THE FLUORODECHLORINATION OF SOME POLYCHLOROAROMATIC COMPOUNDS

A thesis presented for the degree of
Doctor of Philosophy in the Faculty
of Science of the University of London

by

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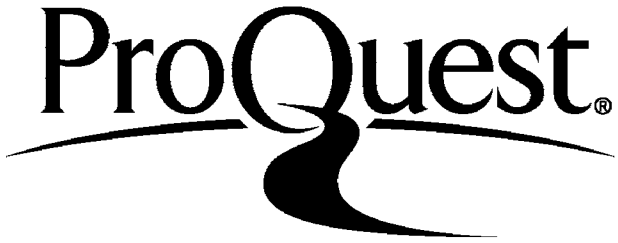

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I am also indebted to Professor G.H. Williams for offering me a place in the Chemistry Department at Bedford College, and to all the technicians in the Department for their kind assistance.

ABSTRACT

The aim of the research reported here was to investigate in detail the fluorodechlorination of some polychloroarenes in aprotic solvents. The particular interest of this work has been directed towards:

1) The identification of minor components in the reaction products, and

2) The isolation of intermediates by competitive and consecutive reactions and the use of such sequences preparatively. Attempts have also been made to bring about the displacement of other groups (Meo-, p-Me-C_6H_4-SO_2-O-) by fluoride ion in sulpholan (tetramethylene sulphone) as methods of preparing aryl fluorides. Detailed studies have been made of the reaction of potassium fluoride with hexachlorobenzene, pentachlorobenzene, fluoropentachlorobenzene, pentachlorotoluene, pentachloroanisole, pentachlorophenyl p-toluenesulphonate, fluoro-2,3,5,6-tetrachlorobenzene, 1,2,3,4-, 1,2,3,5- and 1,2,4,5-tetrachlorobenzenes, tetrachlorophthaloyl chloride, 1,3,5-trichloro-2-nitrosobenzene, 1,3-dichloro-2-nitrosobenzene and octachloronaphthalene.

CONTENTS

CHAPTER 1
INTRODUCTION

1. Theoretical Considerations

A. Bond-breaking Mechanisms

Covalent bonds may be formed and broken in two different ways. If a covalent bond forms from combination of two radicals, (species with an unpaired electron in the outer shell) the process is called a colligative process. Such a bond breaks by the reverse process, called homolysis.

$$A\cdot + B\cdot \underset{\text{homolysis}}{\overset{\text{colligation}}{\rightleftharpoons}} A : B$$

Secondly, covalent bonds may be formed by combination of ions. Such a process is called a heterolytic process and its reverse is called heterolysis.

$$A: + B \underset{\text{heterolysis}}{\overset{\text{co-ordination}}{\rightleftharpoons}} A : B$$

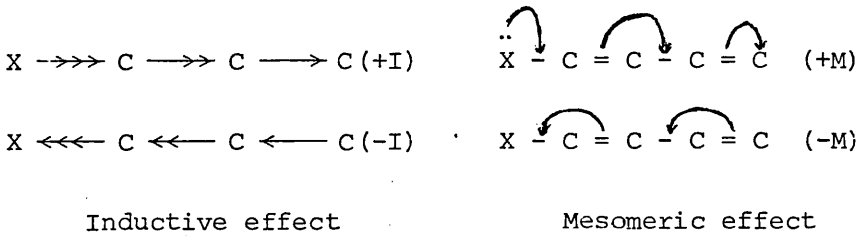
Species A: is called a nucleophile and species B is called an electrophile. Two kinds of reaction are distinguished in heterolytic process, those involving attack of a nucleophile at a site of low electron density (nucleophilic reaction) and those involving attack of an electrophile at a site of high density (electrophilic reaction).

Heterolytic processes are much more sensitive to substituent effects than are homolytic processes. Substituents may extend their electronic effect through space, or by transmission through σ-bonds or π-bonds.

B. Inductive and Mesomeric Effects

Inductive and mesomeric effects are time independent effects of electron displacement; that is, factors controlling the permanent distribution of electrons in the ground states of molecules.

The inductive effect describes the tendency for a substituent to attract or repel electrons according to its electronegativity without changing the arrangement of the electron pairs in the molecule markedly. The mesomeric effect only occurs in unsaturated molecules and describes the tendency of the substituent to extend the configuration path by rearranging the electron pairs in the unsaturated molecules. This involves either donation of electrons to the unsaturated carbon system, or acceptance of electrons from the unsaturated carbon system[1]. These effects may be transmitted through the system:



Inductive effect Mesomeric effect

C. Electronic Effects of the Halogens in Aromatic Systems

From the physical and chemical properties of the halogenated molecules it has been suggested that the halogens have a (-I) effect (electron-attracting) and a (+M) effect (electron-donating) and that these effects are greatest for fluorine and least for iodine[1].

F > Cl > Br > I (-I) F > Cl > Br > I (+M)

It has also been recognised[3] that the inductive effect could be subdivided to two effects:

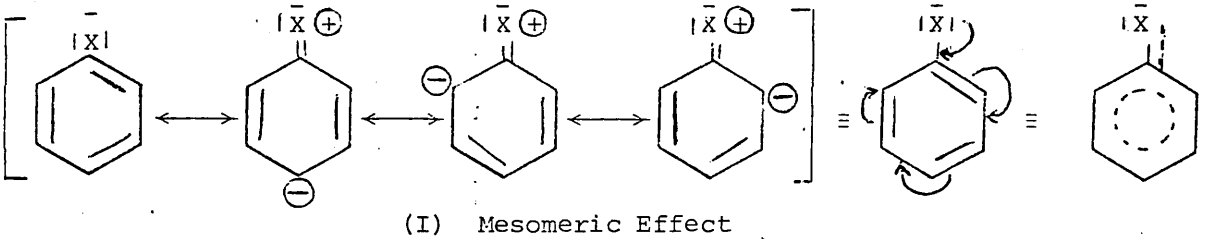
1. Polarisation effects on the σ-bond framework (I_σ).
2. Polarisation effects on the π electrons (I_π)

The classical inductive effects only involved transmission through the σ-bond framework. Transmission through a π-orbital interaction was

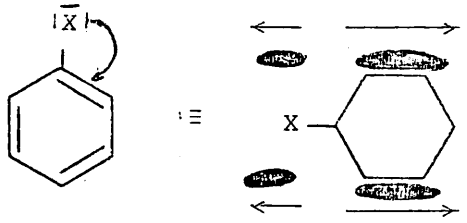
reported[3] in the spectroscopic behaviour of the halogenobenzenes, and named I_π. This name was also given to a mechanism by which the mesomeric effect may be transmitted, by chemists[4] who felt that electron-deficient halogen atoms were energetically unlikely. In the case of halogens which are substituted in an aromatic ring, it has been suggested[3] that they are σ-electron-attracting by virtue of their greater electronegativity than carbon, which arises from their tendency to complete an inert-gas structure, but are π-electron repelling (I_π repulsion) in the order:

$$F > Cl > Br > I$$

This I_π repulsion of halogens in π systems has been explained[3] as arising from the coulombic repulsion between the p-electrons of the halogens and the π-electrons of the neighbouring carbon in the ring, which could be, in fact, an alternative to the mesomeric effect, differing only in the way in which the effect is described. If we compare canonical structures (I) with structures (II) in the Figure 1, both the mesomeric structures and the structures which show the I_π repulsion, lead to similar results:



(I) Mesomeric Effect



(II) I_π Repulsion

Figure 1

In fact, the positive charge upon halogen in the canonical structures is only needed for describing the electron-donating effect of the halogen; as the mesomeric effect (+M effect) only partly reverses the inductive effect (-I effect), the total state of the halogen substituent, attached to an aromatic system, is always electron-rich compared with hydrogen.

In this thesis, the term(M)effect will be used for describing the π-electronic effect of halogens in the following sections.

2. General Properties of Fluorine

A. Fluorine Substituent Effects

Fluorine is the most electronegative element. When bonded to other atoms, fluorine polarises the bond, drawing electrons to it. The electron-attracting inductive effect of fluorine is clearly shown in acetic acid when substituted by fluorine. All fluorinated acetic acids are stronger than the corresponding chlorinated acetic acids.

$$(F_3CCOOH \quad K_a = 5.9 \times 10^{-1}, \quad Cl_3CCOOH \quad K_a = 0.20 \times 10^{-1}).^{5,6a}$$

What is surprising is the ability of fluorine to donate electrons to the benzene ring by a mesomeric effect. In fact fluorine appears significantly better than the other halogens in its ability to donate electrons through resonance (perhaps because carbon and fluorine are similar in size). The electron-donating mesomeric effects of fluorine are shown in the acidity of halogenated aroic acids and phenols in Figure 2.

Table 2 shows that all the fluorinated phenols and benzoic acids are weaker acids than the corresponding chlorinated compounds.

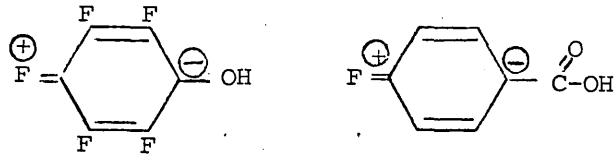


Figure 2

Table 1

Dissociation constants of some selected halogenated benzoic acids and phenols in aqueous solutions

Compound	$Ka^{25^{\circ}}$	Reference
Benzoic acid	6.46×10^{-5}	Handbook of Chemistry and Physics, 51st Ed. (1970-1971) The Chemical Rubber Co.
p-Chlorobenzoic acid	10.4×10^{-5}	Handbook of Chemistry and Physics, 51st Ed. (1970-1971) The Chemical Rubber Co.
p-Fluorobenzoic acid	7.2×10^{-5}	Dippy, Williams and Lewis, J. Chem. Soc., (1935) 343
Phenol	1.3×10^{-10}	Dippy, Williams and Lewis J. Chem. Soc., (1934) 1888
p-Chlorophenol	4.2×10^{-10}	Judson and Kilpatrick, J. Amer. Chem. Soc., 71, (1949) 3110
p-Fluorophenol	1.1×10^{-10}	Bennett, Brooks and Glasstone, J. Chem. Soc., (1935), 1821
Pentachlorophenol	5.5×10^{-6}	Birchall and Haszeldine, J. Chem. Soc., (1959), 3653
Pentafluorophenol	3.0×10^{-6}	

B. Electrophilic Substitution of Fluoroaromatic Compounds

Fluorine, when it is substituted in an aromatic ring, has ortho-para-directing power toward electrophilic substitution. The mesomeric effect of fluorine in the aromatic compounds is high compared to that of other halogens, and this may be due to poorer overlap of the 3p,4p and 5p-orbitals of the other halogens with the π-orbital of the ring. The mesomeric effect of fluorine can be represented either by overlap of the p-orbitals (Figure 3) or by resonance contributing forms (Figure 4):

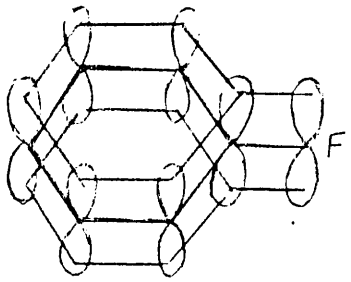


Figure 3

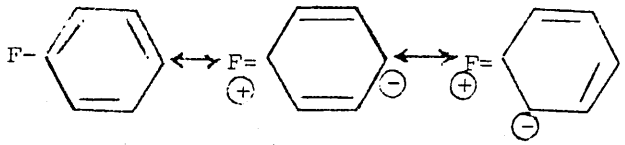


Figure 4

However, use of the resonance pictures shown above is not sufficient to explain the preference of para directivity shown by fluorobenzene over ortho attack. Table 2 shows the striking preference for para directivity of fluorobenzene relative to chloro- and bromo- benzenes. The reason could be explained[6b] by comparing the C-F with other C-Hal bonds. The shortness of the C-F bond and the similar size of the 2p orbitals of fluorine and the π orbitals of the ring lead to a maximum p-π interaction, but because of the short C-F bonds the powerful inductive effect of fluorine is felt most strongly at the ortho-position and becomes much smaller in the para-position. As the result, the increase of electron density by resonance can effectively cancel the small inductive effect at the para-position, but is not large enough to overcome the larger inductive effect at the ortho-position. Figure 5 shows the patterns of electron flow in the σ and π framework in fluorobenzene.

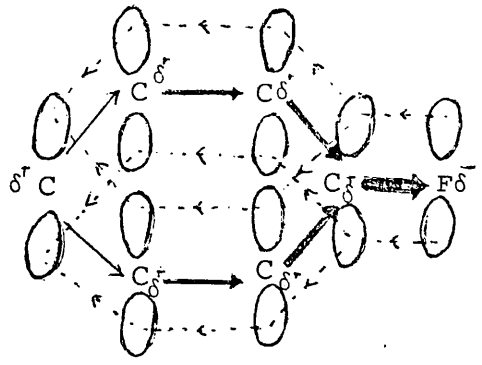


Figure 5

So the positive charge never remains on fluorine (as represented in Figure 4); the great electronegativity of fluorine permits it to withdraw electrons from the σ framework but, by interaction with the π-electrons of the ring this charge is partly fed back to the ring and provides

Table 2

Directive effects in selected electrophilic substitition reactions on halogenobenzenes[a]

Type of Substitution	k_A/k_B (b) PhF	PhCl	PhBr	% Isomer Distribution and Partial Rate Factors (f) Fluorobenzene (PhF) ortho-	meta-	para-	Chlorobenzene (PhCl) ortho-	meta-	para-	Bromobenzene (PhBr) ortho-	meta-	para-
Bromination[c]												
Br_2, $AlBr_3$ in CS_2 at 54-57°C	-	-	-	10.7	0.2	89.1	10.7	0.1	89.2	13.4	0.1	86.5
Chlorination												
Cl_2, HOAc-H_2O 25°C	0.1	0.1	0.072	10.9	-	89.1	32.4	-	67.6	38.6	-	61.4
				f = 0.03	-	0.54	0.1	-	0.41	0.08	-	0.27
Benzylation												
$C_6H_5CH_2Cl$, $AlCl_3$, $MeNO_2$ 25°C	0.46	0.24	0.18	14.7	0.2	85.1	33	0.6	66.4	32.5	0.7	66.8
				f = 0.20	0.0028	2.35	0.24	0.0043	0.96	0.18	0.0038	0.72
Nitration												
NO_2BF_4 $C_4H_8SO_2$ 25°	0.45	0.14	0.12	8.5	-	91.5	22.1	0.7	76.6	25.7	1.1	73.2
				f = 0.11	-	2.47	0.09	0.0029	0.64	0.095	0.0040	0.53

(a) L.M. Stock and H.C. Brown, Advances in Physical Organic Chemistry, Vol. I, (1963), 74-76

(b) Rate of the reaction of halogenbenzene relative to benzene

(c) L.N. Ferguson, A.Y. Gernerand and J.L. Mack, J. Amer. Chem. Soc., 76, (1954), 1250

a "high" electron density at the para-position suitable for attack of an electrophile (Figure 6):

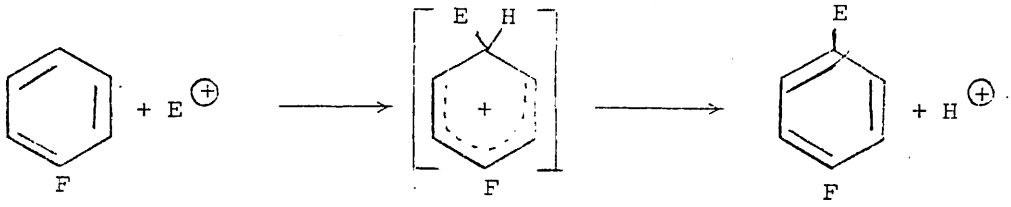


Figure 6

The corresponding effects in nucleophilic substitution will be considered later (page 27ff).

C. Bond Strength

As fluorine replaces hydrogen the C-X bond shortens and simultaneously the bond strength increases. It has been found that the bonds formed by fluorine are among the strongest known, especially to carbon (ionic attraction in C-F bond). Table 3 shows a comparison of the bond strength of fluorine and some other elements when bonded to carbon or hydrogen.

Table 3

Bond strengths of some single bonds[a]

Bond	E. Kcal
C-F	106
C-Cl	81
C-Br	68
C-I	57
C-H	98.7
C-O	85.5
C-N	72.8
C-S	65
HF	135
HCl	103.1
HBr	86.5

(a) T.L. Cottrell, The Strengths of Chemical Bonds, 2nd Ed., Butterworths Scientific Publications, London (1958)

D. Hydrogen Bonding of Fluoride Ion

Because of its small size, fluoride ion has a volume charge density (charge per unit volume) larger than other halide ions and therefore, fluoride ion will more strongly affect dipolar centres of positive charge. As a result it forms stronger hydrogen bonds than other ions do. The strong ability of fluoride ion to form hydrogen bonds is clearly shown in hydrofluoric acid which exists as a polymer $(HF)_n$. This strong tendency to hydrogen bonding is also found where fluorine is covalently bonded to carbon but still has a high electrodensity. Thus on comparing the boiling points of methane and mono-, di-, tri- and tetra-fluoromethanes, the maximum boiling point for the fluorinated methanes occurs for difluoromethane (Table 4), while the chlorinated and the brominated series have the expected continuous rise in boiling points with increasing number of halogen substituents.

Table 4

Boiling points of methane and halogenated methanes

Compounds	b.p. °C (760 mmHg)			
	X = Hydrogen	Fluorine	Chlorine	Bromine
CH_4	-164			
CH_3X		-78.4	-24.2	3.56
CH_2X_2		-51.6	40	97
CHX_3		-82.2	61.70	149.5
CX_4		-129 (a)	76.54	189 - 190

(a) b.p. at 754 mmHg

This increased boiling point in difluoromethane could be due to intermolecular hydrogen bonding in this compound[66].

E. Heat of Hydration of Fluoride Ion

Fluoride ion is tightly bonded by water molecules, when it dissolves in aqueous solvents; as a result the heat of hydration of fluorinated compounds, compared to other correspondingly halogenated compounds, is high. When fluoride ion is dissolved in water five molecules of water are tightly bonded to it while in solvation of chloride three, and bromide two molecules of water are bonded to halogen ions[7]. So fluoride ion compared to other halide ions is a poor nucleophile in a solvent system containing water. (The order of nucleophilic strength of halide ions in aqueous solution is $\bar{I} \sim B\bar{r} > C\bar{l} > \bar{F}$)[8].

3. Nucleophilic Aromatic Substitutions

A. Mechanism

Active research on the nucleophilic aromatic substitition was started about 1950 and three satisfactory mechanisms for these reactions have been found:

Unimolecular (SN_1), bimolecular (SN_2) and elimination-addition (benzyne) mechanisms.

(a) Unimolecular Mechanism

Although the SN_1 mechanism occurs in aliphatic nucleophilic substitutions, it is rare in aromatic systems and is only well established for thermal decomposition of diazonium cations in aqueous solutions.

$$C_6H_5\text{-}N{\equiv}N^{\oplus} \xrightarrow{\text{slow}} C_6H_5^{\oplus} + N{\equiv}N$$

$$C_6H_5^{\oplus} + \bar{X} \xrightarrow{\text{fast}} C_6H_5X$$

The aryl cation formed in this reaction combines with water, halide ions, alcohols and other nucleophilic reagents which might be present, to form phenols, aryl halides, ethers etc. It has been found[9] that diazonium

ion decomposition is a first order reaction, and the effects of substituents on the rate of reaction also support the SN_1 mechanism of these reactions[10]. Electron-releasing groups in the meta-positions accelerate the reaction and electron-attracting groups in all the positions hinder the reaction (Table 5)[11a].

Table 5

Rates of decomposition of aryldiazonium salts in aqueous solution at 28.8°C

Substituent	10^7 k (sec^{-1}) for position shown[(a)]		
	ortho-	meta-	para-
OH	6.8 (0.0092)	9100 (12)	0.93 (0.0013)
OMe	-	3400 (4.6)	0.11 (0.00015)
Ph	1100 (1.5)	1700 (2.3)	37 (0.050)
Me	3700 (5.0)	3400 (4.6)	91 (0.12)
H	740 (1)	740 (1)	740 (1)
COOH	140 (0.19)	410 (0.55)	91 (0.12)
SO_3^{2-}	91 (0.12)	150 (0.21)	41 (0.057)
Cl	0.14 (0.00019)	31 (0.042)	1.4 (0.0019)
NO_2	0.37 (0.00050)	0.69 (0.00093)	3.1 (0.0042)

(a) Values in parentheses are relative to H = 1

What is surprising in aryldiazonium ion reactions is that electron-releasing groups in para-positions inhibit the decomposition of the diazonium cations (Table 5). It has been suggested[11a] that these groups (-OH, -OMe, -Me and -Ph) increase the double bond character of the C-N bond by their(+M)effect and therefore strengthen the bond which must be broken in decomposition (Figure 7).

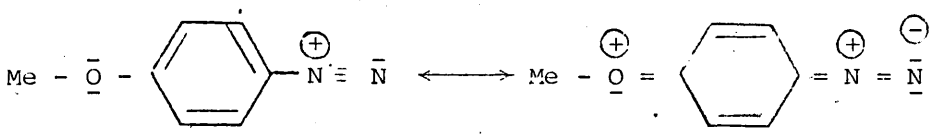
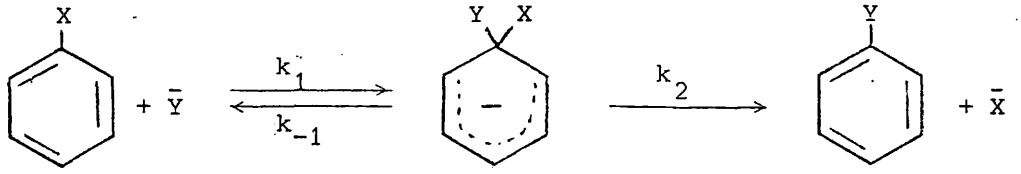


Figure 7. Canonical structures representing para-methoxybenzenediazonium ions.

(b) Bimolecular Mechanism

The great majority of aromatic nucleophilic substitutions occur by a bimolecular mechanism. The following equation represents this reaction:



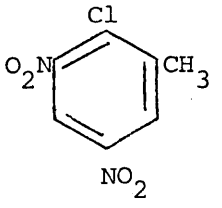
(III)

It has been found that either the first or the second step of the equation might be rate-determining, depending on the relative magnitudes of k_2 and k_{-1}. So if $k_2 >> k_{-1}$, which means X is expelled from the intermediate complex(III) much faster than Y, the rate of the first step would be the rate of overall reaction (the same statement is true when $k_1 >> k_2$), but, if $k_{-1} >> k_2$ the rate would depend on the equilibrium concentration of the intermediate complex(III) and on k_2. The ~~one~~ two step SN_2-like mechanism has been observed in the reaction of 1-halogeno-2,4-dinitrobenzenes with N-methylaniline. It has also been supported by Bunnett and co-workers[13,14], who found that in the reaction of 1-substituted-2,4 -dinitrobenzenes with piperidine in methanol, the rate of displacement of Cl, Br, I, Ph-$\overset{\overset{O}{\|}}{S}$, Ph-$\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}$-S and p-$NO_2$-$C_6H_4$-O- are nearly the same, although bonds like C-S, C-I and C-O usually undergo heterolysis at quite different rates, so the rate determining step in

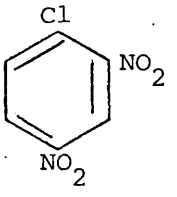
each reaction seems to be the rate of formation of the intermediate complex. In the reaction of 1-halogeno-2,4-dinitrobenzenes with a number of nucleophiles in methanol or ethanol, the order of reactivity being F >> Cl > Br > I[11b] is again another support that the bond-breaking is not the rate determining step and the rate determining step is the formation of intermediate complex (III).

(i) Primary and Secondary Steric Effect in Bimolecular Nucleophilic Substitutions

The presence of bulky ortho-substituents like alkyl groups near the seat of reaction retards the reaction by primary steric effects, e.g. replacement of chlorine in a compound like (IV) with aniline or piperidine has been found to be much slower than the reaction of the same nucleophiles with 2,4-dinitrochlorobenzene (V):

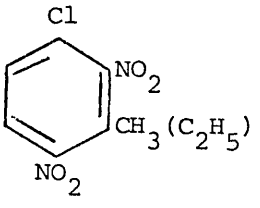


(IV)

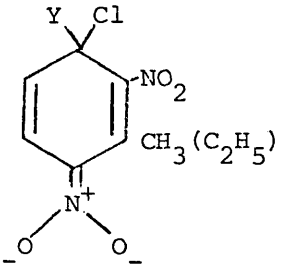


(V)

It is clear that the effect is much more marked with bulkier reagents. Secondary steric effects have been shown[15] in compounds like (VI) where the bulky methyl or ethyl groups are meta to the seat of substitution but ortho to the activating nitro groups.

