Some aspects of fluorocarbanion chemistry

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UNIVERSITY OF DURHAM

A THESIS

entitled

SOME ASPECTS OF FLUOROCARBANION CHEMISTRY

submitted by

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MEMORANDUM

The work described in this thesis was carried out in the University of Durham between October 1965 and April 1968. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

Part of this work has been the subject of the following publications:-

R.D. Chambers, J.A. Cunningham, and D.J. Spring, Tetrahedron, 1968, 24, 3997.

R.D. Chambers, J.A. Cunningham, and D.J. Spring, J. Chem. Soc. (C), 1968, 1560.

R.D. Chambers and D.J. Spring, J. Chem. Soc. (C), in the press.

R.D. Chambers and D.J. Spring, Chem. Comm., 1968,

SUMMARY

Some Aspects of Fluorocarbanion Chemistry

Measurement of the kinetic acidity of the compounds CH_3OCF_2CFClH, CH_3OCF_2CFBrH, $CH_3OCF_2CCl_2H$ indicated that the ability of the α halogens to stabilise a carbanion, in this type of compound, is in the order $F < Cl < Br$. Extension of this to the β halogens, by measuring the kinetic acidity of the compounds CH_3SCF_2CFClH and $CH_3SCFClCFClH$, is impracticable since $CH_3SCFClCFClH$ reacts with base to eliminate HCl. The two diastereomers reacted at markedly different rates, and this indicates that the mechanism is E2 and not Elcb. A more electronegative β group, such as CH_3SO_2, which should make the mechanism more like Elcb, was of no use since $CH_3SO_2CFClCFClH$ appeared to eliminate $CH_3SO_2^-$ rather than Cl^-. Measurement of the kinetic acidity of the compounds XCF_2CFBrH ($X = CH_3O, CH_3S, CH_3SO_2$) indicated that the ability of the β groups to stabilise a carbanion is in the order $CH_3O < CH_3SO_2 < CH_3S$.

Reaction of dimethyl carbonate with polyfluoroaryl-lithiums was shown to be a useful route for the preparation of polyfluoroaryl ketones; thus reaction with pentafluorophenyl-lithium, 2,3,4,5-tetrafluorophenyl-lithium, and octafluoro-2,2'-dilithiobiphenyl leads to the synthesis of decafluorobenzophenone, octafluoro-2,2'-dihydrobenzophenone, and octafluoro-9-fluorenone respectively. However reaction with 2-bromotetrafluorophenyl-lithium is complicated by a lithium/bromine exchange reaction between products and reactants.

Substitution of fluoride by methoxide in decafluorobenzophenone occurs at the 4-position in methanol, and at the 2-position in ether/hexane. This solvent effect is attributed to the different dielectric constants of the two media. Octafluoro-2,2'-dihydrobenzophenone substitutes at the 4-position, and this orientation is attributed to the mesomeric effect of the carbonyl group being stronger than its $I\pi$ effect. Substitution in octafluoro-9-fluorenone occurs at the 2-position, i.e. meta to the carbonyl group, this appears to be attributable to unusual electronic effects in the fluorenone system. Decafluorodiphenyl sulphide, octafluorothianthren, decafluorodiphenyl sulphone, and octafluorodibenzothiophen-5,5-dioxide substitute at the 4,2,4, and 2 positions respectively, and these orientations are rationalised in terms of the known ability of the hetero group to stabilise an adjacent carbanion.

The relative reactivities of some polyfluoroaromatic and heterocyclic systems towards methoxide in methanol were determined by competition reactions. The relative rates of the $(C_6F_5)_2X$ compounds ($X = SO_2$, CO, S, O) correlate with the Hammett substituent constants for X, but such a quantitative correlation is not possible for the corresponding dibenzo compounds $(C_6F_4)_2X$ because of the differing orientations of substitution. Comparison of the rates of octafluoro-2,2'-dihydrobiphenyl and benzophenone with the corresponding decafluoro compounds indicates that replacement of a β fluorine by hydrogen lowers the reactivity considerably, and this is partly attributable to the fact that β fluorines stabilise the intermediate carbanion by a powerful field effect. In octafluorodibenzothiophen and decafluorodiphenyl sulphide it appears that the second methoxyl substitutes into the compound at a faster rate than the first.

CONTENTS

EXPERIMENTAL

General Introduction

The study of fluorocarbon chemistry has, in the past two decades or so, become an important area of research. The reason for this is that fluorine is unique in that extensive and complete replacement of hydrogen, in a hydrocarbon system, by fluorine is possible, and is accompanied by very little distortion of the geometry of the system. As a result, differences in properties between fluorocarbons and hydrocarbons are not dominated by differences in stereochemistry, although, naturally steric effects are involved to some extent. Thus it is possible to envisage a completely synthetic organic chemistry, based on carbon and fluorine, rather than on carbon and hydrogen.

Functional groups, in fluorocarbon systems, tend to be in very different electronic environments, compared to their hydrocarbon analogues. Thus new compounds become available whose reactions and properties are often quite different from the corresponding hydrocarbon compounds, and as a result present a good test for our present theories of reaction processes and factors affecting reactivity. Lastly, but by no means least, the fact that these new compounds are often of potential industrial interest has been a very potent factor in stimulating interest in fluorocarbon chemistry. Substitution of fluorine for hydrogen often tends to promote greater stability in the molecule, and this coupled with industrial demand for inert plastics, polymers, and lubricants of high thermal stability, accounts for industrial interest in this subject.

Investigations into the mechanisms of reactions of unsaturated fluorocarbon compounds have shown that their chemistry complements that of the corresponding hydrocarbon compounds, with the carbanion occupying the position of the carbonium ion as the most important reaction intermediate. Yet, compared with the large amount of information that is available on carbonium ions, relatively much less is known about carbanions, especially those containing fluorine.

The work described in this thesis is a study of three aspects of the chemistry of fluorine-containing carbanions. The first is concerned with aliphatic fluorinated carbanions, and the effect of substituents on their stability; the second with the reaction of polyfluoroaryl-lithiums with dimethylcarbonate; and the third with a study of the factors affecting the orientation and rate of nucleophilic substitution in some polyfluoroaromatic and heterocyclic systems which, of course, involve carbanionic transition states.

INTRODUCTION

Chapter 1

Polyfluoroaryl-lithium Compounds

1.1. Preparation.

The first preparation of a polyfluoroaryl-lithium was by Tatlow and co-workers[1] in 1962, who made pentafluorophenyl-lithium by reaction between bromopentafluorobenzene and butyl-lithium in ether at -78°, and also by direct metallation with lithium amalgam at 0°. They

$$C_6F_5Br + C_4H_9Li \xrightarrow{-78^\circ} C_6F_5Li + C_4H_9Br$$

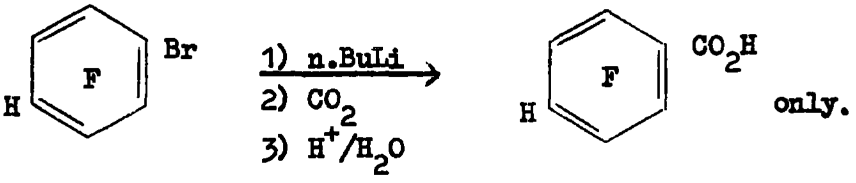
also showed that it was much more stable than monohalogenophenyl-lithiums, since after 24 hours at -10° nearly 60% of the original pentafluorophenyl-lithium was still present.

