic acid; no decomposition or isomerisation was observed over the period of 1 hour at 20°.

4.2.4 Reaction of 4,6-Dichloro-2,3,6-trimethylcyclohexa-2,4-dienone (79)

Chlorine addition to the 2,4-dienone (79), as above, gave a mixture (*c.* 5:2) of the tetrachlorocyclohex-3-enones (37) and (38), (refer Block P) which were separated on a Chromatotron silica gel plate. These tetrachlorocyclohex-3-enones were shown to be identical to the tetrachlorocyclohex-3-enones formed in the reaction of 2,3,6-trimethylphenol (36) with chlorine in acetic acid and hydrochloric acid (*i.e.* compounds (37) and (38) in a ratio (*c.* 3:1), refer Section 2.3.1, Block E).

The tetrachlorocyclohex-3-enones (37) and (38), are formed by *cis* and *trans* 2,5-chlorine addition respectively, to the 2,4-dienone (79). It is likely that chlorine attack is initiated at the C5 ring site and that this initial attack occurs *trans* to the C6-chlorine substituent. The 2,4-dienone (79) was shown to be stable in dry acetic acid; no decomposition or isomerization was observed over the period of 1 hour, at 20°.

4.2.5 Reaction of 2,4,6-Trichloro-3,6-dimethylcyclohexa-2,4-dienone (68)

Chlorine addition to the 2,4-dienone (68), as above, gave a mixture (*c.* 11:8:9:3) of the two pentachlorocyclohex-3-enones (25) and (26) and the pentachlorocyclohex-2-enones (48) and (49) (refer Block P), which were separated on a chromatotron silica gel plate. These four compounds were found to be identical to those formed in the reaction of 2,5-dimethylphenol (41) with chlorine in acetic acid and hydrochloric acid (*i.e.* compounds (25),(26),(48) and (49), refer Section 2.4.1, Block F).

The two pentachlorocyclohex-3-enones (25) and (26) are formed by 2,5-chlorine addition to dienone (68). The stereochemistry of this 2,5-addition of chlorine cannot be determined because the C2-*gem*-dichloro substituents are indistinguishable. The pentachlorocyclohex-2-enones (48) and (49) are formed by 4,5-chlorine addition to 2,4-dienone (68). Again the stereochemistry of this 4,5-chlorine addition is uncertain, because the C4-*gem*-dichloro substituents are indistinguishable. Of note is the fact that both 5,6-*cis*- and 5,6-*trans*-dichloro stereoisomers are formed, in the above reaction, for both the cyclohex-3-enones and the cyclohex-2-enones.

The 2,4-dienone (68) was shown to be stable in dry acetic acid; no decomposition or isomerisation was observed over the period of 1 hour, at 20°.

4.2.6 Reaction of 4,6-Dichloro-2,6-dimethylcyclohexa-2,4-dienone (75)

Chlorine addition to 2,4-dienone (75), as above, gave a mixture (*c*. 18:8:7:12) of the tetrachlorocyclohex-3-enones (40) and (41), the tetrachlorocyclohex-2-enone (113) and the acetoxy compound (114) (refer Block Q), which were separated on a Chromatotron silica gel plate.

The tetrachlorocyclohex-3-enones (40) and (41) were shown to be identical with the tetrachlorocyclohex-3-enones formed in the exhaustive chlorination reaction of 2,6-dimethylaniline (39) in acetic acid and hydrochloric acid; (*i.e.* compounds (40) and (41) in a ratio of (*c*. 2:3), refer Section 2.3.2, Block E).

The structure of the cyclohex-2-enone (113) (refer Block Q) was determined from its spectroscopic properties. The infrared spectrum (ν 1701, C=O and 1640 cm^{-1}, C=C) confirms the presence of a conjugated ketone. The ^{1}H n.m.r. spectrum exhibits the C2-methyl proton resonance, a doublet (δ 1.98), coupled to the C3-H proton, a quartet (δ 7.00) (J 1.5 Hz), consistent with allylic coupling in the cyclohex-2-enone structure. The C5-H methine proton resonance (δ 5.00) and the C6-methyl proton resonance (δ 1.85) are close to those observed for the cyclohex-2-enone (48) (*c.f.* (δ 5.12), C5-H, (δ 1.89), C6-methyl). The stereochemistry of compound (113) is therefore likely to be 5,6-*trans*-dichloro, with both chlorine groups equatorial, by analogy to cyclohex-2-enone (48), the structure of which was determined by single-crystal X-ray analysis.

The structure of the acetoxy compound (114) was determined by single-crystal X-ray analysis. A perspective drawing of this structure (114) is presented in Figure 11 and the corresponding atomic coorindates given in Table 11. the cyclohex-3-enone ring structure is in a "flattened" half-chair conformation, as shown by the relevant torsion angles C(3)-C(4)-C(5)-C(6) -18.9(4)° and C(1)-C(2)-C(3)-C(4) -2.2(4)°. This conformation is notably different from that observed for other cyclohex-3-enones (refer Table 16), which adopt twist-boat conformations. The C(5)-Cl(5) bond is in the pseudoaxial orientation, C(3)-C(4)-C(5)-Cl(5) 106.4(3)°, and the C6-substituents Cl(6) and C(10) adopt the axial and equatorial orientations respectively, as shown by their torsion angles, relative to the carbonyl function, O(1)-C(1)-C(6)-Cl(6) -103.5(3)° and O(1)-C(1)-C(6)-C(10) 12.0(4)°. These structural features are similar to those observed in other cyclohex-3-enones. The C2-substituents, methyl (C7) and acetoxy (021), adopt orientations with torsion angles, relative to the carbonyl function, more similar in magnitude, O(1)-C(1)-C(2)-C(7) 72.7(4)° and O(1)-C(1)-C(2)-O(21) -39.2(4)°. The spectroscopic data recorded for this compound are in accord with the above determined structure.

The tetrachlorocyclohex-3-enones (40) and (41), are formed by *cis*- and *trans*- 2,5-chlorine addition respectively, to the 2,4-dienone (75). Initial attack is likely to occur at C5, *trans*, with respect to the C6-chlorine atom of the 2,4-dienone (75).

Attempts to prepare the acetoxy compound (114) by solvolysis of either the tetrachlorocyclohex-3-enones (40) and (41) or the cyclohex-2-enone (113) in acetic acid at 20°C, over 24 hours, were unsuccessful. The compounds (40), (41) and (113) were shown to be stable under the above conditions. It is therefore likely that the acetoxy compound (114) is formed by 2,5-addition to the 2,4-dienone (75). It seems reasonable to suggest that initially this 2,5-addition involves electrophilic chlorine attack at the C5-position of the 2,4-dienone (75), to give the cationic intermediate (117). Capture of this cationic intermediate (117) by acetate ion at C2, gives the acetoxy compound (114). The acetoxy compound (114) is therefore formed in competition with the tetrachlorocyclohex-3-enones (40) and (41) by competitive capture of the cationic intermediate (117) by either acetate ion or chloride ion respectively.

The 2,4-dienone (75) was shown to be stable in dry acetic acid; no decomposition or isomerisation was observed over the period of 1 hour, at 20°.

4.2.7 Attempted Reaction of 4,5,6-Trichloro-2,3,6-trimethylcyclohexa-2,4-dienone (84) and 3,5,6-Trichloro-2,4,6-trimethylcyclohexa-2,4-dienone (77)

Attempted chlorine addition to the dienone (84), as above, gave only unreacted dienone (84) after 75 minutes. A similar lack of reactivity was observed for the 2,4-dienone (77). In both cases, the 2,4-dienones substrates (84) and (77) are substituted at C5 by chlorine. It is therefore likely that initial electrophilic chlorine attack on these dienones at the C5-position, is hindered sterically, and deactivated electronically.

4.2.8 Reaction of 2,4,6-Trichloro-3,5,6-trimethylcyclohexa-2,4-dienone (72)

Chlorine addition to the 2,4-dienone (72), as above, gave a mixture (*c*. 5:4) of the cyclohex-3-enone (115) and the cyclohex-2-enone (116) (refer Block R), which were separated on a Chromatotron silica gel plate. Conversion of the 2,4-dienone (72) to the above compounds (115) and (116) was shown (^{1}H n.m.r.) to be approximately 10% complete after a reaction time of 1 hour. The reaction time was therefore extended to 18 hours to get full conversion of the 2,4-dienone (72) to the above addition compounds.

The structure of the cyclohex-3-enone (115) was determined by single-crystal X-ray analysis. A perspective drawing of this compound (115) is presented in Figure 12 and the corresponding atomic coordinates are given in Table 12. The structure determined has two independent molecules in the asymmetric unit. These molecules were shown using the programme XFIT,[29] to be non-crystallographic mirror images of each other, with only very minor differences in conformation; therefore, for the purpose of this discussion, only one enantiomer is discussed in detail.

The cyclohex-3-enone ring structure adopts a twist-boat conformation similar to that observed by other cyclohex-3-enones (refer Table 16), as shown by the relevant torsion angles C(13)-C(14)-C(15)-C(16) -27.8(8)° and C(11)-C(12)-C(13-C(14) 5.9(6)°. The C6-substituents Cl(15) and C(19) adopt the axial and equatorial orientations respectively, as shown by their torsion angles, relative to the carbonyl function, O(11)-C(11)-C(16)-Cl(15) -108.7(4)° and O(11)-C(11)-C(16)-C(19) 7.9(6)°. The C2-substituents Cl(11) and Cl(12), adopt positions with torsion angles, relative to the carbonyl function, more similar in magnitude O(11)-C(11)-C(12)-Cl(11) 69.6(5)° and O(11)-C(11)-C(12)-Cl(12) -45.0(5)°. The C(15)-Cl(14) bond adopts the flagpole orientation, as observed in other polychlorocyclohex-3-enones, as shown by the torsion angle C(13)-C(14)-C(15)-Cl(14) 81.0(5)°

(refer Table 16). The spectroscopic data recorded for this compound (115) are in accord with the above structure. Morita and Dietrich[22] reported this compound in admixture with the cyclohex-2-enone (116). The structure proposed by those workers is in accord with that determined in this present work.

The structure of the cyclohex-2-enone (116) was assigned on the basis of its spectroscopic properties and is in agreement with the structure proposed earlier by Morita and Dietrich.[22]

The cyclohex-3-enone (115) is formed by 2,5-chlorine addition to the 2,4-dienone (72). It is probable that both *cis*- and *trans*- 2,5-addition occurs, although no distinction can be made because the C2-substituents (*gem*-dichloro) are indistinguishable. It is likely that this 2,5-chlorine addition is initiated by electrophilic chlorine attack at the C5-position of the 2,4-dienone (72), *trans*, with respect to the C6-chlorine substituent.

The cyclohex-2-enone (116) is formed by 4,5-chlorine addition to the 2,4-dienone (72). It is likely that the reaction is initiated by electrophilic chlorine attack on the 2,4-dienone (72) at C5, *trans* to the C6-chlorine substituent. The 2,4-dienone (72) was shown to be stable in dry acetic acid; no isomerisation or decomposition was observed over a period of 1 hour at 20°.

4.2.9 Reaction of 4,5,6-Trichloro-2,6-dimethylcyclohexa-2,4-dienone (81) and 3,4,6-Trichloro-2,6-dimethylcyclohexa-2,4-dienone (82)

Chlorine addition to the mixture (*c.* 3:2) of the

2,4-dienones (81) and (82), as above, gave a mixture (*c.* 6:5) of the two pentachlorocyclohex-3-enones (43) and (44) (refer Block R), which were separated on a Chromatotron silica gel plate. These two cyclohex-3-enones were shown to be identical with the compounds formed in the exhaustive chlorination reaction of 2,6-dimethylphenol (42) in acetic acid and hydrochloric acid (*i.e.* pentachlorocyclohex-3-enones (43) and (44) in a ratio of (*c.* 3:2), refer Section 2.3.3, Block E).

The pentachlorocyclohex-3-enones (43) and (44) can be formed by either *trans* 2,3-chlorine addition to the 2,4-dienone (81) or *cis*- and *trans*- 2,5-chlorine addition respectively, to 2,4-dienone (82). It is likely that the 2,5-chlorine addition to dienone (82) is initiated by electrophilic chlorine attack at the C5-position, *trans*, with respect to the C6-chlorine substituent.

The 2,4-dienone mixture (*c.* 3:2) (81) and (82) was shown to be stable in dry acetic acid; no decomposition or isomerisation was observed over the period of 1 hour, at 20°.

4.3 Discussion: Chlorine Addition to 6-Chloro-6-methylcyclohexa-2,4-dienones

An examination of the modes of chlorine addition to the 2,4-dienones discussed above, shows two distinct groups: (i) those 2,4-dienones (66), (70) and (81) (refer Block S) which undergo 2,3-addition probably initiated by attack at C 3 and (ii) those 2,4-dienones (79), (68), (75), (82), (72) and (66) (refer Block S) which add chlorine initiated by attack at C5. These latter 2,4-dienones undergo 2,5-addition predominantly, with some 4,5-addition also occurring to give minor products. In order to investigate these various reaction types the reactions of three 2,4-dienone substrates were subjected to detailed examination. The reaction of these 2,4-dienones (70), (66) and (79) with chlorine in acetic acid were repeated with various amounts of either hydrogen chloride or sodium acetate. The products thus formed were identified and their ratios determined by ^{1}H n.m.r. Any previously unidentified products, were isolated and identified. Details of the reaction conditions and product analysis are given in the Experimental Section Relating to Chapter 4.

4.3.1 2,4,6-Trichloro-5,6-dimethylcyclohexa-2,4-dienone (70)

The results of the above range of experiments, with 2,4-dienone (70) as the substrate, are summarized in Block T. Reaction of the 2,4-dienone (70) with dry acetic acid and chlorine in the presence of hydrogen chloride (1.0 mole equivalent) for 30 minutes, gave the two pentachlorocyclohex-3-enones (31) and (32) in a ratio of (*c.* 5:2). Replacing the hydrogen chloride with concentrated hydrochloric acid and repeating the above experiment, gave a mixture (*c.* 1:11:5) of the 2,4-dienone (70) and the pentachlorocyclohex-3-enones (31) and (32). The reaction of the 2,4-dienone (70) with chlorine in dry acetic acid over 30 minutes gave a mixture (*c.* 6:2:1) of the 2,4-dienone (70) and the pentachlorocyclohex-3-enones (31) and (32). Repeating this reaction, in the presence of sodium acetate (0.1 mole equivalent), over 1 hour gave no reaction. The 2,4-dienone (70) was shown to be stable in acetic acid at 20° over the period of 1 hour, and was also shown to be stable in acetic acid in the presence of hydrogen chloride (1.0 mole equivalent).

The formation of the pentachlorocyclohex-3-enones (31) and (32) by 2,3-chlorine addition to the 2,4-dienone (70) is suppressed by the presence of a small amount of sodium acetate in the reaction mixture. In contrast, the formation of these compounds (31) and (32) in the presence of hydrogen chloride occurs more rapidly than is observed in acetic acid alone. The 2,3-double bond of 2,4-dienone (70) is deactivated towards electrophilic attack by the carbonyl functional group, but an alternative mechanism has been shown to be available, which has been described as "nucleophilic".[41] Robertson *et al.*[39,40] established this mechanism as occuring in a range of chlorination and bromination addition reactions of $\alpha\beta$-unsaturated ketones, aldehydes and quinones, in competition with the more conventional electrophilic halogen addition mechanism. It was found that the "nucleophilic" mechanism was enhanced under acidic conditions and that this reaction process was strongly acid-catalysed by the hydrogen hadides. Furthermore these workers were able to suppress this "nucleophilic" process by the addition of a small quantity of sodium acetate to the reaction mixture, with the electrophilic halogen addition being essentially unaffected. It was also found that the presence of water in the reaction mixture profoundly decreases the rate of the "nucleophilic" process, presumably by decreasing the acidity of the reaction mixture. Although the precise steps of this "nucleophilic" reaction are yet unknown, the process almost certainly involves pre-equilibrium protonation of the carbonyl group, followed by either chloride or trichloride ion attack. The halide ion almost certainly has a specific role to play in this mechanism, due to the specific nature of the hydrogen halide catalysis.[41]

The above observations are entirely consistent with a similar nucleophilic reaction mechanism being involved with the 2,3-chlorine addition to 2,4-dienone (70). Such a process might be envisaged to occur along the lines of the reaction scheme outlined in Scheme 6.

4.3.2 2,4,6-Trichloro-6-methylcyclohexa-2,4-dienone (66)

The results of the above range of experiments with the 2,4-dienone (66) as the substrate, are summarized in Block U. Reaction of the 2,4-dienone (66) with chlorine in acetic acid in the presence of hydrogen chloride (1.0 mole equivalent) for 30 minutes, gave the mixture (*c.* 12:12:1) of the pentachlorocyclohex-3-enones (28) and (29) and the cyclohex-2-enone (112). Replacing the hydrogen chloride with concentrated hydrochloric acid and repeating the above experiment, gave a mixture (*c.* 6:6:1) of the pentachlorocyclohex-3-enones (28) and (29) and the cyclohex-2-enone (112). The reaction of the 2,4-dienone (66) with chlorine in acetic acid for 30 minutes, gave a mixture (*c.* 5:5:3:14) of the two pentachlorocyclohex-3-enones (28) and (29), the cyclohex-2-enone (112) and unreacted 2,4-dienone (66). Repeating this experiment in the presence of a small quantity of sodium acetate (0.1 mole equivalent), gave a mixture (*c.* 1:4) of the cyclohex-2-enone (112) and unreacted 2,4-dienone (66).

The formation of the pentachlorocyclohex-3-enones (28) and (29) by 2,3-chlorine addition to the 2,4-dienone (66) is suppressed by the presence of a small amount of sodium acetate in the reaction mixture. In contrast, the formation of the cyclohex-2-enone (112), by 4,5-chlorine addition, is not greatly affected by the presence of sodium acetate.

In the presence of hydrogen chloride the rate of formation of the pentachlorocyclohex-3-enones (28) and (29) is greatly increased, and in fact dominates over the competing electrophilic 4,5-chlorine addition. These observations are consistent with the 2,3-chlorine addition reaction to 2,4-dienone (66) having a mechanism analogous to that proposed for the 2,3-chlorine addition to 2,4-dienone (70) above, *i.e.* the hydrogen chloride acid-catalysed "nucleophilic" mechanism.

4.3.3 4,6-Dichloro-2,3,6-trimethylcyclohexa-2,4-dienone (79)

The results of the above series of experiments with the 2,4-dienone (70) as the substrate, are summarized in Block V. The reaction of the 2,4-dienone (79) with chlorine in acetic acid in the presence of hydrogen chloride (1.0 mole equivalent) for 1 hour, gave the mixture (*c.* 5:4) of the tetrachlorocyclohex-3-enones (37) and (38). This addition reaction is rapid and in fact goes almost to completion in 2 minutes in acetic acid, even without the presence of added hydrogen chloride, giving the tetrachlorocyclohex-3-enones (37) and (38). Some decomposition of the 2,4-dienone (79) to the parent phenol (36), by loss of the *ipso*-chlorine substituent, is observed in acetic acid/hydrogen chloride solution.

The addition of a small quantity of sodium acetate (0.1 mole equivalent) however, gives rise to two additional compounds (118) and (119). Increasing the concentration of the sodium acetate increases the proportion of these two compounds (118) and (119) formed.

The structures of the acetoxy cyclohex-3-enone (118) and the cyclohex-2-enone (119) were determined by comparison of the spectroscopic data (refer Table 4.1) for analogous known compounds, *i.e.* compounds (114) and (48) respectively (refer Block W). The key points of consideration are: (i) The infrared spectrum of acetoxy compound (118) confirms the presence of the acetoxy group and is closely similar to that observed for known compound (114). (ii) The ^{1}H n.m.r. spectrum of acetoxy compound (118) is similar to that observed for the known compound (114) and in particular, the similarity of the C5-H and C6-methyl signals suggests a common 5,6-*trans*-dichloro stereochemistry for both these compounds.

The infrared spectrum of the cyclohex-2-enone (119) (refer Table 4.1) suggests the presence of a conjugated carbonyl group. The difference in carbonyl stretching frequencies between compounds (119) and (48) is attributable to the difference in C2-substituents. The ^{1}H n.m.r. signals for the C5-H and C6-Me protons are similar for compound (119) and known compound (48) suggesting a common 5,6-*trans*-dichloro stereochemistry for both these compounds. The C2-Me and C3-Me signals are consistent with the cyclohex-2-enone structure of compound (119).

The 2,5-addition of chlorine to the 2,4-dienone (79) (refer Block V) could not be suppressed by the addition of sodium acetate to the reaction mixture, even at ten times the concentration required to halt the 2,3-additions of

Infrared data for compounds (118),(119),(114) and (48)

Compound	C=O	AcO	AcO	C=C	(cm^{-1})
(118)	1752	1742	1232		
(114)	1745	1735	1230		
(119)	1697	-	-	1627	
(48)	1718	-	-	1607	

^1H n.m.r. data for compounds (118),(119),(114) and (48)

Compound	C2	OAc	C3	C5	C6	(δ ppm)
(118)	1.90	2.07	1.90(Me)	4.98(H)	1.82	
(114)	1.93	2.07	5.93(H)	4.87(H)	1.79	
(119)	1.98	-	2.35	5.07(H)	1.82	
(48)	-	-	2.57	5.12(H)	1.89	

TABLE 4.1

chlorine to 2,4-dienones (70) and (66). The "nucleophilic" mechanism proposed for the 2,3-additions of chlorine can therefore be excluded as the mechanism for the 2,5-chlorine addition reaction. The formation of the acetoxy compound (119) is consistent with an electrophilic mechanism, as outlined in Scheme 7. Electrophilic chlorine attack occurs at C5, because the C2-position is deactivated towards electrophilic attack by the carbonyl group. The cationic intermediate formed can be expressed in terms of the canonical forms (120) and (121). The majority of the products (37), (38) and (118) are formed by attack of chloride ion at C2 [canonical form (121)] under acidic conditions. In the presence of sodium acetate, chloride ion attack is in competition with attack at C2 by acetate ion. Increasing the sodium acetate concentration would then increase the proportion of acetoxy compound (118) formed, as is observed. The cyclohex-2-enone (119) arises by chloride ion attack at C4 [canonical form (120)] of the cationic intermediate. Increasing proportions of this cyclohex-2-enone (119) are formed upon addition of increasing amounts of sodium acetate to the reaction mixture. It is not clear why increased sodium acetate concentrations should lead to this result.

CHAPTER 5

EXPERIMENTAL METHODS

5.1 Apparatus, Materials and Instrumentation

Infrared spectra were recorded on either a Shimadzu IR-27G or Pye-Unicam SP3 spectrophotometers for liquid films and Nujol mulls. Ultraviolet absorption spectra were obtained using either a Varian Superscan 3 or Varian DMS 100 spectrophotometers with chloroform or cyclohexane as solvent.

Routine ^{1}H n.m.r. spectra were obtained for deuteriochloroform with trimethylsilane as an internal reference on a Varian T60 spectrometer. ^{1}H n.m.r. (variable temperature) and ^{13}C n.m.r. Fourier Transform spectra were recorded on a Varian CFT-20 F.T. N.M.R. spectrometer for deuteriochloroform with trimethylsilane as an internal reference. N.M.R. spectral parameters were derived by first-order analysis and, wherever required or possible, confirmed by double irradiation experiments. All chemical shifts are expressed as parts per million (ppm) downfield from TMS and are quoted as position (δ), multiplycity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet), relative integral (H=1, Me=3) and coupling constants (J,Hz).

Microanalyses were carried out by Professor A.D. Campbell and associates, University of Otago.

Melting points were determined in open tubes and are uncorrected.

Preparative scale chromatography was routinely carried out utilising a Chromatotron (a preparative, centrifugally accelerated, radial, thin-layer chromatograph. Model 7924, Harrison Research Inc.) equipped with rotors coated with Silica gel PF-254 (with $CaSO_4 \cdot \frac{1}{2}H_2O$ type 60 for tlc, Merck: E.M. Laboratories Incorporated, item number 7749) of various thicknesses (generally 2mm).

All solvents used were either of analytical grade (AR) or were purified and dried according to standard procedures.[43] "Light Petroleum" refers to petroleum ether (50-70°C) distilled off phosphorous pentoxide. "Dry acetic acid" refers to Analar glacial acetic acid from which the water had been azeotropically removed with benzene, then fractionated.[46]

The phenols and anilines used were obtained either from various chemical suppliers and used without further purification or were prepared by chlorination of the appropriate alkyl phenol. Those preparations, where only *ortho* and/or *para* chlorination was required, were carried out in chloroform with an appropriate quantity of SO_2Cl_2, and are not further mentioned. Those preparations where *meta* chlorination is involved, usually obtained by indirect methods, are given in Section 5.5.

5.2 Experimental Section Relating to Chapter 2

Chlorination of 3-Chloro-6-methylaniline

Chlorine was bubbled slowly through a stirred solution at 20° of the aniline (5g) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) in a darkened flask for 3 hours. The excess chlorine gas was purged with nitrogen and the solid ammonium chloride produced in the reaction filtered off. The solvents were removed first by distillation under reduced pressure (<35°) and then by drying under reduced pressure for several hours (*c.* 3 mm).

The crude product (5.65 g) was shown (^{1}H n.m.r.) to contain <75% of the required compounds (22) and (23), (*c.* 1:1). Crystallization of the crude material from light petroleum gave a mixture (*c.* 1:1) of the hexachlorocyclohex-3-enones (22) and (23), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

trans-2,2,3,4,5,6-hexachloro-6-methylcyclohex-3-enone (22), m.p. 109.5-110°, (X-ray structure determination, see Appendix 1) ν_{max} (Nujol) 1760, C=O; 1622 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.97, Me; 4.81, H5. [Lit.[21] for compound assigned incorrect structure, m.p. 109-110°, ν_{max} (Nujol) 1760, C=O; 1620 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.99, Me; 4.88, H5.]

Eluted second (pentane):

cis-2,2,3,4,5,6-Hexachloro-6-methylcyclohex-3-enone (23) m.p. 122.5-123°, ν_{max} (Nujol) 1778, C=O; 1752 w; 1612 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.10, Me; 4.79, H5. [Lit.[21] for compound assigned incorrect structure, m.p. 123-124°, ν_{max} (Nujol) 1772, C=O; 1745 w; 1611 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.12, Me; 4.87, H5.]

Chlorination of 2,5-Dimethylaniline

Chlorine was bubbled through a stirred solution at 20° of the aniline (5 g) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) in a darkened flask for 3 hours. Excess chlorine gas was purged with nitrogen, and the solid ammonium chloride produced in the reaction filtered off. The solvents were removed first by distillation under reduced pressure (<35°) and then by drying under reduced pressure (*c.* 3 mm) for several hours.

The crude product (9.39 g) was shown (^{1}H n.m.r.) to contain >60% (total) of the required compounds (25) and (26), (*c.* 2:1). Crystallization of the crude product from diethylether/light petroleum gave a mixture (*c.* 2:1) of the two pentachlorocyclohex-3-enones (25) and (26), which were separated on the Chromatotron on a 2 mm silica plate.

Eluted first (pentane) was: *trans*-2,2,4,5,6-pentachloro-3,6-dimethylcyclohex-3-enone (25), m.p. 129-130° (Found: C, 32.3; H, 2.4; Cl, 59.8. $C_8H_7Cl_5O$ requires C, 32.4; H, 2.4; Cl, 59.8%). ν_{max}(Nujol) 1758, C=O; 1645 cm^{-1}, C=C. ^{1}H n.m.r. (CDCl$_3$) δ 1.94, 6-Me; 2.29, 3-Me; 4.71, br s, H5. [Lit.[22] for compound assigned incorrect structure, m.p. 132-133°, ν_{max} (Nujol) 1747, C=O; 1640 cm^{-1} C=C. ^{1}H n.m.r. (CDCl$_3$) δ 1.93, 6-Me; 2.30, 3-Me; 4.71, H5.]

Eluted second (5% diethylether/light petroleum) was: *cis*-2,2,4,5,6-pentachloro-3,6-dimethylcyclohex-3-enone (26) m.p. 116-118° (dec.) (Found: C, 32.4; H, 2.5; Cl, 59.8. $C_8H_7Cl_5O$ requires C, 32.4; H, 2.4; Cl, 59.8%). ν_{max} (Nujol) 1772, C=O; 1646 cm^{-1}, C=C. ^{1}H n.m.r. (CDCl$_3$) δ 2.08, 6-Me; 2.27, 3-Me; 4.72, br s, H5. [Lit.[22] for compound assigned incorrect structure; data obtained for mixture with (25) above: ^{1}H n.m.r. ($CDCl_3$) δ 2.10, 6-Me; 2.29, 3-Me; 4.75; 4.75, H5.]

Chlorination of 2,4-Dichloro-6-methylphenol

Chlorine was slowly bubbled through a stirred solution at 20° of the phenol (5 g) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) in a darkened flask for 5 hours. Excess chlorine was purged with nitrogen and the solvents removed first by distillation at reduced pressure (<35°) and then by drying under reduced pressure (*c*. 3 mm) for several hours.

The crude product (7.76 g) was shown (^{1}H n.m.r.) to be a mixture (*c*. 3:1) of the required compounds (28) and (29), which were separated on a Chromatotron with a 2 mm Silica gel plate.

Eluted first (pentane) was: *trans*-2,4,5,6,6-pentachloro-2-methylcyclohex-3-enone (29), in admixture with an impurity (*c*. 20%; ^{1}H n.m.r.) formed during chromatography, ν_{max} (Nujol) 1761, C=O; 1654 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.89, 2-Me; 4.97, d, *J* 1.5 Hz, H5; 6.17 d, *J* 1.5 Hz, H3. [Lit.[21] for (29), in admixture with (28), ν_{max} (Nujol) 1760, C=O; 1650 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.89, 2-Me; 4.97, d, *J* 1.5 Hz, H5; 6.24, d, *J* 1.5 Hz, H3.]

Eluted second (pentane) was: *cis*-2,4,5,6,6-pentachloro-2-methylcyclohex-3-enone (28), m.p. 52-53° (X-ray structure determination, see Appendix 1.) ν_{max} (Nujol) 1766, C=O; 1654 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.07, 2-Me; 4.97, d, *J* 1.5 Hz, H5; 6.17, d, *J* 1.5 Hz, H3. [Lit.[21] for (28), in admixture with (29), ν_{max} (Nujol) 1760, C=O; 1650 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.07, 2-Me; 4.98, d, J 1.5 Hz, H5; 6.23, d, J 1.5 Hz, H3.]

Chlorination of 2,3-Dimethylaniline

Chlorine was bubbled slowly through a stirred solution at 20° of the aniline (5 g) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) for 3 hours. Excess chlorine was purged with nitrogen and the solid ammonium chloride produced in the reaction filtered off. The solvents were removed first by distillation under reduced pressure (<35°) and then by drying under reduced pressure (*c.* 3 mm) for several hours.

The crude product (7.31 g) was shown (^{1}H n.m.r.) to be a mixture (*c.* 1:3) of the required compounds (31) and (32), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane):

trans-2,4,5,6,6-pentachloro-2,3-dimethylcyclohex-3-enone (32), m.p. 84-85° (Found: C, 32.5; H, 2.4; Cl, 59.8. $C_8H_7Cl_5O$ requires C, 32.4; H, 2.4; Cl, 59.8%). ν_{max} (Nujol) 1763, C=O; 1646 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.89, 2-Me; 2.14, br s, 3-Me; 5.00, q, J 0.5 Hz, H5. [Lit.^{22} for compound assigned incorrect structure, in admixture with C2-epimer: ν_{max} (Nujol) 1752, C=O; 1640 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.89, 2-Me; 2.14, d, J=0.6 Hz, 3-Me; 5.04, m. J 0.6 Hz, H5.]

Eluted second (pentane) was:

cis-2,4,5,6,6-pentachloro-2,3-dimethylcylohex-3-enone (31), m.p. 128.5-129.5° (Found: C, 32.6; H, 2.6; Cl, 59.6. $C_8H_7Cl_5O$ requires C, 32.4; H, 2.4; Cl, 59.8%). ν_{max} (Nujol) 1770, C=O; 1640 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.06, 2-Me; 2.10, br s, 3-Me; 5.05, q, J 0.5 Hz, H5. [Lit.^{22} for compound assigned incorrect structure: ν_{max} (Nujol 1770, C=O; 1640 cm^{-1}, C=C. ^{1}H n.m.r. (CDCL$_3$) δ 2.06, 2-Me; 2.11, d, J 0.5 Hz, 3-Me; 5.06, m, J 0.4 Hz, H5.]

Chlorination of 3-Chloro-2-methylaniline

Chlorine was bubbled slowly through a stirred solution at 20^o of the aniline (5 g) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) in a darkened flask for 2 hours. Excess chlorine was purged with nitrogen and the solid ammonium chloride produced in the reaction filtred off. The solvents were removed first by distillation under reduced pressure (<35^o) and then by drying under reduced pressure (*c.* 3 mm) for several hours.

The crude product (10.2 gm) was shown (^{1}H n.m.r.) to be a mixture (*c.* 2:3) of the required compounds (34) and (35). Crystallization of the crude product from diethyl ether/ light petroleum gave crystalline material, a mixture (*c.* 2:3) comprised of the two hexachlorocyclohex-3-enones (34) and (35), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

trans-2,3,4,5,6,6-hexachloro-2-methylcyclohex-3-enone (35), m.p. 60-61^o, ν_{max} (Nujol) 1765, C=O; 1623 cm^{-1}, C=C. ^{1}H n.m.r. (CDCl$_3$) δ 1.99, 2-Me; 5.10, H5. [Lit.^{21} m.p. 61-62^o, ν_{max} (Nujol) 1768, C=O; 1620 cm^{-1} C=C. ^{1}H n.m.r. (CDCl$_3$) δ 2.01, 2-Me; 5.51, H5.]

Eluted second (pentane) was:

cis-2,3,4,5,6,6-hexachloro-2-methylcyclohex-3-enone (34), m.p. 111.5-112^o, ν_{max} (Nujol) 1770, C=O; 1620 cm^{-1}, C=C. ^{1}H n.m.r. (CDCl$_3$) δ 2.17, 2-Me; 5.12, H5. [Lit.^{21} m.p. 112, ν_{max} (Nujol) 1758m C=O; 1613 cm^{-1}, C=C. ^{1}H n.m.r. (CDCl$_3$) δ 2.17, 2-Me; 5.17, H5.]

Chlorination of 2,3,6-Trimethylphenol

Chlorine was bubbled slowly through a stirred solution at 20° of the phenol (5 g) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) in a darkened flask for 1 hour. Excess chlorine was purged with nitrogen and the solvents removed first by distillation under reduced pressure (<35°) and then by drying under reduced pressure (*c*. 3 mm) for several hours.

The crude product (10.5 g) was shown (^{1}H n.m.r.) to contain *c*. 50% (total) of the required compounds (37) and (38). Crystallization of the crude material from diethylether/pentane gave a mixture (*c*. 3:1) of the two tetrachlorocyclohex-3-enones (37) and (38), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

r-2,4,*t*-5,*c*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (38), m.p. 106-106.5° (X-ray structure determination, see Appendix 1), ν_{max} (Nujol) 1740, C=O; 1643 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.82, 2-Me; 1.89, 6-Me; 2.14, br s, 3-Me; 4.70, q, J 0.5 Hz, H5. [Lit.[22] for compound assigned incorrect structure, in admixture with C2 epimer: ν_{max} (Nujol) 1755, C=O; 1665 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.82, 1.89, 2- and 6-Me; 2.14, d, J.05 Hz, 3-Me; 4.73, m, J 0.5 Hz, H5.]

Eluted second (pentane) was:

r-2,4,*c*-5,*t*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (37), m.p. 126-127° (Found: C, 39.2; H, 3.7; Cl, 51.6. $C_9H_{10}Cl_4O$ requires C, 39.2; H, 3.7; Cl 51.4%). ν_{max} (Nujol) 1742, C=O; 1648 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.93, 6-Me; 2.02, 2-Me; 2.11, br s, 3-Me; 4.73, q, J 0.5 Hz, H5. [Lit.[22] for compound assigned incorrect structure, in admixture with C2-epimer:

ν_{max} (Nujol) 1755, C=O; 1665 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.92, 6-Me; 2.02, 2-Me; 2.11, d, J 0.5 Hz, 3-Me; 4.76, m, J 0.5 Hz, H5.]

Chlorination of 2,6-Dimethylaniline

Chlorine was bubbled slowly through a stirred solution at 20° of the aniline (6 g) in acetic acid (60 ml) and concentrated hydrochloric acid (6 ml) in a darkened flask for 2 hours. Excess chlorine was purged with nitrogen and the solvents removed first by distillation at reduced pressure (<35°) and then by drying under reduced pressure (*c*. 3 mm) for several hours.

The crude product (9.71 g) was shown (^{1}H n.m.r.) to be a mixture (*c*. 2:3) of the required compounds (40) and (41), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was: *r*-2,4,*t*-5,*c*-6-tetrachloro-2,6-dimethylcyclohex-3-enone (41), was an oil (Found: C, 36.8; H, 3.1; Cl, 54.3. $C_8H_8Cl_4O$ requires C, 36.7; H, 3.1; Cl 54.1%). ν_{max} (Nujol) 1745, C=O; 1649 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.82, 2-Me; 1.89, 6-Me; 4.65, d, J 1.5 Hz, H5; 6.22, d, J 1.5 Hz, H3. [Lit.[22] for compound assigned incorrect structure, in admixture with C2-epimer: ν_{max} (Nujol) 1730, C=O; 1642 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.80, 1.87, 2- and 6-Me; 4.65, d, J 1.5 Hz, H5; 6.18, d, J 1.5 Hz, H3.]

Eluted second (pentane) was: *r*-2,4,*c*-5,*t*-6-tetrachloro-2,6-dimethylcyclohex-3-enone (40), m.p. 41-42° (Found: C, 37.0; H, 3.2; Cl, 54.0. $C_8H_8Cl_4O$ requires C, 36.7; H 3.1; Cl, 54.1%). ν_{max} (Nujol) 1748, C=O; 1652 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.93, 6-Me; 2.02, 2-Me;

4.67, d, J 1.5 Hz, H5; 6.22, d, J 1.5 Hz, H3. [Lit.[22] for compound assigned incorrect structure, in admixture with C2-epimer: ν_{max} (Nujol) 1730, C=O; 1642 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.91, 2- and 6-Me; 4.66, d, J 1.5 Hz; 6.17, d, J 1.5 Hz, H3.]