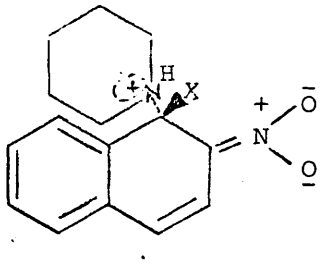


(VI)

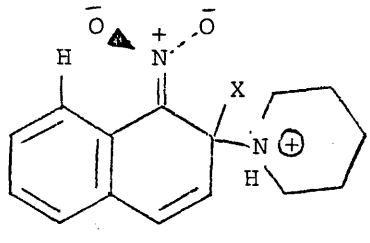


(VII)

In a transition state where the activation by nitro groups involves the coplanarity of the benzene ring with these groups (VII), the presence of a bulky group ortho to the nitro groups disturb this coplanarity of the ring and the activating groups and so affects the degree of mesomeric interaction between them. Primary and secondary steric effects have been observed in nucleophilic subsitution of halogenonaphthalenes. Because of the steric hindrance at α-position, the β-position is generally more reactive towards nucleophilic substitutions[16], but in some cases such as when there is an activating group like a nitro-group in the ortho position, the reactivity of the halogen at α-position is more than that at the β-position[16]. A possible explanation for this has been suggested to be differences in the reaction mechanism of the processes. The reaction of the halogenonaphthalenes has been said to occur in one step (SN_2-like displacement) whereas the reaction of the halogeno-nitronaphthalenes occur in two steps with formation of an intermediate such as(VIIIa):



(VIIIa)



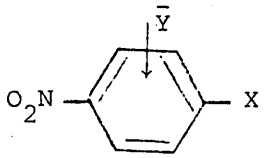
(VIIIb)

Formation of this intermediate needs coplanarity of the nitro-group and the ring,which is not possible for nitro-groups at the α-position (VIIIb).

(ii) Charge-Transfer Complexes

Charge-transfer complexes or π-complexes have been believed to be present in certain activated reactions, such as nitro-activated substitution.

By definition a charge-transfer complex is the result of an electrostatic interaction between the reagent and substrate (IX).



(IX)

The energy profile of the complete reaction could be represented as in Figure 8 if breaking the C-X bond is kinetically important.

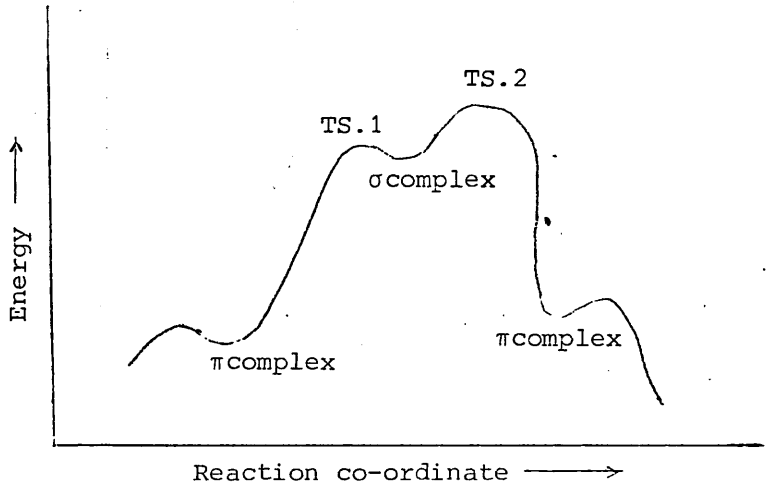
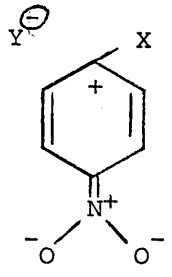
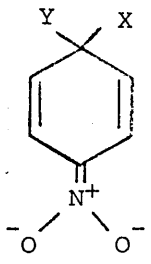


Figure 8

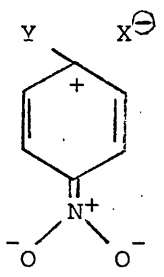
So, for a substitution reaction, activated by a p-nitro substituent, the intermediate σ-complex could be represented as structure (XI) with the two associated possible transition states (X) and (XII):



(X)



(XI)

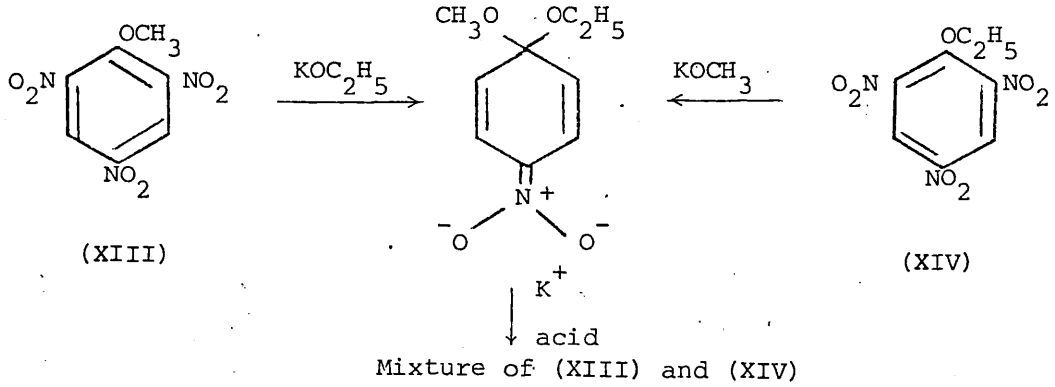


(XII)

Whether general formation of charge-transfer complexes necessarily precedes the formation of covalent intermediate complexes is not clearly known. The presence of charge-transfer complexes has been shown in a number of reactions such as the reaction of 1-chloro-2,4-dinitrobenzene[17] with aniline, of 2,4,6-trinitroanisole with ethoxide ion[18], and of N-methylpyridinium ion with iodide ion[19].

(iii) Isolable Intermediate Complexes

When there is sufficient activation, the intermediate complex like (XI) can actually be isolated. For the first time in 1902 Meisenheimer[20] showed that in the reaction of 2,4,6-trinitroanisole with potassium ethoxide and 2,4,6-trinitrophenetole with potassium methoxide, the adduct for the two processes is the same and on treatment with acid gave the same mixture of 2,4,6-trinitroanisole (XIII) and 2,4,6-trinitrophenetole (XIV).

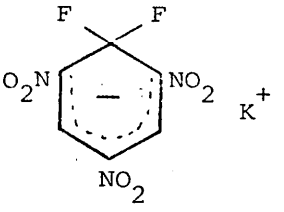


(XIII) (XIV)

Mixture of (XIII) and (XIV)

The presence of stable addition products from poly-nitroaromatic compounds such as 1,3,5-trinitrobenzene and 2,4,6-trinitroanisole, when reacted with potassium methoxide, has been established by ^{1}H n.m.r. spectra[21]. Many other stable intermediates (Meisenheimer-type complexes) have been isolated during the reaction of polynitroaromatic compounds

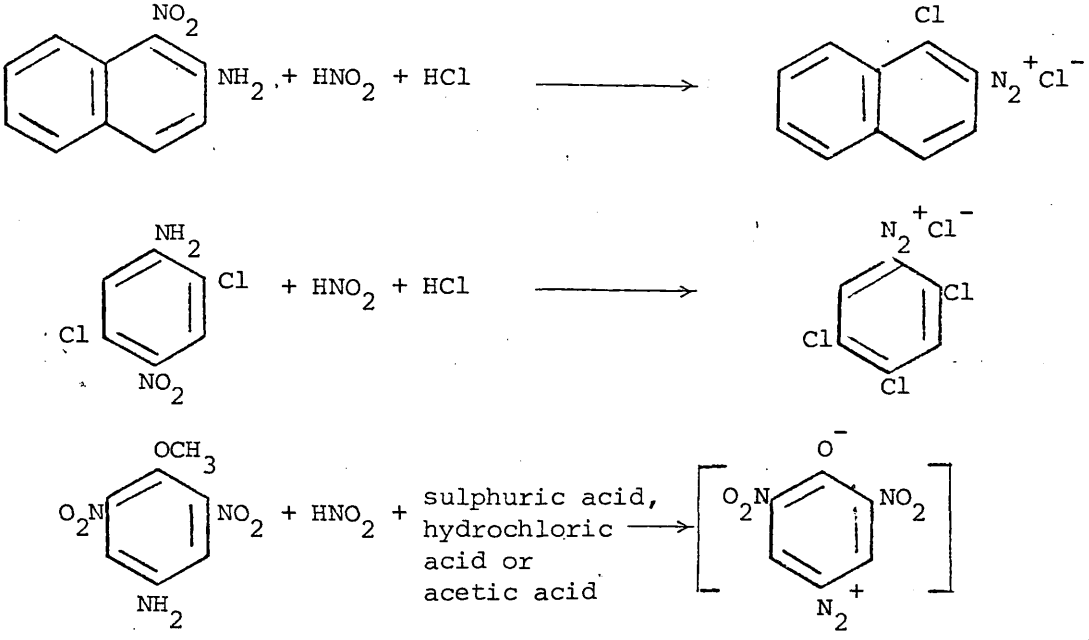
with numbers of nucleophiles[22,23,24]. One example of the kind of stable complexes which has recently been isolated[25] is (XV), which has been reported to be stable at room temperature in the absence of water or hydroxylic solvent.



(XV)

(iv) Reactivity in Bimolecular Displacements

The displacement reaction is facilitated by electron-attracting and retarded by electron-releasing substituents. Diazo groups are known to be the most activating groups, since during the diazotation of ortho or para-nitro, methoxy, or halogeno anilines, the groups at ortho or para positions may undergo displacement by hydroxyl groups (owing to reaction with water) or by chlorine (if hydrochloric acid is used).



The nitro group is another strong activating group which is stable under the basic conditions of most common nucleophilic substitution reactions. The nitro group strongly activates sites ortho and para to it in such reactions. The meta-position is also activated but less than ortho and para so that reaction of meta-fluoronitrobenzene with sodium methoxide requires more vigorous conditions than those of ortho and para-fluoronitrobenzene.

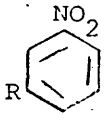
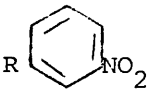
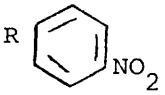
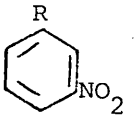
Fluoronitrobenzene	k l sec^{-1} $mole^{-1}$ at 49.5° [29]
ortho-	1.6×10^{-3}
para-	2.37×10^{-3}
meta-	1.59×10^{-7}

The relative extents of ortho and para activation by the nitro group in 2,4-dihalogeno-nitrobenzenes have been studied[30] with many nucleophilic reagents and ortho-halogen has been reported to be preferentially displaced, although in the reactions of ortho- and para-fluoro- and chloro-nitrobenzenes with piperidine the relative rates ($\frac{ortho}{para}$) have been reported to be close to unity[31]. The nitro group itself is displaced by many nucleophiles, one of the examples being the reaction of 1,3,5-trinitrobenzene with sodium methoxide to give 3,5-dinitroanisole which is a preparative method[32]. In 2,3,5,6-tetrachloro- and pentachloro-nitrobenzenes, displacement of the nitro group occurs along with that of chlorine in methoxide ion attack[38], and in the reaction with potassium fluoride in dimethyl-formamide[46] or in sulpholan[33], displacement of the nitro group have been observed.

Halogens are another set of groups which activate all sites, but chiefly the meta- positions. Thus, the rate constants for the reaction of meta-, ortho- and para-dichlorobenzenes with sodium methoxide in methanol at 175 - 176°C are 8.4×10^{-4}, 6.4×10^{-4}, and 1.9×10^{-4} l mole^{-1} min^{-1} respectively[34a]. The activating effect of chlorine groups ortho-, meta- and para- to the site of substitution in many chloronitrobenzenes has been examined[34b] by comparing the rates of the reaction of these compounds with sodium methoxide (Table 6).

Table 6

The activation effect of chlorine A) ortho-, B) meta- and C) para- to the site of reaction

Reaction with sodium methoxide in methanol at 85°C.	 (Cl)	 (Cl)	 (Cl)	 (Cl)
$k_{H\ (R=H)}$	0.231×10^{-1}	0.062×10^{-1}	0.062×10^{-1}	0.062×10^{-1}
k_{Cl} (R=Cl)	2.9×10^{-1}	0.30×10^{-1} (a)	3.3×10^{-1}	0.65×10^{-1}
k_{Cl}/k_{H}	12.5 A	4.8 A	53 B	10.48 C

(a) Steric hindrance between the site of reaction and two bulky groups affected on the rate of reaction.

k_H = rate coefficient when R=H

k_{Cl} = rate coefficient when R=Cl

Miller has predicted[35a] the same order of reactivity for the other halogens; some of his results are listed in Table 7.

Table 7

Reaction of 1-chloro-2-NO_2-4-and-5-X-benzenes with piperidine in benzene at 45°C

Substituent	k (l $mole^{-1}$ sec^{-1})	f_p/f_m
4- and 5-H	3.63×10^{-6}	1
4-Cl	2.29×10^{-5}	0.192
5-Cl	1.17×10^{-4}	
4-Br	3.49×10^{-5}	0.278
5-Br	1.25×10^{-4}	
4-I	4.41×10^{-5}	0.485
5-I	9.07×10^{-5}	

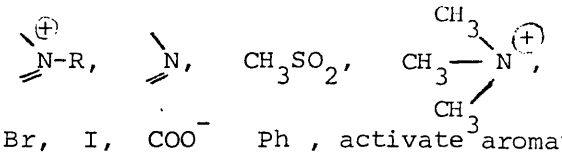
The activation power of the fluorine *para* to the site of reaction in nucleophilic substitution compared to the other halogens, is unexpectedly low (Table 8). In fact fluorine, when it is substituted *para* to the site of reaction, is deactivating compared to hydrogen (Table 9).

Table 8[34c]

Reaction of 4-substituted-2-nitrobromobenzenes with an excess of piperidine as reagent and solvent

Group in 4-position	k (min^{-1}, 25°C)
Br	2.27×10^{-2}
Cl	1.62×10^{-2}
I	1.57×10^{-2}
F	7.55×10^{-4}

Many other activating groups, such as:



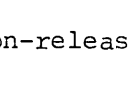
Cl , Br, I, COO^- Ph , activate aromatic nucleophilic substitution[31d]. In contrast, electron-releasing groups like NH_2, OH,  , OCH_3, OC_2H_5, and CH_3 have been shown generally to deactivate the sites of substitution, especially when para to them. The deactivation power of these groups can be shown by the comparison of the rates of reactions of 1-bromo-2-nitro-4-X-benzenes with that of o-nitrobromobenzene (X = H) (Table 9).

Table 9[35b]

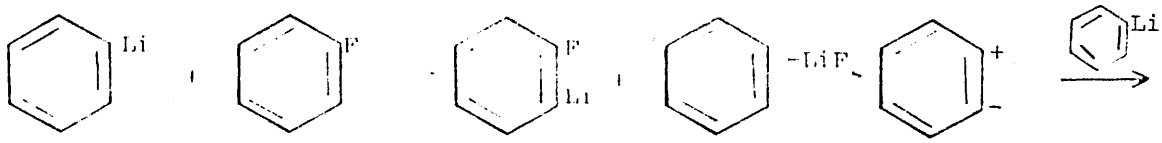
Rates of reaction of 1-bromo-2-nitro-4-X-benzenes with an excess of piperidine (as reagent and solvent) at 25 °C.

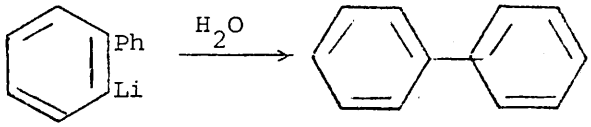
Substituent (4-X)	k (l $mole^{-1}$ sec^{-1})
H	4.83×10^{-5}
NH_2	6.0×10^{-9}
$N(CH_3)_2$	5.87×10^{-8}
OH[(a)]	2.82×10^{-8}
OCH_3	8.70×10^{-7}
OC_2H_5	7.30×10^{-7}
F	1.26×10^{-5}
Cl	2.70×10^{-4}
Br	3.79×10^{-4}
I	2.62×10^{-4}

(a) Because of partial neutralisation -OH group appears to be more deactivating than it really is.

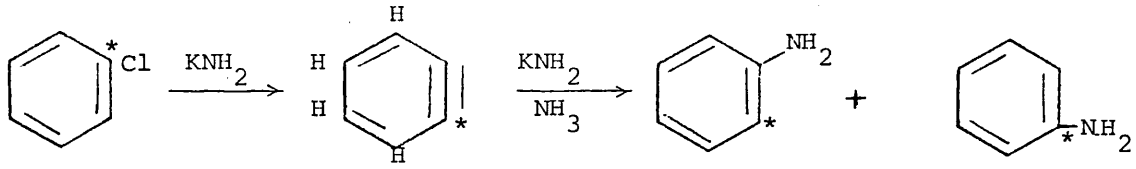
β. The Elimination-Addition (Benzyne) Mechanism

In 1940 Wittig et.al. showed that the reaction of phenyl-lithium with fluorobenzene, to form diphenyl, proceeds via an unusual intermediate.



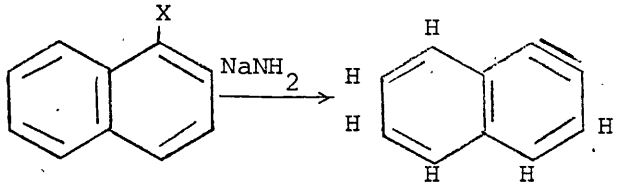


Later on, in the reaction of chlorobenzene with potassium amide in liquid ammonia, Roberts et.al.[36] showed that (1-C^{14}) chlorobenzene gives equal amounts of (1-C^{14}) aniline and (2-C^{14}) aniline when treated with potassium amide in liquid ammonia, and so they suggested the formation of a benzyne intermediate (XVI) in this reaction:

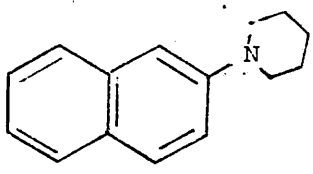


(XVI)

This type of intermediate has been supported by further work on this type of reaction. For example, the formation of an aryne (naphthalyne) intermediate has been observed in the isolation of the two products, α- and β-naphthyl piperidine, from treating α-chloro-,-bromo-, or iodo-napthalene with piperidine and sodium amide[37].



and



Since benzyne mechanisms require the removal of HX from halogenobenzenes, such processes can only occur in the presence of strong base, and where there is at least one ortho-hydrogen atom, but the presence of strong base and an ortho-hydrogen atom in the molecule does not ensure the benzyne mechanism. For example, in the above process where X is fluorine it has been shown[37] that the process involves two mechanisms, both direct SN_2 displacement reaction and a napthalyne mechanism.

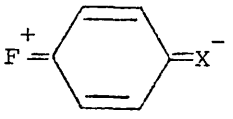
C. Solvation

Solvation, which is the specific interaction between solvent molecules and ions, can affect nucleophilic reactivity. As has been mentioned before (page 17), the order of reactivity of halide ions in water is $I^- \sim Br^- > Cl^- > F^-$. This order seems to be the same in most hydrogen-bonding solvents, but in dipolar aprotic solvents[38] (which may contain hydrogen but cannot donate suitably labile hydrogen atoms to form strong hydrogen bonds with halide ions) the order of reactivity follows the order of increasing bond strength of halogens with carbon atom and is $F^- > Cl^- > Br^- \sim I^-$.[39] The effect of solvation in aromatic nucleophilic substitutions has been shown by Miller and Parker[39]. They reported that such reactions are much faster (10^4-10^5) in dipolar aprotic solvents e.g. N-methylformamide, N,N-dimethylformamide (DMF), N,N-dimethylacetamide (DMAC), tetramethylenesulphone (sulpholan), acetonitrile, benzonitrile, nitromethane, nitrobenzene, acetone and dimethyl sulphoxide (DMSO) than in protic solvents.

4. Aromatic Bimolecular Nucleophilic Substitution in Polyhalogeno Systems

A. Polyfluoroaromatic Systems

Polyhalogenoaromatic compounds undergo nucleophilic substitutions whereas the hydrocarbon analogues undergo mostly electrophilic substitutions. Comparing polyfluoro compounds with other analogous halogeno compounds, the highly electronegative fluorine atom strongly withdraws electrons from the σ framework, but the six unshared electrons in the 2p-orbitals of every fluorine atom interact with the π electrons of aromatic ring more effectively than other halogens, because of the C-F short bond distance and the similar sizes of the overlapping p-orbitals. As a result, the π system appears to have a higher than normal density of electrons so it could interact with an electron-deficient substituent which might be present in the ring:

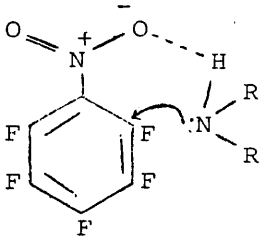


Nucleophilic replacement of a large number of polyfluoroaromatic compounds of the type C_6F_5X are known[35c,40,41]. In most cases where X=H, CH_3, SCH_3, CF_3, $N(CH_3)_2$ and SO_2CH_3, the fluorine *para* to X is the main one replaced but in a few cases (X = NH_2, O^- and S^-) *meta* replacement predominates[35c,42]. It has been suggested that[42,43] activation by four fluorine atoms direct the nucleophile to the para position to X, and X itself may either enhance the effect or oppose it. For example, in the reaction of pentafluoronitrobenzene with amines such as NH_3, NH_2CH_3 and $NH(CH_3)_2$ a high percentage of *ortho*-replacement has been observed for reaction of NH_3 and NH_2-CH_3 but not $NH(CH_3)_2$. The reasons have been

suggested[40] to be:

(i) Hydrogen bonding between amine and nitro-group of the ring which facilitates the replacement at ortho position;

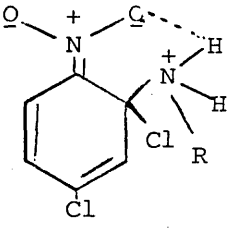
(ii) Steric hindrance between large groups such as $NH(CH_3)_2$ and $-NO_2$ resists the formation of a suitably hydrogen-bonded intermediate (XVII):



(R = H or CH_3)

(XVII)

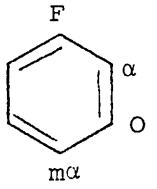
This hydrogen-bonding between amine and nitro-group has also been observed in the reaction of ortho- and para-chloronitrobenzene with piperidine[44] (ortho-chloronitrobenzene reacts faster than its para isomer), and also in the 2,4-dihalogenonitrobenzenes[45] (XVIII) when reacted with different nucleophiles, e.g. 2,4-dichloronitrobenzene reacts with methoxide or ethoxide ion mostly at the para-position relative to nitro-group, but with NH_3 or NH_2-R reacts mainly at the ortho-position relative to nitro-group.



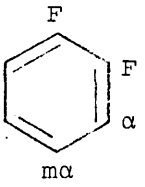
(XVIII)

The nucleophilic attack in C_6F_5X compounds like pentafluorobenzene and chloropentafluorobenzene has been explained[46] by referring to the (-I) and (+M) effects of the fluorine, as mentioned before (page 13) for electrophilic substitution, the (-I) effect of the fluorine atom is partly neutralised by (+M) effect, acting especially at positions ortho- and para to fluorine, so positions meta- to fluorine have the lowest electron density and are therefore most active in nucleophilic attack.

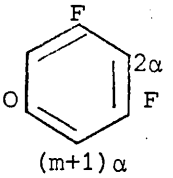
If we show the relative activations of ortho-, meta- and para- sites as α, zero and mα in the electrophilic attack[46] in fluorobenzene (Figure 9) (XIX), the relative activation in ortho- and meta-difluorobenzene may



(XIX)



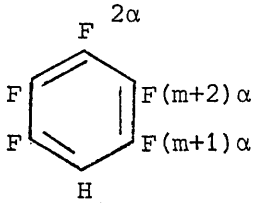
(XX)



(XXI)

Figure 9

be represented as in (XX) and (XXI) where $m > 1$ (preferential attack at para-position). This allows the application of these terms in predicting the orientation of such reactions in nucleophilic attack. Comparing pentachlorobenzene with pentafluorobenzene and using a parameter, β, for chlorine the displacement of each halogen in the C_6Hal_5-H system is aided by the (-I) effect of four other halogens or by (-4I), but deactivated by the (+M) effect of the halogens ortho- and para- to it. Therefore an orientation of attack at positions para > ortho > meta relative to hydrogen could be predicted for both pentafluoro and pentachlorobenzenes (Figure 10).