Tamborski and co-workers[2] showed that solvent was very important in the reaction of pentafluorobenzene with butyl-lithium; lithiation

$$C_6F_5H + C_4H_9Li \xrightarrow{-78^\circ} C_6F_5Li + C_4H_{10}$$

taking over 2 hours in ether/hexane, and 5 minutes or less in ether or ether/tetrahydrofuran (THF). They showed that complete di-lithiation of 1,2,4,5-tetrafluorobenzene (as deduced from carbonation experiments) was possible provided THF was used as solvent; mixtures of di-lithio and mono-lithio derivatives were obtained when ether was employed. However with 1,2,3,4-tetrafluorobenzene, even the use of THF as solvent gave only a mixture of mono and di-lithio derivatives.

As would be expected, bromine is replaced by lithium preferentially to hydrogen,[3] thus

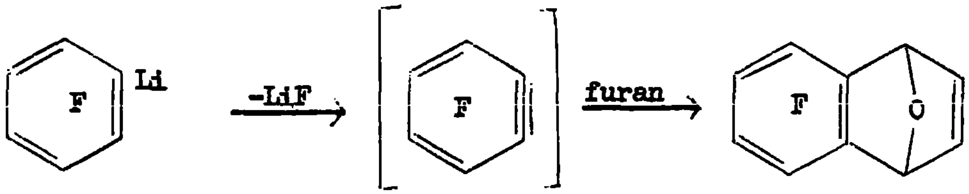


Lithiation of a variety of 4-substituted 2,3,5,6-tetrafluorobenzenes has been accomplished[4] under the usual conditions, except that where the substituent contains an active hydrogen atom an extra equivalent of butyl-lithium must be employed to react with this.

Other polyfluoroaryl-lithiums that have been made, and used in synthesis, are 2-bromotetrafluorophenyl-lithium,[5,6] and octafluoro-2,2'-dilithiobiphenyl[7] (see section 1.4). Similarly 2,3,5,6-tetrafluoro-4-lithiopyridine and 2,4,5,6-tetrafluoro-3-lithiopyridine have been made by Li/H interconversion.[8]

1.2. Decomposition to Benzynes.

The decomposition of pentafluorophenyl-lithium by elimination of LiF was first noted by Tatlow and co-workers,[1] who trapped the tetrafluorobenzyne as its Diels-Alder adduct with furan.



In the absence of a suitable benzyne trap, the tetrafluorobenzyne will react with undecomposed pentafluorophenyl-lithium (see below), to yield a complex polymeric product, from which no tractable organic compound has been isolated.

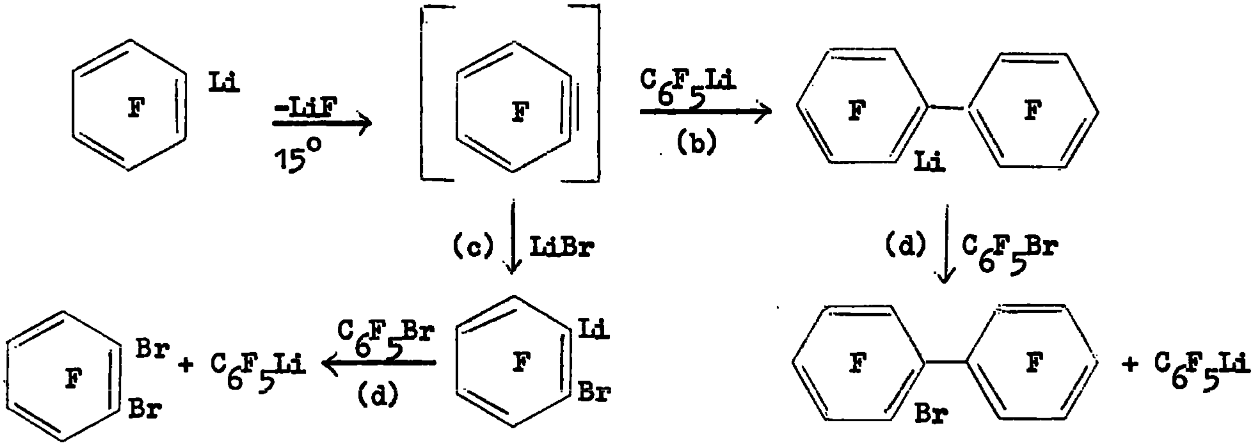
Decomposition of pentafluorophenyl-lithium in the presence of excess bromopentafluorobenzene, gave rise to a complex mixture of products, the formation of which was rationalised[9] on the basis of the following reactions taking place:

(a) nucleophilic attack by $C_6F_5^-$ on C_6F_5Br (see section 1.3),

(b) addition of C_6F_5Li to C_6F_4,

(c) addition of LiBr to C_6F_4,

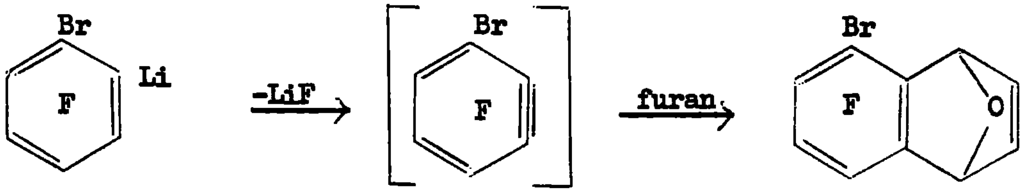
(d) Li/Br exchange reactions.



At 15° the major products are 1,2-dibromotetrafluorobenzene (~80%)

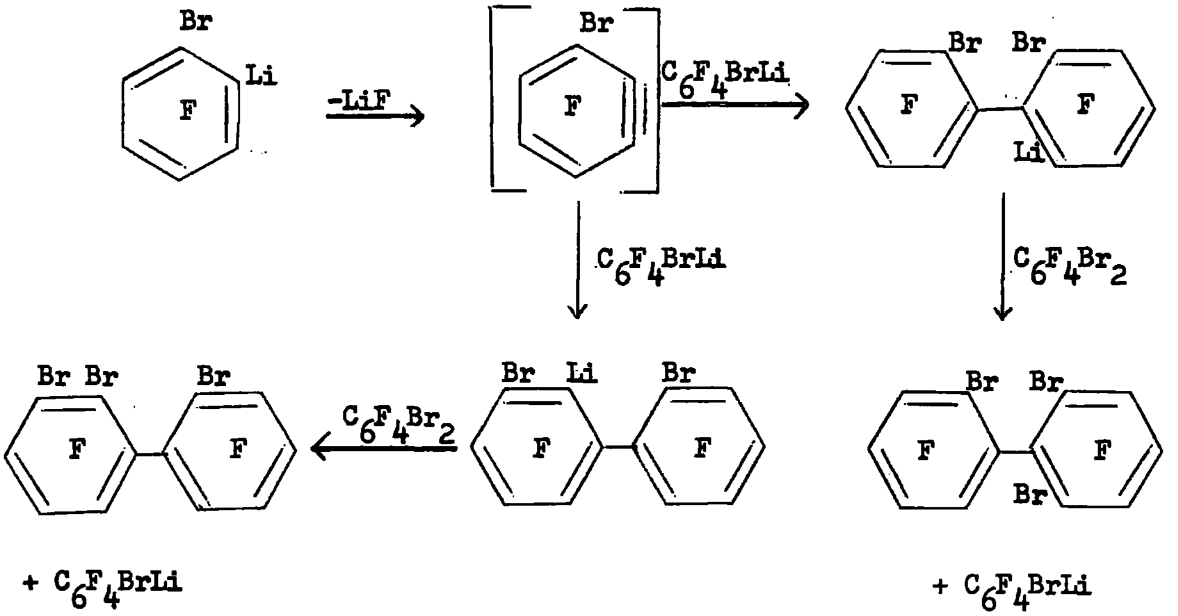
and 2-bromononafluorobiphenyl (~20%); the minor products are those from reaction (a) (see section 1.3), and hydrolysis products of the various intermediate lithium compounds. Evidence for reaction (c) is that if the reaction is carried out in pentane, in which LiBr is insoluble, then the only product isolated is 2-bromononafluorobiphenyl. The Li/Br exchange reaction (d) is a very common one, as will become apparent. Further evidence for this mechanism comes from the fact that if the decomposition of pentafluorophenyl-lithium is carried out in the presence of pentafluorobenzene, then the major products are bromo-2,3,4,5-tetrafluorobenzene and nonafluoro-2-hydrobiphenyl.

