NUCLEOPHILIC DISPLACEMENT IN POLYHALOGENOAROMATIC COMPOUNDS.

PART V.   FLUORODECHLORINATION OF 1,2,3,4- AND 1,2,3,5-TETRA-

CHLOROBENZENES AND 2,3,4,5,6-PENTACHLOROTOLUENE IN SULPHOLAN

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SUMMARY

    Potassium fluoride in sulpholan (tetramethylene sulphone)
reacted readily with 1,2,3,4- and 1,2,3,5-tetrachlorobenzenes
at 250°, but needed temperatures of 270° before fluorodechlorination
of pentachlorotoluene proceeded readily.   Individual rate constants
for the formation and decomposition of some of the fluorochloroarenes
have been isolated; their values are discussed in terms of the
electronic effects of the substituents.

INTRODUCTION

    In our investigations of the fluorodechlorination of poly-
chlorobenzenes in sulpholan we reported the products of reaction
of hexa- and penta-chlorobenzenes, and of fluoro- and nitro-2,3,5,6-
tetrachlorobenzenes [1].   The preparative use of these reactions
was limited to the isolation of fluoropolychlorobenzenes by fluoro-
denitration [2], and the isolation of *m*-difluorotetrachlorobenzene
and 1,3,5-trichlorotrifluorobenzene from attack of hexachlorobenzene
[3,4].   Finger and his colleagues[5] have reported a study of the
fluorodechlorination of the tetrachlorobenzenes, which only had
preparative application in the synthesis of 1,2,3,4,-tetrafluoro-
benzene.

We have repeated the study of the fluorodechlorination of the tetrachlorobenzenes, using sulpholan, a solvent generally most effective in such preparative reactions; we have also derived rate constants for some of the individual displacement processes and compar these with constants found in the earlier report [1].

RESULTS AND DISCUSSION

The course of the reaction with the tetrachlorobenzenes was followed by both ^{19}F-NMR spectroscopy and gas chromatography, using the reported general method [1]; 4-fluorobiphenyl was used as the internal standard.

The reactions were complicated by the concomitant formation of black tars which were not appreciably soluble in water or in fluorotrichloromethane and which contained no fluorine. As these tars indicated a competing side reaction, the preparative use of the reactions was lessened. Table 1 shows the chemical shifts found in the various fluorochlorobenzene derivatives produced by the exchange reactions; products were identified (i) by the chemical shifts of the fluorine atoms which they contained (ii) by the splitting patterns shown by these fluorine atoms (iii) by the general agreement between our results and Finger's [5] and (iv) by the agreement between the relative ease of nucleophilic displacement and the derived values found from these fluorodechlorination studies. In addition, authentic samples were synthesised for comparison in some cases.

Despite the lower reactivity of the tetrachlorobenzenes, only 1,2,4,5-tetrachlorobenzene failed to show appreciable exchange at 250° after twelve hours. Difluorodichlorobenzenes were obtained from both 1,2,3,4- and 1,2,3,5-tetrachlorobenzene by this time, although under no conditions could we obtain an isomerically pure product from either material. The variations in the composition of the reaction mixtures with time are shown in Table 2, together with the associated rate constants. Unlike the previously reported and more rapid exchange reactions [1], the destruction of material to form unidentified materials (tar) was clearly shown in the kinetic results.

TABLE 1

^{19}F-NMR shift and coupling constants of some polychloropolyfluoro-
arenes (shifts, in p.p.m., upfield of trichlorofluoromethane)