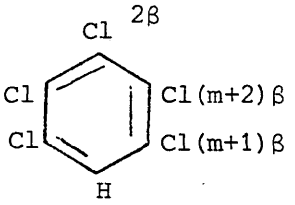


Figure 10

α is greater than β because the (+M) effect of fluorine is more than that of chlorine. The reactions of pentahalogenobenzenes with a variety of reagents also show that hydrogen in C_6Hal_5-H system is more than 90%.para directing[47] relative to the hydrogen substituent. Steric effects are of considerably more significance in the chloro-compounds than in the fluoro-corresponding systems. Russian workers[48] have shown that pentachlorobenzene reacts mainly at the position para to the hydrogen with ammonia, but mainly at the position ortho with the larger groups like dimethylamine. In contrast, pentafluorobenzene gives > 90% para isomer with both the nucleophiles.

B. Polyfluoronaphthalenes

In general naphthyl halides are more susceptable to nucleophilic substitutions than phenyl halides with the similar activating groups[49]. (This could be explained as arising from the second ring). The reaction of octafluoronaphthalene with a number of nucleophiles has been reported[50] to take place at the β-position, with a second nuclephile attack C-6. This orientation of attack has been explained by reference to the transmission of an I_π effect across the naphthalene system[51]. Recent work[52] on 2-X-heptafluoronaphthalenes (X = H, F, Cl, OCH_3 and C_6H_5) involving displacement mainly at C-6 gives support for the previous results, although it offers an alternative mechanism for the transmission of electronic effects across the system.

5. General Survey of Replacement of Chlorine by Fluorine in Polychloroaromatic Compounds

The replacement of chlorine by fluorine in aryl halides began[53] with the reaction of 2,4-dinitrochlorobenzene with potassium fluoride in nitrobenzene at 200°C. Fluoro-2,4-dinitrobenzene has been obtained from

this reaction (30% yield); by changing the solvent to dimethylformamide (DMF) or dimethyl sulphoxide (DMSO) better yields (70-80%) were obtained at somewhat lower temperatures[54]. Replacement of chlorine by fluorine in other activated chlorobenzenes, such as 2,4,6-trichloronitrobenzene, 2,3,4-trichloronitrobenzene and 2,4-dichloronitrobenzene, and also the replacement of a nitro group by fluorine in pentachloro- and 2,3,5,6-tetrachloronitrobenzene and in 2,3,5,6-tetrachloro-1,4-dinitrobenzene has been reported[54] using potassium fluoride in DMF or DMSO. As a result many fluoroaromatic compounds have been prepared by this route. In 1957 Finger et.al. prepared[55] sym-trichlorotrifluorobenzene from hexachlorobenzene with potassium fluoride in DMF and DMSO. Maynard reported[56] the preparation of sym-trichlorotrifluorobenzene by the same method, but changed the solvent to N-methyl-2-pyrollidone.

In 1960, by using the less reactive fluorinating reagents, sodium fluoride, in sulpholan some reactive aryl chlorides, such as cyanuric chloride, were converted to the fluorides[57]. Reaction of polychloropyridines with potassium fluoride in dimethyl sulphone (DMS) has been used for the preparation of 3,5-dichloro-2-fluoropyridine from 2,3,5-trichloropyridine, and 3,5-dichloro-2,6-difluoropyridine from 2,3,5,6-tetrachloropyridine[58]. Russian workers have prepared a number of polyfluoroaromatic compounds by the reaction of the corresponding chlorides with potassium fluoride in an autoclave. They treated hexachlorobenzene[59] and octachloronaphthalene[94] with potassium fluoride at 450 - 500° and 300 - 330° respectively, under such conditions and obtained hexafluorobenzene (21% yield), together with pentafluorochlorobenzene (20%), tetrafluorodichlorobenzene (14%), and sym-trifluorotrichlorobenzene (12%) from hexachlorobenzene. The latter reaction gave octafluoronaphthalene(24%) and a mixture of heptafluoro-naphthalenes (8% yield) which, after reduction with hydrogen over palladium, gave a mixture of 1-H-heptafluoronaphthalene (30%) and 2-H-isomer (70%).

Tetrachlorophthalic anhydride has been treated[60] with potassium fluoride in DMF and gave octafluoroanthraquinone (2% yield) after five hours boiling. A similar reaction at 300°C in the absence of solvent has been reported to give octafluoroanthraquinone (40% yield) after two hours reaction. Tetrachloroterephthaloyl chloride and also tetrachlorophthaloyl chloride have been converted[61,62b] to the corresponding polyfluorophthaloyl fluorides, by using cesium or potassium fluoride without solvent. The reaction of potassium fluoride in tetramethylene sulphone (sulpholan) has been used[63] for the preparation of some polyfluoroaromatic compounds. Polyfluoropolychlorobenzenes were obtained from hexachlorobenzene; octafluorotoluene (2%), 3-chloro-heptafluorotoluene (41%), and 3,5-dichlorohexafluorotoluene (4%), from octachlorotoluene; and octafluoronaphthalene from octachloronaphthalene. Many reactions of hexachlorobenzene have been reported in the patent literature[64]. The preparation of 2,4,6-trifluorodichloropyridine[65] from pentachloropyridine by using potassium fluoride in sulpholan at 190 - 210°C, and also the preparation of many other highly fluorinated compounds such as perfluoroquinoline[65], and perfluoroquinoxaline[67] from the corresponding polychloro-heterocyclic compounds by potassium fluoride in the absence of solvent have been reported by Chambers et.al. Potassium fluoride alone has been reported[68] to react with pentachlorobenzonitrile at 300 - 480°C to give three main products 3,5-dichloro-2,4,6-trifluoro-, 3-chloro-2,4,5,6-tetrafluoro-, and pentafluorobenzonitriles. Recent work on pentachlorobenzene has been reported by Finger et.al[69]. In the presence of potassium fluoride in DMSO at 180°C for 24 hours, pentachlorobenzene was reported to give a mixture of mono-, di-, and tri-fluoro-isomers.

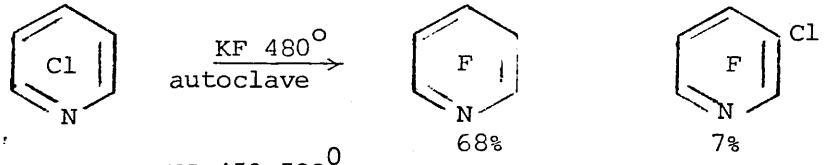
Another study of this system in sulpholan has been reported by Bechtold and Tullock[70]. They obtained a mixture of isomers of difluorotrichlorobenzene, mostly containing 1,3-difluoro-2,4,5-trichlorobenzene. Reaction of tri- and tetra-chlorobenzenes with potassium fluoride, or with a mixture of cesium and potassium fluoride in dimethyl sulphoxide and dimethyl sulphone has been reported to give a mixture of mono-,di- and tri-fluoro compounds[71].

Dimethyl sulphone has been reported to be a better solvent than dimethyl sulphoxide for these reactions; mono-, di-, tri- and tetra-fluoro compounds of these reactions have been identified by ^{19}F n.m.r. and gas chromatography spectroscopy. Recently hexachlorobenzene and pentachloropyridine have been treated with a molten KF-KCl mixture at 630 - 740°C by French workers who obtained a mixture of the di-, tri, tetra-, and penta-fluoro compounds, with a trace of hexafluorobenzene in the case of the former substrate.

6. Reaction of Fluoride Ion with Halogeno-Compounds.

Potassium fluoride, compared to other alkali metal fluorides is the most suitable fluorinating agent[54]. Cesium and rubidium fluorides appear to be more reactive than potassium fluoride, but they are expensive; sodium and lithium fluoride are not very reactive, probably because of their low solubility. Reactions of potassium fluoride in dipolar aprotic solvents has been studied[54,63,71,72]. These solvents are able to dissolve sufficient KF ion pairs (K^+F^-) to permit reaction in solution rather than at the surface of solid potassium fluoride which is easily covered with potassium chloride or other halide. Aprotic solvents that have high dielectric constants can also dissolve and stabilise the highly polarised transition state ions. Aqueous or protic solvent may do a better job in the solvation and stabilisation of transition states but as discussed

before (page17), the high heat of hydration of fluoride ion overcomes all other factors. The replacement reaction of potassium fluoride with perchloroaromatic compounds in aprotic solvents have been shown[63,74] to continue until three fluorine atoms have been introduced, but then further reaction gave significant amounts of hydrogen-containing species. Molten potassium fluoride together with potassium chloride[73] at high temperature 600 - 700°C has been used as fluorinating agent for fluorination of hexachlorobenzene and pentachloropyridine, and a mixture of di-, tri-, and tetra-fluoro isomers have been obtained. Potassium fluoride without solvent at 300 - 500°C has been used in the preparation of highly fluorinated aromatic compounds:



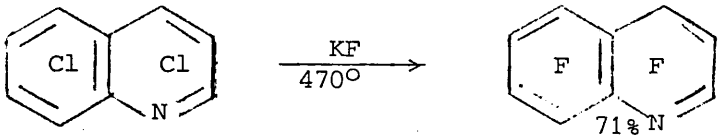
(Ref.65)

$$C_6Cl_6 \xrightarrow[\text{autoclave}]{KF\ 450\text{-}500^0} \underset{21\%}{C_6F_6} + \underset{20\%}{C_6F_5Cl} + \underset{14\%}{C_6F_4Cl_2} + \underset{12\%}{C_6F_3Cl_3}$$

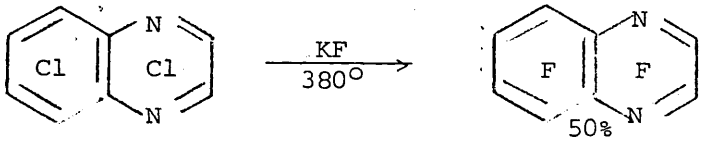
(Ref.59)

$$C_{10}Cl_8 \xrightarrow[25\ \text{hours}]{KF\ 300\text{-}330^\circ} \underset{24\%}{C_{10}F_8} + \underset{8\%}{C_{10}F_7Cl}$$

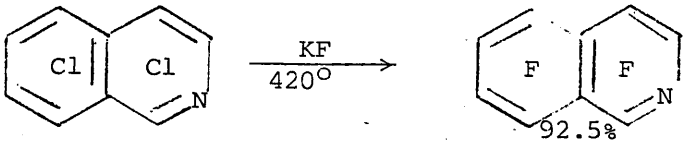
(Ref.94)



(Ref.66)



(Ref.67)



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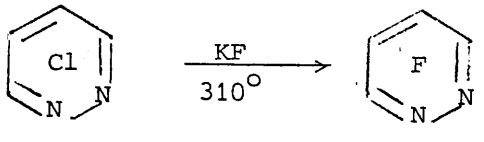
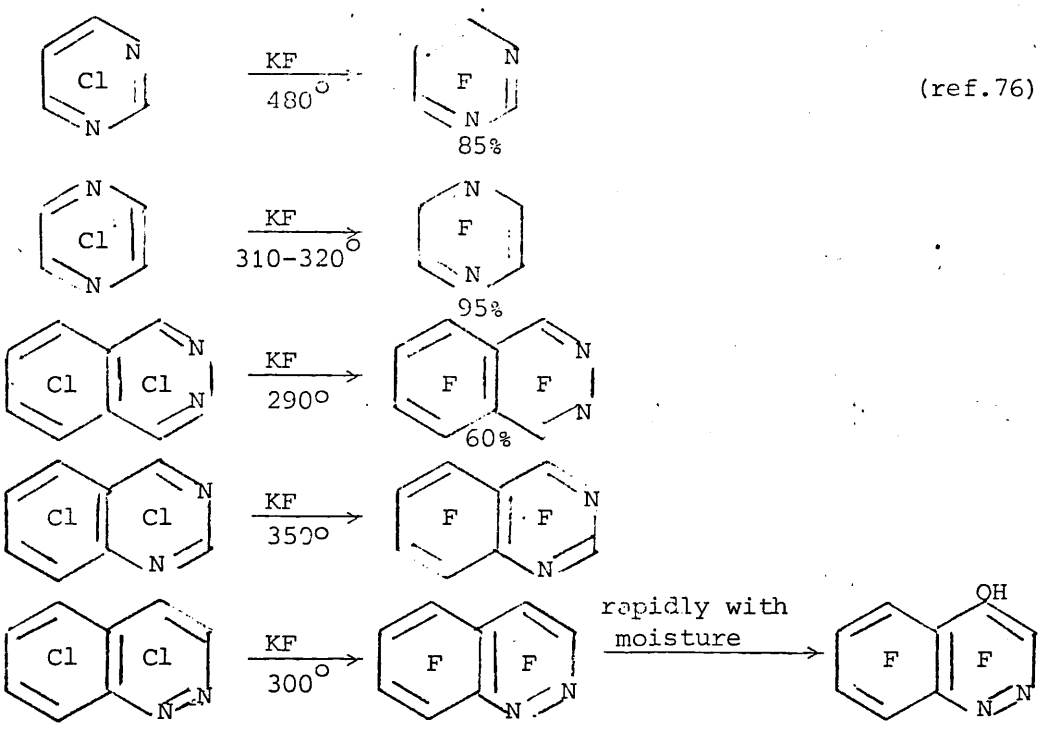


(Ref.75)

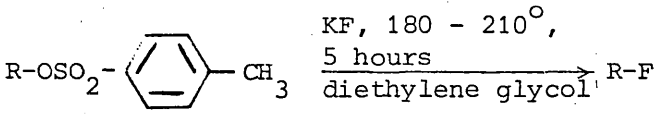


7. Effect of Solvents on Replacement Reactions of Potassium Fluoride

Anhydrous potassium fluoride in polar solvents such as diethylene glycol has been used for replacement of halogens in primary alkyl mono-halides[81]. Secondary and tertiary alkyl halides in non-aqueous solvents usually eliminate hydrogen halide under these conditions, because of the powerful basicity of potassium fluoride toward hydrogen halides[82].

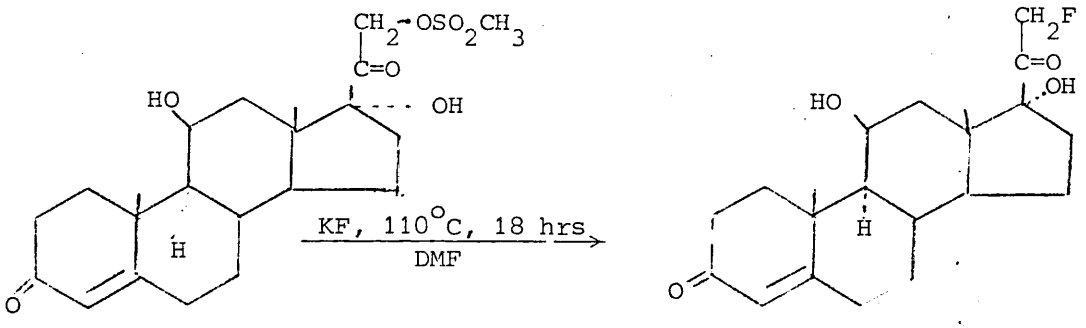
$$-CH_2-\underset{X}{CH}-\underset{H}{CH}-CH_2- + KF \xrightarrow[\text{solvent}]{\text{non-aqueous}} -CH_2-CH=CH-CH_2- + KF \cdot HX$$

In the replacement of oxygen-bonded groups such as methyl sulphonate, and para-toluene sulphonate, dry potassium fluoride in a polar solvent such as diethylene-clycol or dimethyl formamide have been used[83,84].



(Ref.83)

$R = CH_3$, C_2H_5 and C_3H_7

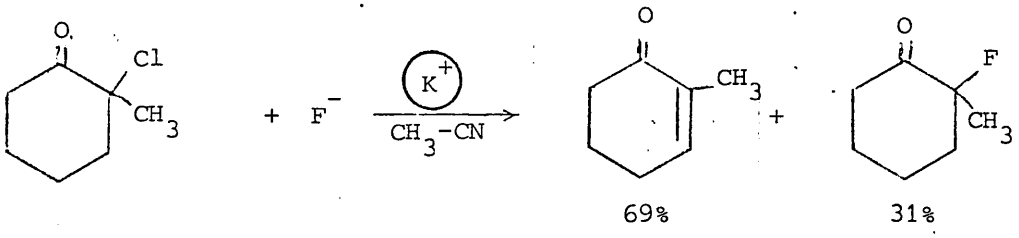


(Ref.84)

In the replacement reactions of polyhalogeno aromatic compounds potassium fluoride has been used in aprotic solvents and sulpholan has been claimed to be the best solvent, especially for the preparation of highly fluorinated aromatic compounds because of its high boiling point (b.p. = 285 - 288°/743 mmHg) and good thermal stability causing low by-product formation from reaction of such solvent fragments with the substrate or the reaction products. Side reactions have been noticed in other aprotic media, like the presence of some thio-ethers which has been reported[54,74] in the replacement of chlorine or the nitro-group by potassium fluoride in DMSO. Some of the problems and limitations of exchange reactions of perchlorinated compounds with potassium fluoride in a solvent have been solved by using a non-solvent method and high temperature. The non-solvent method has the advantage of forming fewer side products, but obtaining the unusually high temperatures and pressures in autoclaves in ordinary preparative laboratories is often difficult.

Recent work[85] on the reaction of potassium fluoride with a number of substrates in the presence of crown ether (18-crown-6) in benzene or acetonitrile showed that potassium fluoride in the presence of crown ethers produces fluoride ion which was called "naked" fluoride, reflecting

the ability of crown ethers to complex cations and dissolve them in polar and non-polar aprotic solvents[86]. Reaction of this "naked" fluoride with a variety of substrates showed that it could react both as a nucleophile and base:



69% 31%

CHAPTER 2

RESULTS AND DISCUSSION

8. Reaction of Hexachlorobenzene with Potassium Fluoride in Sulpholan

A. Products of Fluorodechlorination of Hexachlorobenzene

Table 10

Molar ratios of fluorine-containing products from reaction of hexachlorobenzene (0.1 mole) with KF (1.0 mole) in sulpholan (100 ml) at ca. 250°C

Arene	Molar % of Fluoro-arene at time (t)					
	t = 10	20	30	40	50	60 min
Fluoropentachlorobenzene	85.3	45.9	28.5	-	-	-
1,3-Difluoro-2,4,5,6-tetrachlorobenzene	12.1	39.8	41.4	19.0	7.8	-
1,2 -Difluoro-3,4,5,6-tetrachlorobenzene	2.6	12.0	22.6	9.4	5.7	-
1,4-Difluoro-2,3,5,6-tetrachlorobenzene	-	0.20	2.3	-	-	-
1,3,5-Trifluoro-2,4,6-trichlorobenzene	-	2.1	5.2	48.0	72.2	100
1,2,3-Trifluoro-4,5,6-trichlorobenzene	-	-	-	14.6	10.7	-
1,2,4-Trifluoro-3,5,6-trichlorobenzene	-	-	1.0	9.0	3.6	

Table 10 shows that hexachlorobenzene mainly forms 1,3-difluoro-2,4,5,6-tetrachlorobenzene, this undergoing further rapid exchange to give 1,3,5-trifluoro-2,4,6-trichlorobenzene. Earlier work on the hexachlorobenzene-potassium fluoride system in sulpholan has been reported by Fuller[63] and also by Nyman[64]. When hexachlorobenzene (0.1 mole) was treated with potassium fluoride (1.0 mole) in sulpholan at 230 - 240° for 18 hours the

following molar yields of products were obtained[63] C_6F_6 (0.4%) ; C_6ClF_5 (25%) ; $C_6Cl_2F_4$ (24%) ; $C_6Cl_3F_3$ (30%) . The dichlorotetrafluorobenzene fraction was mostly 1,3-dichlorotetrafluorobenzene (74%) , and the trichloro-trifluorobenzene fraction was largely the symmetrical isomer (72%). In the latter work[64], the dichlorotetrafluorobenzene and trichlorotrifluorobenzenes were identified by n.m.r. spectroscopy. The dichlorotetrafluorobenzene product consisted of a mixture of the 1,3-dichloro- (81%); 1,2-dichloro- (18%): and 1,4-dichlorotetrafluorobenzenes (1.5%), and the trichlorotrifluorobenzene fraction was a mixture of the 1,3,5-trichloro- (95%) and 1,2,3-trichloro-trifluorobenzenes (5%). The present results in Table 10 are in good agreement with these reports.

B. Orientation of Attack upon Hexachlorobenzene

The orientation of attack upon hexachlorobenzene could be predicted by referring to the (-I) and (+M) effects of the halogens. Introducing the first fluorine to the ring directs the second fluorine meta to the existing fluorine because, as shown in (XXII) in Figure 11, the deactivation at positions in the order para > ortho > meta to halogen makes the preferential attack of fluoride at the meta-position relative to fluorine. The orientation of attack in the difluorotetrachlorobenzenes is shown in Figure 11, so the

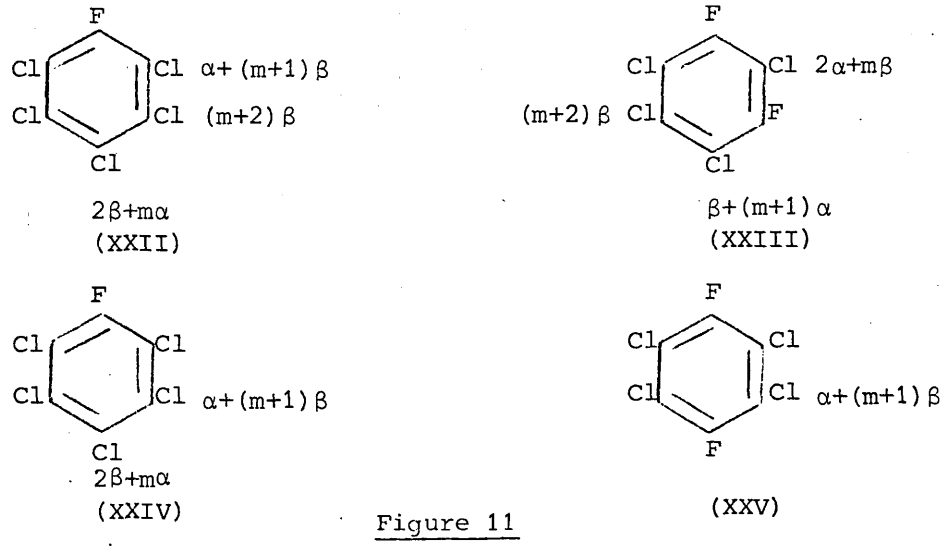


Figure 11

ease of formation of the trifluoro-isomers is in the order:

1,3,5- >> 1,2,3- > 1,2,4-trifluorotrichlorobenzene

This prediction of orientation is in agreement with the results in Table 10, and the more ready attack of positions meta to existing fluorine substitutents allows this ion exchange to be used in the preparation of both 1,3,5-trifluorotrichlorobenzene[63] and also 1,3-difluoro-2,4,5,6-tetrachlorobenzene[46].