Contrary to what one might expect in terms of carbon-halogen bond strengths, LiF rather than LiBr is eliminated in the decomposition of 2-bromotetrafluorophenyl-lithium.[6]

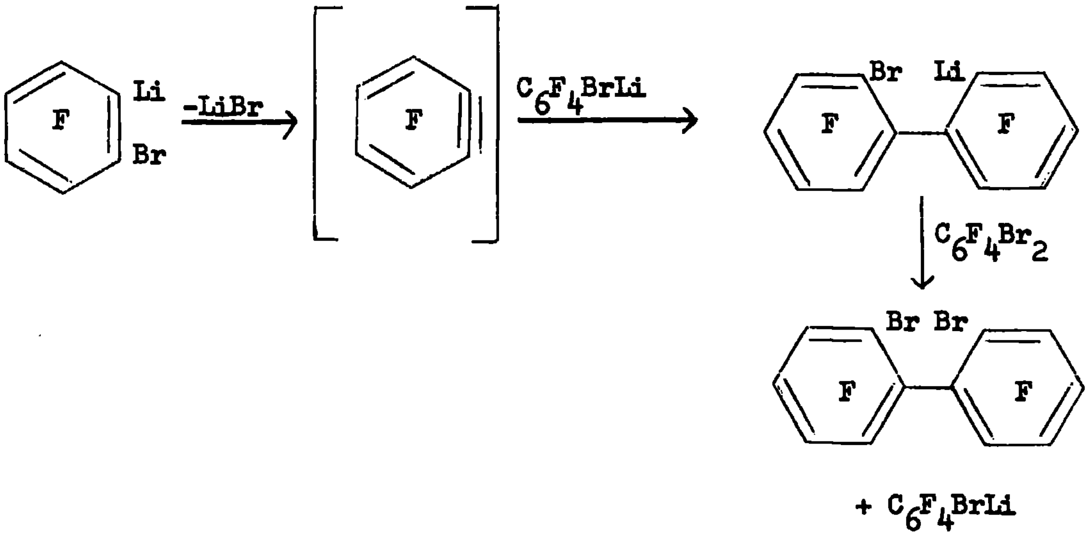


This is attributed to the fact that LiF is insoluble in the solvent used, whereas LiBr is soluble, thus making the elimination of LiBr reversible and that of LiF irreversible.

The decomposition of 2-bromotetrafluorophenyl-lithium in the presence of 1,2-dibromotetrafluorobenzene has been studied;[10] the reaction is again very complicated, giving up to 26 products, but only two of these are present in any large amounts.



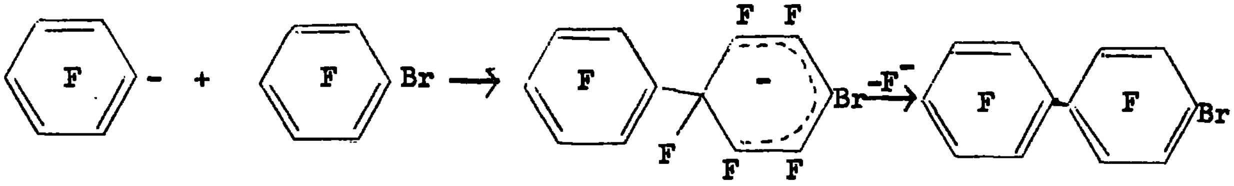
The two isomeric tribromoheptafluorobiphenyls arise from the two possible orientations of addition of the lithium reagent to the benzyne. Trace amounts of 2,2'-dibromo octafluorobiphenyl present in the product mixture, are thought to arise from the reaction



This would appear to confirm the fact that addition of lithium halides to benzynes is an equilibrium process.

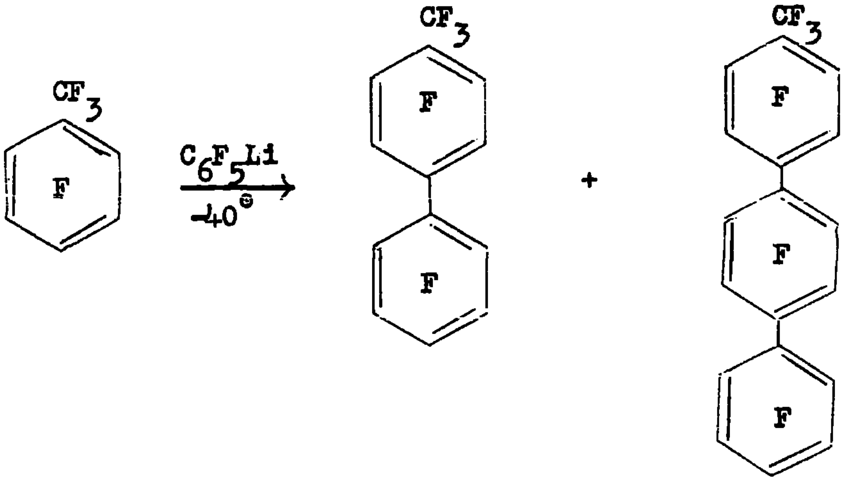
1.3. Pentafluorophenyl-lithium in Nucleophilic Aromatic Substitution.

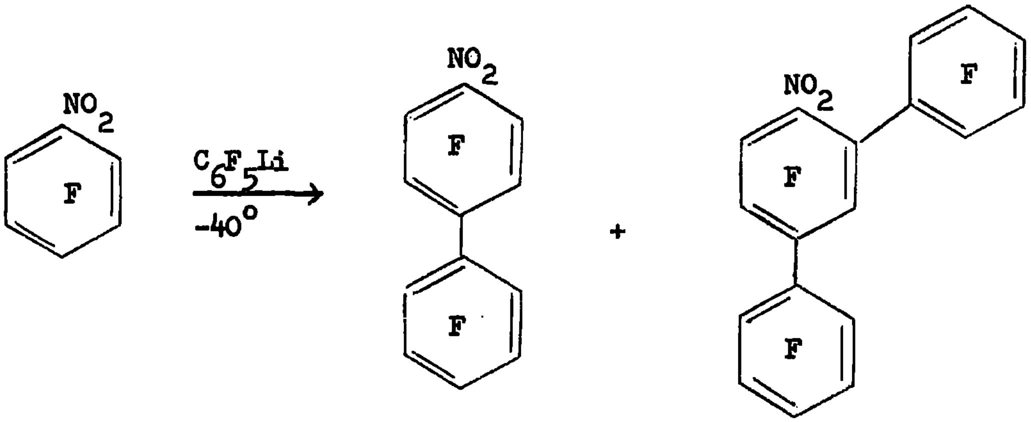
Pentafluorophenyl anion has been shown[9] to act as a nucleophile at a suitable temperature (chosen to minimise benzyne formation). Thus when bromopentafluorobenzene is added to pentafluorophenyl-lithium at -40°, the major product is 4-bromononafluorobiphenyl with only small amounts of the two products resulting from the 'benzyne route' (1,2-dibromotetrafluorobenzene and 2-bromononafluorobiphenyl). The major product arises from a nucleophilic substitution reaction.