Arene	δ(exp)	δ(calc)	Coupling constant (Hz)
2,3,4-Trichlorofluorobenzene	107.2	111.2	F-H$_5$, 4.2; F-H$_6$, 7.8
2,3,5-Trichlorofluorobenzene	106.1	111.8	F-H$_4$, 1.9; F-H$_6$, 8.2
2,3,6-Trichlorofluorobenzene	106.0	109.6	F-H$_4$, 1.4; F-H$_5$, 4.2
2,4,6-Trichlorofluorobenzene	116.6*	109.0	Triplet; F-H$_3$, 6
3,4,5-Trichlorofluorobenzene	110.6	113.4	Triplet; F-H$_2$, 8
1,3-Difluoro-2,5-dichlorobenzene	109.7	108.8	Quartet; F$_1$-H$_6$, 8; F$_1$-H$_4$, 1
1,3-Difluoro-4,5-dichlorobenzene	104.6	107.9	Triplet; F$_1$-H$_2$, 6
	108.5	109.4	Triplet; F$_3$-H$_2$, 8
2-Fluoro-3,4,5,6-tetrachlorotoluene	110	111.2	Quartet; F$_2$-H$_\alpha$, 2.5
3-Fluoro-2,4,5,6-tetrachlorotoluene	107	109.0	Singlet; slightly broadened
4-Fluoro-2,3,5,6-tetrachlorotoluene	108.3	109.6	Singlet
2,4-Difluoro-3,5,6-trichlorotoluene	114	111.2	Broad, not resolved
	111.9	109.6	Sharp singlet
2,6-Difluoro-3,4,5-trichlorotoluene	112.1	111.2	Broad, not resolved
3,5-Difluoro-2,4,6-trichlorotoluene	111.3	111.2	Singlet, slightly broadened

* Authentic compound identical.

In the formation of each intermediate, its instantaneous concentration
is expressed by an equation in which the total rate constants for destructio
of the precursor and of the intermediate itself both appear. An example
is the kinetic term reflecting the concentration of fluoro-2,3,5-
trichlorobenzene from attack of 1,2,3,5-tetrachlorobenzene.

$$[235\text{-}Cl_3F] = \frac{k_1}{a_1 - a_2} \cdot [C_6Cl_4H_2]_o \cdot \{e^{-a_2t} - e^{-a_1t}\}$$

where a_1 and a_2 are the total rate constants associated with destruction
of tetrachlorobenzene and of fluoro-2,3,5-trichlorobezene (235-Cl$_3$F)
respectively, and k_1 is the individual rate constant for the formation
of the fluorotrichlorobenzene. The exact shape of the curve of (235-Cl$_3$F)
against time is defined only by the values of a_1 and a_2; the amount of
fluoro-2,3,5-trichlorobenzene formed at any time is also limited by the
numerical value of the ratio $k_1/(a_1 - a_2)$. As the parameters a_1 and a_2
are the sums of the individual rate constants of formation of products
(e.g. $a_1 = k_1^{(1)} + k_1^{(2)} + k_1^{(3)} + \ldots\ldots$), the rate constant for removal
of any one compound should equal the sum of those for the formation of
the daughter products. This is true, to within the experimental errors
involved, for the values found in the attack of pentachlorobenzene [1],
but it is not so for the analogous reactions of 1,2,3,5-tetrachlorobenzene,
whose total rate of destruction is more than twice the combined rates of
formation of all the fluorotrichlorobenzenes. The rate constants reflect
this, with $a_1 = 11.8 \times 10^{-5}$ s^{-1} and the individual rate constants for
formation being 0.45×10^{-5} (2,4,6-trichlorofluorobenzene), 0.6×10^{-5}
(3,4,5-trichlorofluorobenzene) and 3.5×10^{-5} (2,3,5-trichlorofluoro-
benzene) s^{-1} respectively. The ratios of the terms ($\sum k_1/a_1 = 0.455/1.18 = 0.38$
agrees with the conversion fraction found at each time of sampling (0.31-0.38)
and suggests that the bulk of the starting material in this reaction is
consumed to give non-volatile species which contain no fluorine, since they
are detected neither by NMR nor by g.l.c.