9. Reaction of Pentachlorobenzene with Potassium Fluoride in Sulpholan

A. Products of Fluorodechlorination of Pentachlorobenzene

Table 11

Molar ratios of fluorine-containing products from the reaction of pentachlorobenzene (0.05 mole) with KF (0.5 mole) in sulpholan (50 ml) at ca. 245°C

Arene[a]	Molar % of fluoro-arene at time (t)[b]									
	t = 10	20	30	40	50	60	70	80	90	100min
(A)	30.2	24.1	22.0	15.6	11.2	7.7	6.8	5.9	2.4	-
(B)	32.0	24.1	22.3	15.0	13.3	10.9	5.0	4.0	3.0	-
(C)	37.8	31.6	27.5	20.4	14.3	12.1	7.5	5.9	2.5	-
(D)	-	-	-	-	2.4	5.5	4.9	7.9	5.0	3.0
(E)	-	13.5	20.0	27.2	31.4	34.0	35.0	35.6	38.8	43.5
(F)	-	-	-	7.5	8.3	11.0	13.0	11.9	12.5	14.7
(G)	-	2.4	3.7	5.5	6.0	6.6	9.3	10.9	11.8	12.6
(H)	-	4.3	4.5	5.1	6.1	4.4	6.8	4.0	4.9	3.6
(I)	-	-	-	3.7	7.0	7.7	11.8	13.9	19.0	22.6

(a) Appendix I

(b) Measured from ^{19}F N.M.R. signal integrals

Table 12

Molar ratios of the components from the reaction of pentachlorobenzene (0.05 mole) with KF (0.5 mole) in sulpholan (50 ml) at ca. 245°C

Arene [a]		Molar % of arene at time (t)			
		t = 25	50	75	100 min
(A)	(NMR)	16.4	17.6	14.0	5.5
(B)	(NMR)	14.8	15.6	15.0	8.6
(C)	(NMR)	18.1	20.7	17.5	7.3
A, B, and C	(GLC)	48.5	55.5	44.0	17.0
(D)	(NMR)	0	2.2	3.2	6.0
(E)	(NMR)	3.3	14.6	23.9	34.8
(F)	(NMR)	0.5	4.3	7.1	12.8
(G)	(NMR)	0.5	3.0	4.8	9.3
(H)	(NMR)	0.5	2.5	4.2	5.0
D, E, F, G and H	(GLC)	5.9	25.0	45.1	65.0
(I)	(NMR)	0.5	1.5	4.1	10.7
	(GLC)	0.2	2.3	4.7	15.0
Pentachlorobenzene	(GLC)	45.5	17.2	6.2	0.0

(a) Appendix I

Table 12 shows the relative yields of fluorinated organic products together with that of recovered pentachlorobenzene at four reaction times. Gas chromatography was unable to differentiate between isomeric compounds in most cases, but the relative amounts of tetra-, tri-, and di-chloropolyfluorobenzenes found by g.l.c. were in good agreement with measurements made using ^{19}F n.m.r. spectroscopy. Also gas chromatography

was the only way in which the amounts of unreacted pentachlorobenzene could be measured. Earlier work reported[70] in the patent literature showed that pentachlorobenzene with potassium fluoride in sulpholan at the reflux temperature (255°C, slowly dropping to 233°C) for four hours gives a mixture of di-, and tri-fluoro isomers. Analysis of the difluorotrichlorobenzenes showed that the mixture contained:

Table 13

Arene[(a)]	% Yield
(D)	6.3
(E)	58.2
(F)	15.6
(G)	12.2
(H)	6.8
(J)	0.9

(a) Appendix I

An exchange reaction of pentachlorobenzene with potassium fluoride in DMSO at 180°C for 24 hours has been reported[69] to give three fractions upon distillation:

Table 14

	Fraction a	Fraction b	Fraction c
Arene[(a)]	(I)	(E) (G) (H)	(A) (B) (C)
% of fraction	7.3	30.3	17.1
approximate ratio		2 : 1 : 1	1 : 1 : 1

(a) Appendix I

The results in Tables 11 and 12 are in agreement with the earlier patent reports[70]. The reaction of pentachlorobenzene with potassium fluoride in sulpholan (Tables 11 and 12) gives considerable quantities of (F). This isomer was not found when the reaction was carried out in dimethyl sulphoxide (Table 14). The disparity may be due to a preferential removal of some isomers by nucleophilic attack of products of decomposition of the solvent e.g. Me_2S (page 40). In contrast to the analogous reaction of hexachlorobenzene, ion-exchange of pentachlorobenzene does not afford pure polychlorofluorobenzene isomers readily.

B. Orientation of Attack in Pentachlorobenzene

As shown in Figure 12, the orientation of attack in pentachlorobenzene is para > ortho > meta, relative to the hydrogen substituent, because the deactivation terms are in the order $(m+2)\beta > (m+1)\beta > 2\beta$:

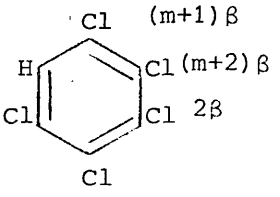


Figure 12

The directive effect of an existing fluorine being preferentially meta is shown in Figure 13.

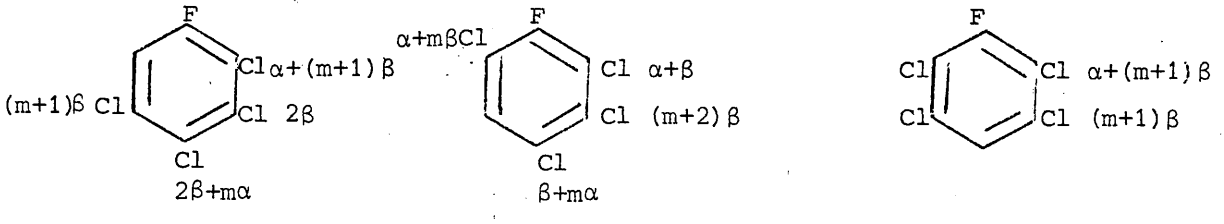


Figure 13

Therefore the ease of formation of the difluorotrichlorobenzenes refer to the deactivating parameters, is in the order (E) > (H) > (G) > (F) > (D). Introduction of the third fluorine to the ring will give preferentially (I):

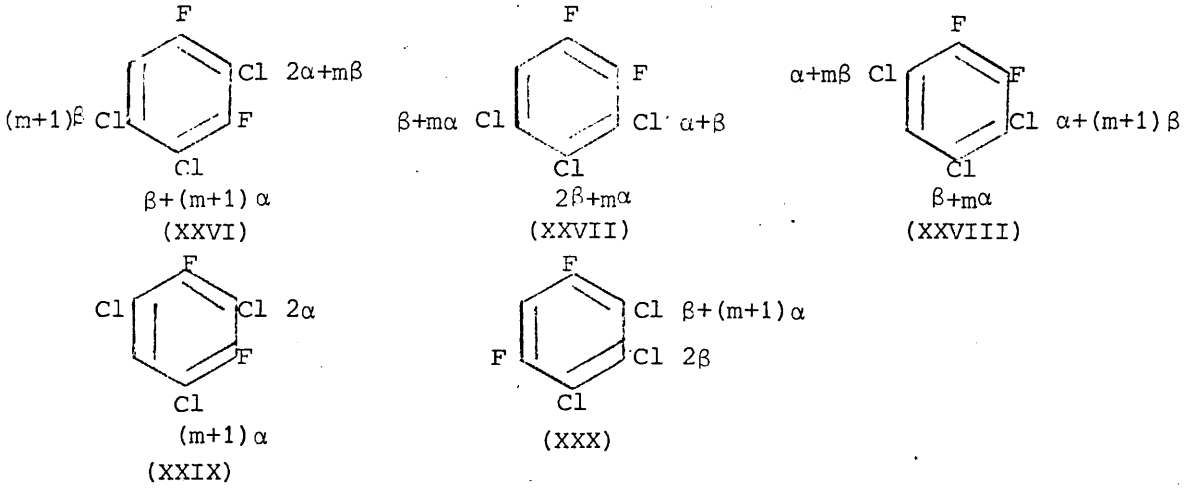


Figure 14

Comparing the deactivating parameters in Figure 14, the ease of formation of the trifluorodichlorobenzenes is in the order:

$$(I) >> (K) > (L) \sim (M)$$

So here again the directive effect of fluorine is meta > ortho $\gg$ para. The results in the Table 11 and 12 are in agreement with this prediction of orientation.

C. Observed Rates of Formation of Fluorotetrachloro- and Difluoro-trichloro-benzenes from Pentachlorobenzene

The pseudo first-order rate constants are distinguished by superscripts which, reading from left to right, indicate the order in which fluorine substituents are introduced into pentachlorobenzene (H=1). Thus $K^{2,4}$ is associated with the attack upon (A) to give (E) (2,4-F_2 (Appendix I)). and $K^{4,2}$ is associated with the attack upon(C)with the formation of the

same difluoro-isomer; a^1 is the rate constant for consumption of the pentachlorobenzene i.e.

$$d[C_6Cl_5H]/dt = a^1.[C_6Cl_5H]$$

Table 15

Arene	$10^5 K^{(a)}$ (sec^{-1}) at 250°C
(A)	$K^2 = 10$
(B)	$K^3 = 9$
(C)	$K^4 = 22$
(D)	$K^{2,3} = 1$ $K^{3,2} = 6$
(E)	$K^{2,4} = 18$ $K^{4,2} = 9$
(F)	$K^{3,4} = 11$ $K^{4,3} = 1.5$
(G)	$K^{3,5} = 8.5$
(H)	$K^{2,6} = 7$
Pentachlorobenzene	$a^1 = -59$

Table 15 shows that the rate of formation of the monofluorotetrachlorobenzenes is in the order para > ortho > meta (relative to the hydrogen) and the most preferentially formed difluorotrichlorobenzene is (E). A similar order has been deduced in the prediction of the orientation (page 47), where the rate of formation of (F) is higher than those of (G) and (H), but in the prediction of orientation the ease of formation of difluoro-trichlorobenzenes was in the order meta- difluoro (i.e.(G) and (H)) > ortho-difluoro-trichlorobenzene (F). The reason could be a ready removal of the 2,6-difluoro-isomer (H) in the formation of trifluoro-dichloro-isomers (e.g. (I)) shown in Table 11. The second fluorine may go preferentially to the meta

positions relative to the existing fluorine, but once (F) and (G) are formed they cannot easily give trifluorodichlorobenzene isomers because the deactivating energies for conversion of these isomers to trifluoro-isomers are high (XXVII and XXIX in Figure 14).

10. Reaction of 2,3,4,5,6-Pentachlorotoluene with Potassium Fluoride in Sulpholan

A. Results of Fluorodechlorination of 2,3,4,5,6-Pentachlorotoluene with Potassium Fluoride

Table 16

Molar ratios of components from the reaction of 2,3,4,5,6-pentachlorotoluene (0.05 mole) with KF (0.5 mole) in sulpholan (50 ml) at ca. 276°C.

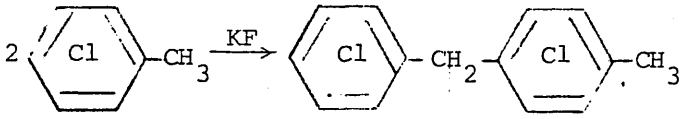
Arene[a]	Molar % of arene at time (t)			
	t= 25	50	75	100
4-Fluoro-2,3,5,6-tetrachlorotoluene (C)	6.30	10.10	10.70	10.25
2-Fluoro-3,4,5,6-tetrachlorotoluene (A)	5.95	7.80	8.74	8.90
3-Fluoro-2,4,5,6-tetrachlorotoluene (B)	4.08	4.50	6.90	5.77
2,4-Difluoro-3,5,6-trichlorotoluene (E)	-	4.20	5.90	8.98
3,5-Difluoro-2,4,6-trichlorotoluene (G)	-	-	1.80	3.20
2,6-Difluoro-3,4,5-trichlorotoluene (H)	-	-	0.46	1.30
2,3,4,5,6-Pentachlorotoluene[b]	83.60	73.40	65.50	61.50

(a) Measured from ^{19}F n.m.r. signal integrals.

(b) Measured from g.l.c.

As is seen by comparing Tables 12 and 16, fluorodechlorination occurs much less readily in pentachlorotoluene than the corresponding reaction in pentachlorobenzene. Attempts were made to continue the exchange reaction

by using longer periods of time, but after 100 minutes, the product of fluorination was an insoluble tar which did not appear to contain any fluorine. This may be some product from nucleophilic attack by fragments from the decomposed solvent at high temperature[54,74] or, perhaps products of polymerisation of highly chlorinated compounds in the presence of potassium fluoride.



B. Orientation of Attack in 2,3,4,5,6-Pentachlorotoluene

The orientation of attack of pentachlorotoluene is similar to that of pentachlorobenzene and is in the order para > ortho > meta relative to the methyl group:

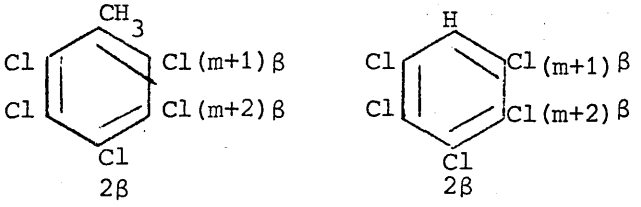
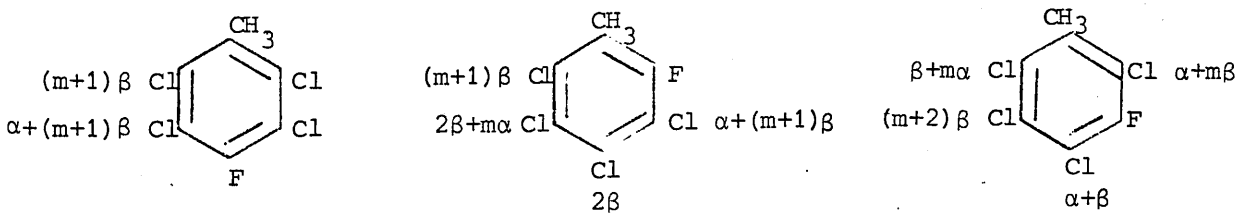


Figure 15

Further fluorination of these mono-fluorotetrachlorotoluenes occur preferentially meta to the existing fluorine:



(See Appendix I, page 110)

Figure 16

and the ease of formation of the difluorotrichlorotoluenes is apparently in the order 2,4-difluoro-(E) > 2,6-difluoro-(H) > 3,5-difluorotrichlorotoluene (G). Table 16 shows that the most preferred isomer among the three difluorotrichlorotoluenes is 2,4-difluoro-3,5,6-trichlorotoluene (E), but the relative amounts of the two other difluorotrichlorotoluenes are not in agreement with the order of reactivity predicted in page 51 . The ease of formation of difluorotrichlorotoluenes is 2,4-difluoro-(E) > 3,5-difluoro-(G) > 2,6-difluoro-(H) trichlorotoluene. This disparity in the order of formation of these isomers, could be due to ready attack at the meta-position relative to fluorine, in the 2,6-difluoro isomer to form 2,4,6-trifluoro-3,5-dichlorotoluene, although this was not observed in the ^{19}F n.m.r. spectra of the reaction mixtures (perhaps because of the low concentration). A methyl group, compared to the hydrogen group in the C_6Cl_5X system, seems to deactivate the system towards nucleophilic attack by potassium fluoride. Here, despite the use of a higher temperature (276°C) and after 100 minutes reaction, still about 60% of unreacted starting material is left (Table 16), whereas in the corresponding reaction of pentachlorobenzene at a lower temperature (245°C) all the starting material was consumed after this time (page 45).

C. Observed Rates of Attack in the Reaction of 2,3,4,5,6-Pentachlorotoluene

Table 17

Arene	$10^5K^{(a)}$ (sec^{-1})
2,3,4,5,6-Pentachlorotoluene	$a^1 = -11.1$
4-Fluoro-2,3,5,6-tetrachlorotoluene (C)	$a^4 = -40$ $K^4 = 7$
2-Fluoro-3,4,5,6-tetrachlorotoluene (A)	$a^2 = -27$ $K^2 = 2.3$
3-Fluoro-2,4,5,6-tetrachlorotoluene (B)	$a^3 = -25$ $K^3 = 2$

Table 17 (continued)

Arene	$10^5 K^{(a)}$ (sec^{-1})
2,4-Difluoro-3,5,6-trichlorotoluene (E)	$K^{2,4} = 8$ $K^{4,2} = 4$
3,5-Difluro-2,4,6-trichlorotoluene (G)	$K^{3,5} = 8$
2,6-Difluoro-3,4,5-trichlorotoluene (H)	$K^{2,6} = 2.4$

(a) a^1, a^2, a^3 and a^4 are the rate constants for removal of the indicated arenes and K are the rates of formation of the arenes. Where there is more than one route for formation of the isomers, the superscripts indicate the source from which the indicated arene has been formed, so $K^{2,4}$ is associated with the attack upon 2-fluoro-3,4,5,6-tetrachlorotoluene to form 2,4-difluoro-3,5,6-trichlorotoluene and $K^{4,2}$ is associated with the attack upon 4-fluoro-2,3,5,6-tetrachlorotoluene to form the same difluoro isomer.

Here again the apparent rate of the formation of 3,5-difluoro-2,4,6-trichlorotoluene (G) is more than that of 2,6-difluoro-3,4,5-trichlorotoluene (H), either $K^{3,5} > K^{2,6}$ which as mentioned before (page 52) may be because of the ready removal of the latter isomer.

11. Reaction of Pentachloroanisole with Potassium Fluoride in Sulpholan

The methoxy-group is known as one of the deactivating group when it is para to the site of reaction in the aromatic nucleophilic substitutions (page 28). The electronic effect of the -OMe group in such reactions has been shown to vary markedly with the position. Miller[11c] has compared

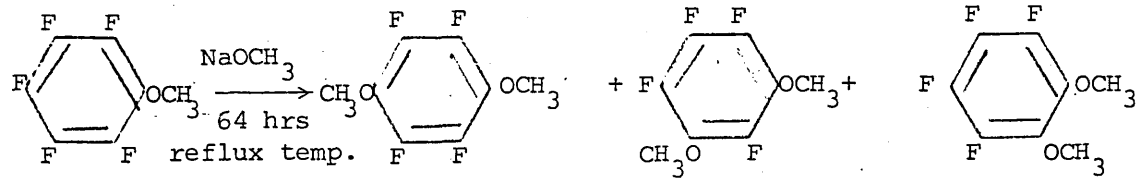
the rate of the methoxydechlorination of the 4-, 5-, and 6-methoxy-2,4- or -2,6-dinitrochlorobenzene and has obtained the deactivating power of the -OMe group to be in the order para > ortho > meta (Table 18):

Table 18

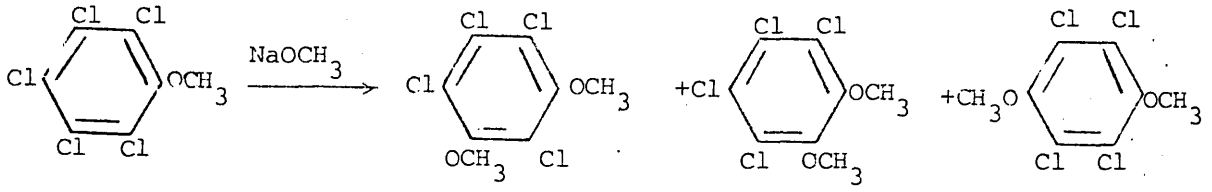
Rates of methoxydechlorination of some chlorodinitro-methoxybenzenes with methoxide ion in methanol at 50°C

Position relative to -Cl	($l.mole^{-1}sec^{-1}$)	f_{OMe} (S.R.F.)
2,6-dinitro-4-methoxy-	1.85×10^{-4}	$f_p = 0.025$
2,4-dinitro-6-methoxy-	4.67×10^{-2}	$f_o = 0.16$
2,4-dinitro-5-methoxy	1.09×10^{-1}	$f_m = 0.38$
2,4-dinitro-	2.88×10^{-1}	1
2,6-dinitro-	7.4×10^{-3}	1

The deactivation power of the -OMe group in the C_6F_5X system could be shown by comparison of the rate of reaction of pentafluoroanisole (X = OMe) with that of pentafluorobenzene (X = H), in the reaction with methoxide ion in methanol at 50°C, ($k_2 = 9.92 \times 10^{-6}$ and 8.66×10^{-5} respectively[11d]) although only 52% attack occurs at the p-position of pentafluoroanisole (see below). The directive effect of the -OMe group in pentafluoroanisole has been reported[87] to be para > meta > ortho in the reaction with sodium methoxide in methanol:



while the methoxydechlorination of the pentachloroanisole occurred[88] at position meta > ortho > para relative to the methoxy group:



70 : 25 : 3

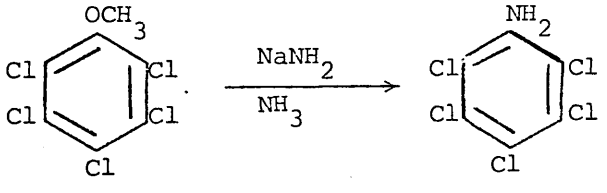
This is because the directive effects of fluorine and chlorine are different. As shown in Table 19, the activating effect of para-fluorine is much less than in any other site, or for chlorine in any position, so that substitution occurs preferentially not at positions p- to fluorine.

Table 19[93b]

Partial rate factors for ortho-, meta- and para-X-groups in the methoxy-dehalogenation of polyhalogeno compounds in methanol at 50°C

Groups	f_o	f_m	f_p
Cl	65	123	26
F	42	180	0.75
OCH_3	0.66	5.5	0.08

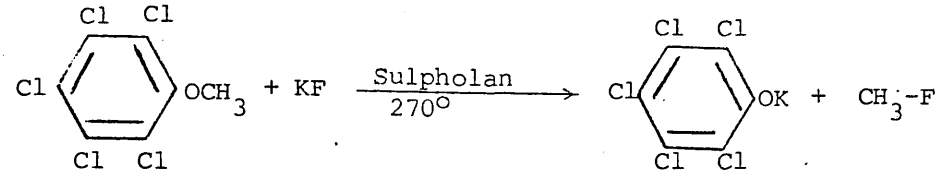
Replacement of the methoxyl group by amine group has been reported[88] in the reaction of pentachloroanisole with sodium amide in liquid ammonia.



64%

In this work attempts upon the displacement reaction of pentachloroanisole by potassium fluoride in sulpholan failed. Under vigorous conditions, potassium fluoride and pentachloroanisole gave some products, but no displacement by fluoride ion took place. It seemed that demethylation

to give potassium pentachlorophenate was the main process under the forcing conditions:



12. Reaction of Fluoropentachlorobenzene with Potassium Fluoride in Sulpholan

A. Products of Fluorodechlorination of Fluoropentachlorobenzene

Table 20

Molar ratios of fluorine-containing components from the reaction of fluoropentachlorobenzene (0.025 mole) with KF (0,25 mole) in sulpholan (25 ml) at ca. 260°C

Fluoro-arene		Molar % of Fluoro-arene at time (t)			
		t = 15	30	45	60 (min)
Fluoropentachlorobenzene	(NMR)	15.37	-	-	-
	(GLC)	14.25	-	-	-
1,3-Difluoro-2,4,5,6-tetrachlorobenzene	(NMR)	44.57	19.84	6.82	2.69
1,2-Difluoro-3,4,5,6-tetrachlorobenzene	(NMR)	16.9	11.3	3.41	1.34
1,4-Difluoro-2,3,5,6-tetrachlorobenzene	(NMR)	1.53	0.70	-	-
Total difluoro-tetrachlorobenzenes	(GLC)	60.1	33.60	12.17	4.80
1,3,5-Trifluoro-2,4,6-trichlorobenzene	(NMR)	19.45	46.20	64.80	67.40
1,2,3-Trifluoro-4,5,6-trichlorobenzene	(NMR)	2.15	14.1	17.0	17.88
1,2,4-Trifluoro-3,5,6-trichlorobenzene	(NMR)	-	7.65	7.87	5.39
Total trifluoro-trichlorobenzenes	(GLC)	25.65	64.89	84.13	86.30
1,2,3,5-Tetrafluoro-4,6-dichlorobenzene	(NMR)	-	-	-	5.39
	(GLC)	-	1.5	3.7	8.70

Table 20 shows that after 15 minutes, all the starting material has reacted and the results are in agreement with those obtained from the reaction of hexachlorobenzene with the same reagent and solvent (page 42). The only tetrafluoro-isomer observed after 60 minutes reaction was 1,2,3,5-tetrafluoro-4,6-dichlorobenzene which has been observed[56,57] to be the main isomer among the tetrafluorodichloroisomers product in the fluorodechlorination of hexachlorobenzene. Table 20 also shows the rapid conversion of 1,3-difluoro-2,4,5,6-tetrachlorobenzene to the kinetically most stable isomer 1,3,5-trifluoro-2,4,6-trichlorobenzene.

B. Orientation of Attack in Fluoropentachlorobenzene

As predicted for the sequence of reaction of hexachlorobenzene, the orientation of attack in fluoropentachlorobenzene is meta > ortho > para relative to fluorine. As can be seen in Table 21 from comparing the free energy parameters for formation of each isomer, the preferentially formed species are 1,3-difluoro-2,4,5,6-tetrachloro- and 1,3,5-trifluoro-2,4,6-trichlorobenzenes. Table 21 also shows that by using the inductive effect, we can put the free energy parameters into an order of reactivity, thus because $I_F > I_{Cl}$ 1,2-difluoro-3,4,5,6-tetrachlorobenzene reacts less readily than 1,2,4-trifluorotrichlorobenzene, when the mesomeric contribution is the same (e.g. $\alpha+(m+1)\beta$) for each site:

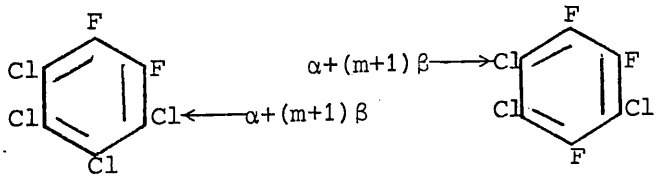


Table 21

Free Energy Parameter	Orientation of Fluorine in Polyfluorochlorobenzene
$4I_{Cl} + 2I_F - \beta(m+2)$	1,3,5-trifluoro-2,4,6-trichlorobenzene
$5I_{Cl} + 1I_F - \beta(m+2)$	1,3-difluoro-2,4,5,6-tetrachlorobenzene
$3I_F + 3I_{Cl} - \alpha+(m+1)\beta$	1,2,3,5-tetrafluoro-4,6-dichlorobenzene
$2I_F + 4I_{Cl} - \alpha+(m+1)\beta$	1,2,3-trifluoro-4,5,6-trichlorobenzene; 1,2,4-trifluoro-3,5,6-trichlorobenzene
$I_F + 5I_{Cl} - \alpha+(m+1)\beta$	1,2-difluoro-3,4,5,6-tetrachlorobenzene
$I_F + 5I_{Cl} - (2\beta+m\alpha)$	1,4-difluoro-2,3,5,6-tetrachlorobenzene

This prediction of orientation is in agreement with the results in Table 20.