The biphenyl produced can react with more $C_6F_5^-$ and, as a result, significant amounts of polymeric phenylenes are produced.

Similarly, pentafluorophenyl-lithium will react with octafluoro toluene, pentafluoronitrobenzene, and other compounds.





1.4. Reaction with Metal and Non-metal Halides.

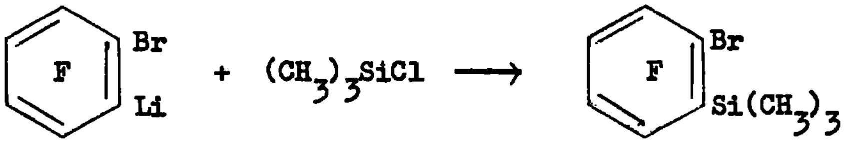
Many pentafluorophenyl derivatives of metals and non-metals[11] have been made by reaction of pentafluorophenyl-lithium with a metal chloride.

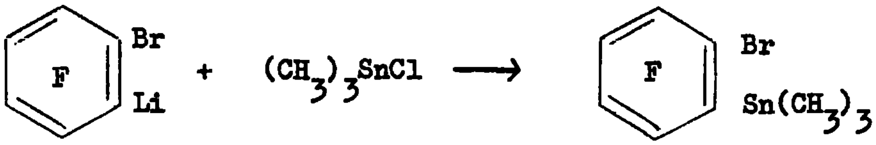
e.g. $C_6F_5Li + SCl_2 \longrightarrow (C_6F_5)_2S$ [5,12]

$C_6F_5Li + HgCl_2 \longrightarrow (C_6F_5)_2Hg$ [5]

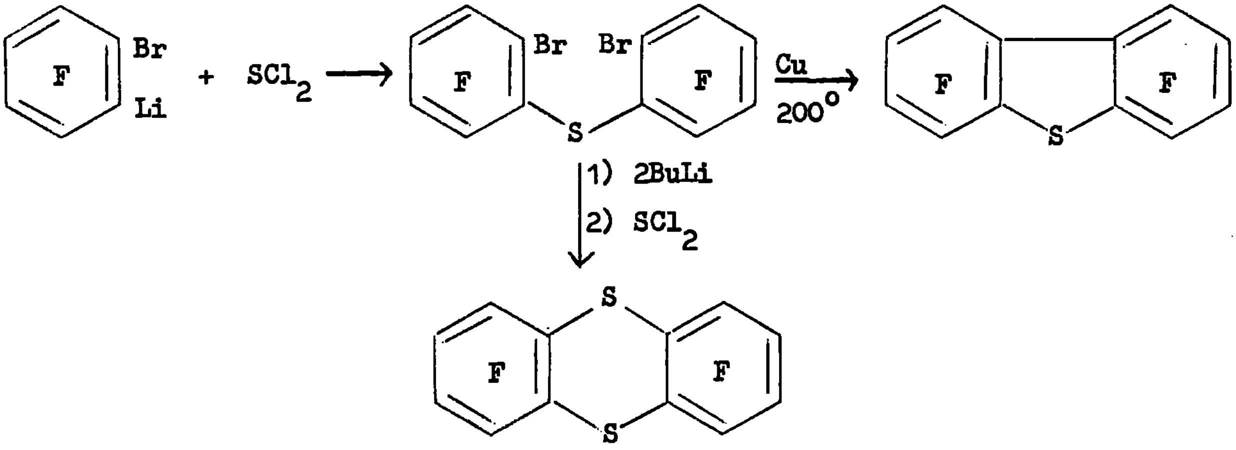
2-Bromotetrafluorophenyl-lithium has also been used in this type of reaction,[5,6]

e.g.