Chlorination of 2,6-Dimethylphenol

Chlorine was bubbled slowly through a stirred solution at 20° of the phenol (20 g) in acetic acid (200 ml) and concentrated hydrochloric acid (20 ml) in a darkened flask for 3 hours. Excess chlorine was purged with nitrogen and the solvents removed first by distillation under reduced pressure (<35°) and then by drying under reduced pressure (*c*. 3 mm) for several hours.

The crude product (35.6 gm) was shown (^1H n.m.r.) to be a mixture (*c*.3:2) of the required compounds (43) and (44). Crystallization of the crude material from diethylether/pentane gave two crops (17.9 g) of compound (43). A further crystallization from diethylether/pentane of the mother liquor gave a mixture (*c*. 1:1) of the two pentachlorocyclohex-3-enones (43) and (44), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

r-2,3,4,*t*-5,*c*-6-pentachloro-2,6-dimethylcyclohex-3-enone (44), m.p. 82-83°, (Found: C, 32.7; H, 2.3; Cl 60.0. $C_8H_9Cl_5O$ requires C, 32.4; H, 2.4; Cl, 59.8%). ν_{max} (Nujol) 1750, C=O; 1625 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.88, 2-Me; 1.92, 6-Me; 4.82, H5.

Eluted second (pentane) was:

r-2,3,4,*c*-5,*t*-6-pentachloro-2,6-dimethylcyclohex-3-enone (43), m.p. 122-123°, ν_{max} (Nujol) 1750, C=O; 1627 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.94, 6-Me; 2.12, 2-Me; 4.82, H5. [Lit.[28]

m.p. 121-123°. ν_{max} (Nujol) 1746, C=O; 1623 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.94, 6-Me; 2.12, 2-Me; 4.83, H5.]
[Lit.[22] m.p. 120-121.5°. ν_{max} (Nujol) 1746, C=O; 1635 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.93, 6-Me; 2.11, 2-Me; 4.83, H5.]

Chlorination of 2,5-Dimethylphenol

Chlorine was bubbled slowly through a stirred solution at 20° of the phenol (3 g) in acetic acid (40 ml) and concentrated hydrochloric acid (4 ml) in a darkened flask for 12 hours. Excess chlorine was purged with nitrogen and the solvents removed first by distillation under reduced pressure and then by drying under reduced pressure (*c.* 3 mm) for several hours. The crude product (7.9 g) was shown (^1H n.m.r.) to be a mixture (*c.* 24:11:5:17:13:9) of the compounds (25), (26), (46), (47), (48) and (49), which were separated on a Chromatotron, with a 2 mm silica gel plate.

Eluted first (pentane) was:
trans-2,2,4,5,6-pentachloro-3,6-dimethylcyclohex-3-enone (25), m.p. 129-130°, ν_{max} (Nujol) 1758, C=O; 1645 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.94, 6-Me; 2.29, 3-Me; 4.71, H5. identical with authentic material.

Eluted second (pentane) was:
cis-2,2,4,5,6-pentachloro-3,6-dimethylcyclohex-3-enone (26), m.p. 116-118°, ν_{max} (Nujol) 1772, C=O; 1646 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.08, 6-Me; 2.27, 3-Me; 4.72, H5. identical with authentic material.

Eluted third (pentane), in admixture with (26), was compound (46), which upon being crystallized from pentane, was able to be mechanically separated:
cis-2,3,4,5,6,6-hexachloro-2,5-dimethylcyclohex-3-enone (46), m.p. 94.5-95°, (X-ray structure determined, see Appendix 1.)

ν_{max} (Nujol) 1759, C=O; 1607 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.17, 2-Me; 2.25, 5-Me. [Lit.[22] m.p. 94°, ν_{max} (Nujol) 1755, C=O; 1610 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.19, 2-Me; 2.25, 5-Me.]

Eluted fourth (diethylether/pentane) (1:20) was: 2,4,4,5-Tetrachloro-3,6-dimethylcyclohexa-2,5-dienone (47), m.p. 55°-56°, pale yellow needles, ν_{max} (Nujol) 1676, C=O; 1616 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.15, 6-Me; 2.52, 3-Me. [Lit.[42] m.p. 55-56°.]

Eluted fifth (diethylether/pentane) (1:20) was: *trans*-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (48), m.p. 92.5-93°, (X-ray structure determined, see Appendix 1.). ν_{max} (Nujol) 1718, C=O; 1607 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.89, 6-Me; 2.57, 3-Me; 5.12, H5. λ_{max} ($CHCl_3$) 252 nm; ε 12,650. [Lit.[22] for compound in admixture with an impurity: ν_{max} (liq.film) 1715, C=O; 1600 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.87, 6-Me; 2.53, 3-Me; 5.08, H5.]

Eluted sixth (diethylether/pentane) (1:20) was: *cis*-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (49), m.p. 84-85°, (X-ray structure determined, see Appendix 1.). ν_{max} (Nujol) 1708, C=O; 1601 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.93, 6-Me; 2.57, 3-Me; 4.80, H5. λ_{max} ($CHCl_3$) 253.2 nm; ε 11,900.

Chlorination of 3,5-Dimethylphenol

Chlorine was bubbled slowly through a stirred solution at 20° of the phenol (2 g) in acetic acid (20 ml) and concentrated hydrochloric acid in a darkened flask for 3 hours. Excess chlorine was purged with nitrogen and the solvents removed first by distillation at reduced pressure (<35°) and then by drying under reduced pressure (*c.* 3 mm) for several hours.

The crude product (4.8 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 9:1) of the required compounds (52) and (51). Crystallization of the crude material from pentane gave:

2,4,4,6-tetrachloro-3,5-dimethylcyclohexa-2,5-dienone (52), 2.2 g, m.p. 107-108°, ν_{max} (Nujol) 1683, C=O; 1613 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.52, 3- and 5-Me. λ_{max} ($CHCl_3$) 257.6 nm, (ε 17,600). [Lit.[28] m.p. 107-108°, ν_{max} (Nujol) 1685, C=O; 1605 cm^{-1}, C=C. ^{1}H n.m.r. (CCl_4) δ 2.50 . [Lit.[22] m.p. 105-106°, ν_{max} (Nujol) 1681, C=O; 1607 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.51.]

Separation of the mother liquor on a Chromatotron with a 2 mm silica gel plate gave the hexachlorocyclohex-3-enone (51):

Eluted first (pentane) was:

2,2,4,5,6,6-hexachloro-3,5-dimethylcyclohex-3-enone (51), m.p. 82-83°. (Found: C, 29.3; H, 1.7; Cl, 64.4. $C_8H_6Cl_6O$ requires C, 29.1; H, 1.8; Cl, 64.3%). ν_{max} (Nujol) 1777, C=O; 1627 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.20, 5-Me; 2.30, 3-Me. [Lit.[22] m.p. 82-83°, ν_{max} (Nujol) 1780, C=O; 1620 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.21, 5-Me; 2.31, 3-Me.]

Chlorination of 2,3,4,6-Tetrachloro-5-methylphenol

Chlorine was bubbled slowly through a stirred solution of the phenol (2 g) in acetic acid (20 ml) and concentrated hydrochloric acid (1 ml) at 20° in a darkened flask for 5 hours. The solvents were then removed under reduced pressure. The crude product (2.4 g) was shown (^{1}H n.m.r.) to be a mixture (*c.* 3:2) of the two compounds (54) and (55), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

2,2,3,4,5,6,6-heptachloro-5-methylcyclohex-3-enone (54), m.p. 100-101°, (Found: C, 23.8; H, 0.9; Cl, 70.6. $C_7H_3Cl_7O$ requires C, 23.9; H, 0.9; Cl 70.7%). λ_{max} (Nujol) 1770, C=O, 1597 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.27, 5-Me. [Lit.[21] m.p. 101-102°, ν_{max} (Nujol) 1770, C=O; 1598 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.26, 5-Me.]

Eluted second (diethylether/pentane) (1:20) was: 2,3,4,4,6-pentachloro-5-methylcyclohexa-2,5-dienone (55), m.p. 89-90°. ν_{max} (Nujol) 1690, C=O; 1582 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.57, 5-Me. λ_{max} ($CHCl_3$) 262.1 nm; ε 14,300. [Lit.[33] m.p. 92°]. [Lit.[21] m.p. 89-90°. ν_{max} (Nujol) 1685, C20; 1590 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$)δ 2.58, 5-Me.]

Chlorination of 2,3-Dimethylphenol

Chlorine was bubbled very slowly through a stirred solution at 20° of the phenol (2 g) in acetic acid (20 ml) and concentrated hydrochloric acid (2 ml) in a darkened flask for 18 hours. The excess chlorine was purged with nitrogen and the solvents removed under reduced pressure. The crude product (5.3 g) was shown (^1H n.m.r.) to consist of a mixture (*c*. 2:8:1) >90% (total) of the hexachlorocyclohex-3-enones (58), (57) and (59), which were separated on a Chromatotron with a 2 mm silica gel/polyethylene glycol plate.

Eluted first (pentane) was: *trans*-2,2,3,4,5,6-hexachloro-5,6-dimethylcyclohex-3-enone (57), m.p. 87-88°, (X-ray structure determination, see Appendix 1.) ν_{max} (Nujol) 1760, C=O; 1603 cm^{-1}, C=C. ν_{max} (CCl_4) 1764, C=O; 1602 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.02, 6-Me; 2.07, 5-Me. [Lit.[22] m.p. 88-89°, ν_{max} (Nujol) 1752, C=O; 1599 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.02, 6-Me; 2.07, 5-Me.]

Eluted second (pentane) was:

2,4,5,5,6,6-hexachloro-2,3-dimethylcyclohex-3-enone (59), m.p. 92-92.5°, (X-ray structure determination, see Appendix 1.) ν_{max} (Nujol) 1761, C=O; 1620 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.98, v-br, 2-Me, 2.19, 3-Me; Low temperature (-12°), δ 1.89, 2-Me; 2.13; 2-Me, 2.20, 3-Me; at 55° 1.97, 2-Me; 2.20, 3-Me.

Eluted third (pentane) was:

cis-2,2,3,4,5,6-hexachloro-5,6-dimethylcyclohex-3-enone (58), m.p. 142-143° (dec.), (X-ray structure determination, see Appendix 1.) ν_{max} (Nujol) 1765, C=O; 1596 cm^{-1}, C=C: ν_{max} (CCl_4) 1772, C=O; 1757, sh, C=O; 1594, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.98, 5- and 6-Me. [Lit.[22] for compound assigned incorrect structure: m.p. 142-143°, ν_{max} (Nujol) 1768, C=O; 1594 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.98, 5- and 6-Me.]

Chlorination of 2,3,4,5-Tetrachloro-6-methylphenol

Chlorine was bubbled slowly through a solution of the phenol (0.5 g) in acetic acid (5 ml) and concentrated hydrochloric acid (0.5 ml) at 20° in a darkened flask for 3 hours.

The flask was then stoppered and left stirring for 48 hours. The excess chlorine was purged with nitrogen, then the solvents removed under reduced pressure. The crude product was shown (^1H n.m.r.) to be essentially a mixture (*c*. 2:3) of the dienone (73) and the heptachlorocyclohex-3-enone (61), which were separated on a Chromatotron with a silica gel plate.

Eluted first (pentane) was:

2,3,4,5,5,6,6-heptachloro-2-methylcyclohex-3-enone (61), m.p. 88.5-89°, ν_{max} (Nujol) 1778, C=O; 1768, C=O; 1598 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.10, v br, 2-Me; at low temperature

(-10°) ($CHCl_3$) δ 2.00, 2-Me; 2.22, 2Me; Coalescence at ≃27°; at 55°, δ 2.08. ^{13}C n.m.r. ($CDCl_3$) (30°) δ 27.34, 2-Me; 30.97, 2-Me; 84.74, C2; 131.82, C4; 135.09, C3; 184.55, C1; C5, C6 not observed. λ_{max} ($CHCl_3$) 240 nm; ε 6723. [Lit.[21] m.p. 88-89°, ν_{max} (Nujol) 1769, C=O; 1600, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.11, s, 2-Me.]

Eluted second (pentane) was:
2,3,4,5,6-hexachloro-6-methylcyclohexa-2,4-dienone (73), m.p. 57-58°, identical with authentic material.

Chlorination of 3-Methylphenol

Chlorine was bubbled slowly through a stirred solution of the phenol (2 g) in acetic acid (20 ml) and concentrated hydrochloric acid (2 ml) at 20° in a darkened flask for 5 hours. The solvents were then removed under reduced pressure. The crude product (5.4 g) was shown (^1H n.m.r.) to comprise >75% (total) of the required compound (64), which crystallized from diethylether/pentane to give:
2,2,4,5,6,6-hexachloro-3-methylcyclohex-3-enone (64), m.p. 117.5-118.5°. (Found: C, 26.4; H, 1.3; Cl, 67.2. $C_7H_4Cl_6O$ requires C, 26.4; H 1.3, Cl, 67.1%). ν_{max} (Nujol) 1769, C=O; 1642 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.30, 3-Me; 5.02, H5. [Lit.[21] m.p. 117-118°, ν_{max} (Nujol) 1770, C=O; 1640 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) 2.30, d, J 0.6 Hz, 3-Me; 5.06, m, J 0.6 Hz, H5.]

5.3 Experimental Section Relation to Chapter 3

Reaction of 2,4-Dichloro-6-methylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (0.5 g) in carbon tetrachloride and pyridine (0.23 ml; 1.01 mole) at 0^{o} was added chlorine (0.22 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The reaction was stirred in a darkened flask for 10 minutes, then poured into ice-water (150 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (0.61 g) was shown (^{1}H n.m.r.) to be:

2,4,6-trichloro-6-methylcyclohexa-2,4-dienone (66), an oil, ν_{max} (liq. film) 1698, C=O; 1625, C-C; 1560 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.83, 6-Me; 6.45, d, J 2.3 Hz, H5; 7.16, d, J 2.3 Hz, H3. [Lit.[21] ν_{max} (liq.film) 1698, C=O; 1627, C=C; 1564 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.83, 6-Me; 6.46, d, J 2.3 Hz, H5; 7.16, d, J 2.3 Hz, H3.]

Reaction of 2,4-Dichloro-3,6-dimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (1 g) in carbon tetrachloride (10 ml) and pyridine (0.46 ml; 1.1 mole) at 0^{o} was added chlorine (0.4 g; 1.2 mol) as a chlorine/carbon tetrachloride solution. The solution was stirred in a darkened flask for 10 minutes, then poured into ice-water (150 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (1.12 g) was shown (^{1}H n.m.r.) to be the cyclohexa-2,4-dienone (68), which crystallized from

dichloromethane/pentane to give:
2,4,6-trichloro-3,6-dimethylcyclohexa-2,4-dienone (68), (0.44 g), m.p. 57-58°. ν_{max} (Nujol) 1695, C=O; 1630, C=C; 1554 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.81, 6-Me; 2.40, br s, 3-Me; 6.52, br s, H5. [Lit.[22] m.p. 57-58°, ν_{max} 1685, C=O; 1630, C=C; 1558 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.78, 6-Me; 2.37, d, J 0.4 Hz, 3-Me; 6.48, m, J 0.4 Hz, H5.]

Reaction of 2,4-Dichloro-5,6-dimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (1 g) in carbon tetrachloride (10 ml) and pyridine (0.41 ml; 1.01 mole) at 0° was added chlorine (0.31 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The reaction was stirred in a darkened flask for 10 minutes, then poured into ice-water (200 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product was (^1H n.m.r.) shown to be:
2,4,6-trichloro-5,6-dimethylcyclohexa-2,4-dienone (70), a yellow oil, (Found: C, 42.4; H, 3.1; Cl, 47.2. $C_8H_9Cl_3O$ requires C, 42.6; H, 3.1; Cl 47.3%). ν_{max} (liq. film) 1700, C=O; 1625, C=C; 1575 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.85, 6-Me; 2.17, 5-Me; 7.17, H3. [Lit.[22] ν_{max} (liq. film) 1690, C=O; 1620, C=C; 1572 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.84, 6-Me; 2.18, 5-Me; 7.26, m, J 0.4 Hz, H3.]

Reaction of 2,4-Dichloro-3,5,6-trimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (0.5 g) in carbon tetrachloride (5 ml) and pyridine (0.2 ml; 1.1 mole) at 0° was added chlorine (0.2 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 10 minutes, then poured into ice-water (150 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (593 mg) was shown (^{1}H n.m.r.) to be the required compound:

2,4,6-trichloro-3,5,6-trimethylcyclohexa-2,4-dienone (72), a yellow oil, ν_{max} (liq. film) 1690, C=O; 1620, C=C; 1560 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.80, 6-Me; 2.20, m, J≃0.5 Hz, 5-Me; 2.42, m, J≃0.5 Hz, 3-Me. [Lit.[22] ν_{max} (liq. film) 1685, C=O; 1616, C=C; 1563 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.82, 6-Me; 2.20, m, 5-Me; 2.42, m, 3-Me.]

Reaction of 2,3,4,5-Tetrachloro-6-methylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a stirred solution of the phenol (0.5 g) in carbon tetrachloride (5 ml) and pyridine (0.16 ml; 1.01 mole) at 0^{o} was added chlorine (0.15 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 10 minutes, then poured into ice-water (150 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (.56 g) was shown (^{1}H n.m.r.) to be the required compound (73), which crystallized from pentane:

2,3,4,5,6-pentachloro-6-methylcyclohexa-2,4-dienone (73), m.p. 57-58^{o}, (Found: C, 29.8; H, 1.0; Cl, 63.1. $C_7H_3Cl_5O$ requires C, 30.0; H, 1.1; Cl, 63.2%). ν_{max} (Nujol) 1700, C=O; 1585, C=C; 1532 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.97, 6-Me. λ_{max} ($CHCl_3$) 239, 363 nm; (ε 5522, 3951.) [Lit.[21]

m.p. 60-61° (*ex.* light petroleum), ν_{max} (Nujol) 1695, C=O; 1580, C=C; 1530 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.00, 6-Me.]

Reaction of 4-Chloro-2,6-dimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (2 g) in carbon tetrachloride (20 ml) and pyridine (1.1 ml; 1.01 mole) at 0° was added chlorine (1.0 m; 1.2 mole) as a chlorine/carbon tetrachloride solution. The reaction was stirred in a darkened flask for 10 minutes, and then poured into ice-water (400 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (2.44 g) was shown (^{1}H n.m.r.) to be the required compound:

4,6-dichloro-2,6-dimethylcyclohexa-2,4-dienone (75), a yellow oil, ν_{max} (liq. film) 1690, C=O; 1643, C=C; 1593 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.77, 6-Me; 2.00, m, J 0.5 Hz, 2-Me; 6.33, d, J 1.5 Hz, H5; 6.70, m, J 0.5, H3. [Lit.[22] ν_{max} (liq. film) 1678, C=O; 1636, C=C; 1586 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.73, 6-Me; 2.00, m, 2-Me; 6.35, m, H5; 6.72, m, H3.]

Reaction of 3,5-Dichloro-2,4,6-trimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (0.3 g) in carbon tetrachloride (3 ml) and pyridine (0.15 ml; 1.01 mole) at 0° was added chlorine (0.12 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 10 minutes, then poured into ice-water (100 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (0.34 g) was shown to be the required compound (77):

3,5,6-trichloro-2,4,6-trimethylcyclohexa-2,4-dienone (77), a yellow oil, (Found: C, 45.2; H, 3.7; Cl, 44.3. $C_9H_9Cl_3O$ requires C, 45.1; H, 3.8; Cl, 44,4%). ν_{max} (liq. film) 1675, C=O; 1623, C=C; 1568 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.90, 6-Me; 1.12, 2-Me; 2.29, 4-Me.

Reaction of 4-chloro-2,3,6-trimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (0.5 g) in carbon tetrachloride (10 ml) and pyridine (0.24 ml; 1.01 mole) at 0^o was added chlorine (0.21 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The reaction was stirred in a darkened flask for 10 minutes, then poured into ice-water (150 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (0.58 g) was shown (^1H n.m.r.) to be >90% (total) of the required compound (79), but could not be further purified by either crystallization or chromatographic techniques.

4,6-dichloro-2,3,6-trimethylcyclohexa-2,4-dienone (79), a yellow oil, ν_{max} (liq. film) 1679, C=O; 1640, C=C; 1599 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.77, 6-Me; 1.97, m, J 1.5 Hz, 3-Me; 2.13, m, J 0.5 Hz, 2-Me; 6.77, q, J 1.5 Hz, H5. λ_{max} ($CHCl_3$) 246, 344 nm (ε 2670, 3190). [Lit.[22] for compound assigned incorrect structure: ν_{max} (liq. film) 1677, C=O; 1639, C=C; 1599 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.74, 6-Me; 1.96, m, J 1.4 Hz, 2-Me; 2.10, m, 5-Me; 6.80, m, J 1.4 Hz, H3.]

The minor component (79a) (*c*. 1.11) could not be isolated from the reaction mixture. The ^1H n.m.r. spectrum of the mixture shows only the olefinic proton as a resolved peak (δ 6.42). It is probable that this minor component is the 4,6-dichloro-2,5,6-trimethylcyclohexa-2,4-dienone (79a).

Reaction of 3,4-Dichloro-2,6-dimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (0.5 g) dissolved in carbon tetrachloride (5 ml) and pyridine (0.21 ml; 1.01 mole) at 0^{o} was added chlorine (0.19 gm; 1.2 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 10 minutes, then poured into ice-water (150 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (0.54 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 3:2) of the required compounds (81) and (82), which could not be further separated.

4,5,6-trichloro-2,6-dimethylcyclohexa-2,4-dienone (81), (an oil, in admixture with (82)): ν_{max} (liq. film) 1687, C=O; 1634, C=C; 1575 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.82, 6-Me; 1.92, d, J 1.5 Hz, 2-Me; 6.57, q, J 1.5 Hz, H3. [Lit.[22] for compound in admixture with (82), (*c.* 2:3): ν_{max} (liq. film) 1687, C=O; 1650, C=C; 1575 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.88, 6-Me; 2.00, d, J 1.5 Hz, 2-Me; 6.85, m, J 1.5 Hz, H3.]

3,4,6-trichloro-2,6-dimethylcyclohexa-2,4-dienone (82), (an oil, in admixture with (81)): ν_{max} (liq. film) 1682, C=O; 1620, C=C; 1562 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.70, 6-Me; 2.05, d, J 0.8 Hz, 2-Me; 6.30, q, J 0.8 Hz, H5. [Lit.[22] for compound in admixture with (81) (*c.* 3:2): ν_{max} (liq. film) 1687, C=O; 1618, C=C; 1575 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.77, 6-Me; 2.14, d, J 0.8 Hz, 2-Me; 6.54, m, J 0.8 Hz, H5.]

Reaction of 3,4-Dichloro-2,5,6-trimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a solution of the phenol (0.5 g) in carbon tetrachloride (5 ml) and pyridine (0.21 ml; 1.01 mole) at 0° was added chlorine (0.2 gm; 1.2 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 10 minutes, then poured into ice-water (150 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (0.58 g) was shown (^{1}H n.m.r.) to be >90% (total of the required compound: 4,5,6-trichloro-2,3,6-trimethylcyclohexa-2,4-dienone (84), a yellow oil, ν_{max} (liq. film) 1678, C=O; 1613, C=C; 1575 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.80, 6-Me; 2.15, br s, 2-Me; 2.25, br s, 3-Me, [Lit.[22] for compound assigned incorrect structure: ν_{max} (liq. film) 1677, C=O; 1612, C=C; 1563 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.77, 6-Me; 2.13, m, J 0.6 Hz, 2-Me; 2.24, m, J 0.6 Hz, 5-Me.]

The minor component (85) (<10%) could not be isolated from the above mixture, but could be seen in the ^{1}H n.m.r. spectrum of the above mixture. ($CDCl_3$) 1.90, 6-Me; 2.04, 2-Me; 2.24, 5-Me. On the basis of this data the structure of the minor component is probably the 3,4,6-trichloro-2,5,6-trimethylcyclohexa-2,4-dienone (85).

Reaction of 2-Chloro-3,4,6-trimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a stirred solution of the phenol (0.5 g) in carbon tetrachloride (5 ml) and pyridine (0.24 ml; 1.0 mole) at 20° was added chlorine (0.21 gm; 1.1 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred for 5 minutes in a darkened flask, then the solvents removed under reduced pressure. The crude product (0.68 g) was shown (^1H n.m.r.) to consist >75% (total) of a mixture (*c*. 2:1) of the compounds (87) and (88), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was: *trans*-2,5,6-trichloro-3,6-dimethyl-4-methylenecyclohex-2-enone (87), m.p. 100-101°, (Found) C, 45.2; H, 3.8; Cl, 44.7. $C_9H_9Cl_3O$ requires C, 45.1; H, 3.8; Cl, 44.4%). ν_{max} (Nujol) 1700, C=O; 1570 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.87, 6-Me; 2.31, 3-Me; 4.88, H5; 5.72, 4-CH_2. ^{13}C n.m.r. ($CDCl_3$) δ 17.92, 3-Me; 23.72, 6-Me; 65.86, C6; 66.45, C5; 122.16, 4-CH_2; 128.16, C2; 140.41, C3; 145.54, C4; 182.86, C1. λ_{max} ($CHCl_3$) 294 nm; ε 14,150.

Eluted second (diethylether/pentane) (1:9) was: 2,4-dichloro-3,4,6-trimethylcyclohexa-2,5-dienone (88), m.p. 45.5-46.5°, (Found: C, 52.9; H, 5.0; Cl, 34.5. $C_9H_{10}Cl_2O$ requires C, 52.7; H, 4.9; Cl, 34.6%). ν_{max} (Nujol) 1661, C=O; 1608 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.82, 4-Me; 1.98, d, J 1.5 Hz, 6-Me; 2.31, 3-Me; 6.78, q, J 1.5 Hz, H5. λ_{max} ($CHCl_3$) 2.48 nm; ε 10,000.

Reaction of 2-chloro-4,6-dimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a stirred solution of the phenol (0.5 g) in carbon tetrachloride (10 ml) and pyridine (0.26 ml; 1.01 mole) at -10° was added chlorine (0.23 g; 1.1 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 2 minutes, then poured into ice-water (150 ml). The organic phase was separated, dryed over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (0.62 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 95:5) of the dienone (90), which could not be further purified, and the exocyclic-methylene compound (91).

2,6-dichloro-4,6-dimethylcyclohexa-2,4-dienone (90), a yellow oil, ν_{max} (liq. film) 1698, C=O; 1662, C=C; 1570 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.77, 6-Me; 1.98, d, J≃2.0 Hz, 4-Me; 6.08, m, J≃2.0 Hz, H5; 7.03, d, J≃2.0 Hz, H3. λ_{max} ($CHCl_3$) 243, 345 nm; (ε 3312, 2748).

Isolated, as below:

trans-2,5,6-trichloro-6-methyl-4-methylenecyclohex-2-enone (91), colourless crystalline solid, m.p. 65-67.5°, (Found: mass 223.956590. $C_8H_7OCl_3{}^{35}$ requires 223.956247, $\Delta \simeq 1$ p.p.m.) ν_{max} (Nujol) 1695 (br), C=O; 1625, C=C; 1579 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 1.92, 6-Me; 4.87, d, J 2.0 Hz, H5; 5.58 and 5.67, 4-CH_2; 7.20, d, J 2.0 Hz, H3. λ_{max} ($CHCl_3$) 292 nm; ε 12,000. ^{13}C n.m.r. ($CDCl_3$) δ 23.56, 6-Me; 64.96, C5; 66.09, C6; 124.82, 4-CH_2; 128.94, C2; 138.90, C3; 142.50, C4; 183.16, C1.

Absorption of a sample (0.35 g) of the above mixture onto a 2 mm silica gel plate and elution with pentane on a Chromatotron gave:

trans-2,5,6-trichloro-6-methyl-4-methylenecyclohex-2-enone (91) m.p. 65-67°, identical with authentic material.

Eluted second (diethylether/pentane) (1:5) was:

2,4-dichloro-4,6-dimethylcyclohexa-2,5-dienone (92) a lightly coloured oil, (Found: C, 50.1; H, 4.3; Cl, 37.1. $C_8H_8Cl_2O$ requires C, 50.3; H, 4.2; Cl, 37.1%). ν_{max} (liq. film) 1685, C=O; 1667, C=C; 1620 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) 1.83, 4-Me;

1.93, d, J 1.5 Hz, 6-Me; 6.67, m, J 1.5 Hz, H5; 7.02, d, J 3.0 Hz, H3. λ_{max} ($CHCl_3$) 246 nm; ε 13,609.

Eluted third (diethylether) was:

2-chloro-4-hydroxy-4,6-dimethylcyclohexa-2,5-dienone (93), a colourless oil, (Found: C, 55.5; H, 5.4; Cl; 20.6. $C_8H_9Cl\,O_2$ requires C, 55.7; H, 5.3; Cl, 20.5%). ν_{max} (liq. film) 3450, OH; 1678 C=O; 1660, C=C; 1609 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.48, 4-Me; 1.90, d, J 1.5 Hz, 6-Me; 3.00, v-br, 4-OH; 6.63, m, J 1.5 Hz, H5; 7.00, d, J 3.0 Hz, H3. λ_{max} ($CHCl_3$) 243 nm; ε 10,499.

Reactions of 2,6-Dichloro-4,6-dimethylcyclohexa-2,4-dienone (90):

(a) Reaction of 2,6-Dichloro-4,6-dimethylcyclohexa-2,4- (90) with Chlorine in Carbon Tetrachloride and Pyridine

To a stirred solution of the dienone (90), in admixture with (91) (*c*. 95:5) (0.2 g) in carbon tetrachloride (2 ml) and pyridine (0.1 ml, 1.01 mole) at 20° was added chlorine (0.11 g; 1.1 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 10 minutes, then poured into ice-water (50 ml). The organic phase was separated, dryed over anhydrous magnesium sulphate and the solvents removed under reduced pressure.

The crude product (0.25 g) was shown (^1H n.m.r.) to be essentially:

trans-2,5,5-trichloro-6-methyl-4-methylenecyclohex-2-enone (91), m.p. 65-67.5°, identical with authentic material.

(b) Rearrangement of 2,6-Dichloro-4,6-dimethylcyclohexa-2,4-dienone (90) in Acetic Acid

The dienone (90), (0.5 g) in admixture with (91) (*c*. 95:5), was dissolved in acetic acid (5 ml) and left stirring in a darkened flask for 21 hours, at 20°. The solvents were removed by distillation under reduced pressure and by drying under reduced pressure (*c.* 3 mm) for several hours. The crude product (0.5 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 10:6:1) of the compounds (92), (94) and (91), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:
2,3-dichloro-4,6-dimethylphenol (94), colourless needles, m.p. 64-65°, (Found: C, 50.2; H, 4.1; Cl, 37.0. $C_8H_8Cl_2O$ requires C, 50.3; H, 4.2; Cl 37.1%). ν_{max} (Nujol) 3400, OH; 1605(w) cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.23, br s, 6-Me; 2.30, br s, 4-Me; 5.53, D_2O exch., OH; 6.92, m, H5. ^{13}C n.m.r. ($CDCl_3$) δ 15.17, 6-Me; 20.05, 4-Me; 118.49, C2; 123.41, C6; 128.50, C4; 128.99, C3; 148.66, Cl.

Eluted second (pentane) was:
trans-2,5,6-trichloro-6-methyl-4-methylenecyclohex-2-enone (91), m.p. 65-67.5°, identical with authentic material.

Eluted third (diethylether/pentane) (1:5) was:
2,4-dichloro-4,6-dimethylcyclohexa-2,5-dienone (92), a lightly coloured oil, identical with authentic material.

Attempted Reaction of 2,4,Dichloro-4,6-dimethylcyclohexa-2,5-dienone (92) with Chlorine in Carbon Tetrachloride and Pyridine

To a stirred solution of the dienone (92) (0.2 g) in carbon tetrachloride (2 ml) and pyridine (0.1 ml; 1.0 mole) at 20° was added chlorine (0.11 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The mixture was left stirring for 10 minutes, then poured into ice-water (50 ml). The organic phase was separated, dryed over anhydrous magnesium sulphate and the solvents removed under reduced pressure.

The crude product (0.27 g) was shown (^{1}H n.m.r.) to consist >95% (total) of the unreacted dienone (92).

5.4 Experimental Section Relating to Chapter 4

Reaction of 2,4,6-Trichloro-5,6-dimethylcyclohexa-2,4-dienone (70) with Chlorine in Acetic Acid

To a stirred solution of the dienone (70) (0.55 g) in acetic acid (5 ml) at 20° was added chlorine (0.21 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 3 hours, then the solvents removed under reduced pressure (*c.* 3 mm). The crude product (0.61 g) was shown (^{1}H n.m.r.) to be a mixture (*c.* 3:2) of the required compounds (31) and (32), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:
trans-2,4,5,6,6-pentachloro-2,3-dimethylcyclohex-3-enone (32), m.p. 84-85°, identical with authentic material.

Eluted second (pentane) was:
cis-2,4,5,6,6-pentachloro-2,3-dimethylcyclohex-3-enone (31), m.p. 128.5-129.5°, identical with authentic material.

Reaction of 2,4-Dibromo-5,6-dimethylphenol with Chlorine in Acetic Acid

To a solution of the phenol (1 g) in anhydrous acetic acid (10 ml) was added chlorine (0.63 g; 2.2 mole) as a chlorine/acetic acid solution. The mixture was stirred at 20° in a darkened flask for 1 hour, then the solvents were removed by distillation under reduced pressure and then by drying under reduced pressure (*c.* 3 mm) for several hours.

The crude product (1.31 g) was shown (^{1}H n.m.r.) to be a mixture (*c.* 5:8:2:2) of the required compounds (107), (108), (109) and (110), which were separated on a Chromatotron with either a 2 mm silica gel plate, or a 2 mm silica gel/polyethylene glycol (m.w. 6000) plate.

Eluted first (pentane) was:

4,*r*-6-dibromo-*t*-2,*c*-5,6-trichloro-2,3-dimethylcyclohex-3-enone (109), m.p. 68-71°, for compound in admixture with (11), (*c*. 1:1), (Found: C, 24.7; H, 1.84; Br, 41.2; Cl, 27.3. $C_8H_7Br_2Cl_3O$ requires C, 24.9; H, 1.8; Br, 41.5, Cl 27.6%). ν_{max} (Nujol) 1757, C=O; 1640 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.88, 2-Me; 2.15, 3-Me; 5.14, H5. λ_{max} ($CHCl_3$) 223 nm; ε 891.

Eluted second (pentane) was:

4,*r*-6-dibromo-*c*-2,*t*-5,6-trichloro-2,3-dimethylcyclohex-3-enone (110), m.p. 85-86°, (Found: C, 24.9; H, 1.88; Br, 41.6; Cl 29.5. $C_8H_7Br_2Cl_3O$ requires C, 24.9; H, 1.8; Br 41.5; Cl, 27.6%). ν_{max} (Nujol) 1753, C=O; 1640 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.88, 2-Me; 2.15, 3-Me; 5.18, H5. λ_{max} ($CHCl_3$) 222 nm; ε 962.

Eluted third (pentane) was:

4,*r*-6-dibromo-*c*-2,*c*-5,6-trichloro-2,3-dimethylcyclohex-3-enone (107), m.p. 130-131°, (X-ray structure determined, see Appendix 1). ν_{max} (Nujol) 1764, C=O; 1633 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.05, 2-Me; 2.13, 3-Me; 5.18, H5. λ_{max} ($CHCl_3$) 221 nm; ε 935.

Eluted fourth (pentane) was:

4,*r*-6-dibromo-*t*-2,*t*-5,6-trichloro-2,3-dimethylcyclohex-3-enone (108), m.p. 141.5-142°. (Found: C, 25.1; H, 1.9; Br, 41.6; Cl, 27.8. $C_8H_7Br_2Cl_3O$ requires C, 24.9; H, 1.8; Br, 41.5; Cl, 27.6%). ν_{max} (Nujol) 1754, C=O; 1670 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 2.13, 2- and 3-Me; 5.23, H5. λ_{max} ($CHCl_3$) 226 nm; ε 1010.

Attempted Reaction of 2,4-Dibromo-5,6-dimethylphenol with Chlorine in Carbon Tetrachloride and Pyridine

To a stirred solution of the phenol (1g) in carbon tetrachloride (10 ml) and pyridine (0.32 ml; 1.0 mole) at 0° was added chlorine (0.28 g; 1.1 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred for 2 minutes in a darkened flask, then poured into ice-water (250 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (1.2 g) was shown (^{1}H n.m.r.; ir.) to contain a mixture of compounds, which decomposed upon attempting to crystallize from dichloromethane/pentane.

Reaction of 2,4,6-Trichloro-6-methylcyclohexa-2,4-dienone (66) with Chlorine in Acetic Acid

To a stirred solution of the dienone (66) (0.6 g) in acetic acid (6 ml) was added chlorine (0.24 g; 1.2 mole) as a chlorine acetic acid solution. The mixture was stirred at 20° in a darkened flask for 3 hours, then the solvents removed under reduced pressure (*c.* 3 mm). The crude product (0.77 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 5:5:1) of the compounds (28), (29) and (112), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was: *trans*-2,4,5,6,6-pentachloro-2-methylcyclohex-3-enone (29), a colourless oil, in admixture with an impurity (*c.* 20%, ^{1}H n.m.r.) during chromatography, ν_{max} (liq. film) 1761, C=O; 1654 cm^{-1}, C=C. ^{1}H n.m.r. (CDCl$_3$) δ 1.89, 2-Me; 4.97, d, J 1.5 Hz, H5; 6.17, d, J 1.5 Hz, H3.

Eluted second (pentane) was: *cis*-2,4,5,6,6-pentachloro-2-methylcyclohex-3-enone (28), m.p. 52-53°, identical with authentic material.

Eluted third (diethylether/pentane) (1:9) was: *trans*-2,4,4,5,6-pentachloro-6-methylcyclohex-2-enone (112), a yellow oil, (Found: C, 29.6; H, 1.6; Cl, 62.5. $C_7H_5Cl_5O$ requires C, 29.8; H, 1.8; Cl, 62.8%). ν_{max} (liq. film) 1721, C=O; 1614 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.90, 6-Me; 5.03, H5; 7.40, H3. λ_{max} ($CHCl_3$) 246 nm; ε 11,700.