13. Reaction of 1,2,3,5-Tetrachlorobenzene with Potassium Fluoride in Sulpholan

A. Products of Fluorodechlorination of 1,2,3,5-Tetrachlorobenzene

Table 22

Composition (moles) of components from the reaction of 1,2,3,5-tetrachlorobenzene (0.05 mole) with KF (0.5 mole) in sulpholan (50 cc) at ca. 250°C

Arene[a]		10^3 moles of components at time (t) t = 2	4	6	8 hours
(O)	(NMR)	8.02	10.02	10.02	9.6
	(GLC)	9.37	9.62	10.05	11.1
(P)	(NMR)[b]	0	1.35	1.50	1.85
(Q)	(NMR)	1.35	1.35	2.25	2.55
(R)	(NMR)	0	0.054	1.47	2.67
	(GLC)	0.038	0.069	1.53	2.13
1,2,3,5-Tetrachlorobenzene	(GLC)	14.00	8.20	4.40	1.99

(a) Appendix II

(b) GLC was not able to differentiate between (P) and (Q).

Table 23

Composition (moles) of components from the reaction of 1,2,3,5-tetrachlorobenzene (0.05 mole) with KF (0.5 mole) with KF (0.5 mole) in sulpholan (50 cc) at ca. 250°C

Arene[a]		10^3 moles of components at t (t) t = 3	6	9	12	15	18(hrs)
(O)	(NMR)	10.01	10.02	9.20	6.0	5.8	5.0
	(GLC)[c]	10.47	10.52	9.50	6.01	6.0	5.2
(P)	(NMR)	0	1.80	2.40	2.0	1.90	-
(Q)	(NMR)	2.45	2.55	2.70	2.15	-	-
(P) and (Q)	(GLC)[d]	7.30	8.5	10.0	8.5	6.5	5.8
(R)	(NMR)	0	1.47	2.45	2.73	2.73	2.51
(S)	(NMR)	0	0.81	1.47	1.74	2.01	1.36
(R) and (S)	(GLC)	0.04	1.95	2.73	3.66	2.95	3.0
(T)	(NMR)	-	-	-	0.09	1.09	-
1,2,3,5-Tetrachlorobenzene	(GLC)	9.44	4.76	3.51	1.94	1.52	0.046
1,2,3-Trichlorobenzene	(GLC)	-	-	-	-	-	1.6[e]

(a) See Appendix II.

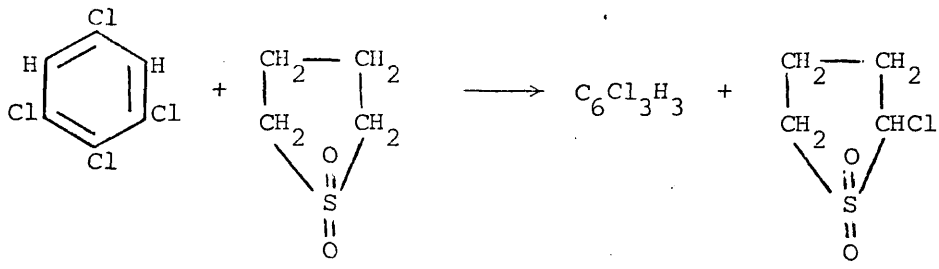
(b) The reaction mixtures were left for 15 hours (overnight) and reheated.

(c) (N) together with products of reduction probably 1,2,3-trichlorobenzene.

(d) Both the monofluoro-trichlorobenzenes (Appendix II) together with small quantity of sulpholan and also, products of reduction.

(e) Measured from GLC analysis of the steam volatile species of the reaction mixture.

Tables 22 and 23 show that fluorodechlorination of 1,2,3,5-tetrachlorobenzene occurs mainly at positions ortho and para to hydrogen and meta to chlorine with the preferential formation of (O) and (R) (see Appendix II). Similar exchange reactions of 1,2,3,5-tetrachlorobenzene with potassium fluoride in DMSO has been reported by Finger et.al[71a] to give (O) 7.2% (mole %) as the only mono-fluorinated product, after 72 hours heating at 183°C. They also reported the presence of two difluoro-isomers, (R), 0.4% and 1,2-difluoro-3,5-dichlorobenzene (U), 0.4% with this mono-fluorinated product (O). 1.2-Difluoro-3,5-dichlorobenzene was not observed after heating the 1,2,3,5-tetrachlorobenzene with potassium fluoride in sulpholan for 18 hours. The reason could be the preferential attack at meta position relative to chlorine rather than ortho (Figure 18). As shown in Table 23. the presence of some products of reduction (T) has been deduced from the ^{19}F n.m.r. spectra of the reaction mixture, and also in the g.l.c. analysis of the steam-volatile substances of the reaction mixture. Compared to the similar reaction with pentachlorobenzene, considerable amounts of non-volatile species (tar) which contained no fluorine were obtained in this reaction. Extraction of these tars by petroleum ether did not give any pure compound, but the presence of 1,2,3-trichlorobenzene was shown by g.l.c. analysis of the volatile species of the reaction mixture formed after 18 hours (Table 23). Presence of other products of reduction (e.g. 1,3,5- and 1,2,4-trichlorobenzenes) was not observed in the g.l.c. analysis of the reaction mixtures because they coincide with the monofluorotrichlorobenzenes (Table 23). The formation of trichloro-benzenes may be represented by the equation:



and the resultant chlorosulphone can be regarded as a source of the tarry materials. Protiodechlorination has been observed in the exchange reactions of some polychloroaromatic compounds in sulpholan, e.g. presence of 2,4-dichloro-1,3,5-trifluorobenzene among the products of reaction of hexachlorobenzene with potassium fluoride in sulpholan[46].

B. Orientation of Attack in 1,2,3,5-Tetrachlorobenzene

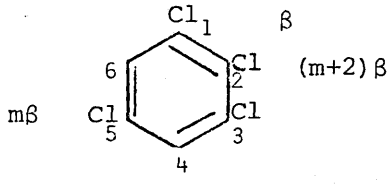
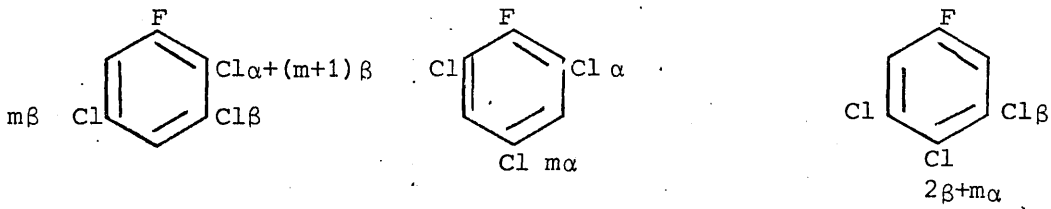


Figure 17

Figure 17 shows that chlorine atoms at C-1 (≡C-3) and C-5 are more readily attacked than chlorine at C-2, (deactivating parameters are β < mβ < (m+2)β respectively). The extent of formation of mono-fluoro-derivatives is therefore predicted to be:

2,3,5-(O) > 3,4,5-(P) > 2,4,6-trichlorofluorobenzene (Ω).

Attack by the second fluoride ion is expected to take place at the less deactivated positions shown in Figure 18:



(XXXI) (XXXII) (XXXIII)

Figure 18

which gives the ease of formation of the difluoro-isomers in the order: (R) $\simeq$ (S) >> (U). The order of formation of these difluoro-isomers shown in Tables 17 and 18 is (R) > (S). Figure 18 shows that (R) can only be formed from attack on (XXXI), but (S) may be formed from the attack on both (XXXI) and (XXXIII) [mostly from (XXXIII) because the deactivating parameters at the sites of attack are mβ and β for (XXXI) and (XXXIII) respectively]. As the ratio of the concentrations of (XXXI) to (XXXIII) is about 5:1 ((O)/(Q) in Table 23) the amount of isomers formed from (XXXI) is therefore more than that formed from (XXXIII). These differences in the amount of difluoro-compounds formed from the different mono-fluoro derivatives are seen in Table 24, which shows that the rate of formation of (R) from the only mono-fluoro isomer formed (O), is more ($K^{2,4} = 0.8 \times 10^{-5}$ sec^{-1}) than that of (S) from (O) and (Q) ($K^{2,6} = 0.5 \times 10^{-5}$ and $K^{6,2} = 0.22 \times 10^{-5}$ sec^{-1} respectively).

C. Observed Rates of Attack in the Reaction of 1,2,3,5-Tetrachloro-benzene (0.05 mole) with Potassium Fluoride (0.5 mole) in Sulpholan (50 ml) at ca. 250°C.

Table 24

Arene	$10^5 K^{(a)}$ (sec^{-1})
1,2,3,5-Tetrachlorobenzene	$a^1 = -11.8$
(O)	$K^2 = 1.75$
(P)	$K^3 = 0.45$
(Q)	$K^6 = 0.6$
(R)	$K^{2,4} = 0.80$
(S)	$K^{2,6} = 0.5$, $K^{6,2} = 0.22$

(a) a^1 is the rate of consumption of starting material, other superscripts are the same as that stated for pentachlorobenzene, and pentachloro-toluene.

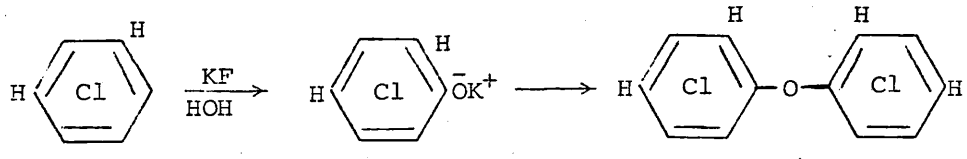
As was mentioned before (page 60) the amount of non-volatile species (tar) obtained in this reaction was more than those obtained in the similar reaction of pentachlorobenzene. In Table 24 a^1 should be equal to the rates of formation of the daughter products, i.e.

$$a^1 = 2K^2 + K^3 + K^6$$

But the total sum of the rate constants for the formation of mono-fluoro-isomers is:

$$2K^2 + K^3 + K^6 = 4.55 \times 10^{-5}$$

which is not equal to $a^1 = 11.8 \times 10^{-5}$; $\left(\sum K^1/a^1 = \frac{0.455}{1.18} = 0.38\right)$. Although much of the starting material in this reaction is consumed to give volatile species (including trichlorobenzenes and 3,5-dichlorofluorobenzene), some non-volatile species which contain no fluorine and cannot be detected by ^{19}F n.m.r. or g.l.c. are evidently also formed. They might be biaryl ethers[78] formed from the reaction of starting material or trichlorobenzenes with the atmospheric moisture, e.g.



14. Reaction of 1,2,3,4- and 1,2,4,5-Tetrachlorobenzene with Potassium Fluoride in Sulpholan

A. Products of Fluorodechlorination of 1,2,3,4-Tetrachlorobenzene

Table 25

Composition of compounds from reaction of 1,2,3,4-tetrachlorobenzene (0.035 mole) with potassium fluoride (0.35 mole) in sulpholan (35 ml) at ca 250°C

Arene[a]	10^3 moles of components at time(t) t = 2	4 hours
(V) (NMR)	4.55	7.50
(W) (NMR)	1.96	3.36
(V) and (W) (GLC)	6.60	11.20
1.2.3.4-Tetrachlorobenzene ^1H (NMR)[b]	28.20	23.80
(GLC)	26.00	20.00

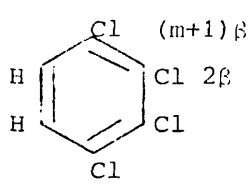
(a) Appendix II.

(b) δ = 7.3 p.p.m. downfield of T.M.S. using tetrachloromethane as solvent.

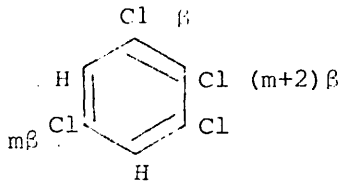
Table 25 shows that after four hours heating at 250°C, 1,2,3,4-tetrachlorobenzene gives only two mono-fluorotrichloro isomers, with about 60% of the starting material still unreacted. Similar results have been reported by Finger et.al.[71a]. Tetrachlorobenzene (0.2 mole) with potassium fluoride (1.8 mole) at 200°C in dimethyl sulphone gave (V) 46.7% mole %, (W) 8.3%, and three difluorodichloro-isomers; 1,3-difluoro-2,4-dichloro- (X) 10.7%; 2,3-difluoro-1,4-dichloro- (Y) 7.5%; and 1,2,-difluoro-3,4,-dichlorobenzene (Z) 1.4 %.

The results in Table 25 are in general agreement with these results so far as mono-fluorodechlorination is concerned.

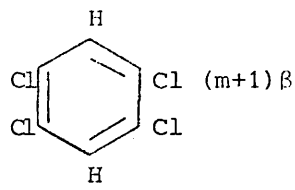
B. Orientation of Attack in 1,2,3,4-Tetrachlorobenzene



(XXXIV)



(XXXV)



(XXXVI)

As shown in (XXXIV), the orientation of attack in 1,2,3,4-tetrachlorobenzene is expected to be para > ortho relative to hydrogen. So the order of formation of monofluorotrichloro-compound is (V) > (W). Comparing the three tetrachlorobenzenes together, the reactivity of 1,2,3,5-tetrachlorobenzene (XXXV) towards the exchange reaction is more than those of 1,2,3,4- and 1,2,4,5-tetrachlorobenzenes. [(XXXIV) and (XXXVI) respectively].

C. Observed Rates of Attack in the Reaction of 1,2,3,4-Tetrachlorobenzene (0.05 mole), Potassium Fluoride (0.5 mole) and Sulpholan (50 ml) at ca. 250°C

Table 26

Arene	$10^5 K$ (sec^{-1})
1,2,3,4-Tetrachlorobenzene	$a^1 = -2.7$
(V)	$K^2 = 0.95$
(W)	$K^1 = 0.4$

Table 26 shows that the reaction of 1,2,3,4-tetrachlorobenzene is slower ($a^1 = -2.7 \times 10^{-5}$ sec^{-1}) than that of 1,2,3,5-tetrachlorobenzene.

($a^1 = -11.8 \times 10^{-5}$ sec^{-1}) which is in agreement with that predicted in page 65. The rate constants for formation of monofluorotrichloro-compounds (K^2 and K^1) are also in agreement with the order of reactivity predicted in page 65. In contrast 1,2,4,5-tetrachlorobenzene gave no 2,4,5-trichlorofluorobenzene with potassium fluoride in sulpholan at 250°C even after 12 hours (So $a^1 \not> 5 \times 10^{-6}$ sec^{-1}).

15. Reaction of 2,3,5,6-Tetrachlorofluorobenzene with Potassium Fluoride in Sulpholan

A. Products of Fluorodechlorination of 2,3,5,6-Tetrachloro-fluorobenzene

Table 27

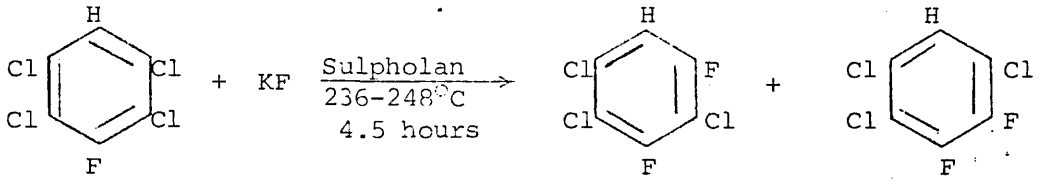
Molar ratios of fluorine containing compounds from the reaction of 2,3,5,6-tetrachlorofluorobenzene (0.1 mole) with potassium fluoride (1.0 mole) in sulpholan (100 ml) at ca. 260°C

Fluoro-arene[a]		Molar % of fluoro-arene at time (t)				
	t =	15	30	45	60	75 (min)
2,3,5,6-Tetrachlorobenzene						
(C)	(NMR)	58.90	35.60	18.20	10.10	8.00
	(GLC)	63.40	32.20	6.90	6.70	5.20
(E)	(NMR)	32.30	48.0	56.70	59.40	64.0
(F)	(NMR)	7.80	10.90	13.70	14.80	10.70
(E) and (F)	(GLC)	35.20	61.40	80.60	78.80	73.90
(I)	(NMR)	1.00	5.40	11.40	14.80	16.10
	(GLC)	1.40	6.40	12.40	17.30	19.40
(N)[b]	(GLC)	0	<0.09	0.1	0.7	1.5
	(NMR)	0	0	0	0.3	1.3

(a) Appendix I.

(b) Reduction product.

The results in Table 27 are in agreement with the results obtained from the corresponding reaction of pentachlorobenzene with potassium fluoride. An earlier report[70] was made of the reaction of 2,3,5,6-tetrachlorofluorobenzene which gave the two possible difluorotrichlorobenzenes:



(39% overall conversion)

The results in Table 27 confirm this report.

B. Orientation of Attack in 2,3,5,6-Tetrachlorofluorobenzene

As was predicted in the attack of pentachlorobenzene (page 48), further fluorination of 2,3,5,6-tetrachlorofluorobenzene (C) gave (E) more readily than (F). The trifluorodichloro-isomers formed from these difluoro-compounds were in the order: (I) >> (K); this orientation of attack has been observed (Table 27) in this reaction.

C. Observed Rates of Attack in the Reaction of 2,3,5,6-Tetrachlorofluorobenzene (0.1 mole), Potassium Fluoride (2.0 mole) and Sulpholan (100 ml) at ca. 260°C

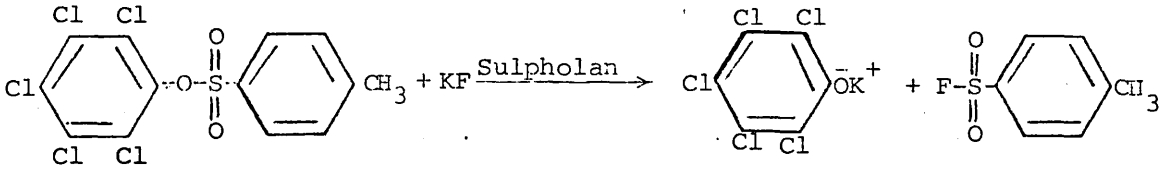
Table 28

Arene	10^5 K(sec^{-1})
2.3.5.6-Tetrachlorofluorobenzene (C)	$a^1 = -60$
(E)	$K^{2,4} = 24.5$
(F)	$K^{2,3} = 5$
(I)	$K^{2,4,6} = 10$

The main difluorotrichloro-compound in this reaction was predicted to be (E) and the main trifluorotrichlorobenzene to be (I). The rate constants in Table 28 are in agreement with this prediction of orientation.

16. Reaction of Pentachlorophenyl p-toluenesulphonate with Potassium Fluoride in Sulpholan

Replacement of the p-toluenesulphonate group by fluorine has been reported[83] in the preparation of the alkyl halides such as fluoroethane, fluoroethylene, and 1-fluoroheptane from the corresponding alkyl p-toluenesulphonate with dry potassium fluoride either in diethylene glycol or without a solvent (preparation of fluoroethane[83]). Similar replacement has been reported[84] in the synthesis of some fluoro-steroids (page 40); diethylene glycol[89] and dimethyl sulphoxide[90] have been used as solvents in these ion exchange reactions. In the present work attempts to replace the p-toluenesulphonate group from pentachlorophenyl p-toluenesulphonate failed. Anhydrous potassium fluoride in sulpholan at different temperatures (240, 250, 270 and 280°C) was used, but no such replacement by fluorine took place. This may be due to a primary steric effect from the p-toluenesulphonate group, or because p-toluenesulphonyl fluoride may be formed by the preferential displacement of pentachlorophenoxide ion:



17. Attempted Replacement Reaction of Tetrachlorophthaloyl Chloride with Potassium Fluoride in Sulpholan

The reaction of tetrachloroterephthaloyl chloride with anhydrous potassium fluoride at 230°C for 30 hours, or with cesium fluoride at 190°C

for two hours in the absence of solvent, has been reported to give 72 - 87% tetrachloroterephthaloyl fluoride[62b]. A similar reaction of tetrachloroterephthaloyl fluoride with cesium fluoride at 220° for 26 hours has been reported[62b] to give 52% tetrafluoroterephthaloyl fluoride. Reaction of tetrachlorophthaloylchloride has also been reported[61] to give tetrafluorophthaloyl fluoride, using potassium fluoride in the absence of solvent. In the present work, tetrachlorophthaloyl chloride was treated with anhydrous potassium fluoride in sulpholane at 260°, but no ion-exchange reaction observed over 2 hours, although the method of analysis would not detect acid fluoride formation. The potassium fluoride-sulpholan systems seems not to be effective for this ion-exchange reaction.

18. Replacement Reactions of 1,3,5-Trichloro- and 1,3-Dichloro-2-nitrosobenzenes with potassium fluoride in DMSO and Sulpholan

Comparing the relative rates of the reaction of 2,4-dinitrochlorobenzene and 2-nitroso-4-nitrochlorobenzene with sodium methoxide at 0° shows that the latter is more reactive [rate constants relative to 4-nitrochlorobenzene (K=1) are 6.73×10^5 and 5.22×10^6 respectively]. 2,4,6-Trichloronitrobenzene and also 2,4-dichloronitrobenzene with potassium fluoride in DMSO has been reported[54] to give the corresponding fluoro-compounds after 2 and 8 hours heating at 180°. The similar reaction with the di-, and tri- nitroso-benzenes was therefore expected to give the aromatic polyfluoro-nitroso-compounds, but the reaction failed to give any detectable ion-exchange products. The reaction of p-chloronitrosobenzene with methoxide ion in methanol has been reported[92] to give 4,4'-dichloroazoxybenzene instead of normal exchange reaction.

The result has been explained by the reactivity of the nitroso-group being greater towards reduction than substitution reactions. As the products of the reaction of 1,3,5-trichloro- and 1,3-dichloro-2-nitrosobenzenes with potassium fluoride after 2 and 6 hours reflux in dimethyl sulphoxide and also in sulpholan did not contain any fluorine, similar reduction processes may have taken place. The reaction mixtures were insoluble tars and attempts for the isolation of any pure substance from the tars failed.

19. The reaction of Octachloronaphthalene with Potassium Fluoride in Sulpholan and DMSO

A. Products of Fluorodechlorination of Octachloronaphthalene

In contrast to the corresponding reactions of polychlorobenzenes, reaction of octachloronaphthalene with potassium fluoride did not permit a full investigation of the exchange reaction because of the following reasons:

(i) The presence of many possible similar isomers of fluorochloronaphthalenes in every sample did not permit a clear identification of the individual isomer by ^{19}F n.m.r. spectroscopy, because of the lower signal-to-noise ratios.

(ii) The similarity of the chemical shifts of many isomers of the polyfluorochloronaphthalenes and the complex interaction of their fluorine absorption signals.

(iii) The lower solubility of octachloronaphthalene than those of fluorochloronaphthalene products, in the organic solvent caused difficulties in the analysis of the reaction mixtures.

The results of the fluorodechlorination of octachloronaphthalene using different conditions are listed in Tables 29, 30, 31 and 32.

Table 29

Molar % of the components of reaction of octachloronaphthalene (0.012 mole) with potassium fluoride (0.12 mole) in DMSO (20 ml) at ca. 140°C

Arene	Molar % of the components at time (t) t = 15	30	45	60 min
2-Fluoroheptachloronaphthalene				
(GLC)	42.3	10	-	-
(NMR)	45	12.00		
1-Fluoroheptachloronaphthalene				
(GLC)	38.8[a]	44.5[a]		
(NMR)	28[b]	43.50[b]		
2,7-Difluorohexachloronaphthalene				
(GLC)	8.9			
(NMR)	8.3	12.0	14.8	11.8
1,3-Difluorohexachloronaphthalene				
(NMR)	-	12.1	27	36
1,6-Difluorohexachloronaphthalene				
(NMR)	-	12.0	14.6	12.0
1,8-Difluorohexachloronaphthalene				
(GLC)	-	-	19.5[c]	17.8[c]
(NMR)	-	-	14	11.2
Total 1,3-, 1,6- and 2,7-Difluorohexachloronaphthalenes				
(GLC)	-	33.6	52.0	53.0
1,3,6-Trifluoropentachloronaphthalene				
(NMR)	-	3.8	8.1	12.0
1,3,8-Trifluoropentachloronaphthalene				
(NMR)	-	-	18.5[d]	17[d]
Total Trifluoropentachloronaphthalenes				
(GLC)	-	7.3	25.5	29.2
Octachloronaphthalenes				
(GLC)	10	4.6	3.0	-

(a) 1-Fluoroheptachloronaphthalene together with products of reduction.