The apparent first-order rate constants associated with these side
reactions are larger for the attack of 1,2,3,5-tetrachlorobenzene
($k = 7.6 \times 10^{-5}$ s^{-1}) than for the attack of 2,3,5-trichlorofluorobenzene
(0.98×10^{-5}) or for 3,4,5-trichlorofluorobenzene (0.9×10^{-5}). The
presence of the fluorine substituent in the arene deactivates this
reaction. There are two groups of process which might be involved.
The first is a direct nucleophilic attack upon aromatic carbon, similar
to the fluorodechlorination process by which these mixed halogenoaromatic
compounds were obtained and involving a nucleophile derived from some
unconsidered reaction between KF and, perhaps, the solvent. Although the
relative ease of displacement of fluorine and of chlorine from aromatic
sites varies considerably according to the solvent system and the attacking

nucleophile [6], we believe that in the present system fluorine is much more readily displaced than chlorine, the 'usual' order of reactivity found both generally [7] and in the attack of methoxide ion upon poly-halogenoaromatic systems [8] falling in the order F, NO_2 > Cl.

TABLE 2

Experimental and calculated compositions of mixtures formed from fluorodechlorination (KF) of tetrachlorobenzene in sulpholan (250°)

Arene		t = 120	[Arene] at 180	240	360	480	540 mins	$10^5 k$ (a)
		1,2,3,4-Tetrachlorobenzene						
$C_6Cl_4H_2$	exp :	0.806		0.680				a_1 = -2.7
	calc :	0.823		0.678				
234-Cl_3F (b)	exp :	0.056		0.096				k^1 = 0.4
	calc :	0.052		0.095				
236-Cl_3F	exp :	0.136		0.224				k^2 = 0.95
	calc :	0.125		0.227				
		1,2,3,5-Tetrachlorobenzene						
$C_6Cl_4H_2$	exp :	0.28		0.164	0.089	0.039		a_1 = -11.8
	calc :	0.42		0.174	0.072	0.030		
235-Cl_3F	exp :	0.160	0.188	0.200	0.199	0.192	0.180	k^1 = 1.75
	calc :	0.155	0.185	0.199	0.199	0.187	0.178	
246-Cl_3F	exp :	0	0	0.027	0.033	0.037	0.048	k^2 = 0.45
	calc :	0.022	0.027	0.031	0.034	0.036	0.037	
345-Cl_3F	exp :	0.027	0.040	0.030	0.048	0.051	0.054	k^5 = 0.6
	calc :	0.028	0.034	0.038	0.041	0.040	0.040	
13F_2-25Cl_2	exp :	0.008	0.011	0.013	0.030	0.044	0.049	k = 0.8
	calc :	0.005	0.010	0.015	0.028	0.044	0.048	
15F_2-23Cl_2	exp :	0		0.004	0.008	0.011		k^{13} = 0.22
	calc :	0.002		0.005	0.011	0.013		k^{15} = 0.5

(a) Rate constants in s^{-1} ([KF] = 10 M; pseudo-first order process).

(b) Nomenclature similar to that used previously [1]; thus 234-Cl_3F is 2,3,4-trichlorofluorobenzene, and 13F_2-25Cl_2 is 1,3-difluoro-2,5-dichloro-benzene.

In the fluoride ion attack of a number of polyhalogenobenzenes,
the order of displacement found [1, 8, 9] is $NO_2 > Cl$, and we
deduce from this that the 'usual' order of reactivity is again
found in the reactions under study. If this deduction is correct,
the lower reactivity of fluorotrichlorobenzenes towards the side
reaction suggests that this reaction does not involve nucleophilic
attack upon aromatic carbon.

The alternative process involves nucleophilic attack upon
chlorine. Similar reactions have been recently reported involving
displacement of iodine [10] and of bromine [11] from similar
systems, and chlorodeprotonation has been detected [8] in exchange
reactions carried out in sulpholan. The process may be simply
represented by the equation