Reaction of 4,6-Dichloro-2,3,6-trimethylcyclohexa-2,4-dienone (79) with Chlorine in Acetic Acid

To a solution of the dienone (79) (0.5 g) in acetic acid (5 ml) at 20° was added chlorine (0.18 g; 1.1 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure (*c*. 3 mm). The crude product (0.51 g) was shown (^1H n.m.r.) to be a mixture (*c*. 5:4) of the required compounds (37) and (38), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was: *r*-2,4,*t*-5,*c*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (38), m.p. 106-106.5°, identical with authentic material.

Eluted second (pentane) was: *r*-2,4,*c*-5,*t*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (37), m.p. 126-127°, identical with authentic material.

Reaction of 2,4,6-Trichloro-3,6-dimethylcyclohexa-2,4-dienone (68) with Chlorine in Acetic Acid

To a stirred solution of the dienone (68) (1.25 g) in acetic acid (10 ml) at 20° was added chlorine (0.41 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 2 hours, then the solvents removed under reduced pressure (*c*. 3 mm). The crude product (1.5 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 11:8:9:3) of the required compounds, (25), (26), (48) and (49) which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

trans-2,2,4,5,6-pentachloro-3,6-dimethylcyclohex-3-enone (25), m.p. 129-130°, identical with authentic material.

Eluted second (pentane) was:

cis-2,2,4,5,6-pentachloro-3,6-dimethylcyclohex-3-enone (26), m.p. 116-118°, identical with authentic material.

Eluted third (diethylether/pentane) (1:20) was:

trans-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (48), m.p. 92.5-93°, identical with authentic material.

Eluted fourth (diethylether/pentane) (1:20) was:

cis-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (49), m.p. 84-85°, identical with authentic material.

Reaction of 4,6-dichloro-2,6-dimethylcyclohexa-2,4-dienone (75) with Chlorine in Acetic Acid

To a stirred solution of the dienone (75) (0.5g) in acetic acid (5 ml) at 20° was added chlorine (0.21; 1.1 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure (*c*. 3 mm). The crude product (0.59 g) was shown (^{1}H n.m.r.) to be a mixture (*c*. 8:18:7:12) of the required compounds (41), (40), (113) and (114), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

r-2,4,*t*-5,*c*-6-tetrachloro-2,6-dimethylcyclohex-3-enone (41), a colourless oil, identical with authentic material.

Eluted second (pentane) was:

to be essentially unreacted dienone (77).

Reaction of 2,4,6-Trichloro-3,5,6-trimethylcyclohexa-2,4-dienone (72) with Chlorine in Acetic Acid

To a stirred solution of the dienone (72) (0.57 g) in acetic acid (5.5 ml) at 20° was added chlorine (0.2 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 18 hours, then the solvents removed under reduced pressure. The crude product (0.66 g) was shown (^{1}H n.m.r.) to be essentially a mixture (*c.* 5:4) of the two compounds (115) and (116), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:

trans-2,2,4,5,6-pentachloro-3,5,6-trimethylcyclohex-3-enone (115), m.p. 81-82°, (X-ray structure determination, see Appendix 1). ν_{max} (Nujol) 1766, C=O; 1635 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.00, 6-Me; 2.03, 5-Me; 2.30, 3-Me. [Lit.[22] for compound in admixture with (116): ν_{max} (liq. film) 1760, C=O; 1635 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.01, 6-Me; 2.03, 5-Me; 2.29, 3-Me.]

Eluted second (pentane) was:

trans-2,4,4,5,6-pentachloro-3,5,6-trimethylcyclohex-2-enone (116), m.p. 38-39°, (Found: C, 35.0; H, 3.0; Cl, 57.1. $C_9H_9Cl_5O$ requires C, 34.8; H, 2.9; Cl 57.1%). ν_{max} (Nujol) 1719, C=O; 1609 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.07, 6-Me; 2.22, 5-Me; 2.50, 3-Me. [Lit.[22] for compound in admixture with (115): ν_{max} (liq. film) 1725, C=O; 1610 cm^{-1}, C=C. ^{1}H n.m.r. ($CDCl_3$) δ 2.07, 6-Me; 2.21, 5-Me; 2.47, 3-Me.]

r-2,4,*c*-5,*t*-6-tetrachloro-2,6-dimethylcyclohex-3-enone (40), m.p. 41-42°, identical with authentic material.

Eluted third (diethylether/pentane) (1:15) was: *trans*-4,4,5,6-tetrachloro-2,6-dimethylcyclohex-2-enone (113), a yellow oil, (Found: C, 36.9; H, 3.3; Cl, 54.3. $C_8H_8Cl_4O$ requires C, 36.7; H, 3.1; Cl, 54.1%). ν_{max} (liq. film) 1701, C=O; 1640, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.85, 6-Me; 1.98, d, J 1.5 Hz, 2-Me; 5.00, H5; 7.00, q, J 1.5 Hz, H3.

Eluted fourth (diethylether/pentane) (1:9) was: *r*-2-acetoxy-4-,*c*-5,*t*-6-trichloro-2,6-dimethylcyclohex-3-enone (114), colourless needles, m.p. 125-125.5°, (X-ray structure determination, see Appendix 1.) ν_{max}, (Nujol) 1745 (sh), C=O; 1735, C=O; 1230 cm^{-1}, acetoxy. ^1H n.m.r. ($CDCl_3$) δ 1.79, 2-Me 1.93, 6-Me; 2.04, 2-OAc; 4.87, H5; 5.93, H3. λ_{max} ($CHCl_3$) 241 nm; ε 1010.

Attempted reaction 4,5,6-Trichloro-2,3,6-trimethylcyclohexa-2,4-dienone (84) with Chlorine in Acetic Acid

To a stirred solution of the dienone (84) (0.5 g) in acetic acid (5 ml) at 20° was added chlorine (0.19 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 75 minutes, then the solvents removed under reduced pressure. the crude product (0.5 g) was shown (^1H n.m.r.) to be essentially unreacted dienone (84).

Attempted Reaction of 3,5,6-Trichloro-2,4,6-trimethylcyclohexa-2,4-dienone (77) with Chlorine in Acetic Acid

To a stirred solution of the dienone (77) (0.33 g) in acetic acid (3 ml) at 20° was added chlorine (0.12 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product was shown (^1H n.m.r.)

Reaction of 4,5,6-Trichloro-2,6-dimethylcyclohexa-2,4-dienone (81) and 3,4,6-Trichloro-2,6-dimethylcyclohexa-2,4-dienone (82) with Chlorine in Acetic Acid

To a stirred solution of the dienones (81) and (82) (*c*. 3:2) (1.5 g) in acetic acid (10 ml) at 20° was added chlorine (0.57 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 6 hours, then the solvents removed under reduced pressure. The crude product (2.9 g) was shown (^{1}H n.m.r.) to be essentially a mixture (*c*. 6:5) of the two compounds (43) and (44), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:
r-2,3,4,*t*-5,*c*-6-pentachloro-2,6-dimethylcyclohex-3-enone (44), m.p. 82-83°, identical with authentic material.

Eluted second (pentane) was:
r-2,3,4,*c*-5,*t*-6-pentachloro-2,6-dimethylcyclohex-3-enone (43), m.p. 122-123°, identical with authentic material.

Reactions of 2,4,6-Trichloro-5,6-dimethylcyclohexa-2,4, dienone (70)

(a) Acetic Acid with Chlorine and Hydrogen Chloride; 30 min.

To a stirred solution of the dienone (70) (0.5 g) in acetic acid (5 ml) and hydrogen chloride (0.09 g; 1.0 mole) at 20° was added chlorine (0.19 g; 1.2 mole) as a chlorine/ acetic acid solution. The mixture was stirred for 30 min in a darkened flask, then the solvents removed under reduced pressure. The crude product (0.63 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 5.2) of the pentachlorocyclohex-3-enones (31) and (32).

(b) Acetic Acid with Chlorine and Concentrated Hydrochloric Acid; 30 min.

To a stirred solution of the dienone (70) (0.5 g) in acetic acid (5 ml) and concentrated hydrochloric acid (0.05 ml) at 20° was added chlorine (0.19 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 30 minutes, then the solvents removed under reduced pressure. The crude product (0.61 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 1:11:5) of the unreacted dienone (70) and the two pentachlorocyclohex-3-enones (31) and (32).

(c) Acetic Acid and Chlorine; 30 min.

To a stirred solution of the dienone (70) (0.5 g) in acetic acid (5 ml) at 20° was added chlorine (0.19 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 30 minutes, then the solvents removed under reduced pressure. The crude product (0.53 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 6:2:1) of the unreacted dienone (70) and the pentachlorocyclohex-3-enones (31) and (32).

(d) Acetic Acid and Chlorine with Sodium Acetate; 1 hour.

To a stirred solution of the dienone (70) (0.6 g) in acetic acid (6 ml) and sodium acetate (0.02 g; 0.1 mole) at 20° was added chlorine (0.23 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (0.64 g) was shown (^{1}H n.m.r.) to contain essentially unreacted dienone (70).

(e) Acetic Acid and Hydrogen Chloride; 15 minutes.

To a stirred solution of the dienone (70) (0.46 g) in acetic acid (6 ml) at 20° was added hydrogen chloride (0.08 g; 1.0 mole) as a hydrogen chloride/acetic acid solution. The mixture was stirred in a darkened flask for 15 minutes, then the solvents removed under reduced pressure. The crude product (0.45 g) was shown (^{1}H n.m.r.) to be essentially unreacted dienone (70).

(f) Attempted Rearrangement in Acetic Acid; 1 hour.

A solution of the dienone (70) (0.5 g) in acetic acid (5 ml) at 20° was stirred in a darkened flask for 1 hour. The solvents were then removed under reduced pressure. The crude product was shown (^{1}H n.m.r.) to be essentially unreacted dienone (70).

Reactions of 2,4,6-Trichloro-6-methylcyclohexa-2,4-dienone (66)

(a) Acetic Acid with Chlorine and Hydrogen Chloride; 30 minutes

To a stirred solution of the dienone (66) (0.5 g) in acetic acid (5 ml) and hydrogen chloride (0.09 g; 1.0 mole) at 20° was added chlorine (0.2 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 30 minutes, then the solvents removed under reduced pressure. The crude product (0.59 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 1:12:12) of pentachlorocyclohex-2-enone (112) and the pentachlorocyclohex-3-enones (28) and (29).

(b) Acetic Acid with Chlorine and Concentrated Hydrochloric Acid; 30 minutes

To a stirred olution of the dienone (66) (0.5 g) in acetic acid (5 ml) and concentrated hydrochloric acid (0.05 ml) at 20° was added chlorine (0.2 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 30 minutes, then the solvents removed under reduced pressure. The crude product (0.58 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 2:12:12) of the pentachlorocyclohex-2-enone (112) and the pentachlorocyclohex-3-enones (28) and (29).

(c) Acetic Acid and Chlorine; 30 minutes

To a stirred solution of the dienone (66) (0.5 g) in acetic acid (5 ml) at 20° was added chlorine (0.2 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 30 minutes, then the solvents removed under reduced pressure. The crude product (0.53 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 14:3:5:5) of unreacted dienone (66), the pentachlorocyclohex-2-enone (112) and the pentachlorocyclohex-3-enones (28) and (29).

(d) Acetic Acid with Chlorine and Sodium Acetate; 30 minutes

To a stirred solution of the dienone (66) (0.5 g) in acetic acid (5 ml) and sodium acetate (0.02 g; 0.1 mole) at 20° was added chlorine (0.2 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 30 minutes, the solvents removed under reduced pressure. The crude product (0.52 g) was shown (^{1}H n.m.r.) to be essentially a mixture (*c*. 4:1) of unreacted dienone (66) and the pentachlorocyclohex-2-enone (112).

Reactions of 4,6-Dichloro-2,3,6-trimethylcyclohexa-2,4-dienone (79):

(a) Acetic Acid and Chlorine with Hydrogen Chloride; 1 hour

To a stirred solution of the dienone (79) (0.6 g) in acetic acid (6 ml) and hydrogen chloride (0.11 g; 1 mole) at 20° was added chlorine (0.25 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (0.79 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 5:4) of the tetrachlorocyclohex-3-enones (37) and (38).

(b) Acetic Acid and Chlorine; 2 minutes

To a stirred solution of the dienone (79) (0.62 g) in acetic acid (6 ml) at 20° was added chlorine (0.26 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 2 minutes, then the solvents removed under reduced pressure. The crude product (0.67 g) was shown (^{1}H n.m.r.) to be a mixture (*c.* 1:9:7) of unreacted dienone (79) and the tetrachlorocyclohex-3-enones (37) and (38).

(c) Acetic Acid and Chlorine with (0.1 mole) Sodium Acetate

To a stirred solution of the dienone (79) (0.6 g) in acetic acid (6 ml) and sodium acetate (0.024 g; 0.1 mole) at 20° was added chlorine (0.25 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (0.79 g) was shown (^{1}H n.m.r.)

to consist of a mixture (*c*. 34:26:10:7) of the tetrachlorocyclohex-3-enones (37) and (38) and the compounds (119) and (118), which were separated on a Chromatotron with a 2 mm silica gel plate.

Eluted first (pentane) was:
r-2,4,*t*-5,*c*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (38), m.p. 106-107°, identical with authentic material.

Eluted second (pentane) was:
r-2,4,*c*-5,*t*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (39), m.p. 126-127°, identical with authentic material.

Eluted third (diethylether/pentane) (1:9) was:
trans-4,4,5,6-tetrachloro-2,3,6-trimethylcyclohex-2-enone (119), an oil, (Found: C, 39.3; H, 3.7; Cl, 51.2. $C_9H_{10}Cl_4O$ requires C, 39.2; H, 3.7; Cl, 51.5%). ν_{max} (liq. film) 1697, C=O; 1627 cm^{-1}, C=C. ^1H n.m.r. ($CDCl_3$) δ 1.82, 6-Me; 1.98, 2-Me; 2.35, 3-Me; 5.07, H5.

Eluted fourth (diethylether/pentane) (1:9) was:
r-2-acetoxy,4,*c*-5,*t*-6-trichloro-2,3,6-trimethylcyclohex-3-enone (118), m.p. 100-101°, (Found: C, 44.2; H, 4.5; Cl, 35.8. $C_{11}H_{13}Cl_3O$ requires C, 44.1; H, 4.4; Cl, 35.5%). ν_{max} (Nujol) 1752, C=O; 1742, C=O; 1657, C=C; 1232 cm^{-1}, acetoxy. ^1H n.m.r. ($CDCl_3$) δ 1.82, 6-Me; 1.90, 2-Me and 3-Me; 2.07, OAc; 4.98, H5. λ_{max} ($CHCl_3$) 235 nm; ε 2200.

(d) Acetic Acid and Chlorine with 0.5 mole Sodium Acetate

To a stirred solution of the dienone (79) (0.54 g) in acetic acid (5.5 ml) and sodium acetate (0.11 g; 0.5 mole) at 20° was added chlorine (0.22 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (0.71 g) was shown (^1H n.m.r.) to consist of a mixture (*c*. 15:12:10:8) of the tetrachlorocyclohex-3-enones (37) and (38) and the compounds (119) and (118).

(e) Acetic Acid and Chlorine with 1.0 mole Sodium Acetate:

To a stirred solution of the dienone (79) (0.59 g) in acetic acid (6 ml) and sodium acetate (0.24 g; 1.0 mole) at 20° was added chlorine (0.24 g; 1.2 mole) as a chlorine/acetic acid solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (1.1 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 15:12:11:13) of the tetrachlorocyclohex-3-enones (37) and (38) and the compounds (119) and (118).

(f) Attempted Rearrangement in Acetic Acid:

A solution of the dienone (79) (0.5 g) in acetic acid (5 ml) at 20° was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (0.49 g) was shown (^{1}H n.m.r.) to be essentially unreacted dienone (79).

(g) Attempted Rearrangement in Acetic Acid and Sodium Acetate:

A solution of the dienone (79) (0.5 g) in acetic acid (5 ml) and sodium acetate (0.024; 0.1 mole) was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (0.52 g) was shown (^{1}H n.m.r.) to be essentially unreacted dienone (79).

(h) Attempted Reaction with Chlorine in Carbon Tetrachloride:

To a solution of the dienone (79) (0.5 g) in carbon tetrachloride (5 ml) at 20° was added chlorine (0.22 g; 1.2 mole) as a chlorine/carbon tetrachloride solution. The mixture was stirred in a darkened flask for 1 hour, then the solvents removed under reduced pressure. The crude product (0.5 g) was shown (^{1}H n.m.r.) to be essentially unreacted dienone (79).

(h) Acetic Acid and Hydrogen Chloride:

A solution of the dienone (79) (0.5 g) in acetic acid (5 ml) and hydrogen chloride (0.11; 1.0 mole) at 20° was stirred in a darkened flask for 15 minutes, then the solvents removed under reduced pressure. The crude product (0.47 g) was shown (^{1}H n.m.r.) to consist of a mixture (*c*. 9:1) of unreacted dienone (79) and the parent phenol (78).

5.5 Selected Preparations of Chlorophenols

Preparation of 2,3,4,6-Tetrachloro-5-methylphenol

Chlorine was bubbled slowly through a stirred solution of thymol (5 g) in carbon tetrachloride (30 ml) with finely divided iron dust (1.5 g) in a darkened flask at 0°, for 5 hours. The mixture was then stirred for a further 18 hours at room temperature, then the solids filtered off. The filtrate was then washed with water (3 x 200 ml), then dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (9.8 g) was shown by (^{1}H n.m.r.) to be essentially the dienone (123).

2,3,4,4,6-pentachloro-5-methylcyclohexa-2,5-dienone (123) m.p. 92° (ex. light petroleum) ^{1}H n.m.r. ($COCl_3$) 2.55, 5-Me. [Lit.^{33} m.p. 92°.]

The above material was dissolved in acetic acid (80 ml) and finely divided zinc dust (6 g) added to the rapidly stirred solution. Reaction was almost immediate. The solids were filtred off and the filtrate poured into water (220 ml) and then extracted into light petroleum (3 x 100 ml). The extracts were combined, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (6.3 g) was shown to be essentially pure tetrachlorophenol, which crystallized from light petroleum to give:

2,3,4,6-Tetrachloro-5-methyl phenol (53) m.p. 189-190°C, ν_{max} (Nujol) 3540 cm^{-1}, OH. ^{1}H n.m.r. ($CDCl_3$) δ 2.50, 5-Me; 5.95, D_2O exch., OH. [Lit.^{33} m.p. 189-190°.]

Preparation of 2,3,4-Trichloro-6-methylphenol

Chlorine was bubbled slowly through a stirred solution of 3-chloro-6-methylaniline (15 g) in acetic acid (120 ml) and concentrated hydrochloric acid (10 ml) at 20° in a darkened flask for 2 hours. The solid ammonium chloride formed during the reaction was filtered off and the solvents removed first by distillation under reduced pressure and then by drying under reduced pressure (*c.* 3 mm) for several hours.

The crude product (16 g) was shown (^1H n.m.r.) to be essentially a mixture (*c.* 1:1) of the hexachlorocyclohex-3-enones (22) and (23), which were crystallized from pentane before proceeding with the next step.

The hexachlorocyclohex-3-enones (22) and (23) (8 g) were dissolved in acetic acid (130 ml) and rapidly stirred while finely divided zinc dust (8 g) was added. The mixture was then stirred at 20° for 1 hour, then the solids filtered off. The filtrate was poured into water (200 ml) and then extracted into light petroleum (3 x 100 ml). The extracts were combined, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (6.1 g) was shown (^1H n.m.r.) to be essentially the trichlorophenol, which crystallized from light petroleum to give:

2,3,4-trichloro-6-methylphenol (122) (4.4 g) as colourless needles, m.p. 75-76°. ν_{max} (Nujol) 3425 cm^{-1}, OH. ^1H n.m.r. ($CDCl_3$) δ 2.25, d, J 0.5 Hz, 6-Me; 5.67, D_2O exch., OH; 7.17, q, J 0.5 Hz, H5. [Lit.[45] m.p. 77°C.]

Preparation of 3,4-Dichloro-2,6-dimethylphenol

Chlorine was bubbled through a stirred solution of 2,6-dimethylphenol (20 g) in acetic acid (200 ml) and concentrated hydrochloric acid (20 ml) at 20° in a darkened flask, rapidly for 30 minutes, and then slowly for a further 2 hours. The excess chlorine was purged with nitrogen, then the solvents removed first by distillation under reduced pressure, and then by drying under reduced pressure for several hours. The crude product (30 g) was shown (^{1}H n.m.r.) to be essentially the pentachlorocyclohex-3-enones (43) and (44), which crystallised from diethylether/ pentane to give (20 g) of a crystalline mixture (*c.* 2:3) of the above compounds.

The pentachlorocyclohex-3-enones (43) and (44) (26 g) were dissolved in acetic acid (300 ml) and zinc dust (15 g) added to the rapidly stirred solution, then left stirring for 1 hour at 20°. The solids were filtered off and the filtrate poured into water (300 ml), then extracted with light petroleum (3 x 100 ml). The extracts were combined, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (12.2 g) was shown (^{1}H n.m.r.) to be essentially pure dichlorophenol, which recrystallized from light petroleum to give: 3,4,-dichloro-2,6-dimethylphenol (80) (7.8 g) as colourless needles, m.p. 87.5-88.5°. ν_{max} (Nujol) 3616 cm^{-1}, OH. ^{1}H n.m.r. ($CDCl_3$)δ 2.17, d, J 0.5 Hz; 2.30, 2-Me; 4.67, D_2O exch., OH; 7.05, q, J 0.5 Hz, H5. [Lit.[28] m.p. 87-88°, ν_{max} (CCl_4) 3615 cm^{-1}, OH. ^{1}H n.m.r. (CS_2)δ 2.17, d, J 0.7 Hz, 6-Me; 2.28, d, J 0.5 Hz, 2-Me; 4.54, OH; 6.98, septet, J 0.6 Hz, H5.]

Preparation of 2,3,4,5-Tetrachloro-6-methylphenol

Chlorine was bubbled through a stirred solution of 2,4-dichloro-6-methylphenol (4 g) in carbon tetrachloride (100 ml) and finely divided iron dust (4 g) at 20° in a darkened flask for 3 hours. The solids were filtered off and the filtrate washed with water (3 x 100 ml). The organic phase was separated, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (6.4 g) was shown (^{1}H n.m.r.) to be essentially the chlorodienone (124).

2,3,4,4,5-pentachloro-6-methylcyclohexa-2,5-dienone (124) m.p. 63-64°, ν_{max} ν(Nujol) 1695, C=O; 16-1 cm^{-1}, C=C. ^{1}H n.m.r. (CDCl$_3$) δ 2.18, 6-Me. [Lit.[44] m.p. 64°.]

The above material was dissolved in acetic acid (100 ml) and zinc dust (8 g) added to the rapidly stirred solution. The reaction was rapid and complete in 10 minutes. The solids were filtered off and the filtrate poured into water (200 ml) and extracted with light petroleum (3 x 50 ml). The extracts were combined, dried over anhydrous magnesium sulphate and the solvents removed under reduced pressure. The crude product (4.0 g) was shown (^{1}H n.m.r.) to be essentially the tetrachlorophenol, which recrystallized from diethylether/pentane to give:

2,3,4,5-tetrachloro-6-methylphenol (60), (3.2 g) as buff coloured needles, m.p. 190-191°, ν_{max} (Nujol) 3550 cm^{-1}, OH. ^{1}H n.m.r. (CDCl$_3$) δ 2.37, 6-Me; 5.80, D$_2$O exch., OH. [Lit.[44] m.p. 190°.

APPENDIX 1

Single-crystal X-ray Structure Analyses

1.1 Crystal Structure: *trans*-2,2,3,4,5,6-hexachloro-6-methylcyclohex-3-enone (22)

Crystal unit cell data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was unambiguously determined from the systematic absences (oko, k=2n; ool, hol, l=2n) and the distribution of normalized structure factors.

Molybdenum X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 23.3° at room temperature. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections (25°<2θ<35°). Absorption corrections were applied empirically from azimuthal scans of selected reflections.

Crystal Data for: *trans*-2,2,3,4,5,6-hexachloro-6-methylcyclohex-3-enone (22)

$C_7H_4Cl_6O$, M 316.83, monoclinic, space group $P2_1/_c$, a 8.410(2), b 10.194(2), c 13.329(2) Å, β 98.04(1)°, U 1131.5 $Å^3$, Dm 1.82 g cm^{-3}, Dc 1.84 g cm^{-3}, Z 4. The crystal was colourless and of approximate dimensions 0.22 x 0.13 x 0.19 mm. Absorption corrections, maximum 0.86, minimum 0.60. Number of independent reflections measured 1883, number of observed reflections with $I>3\sigma(I)$ 1336, g 0.0014, R-factor 0.039, Rw 0.043.

The structure was solved by direct methods and difference Fourier syntheses. Blocked-cascade least-squares refinements were employed with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo|-|Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors. Final Fourier synthesis showed no significant residual electron density and there were no abnormal discrepancies between the observed and calculated structure factors.

1.2 Crystal Structure: *cis*-2,4,5,6,6-Pentachloro-2-methylcyclohex-3-enone (28)

Crystal unit cell data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was unambiguously determined from the systematic absences (oko, k=2n; ool, hol, l=2n) and the distribution of normalized structure factors.

Molybdenum X-radiation from a crystal monochromator [λ(Mokα) 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 25° at room temperature. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections ($25° < 2\theta < 30°$). Absorption corrections were applied empirically from azimuthal scans of selected reflections.

Crystal Data for: *cis*-2,4,5,6,6-Pentachloro-2-methylcyclohex-3-enone (28)

$C_7H_5Cl_5O$, M 282.38, monoclinic, space group $P2_1/c$, a 7.421(4), b 14.319(8), C 10.178(b) Å, β 97.69(5)° U 1071.8 $Å^3$, Dm 1.70 g cm^{-3}, Dc 1.73 g cm^{-3}, Z 4, the crystal was colourless and of approximate dimensions 0.18 x 0.15 x 0.07 mm. Absorption corrections, maximum 0.96, minimum 0.92. Number of independent reflections measured 1885, observed reflections with $I>3\sigma(I)$ 1336, g 0.0023, R-factor 0.046, Rw 0.048.

The structure was solved using direct methods and difference Fourier syntheses. Blocked-cascade least-squares refinements were employed with reflections weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors. Final Fourier synthesis showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.3 Crystal Structure: *r*-2,4,*t*-5,*c*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (38)

Crystal unit cell data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was unambiguously determined from the systematic absences (oko, k=2n; ool, hol, l=2n).

Molybdenum X-radiation from a crystal monochromator [λ(Mokα) 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 22.5° at room temperature.

The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections (25°>2θ>30°). Absorption corrections were applied empirically from azimuthal scans of selected reflections.

Crystal Data for *r*-2,4,*t*-5,*c*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (38)

$C_9H_{10}Cl_4O$, M 275.98, monoclinic, space group $P2_1/c$, a 8.533(2), b 10.187(4), c 13.526(4) Å, β 97.97(2)°, U 1162.3 $Å^3$, Dm 1.55 g cm^{-3}, Dc 1.57 g cm^{-3}, Z 4, the crystal was colourless and of approximate dimensions 0.15 x 0.09 x 0.20 mm. Absorption corrections, maximum 0.77, minimum 0.66. Number of independent reflections measured 703, observed reflections with $I>2\sigma(I)$ 634, g 0.0002, R-factor 0.058, Rw 0.057.

The structure was solved using direct methods and difference Fourier synthesis. Blocked-cascade least-squares refinements were employed with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. Anisotropic temperature factors were assigned to the chlorine and oxygen atoms. Final Fourier synthesis showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.4 Crystal Structure: 2,2,4,5,6,6-Hexachloro-3,5-dimethylcyclohex-3-enone (46)

Crystal unit cell data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four circle diffractometer, are given below. The space group was unambiguously determined from the systematic absences (hoo, h=2n; oko, k=2n; ool, l=2n; hol, h+l=2n).

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the omega scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 23° at room temperature. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections ($28° < 2\theta < 30°$). Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for 2,2,4,5,6,6-Pentachloro-3,5-dimethylcyclohex-3-enone (46)

$C_8H_6Cl_6O$, M 330.85, monoclinic, space group $P2_1/n$ a 8.426(3), b 13.437(5), C 11.232(4) Å, β 105.81° (3), U 1223.5 (7), Dm 1.80 g cm^{-3}, Dc 1.79 g cm^{-1}, Z 4, μ(MoKα) 13.83 cm^{-1}. The crystal was colourless and of approximate dimensions 0.16 x 0.39 x 0.61 (mm). Transmission factors (after absorption correction) minimum 0.56, maximum 0.79. Number of independent reflections measured 1732, observed reflections with $I > 3\sigma(I)$ 985, g 0.00001, R factor 0.068, Rw 0.046.

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors. Final

Fourier syntheses showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.5 Crystal Structure: *trans*-2,4,4,5,6-Pentachloro-3,6-dimethylcyclohex-2-enone (48)

Crystal unit cell data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four-circle diffractometer are given below. The space group was determined unambiguously from the systematic absences (oko, k=2n; ool, hol, l=2n) and the distribution of normalized structure factors.

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the Wychoff scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 23° at 160° K. The cell parameters were determined by least-squares refinement using the setting angles of 15 accurately centred reflections ($28° < 2\theta < 30°$). Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data: *trans*-2,4,4,5,6-Pentachloro-3,6-dimethylcyclohex-2-enone (48)

$C_8H_7Cl_5O$, M 296.409, monoclinic, space group $P2_1/c$, a 10.875(3), b 16.195(7), c 12.709(5) Å, β 91.45(3)°, U 2237.6(9) Å^3, Dm 1.75 g cm^3, Dc 1.76 g cm^3, Z=8 (two molecules in asymmetic unit), μ(MoKα) 12.68 cm^{-1}. The crystal was colourless and of approximate dimensions 0.32 x 0.32 x 0.61 (mm). Transmission factors (after absorption correction) minimum 0.67, maximum 0.75. Number of independent reflections measured 2983, observed reflections with $I>3\sigma(I)$ 1945, g 0.00056 R factor 0.045, Rw 0.053.

The structure was solved using direct methods and difference Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflection wrights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo|-|Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. Hydrogen atoms H5 and H15 were included as riding atoms with the appropriate geometrical constraints. All non-hydrogen atoms were assigned anisotropic temperature factors. Final Fourier syntheses showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.6 Crystal Structure: *cis*-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (49)

Crystal unit cell data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was indicated by the systematic absences (hoo, h=2n; oko, k=2n; ool, l=2n) and the distribution of normalized structure factors and was confirmed by this structure analysis.

Molybdenium x-radiation from a crystal monochromator [$\lambda(\text{MoK}\alpha)$ 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 25° at 130° K. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections ($28° < 2\theta < 30°$). Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for: *cis*-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (49)

$C_8H_7Cl_5O$, M 296.409, orthorhombic, space group $P2_12_12_1$, a 9.491(4), b 16.096(8), c 7.528(3) Å, U 1150.0 (9) $Å^3$, Dm 1.70 g cm^{-3}, Dc 1.71 g cm^{-3}, Z 4, μ(MoKα) 12.34 cm^{-1}. The crystal was colourless and of approximate dimensions 0.28 x 0.44 x 0.79 (mm). Transmission factors (after absorption correction) minimum 0.55, maximum 0.71. Number of independent reflections measured 1670, observed reflections with $I>3\sigma(I)$ 1511, *g* 0.00015, R factor 0.039, Rw 0.049.

The structure was solved using direct methods and difference-Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. Hydrogen atom H5 was included as a riding atom with the appropriate geometrical constraints. All non-hydrogen atoms were assigned anisotropic temperature factors. Final Fourier syntheses showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.7 Crystal Structure: *trans*-2,2,3,4,5,6-Hexachloro-5,6-dimethylcyclohex-3-enone (57)

Crystal unit cell data, established from precession photographs and measured accurately using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was determined unambiguously from the systematic absences (hoo, h=2n; oko, k=2n; ool, l=2n; hol, h+l=2n).

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the Wychoff scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 25° at 120° K. The cell parameters were determined by least-squares refinement using the setting angles of 15 accurately centred reflections ($28° < 2\theta < 30°$). Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for: *trans*-2,2,3,4,5,6-Hexachloro-5,6-dimethylcyclohex-3-enone (57)

$C_8H_6Cl_6O$, M 330.854, monoclinic, space group $P2_1/n$, a 6.146(2), b 12.512(5), c 15.654(7) Å, β 91.86(3)°, U 1203.1(8) Å^3, Dm 1.82 g cm^{-3}, Dc 1.83 g cm^{-3}, Z 4, μ(MoKα) 14.07 cm^{-1}. The crystal was colourless and of approximate dimensions 0.22 x 0.38 x 0.22 mm. Transmission factors (after absorption correction) minimum 0.74, maximum 0.80. Number of independent reflections measured 2114, observed reflections with $I > 3\sigma(I)$ 1821, g 0.00018, R factor 0.029, Rw 0.037.

The structure was solved by direct methods and difference-Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflections weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors. Final Fourier syntheses showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.8 Crystal Structure: *cis*-2,2,3,4,5,6-Hexachloro-5,6-dimethylcyclohex-3-enone (58)

Crystal cell unit data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was suggested by the distribution of normalized structure factors and confined by this structure analysis.

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the omega scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 23° at 160° K. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections (28°<2θ<30°).

Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for *cis*-2,2,3,4,5,6-Hexachloro-5,6-dimethylcyclohex-3-enone (58)

$C_8H_6Cl_6O$, M 330.854, triclinic, space group $P\bar{1}$, a 6.005(2), b 8.238(2), C 12.901(4) Å α 94.12(2), β 102.54(3), γ 108.69(3)°, U 583.2(3) $A^{\circ 3}$, Dm 1.87 g cm^{-1}, Dc 1.88 g cm^{-1}, Z 2, μ(MoKα) 14.51 cm^{-1}. The crystal was colourless and of approximate dimensions 0.24 x 0.34 x 0.59 (mm). Transmission factors (after absorption correction) minimum 0.58, maximum 0.74. Number of independent reflections measured 1625, observed reflections with $I>3\sigma(I)$ 1514, g 0.00029, R factor 0.029, Rw 0.044.

The structure was solved using direct methods and difference Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atom were assigned anisotropic temperature factors. Final Fourier syntheses showed no significant residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.9 Crystal Structure: 2,4,5,5,6,6-Hexachloro-2,3-dimethylcyclohex-3-enone (59)

Crystal unit cell data, established from precession photographs, and measured accurately using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was suggested by the distribution of normalised structure factors and was confirmed by this structure analysis.

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 25° at 120° K. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections ($30<2\theta<32°$). Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for: 2,4,5,5,6,6-Hexachloro-2,3-dimethylcyclohex-3-enone (59)

$C_8H_6Cl_6O$, M 330.85, triclinic, space group P$\bar{1}$, a 6.104(1) b 8.423(2), c 12.410(3) Å, α 78.18(2), β 84.79(2), γ 70.86(2)°, U 589.8(2) Å^3, Dm 1.85 g cm^{-3}, Dc 1.86 g cm^{-1}, Z 2, μ(MoKα) 14.35 cm^{-1}. The crystal was colourless and of approximate dimensions 0.20 x 0.21 x 0.62 (mm). Transmission factors (after absorption correction) minimum 0.72, maximum 0.76. Number of independent reflections measured 2042, observed reflections with $I>3\sigma(I)$ 1995, g 0.00009, R factor 0.041, Rw 0.067.

The structure was solved using direct methods and difference Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

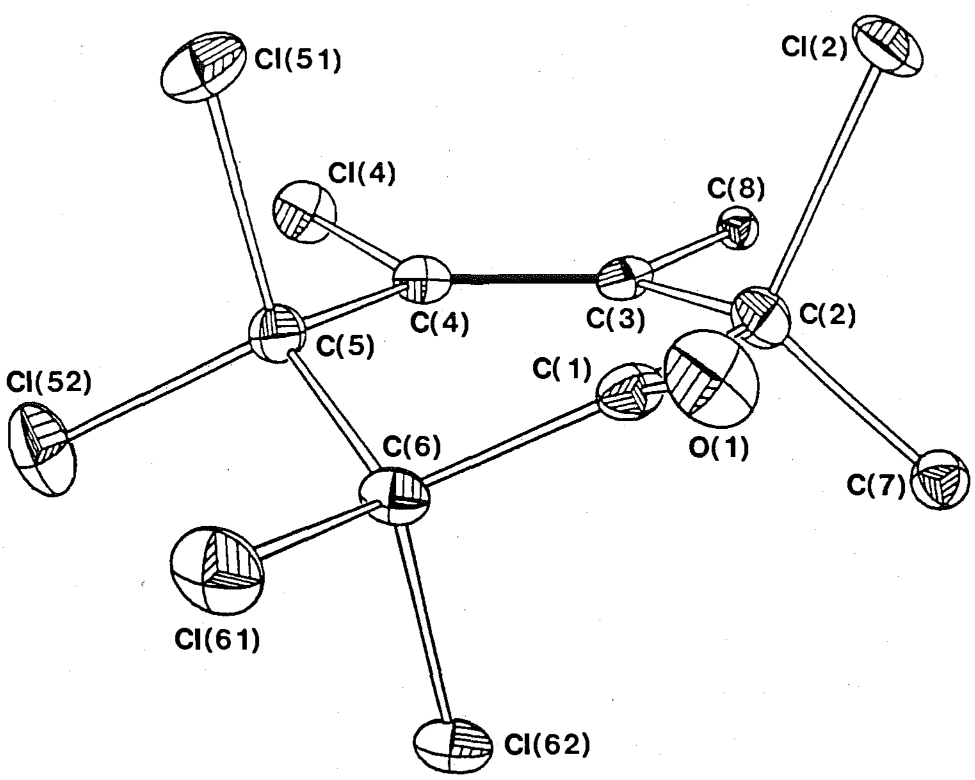
The model first refined (molecule 1); R 0.065, showed significant residual electron density around methyl carbon atom C7 in the difference-Fourier map. This discrepancy could not be explained satisfactorily by a translational disordering of the methyl group or by total interchange of the substituents C7 and Cl2 attached to carbon atom C2 (*vis* molecule 2). The best model produced from the data consists of a non-stoichiometric disordering of the substituent atoms C7 and Cl2 about carbon atom C2. The site occupancy factors of the resulting atom pairs C7, C7' and Cl2, Cl2' were allowed to refine within the appropriate constraints. The result was a S.O.F. of 0.85 for the atoms C7 and Cl2 in the positions represented by molecule 1 and a S.O.F. of 0.15 for the disordered atoms C7' and Cl2' in the positions represented by molecule 2, R 0.041.