(b) 1-Fluoroheptachloronaphthalene together with 1,8-difluorohexachloronaphthalene.

(c) 1,8-Difluorohexachloronaphthalene together with products of reduction.

(d) Together with tetrafluorotetrachloro-isomers or perhaps products from the reduction processes.

Table 30

Molar % of the components from the reaction of octachloronaphthalene (0.012 mole) with potassium fluoride (0.12 mole) in sulpholan (25 ml) at 142-145°C

Arene	Molar % of the components[a] at time (t) t = 1	2	3	4	5hrs
2-Fluoroheptachloronaphthalene	32.3	41.7	41.5	41.4	31.8
1-Fluoroheptachloronaphthalene[b]	5.7	14.8	25.0	36.5	46
2,7-Difluorohexachloronaphthalene	-	1.8	5.5	9.8	15.4
Octachloronaphthalene	62.0	41.7	28.0	12.3	6.8

(a) Results from GLC analysis

(b) Together with monofluorohexachloronaphthalene, a product of reduction, this isomer has been identified in ^{19}F n.m.r. spectroscopy of the reaction mixture.

Table 31

Yields (moles) of some major components from the reaction of octachloronaphthalene (0.025 mole), potassium fluoride (0.25 mole) in DMSO (30 ml) at ca. 150-160°C. (0.017 M 4-fluorobiphenyl has been used as a marker).

Arene	Moles of arenes[a] at time (t) t = 30	60	120 (mins)
2-Fluoroheptachloronaphthalene	0.0014	-	-
1-Fluoroheptachloronaphthalene	0.0019[b]	-	-
1,3-Difluorohexachloronaphthalene	-	0.01	0.0079

(a) From ^{19}F n.m.r. signal integrals.

(b) Together with 1,8-difluorohexachloronaphthalene.

Table 31 shows the molar yields of some components of the reaction of octachloronaphthalene with potassium fluoride in DMSO. These compounds were formed together with some other polyfluorochloronaphthalenes during this reaction, but the amount of none of the identified compounds exceed 0.01 M

during 2 hours reaction. The identification and determination of structure of all the products formed during this reaction was not possible, because of the difficulties mentioned before. G.l.c. analysis also failed to differentiate between isomeric compounds, but it showed that all the octachloronapthalene was consumed after one hour.

Table 32

Steam distilled products of the reaction of octachloronaphthalene (0.025 mole), and potassium fluoride (0.25 mole) sulpholan (25 ml) at ca. 220-225°C for 5 hours

Arene	Molar % of the fluoro-arene	
	GLC	Mass spec.
Tetrachlorotetrafluoronaphthalenes	4.9	1 - 2
Trichloropentafluoronaphthalenes	31.8	36
Dichlorohexafluoronaphthalenes	50 (a)	50
Monochloroheptafluoronaphthalenes	12.3	12 (b)
Octafluoronaphthalene	1.0	1 - 2

(a) Mixture of three isomers with ratios of 1 : 14 : 1

(b) Mixture of 60% α and 40% β-Chloroheptafluoronaphthalene

As seen in Tables 29 and 30 nucleophilic attack occurs more at β than α positions. The same preference has been reported for the reaction of octafluoronaphthalene by a number of nucleophiles[50,51] and some 2-X-heptafluoronaphthalenes have been prepared by this route. Reaction of 2-methoxy-heptafluoronaphthalene with methoxide ion in

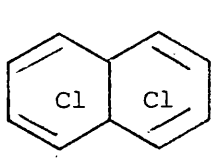
methanol has been reported[93] to give mainly the 2,6-disubstituted isomer, but some attack at C-7 has also been observed. In the present work ^{19}F n.m.r. spectroscopy showed a singlet at 102.8 p.p.m. for the fluorine signal of the first difluorohexachloronaphthalene was formed in the fluorodechlorination of the octachloronaphthalene (Table 42). This could be either 2,7-difluoro- or 2,6-difluorohexachloronaphthalene (both have two equivalent fluorine in the β-position), but because 2,7-difluoro-hexachloronaphthalene is the more preferred compound (page 73) the fluorine signal at 102.8 p.p.m. was assigned to this isomer.

Another investigation of the system is shown in Table 32. After 5 hours reaction in sulpholan the isomers of dichlorohexafluoronaphthalenes are the major products, while at higher temperatures (255-260°) after the same period, ocatchloronaphthalene (0.025 mole) with potassium fluoride (0.25 mole) in sulpholan (30 ml) gave octafluoronaphthalene as the main product (57 % yield). Octachloronaphthalene has been reported[63] to give octafluoronaphthalene (50-60% yield) after 14 hours heating with potassium fluoride at 230-240°C in sulpholan. Without added solvent, octachloronaphthalene gave[94] octafluoronaphthalene (28 %) and 1-chloroheptafluoronaphthalene (8 %) after 25 hours at 300-330°C. The results in Table 32 are in agreement with the earlier work. Table 31 shows that considerable amounts of 1,3-difluorohexachloronaphthalene (0.01 M) are obtained after one hour reaction. In the reaction of 2-methoxyheptafluoronaphthalene, however, displacement at C-1, C-3 and C-4 has not been observed[93a], because the methoxy substituent has only a weak activating effect upon positions meta to it compared to that of fluorine (Table 19, page 55), and deactivates sites ortho- and para- to it (Table 18, page 54).

In this work again the presence of the other isomers in each sample makes the preparation of the pure samples of the 1,3-difluorohexachloro-naphthalene of little value.

B. Orientation of Attack in Octachloronaphthalene

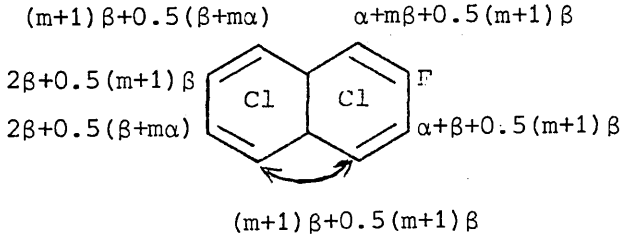
If we show the mesomeric effect of α- and β-chlorine transmitted across the ring in octachloronaphthalene (Figure 19, page 76), it could be predicted that α-position is deactivated by (+M) effect of one ortho- and one para-chlorine to it and also by (+M) effect of two chlorine from the second ring. Similarly β-position is deactivated by (+M) effect of two ortho-chlorine to it and also by (+M) effect of two chlorine from the second ring. The deactivating effects arising from the second ring has been found to be half of the effects if they arise from the same ring[93a]. Therefore the deactivating parameters at α- and β-positions is predicted to be [(m+1)β + 0.5 (m+1)β], and [2β + 0.5 (m+1)β] respectively:



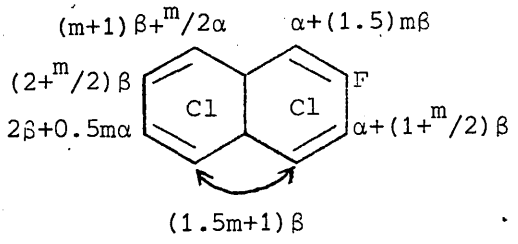
$(m+1)\beta+0.5(m+1)\beta$ or subtracting $(^{m}/_{2}+1)\beta = (m+0.5)\beta$

$2\beta+0.5(m+1)\beta$ $= 1.5\beta$

and the ease of formation of monofluoro-isomers is in the order β > α. Orientation of attack for the second fluorine is expected to be:



or: subtracting β/2:



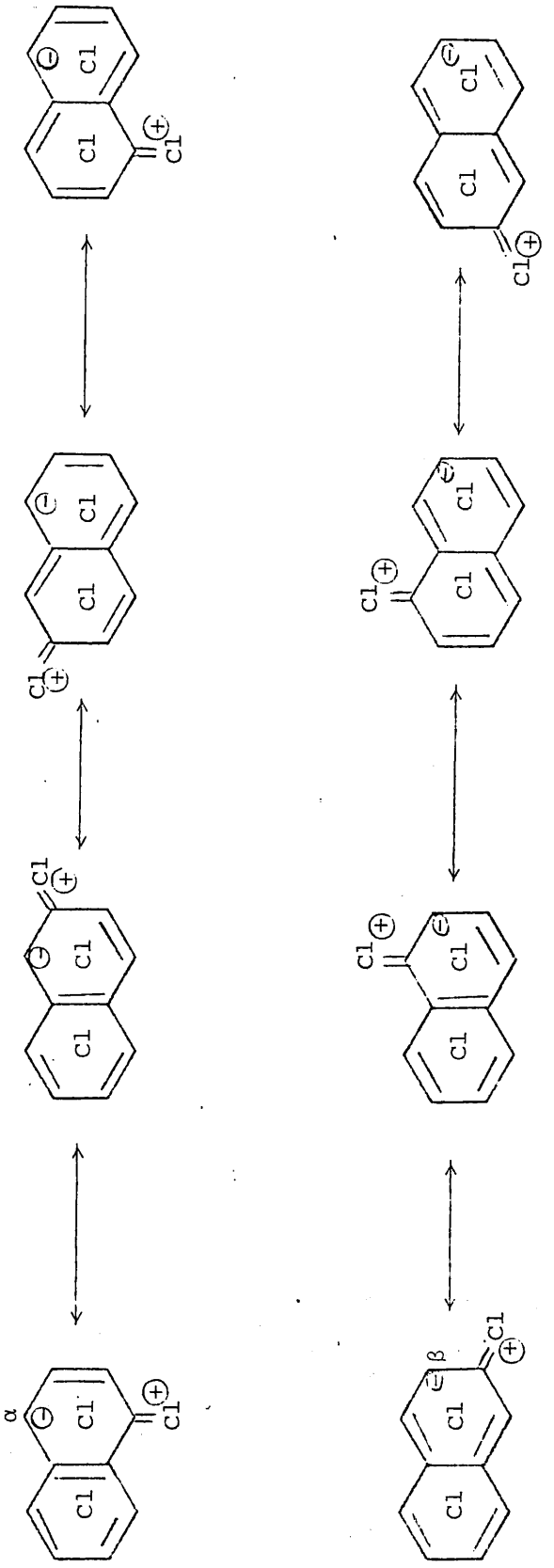
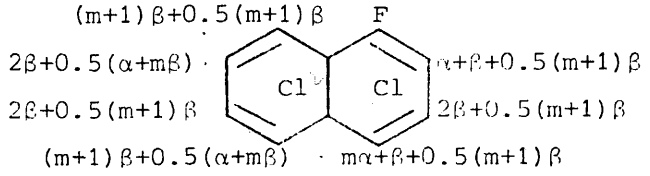
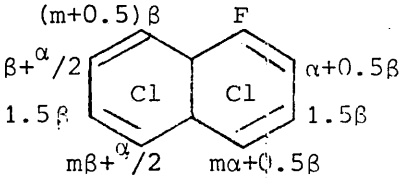


Figure 19

Therefore the order of attack is: C-7 > C-4 = C-5 > C-8 > C-6 > C-3 >C-1

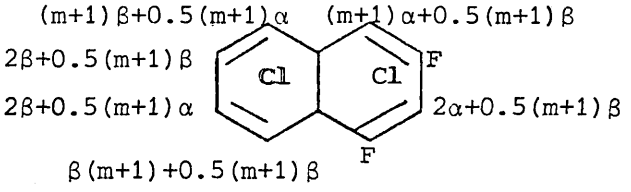


or: subtracting $(^{m}/2 + 1)\beta$

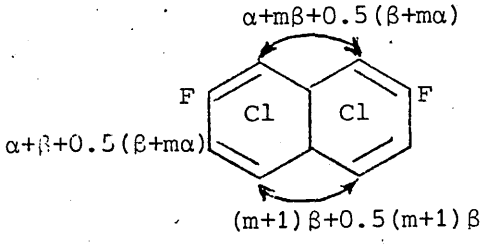


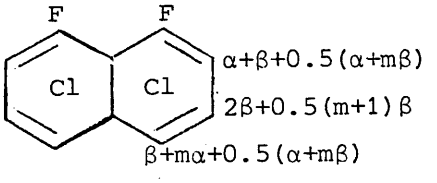
and order of attack is: C-3 = C-6 > C-8 > C-7 > C-5 > C-2 > C-4.

Orientation of attack for the third fluorine is predicted as below:



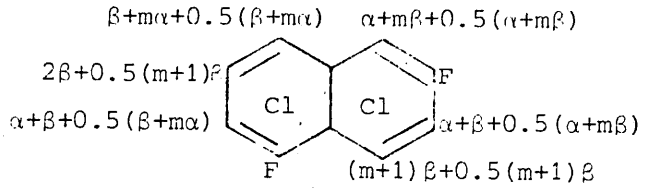
or attack C-7 > C-5 > C-6 > C-8 > C-3 > C-1





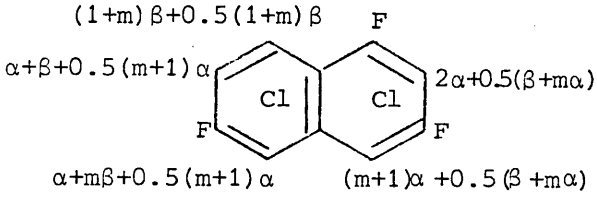
order of attack:

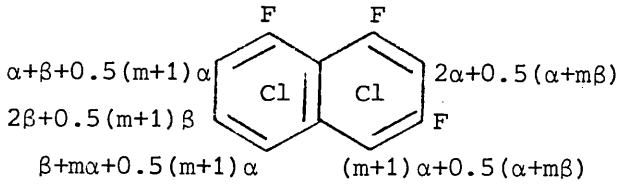
C-4 = C-5 > C-3 = C-6 > C-8 = C-1 , C-3 = C-6 > C-2 = C-7 > C-4 = C-5



The order of attack is: C-7 > C-4 > C-3 > C-1 > C-6 > C-8. So from this prediction of orientation the ease of formation of difluorohexachloronaphthalenes is in the order: 1,3-difluoro- $\cong$ 1,6-difluoro- $\cong$ 2,7-difluoro- > 1,8-difluorohexachloronaphthalene, and the ease of formation of trifluoropentachloronaphthalenes is in the order: 1,3,6-trifluoro->1,3,8-trifluoropentachloronaphthalene.

Orientation of attack for the fourth fluorine expected to be:





Therefore the order of attack is:

C-8 > C-7 > C-5 > C-2 > C-4 and C-6 > C-7 > C-2 > C-5 > C-4

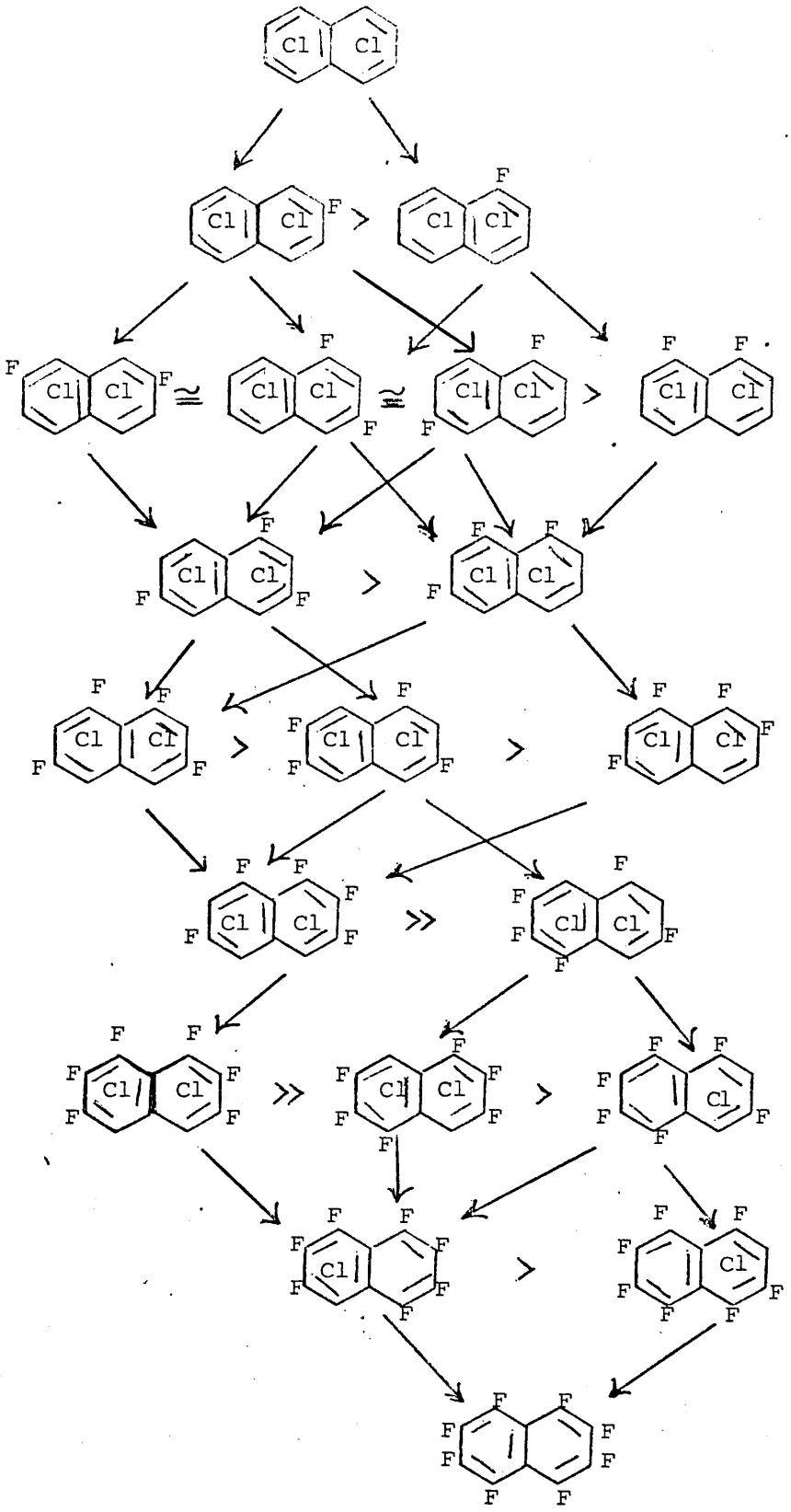
and the ease of formation of tetrafluorotetrachloronaphthalene is in the order: 1,3,6,8-tetrafluoro- > 1,3,6,7-tetrafluoro- > 1,3,7,8-tetrafluorotetrachloronaphthalene.

The similar prediction of orientation for formation of penta-, hexa- and hepta-fluoro isomers shows that the ease of formation of the

pentafluorotrichloronaphthalenes is in the order: 1,2,3,6,8-pentafluoro- > 1,2,3,5,7-pentafluorotrichloronaphthalene, that of hexafluorodichloronaphthalenes is 1,2,3,6,7,8-hexafluoro- >> 1,2,3,5,6,7-hexafluoro- > 1,2,3,4,5,7-hexafluorodichloronaphthalene and formation of heptafluoromonochloronaphthalenes is in the order: α-chloroheptafluoro- > β-chloroheptafluoronaphthalene. Results in the Tables 29 and 30 are in agreement with this prediction of orientation. Table 32 shows that the hexafluoro isomers are a mixture of three isomers in the ratios 1:14:1 (50% yield). The major components in this mixture could be 1,2,3,6,7,8-hexafluorodichloronaphthalene, which was predicted to be the most preferential isomer among the hexafluoro- isomers. Table 32 also shows that heptafluoromonochloronaphthalenes are a mixture of α-chloroheptafluoronaphthalene (60%) and β-chloroheptafluoronaphthalene (40%) which again is in agreement with the prediction of orientation. The formation of some isomers preferentially in fluorodechlorination of octachloronaphthalene could be shown in Scheme (I).

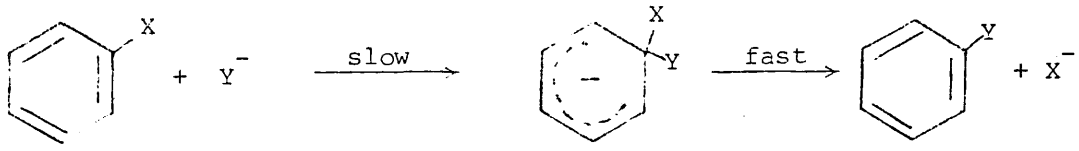
Scheme (I)

Sequential attack of octachloronaphthalene by fluoride ion



20. Investigation of the Mechanism of the Reaction of Polychloroaromatic Compounds with Potassium Fluoride in Sulpholan in the Presence of the Crown Ethers

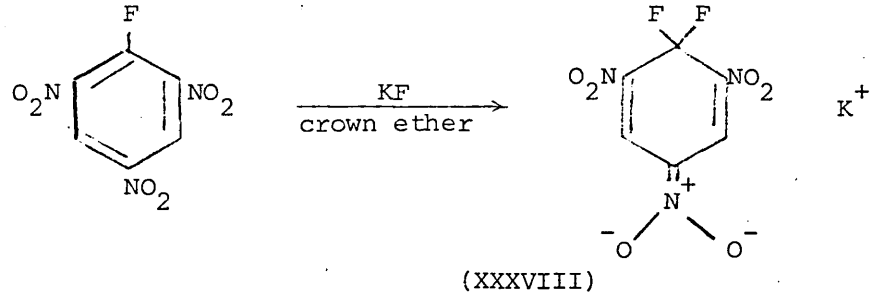
Aromatic nucleophilic substitution mechanisms was discussed before (page 17). Halogen displacement reaction could be represented as below:



(XXXVII)

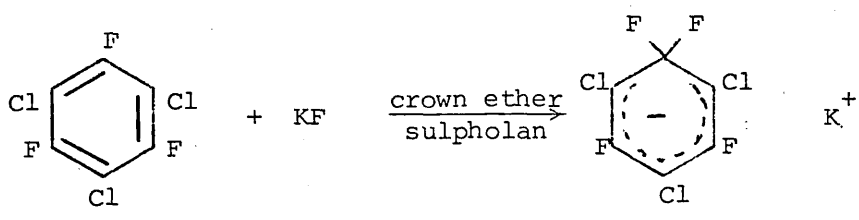
The first step is usually rate-determining in this reaction, since fluorine has been known to be by far the best leaving group among the halogens in the displacement reactions of activated halogeno-aromatic compounds and so, the second step of the above mechanism cannot be involved in the slow process. The effect of solvents on the displacement reactions was discussed earlier in pages 39-40 . Fluoride ion in dipolar aprotic solvents is a powerful nucleophile so that, SNAr fluoride-halogen exchange are at least 10^3 times faster in dipolar aprotic solvents than in alcohols[50] and dipolar aprotic solvents have been known[96] to increase the rates of many aromatic nucleophilic substitutions. These solvents facilitate the reactions by solvation of the charged intermediate complex (XXXVII), but the original charged nucleophile is less solvated in these solvents[97], because it is easier for the large anions to be solvated by the aprotic solvents since aprotic solvents have much looser structures to hold the small ions than the protic solvents which have structures held together by hydrogen bonds. Whether the intermediate complex (XXXVII) exists in all the reactions of polyhalogeno-aromatic compounds and is stable enough to permit its direct spectroscopic

observations is not known. The presence of stable intermediates have been observed in the activated nitrohalogenobenzenes (page 23). Liotta et. al.[85] have shown that the displacement reaction of 2,4-dinitrochlorobenzene with "naked" fluoride in acetonitrile occurs smoothly at room temperature and at reflux temperature rapid exchange reaction occurs to give 100% conversion to the corresponding fluoride, while the same reaction of the 2,4-dinitrochlorobenzene with potassium fluoride in aprotic solvents without presence of crown ethers has been reported[54] to give 77% yield after 60 minutes reaction at 140-150°C. Recent reaction of potassium fluoride with picryl fluoride in acetonitrile in the presence of 18-crown-6-ether has been reported to give a Meisenheimer-type intermediate complex (XXXVIII) which was sufficiently stable for direct n.m.r. observation:



(XXXVIII)

The ^{19}F n.m.r. spectroscopy on (XXXVIII) showed that the fluorine signal was shifted downfield ($\Delta\delta$ = 54 p.p.m.) compared with that of picryl fluoride. In the present work, sym-trifluorotrichlorobenzene was reacted with potassium fluoride in sulpholan, in the presence of crown-ether. If a similar intermediate complex existed there, the presence of structures such as (XXXIX) could have been observed by direct n.m.r. spectroscopy of the reaction mixture:



(XXXIX)

No intermediate complex could be observed in this case and in fact the reaction of fluoropentachlorobenzene, 2,3,5,6-tetrachlorofluorobenzene, or pentachlorotoluene with equal amount of crown-ethers (dicyclohexyl-18-crown-6-, and 18-crown-6-ethers) in the presence of an excess of potassium fluoride showed that, the reaction of polychlorofluoro arenes with "naked" fluoride does not lead to the rapid displacement reaction reported[85] for the reaction of 2,4-dinitrochlorobenzene. "Naked" fluoride here may mainly act as a base in aiding the polymerisation of the polychlorofluoro arenes or starting materials, and only traces of fluorodechlorination products were observed in ^{19}F n.m.r. spectroscopy of the reaction mixtures.