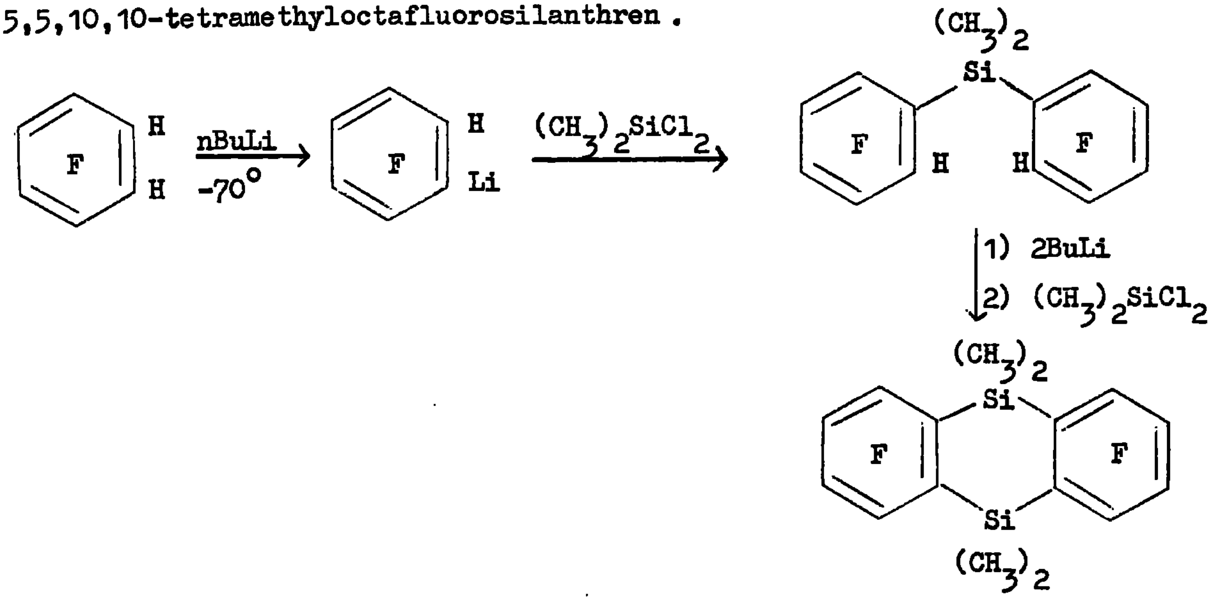




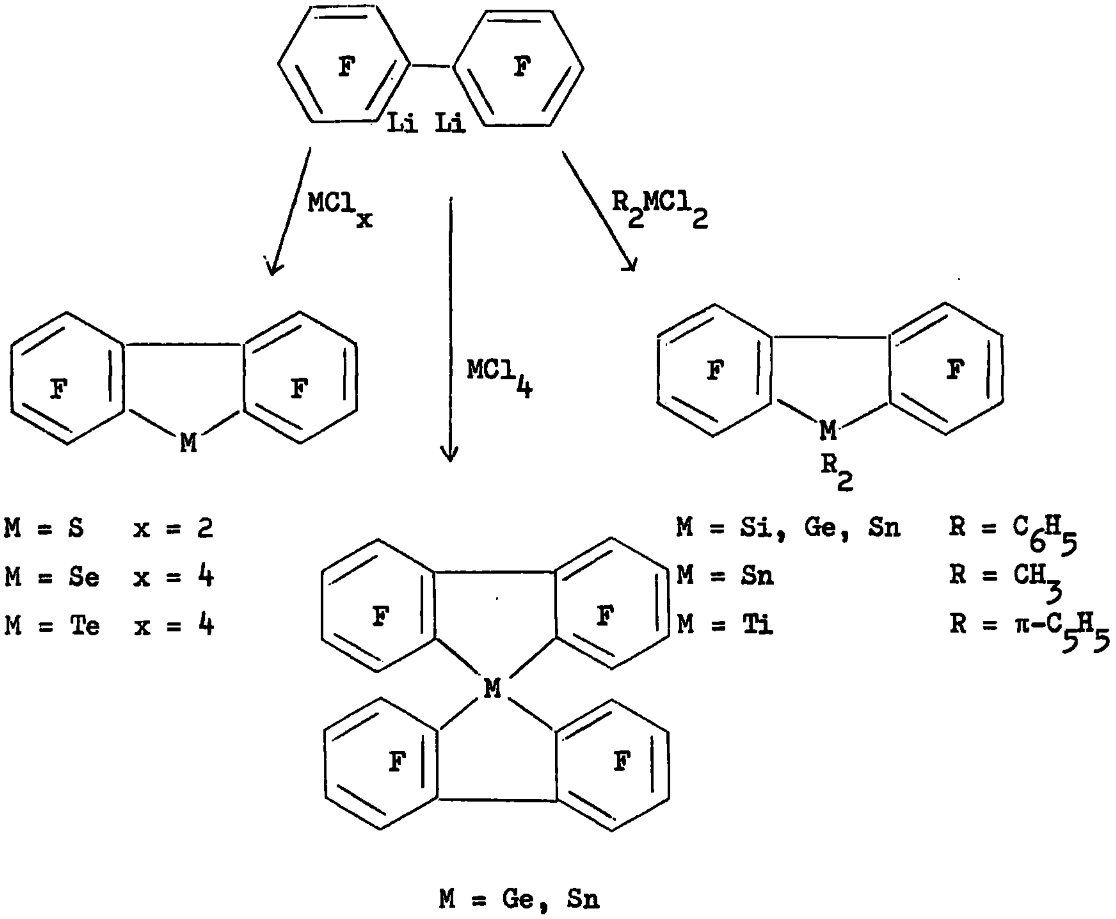
and its reaction with sulphur dichloride has been used as the first step in the synthesis of the perfluoro sulphur heterocycles, octafluorothianthren[5] and octafluorodibenzothiophen.[13]



Gilman and co-workers[14] have used a similar route to prepare 5,5,10,10-tetramethyloctafluorosilanthren.



Massey has made extensive use of octafluoro-2,2'-dilithiobiphenyl to prepare perfluoroheterocycles of the dibenzo series[7,12].



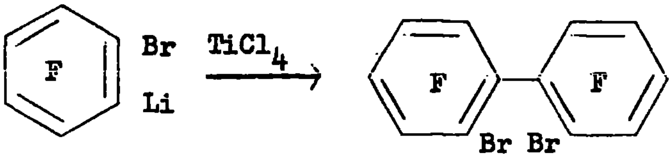
M = S x = 2
M = Se x = 4
M = Te x = 4

M = Si, Ge, Sn R = C_6H_5
M = Sn R = CH_3
M = Ti R = π-C_5H_5

M = Ge, Sn

Reaction of polyfluoroaryl-lithiums with excess titanium tetrachloride at -78° yields a titanium derivative, which on standing at room temperature decomposes to give a biaryl[15] (though in lower yields than the classical Ullmann route).

e.g. $C_6F_5Li \xrightarrow{TiCl_4} C_6F_5 \cdot C_6F_5$ 70%



50%

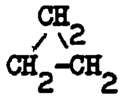
The active intermediate is thought[7] to be Ar_2TiCl_2, which splits up on warming to Ar·Ar and $TiCl_2$, the latter being oxidised during work up.

Chapter 2

Stabilisation of Carbanions by Substituents

2.1. Unsubstituted Carbanions

In the absence of strongly acidifying substituents, the factor which determines the stability of the carbanion is the amount of 2s character of the orbital which contains the electron pair;[16] this is shown by the following results:

Compound	$HC\equiv CH$	$CH_2=CH_2$		CH_4
pKa	25	36•5	39	42
hybridisation	sp	sp^2	$sp^{2\cdot 28}$	sp^3
%2s	50	33	30	25

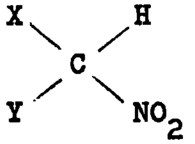
In fact a plot of pKa against %2s character gives a reasonable straight line. Electrons in an s orbital are held closer to the nucleus than those in a p orbital, and so are more stabilised by the nuclear positive charge, thus accounting for the increase in acidity with increasing s character.

2.2. α-Halogen Substituents

The ability of halogens to stabilise an adjacent (i.e. α) carbanion in the order F < Cl < Br < I was noted by Hine[17] in the course of his classic work on the hydrolysis of haloforms. He measured the kinetic acidity (rate of base catalysed hydrogen/deuterium exchange) of a series of these haloforms, and observed the above order for the ability of the halogens to acidify the carbon acid. The same order was also obtained when the kinetic acidity of compounds of the type CF_3CXYH (X and Y are Cl, Br, I) was investigated.[18]

Other workers investigating the acidity of some nitroalkanes, found that α fluorine is less acidifying than an α hydrogen. Thus the pKa of $CHF(NO_2)_2$ was found to be ~4 units larger than that of $CH_2(NO_2)_2$;[19] that of CH_2FNO_2 ~ 2 units larger than that of CH_3NO_2;[20] and that of CF_3CHFNO_2 ~2 units larger than that of $CF_3CH_2NO_2$.[20]

Adolph and Kamlet[21] measured the pKa values of a series of nitromethanes of the type



where Y = Cl, $COOC_2H_5$, $CONH_2$, NO_2

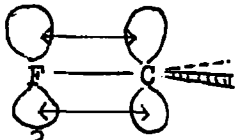
X = F, Cl, H.

Their results indicate that the pKa values lie in the order F > H > Cl for a given Y group (except for Y = NO_2, where Cl ~ H).

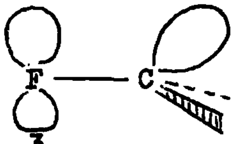
Hine has recently shown[22] that the effect of fluorine on carbanion stability depends strongly on the conformation of the carbanion concerned (and also on the electronic configuration of the carbanionic carbon atom). If the carbanion is sp^3 in electronic configuration, then fluorine is strongly stabilising and the decrease in pKa or increase in kinetic acidity correlates well with that which would be expected in terms of the inductive effect of fluorine alone. Thus the kinetic acidities of $CHFX_2$ compounds are 10^4 to 10^5 times greater than those for the corresponding CH_2X_2 compounds. Carbanions with substituents which exert strong mesomeric effects (e.g. NO_2) tend towards planarity, the actual degree of planarity depending on the extent to which the mesomeric effect can overcome the preference of the electron pair to reside in the orbital of highest s character (i.e. sp^3 rather than p), thus we get a spectrum of carbanion conformations. The greater the flattening of such carbanions then the smaller becomes the stabilising effect of fluorine, and if the carbanion is sufficiently flattened,it becomes destabilising relative to hydrogen. Thus the σ inductive stabilising effect of fluorine is being counterbalanced by a destabilising effect which depends on carbanion conformation.