The C8 methyl group hydrogen atoms were included as a rigid group pivoting about the carbon atom. The disordered atoms C7, C7' and Cl2, Cl2' were allowed to refine within appropriate distance constraints. All non-hydrogen atoms except Cl2' were assigned anisotropic temperature factors. The SHELXTL system was used for all computations.
Final Fourier syntheses showed little residual electron density ($0.8e^{-}$ Å^{-3}) and there were no abnormal discrepancies between observed and calculated structure factors.

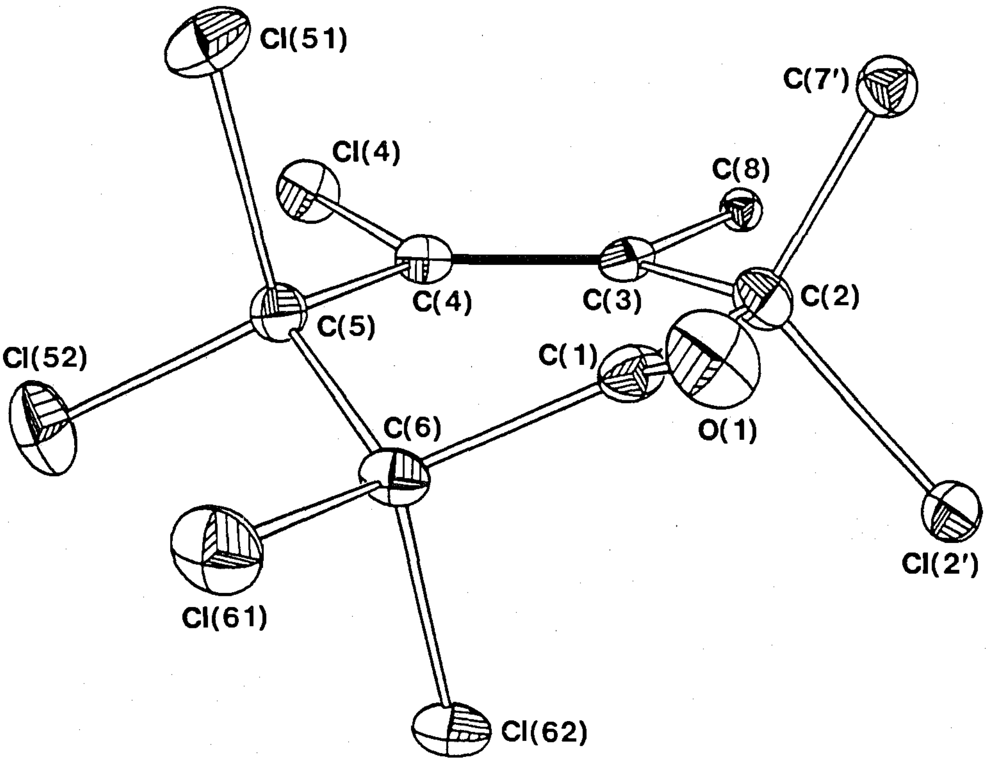
1.10 Crystal Structure: 4,*r*-6-Dibromo*t*-2,*c*-5,6-trichloro-2,3-dimethylcyclohex-3-enone (107)

Crystal unit cell data, established from precession photographs and accurately measured, using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was determined unambiguously from the systematic absences (oko, k=2n; ool, hol, l=2n) and was confirmed by this structure analysis.

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 25° at 160° K. The cell parameters were determined by least squares refinement using the setting angles of 25 accurately centred reflections ($28° < 2\theta < 30°$). Absorption



MOLECULE 1



MOLECULE 2

corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for: 4,*r*-6-Dibromo-*t*-2,*c*-5,6-trichloro-2,3-dimethylcyclohex-3-enone (107)

$C_8H_7Br_2Cl_2O$, M 385.32, monoclinic, space group $P2_1/c$, a 118.79(3), b 6.299(2), c 15.889(3) Å, β 95.06(2)°, U 1139.4(4) $Å^3$, Dm 2.24 g cm^{-3}, Dc 2.25 g cm^{-3}, Z 4. μ(MoKα) 77.2 cm^{-1}. The crystal was colourless and of approximate dimensions 0.15 x 0.045 x 0.4 (mm). Transmission factors (after absorption correction) minimum 0.38, maximum 0.73. Number of independent reflections measured 2020, number of observed reflections with $I>3\sigma(I)$ 1488, *g* 0.0016, R factor 0.071 Rw 0.096.

The structure was solved using direct methods and difference-Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anamolous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors.

Final Fourier syntheses showed little residual electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.11 Crystal Structure: *r*-2-acetoxy-4,*c*-5,*t*-6-trichloro-2,6-dimethylcyclohex-3-enone (114)

Crystal unit cell data, established from precession photographs and measured accurately using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was determined unambiguously from the systematic absences (oko, k=2n; ool, hol, l=2n).

Molybdenium X-radiation from a crystal monochromater [λ(MoKα) 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 24°.

The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections ($28° < 2\theta < 30°$). Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for *r*-2-Acetoxy-4,*c*-5,*t*-6-trichloro-2,6-dimethylcyclohex-3-enone (114)

$C_{10}H_{11}Cl_3O_3$, M 285.555, monoclinic, space group $P2_1/c$, a 12.971(2), b 12.650(2), c 8.541(1) Å, β 93.65(1)°, U 1234.8(3) Å^3, Dm 1.53 g cm^{-3}, Dc 1.54 g cm^{-1}, Z 4, μ(MoKα) 7.32 cm^{-1}. The crystal was colourless and of approximate dimensions 0.08 x 0.22 x 0.22 (mm). Transmission factors (after absorption correction) minimum 0.72, maximum 0.82. Number of independent reflections measured. 1838, number of observed reflections with $I > 1\sigma(I)$ 1605, *g* 0.001, R factor 0.045, Rw 0.059.

The structure was solved using direct methods and difference-Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors.

Final Fourier syntheses showed no significant residual electron density and there were no abnormal discrepancies between the observed and calculated structure factors.

The SHELXTL[48] system of computer programmes was used in all calculations.

1.12 Crystal Structure: *trans*-2,2,4,5,6-Pentachloro-3,5,6-trimethylcyclohex-3-enone (115)

Crystal unit cell data, established from precession photographs and measured accurately, using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was suggested by the distribution of the normalised structure factors and was confirmed by this structure analysis.

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the omega scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 23°. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections ($28° < 2\theta < 30°$). Absorption corrections were applied using the indexed bounding faces of the crystal and numerical integration.

Crystal data for: *trans*-2,2,4,5,6-Hexachloro-3,5,6-trimethylcyclohex-3-enone (115)

$C_9H_9Cl_5O$, M 310.436, triclinic, space group P$\bar{1}$, a 8.305(2), b 13.356(4), c 13.624(4) Å, α 114.64(2), β 98.89(2), γ 105.69(2)°, U 1259.3(6) Å^3, Dm 1.63 g cm^{-3}, Dc 1.64 g cm^{-1}, Z 4 (two molecules in asymmetric unit), μ(MoKα) 11.3 cm^{-1}. The crystal was colourless and of approximate dimensions 0.16 x 0.38 x 0.59 (mm). Transmission factors (after absorption correction) minimum 0.64, maximum 0.85. Number of independent reflections measured 3286, observed reflections with $I>2.5\sigma(I)$ 2436, g 0.00045, R factor 0.051, Rw 0.065.

The structure was solved using direct methods and difference-Fourier syntheses. Blocked-cascade least-squares refinements were employed, with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors.

Final Fourier syntheses showed no significant electron density and there were no abnormal discrepancies between observed and calculated structure factors.

1.13 Crystal Structure: (E)-(2RS,5RS)-2,4,5,6,6-pentachloro-2-methyl-6-nitrohex-3-enoic acid (131)

Crystal unit cell data, established from precession photographs and measured accurately using a Nicolet XRD-P3 four-circle diffractometer, are given below. The space group was suggested by the distribution of the normalized structure factors and confirmed by this structure analysis.

Molybdenium X-radiation from a crystal monochromator [λ(MoKα) 0.71069 Å] and the $\theta/2\theta$ scan technique were used to collect reflection intensities out to a maximum Bragg angle θ 29° at room temperature. The cell parameters were determined by least-squares refinement using the setting angles of 25 accurately centred reflections ($25° > 2\theta > 35°$).

Absorption corrections were applied empirically from azimuthal scans of selected reflections.

Crystal Data for: (E)-(2RS,5RS)-2,4,5,6,6-pentachloro-2-methyl-6-nitrohex-3-enoic acid (131)

$C_7H_6Cl_5NO_4$, M 345.39, triclinic, space group $P\bar{1}$, a 7.985(1), b 9.119(2), c 10.799(2) Å, α 107.4(1), β 105.99(1), γ 105.74(1)°, U 655.2 $Å^3$, Dm 1.71 g cm^{-3}, Dc 1.73 g cm^{-3}, Z 2, $\mu(MoK\alpha)$ 10.96 cm^{-1}, the crystal was colourless and of approximate dimensions 0.14 x 0.19 x 0.15 mm. Absorption corrections, maximum 0.83, minimum 0.76. Number of independent reflections measured 3747, observed reflections with $I>3\sigma(I)$ 2660, g 0.00012, R-factor 0.039, Rw 0.042.

The structure was solved using direct methods and difference Fourier synthesis. Blocked-cascade least-squares refinements were employed with reflection weights $1/[\sigma^2(F)+g(F)^2]$. The function minimised was $\Sigma w(|Fo| - |Fc|)^2$. Anomalous dispersion corrections were from Cromer and Liberman.[47]

Methyl hydrogen atoms were included as rigid groups pivoting about their carbon atoms. All non-hydrogen atoms were assigned anisotropic temperature factors. Final Fourier synthesis showed no significant residual electron density and there were no abnormal discrepancies between the observed and calculated structure factors.

TABLE 1. Fractional coordinates for non-hydrogen atoms in *trans*-2,2,3,4,5,6-hexachloro-6-methylcyclohex-3-enone (22), $C_7H_4Cl_6O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(6)	7107(1)	1616(1)	3298(1)	47(1)
Cl(3)	10354(1)	2299(1)	735(1)	59(1)
Cl(4)	7341(1)	464(1)	226(1)	51(1)
Cl(5)	4527(1)	3845(1)	487(1)	58(1)
Cl(21)	8661(2)	5182(1)	1048(1)	61(1)
Cl(22)	10200(1)	3837(1)	2839(1)	59(1)
O(1)	6762(4)	4965(3)	2747(3)	50(1)
C(4)	7337(4)	1794(4)	1018(3)	34(1)
C(6)	5970(5)	2746(4)	2419(3)	37(1)
C(2)	8555(5)	3785(4)	1843(3)	37(1)
C(3)	8602(5)	2564(4)	1222(3)	36(1)
C(5)	5779(5)	2034(4)	1412(3)	38(1)
C(7)	4414(5)	3078(4)	2793(3)	44(1)
C(1)	7038(5)	3947(4)	2365(3)	34(1)

TABLE 2. Fractional coordinates for non-hydrogen atoms in *cis*-2,4,5,6,6-pentachloro-2-methylcyclohex-3-enone (28), $C_7H_5Cl_5O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(61)	6263(2)	4630(1)	3613(2)	64(1)
Cl(62)	7273(2)	5952(1)	1708(2)	69(1)
Cl(2)	11984(2)	3310(1)	2255(2)	62(1)
Cl(5)	7702(2)	4321(1)	-331(1)	64(1)
Cl(4)	5582(2)	2312(1)	824(2)	72(1)
C(1)	9511(7)	4566(3)	2773(5)	43(2)
C(7)	10434(9)	3356(4)	4506(5)	64(2)
C(4)	7119(6)	3122(3)	1576(5)	42(2)
O(1)	10612(5)	5168(3)	3009(4)	60(1)
C(2)	9950(7)	3535(3)	3028(5)	42(2)
C(3)	8534(7)	2866(4)	2395(5)	45(2)
C(6)	7512(7)	4786(3)	2227(5)	44(2)
C(5)	6721(8)	4101(4)	1166(5)	43(2)

TABLE 3. Fractional coordinates for non-hydrogen atoms in *r*-2,4,*t*-5,*c*-6-tetrachloro-2,3,6-trimethylcyclohex-3-enone (38) $C_9H_{10}Cl_4O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(6)	7879(3)	1561(3)	1689(2)	52(1)
Cl(2)	4773(4)	3714(3)	2175(2)	73(2)
Cl(4)	7766(3)	385(3)	4731(2)	54(1)
Cl(5)	10461(4)	3018(3)	4447(2)	63(1)
C(4)	7674(11)	1737(10)	3943(7)	32(3)
O(1)	8156(8)	4924(7)	2257(5)	42(3)
C(9)	10510(12)	3067(10)	2152(7)	48(3)
C(6)	8956(12)	2715(10)	2562(7)	35(3)
C(2)	6446(12)	3731(10)	3175(7)	43(3)
C(8)	4901(12)	2187(10)	4210(7)	49(3)
C(5)	9211(12)	2005(10)	3544(7)	41(3)
C(1)	7868(12)	3900(11)	2624(7)	34(3)
C(3)	6412(12)	2496(10)	3779(7)	33(3)
C(7)	6349(13)	4994(10)	3899(7)	48(3)

TABLE 4. Fractional coordinates for non-hydrogen atoms in 2,2,4,5,6,6-hexachloro-3,5-dimethylcyclohex-3-enone (46), $C_8H_6Cl_6O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(2)	3414(3)	4596(2)	8960(2)	86(1)
Cl(3)	212(3)	5338(2)	6702(2)	83(1)
Cl(4)	-2686(3)	4629(2)	7656(2)	72(1)
Cl(5)	49(3)	3482(2)	10355(2)	66(1)
Cl(61)	-294(3)	1875(2)	6965(2)	66(1)
Cl(62)	768(3)	1293(2)	9537(2)	85(1)
O(1)	3383(7)	2413(5)	9066(5)	76(3)
C(1)	2080(10)	2804(6)	8567(7)	49(4)
C(2)	2031(10)	3783(6)	7887(7)	48(4)
C(3)	382(10)	4286(6)	7561(6)	42(3)
C(4)	-877(10)	3963(5)	7969(7)	42(3)
C(5)	-795(9)	3056(6)	8767(6)	44(3)
C(6)	440(10)	2316(6)	8518(7)	46(3)
C(7)	2687(11)	3639(7)	6771(8)	70(4)
C(8)	-2469(10)	2576(7)	8681(8)	68(4)

TABLE 5. Fractional coordinates for non-hydrogen atoms in *trans*-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (48), $C_8H_7Cl_5O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(1)	7556(2)	6652(1)	7237(1)	43(1)
Cl(2)	4760(2)	6557(1)	3981(1)	49(1)
Cl(3)	3476(1)	7325(1)	5735(1)	43(1)
Cl(4)	4477(2)	8551(1)	3929(1)	47(1)
Cl(5)	6973(2)	9313(1)	4951(1)	42(1)
O(1)	7648(4)	8368(3)	6788(4)	50(2)
C(1)	6865(5)	8033(4)	6298(5)	29(2)
C(2)	6612(5)	7157(4)	6373(4)	24(2)
C(3)	5732(5)	6744(4)	5881(4)	24(2)
C(4)	4962(5)	7201(4)	5112(4)	28(2)
C(5)	5516(5)	8007(4)	4724(4)	29(2)
C(6)	6025(5)	8549(3)	5591(4)	24(2)
C(7)	5475(5)	5851(4)	6092(5)	36(2)
C(8)	5092(5)	8994(4)	6297(5)	35(2)
Cl(11)	2294(1)	9555(1)	2017(1)	42(1)
Cl(12)	-1027(2)	11278(1)	3986(1)	43(1)
Cl(13)	-2110(1)	10519(1)	2182(1)	44(1)
Cl(14)	-1527(1)	12431(1)	1922(1)	43(1)
Cl(15)	990(2)	12476(1)	521(1)	43(1)
O(11)	2255(4)	10906(3)	583(4)	55(2)
C(11)	1370(5)	10918(4)	1150(5)	28(2)
C(12)	1164(5)	10294(4)	1969(5)	27(2)
C(13)	230(5)	10274(4)	2672(5)	26(2)
C(14)	-707(5)	10955(4)	2666(4)	27(2)
C(15)	-312(5)	11711(4)	2037(4)	27(2)

C(16)	330(5)	11540(4)	1004(4)	27(2)
C(17)	25(5)	9578(4)	3473(5)	34(2)
C(18)	-483(6)	11200(5)	122(5)	46(3)

TABLE 6. Fractional coordinates for non-hydrogen atoms in *cis*-2,4,4,5,6-pentachloro-3,6-dimethylcyclohex-2-enone (44), $C_8H_7Cl_5O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(2)	584(1)	1241(1)	3046(1)	32(1)
Cl(41)	-103(1)	-341(1)	-2831(1)	43(1)
Cl(42)	-2129(1)	-964(1)	-316(2)	40(1)
Cl(5)	508(1)	-2159(1)	-984(1)	40(1)
Cl(6)	-427(1)	-1648(1)	3215(1)	33(1)
O(1)	2024(3)	-256(1)	4016(4)	29(1)
C(1)	1258(4)	-369(2)	2761(5)	20(1)
C(2)	447(4)	306(2)	1952(5)	22(1)
C(3)	-342(4)	248(2)	479(5)	24(1)
C(4)	-385(4)	-558(2)	-528(5)	26(1)
C(5)	772(4)	-1171(2)	10(4)	23(1)
C(6)	1051(4)	-1241(2)	2007(5)	23(1)
C(7)	-1177(5)	952(3)	-219(6)	38(1)
C(8)	2322(5)	-1775(2)	2398(6)	36(1)

TABLE 7. Fractional coordinates for non-hydrogen atoms in *trans*-2,2,3,4,5,6-hexachloro-5,6-dimethylcyclohex-3-enone (57), $C_8H_6Cl_6O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(21)	9811(1)	7199(1)	-448(1)	25(1)
Cl(22)	5959(1)	6414(1)	386(1)	28(1)
Cl(3)	10736(1)	5522(1)	1080(1)	30(1)
Cl(4)	11537(1)	6717(1)	2808(1)	28(1)
Cl(5)	6216(1)	8059(1)	2461(1)	30(1)
Cl(6)	11499(1)	9269(1)	959(1)	25(1)
O(1)	6185(3)	8757(2)	178(1)	26(1)
C(1)	7585(4)	8395(2)	634(2)	18(1)
C(2)	8343(4)	7222(2)	523(2)	16(1)
C(3)	9725(4)	6784(2)	1247(2)	17(1)
C(4)	10046(4)	7306(2)	1981(2)	19(1)
C(5)	9017(4)	8384(2)	2162(2)	22(1)
C(6)	8774(4)	9050(2)	1338(2)	20(1)
C(7)	10098(5)	8991(3)	2905(2)	33(1)
C(8)	7665(5)	10132(2)	1445(2)	30(1)

TABLE 8. Fractional coordinates for non-hydrogen atoms in *cis*-2,2,3,4,5,6-hexachloro-5,6-dimethylcyclohex-3-enone (58), $C_8H_6Cl_6O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(21)	15404(1)	15864(1)	7230(1)	30(1)
Cl(22)	10190(1)	14407(1)	6313(1)	33(1)
Cl(3)	13664(1)	12835(1)	5199(1)	29(1)
Cl(4)	12829(1)	9259(1)	5955(1)	30(1)
Cl(5)	8798(1)	10110(1)	7519(1)	30(1)
Cl(6)	12406(1)	11998(1)	9851(1)	33(1)
O(1)	11690(3)	14622(2)	8641(1)	29(1)
C(1)	12471(4)	13718(3)	8171(2)	18(1)
C(2)	12767(4)	13974(3)	7034(2)	20(1)
C(3)	13045(4)	12482(3)	6411(2)	19(1)
C(4)	12704(4)	10964(3)	6751(2)	19(1)
C(5)	12085(4)	10615(3)	7805(2)	21(1)
C(6)	13322(5)	12299(3)	8633(2)	21(1)
C(7)	12595(5)	9061(4)	8220(2)	31(1)
C(8)	16106(5)	12879(4)	8905(2)	25(1)

TABLE 9. Fractional coordinates for non-hydrogen atoms in 2,4,5,5,6,6-hexachloro-2,3-dimethylcyclohex-3-enone (59), $C_8H_6Cl_6O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(2)	4595(2)	-940(2)	1981(1)	22(1)
Cl(4)	6186(1)	1740(1)	4903(1)	21(1)
Cl(51)	783(1)	2956(1)	3541(1)	26(1)
Cl(52)	3223(2)	5288(1)	3754(1)	34(1)
Cl(61)	997(2)	5703(1)	1369(1)	29(1)
Cl(62)	5980(1)	4667(1)	1469(1)	22(1)
O(1)	2552(4)	2497(3)	662(2)	29(1)
C(1)	3742(5)	2454(4)	1374(2)	17(1)
C(2)	5749(5)	827(4)	1822(2)	18(1)
C(3)	6552(5)	782(4)	2955(2)	15(1)
C(4)	5439(5)	1974(4)	3551(2)	14(1)
C(5)	3390(5)	3527(4)	3153(3)	17(1)
C(6)	3465(5)	4033(4)	1884(3)	17(1)
C(7)	7649(7)	563(6)	951(3)	17(1)
Cl(2')	8093(10)	694(8)	849(5)	18(2)
C(7')	4928(33)	-659(16)	1869(17)	17(1)
C(8)	8626(5)	-795(4)	3394(2)	12(1)

TABLE 11. Fractional coordinates for non-hydrogen atoms in *r*-2-acetoxy-4,*c*-5,*t*-6-trichloro-2,6-dimethylcyclohex-3-enone (114), $C_{10}H_{11}Cl_3O_3$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(5)	3521(1)	-209(1)	10660(1)	64(1)
Cl(6)	3613(1)	686(1)	5168(1)	61(1)
Cl(4)	4358(1)	-2298(1)	8292(1)	72(1)
O(21)	742(1)	-1280(2)	6764(3)	42(1)
O(1)	1214(2)	853(2)	6807(3)	60(1)
C(1)	1904(2)	231(2)	6785(4)	39(1)
C(5)	3660(2)	-276(3)	8302(4)	47(1)
C(2)	1721(2)	-901(2)	6138(4)	37(1)
C(3)	2568(2)	-1652(2)	6722(4)	41(1)
O(22)	1248(2)	-873(2)	9557(3)	61(1)
C(8)	603(2)	-1209(2)	8508(4)	41(1)
C(6)	3021(2)	574(2)	7295(4)	44(1)
C(4)	3416(2)	-1366(2)	7661(4)	43(1)
C(7)	1528(3)	-918(3)	4117(4)	52(1)
C(9)	-441(3)	-1601(3)	8921(5)	59(1)
C(10)	3060(3)	1660(3)	8149(5)	66(1)

TABLE 12. Fractional coordinates for non-hydrogen atoms in *trans*-2,2,4,5,6-pentachloro-3,5,6-trimethylcyclohex-3-enone (115), $C_9H_9Cl_5O$.

atom	$10^4x/a$	$10^4y/b$	$10^4z/c$	10^3U (Å)^2
Cl(11)	1135(2)	3725(1)	6634(1)	71(1)
Cl(12)	-65(2)	1211(1)	5066(2)	84(1)
Cl(13)	-5554(2)	1621(2)	5807(2)	92(1)
Cl(14)	-4485(3)	746(1)	3143(1)	90(1)
Cl(15)	-2137(2)	4496(1)	5495(1)	71(1)
0911)	27(5)	2723(3)	4003(3)	75(2)
C(11)	-990(7)	2725(4)	4525(4)	47(2)
C(12)	-705(7)	2471(4)	5525(4)	49(3)
C(13)	-2224(7)	2207(4)	5947(4)	43(3)
C(14)	-3749(7)	2099(4)	5403(4)	48(3)
C(15)	-4174(7)	2218(5)	4348(5)	61(3)
C(16)	-2582(8)	3029(5)	4292(4)	62(3)
C(17)	-1932(9)	2010(6)	6953(5)	76(4)
C(18)	-5813(8)	2471(6)	4118(6)	86(4)
C(19)	-2791(10)	3149(6)	3220(5)	81(4)
Cl(21)	4172(3)	1146(1)	109(2)	88(1)
Cl(22)	4167(3)	2060(1)	-1480(1)	83(1)
Cl(23)	-1837(2)	1263(2)	-705(2)	107(1)
Cl(24)	1683(3)	2932(1)	1991(1)	78(1)
Cl(25)	2378(2)	4206(1)	-407(1)	70(1)
O(21)	5591(5)	3732(3)	1145(3)	69(2)
C(21)	4066(7)	3280(4)	598(4)	45(3)
C(22)	3291(7)	2004(4)	-367(4)	51(3)
C(23)	1362(7)	1434(4)	-792(4)	53(3)
C(24)	408(7)	1983(4)	-272(4)	50(3)
C(25)	1102(8)	3191(5)	759(4)	57(3)
C(26)	2865(7)	3955(4)	807(4)	54(3)
C(27)	575(11)	211(5)	-1787(6)	102(4)
C(28)	-164(9)	3818(6)	966(6)	85(4)
C(29)	3790(9)	5167(4)	1889(5)	74(3)

TABLE 13. Fractional coordinates for atoms in (E)-(2RS,5RS)-2,4,5,6,6-pentachloro-2-methyl-6-nitrohex-3-enoic acid (131), $C_7H_6Cl_5NO_4$.

Atom	X/a	Y/b	Z/c	10^3 ($Å^2$)
Cl(2)	0.2814(1)	0.1256(1)	0.9474(1)	52(1)
Cl(4)	0.8072(1)	0.1329(1)	0.8067(1)	64(1)
Cl(5)	0.7235(1)	0.4604(1)	0.9740(1)	66(1)
Cl(61)	0.4217(1)	0.1858(1)	0.5263(1)	66(1)
Cl(62)	0.8016(1)	0.4242(1)	0.6908(1)	101(1)
O(11)	0.0953(2)	0.0986(2)	0.6689(2)	49(1)
O(12)	0.0953(3)	-0.1467(2)	0.5478(2)	61(1)
O(61)	0.3435(5)	0.4574(4)	0.7084(3)	108(2)
O(62)	0.5928(5)	0.6216(3)	0.7079(3)	130(2)
N(6)	0.4961(5)	0.4912(3)	0.7024(3)	80(2)
C(1)	0.1416(3)	-0.0177(3)	0.6628(2)	39(1)
C(2)	0.2680(3)	-0.0303(3)	0.7912(2)	39(1)
C(3)	0.4634(3)	-0.0007(3)	0.7908(2)	37(1)
C(4)	0.5879(3)	0.1347(3)	0.7986(2)	39(1)
C(5)	0.5628(3)	0.2948(3)	0.8086(2)	41(1)
C(6)	0.5770(4)	0.3495(3)	0.6897(3)	55(1)
C(7)	0.1814(4)	-0.2007(3)	0.7937(3)	60(1)

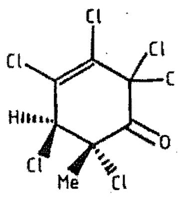
TABLE 14. Interatomic distances in (131)

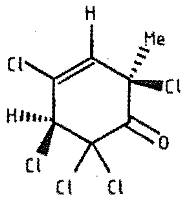
Atoms	Distance (Å)	Atoms	Distance (Å)
Cl(5)-C(5)	1.780(2)	Cl(2)-C(2)	1.804(2)
Cl(61)-C(6)	1.757(2)	Cl(62)-C(6)	1.732(3)
Cl(4)-C(4)	1.734(2)	C(5)-C(4)	1.502(4)
C(5)-C(6)	1.539(2)	C(4)-C(3)	1.321(3)
C(1)-C(2)	1.530(3)	C(3)-C(2)	1.511(3)
C(2)-C(7)	1.532(4)	C(1)-O(11)	1.205(3)
C(1)-O(12)	1.303(3)	C(6)-N(6)	1.582(5)
N(6)-O(61)	1.198(6)	N(6)-O(62)	1.203(4)

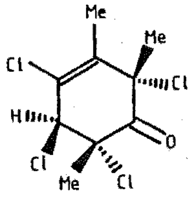
TABLE 15. Torsion angles in (131)

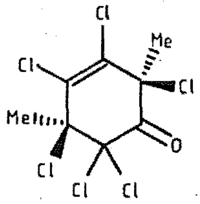
Atoms	Angle (degrees)	Atoms	Angle (degrees)
Cl(5)-C(5)-C(4)-Cl(4)	-61.5(2)	Cl(5)-C(5)-C(4)-C(3)	114.8(2)
H(5)-C(5)-C(4)-Cl(4)	179.0(1)	H(5)-C(5)-C(4)-C(3)	-4.7(2)
C(6)-C(5)-C(4)-Cl(4)	63.6(2)	C(6)-C(5)-C(4)-C(3)	-120.1(3)
Cl(5)-C(5)-C(6)-Cl(61)	179.0(2)	Cl(5)-C(5)-C(6)-Cl(62)	53.2(2)
Cl(5)-C(5)-C(6)-N(6)	-68.0(2)	H(5)-C(5)-C(6)-Cl(61)	-61.2(2)
H(5)-C(5)-C(6)-Cl(62)	172.9(1)	H(5)-C(5)-C(6)-N(6)	51.8(2)
C(4)-C(5)-C(6)-Cl(61)	53.0(3)	C(4)-C(5)-C(6)-Cl(62)	-72.9(2)
C(4)-C(5)-C(6)-N(6)	166.0(2)	Cl(4)-C(4)-C(3)-H(3)	-3.9(2)
Cl(4)-C(4)-C(3)-C(2)	176.1(2)	C(5)-C(4)-C(3)-H(3)	179.8(2)
C(5)-C(4)-C(3)-C(2)	-0.2(4)	O(11)-C(1)-C(2)-Cl(2)	14.0(3)
O(11)-C(1)-C(2)-C(3)	-106.1(3)	O(11)-C(1)-C(2)-C(7)	131.3(3)
O(12)-C(1)-C(2)-Cl(2)	-167.3(2)	O(12)-C(1)-C(2)-C(3)	72.6(2)
O(12)-C(1)-C(2)-C(7)	-49.9(3)	C(2)-C(1)-O(12)-H(1)	-178.0(2)
O(11)-C(1)-O(12)-H(1)	1.0(2)	C(4)-C(3)-C(2)-Cl(2)	-56.5(3)
C(4)-C(3)-C(2)-C(1)	62.5(3)	C(4)-C(3)-C(2)-C(7)	-174.9(2)
H(3)-C(3)-C(2)-Cl(2)	123.5(1)	H(3)-C(3)-C(2)-C(1)	-117.5(1)
H(3)-C(3)-C(2)-C(7)	5.1(2)	Cl(61)-C(6)-N(6)-O(61)	64.5(3)
Cl(61)-C(6)-N(6)-O(62)	-116.9(3)	C(5)-C(6)-N(6)-O(61)	-51.6(3)
C(5)-C(6)-N(6)-O(62)	126.9(3)	Cl(62)-C(6)-N(6)-O(61)	-177.2(2)
Cl(62)-C(6)-N(6)-O(62)	1.3(3)		

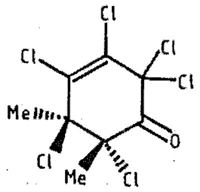
TABLE 16. Selected torsion angles for polychlorocyclohex-3-enones. (degrees)

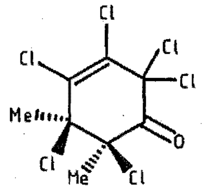


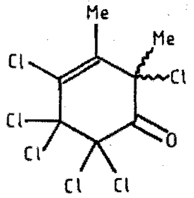


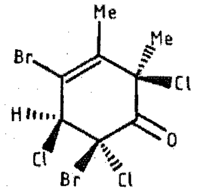


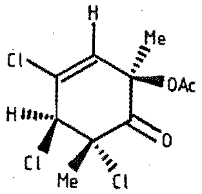


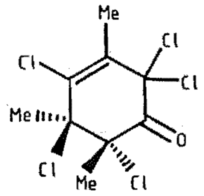












Compound	(22)	(28)	(38)	(46)	(57)	(58)	(59)	(107)	(114)	(115)
C3-C4-C5-C6	-29.0(5)	-27.9(8)	-31(1)	-28.3(9)	-32.8(3)	-32.6(3)	-26.9(5)	-27(1)	-18.9(4)	-27.8(8)
C1-C2-C3-C4	9.6(5)	6.7(8)	11(1)	8(1)	8.5(4)	9.5(3)	6.6(5)	7(1)	-2.2(4)	5.9(6)
C3-C4-C5-Cl5	90.5(4)	92.2(6)	89(1)	86.2(8)	80.2(2)	82.9(2)	90.4(3)	93(1)	106.4(3)	81.0(5)
O1-C1-C6-X1	-107.5(4)	-104.4(5)	-108.5(9)	-104.5(8)	-108.6(2)	-106.8(3)	-111.1(3)	-110(1)	-103.5(3)	-108.7(4)
X1	Cl(6)	Cl(61)	Cl(6)	Cl(61)	Cl(6)	C(8)	Cl(62)	Cl(6)	Cl(6)	Cl(15)
O1-C1-C6-X2	12.2(5)	12.3(7)	9(1)	12(1)	8.8(3)	10.7(3)	7.0(4)	7(1)	12.0(4)	7.9(6)
X2	C(7)	Cl(62)	C(9)	Cl(62)	C(8)	Cl(6)	Cl(61)	Br(6)	C(10)	C(19)
O1-C1-C2-X3	68.6(4)	65.2(7)	73(1)	65.5(a)	71.3(3)	75.7(2)	70.5(5)/77.3(5)	69(1)	72.7(4)	69.6(5)
X3	Cl(22)	C(7)	Cl(2)	C(7)	Cl(21)	Cl(21)	C7/Cl(2)'	C(7)	C(7)	Cl(11)
O1-C1-C2-X4	-47.0(4)	-50.5(6)	-44(1)	-51.2(9)	-44.8(3)	-40.4(2)	-44.1(4)/-39.3(9)	-45(1)	-39.2(4)	-45.0(5)
X4	Cl(21)	Cl(2)	C(7)	Cl(2)	Cl(22)	Cl(22)	Cl(21)/C(7)'	Cl(2)	OAc	Cl(12)