CHAPTER 3

EXPERIMENTAL

21. Purification and Preparation of Reagents and Solvents

A. Purification

Anhydrous potassium fluoride used in all the reactions was commercial anhydrous material, dried at 140°C for three hours and ground in a hot mortar before use. Sulpholan, was commercial material, solid at room temperature and was redistilled when necessary (b.p. 140/15 mm). DMF and DMSO were commercial materials. Hexa-, penta- and the tetrachlorobenzenes were commercial materials, purified by recrystallisation from ethanol before use. All other starting materials were prepared by literature methods (Section B).

B. Preparation

(a) Fluoropentachlorobenzene and 2,3,5,6-tetrachlorofluorobenzene

Fluoropentachlorobenzene (m.p. 138-9°) and 2,3,5,6-tetrachlorofluorobenzene (m.p. 71.5-72.5°) were prepared[54] from pentachloro-, and 2,3,5,6-tetrachloronitrobenzene respectively. The m.p. for both the products were in good agreement with the literature values. ^{1}H and ^{19}F n.m.r. spectroscopy were used for identification of the products:

Product	δ H[(a)] p.p.m.	δ F[(b)] p.p.m.	Coupling constant (Hz)
Fluoropentachloro-benzene	-	105	singlet
2,3,5,6-tetrachloro-fluorobenzene	7.5	103.7	F-H, 2.5

(a) Downfield of T.M.S. as an internal reference.

(b) Upfield of $CFCl_3$ as an internal reference.

(b) 2,3,4,5,6-Pentachlorotoluene

2,3,4,5,6-Pentachlorotoluene was prepared by the catalysed ($AlCl_3$, S_2Cl_2) chlorination (SO_2Cl_2) of toluene[98]. Presence of some condensation products of pentachlorotoluene ($C_6Cl_5-CH_2-C_6Cl_4-CH_3$) was identified in the proton n.m.r. spectra of the products:

Product	δ H[(a)] p.p.m.	group
2,3,4,5,6-Pentachlorotoluene	2.2[(b)]	$-CH_3$
Pentachlorophenyl-tetrachloro-tolyl methane	2.6	$-CH_2$

(a) Downfield of T.M.S. using $CDCl_3$ as solvent.

(b) Together with the $-CH_3$ proton signals of the pentachlorophenyl-tetrachlorotolyl methane.

Therefore many recrystallisations from benzene were needed to obtain pure material (m.p. 218-219°). The presence of five chlorine atoms in each molecule of the product was also identified by mass spectroscopy, which showed a molecular ion containing six peaks at: M/e = 262, 264, 266, 268, 270 and 272, in the relative amounts found (16:27:18:6:1:0.06).

(c) 2,3,4,5,6-Pentachloroanisole

Pentachloroanisole was prepared by the reaction of sodium pentachlorophenoxide and dimethyl sulphate, using the method described[99] for preparation of anisole (m.p. = 105°, lit. m.p. 108°).

^1H n.m.r. spectroscopy showed a sharp singlet downfield of T.M.S. at 3.93 p.p.m. referring to the presence of methoxyl-group.

(d) Pentachlorophenyl p-toluenesulphonate was prepared by the reaction of pentachlorophenol with p-toluenesulphonyl chloride in pyridine, the general method[100] described for preparation of the esters of phenols. The crude product was recrystallised from mixtures of ethanol and acetone and gave white needles melted at 150-152°.

Anal.	calc.	found
%C	37.09	37.00
%H	1.66	1.60

(e) Tetrachlorophthaloyl chloride (unsym-)

Tetrachlorophthalic anhydride was treated with phosphorus pentachloride at about 150° for 12 hours[101,102a]. After many recrystallisations from petroleum ether, white needles (m.p. 127-130°) were obtained (lit[102] m.p. sym-tetrachlorophthaloyl chloride 48°, unsym-tetrachlorophthaloyl chloride 137°).

Anal.	calc.	found
%C	28.15	28.50

(f) 1,3-Dichloro-, and 1,3,5-trichloro-2-nitrosobenzenes

Nitroso-compounds were prepared[103] from oxidation of the corresponding amines with mixtures of glacial acetic acid and aqueous hydrogen peroxide in concentrated sulphuric acid.

1,3,5-Trichloro-2-nitrosobenzene (m.p. 140°, lit.[103] m.p. 145-146°)

Anal.	calc.	found
%C	34.20	35.0
%H	0.95	0.95
%N	6.65	6.67

1,3-Dichloro-2-nitrosobenzene (m.p. = 170-172°, lit.[103] m.p. = 173-175°).

Anal.	calc.	found
%C	40.90	43.1
%H	1.70	1.70
%N	7.95	8.0

(g) Octachloronaphthalene

Naphthalene was reacted with chlorine in sulphuryl chloride, with powdered iron as the catalyst. G.l.c. analysis was used to estimate the purity of the sample. The purest compound obtained after several recrystallisations from mixture of bezene and petroleum ether contained 1% heptachloronaphthalene (m.p. 200°, lit[104] m.p. 208, lit.[102] m.p. 190-196°).

(h) 2-Chloroheptafluoronaphthalene

Octafluoronaphthalene gave heptafluoro-2-naphthylhydrazine on treatment with hydrazine hydrate in ethanol[50]. This reacted with cupric chloride in concentrated hydrochloric acid to give the corresponding chloride (m.p. 59-60°). G.l.c. and ^{19}F n.m.r. were used for the identification of the product (Table 33).[52]

(i) Fluoroheptachloronaphthalenes

An attempt was made to prepare α-, and β-fluoroheptachloronaphthalene from α- and β-fluoronaphthalenes but neither prolonged chlorination with chlorine in the presence of a catalyst ($FeCl_3$) at 50-60°, nor chlorination with sulphuryl chloride in the presence of S_2Cl_2 and $AlCl_3$ gave satisfactory results. In all cases presence of aromatic protons in the ^1H n.m.r. spectra of the products showed that hydrogen had not been completely replaced by chlorine.

22. Instrumentation

A. ^{19}F N.M.R.

The n.m.r. machine (Perkin-Elmer R12B) was operated at 60 MHz for ^{1}H nuclei and 56.4 MHz for ^{19}F nuclei. ^{1}H chemical shifts are to low field of tetramethylsilane (TMS) the internal standard and reference, and ^{19}F chemical shifts to upfield of trichlorofluoromethane, the internal or in some cases, external reference. All the chemical shifts are in p.p.m. from the named reference signal, and for ^{19}F the shifts occurred within the range δ = 99 to ca. 160 p.p.m.

Analysis of the system was assisted by:

1. The splitting of the fluorine signals arising from the coupling of the fluorine atoms to both fluorine and hydrogen atoms.

2. Synthesis of authentic samples for comparison in some cases.

3. Comparing the chemical shifts with those calculated from the additivity calculus method[46].

4. The agreement between the relative ease of nucleophilic displacement and the derived values found from these fluorodechlorination studies.

B. Gas Chromatography (G.L.C.)

G.l.c. (Pye 104) analysis was the only method for measuring the amount of the unreacted polychloroarenes (starting materials). Methyl silicone (OV-1) and Apiezon L were used as liquid phase, but methyl silicone gum has been found to be more effective than the other phases. Although differentiation between isomeric compounds in most cases was not possible by this analytical method, the relative amounts of total isomers of mono-, di-, tri-, tetra-,..... fluorochloroarenes found by n.m.r. and g.l.c. were in good agreement. G.l.c. analysis of the components in each reaction was assisted by:

1. Comparison with other spectroscopic methods (n.m.r., mass spectroscopy).

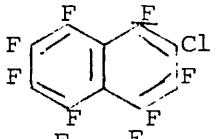
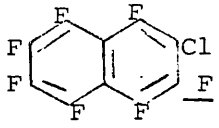
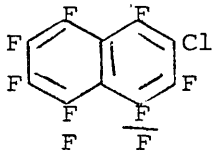
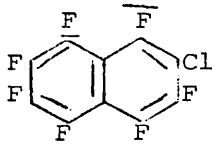
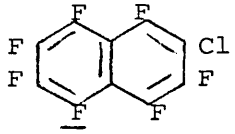
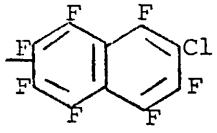
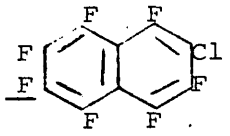
2. Comparison with authentic samples in some cases.

C. Tables

Table 33

^{19}F N.m.r. and g.l.c. properties of 2-chloroheptafluoronapthalene

^{19}F N.m.r.

Position of F	δ p.p.m.	Coupling constant (Hz)
	119.5	F_1-F_8 , 64
	135.5	o, F-F , 20 m, F-F , 2.5
	143.3	F_4-F_5 , 56.5
	144.5	F_1-F_8 , 64
	145.6	F_4-F_5 , 56.5
	153	o, F-F , 30
	154	o, F-F , 33

G.l.c. analysis. Column OV-1. Temp. 150°C

Arene	retention time (min)
2-Chloroheptafluoronaphthalene	1.4

Table 34

^{19}F n.m.r. chemical shifts and coupling constants of fluorine containing products from the reaction of hexachlorobenzene with potassium fluoride in sulpholan at ca. 250°

Arene	F atom	Exp.δ	lit.δ	Coupling constants(Hz)
Fluoropentachlorobenzene	1	105.0	106[b]	
1,3-Difluoro-2,4,5,6-tetrachlorobenzene	1,3	109.0	109.1[a]	
1,2-Difluoro-3,4,5,6-tetrachlorobenzene	1.2	130.5	130.9[a]	
1,4-Difluoro-2,3,5,6-tetrachlorobenzene	1,4	110.8	111.1[a]	
1,3,5-Trifluoro-2,4,6-trichlorobenzene	1,3,5	112.6	112.5[a]	
1,2,3-Trifluoro-4,5,6-trichlorobenzene	1,3	130.0	130.1[a]	F_1-F_2 , 18.6
	2	155.5	155.3[b]	
1,2,4-Trifluoro-3,5,6-trichlorobenzene	1	136.0	135.8[a]	F_1-F_2 , 18.6
	2	134.5	134.2[a]	F_1-F_4 , 10
	4	114.4	114.3[a]	
1,2,3,5-Tetrafluoro-4,6-dichlorobenzene[c]	5	118.3	118.4[b]	F_2-F_5 , 10
	1,3	134.5	134.5[b]	F_1-F_2 = F_2-F_3 , 18.6
				F_3-F_5 = F_1-F_5 , 2
	2	160.5	160.60[b]	F_2-F_1 = F_2-F_3 , 18.6

(a) C.H. Dungan and J.R. Van Wazer, Compilation of Reported ^{19}F n.m.r. Chemical Shifts, Wiley Interscience, N.Y. (1970)

(b) Emsley, Feeney and Sutcliffe, Progress In Nuclear Resonance Spectroscopy, Vol. 7, (1971)

(c) Product from the reaction of fluoropentachlorobenzene with potassium fluoride (page 56).

Table 35

^{19}F N.m.r. chemical shifts of fluorine-containing products from the reaction of pentachlorobenzene and 2,3,5,6-tetrachlorofluorobenzene with potassium fluoride in sulpholan

Arene[(a)]	F atom	exp. δ	calc.δ[(b)]	Coupling constant (Hz)
(A)	1	109.5	111.2	F-H , 9.6
(B)	1	110.0	109.0	F-H , 7.2
(C)	1	103.7	109.6	F-H , 2.4
(D)	1	133.9	135.7	F_1-F_2 , 21.6 ; F_2-H_6
	2	132.2	133.5	7.8 ; F_1-H_6 , 10
(E)[(c)]	1	113	111.2	F_1-F_3 , 2 ; F_1-H_6 , 8.4
	3	106.7	109.6	F_3-H_6 , 2
(F)	1	135.5	133.5	F_1-F_2 , 19 ; F_1-H_5 , 7
	2	128.8	134	F_2-H_5 , 2
(G)	2,4	112.6	109	F-H , 7.2
(H)	1,5	107.8	111.2	F-H , 9.6
(I)[(d)]	1,5	110.4	111.2	F_1-F_3 , 2 ; F_3-H_6 ,
	3	111.8	109.6	not resolved; F_1-H_6 , 9.6
(N)[(e)]	2,3	142	-	F-F , 18.0 ; F-H , 6.0

(a) Appendix I, page 110.

(b) Ref. 46.

(c) Same structure with the same coupling constant has been observed in ^1H n.m.r. spectrum of the mixture.

(d) Reported[74], $F_1 = F_5$ at 110.3; F_3 at 111.9 p.p.m.

(e) Structure suggested by quartet in n.m.r. spectroscopy and also on the appearance of a peak with retention time of slightly greater than those of polyfluoro-2,4-dichlorobenzenes.

Table 36

^{19}F N.m.r. chemical shifts and coupling constants of components of reaction of 1,2,3,5-tetrachlorobenzene and 1,2,3,4-tetrachlorobenzene with potassium fluoride in sulpholan.

Arene[a]	exp.δ[b]	calc.δ[c]	Coupling constants (Hz)
(O)	106.1	111.8	F_1-H_4 , 1.9 ; F_1-H_6 , 8.2
(V)	106.0	109.6	F_1-H_4 , 1.4 ; F_1-H_5 , 4.2
(W)	107.2	111.2	F_1-H_5 , 4.2 ; F_1-H_6 , 7.8
(P)	116.6[d]	109.0	triplet ; F_1-H_3 , 6
(Q)	110.6	113.4	triplet ; F_1-H_2 , 8
(R)	109.7	108.8	quartet ; F_1-H_6 , 8 ; F_1-H_4 , 1
(S)	104.6	107.9	triplet ; F_1-H_2 , 6 ;
	108.5	109.4	triplet ; F_3-H_2 , 8
(T)	110		triplet ; F_1-H_2 = F_1-H_6, 8

(a) Appendix II, page 112.

(b) Using tetrachloromethane as solvent and trichlorofluoromethane as external reference.

(c) Ref. 46.

(d) Authentic compound was prepared[105] and gave the identical chemical shift.

Table 37

Retention times of the isomers of trichlorobenzenes

Trichlorobenzene	Retention time (min)
Column: Temp.°C	Apiezon L 120
1,2,3-Trichlorobenzene	20
1,2,4-Trichlorobenzene	15
1,3,5-Trichlorobenzene	13

Table 38

Retention times of the components of reaction of 1,2,3,5-tetrachlorobenzene with potassium fluoride in sulpholan

Arene	Retention time (min) Column OV-1	OV-1	Apiezon L
	Temp. °C 65	80	120
(R)	4	2	2.2
(S)	5.2	2.5	4.4
(T)	6.3	3	5.1
(Q) and (P)	17.2	7.9	16.4
(O)	22.4	9	16.4
1,2,3-Trichlorobenzene	-	-	18.5 (a)
1,2,3,5-Tetrachlorobenzene	-	25.2	48.5
4-Fluorobiphenyl (b)	-	35.6	48.5
Sulpholan	-	7	10

(a) Authentic compound identical

(b) Was used as a marker in the exchange reaction.

Table 39

Retention times of components of reaction of 1,2,3,4-tetrachlorobenzene with potassium fluoride in sulpholan

Arene	Retention time (min) Column OV-1	Temp. °C 90
(V) and (W)		6.8
1,2,3,4-Tetrachlorobenzene		21

Table 40

^{19}F N.m.r. chemical shifts and coupling constants of fluorine-containing products from the reaction of 2,3,4,5,6-pentachlorotoluene with potassium fluoride in sulpholan

Arene[a]	F atom	Exp.δ	Calc.δ[b]	Coupling constant (Hz)
2-Fluoro-3,4,5,6-tetrachlorotoluene (A)		110	111.2	quartet F_2-H_α, 2.5
3-Fluoro-2,4,5,6-tetrachlorotoluene (B)		107	109	singlet; slightly broadened
4-Fluoro-2,3,5,6-tetrachlorotoluene (C)		108.3	109.6	singlet
2,4-Difluoro-3,5,6-trichlorotoluene (E)	F_2	114	111.2	broad, not resolved
	F_4	111.9	109.6	sharp singlet
2,6-Difluoro-3,4,5-trichlorotoluene (H)		112.1	111.2	broad, not resolved
3,5-Difluoro-2,4,6-trichlorotoluene (G)		111.3	111.2	singlet, slightly broadened

(a) Appendix I

(b) Ref. 46

Table 41

^{19}F N.m.r. chemical shifts and coupling constants of fluorine-containing products from reaction of octachloronaphthalene with potassium fluoride

Arene	F atom	δ $CFCl_3$	Coupling constant (Hz)
1-Fluoroheptachloronaphthalene	-	108.8	
2-Fluoroheptachloronaphthalene	-	102 (a)	
2,7-Difluorohexachloronaphthalene	-	102.8	
1,8-Difluorohexachloronaphthalene	-	109	
1,3-Difluorohexachloronaphthalene	F_3	102	F_1-F_3 , 1.5
	F_1	111.8	
1,6-Difluorohexachloronaphthalene	F_6	101	F-F , 3.7
	F_1	111.0	
1,3,6-Trifluoropentachloronaphthalene	F_3	101	F_1-F_6 , 3.7
	F_6	107.9	F_3-F_6 , 5
	F_1	112.8	
1,3,8-Trifluoropentachloronaphthalene	F_1	106	not resolved
	F_8	105.5	
	F_3	104.9	
6-Fluoro-2H-hexachloronaphthalene (b)		99	singlet
4-Fluoro-1H-hexachloronaphthalene (b)		109.5	F-H , 3

(a) lit.[106] δ = 103 p.p.m.

(b) Reduction products. Presence of these reduction products has also been observed in the ^1H spectrum of the mixture.

Table 12

Observed and calculated[(a)] ^{19}F n.m.r. shifts of polychlorofluoronapthalenes formed during the reaction of octachloronaphthalene with potassium fluoride

Arene	F atom	δ $CFCl_3$ obs.	δ calc.
1-Fluoroheptachloronaphthalene		108.8	112.45
2-Fluoroheptachloronaphthalene		102	102.75
2,7-Difluorohexachloronaphthalene	2,7	102.8	100.75
1,8-Difluorohexachloronaphthalene	1,8	109	110.45
1,3-Difluorohexachloronaphthalene	1	111.8	108.45
	3	102	98.75
1,6-Difluorohexachloronaphthalene	1	111.0	110.45
	6	101	100.75
1,3,6-Trifluoropentachloronaphthalene	1	112.8	106.45
	3	101.0	96.75
	6	107.9	98.75
1,3,8-Trifluoropentachloronaphthalene	1	105.5	106.45
	3	104.9	96.75
	8	106.5	108.45
4-Fluoro-1H-hexachloronaphthalene	4	109.5	110.95
6-Fluoro-2H-hexachloronaphthalene	6	99	102.0

(a) Using octafluoronaphthalene (δ F_1 = 146, δ F_2 = 155 p.p.m.)[107] as standard and considering that in fluorobenzene, o-F raises δ by 25 p.p.m., m-F lowers δ by 4 p.p.m., p-F raises δ by 6 p.p.m., o-Cl raises δ by 1.8 p.p.m., m-Cl raises δ by 0 p.p.m. and p-Cl raises δ by 1.5 p.p.m. The effect of second ring halogens on each ring, has been considered as half of the effect of its own halogens. Thus, δ for 2-fluoroheptachloro naphthalene is:

155 - 2 x 25 - 15.5 + 4 + 2 + 2 + 1.8 + 1.8 + 1.65 = 102.75 p.p.m. and

δ for 1-fluoroheptachloronaphthalene is:

146 - 25 - 6 - 15.5 + 4 + 2 + 2 + 1.8 + 1.5 + 1.65 = 112.45 p.p.m.

Table 43

Retention times of the components in the reaction of pentachlorobenzene with potassium fluoride

Arene[a]	Retention time (min)	
Column	OV-1	OV-1
Temp. °C	100	80
Trifluorodichlorobenzene (I)	1	2.3
Total difluorotrichlorobenzenes (D), (E), (F), (G) and (H)	3.2	7.8
Total monofluorotetrachlorobenzenes (A), (B) and (C)	9.9	24.4
Pentachlorobenzene	27.6	-

(a) Appendix I

Table 44

G.l.c. analysis on the products from the reaction of octachloronaphthalene with potassium fluoride in sulpholan at 220-225° for 5 hours

Arene	Retention time (min)	
	Column	Apiezon L	OV-1
	Temp.°C	200	150
Tetrachlorotetrafluoronaphthalenes		30	21
Trichloropentafluoronaphthalenes		21	9 - 9.6[a]
Dichlorohexafluoronaphthalenes		8	3.6 - 3.8[a]
Monochloroheptafluoronaphthalenes		3	1.4[b]
Octafluoronaphthalene		1	0.5

(a) Two peaks for each mixture of isomers

(b) Authentic sample identical

Table 45

Mass spectroscopy on the products from the reaction of octachloronaphthalene with potassium fluoride in sulpholan at 220 - 225°C for 5 hours

Arene	M/e (top peak)	Ratios
Tetrachlorotetrafluoronaphthalenes	336-338-340-342-344	81:108:54:12:1
Trichloropentafluoronaphthalenes	320-322-324-326	27:27:9:1
Dichlorohexafluoronaphthalenes	304-306-308	9:6:1
Monochloroheptafluoronaphthalenes	288-290	3:1
Octafluoronaphthalene	272	-

Table 46

^{19}F N.m.r. chemical shifts and retention times of the components from the reaction of octachloronaphthalene with potassium fluoride in sulpholan at 142 - 144° for 5 hours

Arene	Retention time (min) G.L.C.(a)	δ $CFCl_3$ ^{19}F N.M.R.
2-Fluoroheptachloronaphthalene	14.4	102.0
1-Fluoroheptachloronaphthalene	8	108.8
2,7-Difluorohexachloronaphthalene	4	102.8
Octachloronaphthalene	23.8	-

(a) Using OV-1 Column at 240°C.

Table 47

^{19}F N.m.r., g.l.c. and mass spectroscopy of products from the reaction of octachloronaphthalene with potassium fluoride in sulpholan at 255 - 260° for 5 hours

Arene	G.l.c.(b) ret.time (min)	Mass spect. M/e	No. of F	δ $CFCl_3$	Coupling constant (Hz)
Octafluoro-naphthalene(a)	1.6	272	F_1	145	o F-F , 17
			F_2	154	m F-F , 2.8
Monochlorohepta-fluoronaphthalenes	10	288-290	-		
Dichlorohexafluoro-naphthalenes	-	304-306-308	-		

(a) Main product (57% yield)

(b) Apiezon L Column at 180°C

23. General Method of Following the Course of the Reactions

A stirred mixture of the organic polychloroarene with anhydrous dry potassium fluoride (molar ratios 0.1 : 1.0) in the aprotic solvents (sulpholan or in some cases DMSO) were heated under reflux with the exclusion of moisture at the temperatures indicated in each case (Chapter 2). Samples were taken from the boiling reaction mixtures and were quenched in water. Organic compounds were usually extracted by fluorotrichloromethane or in some cases, by other solvents like tetrachloro-, or trichloromethane. The compounds of these extracts were then characterised by ^{19}F n.m.r. spectroscopy and g.l.c. In some cases where the calculation of the composition of the reaction mixtures from ^{19}F n.m.r. integrals was not accurate (poor signal-to-noise ratios), mass spectroscopy together with gas chromatography were used for the analysis of the mixtures. In some reactions 4-fluorobiphenyl has been used as a marker for calculation of the composition of the reaction mixtures.

24. Extraction of the Tars

In some exchange reactions considerable amount of tars were formed which were not soluble in chlorinated organic solvents, such as fluorotrichloromethane, chloroform, carbon tetrachloride, dichloromethane or in benzene and toluene. Reaction of 2,3,4,5,6-pentachlorotoluene or 1,2,3,5-tetrachlorobenzene with potassium fluoride in sulpholan gave a considerable amount of tarry materials. After the isolation of steam volatile products from these tars, the residues were Soxhlet extracted (using petroleum ether b.p. ($60-80^{\circ}$)) and then purified by column chromatography (using alumina column) or by recrystallisation, without obtaining any pure products for identification.

25. Reaction of Polychloro-arenes with Potassium Fluoride in Sulpholan in the Presence of Crown Ethers

The polychloroarene (2.5 g) with anhydrous dry potassium fluoride (1.0 g) and 18-crown-6-ether (2.5 g) in sulpholan (10 ml) were stirred and heated at about 200° (for 2,3,4,5,6-pentachlorotoluene, about 270°). Samples were taken at 30 and 60 minutes for direct ^{19}F n.m.r. observation. The rest of the reaction mixtures were heated under reflux for one more hour, then quenched in water and extracted with trichlorofluoromethane or tetrachloromethane and analysed as before.