As an explanation for this, Hine suggests that the bond between halogen and sp^2 carbon is weaker than that between halogen and sp^3 carbon, since the former is more electronegative. This bond weakening effect is larger for fluorine than for chlorine or hydrogen, since it depends on the square of the electronegativity difference between the atoms involved. Thus the formation of an sp^2 hybridised carbanion from an sp^3 carbon acid would tend to be more energetically unfavourable when the substituent is fluorine than when it is chlorine or hydrogen. The magnitude of this effect will decrease as the geometry of the carbanion formed becomes less and less planar.

Adolph and Kamlet,[21] mention however, that these results can also be rationalised in terms of the Iπ effect. When the carbanion is planar, and the electron pair in a p orbital on the carbon atom, it is possible to get repulsion between these electrons and those in a filled p orbital on the fluorine. This is attributed to simple coulomb repulsion of these electrons,[23] or to unfavourable penetration of the carbanion π system by the halogen p electrons.[24] As the carbanion becomes less and less planar this effect will diminish because the unfavourable overlap of the orbitals is reduced.



sp^2 carbanion



sp^3 carbanion

In the case of chlorine, such effects would not be so important because of reduced overlap between the p orbitals on the halogen and those of the π system. The order of Iπ repulsion effects has been shown[23] for the halogens to be F $>$ Cl $>$ Br $>$ I. Hydrogen should have no Iπ effect since it has no p electrons.

However the results for the nitromethane series[21] show the order Cl $>$ H $>$ F in carbanion stabilising ability; thus it is probable that in the case of chlorine we have an effect which works in the reverse sense superimposed onto the Iπ effect. This could be delocalisation of the negative charge into vacant 3d orbitals on chlorine. That this is possible is shown by the results of Doering and Hoffmann[25] who found that the kinetic acidity of $(CH_3)_4P^+$ was $2{\cdot}4 \times 10^6$ times greater than that of $(CH_3)_4N^+$. However for the halogens this effect would be expected to decrease in the order Cl $>$ Br $>$ I $>$ F, because the effective overlap of the d orbitals with the π system will decrease with increasing atomic number, since a similar order P $>$ As $>$ Sb $>$ N was found for the $(CH_3)_4M^+$ series.[25] It should be remembered though that these carbanions are probably pyramidal, and the same order may or may not apply to planar or near planar carbanions (see section 2.4).

Hine[17] has suggested that the order F $<$ Cl $<$ Br $<$ I, determined from the acidities of the haloforms, could also be explained in terms of electrostatic polarisation of the halogen by the carbanionic charge, since the polarisabilities of the halogens increase with increasing atomic size.

As can be seen, the effects of the halogens on an adjacent carbanion can be quite complicated, since they depend on the geometry of the carbanion which in turn depends on the degree of delocalisation of the negative charge. As a result, introducing a carbanion stabilising substituent may change the geometry of the carbanion sufficiently to change the overall nature of the mode of interaction of some of the other substituents. A variety of effects are involved; inductive effects, field effects, polarisabilities, Iπ effect, mesomeric effect, d-orbital effects, and bond energy-electronegativity effects, and all should be considered ideally. To pick out just one of these for some rationalisation of results is a gross oversimplification which may or may not be justified, only experimental verification of its predictions will decide.

Whatever the nature of the effects which determine the relative abilities of the halogens to stabilise an adjacent carbanion, the order $F < Cl < Br < I$ has found extensive use in the rationalisation of orientation of nucleophilic substitution of polyhalocyclobutenes,[26,27] cyclopentenes[27,28] and polyfluoroaromatic compounds.[51] In these systems the ring constraints enforce a planar geometry on the intermediate carbanions so one is not troubled by any effects due to variable geometry.

2.3. β-Halogen Substituents

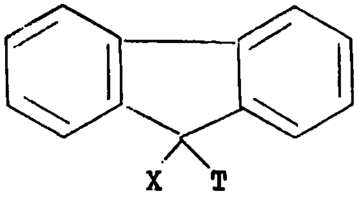
Andreades[29] showed that fluorine was strongly stabilising from the β position, by measuring the kinetic acidity of a series of monohydrofluorocarbons.

	CF_3H	$CF_3(CF_2)_5CF_2H$	$(CF_3)_2CFH$	$(CF_3)_3CH$
k(rel.)	1·0	6	2×10^5	10^9

Analogous results were obtained by Hine[18] who found that the kinetic acidity of CF_3CCl_2H was ~40 times that of $CFCl_2H$.

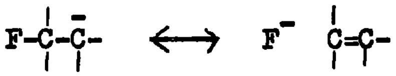
The acid strengths of the nitroethanes $CF_3CH_2NO_2$ and $CH_3CH_2NO_2$ were determined by Knunyants[20] to be $4{\cdot}0 \times 10^{-8}$ (K_a) and $6{\cdot}1 \times 10^{-11}$ respectively.

Streitweiser, in the course of measuring the rates of protodetritiation of a series of 9-substituted fluorenes,[30] found that X = CF_3 increased the kinetic acidity by a factor of 2×10^4 compared



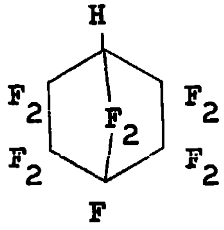
to X = H.

Andreades attributed[29] this stabilisation of a carbanion by a β fluorine atom to a negative hyperconjugation effect.



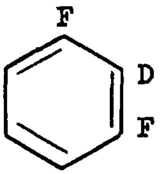
$$F-\overset{|}{\underset{|}{C}}-\overset{-}{\underset{|}{C}}- \longleftrightarrow F^- \ \overset{|}{\underset{|}{C}}=\underset{|}{C}-$$

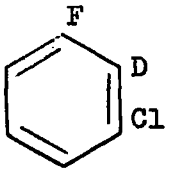
However it has been conveniently explained by Streitweiser in terms of the inductive effect,[31] since a determination of the kinetic acidity of the bicyclic fluorocarbon below showed it to be $\sim 5 \times 10^9$ (relative to CF_3H).

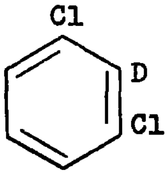


This carbanion should have an enforced pyramidal conformation and should, as a result, be incapable of negative hyperconjugation (this is also supported by the fact that its lithium derivative is much more stable than most perfluoroalkyl lithiums towards elimination of LiF, indicating the instability of a bridgehead olefin[68]). Thus one concludes that a β fluorine atom stabilises a carbanion primarily by its inductive effect. This is further confirmed by the fact that in the 9-substituted fluorene series,[30] the observed rate enhancement due to CF_3 correlates well with its σ_I value. It is also worth noting that the stabilising effect of a β fluorine atom on a pyramidal carbanion is greater than that due to an α fluorine atom, since Andreades compounds[29] almost certainly give pyramidal carbanions.

There is very little evidence for the effect of the other halogens on a β carbanion. Hine[32] determined the rates of proto-dedeuteration of the m-dihalobenzenes shown





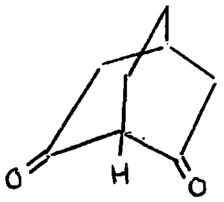


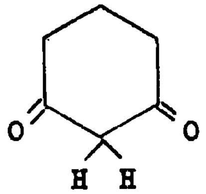
10^6k (100°)	978	151	20·2

which indicates that replacement of β chlorine by β fluorine increases the rate of carbanion formation by a factor of 7. This was attributed to inductive effective, which one would expect to be in the order F > Cl.