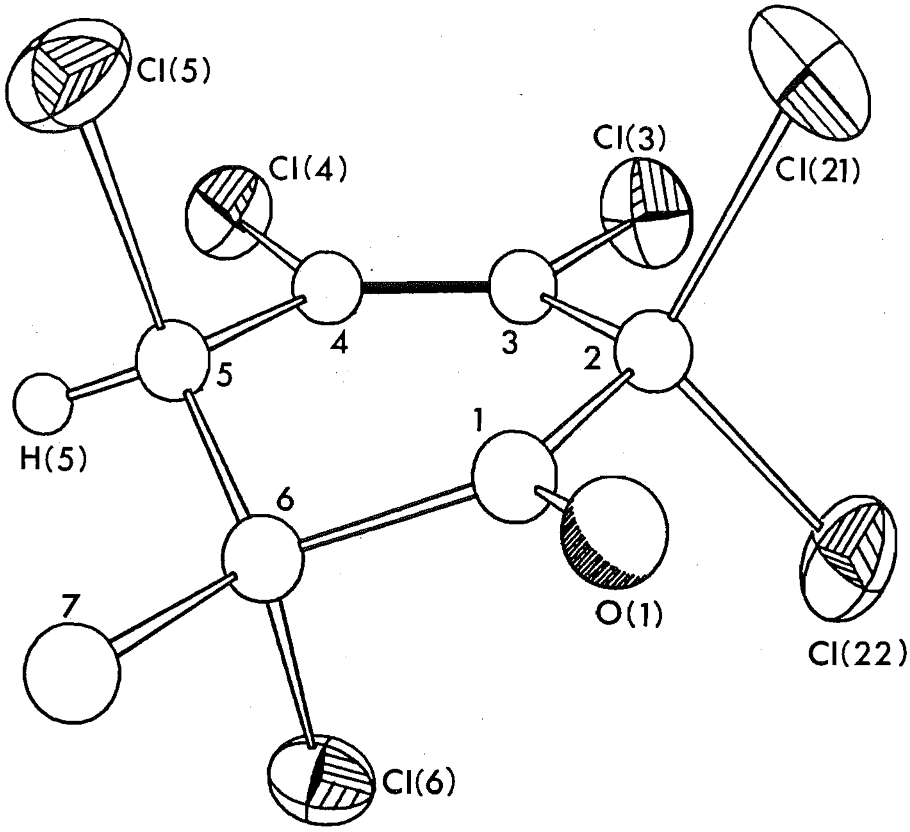


FIGURE 1

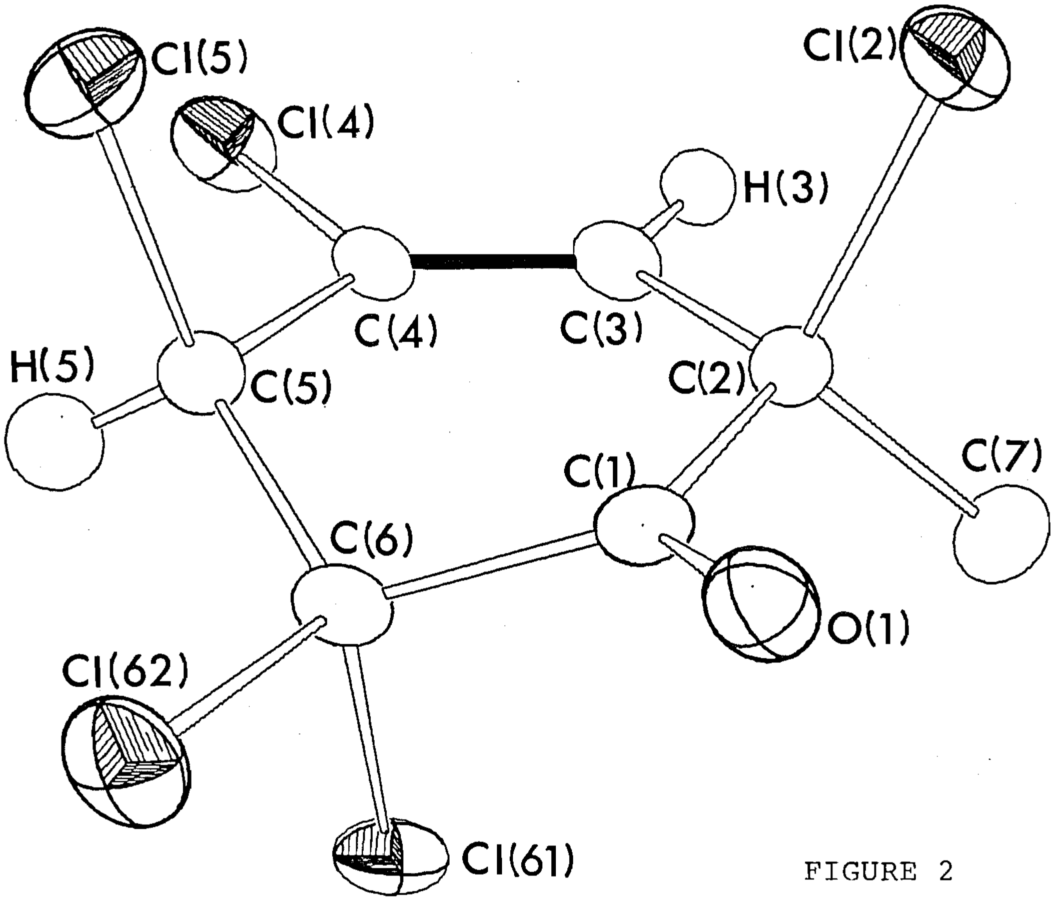


FIGURE 2

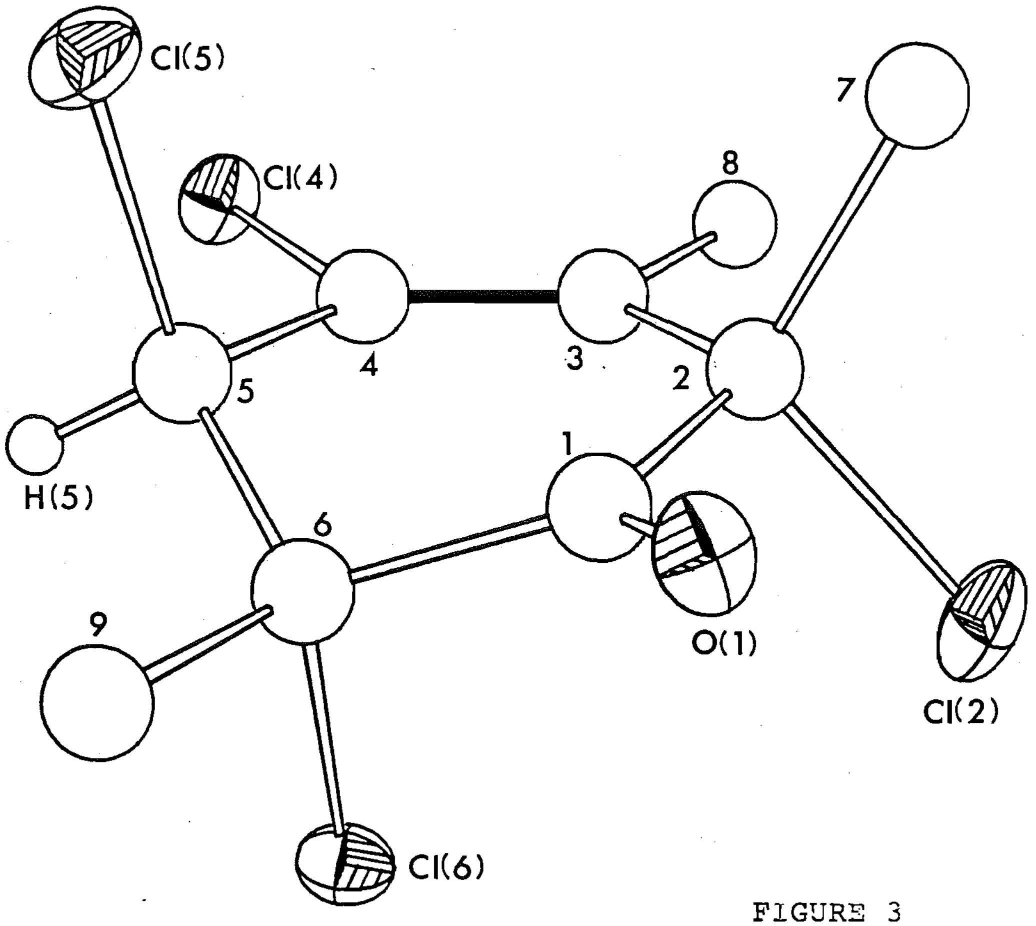


FIGURE 3

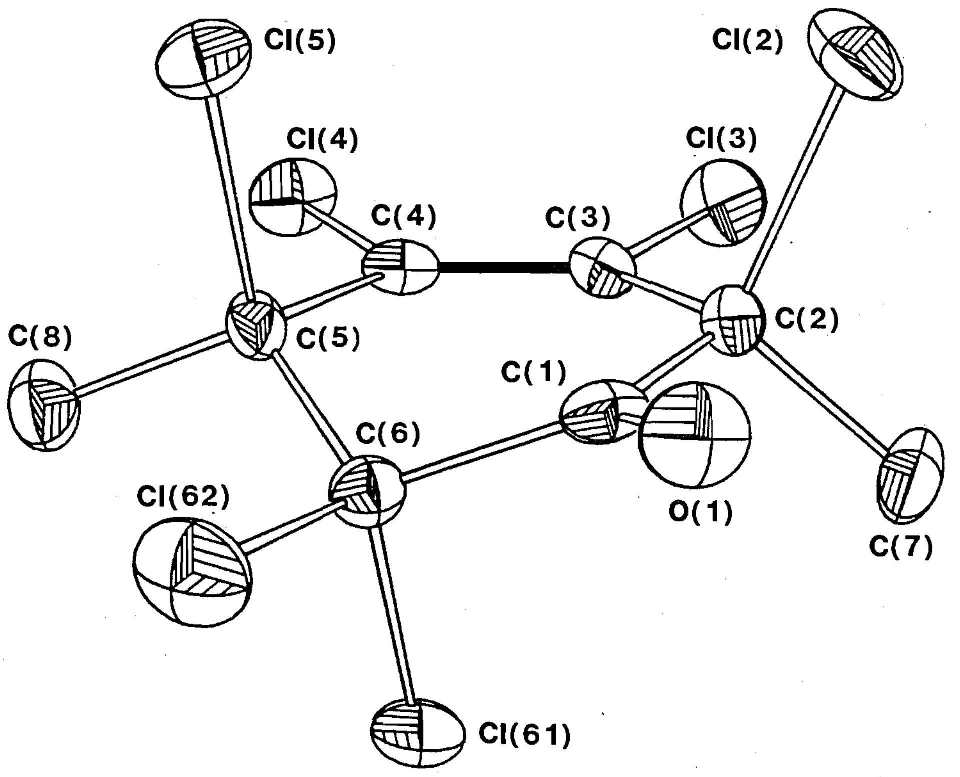
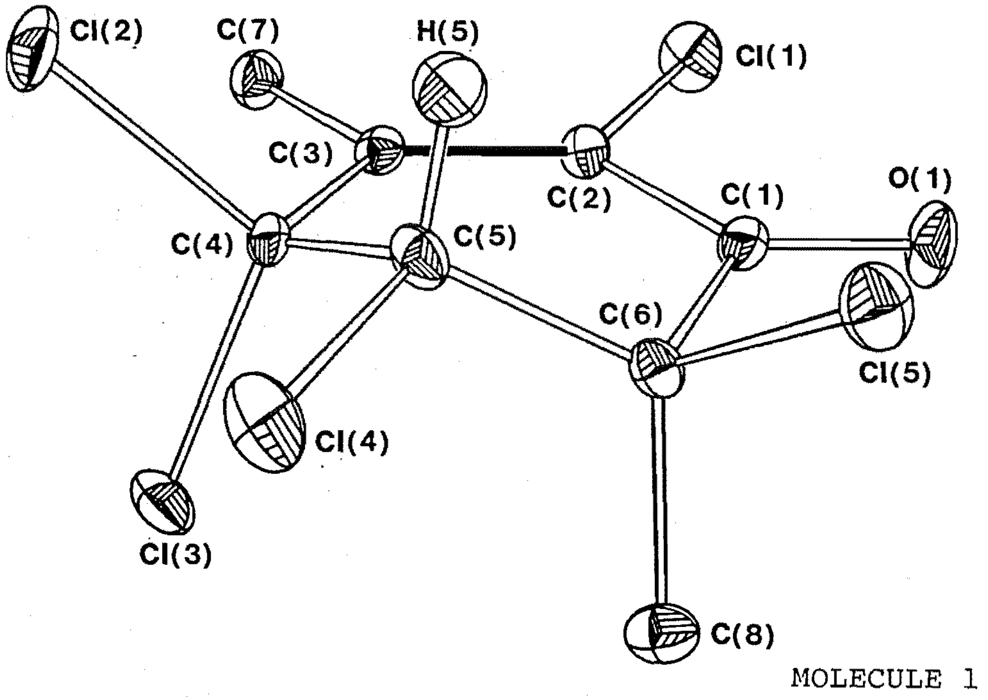


FIGURE 4


Cl(2)
C(7)
H(5)
Cl(1)
C(3)
C(2)
C(1)
O(1)
C(4)
C(5)
C(6)
Cl(5)
Cl(4)
Cl(3)
C(8)
MOLECULE 1

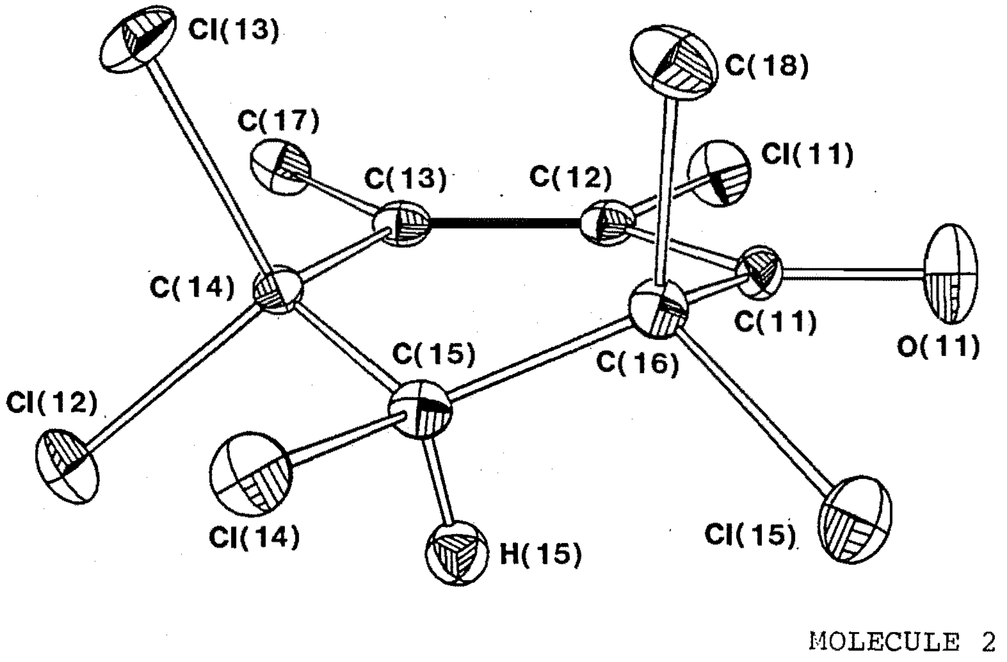

Cl(13)
C(18)
C(17)
Cl(11)
C(13)
C(12)
C(14)
C(11)
O(11)
C(15)
C(16)
Cl(12)
Cl(14)
H(15)
Cl(15)
MOLECULE 2

FIGURE 5

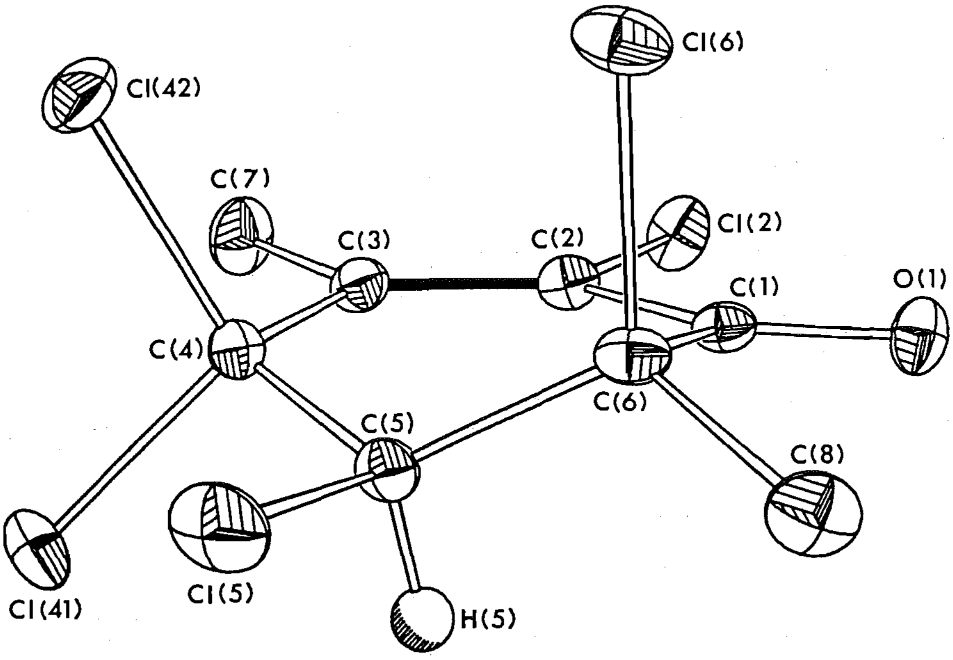


FIGURE 6

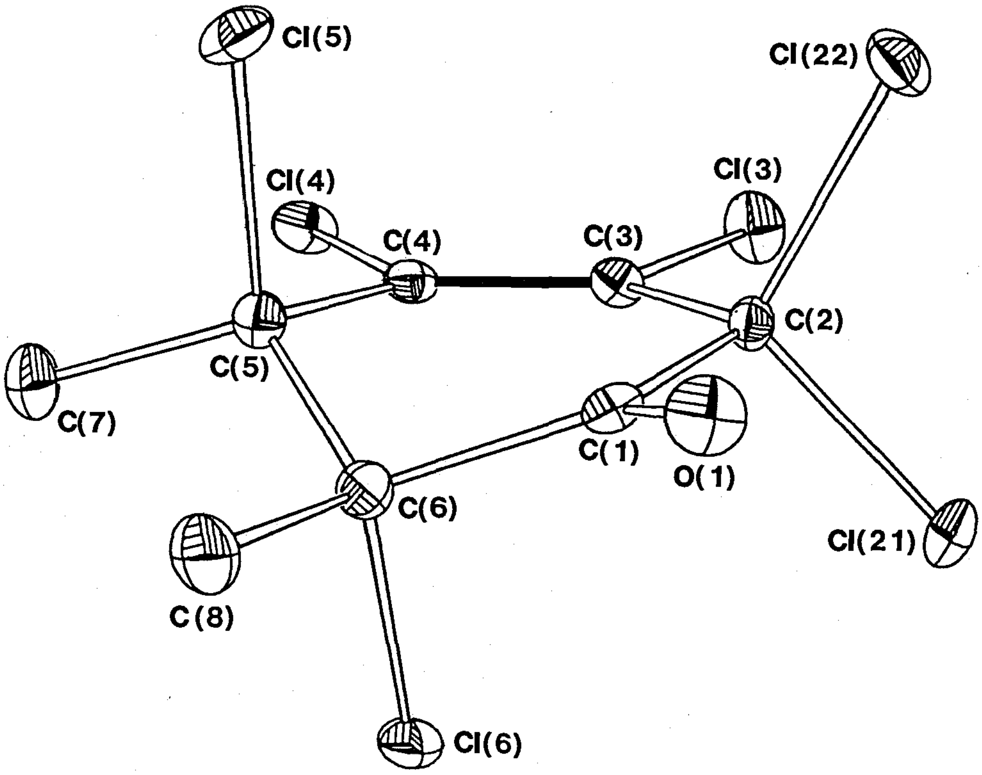


FIGURE 7

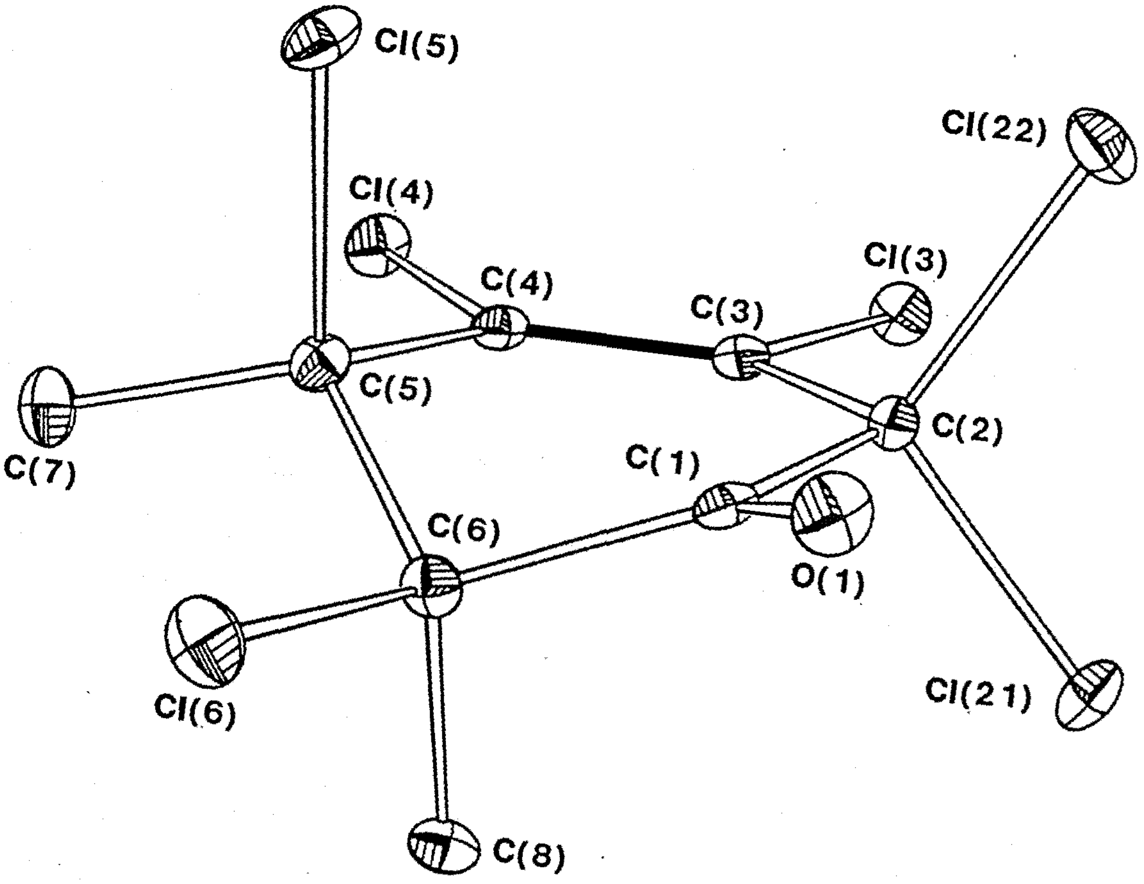


FIGURE 8

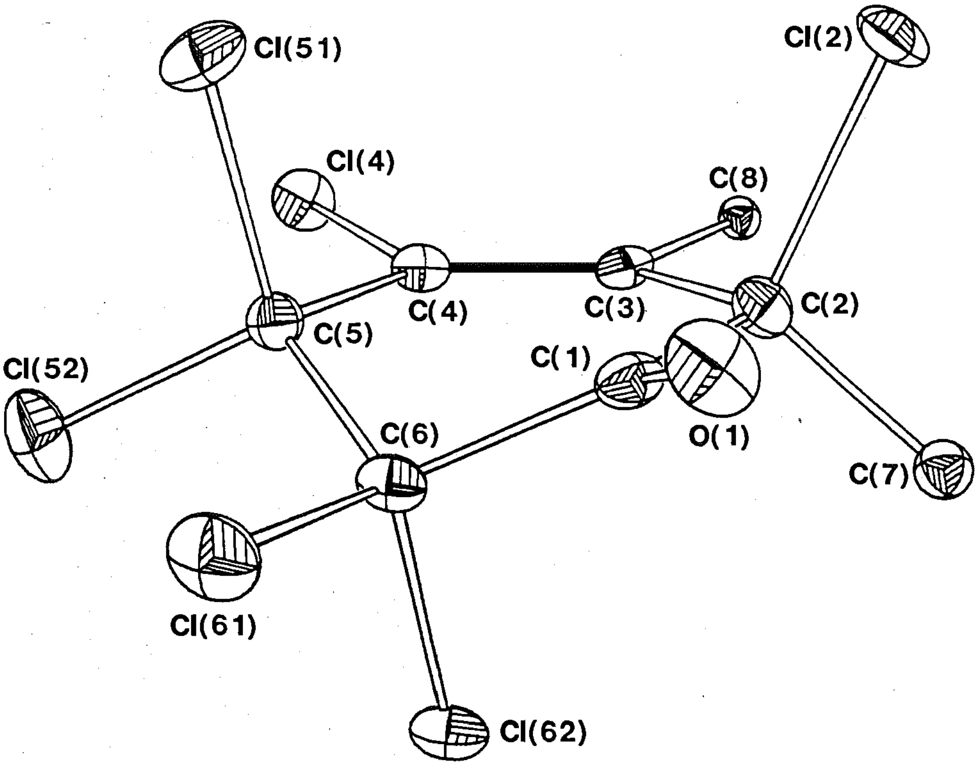


FIGURE 9a

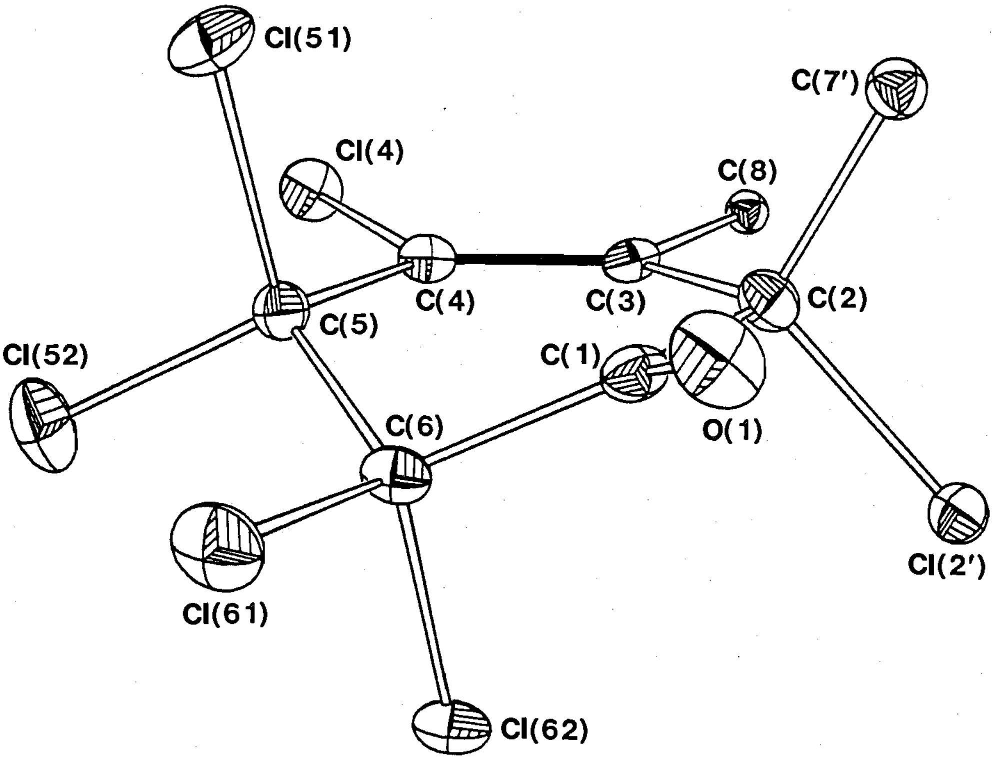


FIGURE 9b

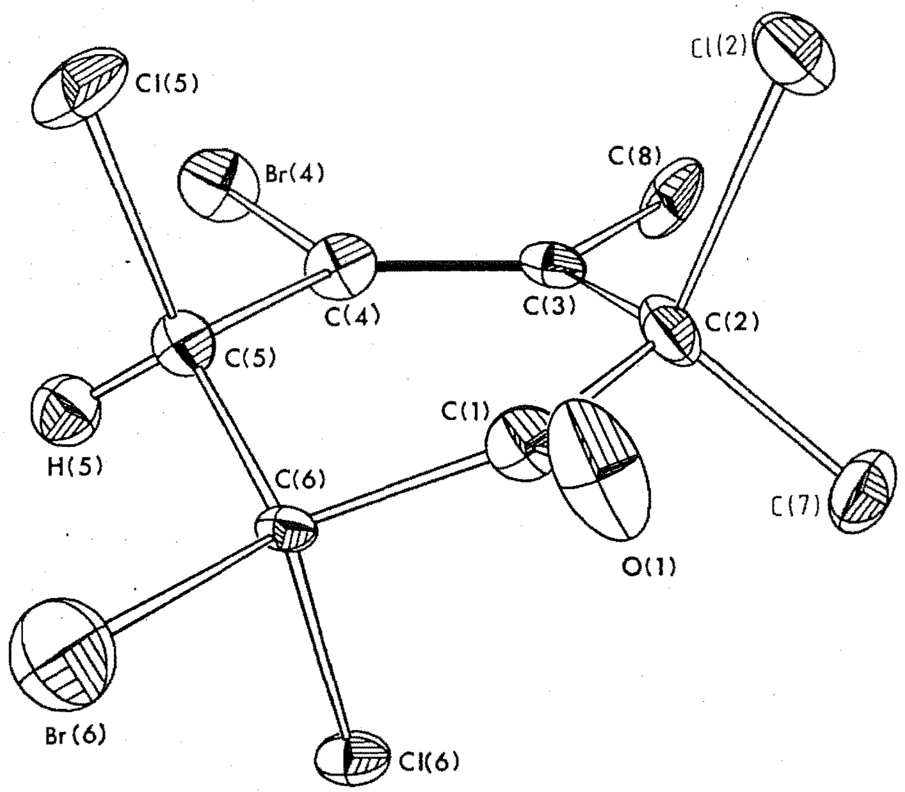


FIGURE 10

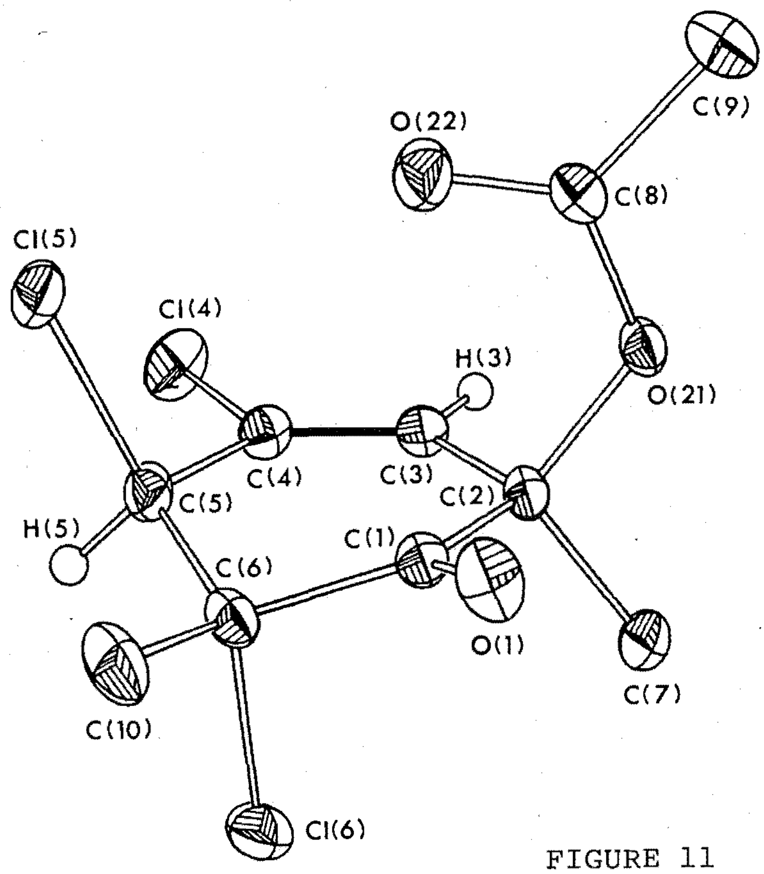
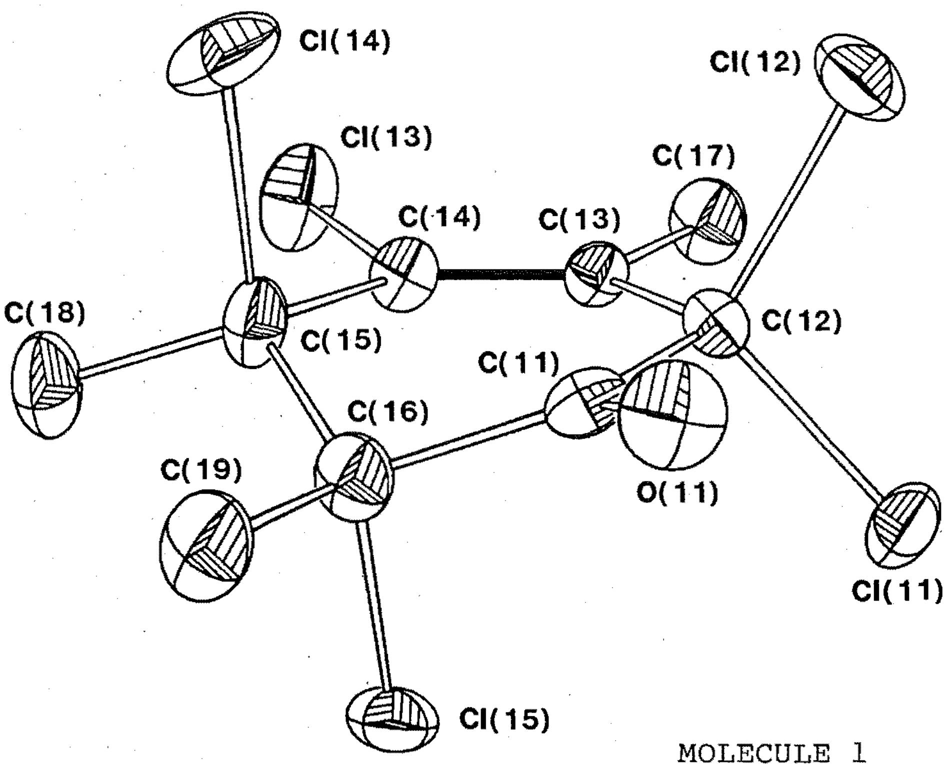
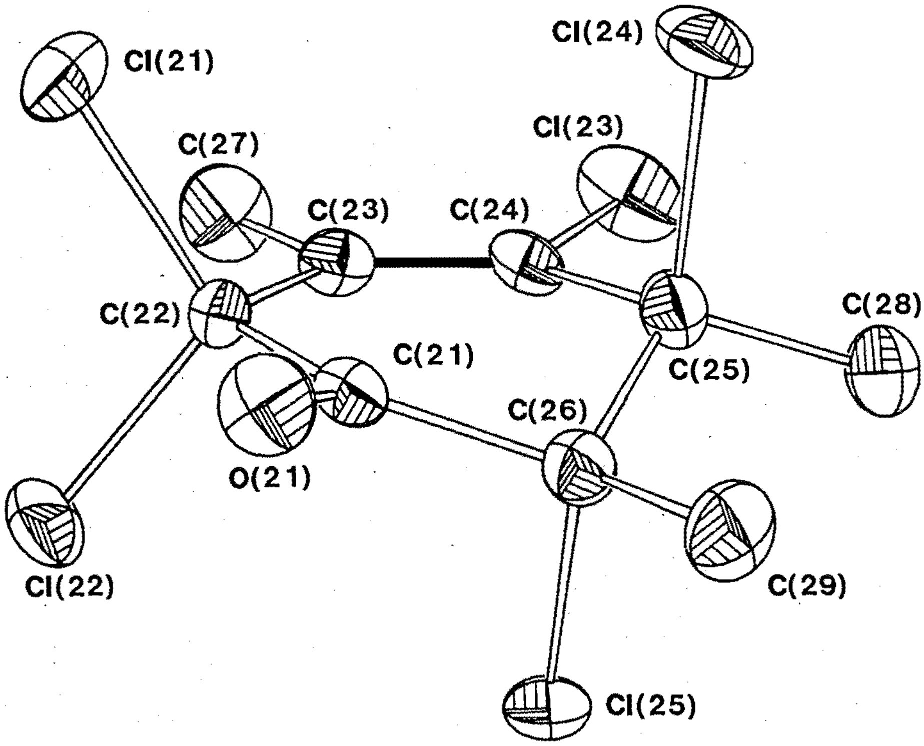


FIGURE 11



MOLECULE 1



MOLECULE 2

FIGURE 12

APPENDIX 2

Chlorination of 2-Nitrophenols; Formation of (E)-(2RS,5RS)-2,4,5,6,6-Pentachloro-2-methyl-6-nitrohex-3-enoic Acid

2.1 Introduction

In 1887 Hantzsch reported the chlorination of phenol in alkaline conditions to yield an acidic product to which he assigned structure (125)[49,50] (refer Block X). The structure of this acid was subsequently confirmed by Moyle *et.al.*[54] The 2,4,6-trichlorophenol (126) was established as being an intermediate in the above reaction process,[49] which was suggested to involve ring contraction by a benzilic acid type rearrangement of the α-diketone (127).[49,50] In order to test this hypothesis, the preparation of this α-diketone was attempted.

It seemed reasonable to expect that 2,4-dichloro-6-nitrophenol (128) would react with chlorine in acetic acid and concentrated hydrochloric acid to yield the pentachlorocyclohex-3-enone (129), by analogy with the observations discussed previously in this work. The pentachlorocyclohex-3-enone (129) would be expected to yield the α-diketone (127) by rearrangement and loss of the elements NOCl, by analogy with previous work.[53] However, this phenolic substrate (128) failed to react with chlorine under these reaction conditions, even over a period of 27 days. In order to overcome this lack of reactivity the 4-chloro-6-methyl-2-nitrophenol (130) was reacted under the above conditions in the expectation that the C6-methyl group would activate the phenolic ring system to electrophilic chlorine attack. In the event, the reaction of 4-chloro-6-methyl-2-nitrophenol with chlorine in acetic acid and concentrated hydrochloric acid gave a high yield of the epimeric pair of acyclic pentachloronitrohex-3-enoic acids (131) and (132).

2.2 Discussion

Chlorine was bubbled slowly through a stirred solution of the 4-chloro-6-methyl-2-nitrophenol (130) in acetic acid and hydrochloric acid for 14 days. The crude material, isolated after removal of the solvents was shown (^{1}H n.m.r.) to consist of a mixture (*c.* 1:1) of the tetrachloronitrohex-3-enoic acids (131) and (132). Fractional crystallization of the crude product from dichloromethane/pentane gave first the pure epimer (131), followed by successive crops of a mixture (*c.* 1:1) of the epimeric pair (131) and (132). The epimer (132) could not be isolated from this mixture by either fractional crystallization or chromatographic techniques. The structure of the pure isomer (131), $C_7H_6Cl_5NO_4$, m.p. 143-144°, was determined by single-crystal X-ray analysis. A perspective drawing of this compound is presented in Figure 13 (as a foldout at the end of Appendix 2) and the corresponding atomic coordinates, bond lengths and torsion angles are presented in Table 13, Table 14 and Table 15 respectively (refer Appendix 1).

In the solid state, compound (131) exists in a conformation in which the substituents about the C(5)-(C6) bond are almost perfectly staggered, and with the C(5)-H(5) bond close to eclipsed with the C(3)-C(4) bond. The C(2)-C(7) bond is close to eclipsed with the C(3)-H(3) bond, and the double bond has the (E)-configuration, consistent with the mode of formation of compound (131) (see below).

The analytical data for the mixture (*c.* 1:1) of the isomers (131) and (132) confirmed their common molecular formula, and their assignment as epimers was consistent with the close similarity between their ^{1}H n.m.r. spectra. The chemical shifts of the resonances due to the C2-methyl groups are the same for the two epimers (δ 2.07) as are the C(5)-H proton resonances (δ 6.48), while the chemical shifts of the C(3)-H protons (δ 6.78) and (δ 6.75), for compounds (131) and (132) respectively, are closely similar.

Little experimental evidence is available which points to the mode of formation of compounds (131) and (132) from the 4-chloro-6-methyl-2-nitrophenol (130), but some comment can be made. The composition of the reaction mixture was monitored during the chlorination reaction by the ^1H n.m.r. spectra of withdrawn aliquots. At no time was evidence obtained for the presence of intermediates, and the compounds (131) and (132) were the only compounds detected. It seems likely that initial attack on the phenol (130) would occur at C6 to give the 6-chloro-6-methylcyclohexa-2,4-dienone (133) (refer Scheme 8). On this assumption, and given the presence of a chlorine atom at C5 in the substituted hex-3-enoic acids (131) and (132), it appears that 2,3-addition of chlorine to the 6-chloro-6-methylcyclohexa-2,4-dienone (133) occurs to give the 2,4,5,6-tetrachlorocyclohex-3-enone (134). This 2,3-addition of chlorine is likely to be acid-catalysed, particularly by hydrogen chloride, because the formation of the hex-3-enoic acids (131) and (132) from the phenol (130) only occurs in the presence of added HCl. The 2,3-addition of chlorine to 2,4-dienone (133), promoted by the electron-withdrawing 2-NO_2 substituent, is therefore likely to occur by a mechanism similar to that proposed for the 2,3-addition of chlorine to other 2,4-dienones discussed in Chapter 4, *i.e.* the "nucleophilic" process involving pre-equilibrium protonation of the 2,4-dienone ketone function.