$$ArCl + R^- = Ar^- + RCl$$

with both the products undergoing rapid subsequent reactions to give
the hydrocarbon, ArH, and the multiplicity of products arising from
the generation of an alkyl halide in basic media. In our present
system, ArH would correspond to a trichlorobenzene or a
dichlorofluorobenzene, R^- would be a carbanion arising from
deprotonation of the solvent (presumably at the methylene group
adjacent to the hetero atom), and the resultant chlorosulphone can
be regarded as the source of the tarry material. Although the
trichlorobenzene component should be readily detected by g.l.c.,
it may well coincide with the fluorotrichlorobenzene products and
so be hidden; perhaps it is significant that the discrepancy
between the results from the two analytical methods was greater
for the fluorotrichlorobenzenes than for the difluorodichlorobenzenes,
where the agreement was as close as the accuracies of the two
methods permitted. Nucleophilic attack upon aromatic chlorine will
explain the results, although the evidence for it is not conclusive;
certainly the solvent appears to be involved, for the yield of fluoro-
dechlorination products falls considerably in the presence of twice th
amount of sulpholan.

2,3,4,5,6-Pentachlorotoluene The results of a similar investigation
of fluorodechlorination in pentachlorotoluene are given in Table 3.

TABLE 3

Experimental and calculated compositions of mixtures formed from
KF (0.50 mole) - pentachlorotoluene (0.05 mole) - sulpholan (50 ml)
at ca. 275°

Arene		[Arene] at t = 25	50	75	100 min	$10^5 k$ (a)
2,3,4,5,6-Pentachloro-	exp :	0.848	0.734	0.654	0.615	a_1 = -11.1
toluene	calc :	0.845	0.717	0.607	0.514	
2-Fluoro-3,4,5,6-	exp :	0.055	0.078	0.088	0.090	a_2 = -27
tetrachlorotoluene	calc :	0.051	0.077	0.088	0.093	k_2 = 2.3
3-Fluoro-2,4,5,6-	exp :	0.038	0.046	0.069	0.058	a_3 = -25
tetrachlorotoluene	calc :	0.038	0.058	0.067	0.068	k_3 = 2
4-Fluoro-2,3,5,6-	exp :	0.059	0.100	0.106	0.103	a_4 = -40
tetrachlorotoluene	calc :	0.072	0.101	0.107	0.103	k_4 = 7
2,4-Difluoro-3,5,6-	exp :		0.041	0.060	0.090	k^{42} = 4
trichlorotoluene	calc :	0.020	0.043	0.060	0.076	k^{24} = 8
2,6-Difluoro-3,4,5-	exp :			0.004$_6$	0.012$_8$	k^{26} = 2.4
trichlorotoluene	calc :			0.009$_2$	0.012$_1$	
3,5-Difluoro-2,4,6-	exp :			0.018	0.032	k^{35} = 8
trichlorotoluene	calc :			0.020	0.026	

(a) Rate constants in s^{-1}. a are composite rate constants for the removal
of the indicated arene; k are the rates of formation of the arene. Where
there is more than one route, the source is indicated by numbering the
fluorine atoms inserted in sequence; thus k^{24} refers to the attack of
2-fluoro-3,4,5,6-tetrachlorotoluene at the 4-position.

These results are less reliable than the previously reported figures.
Error arises partly because of the higher temperature, when much of
the organic reagents was in the gas phase, and also because of the lower
solubility of the products in fluorotrichloromethane, giving lower
signal-to-noise ratios and the obscuring of some fine structure. The
concomitant tar also lowered the ease of extraction of the products
and complicated an already difficult operation. For this reason, we
shall consider the results from the attack of pentachlorotoluene
separately.

Two points are immediately evident: (i) the exchange occurs much less readily than the corresponding reaction with pentachlorobenzene, and (ii) the orientation of attack of both perchloro-arenes is similar. A more detailed comparison of the sets of rate constants associated with individual stages in each fluorodechlorination suggests the parallel to hold throughout the reaction, so that the general observation may be made that the methyl group deactivates the system to nucleophilic attack and that, to within the limits of our analysis, this deactivation applies equally to all sites in the aromatic system. Fig. 1 shows this for attack of the parent pentachloroarenes.