2.4. Other Groups

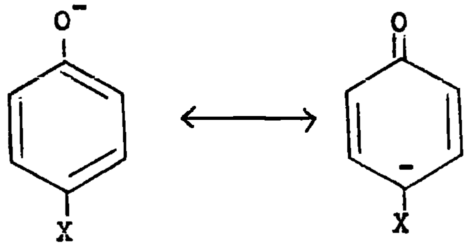
Substituents capable of delocalising the electron pair onto more electronegative elements require an sp^2 hybridisation of the carbanion in order to maximise overlap. Such groups include nitro, cyano, and carbonyl. Thus the tricyanomethide anion $\bar{C}(CN)_3$ has been shown by X-ray crystallographic work to be virtually planar.[33] Any solvation, steric, or ring constraint effects which reduce the planarity of the carbanion, reduce the orbital overlap, hence reducing the conjugation and the stability of the carbanion. This is evidenced by the fact that the bicyclic β-diketone shown is a much weaker carbon acid than is cyclohexa-1,3-dione,[33]





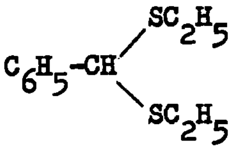
since ring constraint in the former prevents planarity of the carbanion.

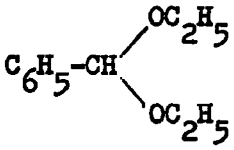
Studies on the ability of meta and para substituents to acidify phenols show that the inductive effect makes an important contribution



to the total stabilisation, even for groups that conjugate well with the carbanion.[34]

Another important effect, which was mentioned in section 2.2., is stabilisation due to vacant d-orbitals on the substituent,[35] thus the observed kinetic acidities of the two compounds shown are,


$C_6H_5-CH(SC_2H_5)_2$


$C_6H_5-CH(OC_2H_5)_2$

k(rel.) 10^6 1·0

But for the fact that the inductive effect will tend to favour oxygen, the extra stabilising effect due to sulphur would have been even larger. Even for groups such as CH_3SO and CH_3SO_2, their effect, on phenol acidity, suggests that their d-orbital resonance effect is at least as important as their inductive effects. Studies also suggest that the ability of a hetero atom to stabilise a carbanion by d orbital resonance is little affected by the geometry of the carbanion, unlike p orbital resonance effects.

Chapter 3

Nucleophilic Substitution in Polyfluoroaromatic and Heterocyclic Compounds

The most extensively studied reaction of polyfluoroaromatic compounds, is that involving displacement of a fluoride ion by a nucleophile. These reactions of polyfluorohomocyclic compounds have been studied principally by research workers at the University of Birmingham. Only relatively recently have some perfluoroheterocyclic compounds been synthesised; and the similar reactions of these compounds have been studied principally in these laboratories and at the University of Manchester.

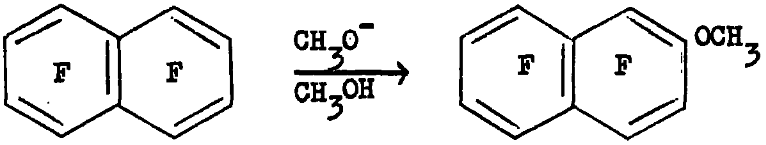
3.1. Nucleophilic Substitution in Polyfluoroaromatic Compounds.

The reaction of hexafluorobenzene with a wide variety of nucleophilic reagents such as $^-OCH_3$,[36], ^-OH,[37] NH_3,[38] $NH_2NH_2.H_2O$,[38] ^-SH,[39] CH_3NH_2,[38] CH_3^- [40], and $C_6H_5^-$,[41] results in replacement of a single fluorine atom under moderate conditions to give a good yield of the corresponding pentafluorophenyl compound.

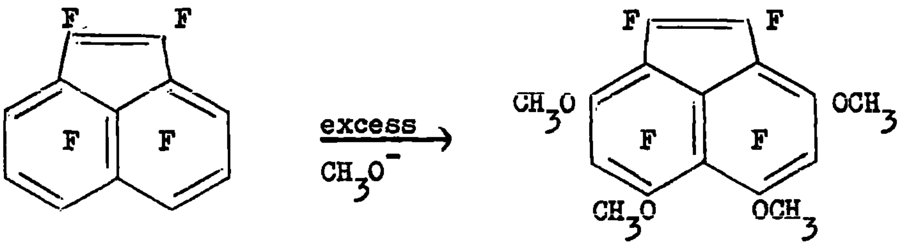
Nucleophilic replacement reactions of the C_6F_5X compounds have been carried out, and are of considerable interest because different positional isomers can be formed. In most cases, the fluorine para to X was replaced[42] ($>$ 90%) when for example X = H, CH_3, CF_3, SCH_3, SO_2CH_3, $N(CH_3)_2$, Cl, Br, and I. However when X = O^- [43] and NH_2[44] meta replacement occurs predominantly, and when X = OCH_3[43] and $NHCH_3$[44] para and meta replacement occur to a similar extent. In these examples the nucleophile had little effect in determining the orientation; however in certain cases[45,46,47] (X = NO_2, NO, CO_2^-) it was observed that reaction took place at the para position with $NaOCH_3$ in CH_3OH, but gave high ortho replacement (> 50% in some cases) with certain amines. This is attributed to specific hydrogen bonding between the nucleophile and the substituent. Solvent can also have an effect on orientation; thus in ether (containing a little methanol) $NaOCH_3$ reacts with pentafluoronitrobenzene to give over 50% ortho replacement.[48]

Nucleophilic substitution reactions of perfluoropolycyclic aromatic systems have been studied: octafluoronaphthalene reacts readily with nucleophiles,[49] to give good yields of 2-substituted heptafluoronaphthalene derivatives.

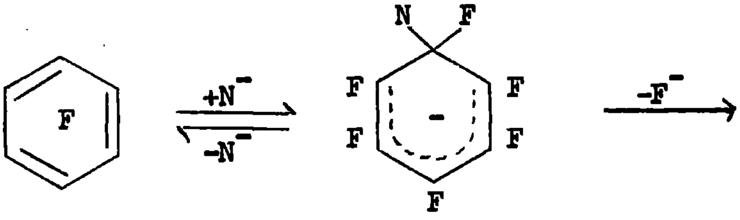
e.g.



Substitution in octafluoroacenaphthalene[50] occurs sequentially at the 3,8,5, and 6 positions; the tetramethoxy tetrafluoroacenaphthalene being formed when 4 or more equivalents of sodium methoxide are used.



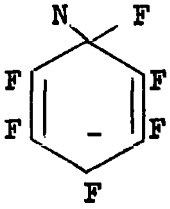
The most successful attempt at a general rationalisation of orientation of substitution in polyfluoroaromatic compounds is that proposed by Burdon.[51] The substitution reaction is assumed to involve an addition-elimination mechanism proceeding through a definite intermediate; thus reaction of C_6F_6 with a nucleophile is represented,



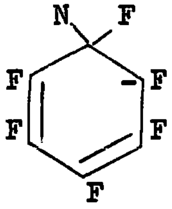
(I)

Recently kinetic evidence in favour of this type of mechanism[52] has been published.