As to the ring opening step, it may occur *via* the ketone hydrate (135), followed by chlorine substitution at C6 of the acyclic structure (136). Unfortunately, attempts to prepare the proposed intermediates (133) and (134) were unsuccessful.

In an attempt to gain more information about the ring-opening reaction we sought analogues to the proposed intermediate (134) of Scheme 8. To this end,cyclohex-3-enones (28) + (29) and cyclohex-3-enone (137) were subjected to the above reaction conditions but failed to undergo any ring-opening reaction. This behaviour is in keeping with our belief that the strongly electron-withdrawing 6-NO_2 group is a required feature for the ring-opening process. Such an electron-withdrawing group at C6 would stabilise the intermediate carbanion (136), formed upon rearrangement of the ketone hydrate (135).

2.3 Experimental

Chlorination of 4-chloro-2-methyl-6-nitrophenol (13)

(a) In Acetic Acid/Concentrated Hydrochloric Acid

Chlorine was bubbled slowly for 14 days through a stirred solution of the phenol (130) (5 g) in acetic acid (50 ml) and concentrated hydrochloric acid (5 ml) in the dark. The solvents were then removed under reduced pressure at <40° to give a residual yellow oil (7.98 g), which was shown (^1H n.m.r.) to contain *c.* 80% of a mixture (1:1) of two compounds.

Crystallization of this crude material from dichloromethane/pentane gave one of the major products, (E)-(2RS,5RS)-2,4,5,6,6-pentachloro-2-methyl-6-nitrohex-3-enoic Acid (131) (1 g), m.p. 143-144° (X-ray crystal structure determination, see Appendix 1.) ν_{max} (Nujol) 3000 br, CO_2H; 1725, C=O; 1620, C=C; 1595 cm^{-1}, NO_2. ^1H n.m.r. ($CDCl_3$) δ 2.07, 2-Me; 6.48, H5; 6.78, H3; 7.60, D_2O exch., CO_2H. ^{13}C n.m.r.

(CD_3COCD_3) δ 31.1, 2-Me; 60·8, C5; 65.0, C2; 113.7, C6; 131.6, C4; 139.9, C3; 169.6, Cl.

Recrystallization of the material, from the above filtrate, from dichloromethane/pentane gave a mixture (720 mg) (1:1) (^1H n.m.r.) of the carboxylic acid (131) and an isomeric compound (132). This mixture could not be separated; It had m.p. 101-104° (Found: C, 24.2; H, 1.6; Cl, 51.0; N, 3.9. $C_7H_6Cl_5NO_4$ requires C, 24.3; H, 1.8; Cl, 51.3; N, 4.1%). ν_{max} (Nujol) 3000 br, CO_2H; 1720, C=O; 1620, C=C; 1596 cm^{-1}, NO_2. ^1H n.m.r. ($CDCl_3$) δ 2.07 C2-Me's; 6.48, H5 for (131) and (132); 6.75, H3 for (132); 6.78, H3 for (131).

The residue from the above crystallization was shown (^1H n.m.r. and infrared spectra) to consist largely of the isomeric carboxylic acids (131) and (132).

(b) <u>In Acetic Acid</u>

Chlorine was bubbled slowly for 21 days through a stirred suspension of the phenol (130) (2 g) in acetic acid (20 ml) in the dark. The solvents were then removed under reduced pressure at <40° to give an essentially quantitative recovery of starting material (130), identical (m.p., m.m.p., infrared and ^1H n.m.r. spectra) with an authentic sample.

Attempted Chlorination of 2,4-Dichloro-6-nitrophenol (128)

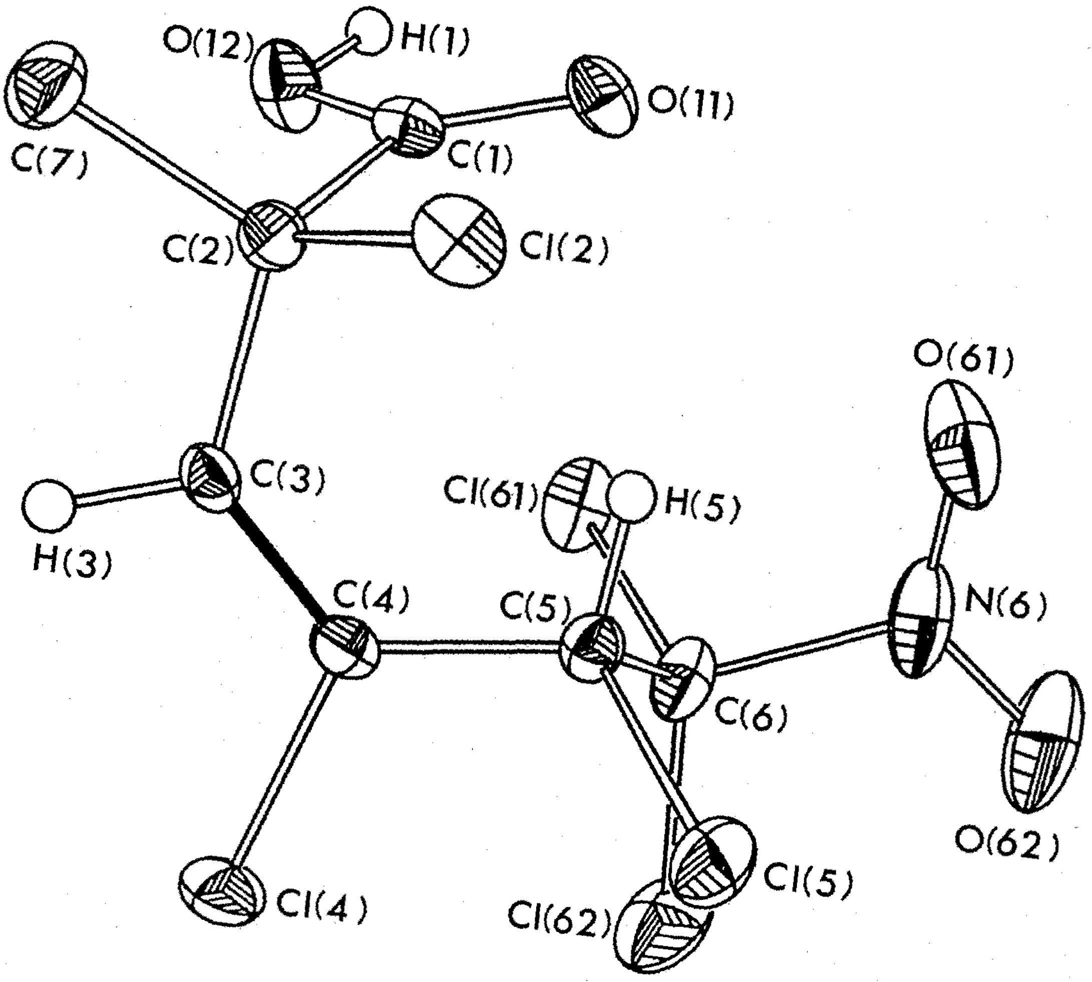
Reaction of 2,4-dichloro-6-nitrophenol (128) (2 g), as for reaction (a) above except that the reaction time was extended to 27 days, gave essentially pure phenol (128) (1.98 g) identical (m.p., m.m.p., infrared and ^1H n.m.r. spectra) with authentic material.

Attempted ring opening of 2,2,4,5,6,6-hexachlorocyclohex-3-enone (137)

Reaction of the chloro-ketone (137) (2 g), as for reaction (a) above except that the reaction time was extended to 16 days, gave only the pure chloro ketone (137) (1.95 g) identical (m.p., m.m.p.; ^1H n.m.r. and infrared spectra) with authentic material.

Preparation and Attempted Ring Opening of 2,2,4,5,6-Pentachloro-6-methylcyclohex-3-enones (28) and (29)

Reaction of 2,4-dichloro-6-methylphenol (27) (2 g), as for reaction (a) above except that the reaction time was extended to 30 days, gave only a mixture (3.1 g) of the known pentachlorocyclohex-3-enones (28) and (29);[55] no trace of any other material was detected.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O(11)
C(7)
C(1)
C(2)
Cl(2)
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C(3)
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H(5)
H(3)
C(4)
C(5)
N(6)
C(6)
O(62)
Cl(4)
Cl(62)
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FIGURE 13

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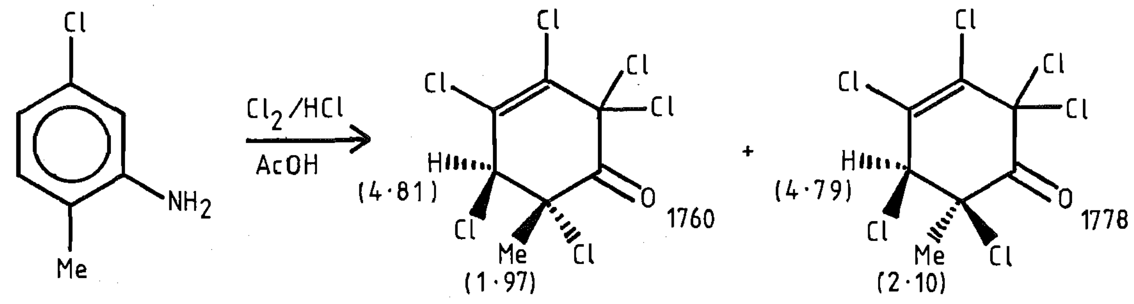

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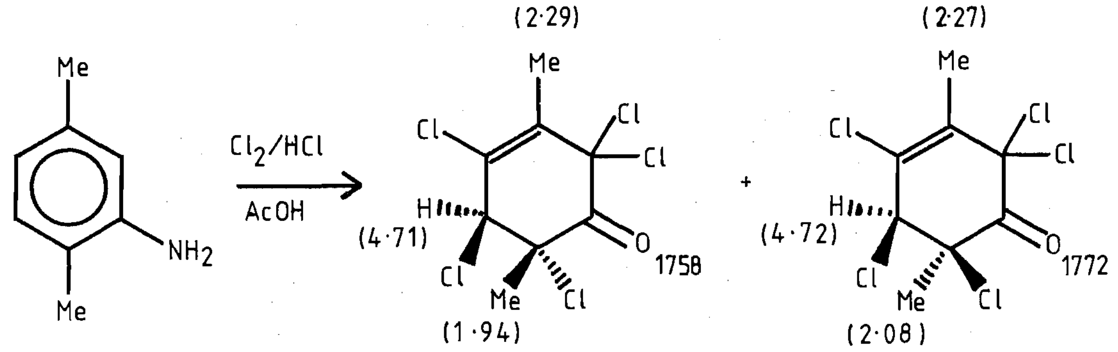

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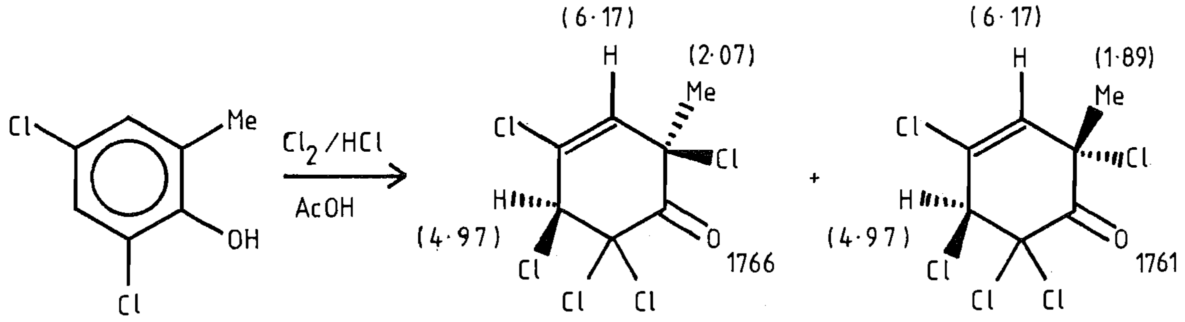

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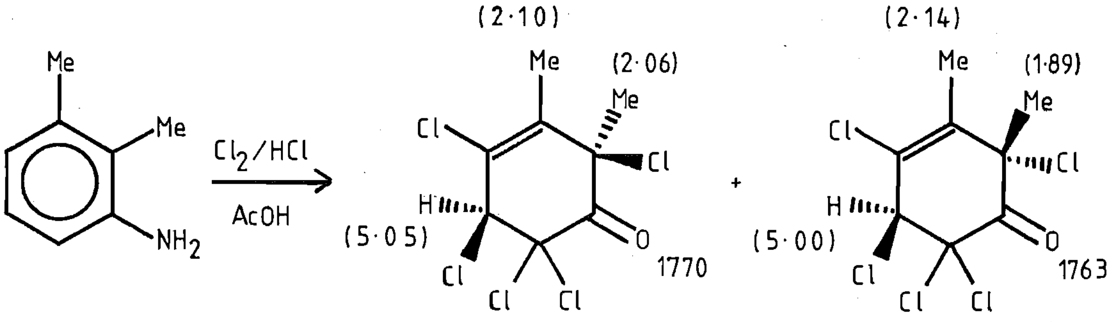

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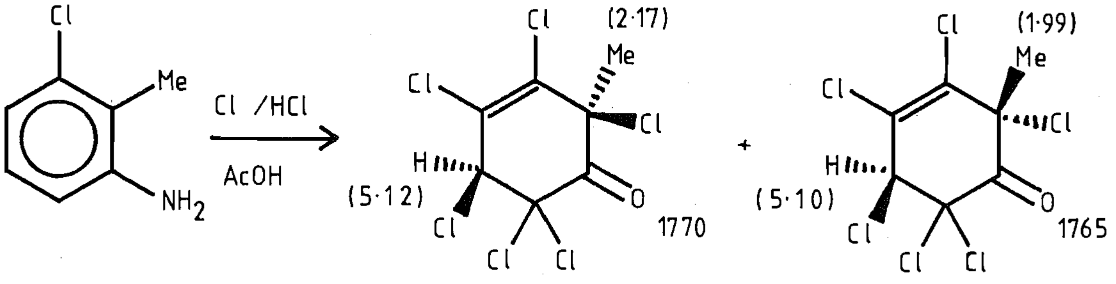

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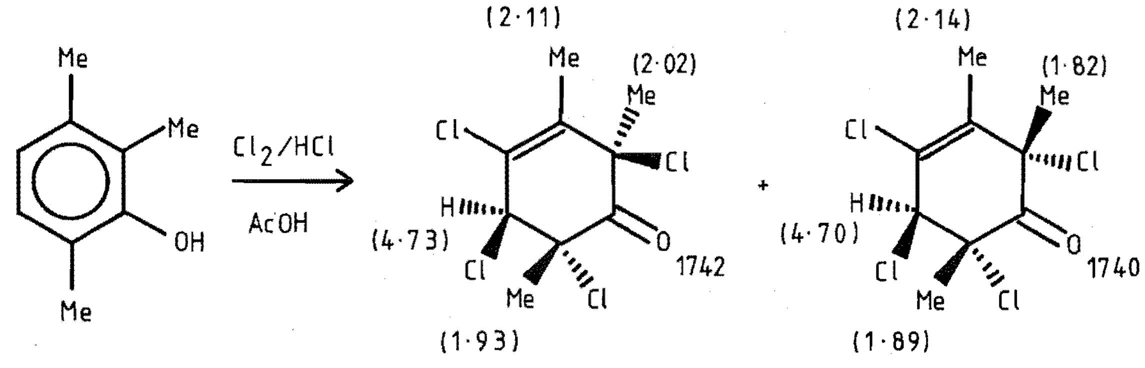

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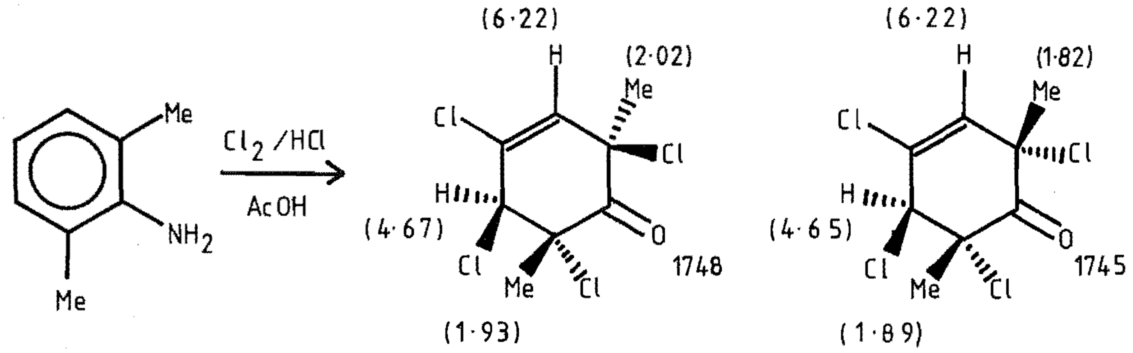

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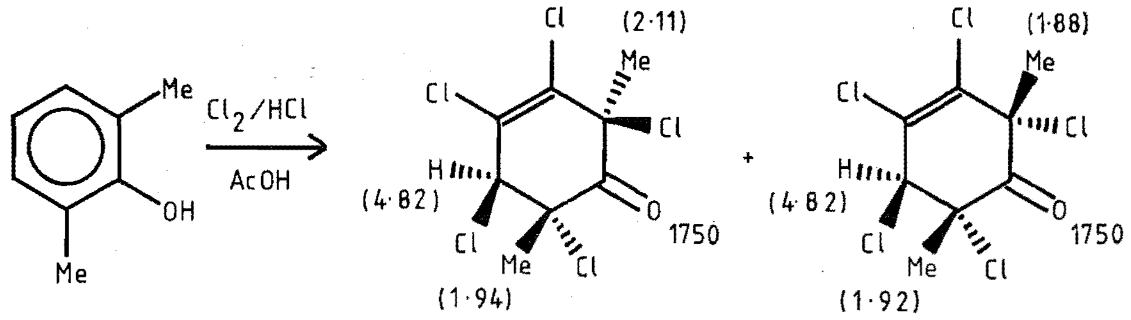

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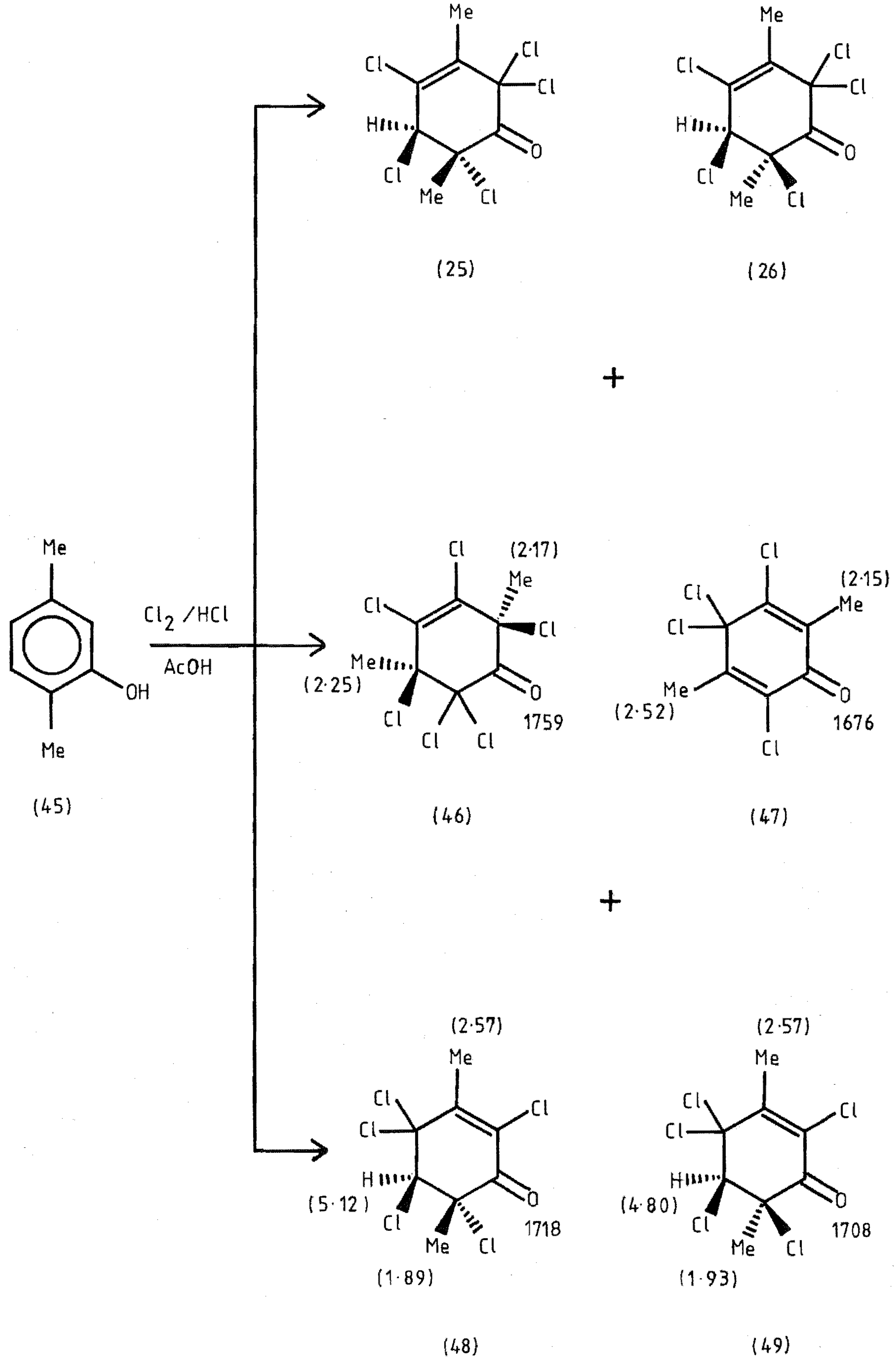
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(47)
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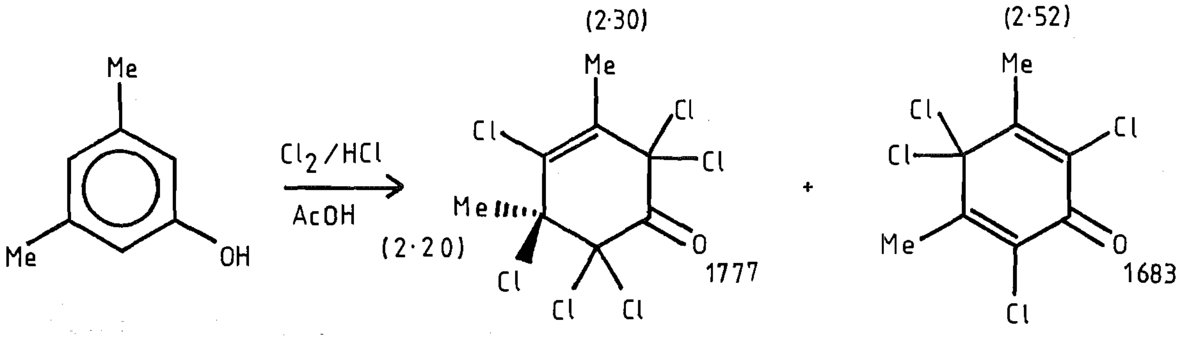

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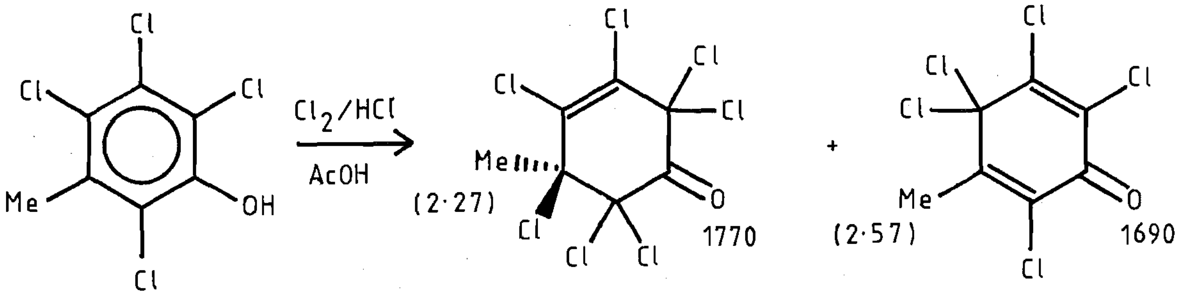

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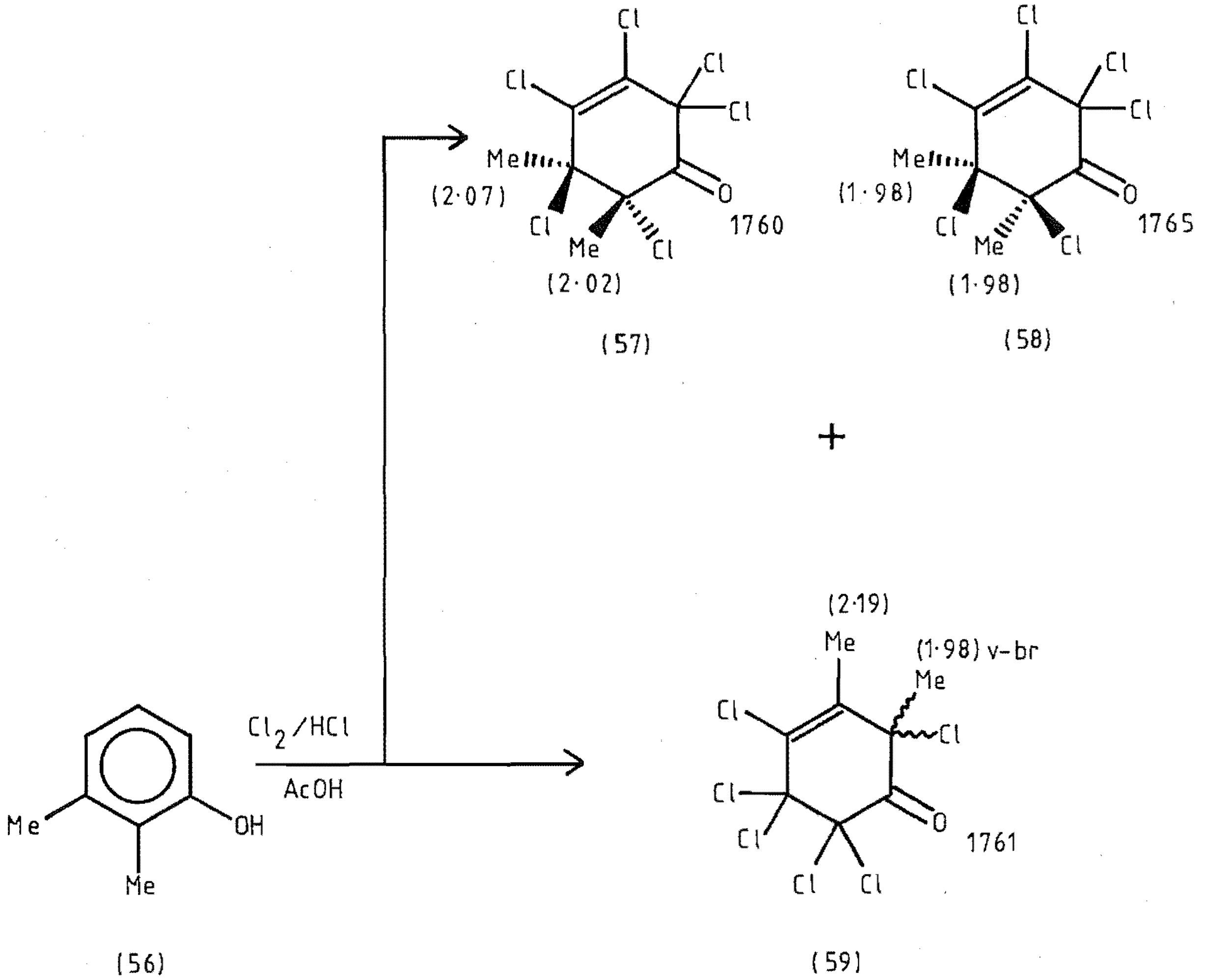
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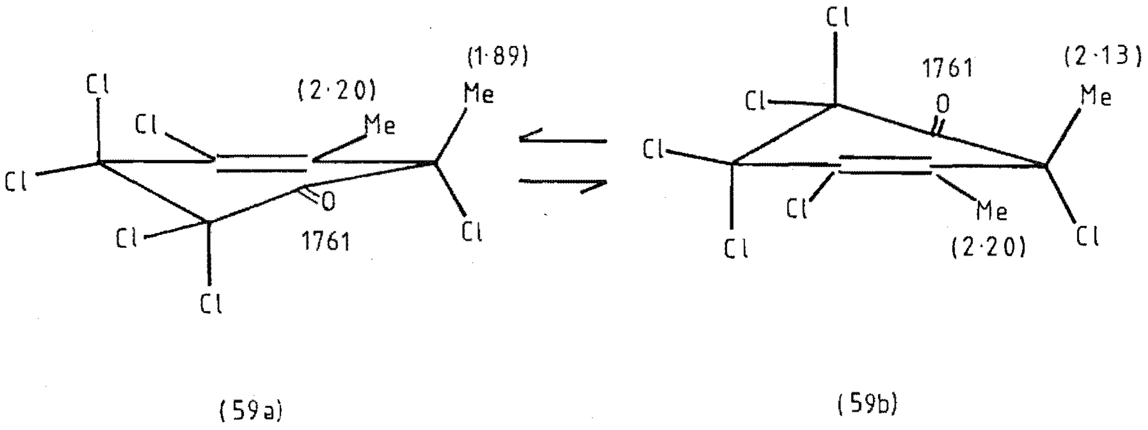
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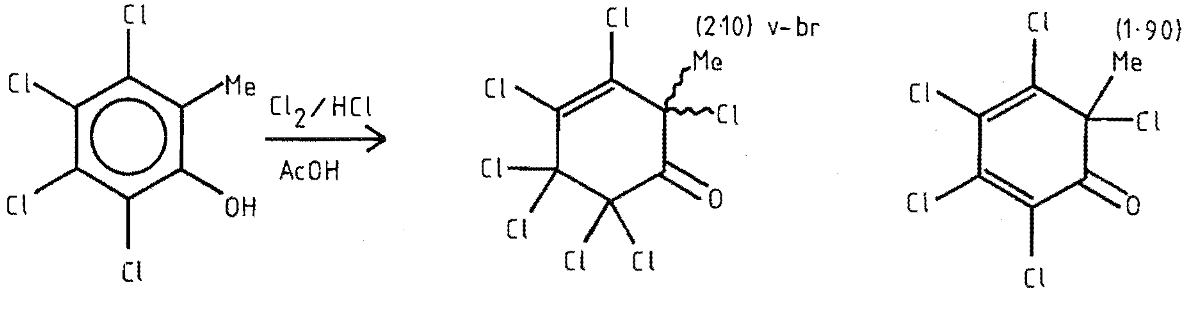

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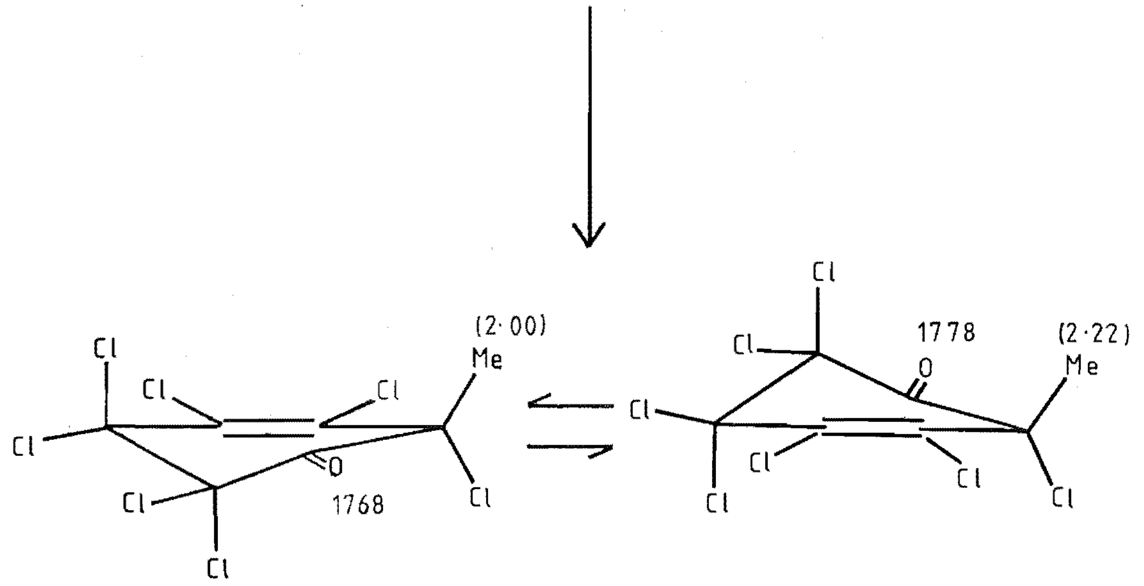

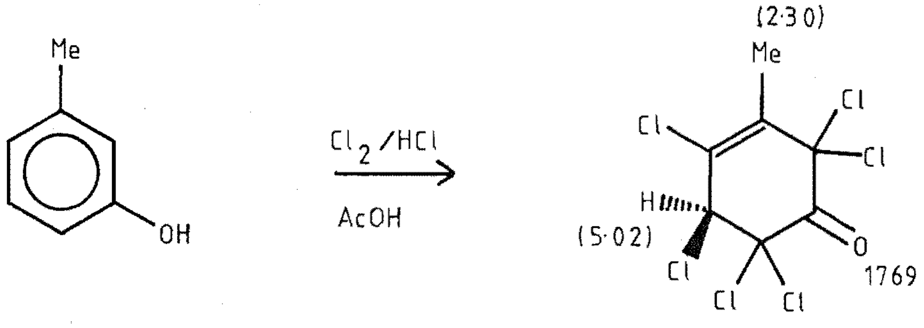

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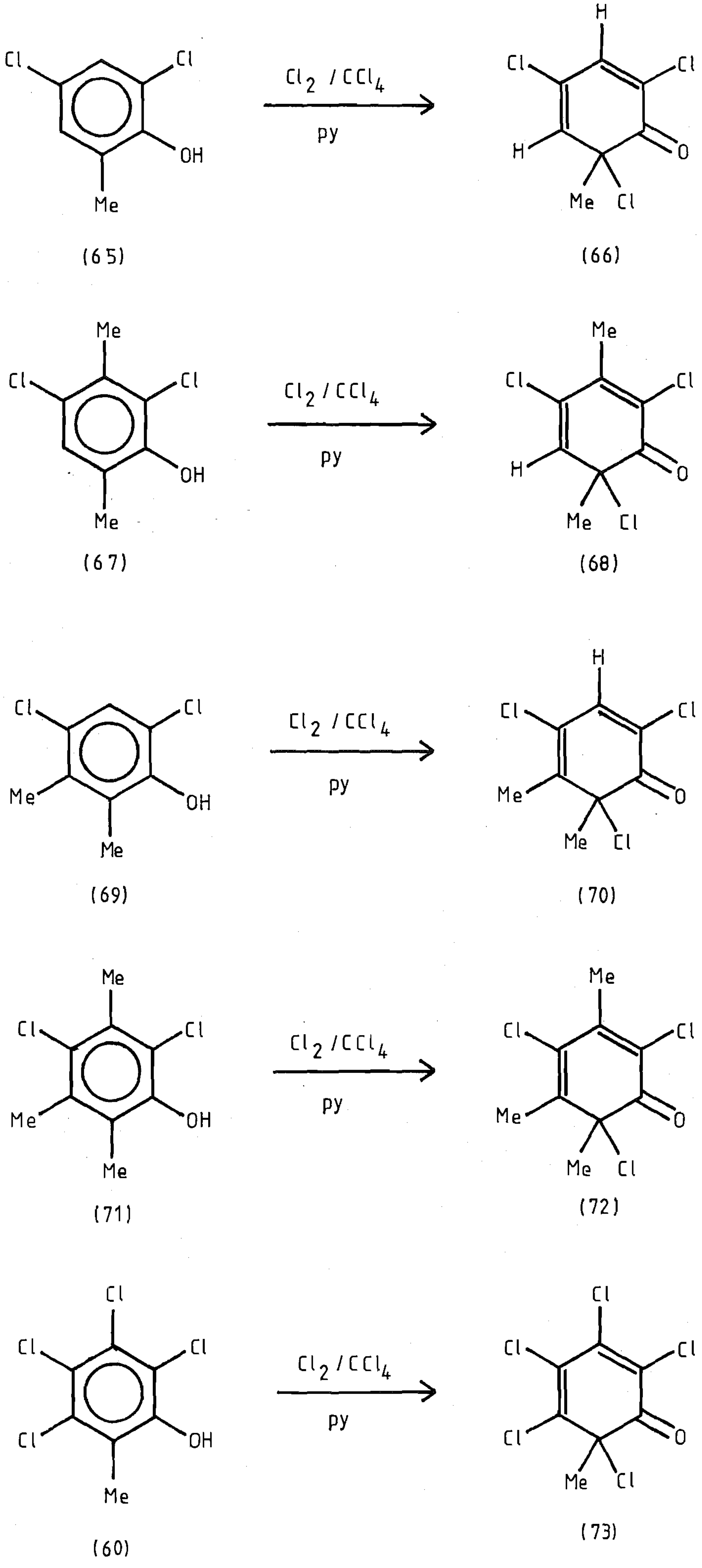

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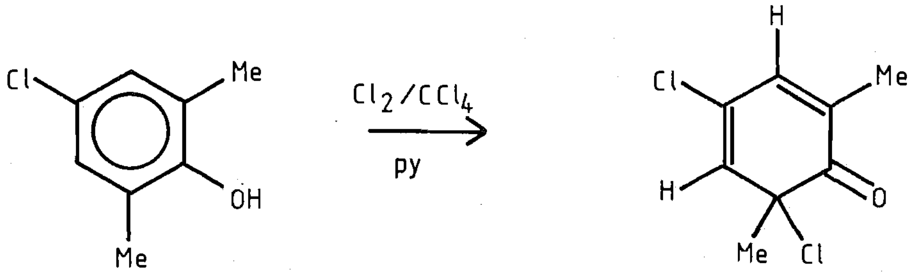