Fig. 1 Orientation and associated rate constants for fluorodechlorination of pentachlorobenzene (250°) and pentachlorotoluene (275°)

The significance of the rate constants. We now have a number of rate constants associated with the fluorodechlorination of penta- and of two tetra-chlorobenzenes, and of their various exchange products, in the presence of a large excess of potassium fluoride in sulpholan at ca.250°. These are now gathered together in Table 4, where the various electronic effects may be deduced. In such interpretations, the implicit errors in some values must not be forgotten, and nor should the assumptions made in obtaining these figures be neglected. The reactions have been assumed to be first order with respect to the arene, which may be justified by recourse both to other studies in which the molecularity of the reaction has been more rigorously studied [12] and to the agreement between calculated and experimental results, although this may merely reflect the degree to which the experimental figures can be forced to fit an incorrect hypothesis. The reactions are also held in the presence of a large excess of potassium fluoride, and will show pseudo-first order kinetic behaviour whether all of the fluoride ion is involved in the kinetic form, or only that present in the saturated solution.

TABLE 4

Rate constants associated with fluorodechlorination in sulpholan in
the presence of KF at 250°

Arene	$10^{5}k_{(x)}$ where x is the site of attack
1,2,3,4,5-Pentachlorobenzene	k_1 = 10; k_2 = 9; k_3 = 22
2,3,4,5-Tetrachlorofluorobenzene	k_2 = 1; k_3 = 18; k_5 = 7
1,3,4,5-Tetrachloro-2-fluorobenzene	k_1 = 6; k_3 = 11; k_4 = 8.5
1,2,4,5-Tetrachloro-3-fluorobenzene	k_1 = 9; k_2 = 1.5
1,2,3,4-Tetrachlorobenzene	k_1 = 0.4; k_2 = 0.95
1,2,3,5-Tetrachlorobenzene	k_1 = 1.75; k_2 = 0.45; k_5 = 0.6
2,3,5-Trichlorofluorobenzene	k_3 = 0.8; k_5 = 0.5
3,4,5-Trichlorofluorobenzene	k_3 = 0.22

Substituent rate factors can be adduced for both halogen groups, but only
in the ortho- and meta-positions for fluorine; the 'deactivating'
effect of fluorine substituents upon the para-position, which appears
because of the relatively much greater effect of the substituent upon ortho-
and meta-positions, is sufficient that no appreciable amount of attack
occurs at any site para- to a fluorine atom already placed in the system.
These SRF's fall consistently in the order meta > ortho > para (Table 5);
in terms of our three parameter equation [1, 8], the I_{Hal} term is almost

TABLE 5

Substituent rate factors (SRF's) and other parameters derived for
fluorine and chlorine substituents in fluorodechlorination at 250°

Halogen	SRF			I_{Hal} *	μ *
	ortho	meta	para		
Fluorine	ca. 4	18	–	3.0 kcal mol^{-1}	-1.6 kcal mol^{-1}
Chlorine	ca 17	22	10	3.2	-0.3

* I_{Hal} is defined by the term $RT\ln(k_{m-x}/k_{H})$ μ is defined by the term $RT\ln(k_{o-x}/k_{m-x})$

identical for each halogen, and the deactivating term is entirely responsible for the observed orientation of attack, which, like the methyl group substituent effect seen in pentachlorotoluene, is indicative of a nucleophilic substitution process.

EXPERIMENTAL

2,3,4,5,6-Pentachlorotoluene was obtained by the catalysed $(AlCl_3 - S_2Cl_2)$ chlorination (SO_2Cl_2) of toluene [13]. Proton NMR was used to estimate the purity of the sample, for many recrystallisations from benzene were needed to obtain pure material, and m.p. was not sufficiently sensitive criterion. 1,2,3,4- and 1,2,3,5-Tetrachlorobenzenes were commercial samples, purified by recrystallisation from ethanol to constant m.p.; g.l.c. was used as the criterion of purity. The reactions were carried out and analysed by exactly analogous methods to that already described [1], with the exception that 4-fluorobiphenyl was used as a marker in the exchange reactions of 1,2,3,5-tetrachlorobenzene.

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