26. Derivation of the Kinetic Form

In this section of the thesis, the basis for the complex kinetic form is established. Although the following derivation is not rigorous it indicates the way in which the more complicated kinetic equations are obtained.

If compound A_o with an initial concentration of $C_o^{(o)}$ reacts with an excess of B by a first order kinetic process, to give A_1, and this A_1 is converted to A_2 which in the third stage is transformed into A_3. The specific first order rate constants for these reactions are, respectively, k_1, k_2 and k_3.

The course of the reactions is shown in the scheme below:

$$\underset{C_o^{(o)}}{A_o} \xrightarrow{k_1} \underset{C_1}{A_1} \xrightarrow{k_2} \underset{C_2}{A_2} \xrightarrow{k_3} \underset{C_3}{A_3}$$

where C_o, C_1, C_2 and C_3 are the concentrations at time (t,) and and $C_o^{(o)}$ is the initial concentration of the starting material A_o.

The concentration of any substance which has reacted by the time (t,) can be expressed by one of the following equations:

For substance A_o $\quad C_o^{(o)} - C_o$,

For substance A_1 $\quad C_o^{(o)} - C_o - C_1$,

For substance A_2 $\quad C_o^{(o)} - C_o - C_1 - C_2$,

For substance A_3 $\quad C_o^{(o)} - C_o - C_1 - C_2 - C_3 = o$

Assuming the rate at which each substance is consumed, to be proportional to its concentration, we can write the following set of equations:

$$\frac{d(C_o^{(o)} - C_o)}{dt} = k_1' C_o Z \qquad \ldots\ldots (1)$$

$$\frac{d(C_o^{(o)} - C_o - C_1)}{dt} = k_2' C_1 Z \qquad \ldots\ldots (2)$$

$$\frac{d(C_o^{(o)} - C_o - C_1 - C_2)}{dt} = k_3' C_2 Z \qquad \ldots\ldots (3)$$

$$\frac{d(C_o^{(o)} - C_o - C_1 - C_2 - C_3)}{dt} = o \qquad \ldots\ldots (4)$$

Where Z is a constant proportional to the concentration of B. As $[B] >> [A_o]$, we can introduce the constant Z into the rate constants and after a few rearrangements we have:

$$\frac{dC_o}{dt} = K_1 C_o \qquad \ldots\ldots (5)$$

$$\frac{dC_1}{dt} = K_1 C_o - K_2 C_1 \qquad \ldots\ldots (6)$$

$$\frac{dC_2}{dt} = K_2 C_1 - K_3 C_2 \qquad \ldots\ldots (7)$$

$$\frac{dC_3}{dt} = K_3 C_2 - o \qquad \ldots\ldots (8)$$

Here $K_1=K'_1Z$, $K_2=K'_2Z$, $K_3=K'_3Z$.

If we replace the unknown functions $(\frac{d}{dt})$ by their transforms (P), the above equations will change to the following equations:

$$PC_o - PC_o^{(o)} = -K_1C_o \quad \ldots\ldots (9) \quad \text{or:} \quad C_o = \frac{PC_o^{(o)}}{(P+K_1)}$$

$$PC_1 = K_1C_o - K_2C_1 \quad \ldots\ldots (10) \quad \text{or:} \quad C_1 = \frac{K_1PC_o^{(o)}}{(P+K_2)(P+K_1)}$$

$$PC_2 = K_2C_1 - K_3C_2 \quad \ldots\ldots (11) \quad \text{or:} \quad C_2 = \frac{K_1K_2pC_o^{(o)}}{(P+K_3)(P+K_2)(P+K_1)}$$

$$PC_3 = K_3C_2 - 0 \quad \ldots\ldots (12) \quad \text{or:} \quad C_3 = \frac{K_1K_2K_3C_o^{(o)}}{(P+K_3)(P+K_2)(P+K_1)}$$

(The initial concentration of substance A_o is $C_o^{(o)}$, while the initial concentrations of each of the other substances is zero).

We shall next use formulas 4,5,6 and 7 in Appendix (III). To replace the transforms of the unknown function C_o, C_1, C_2 and C_3 by their originals:

$$C_o = C_o^{(o)} \; e^{-Kt} \quad \ldots\ldots (13)$$

$$C_1 = C_o^{(o)} \left[\frac{K_1}{K_1-K_2} e^{-K_1t} + \frac{K_1}{K_1-K_2} e^{-K_2t}\right] \quad \ldots\ldots (14)$$

$$C_2 = C_o^{(o)} \left[\frac{K_1K_2}{(K_2-K_1)(K_3-K_1)} e^{-K_1t} + \frac{K_1K_2}{(K_1-K_2)(K_3-K_2)} e^{-K_2t}\right.$$

$$\left. + \frac{K_1K_2}{(K_1-K_3)(K_2-K_3)} e^{-K_3t} , \right] , \quad \ldots\ldots (15)$$

$$C_3 = C_o^{(o)} \left[1 - \frac{K_2K_3}{(K_2-K_1)(K_3-K_1)} e^{-K_1t} - \frac{K_1K_3}{(K_1-K_2)(K_3-K_2)} e^{-K_2t}\right.$$

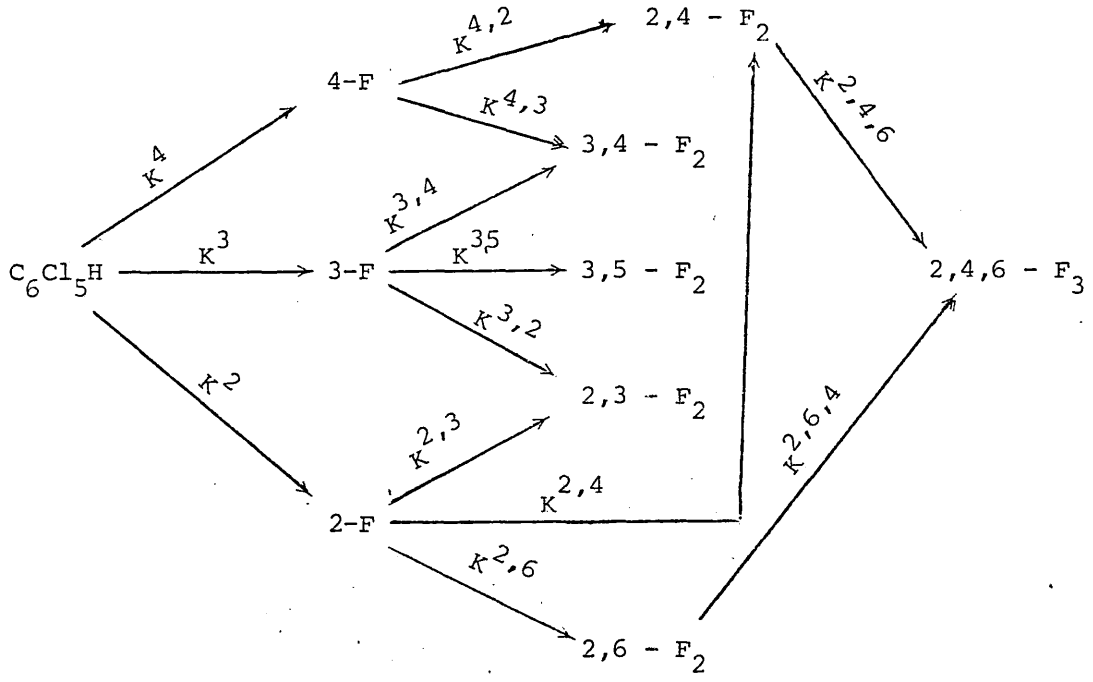
$$\left. - \frac{K_1K_2}{(K_1-K_3)(K_2-K_3)} e^{-K_3t} \right] \quad \ldots\ldots (16)$$

The concentration of the last substance C_3, can also be determined by another method, as the difference between the initial concentration of the initial substance and the sum total of all the concentrations of all substances participating in the reaction:

$$C_3 = C_o^{(o)} - (C_o + C_1 + C_2) \qquad \ldots\ldots \quad (17)$$

Reaction of pentachlorobenzene with potassium fluoride:

If we show all the necessary steps in the reaction of pentachlorobenzene with potassium fluoride in the Scheme II, where the pseudo first-order rate constants are distinguished by superscripts which, reading from left to right, indicate the order in which fluoride ions are introduced into pentachlorobenzene (H = 1).



Scheme (II)

Therefore, the formation of 1,2-difluoro-3,4,5-trichlorobenzene (2,3 - F_2) is controlled by two rate constants : $K^{3,2}$ is associated with attack upon the 2,4,5,6-tetrachlorofluorobenzene (3-F), and $K^{2,3}$ with attack upon the 2,3,4,5-tetrachlorobenzene (2-F). If a^1 is the rate

constant for the consumption of the pentachlorobenzene, so the concentration of the pentachlorobenzene at time (t,) according to the equation (9) is:

$$[C_6Cl_5H]_t = \frac{p[C_6Cl_5H]_o}{p + a^1}$$

or $$[C_6Cl_5H]_t = [C_6Cl_5H]_o \, e^{-a^1 t}$$

Taking a^1, a^2, a^3 and a^4 as the rates of consumption of starting materials and the monofluorinated isomers then:

$$a^1 = 2K^2 + 2K^3 + K^4$$

$$a^2 = K^{2,3} + K^{2,4} + K^{2,6}$$

$$a^3 = K^{3,4} + K^{3,5} + K^{3,2}$$

$$a^4 = K^{4,2} + K^{4,3}$$

and the instantaneous concentration of the mono-fluorinated isomers according to the equation (10) becomes:

$$p[4\text{-}F]_t = K^4[C_6Cl_5H]_t - a^4[4\text{-}F]_t$$

$$p[3\text{-}F]_t = K^3[C_6Cl_5H]_t - a^3[3\text{-}F]_t$$

$$p[2\text{-}F]_t = K^2[C_6Cl_5H]_t - a^2[2\text{-}F]_t$$

or $$[4\text{-}F]_t = \frac{K^4[C_6Cl_5H]_t}{[p + a^4]}$$

$$[3\text{-}F]_t = \frac{K^3[C_6Cl_5H]_t}{[p + a^3]}$$

$$[2\text{-}F]_t = \frac{K^2[C_6Cl_5H]_t}{[p + a^2]}$$

Then,

$$[4\text{-F}]_t = \frac{K^4 p[C_6Cl_5H]_o}{(p+a^1)(p+a^4)}$$

$$[3\text{-F}]_t = \frac{K^3 p[C_6Cl_5H]_o}{(p+a^1)(p+a^3)}$$

$$[2\text{-F}]_t = \frac{K^2 p[C_6Cl_5H]_o}{(p+a^1)(p+a^2)}$$

and according to the equation (14)

$$[4\text{-F}]_t = K^4[C_6Cl_5H]_o\left[\frac{e^{-a^1 t}}{a^4 - a^1} + \frac{e^{-a^4 t}}{a^1 - a^4}\right]$$

or:

$$= \frac{K^4}{a^1 - a^4}[C_6Cl_5H]_o\ [e^{-a^4 t} - e^{-a^1 t}]$$

similarly:

$$[3\text{-F}]_t = \frac{K^3}{a^1 - a^3}[C_6Cl_5H]_o\ [e^{-a^3 t} - e^{-a^1 t}]$$

and:

$$[2\text{-F}]_t = \frac{K^2}{a^1 - a^2}[C_6Cl_5H]_o\ [e^{-a^2 t} - e^{-a^1 t}]$$

and the instantaneous concentrations of the difluoro-isomers according to the equations (10), (11) and (12) are:

$$p[2,4\text{-F}_2]_t = K^{4,2}[4\text{-F}]_t + K^{2,4}[2\text{-F}]_t - K^{2,4,6}[2,4\text{-F}_2]_t$$

$$p[3,4\text{-F}_2]_t = K^{4,3}[4\text{-F}]_t + K^{3,4}[3\text{-F}]_t$$

$$p[3,5\text{-}F_2]_t = K^{3,5}[3\text{-}F]_t$$

$$p[2,3\text{-}F_2]_t = K^{3,2}[3\text{-}F]_t + K^{2,3}[2\text{-}F]_t$$

$$p[2,6\text{-}F_2]_t = K^{2,6}[2\text{-}F]_t - k^{2,6,4}[2,6\text{-}F_2]_t$$

or:

$$[2,4\text{-}F_2]_t = \frac{K^{4,2}[4\text{-}F]_t + K^{2,4}[2\text{-}F]_t}{p + K^{2,4,6}}$$

$$[3,4\text{-}F_2]_t = \frac{K^{4,3}[4\text{-}F]_t + K^{3,4}[3\text{-}F]_t}{p}$$

$$[3,5\text{-}F_2]_t = \frac{K^{3,5}[3\text{-}F]_t}{p}$$

$$[2,3\text{-}F_2]_t = \frac{K^{3,2}[3\text{-}F]_t + K^{2,3}[2\text{-}F]}{p}$$

$$[2,6\text{-}F_2]_t = \frac{K^{2,6}[2\text{-}F]_t}{p + K^{2,6,4}}$$

or: $$[2,4\text{-}F_2]_t = \frac{K^{4,2}\,K^{4}\,p[C_6Cl_5H]_o}{(p+K^{2,4,6})\,(p+a^1)\,(p+a^4)} + \frac{K^{2,4}\,K^{2}\,p[C_6Cl_5H]_o}{(p+K^{2,4,6})\,(p+a^1)\,(p+a^2)}$$

$$[3,4\text{-}F_2]_t = \frac{K^{4,3}K^{4}\not{p}[C_6Cl_5H]_o}{\not{p}(p+a^1)\,(p+a^4)} + \frac{K^{3,4}K^{3}\not{p}[C_6Cl_5H]_o}{\not{p}(p+a^1)\,(p+a^3)}$$

$$[3,5\text{-}F_2]_t = \frac{K^{3,5}K^{3}\not{p}[C_6Cl_5H]_o}{\not{p}(p+a^1)\,(p+a^3)}$$

$$[2,3\text{-}F_2]_t = \frac{K^{3,2}K^{3}\not{p}[C_6Cl_5H]_o}{\not{p}(p+a^1)\,(p+a^3)} + \frac{K^{2,3}\,k^{2}\not{p}[C_6Cl_5H]_o}{\not{p}(p+a^1)\,(p+a^2)}$$

and finally:

$$[2,6\text{-}F_2]_t = \frac{K^{2,6}K^{2}p[C_6Cl_5H]_o}{(p+K^{2,6,4})(p+a^1)(p+a^2)}$$

After replacement of the transforms we have:

$$[2,4\text{-}F_2]_t = [C_6Cl_5H]_o K^{4,2}K^4 \left[\frac{e^{-a^1t}}{(a^4-a^1)(K^{2,4,6}-a^1)} + \frac{e^{-a^4t}}{(a^1-a^4)(K^{2,4,6}-a^4)}\right.$$

$$\left. + \frac{e^{-K^{2,4,6}t}}{(a^1-K^{2,4,6})(a^4-K^{2,4,6})}\right] + [C_6Cl_5H]_o K^{2,4}K^2 \left[\frac{e^{-a^1t}}{(a^2-a^1)(K^{2,4,6}-a^1)}\right.$$

$$\left. + \frac{e^{-a^2t}}{(a^1-a^2)(K^{2,4,6}-a^2)} + \frac{e^{-K^{2,4,6}t}}{(a^1-K^{2,4,6})(a^2-K^{2,4,6})}\right]$$

$$[3,4\text{-}F_2]_t = [C_6Cl_5H]_o K^{4,3}K^4 \left[\frac{1}{a^1a^4} - \frac{e^{-a^1t}}{a^1(a^4-a^1)} - \frac{e^{-a^4t}}{a^4(a^1-a^4)}\right]$$

$$+ [C_6Cl_5H]_o K^{3,4}K^3 \left[\frac{1}{a^1a^3} - \frac{e^{-a^1t}}{a^1(a^3-a^1)} - \frac{e^{-a^3t}}{a^3(a^1-a^3)}\right]$$

$$[3,5\text{-}F_2]_t = [C_6Cl_5H]_o K^{3,5}K^3 \left[\frac{1}{a^1a^3} - \frac{e^{-a^1t}}{a^1(a^3-a^1)} - \frac{e^{-a^3t}}{a^3(a^1-a^3)}\right]$$

$$[2,3\text{-}F_2]_t = [C_6Cl_5H]_o K^{3,2}K^3 \left[\frac{1}{a^1a^3} - \frac{e^{-a^1t}}{a^1(a^3-a^1)} - \frac{e^{-a^3t}}{a^3(a^1-a^3)}\right]$$

$$+ [C_6Cl_5H]_o K^{2,3}K^2 \left[\frac{1}{a^1a^2} - \frac{e^{-a^1t}}{a^1(a^2-a^1)} - \frac{e^{-a^2t}}{a^2(a^1-a^2)}\right]$$

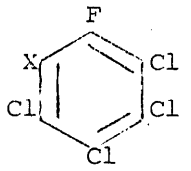
and:

$$[2,6\text{-}F_2]_t = [C_6Cl_5H]_o \, K^{2,6} \, k^2 \left[\frac{e^{-a^1 t}}{(a^2 - a^1)(K^{2,6,4} - a^1)} + \frac{e^{-a^2 t}}{(a^1 - a^2)(K^{2,6,4} - a^2)} + \frac{e^{-K^{2,6,4} t}}{(a^1 - K^{2,6,4})(a^2 - K^{2,6,4})} \right]$$

Similarly the instantaneous concentration of the components in all other fluorodechlorination processes, can be calculated by using similar equations because, in all the processes, the concentration of potassium fluoride is more than that of arylchloride, i.e. [KF] >> [ArCl].

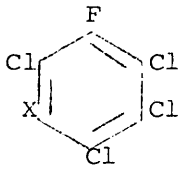
APPENDIX I

Fluorotetrachlorobenzenes (X=H) or toluenes (X=Me)



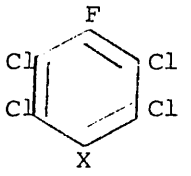
(A)

2,3,4,5-Tetrachloro-fluorobenzene (X=H)



(B)

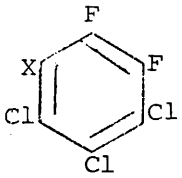
2,3,4,6-Tetrachloro-fluorobenzene (X=H)



(C)

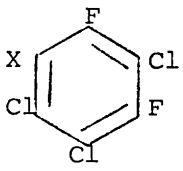
2,3,5,6-Tetrachloro-fluorobenzene (X=H)

Difluorotrichloro- and dichlorotrifluorobenzenes (X=H) or toluenes (X=Me)



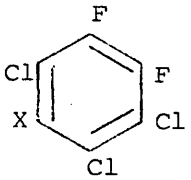
(D)

1,2-Difluoro-3,4,5-trichloro-($2,3\text{-}F_2$-4,5,6-trichlorobenzene; X=H $2,3\text{-}F_2$)



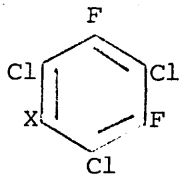
(E)

1,3-Difluoro-2,4,5-trichloro-($2,4\text{-}F_2$-3,5,6-trichlorobenzene; X=H $2,4\text{-}F_2$)



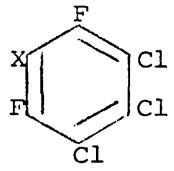
(F)

1,2-Difluoro-3,4,6-trichloro-($3,4\text{-}F_2$-2,5,6-trichloro-, $4,5\text{-}F_2$-2,3,6-trichlorobenzene, X=H $3,4\text{-}F_2$)



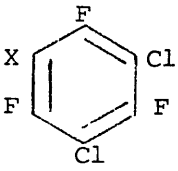
(G)

2,4-Difluoro-1,3,5-trichloro-($3,5\text{-}F_2$-2,4,6-trichlorobenzene; X=H $3,5\text{-}F_2$)



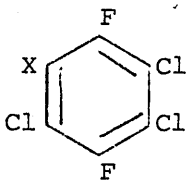
(H)

1,5-Difluoro-2,3,4-trichloro-($2,6\text{-}F_2$-3,4,5-trichlorobenzene; X=H $2,6\text{-}F_2$)



(I)

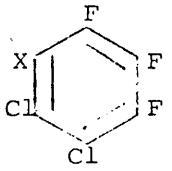
1,3,5-Trifluoro-2,4-dichloro-($2,4,6\text{-}F_3$-3,5-dichlorobenzene; X=H $2,4,6\text{-}F_3$)



(J)

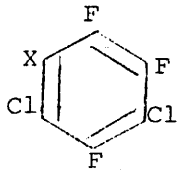
1,4-Difluoro-2,3,5-trichlorobenzene (X=H)

Appendix I (continued)



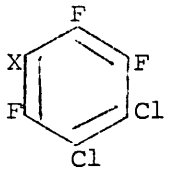
(K)

1,2,3-Trifluoro-4,5-dichloro-benzene (X=H)



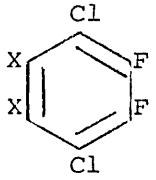
(L)

1,2,4-Trifluoro-3,5-dichloro-benzene (X=H)



(M)

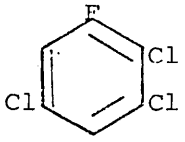
1,2,5-Trifluoro-3,4-dichlorobenzene (X=H)



(N)

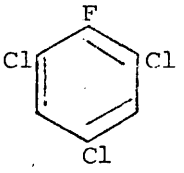
2,3,-Difluoro-1,4-dichlorobenzene (X=H)

Appendix II



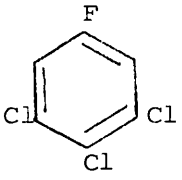
(O)

2,3,5-Trichlorofluorobenzene



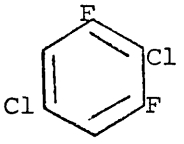
(P)

2,4,6-Trichlorofluorobenzene



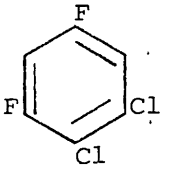
(Q)

3,4,5-Trichlorofluorobenzene



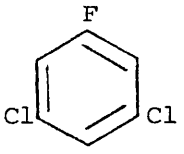
(R)

1,3 - Difluoro-2,5-dichlorobenzene



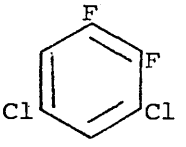
(S)

1,3-Difluoro-4,5-dichlorobenzene



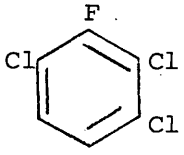
(T)

3,5-Dichlorofluorobenzene



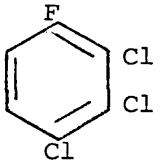
(U)

1,2-Difluoro-3,5,-dichlorobenzene



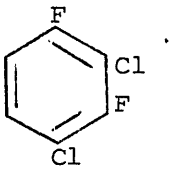
(V)

2,3,6-Trichlorofluorobenzene



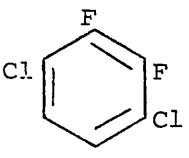
(W)

2,3,4-Trichlorofluorobenzene



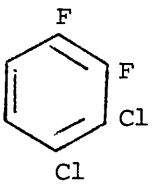
(X)

1,3-Difluoro-2,4,-dichloro-benzene



(Y)

2,3-Difluoro-1,4-dichloro-benzene



(Z)

1,2-Difluoro-3,4-dichlorobenzene

Appendix III[(a)]

Table of Transforms and Originals

No.	Transforms	Originals
1	$\frac{1}{p}$	t
2	$\frac{1}{p^n}$	$\frac{t^n}{n}$
3	$\frac{1}{p \pm a}$	$\frac{1}{\pm a} - \frac{1}{\pm a} e^{\pm at}$
4	$\frac{p}{p \pm a}$	$e^{\pm at}$
5	$\frac{p}{(p+a^1)(p+a^2)}$	$\frac{1}{a^2-a^1} e^{-a^1 t} + \frac{1}{a^1-a^2} e^{-a^2 t}$
6	$\frac{p}{(p+a^1)(p+a^2)(p+a^3)}$	$\frac{1}{(a^2-a^1)(a^3-a^1)} e^{-a^1 t} + \frac{1}{(a^1-a^2)(a^3-a^2)} e^{-a^2 t} + \frac{1}{(a^1-a^3)(a^2-a^3)} e^{-a^3 t}$
7	$\frac{1}{(p+a^1)(p+a^2)(p+a^3)}$	$\frac{1}{a^1 a^2 a^3} - \frac{1}{a^1(a^2-a^1)(a^3-a^1)} e^{-a^1 t} - \frac{1}{a^2(a^1-a^2)(a^3-a^2)} e^{-a^2 t} - \frac{1}{a^3(a^1-a^3)(a^2-a^3)} e^{-a^3 t}$

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