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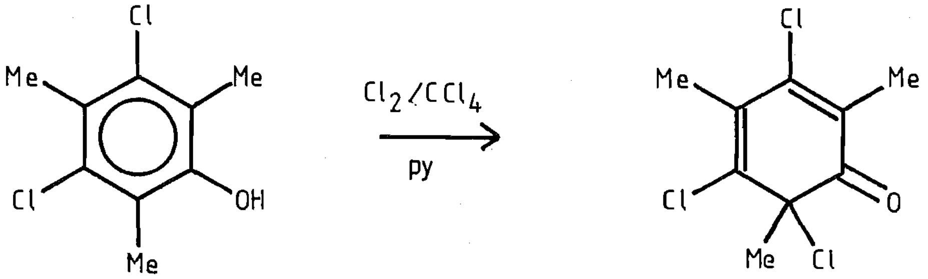
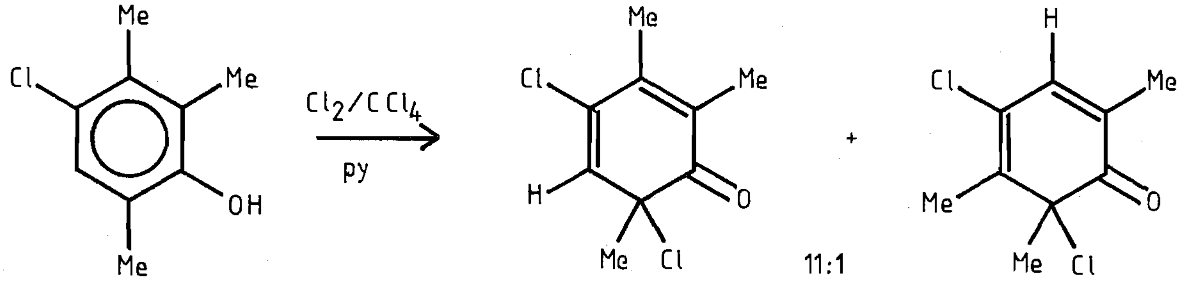
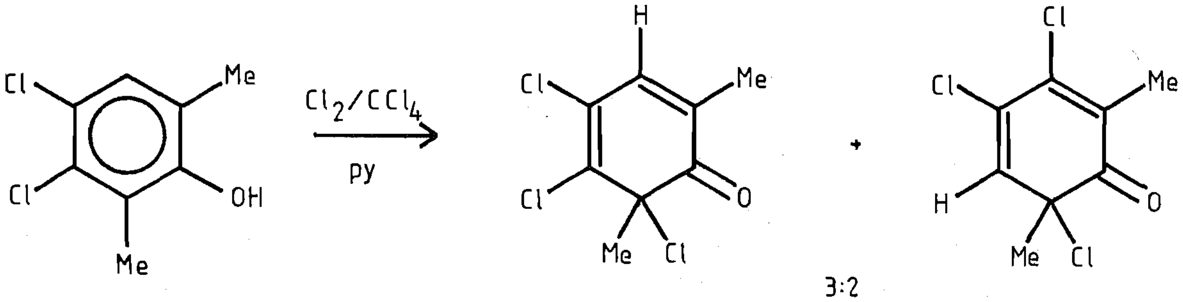


(76) (77)

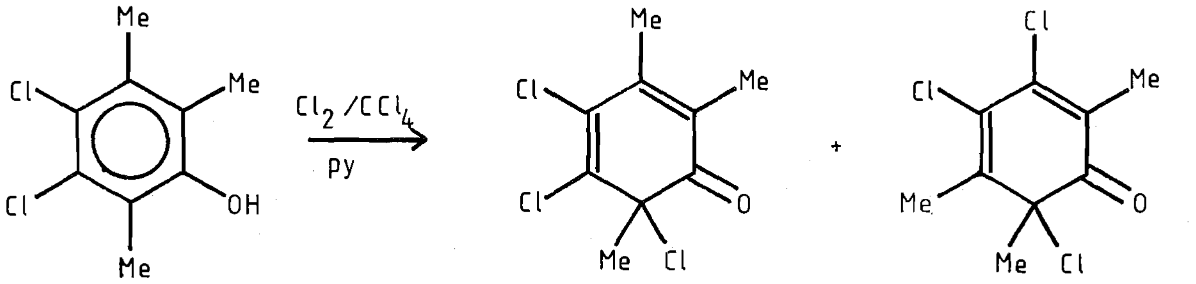


(78) (79) (79a)

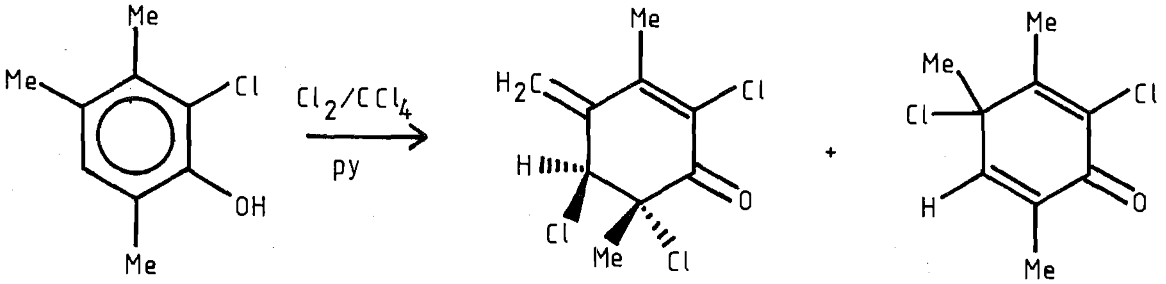


(80) (81) (82)

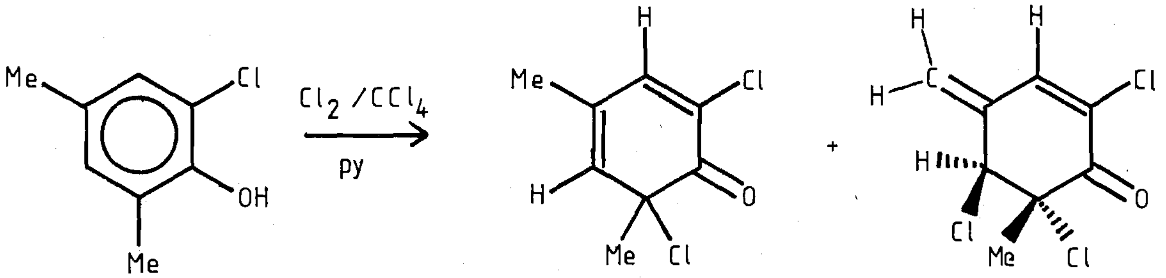
BLOCK L



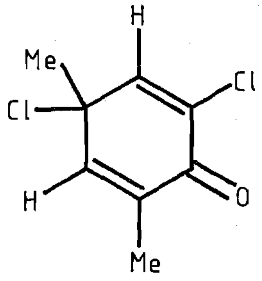
(83) (84) (85)



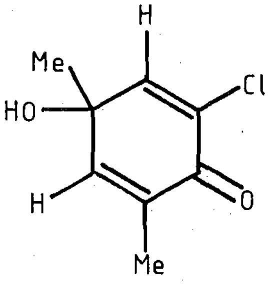
(86) (87) (88)



(89) (90) (91)

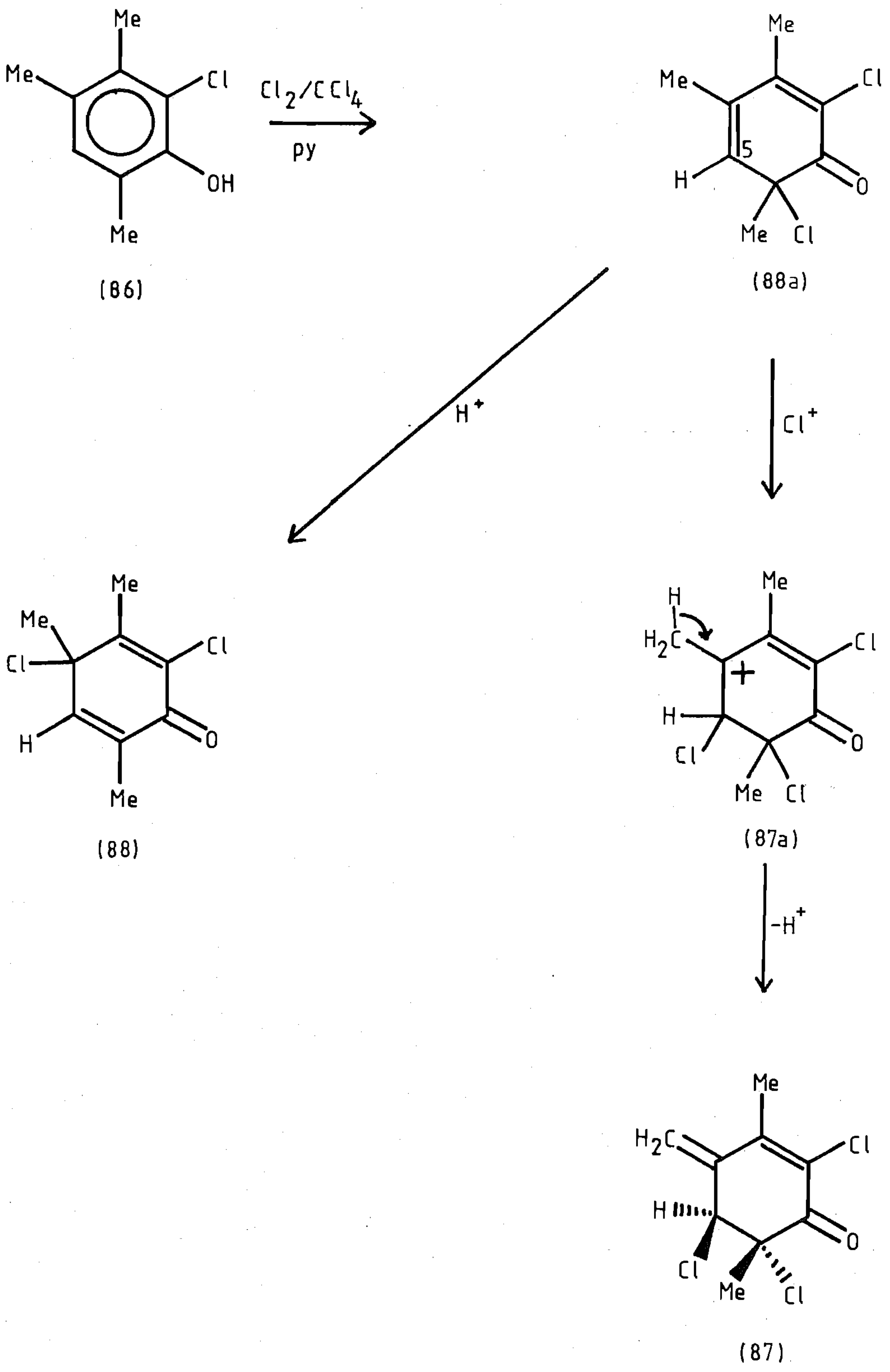


(92)

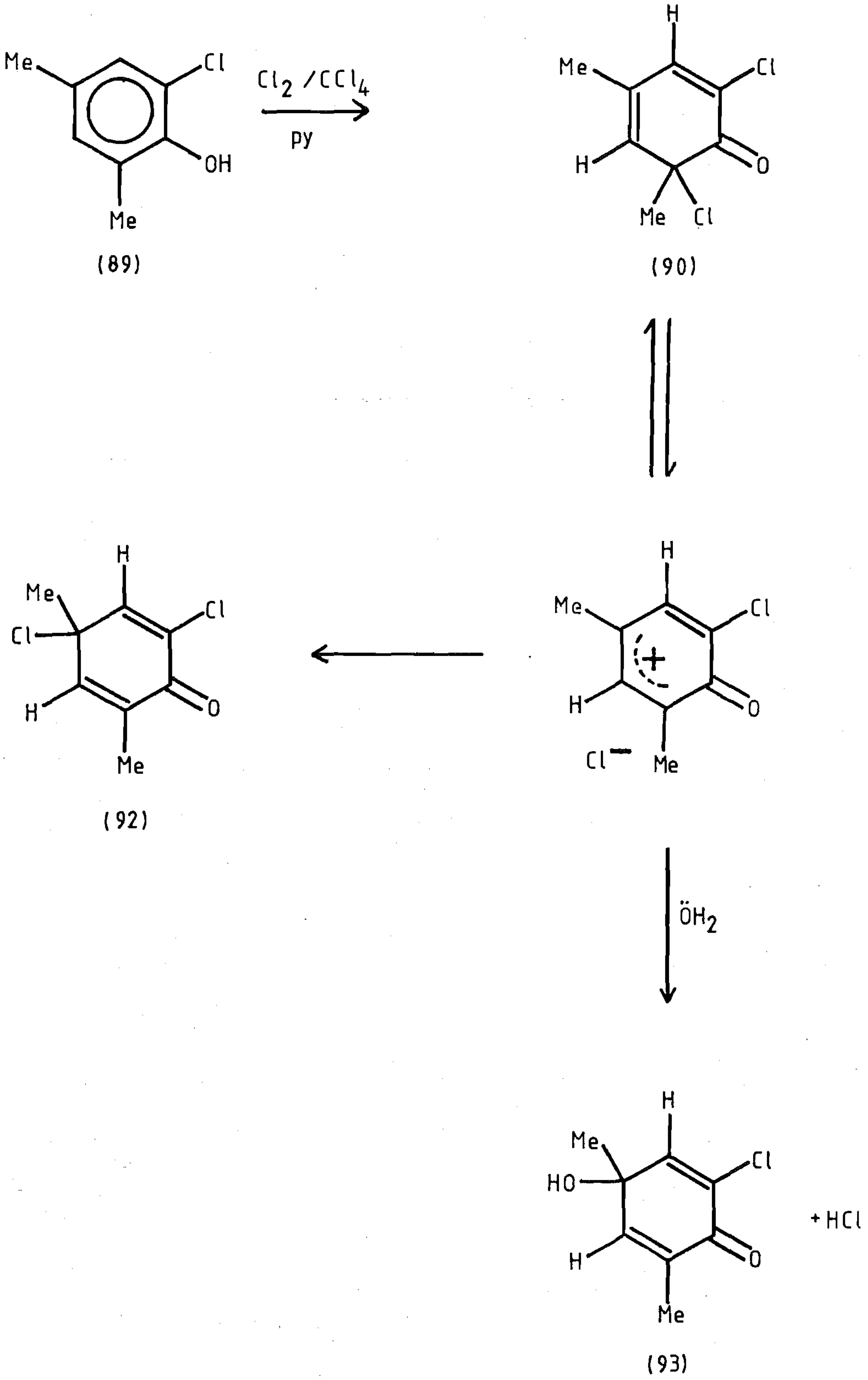


(93)

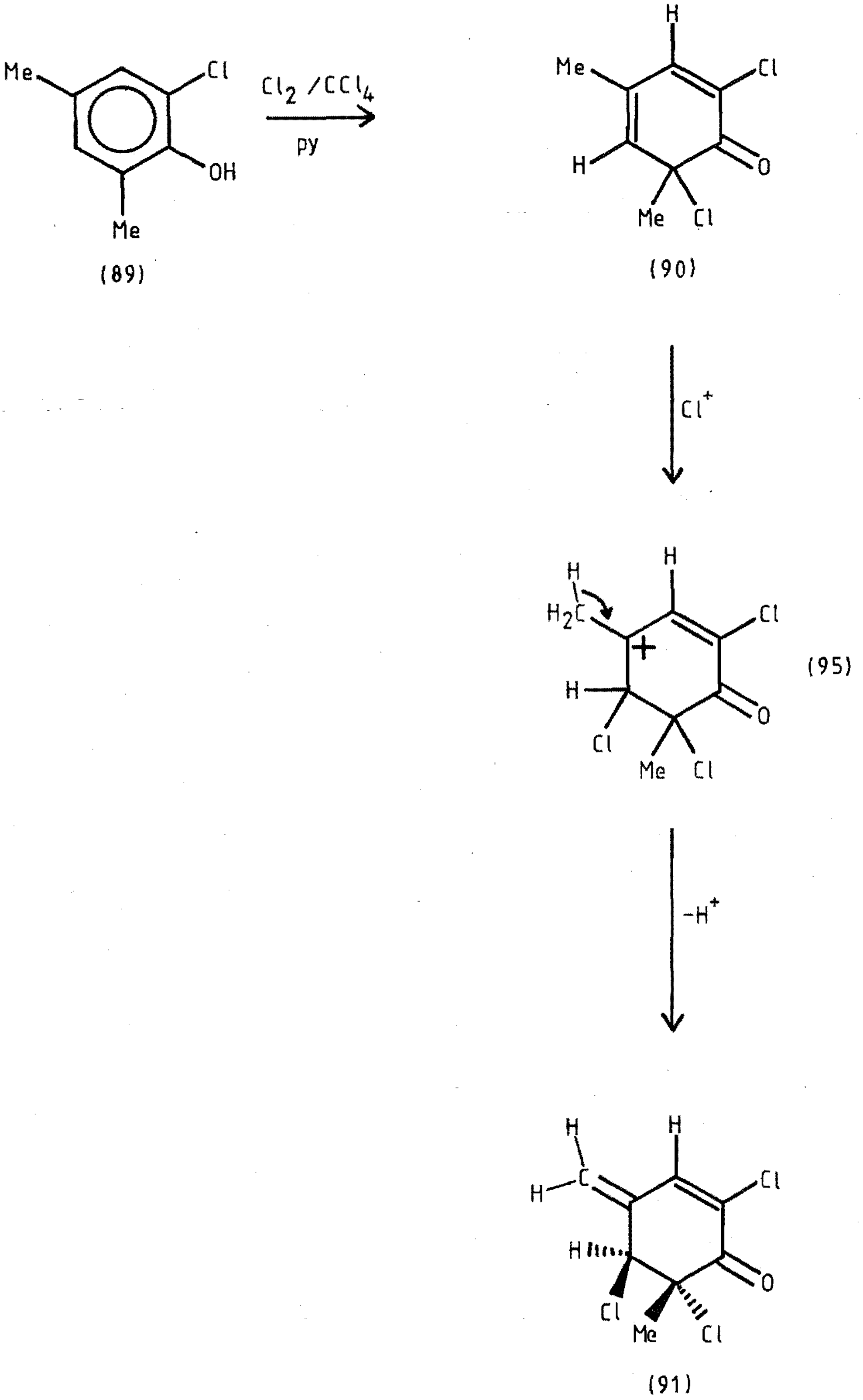
SCHEME 2


Me
Me
Cl
OH
Me
(86)
Cl_2/CCl_4
py
Me
Me
Cl
5
H
O
Me Cl
(88a)
H^+
Cl^+
Me
Me
Cl
Cl
H
O
Me
(88)
Me
H
H_2C
Cl
H
Cl
O
Me Cl
(87a)
$-H^+$
Me
H_2C
Cl
H
O
Cl
Me
Cl
(87)

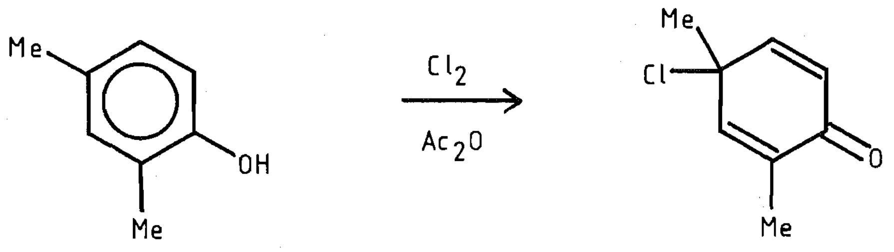
SCHEME 3


Me
Cl
OH
Me
(89)
Cl2 /CCl4
py
H
Me
Cl
H
O
Me
Cl
(90)
H
Me
Cl
Cl
H
O
Me
(92)
H
Me
Cl
+
H
O
Cl−
Me
ÖH2
H
Me
Cl
HO
H
O
Me
+ HCl
(93)

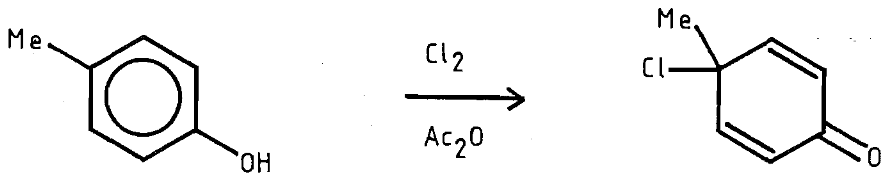
SCHEME 4


Me
Cl
OH
Me
(89)
Cl_2 / CCl_4
py
H
Me
Cl
H
O
Me
Cl
(90)
Cl^+
H
H_2C
H
Cl
H
O
Cl
Me
Cl
(95)
$-H^+$
H
H
C
H
Cl
H
O
Cl
Me
Cl
(91)

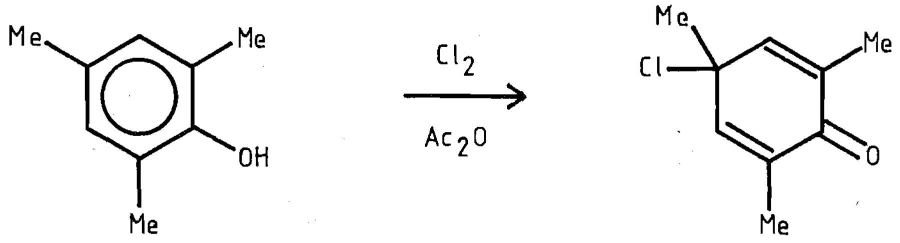
BLOCK M



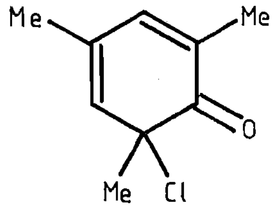
(96) (97)



(98) (99)

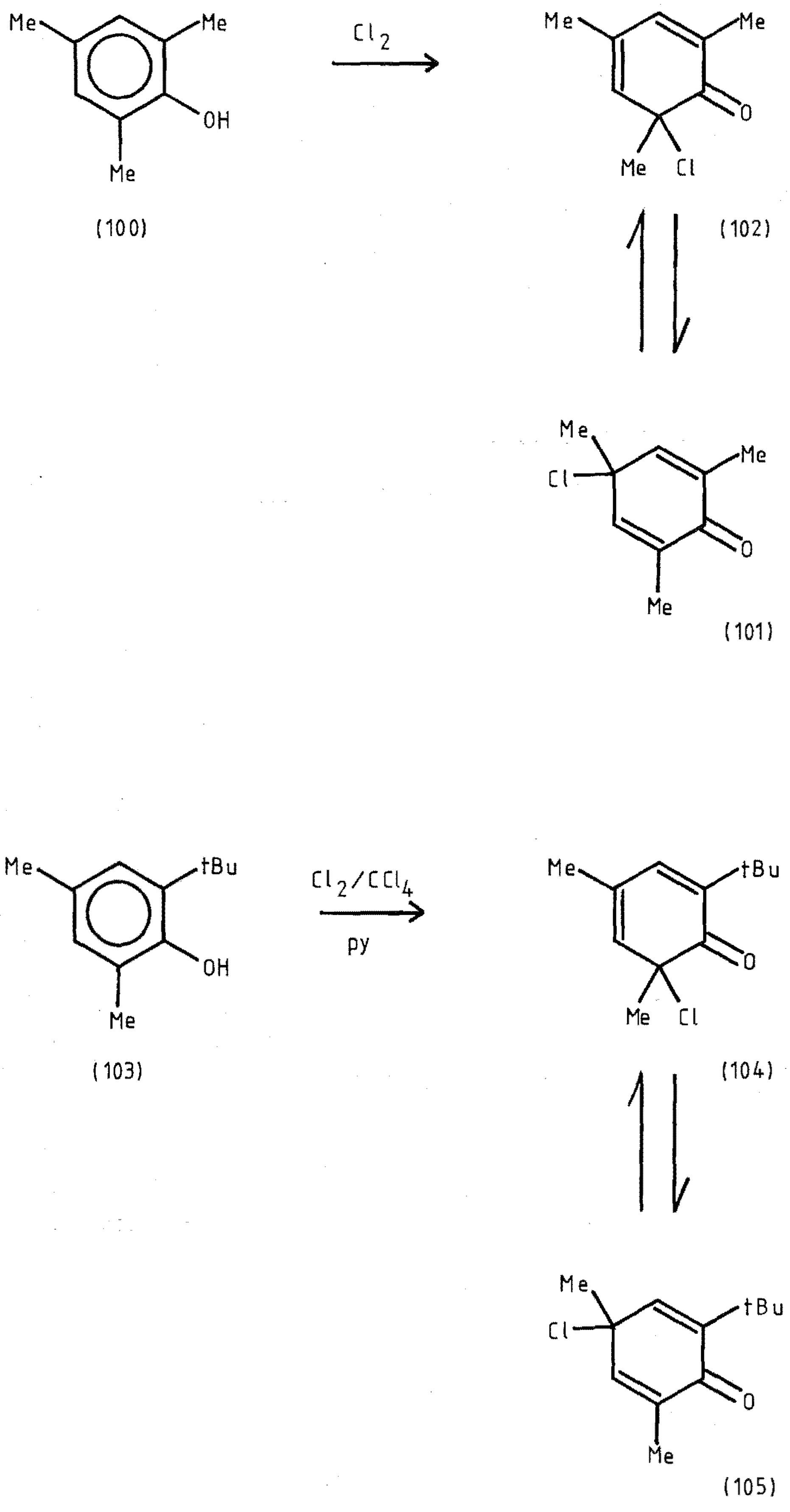


(100) (101)

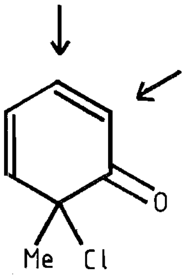


(102)

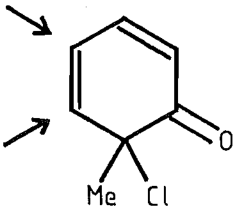
SCHEME 5a


Me
Me
OH
Me
(100)
Cl_2
Me
Me
O
Me
Cl
(102)
Me
Cl
Me
O
Me
(101)
Me
tBu
OH
Me
(103)
Cl_2/CCl_4
py
Me
tBu
O
Me
Cl
(104)
Me
Cl
tBu
O
Me
(105)

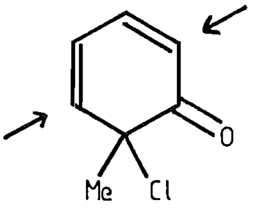
BLOCK N



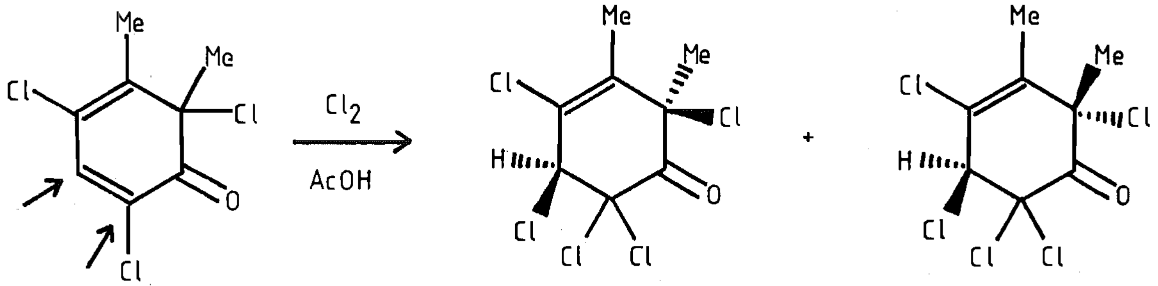
2,3-



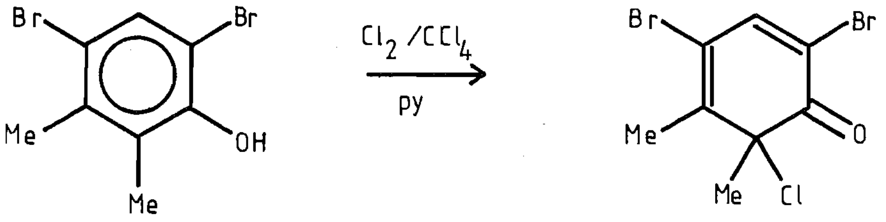
4,5-



2,5-

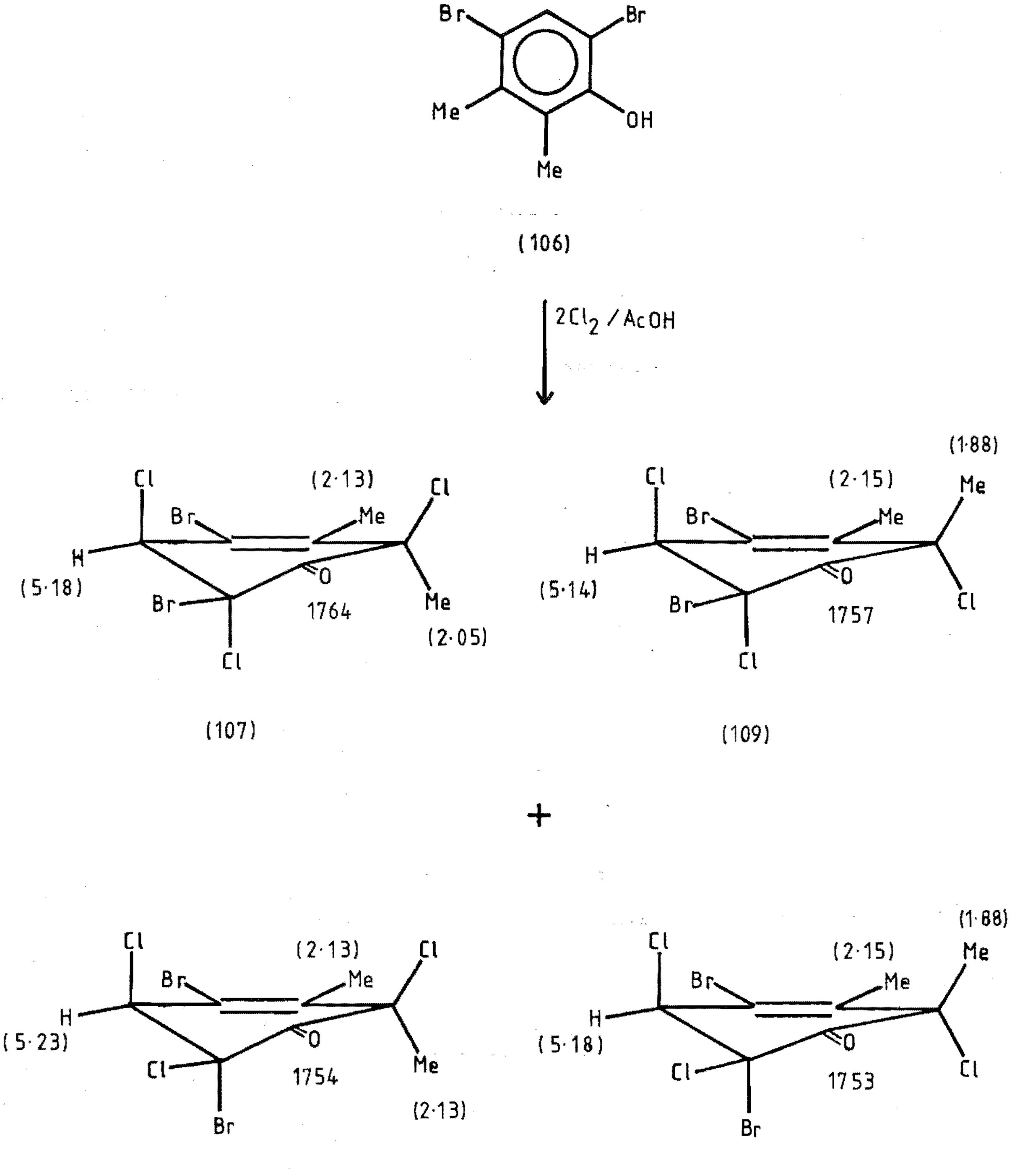


(70) (31) (32)

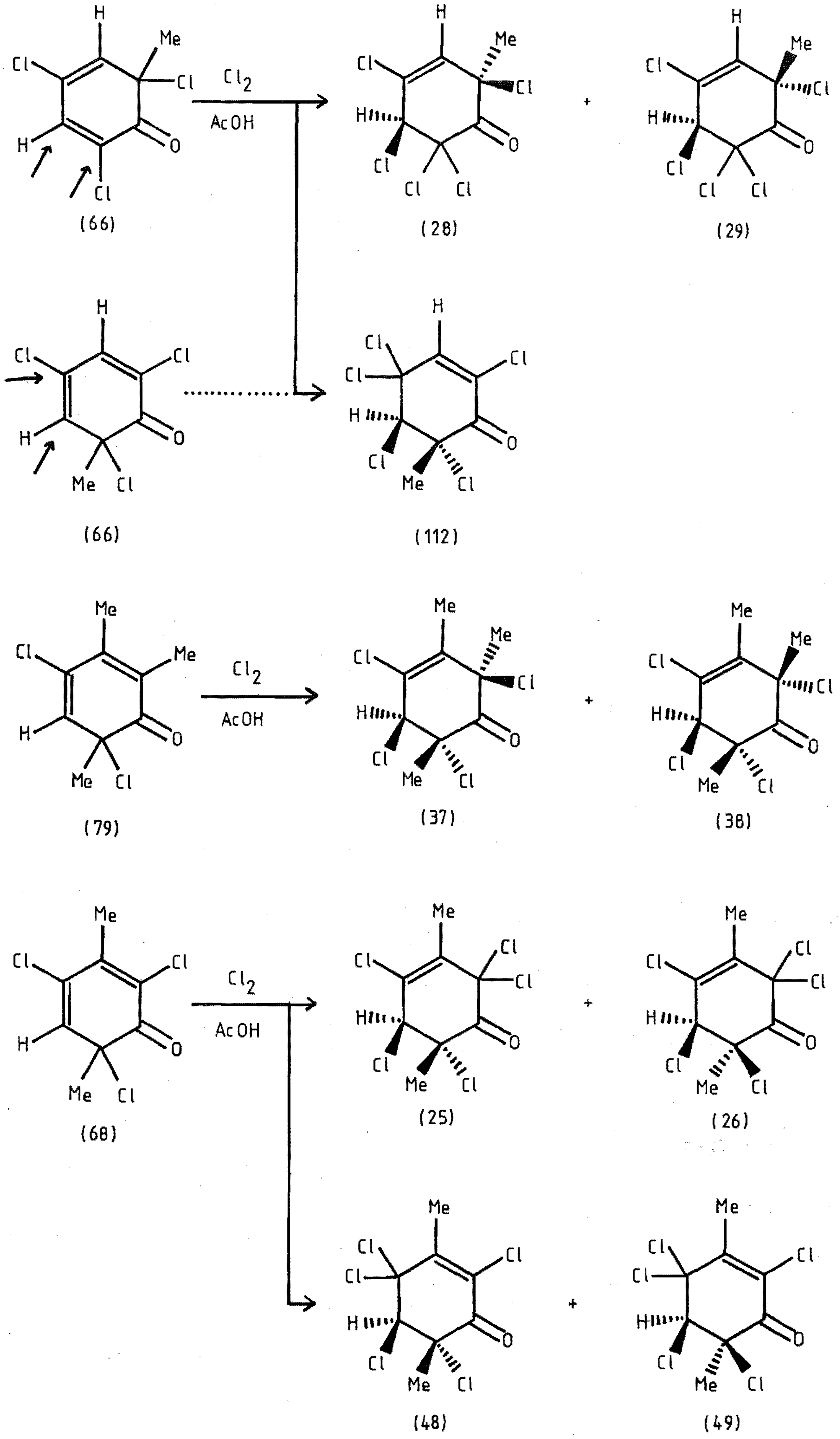


(106) (111)

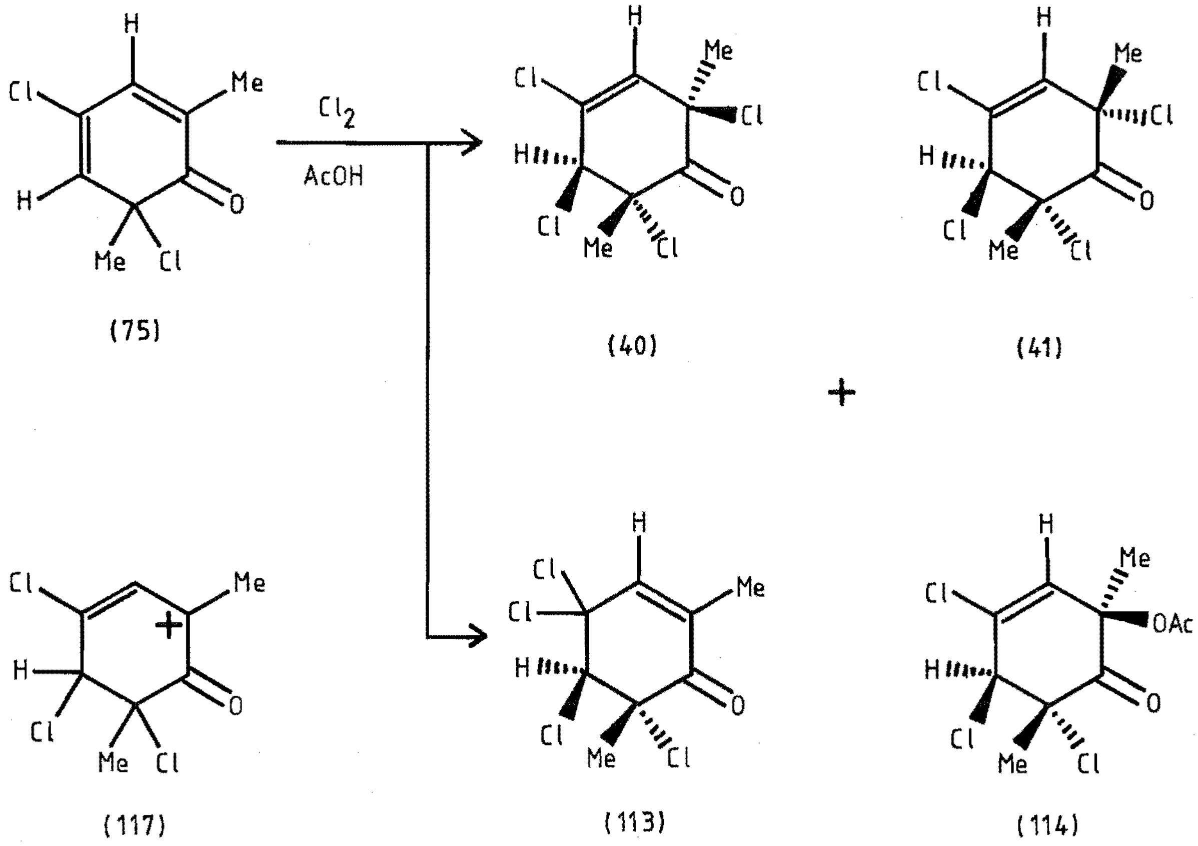
BLOCK O

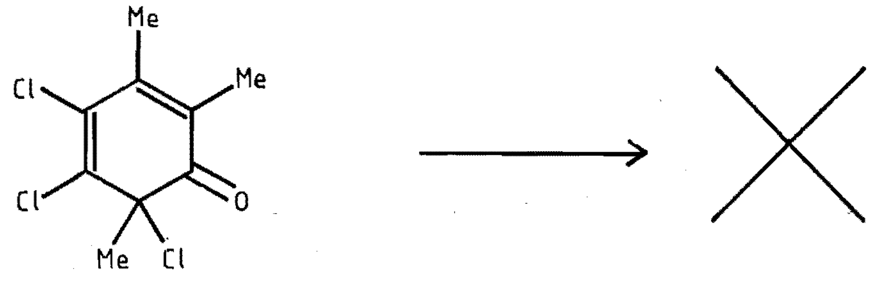

Br
Br
Me
OH
Me
(106)
2Cl2 / AcOH
Cl
H
(5·18)
Br
Br
Cl
(2·13)
Me
Cl
O
1764
Me
(2·05)
(107)
(1·88)
Cl
H
(5·14)
Br
Br
Cl
(2·15)
Me
Me
O
1757
Cl
(109)
+
Cl
H
(5·23)
Br
Cl
Br
(2·13)
Me
Cl
O
1754
Me
(2·13)
(108)
(1·88)
Cl
H
(5·18)
Br
Cl
Br
(2·15)
Me
Me
O
1753
Cl
(110)

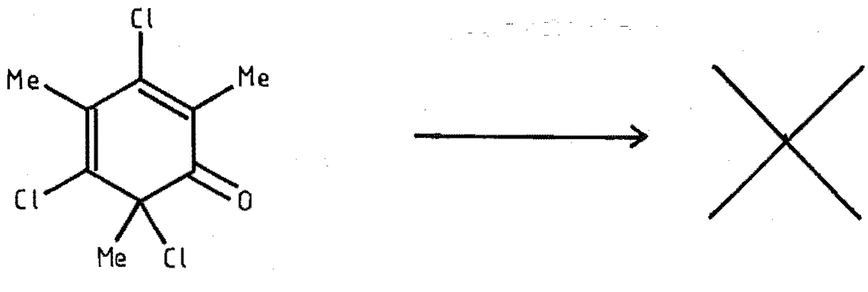
BLOCK P



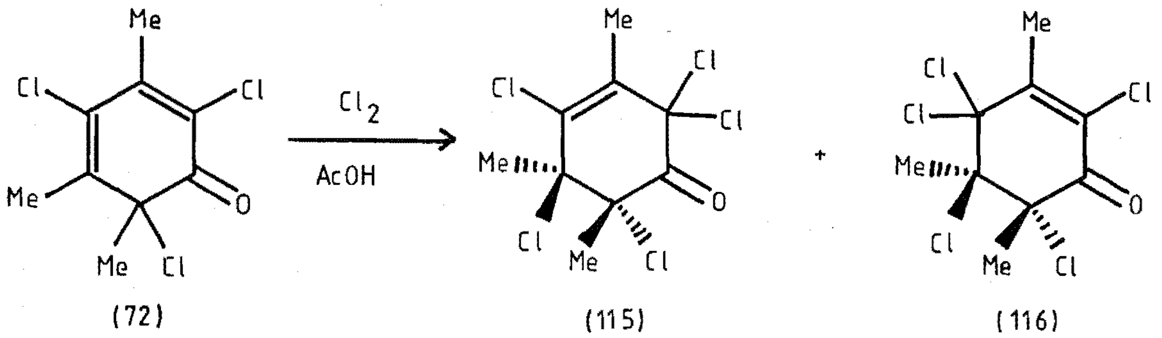
BLOCK Q

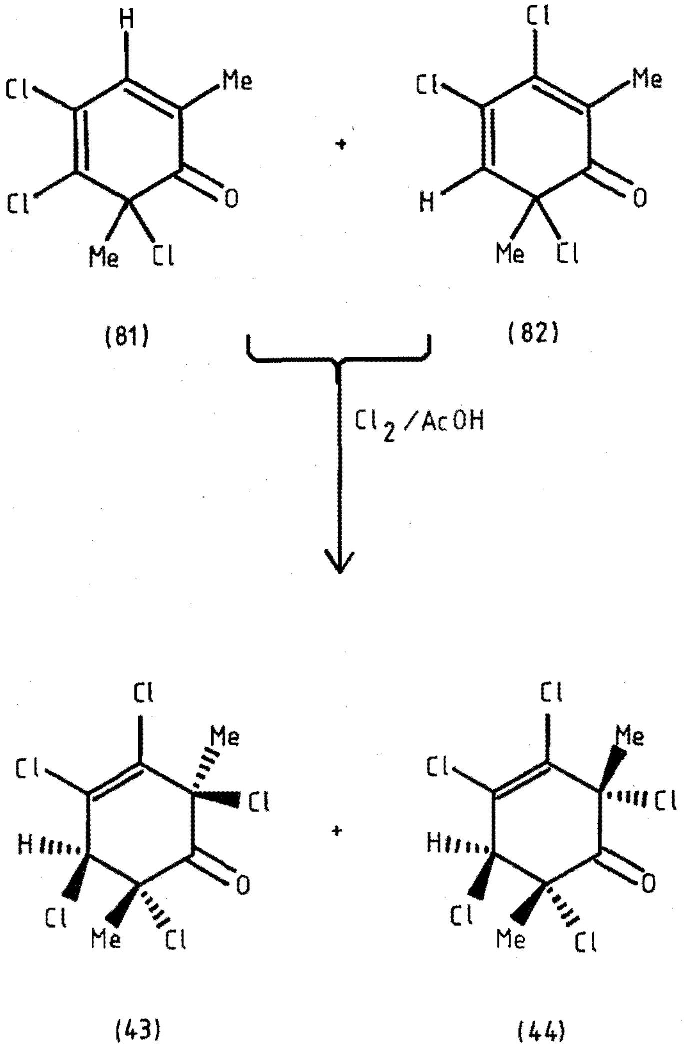



(84)


(77)

BLOCK R



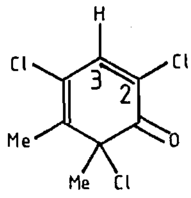


BLOCK S

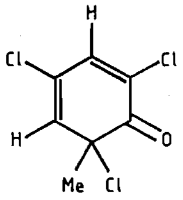
2,3-

4,5-

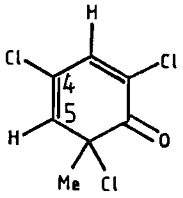
2,5-



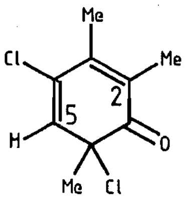
(70)



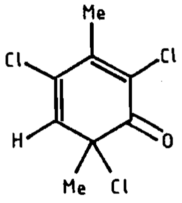
(66)



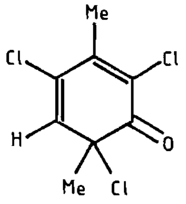
(66)



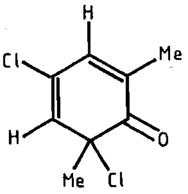
(79)



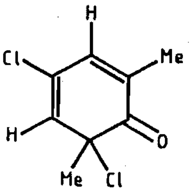
(68)



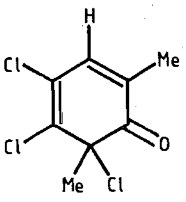
(68)



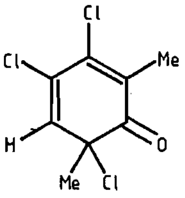
(75)



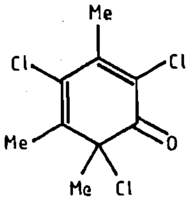
(75)



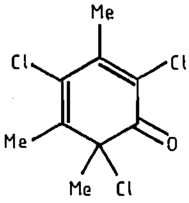
(81)



(82)

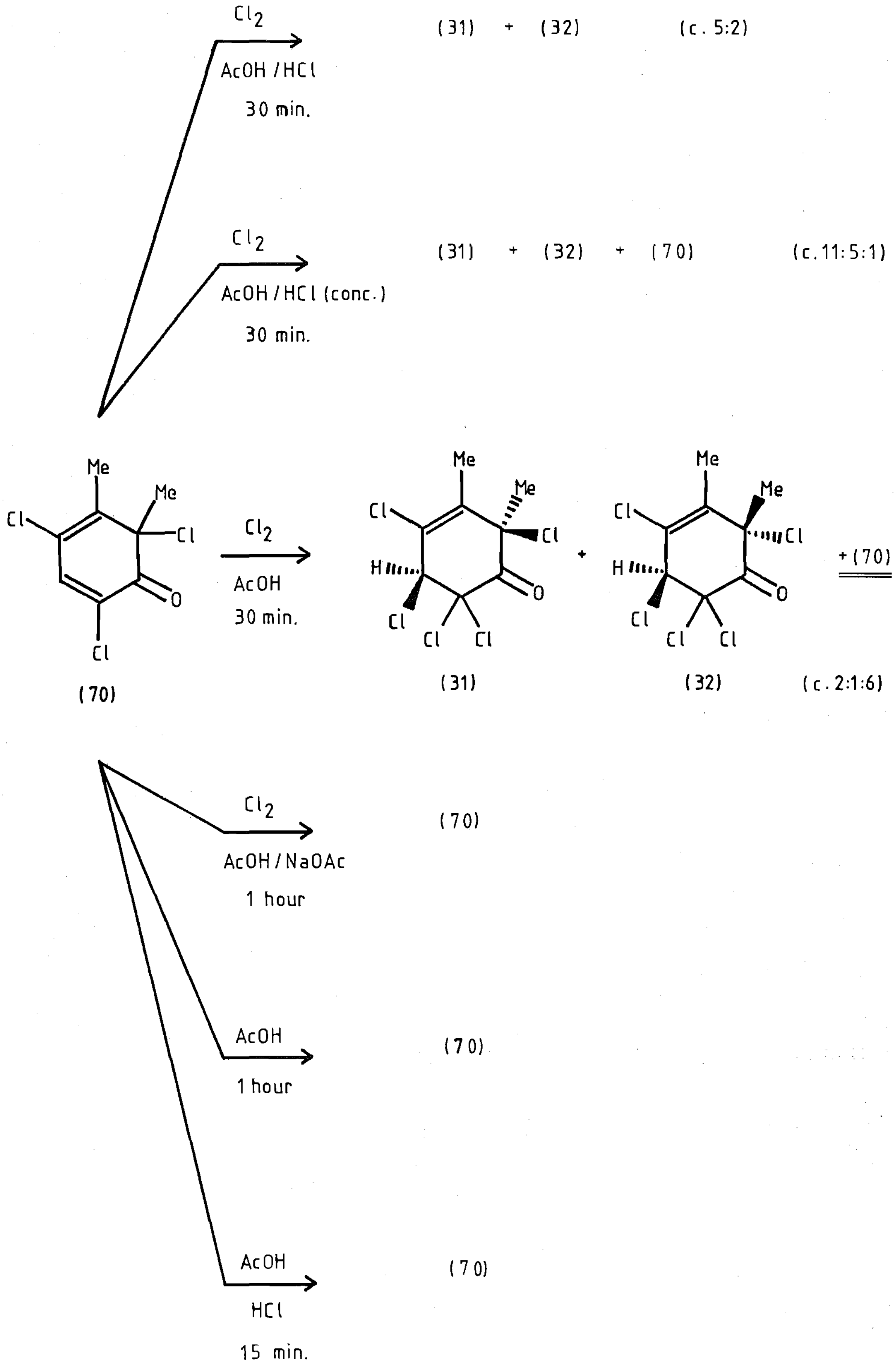


(72)

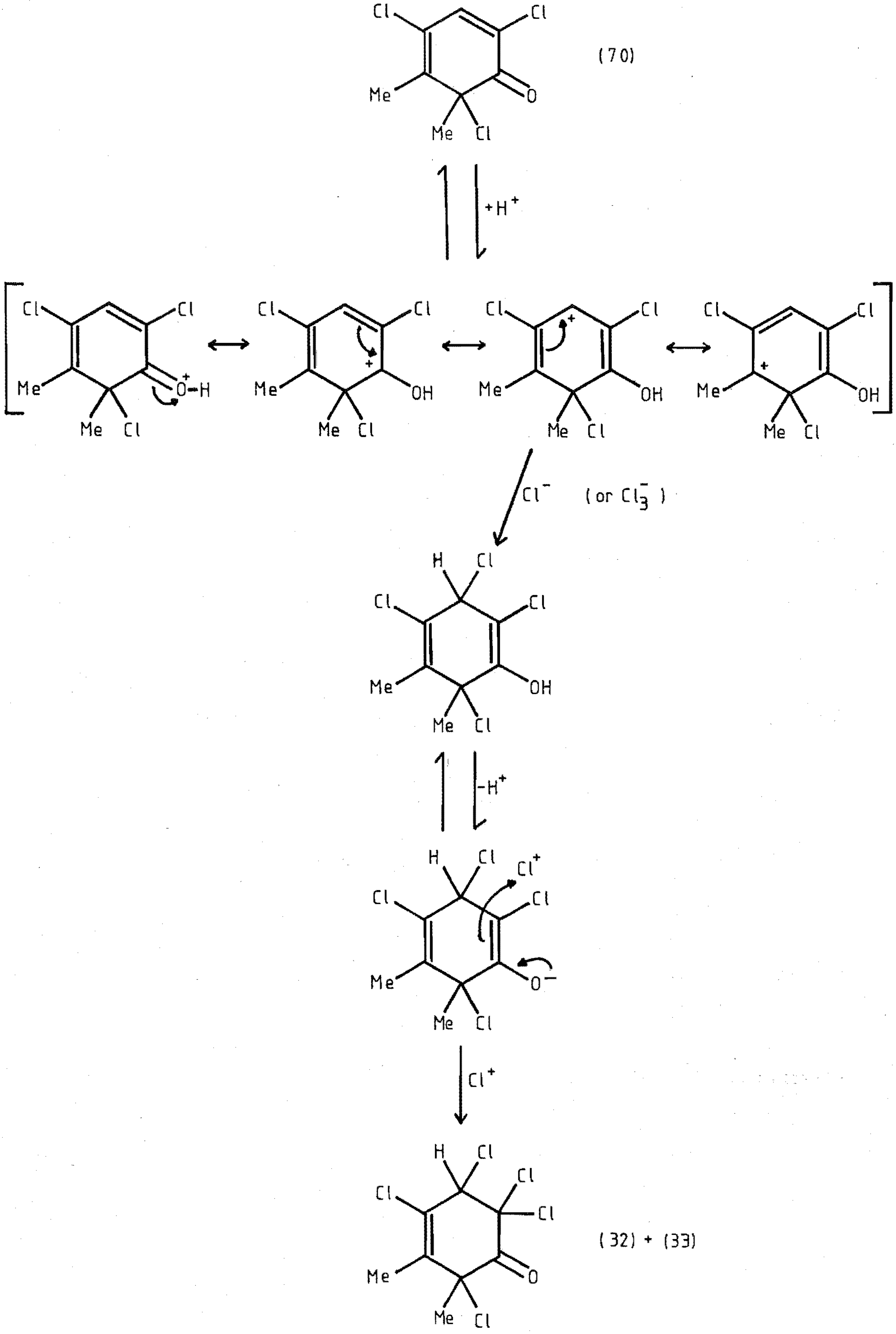


(72)

BLOCK T


Cl2
AcOH / HCl
30 min.
(31) + (32) (c. 5:2)
Cl2
AcOH / HCl (conc.)
30 min.
(31) + (32) + (70) (c. 11:5:1)
Me
Me
Cl
Cl
O
Cl
(70)
Cl2
AcOH
30 min.
Me
Me
Cl
Cl
H
Cl
Cl
Cl
O
(31)
+
Me
Me
Cl
Cl
H
Cl
Cl
Cl
O
(32)
+ (70)
(c. 2:1:6)
Cl2
AcOH / NaOAc
1 hour
(70)
AcOH
1 hour
(70)
AcOH
HCl
15 min.
(70)

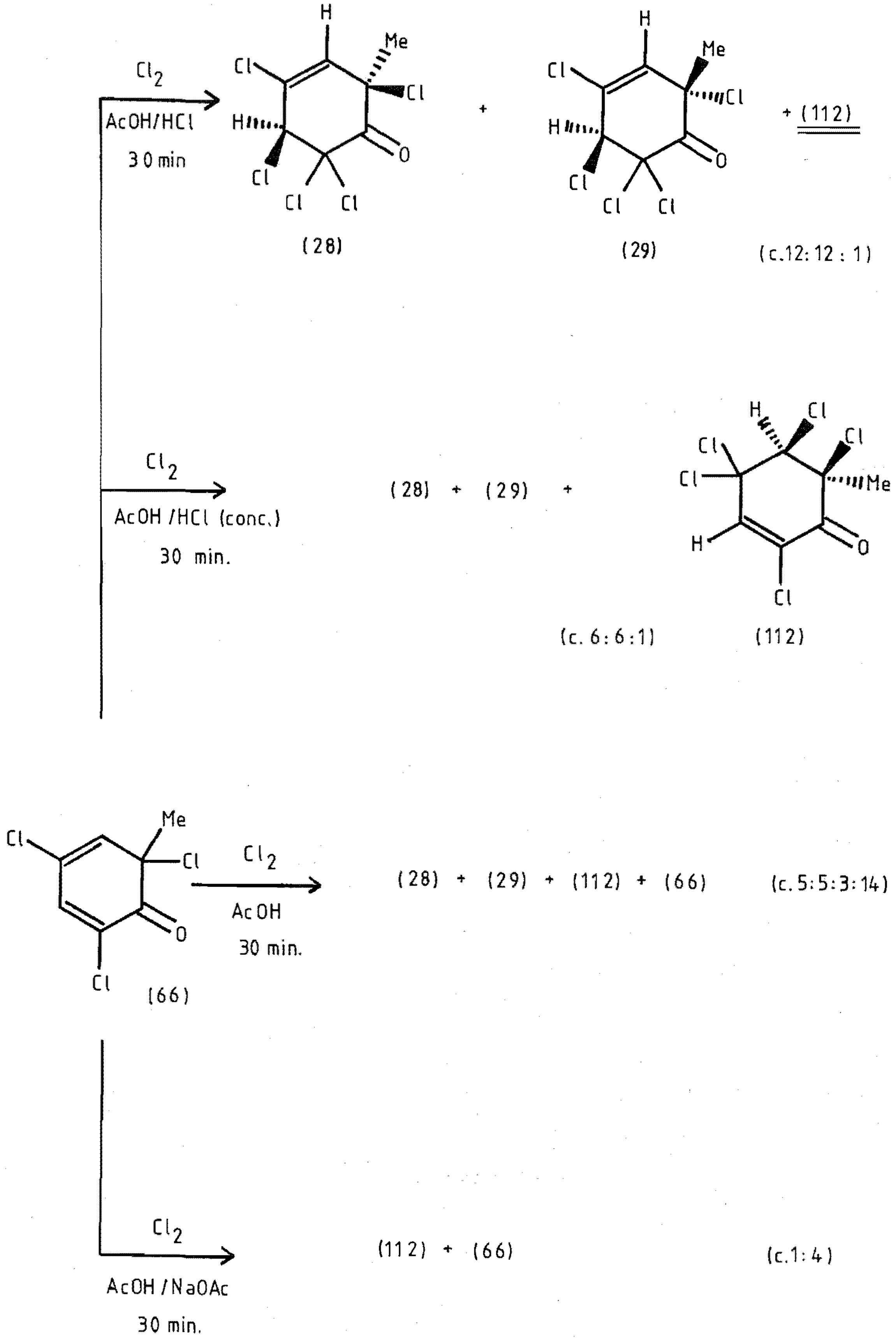
SCHEME 6



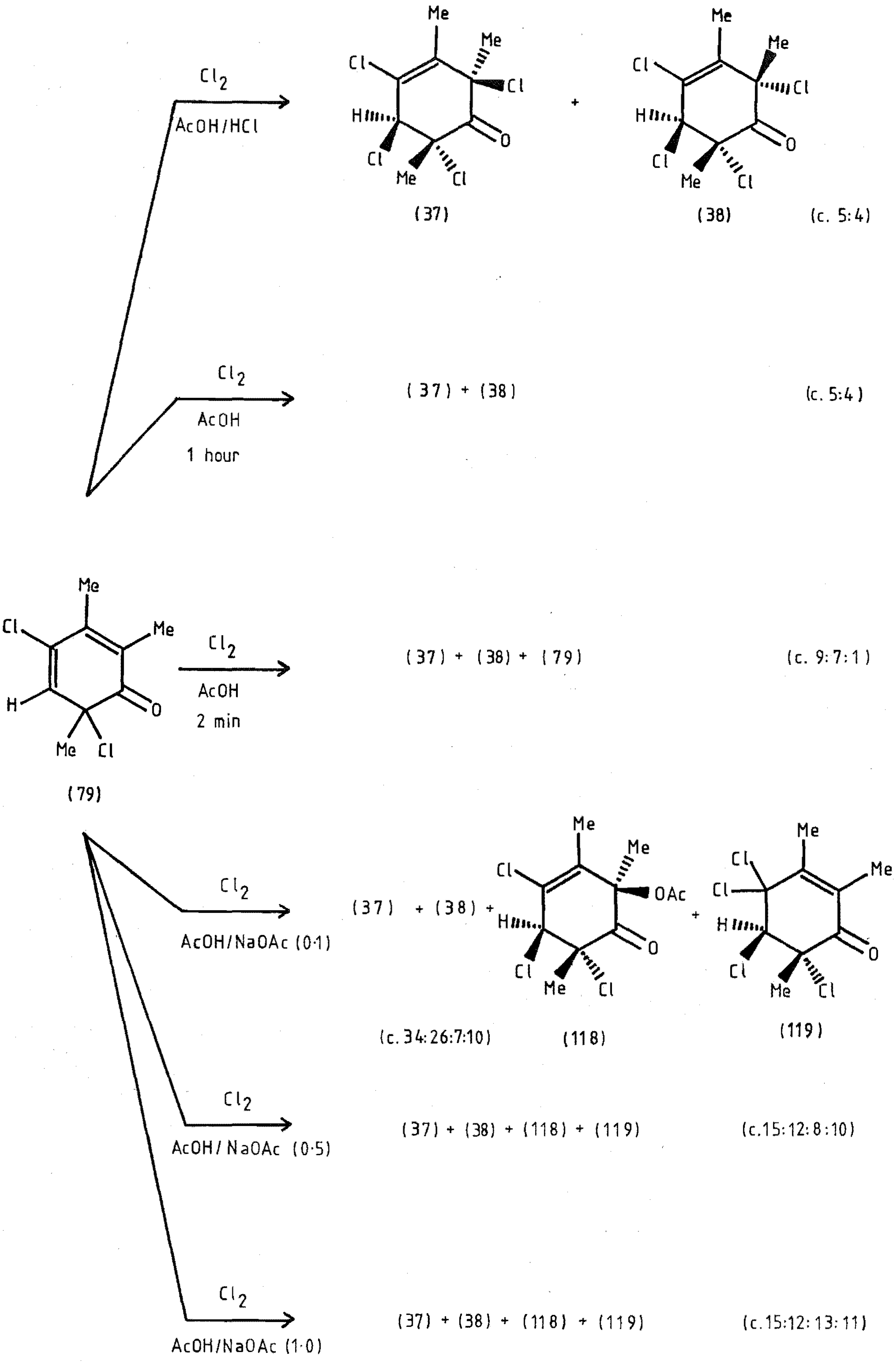
(70)

(32) + (33)

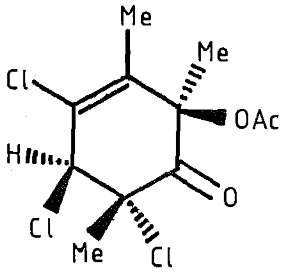
BLOCK U


Cl2
AcOH/HCl
30 min
(28)
+
(29)
+ (112)
(c.12: 12 : 1)
Cl2
AcOH /HCl (conc.)
30 min.
(28) + (29) +
(c. 6 : 6 :1)
(112)
(66)
Cl2
AcOH
30 min.
(28) + (29) + (112) + (66)
(c. 5:5:3:14)
Cl2
AcOH / NaOAc
30 min.
(112) + (66)
(c.1: 4)
H
Me
Cl
O

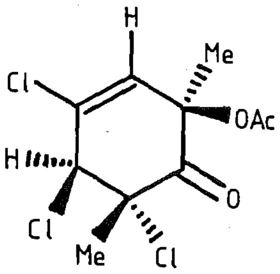
BLOCK V


Cl2
AcOH/HCl
(37)
(38)
(c. 5:4)
Cl2
AcOH
1 hour
(37) + (38)
(c. 5:4)
(79)
Cl2
AcOH
2 min
(37) + (38) + (79)
(c. 9:7:1)
Cl2
AcOH/NaOAc (0·1)
(37) + (38) +
(c. 34:26:7:10)
(118)
(119)
Cl2
AcOH/NaOAc (0·5)
(37) + (38) + (118) + (119)
(c.15:12:8:10)
Cl2
AcOH/NaOAc (1·0)
(37) + (38) + (118) + (119)
(c.15:12:13:11)

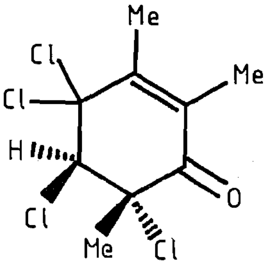
BLOCK W



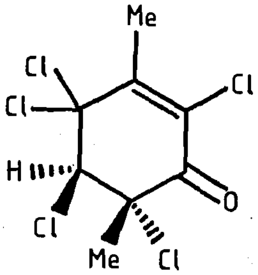
(118)



(114)

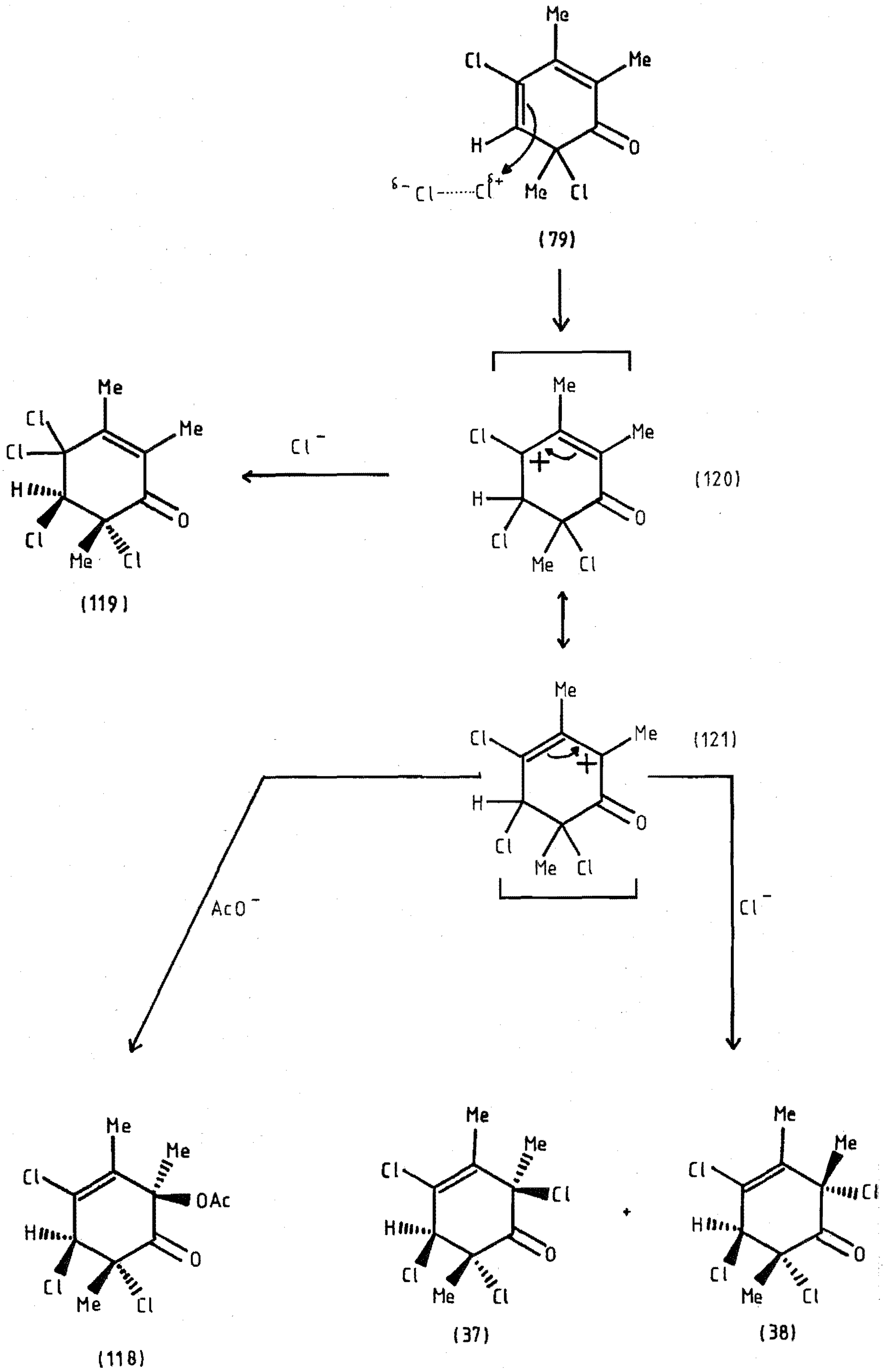


(119)

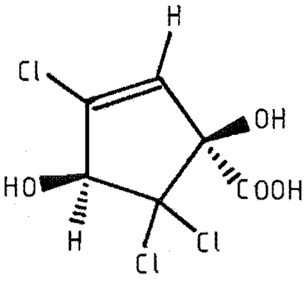


(48)

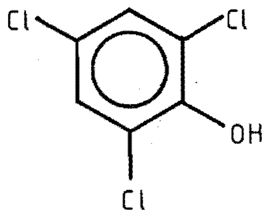
SCHEME 7


Me
Cl
Me
H
O
δ− Cl·········Cl δ+
Me
Cl
(79)
Me
Cl
Cl
Me
H
Cl
Me
Cl
O
(119)
Cl⁻
Me
Cl
Me
+
H
O
Cl
Me
Cl
(120)
Me
Cl
Me
(121)
+
H
O
Cl
Me
Cl
AcO⁻
Cl⁻
Me
Me
Cl
OAc
H
O
Cl
Me
Cl
(118)
Me
Me
Cl
Cl
H
O
Cl
Me
Cl
(37)
+
Me
Me
Cl
Cl
H
O
Cl
Me
Cl
(38)

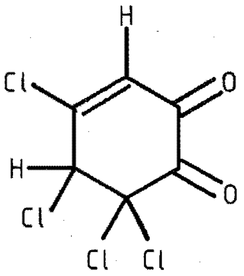
BLOCK X



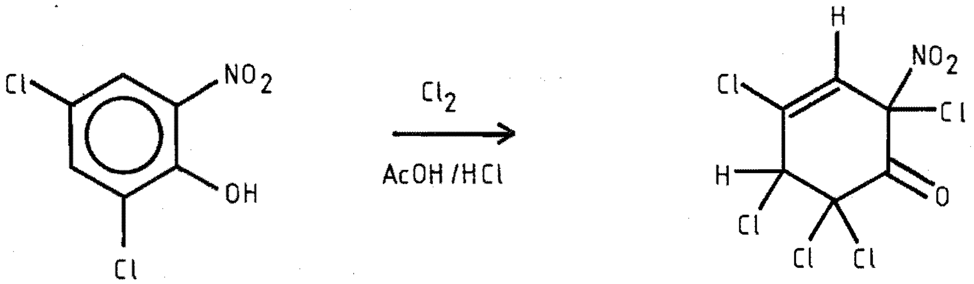
(125)



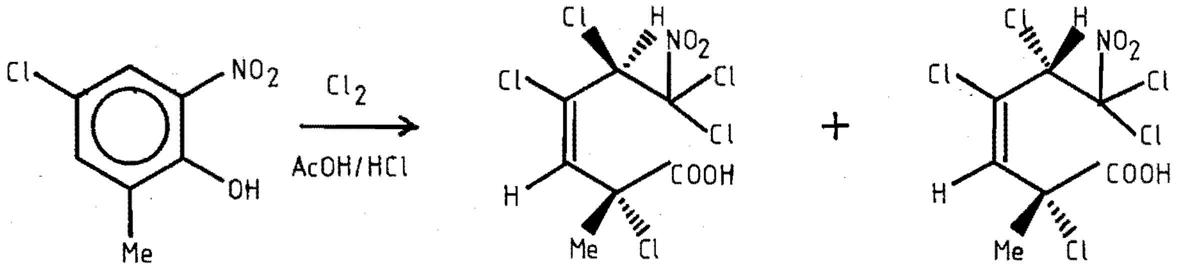
(126)



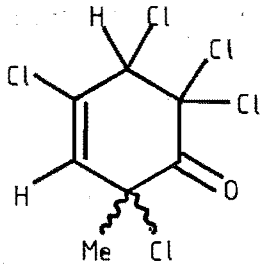
(127)



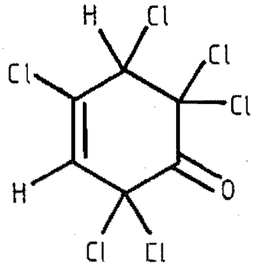
(128) (129)



(130) (131) (132)

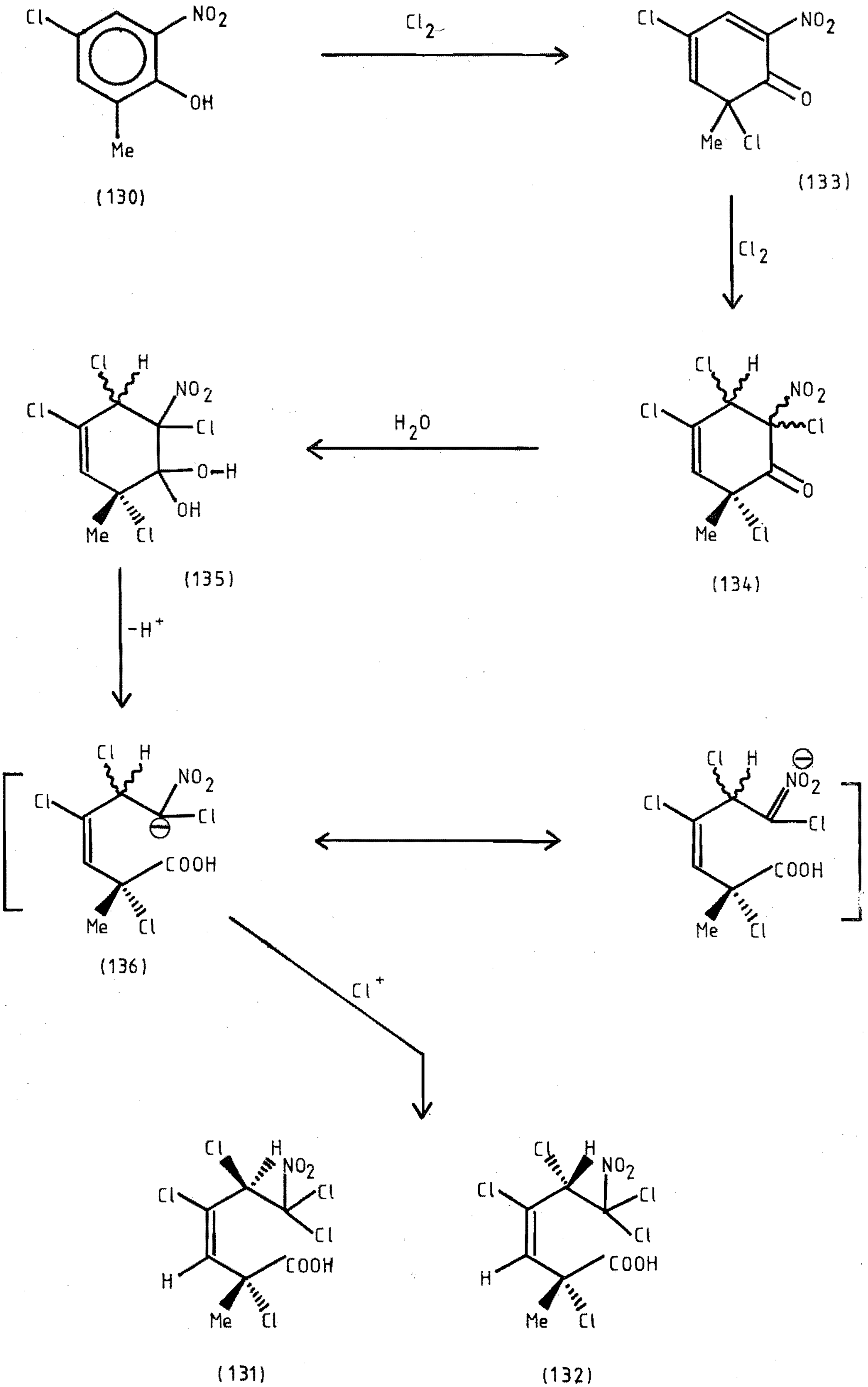


(28 & 29)



(137)

SCHEME 8



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