The Wheland intermediate (I) was used as an approximation to the transition state of the substitution reaction, with the resonance canonical II assumed to be the main contributor to this transition state, and with III of only minor importance.



II



III

Apparently this assumption receives considerable justification from the results of advanced molecular orbital calculations. The results can be rationalised by a consideration of the relative stabilities of the transition states concerned, except where solvent, steric and specific nucleophile-substituent interactions are in operation.

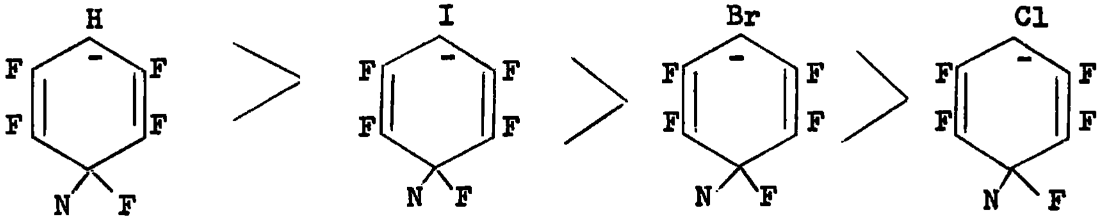
In considering substitution in C_6F_5X compounds, the problem resolves itself into a consideration of the effect of the substituent on the carbanion localised adjacent to itself. If the substituent X is capable of stabilising the carbanion more effectively than fluorine, then substitution will occur para to X and to a lesser extent at the ortho position (since canonicals of type III, while of lesser importance, are not completely negligible). If the substituent X stabilises the carbanion less effectively than fluorine, then substitution will occur meta to X; and if to exactly the same extent as fluorine, then the ortho: meta: para replacement ratio will be the statistical 2:2:1.

The halogens were assumed to stabilise an adjacent carbanion in the order $F < Cl < Br < I < H$, and this was attributed[51] to the $I\pi$ effect. It should be noted however, that because of the effect of the ring, these are planar carbanions, and will maximise such an effect (see section 2.2). The magnitude of the $I\pi$ repulsion effects for N and O were not obtainable, but were assumed to be in the order $N > O > F$.

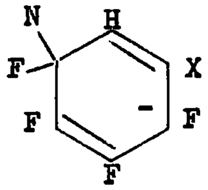
Thus one can understand the increasing amount of ortho substitution in the series

Compound	C_6F_5H	C_6F_5I	C_6F_5Br	C_6F_5Cl	C_6F_6
% ortho	3	5	12	17	(40)

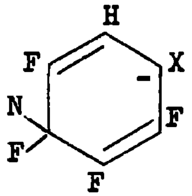
since this is the order for decreasing stability of canonicals of type II, relative to the corresponding canonicals for ortho and meta substitution.[53]



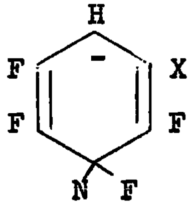
It has also been extended to the tetrafluorohalobenzenes;[54] the predominance of substitution para to hydrogen rather than para to halogen in 1,2,3,4-tetrafluoro-5-halobenzenes can be rationalised by a consideration of the relevant canonicals of type II,



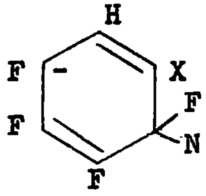
IV



V



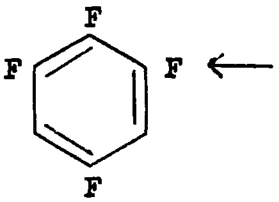
VI

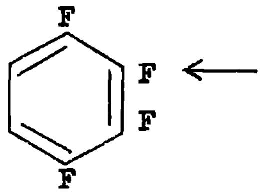


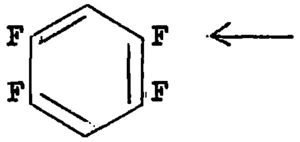
VII

Thus VI would be considered to be more stable than V, and both should be considerably more stable than IV and VII (which should be of equal stability on this simple approach). It also follows that the relative proportion of V in the product should increase in the order Cl < Br < I, and this in fact is observed. Similar results have been found in the 1,2,3,5-tetrafluoro-4-halobenzenes[54] (though see below).

The orientation of nucleophilic substitution in the three isomeric tetrafluorobenzenes[55] can also be understood in terms of the ability of fluorine to stabilise an adjacent carbanion less effectively than hydrogen, in systems of this type. The position of attack in each case is indicated with an arrow. Relevant to this is the fact that

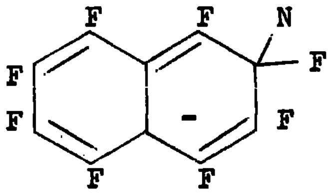




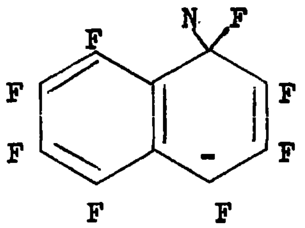


1,2,4,5-tetrafluorobenzene reacts $\sim 10^3$ times slower than the other two isomers.

The orientation of nucleophilic substitution in octafluoronaphthalene[49] can be rationalised in terms of the $I\pi$ destabilising effect of fluorine. Though, of course, an alternative explanation



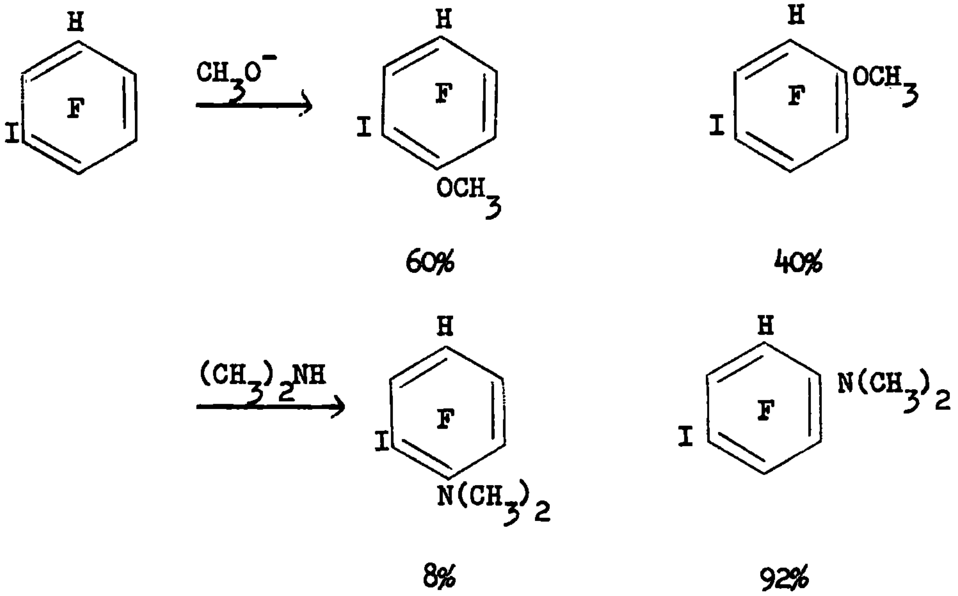
more stable than



is that 2-substitution permits maximum delocalisation of the negative charge into the unsubstituted ring.

Steric factors must be taken into account in some cases;

e.g.



This was rationalised[54] on the basis of a steric interaction between the bulky iodine atom and the dimethylamino group.

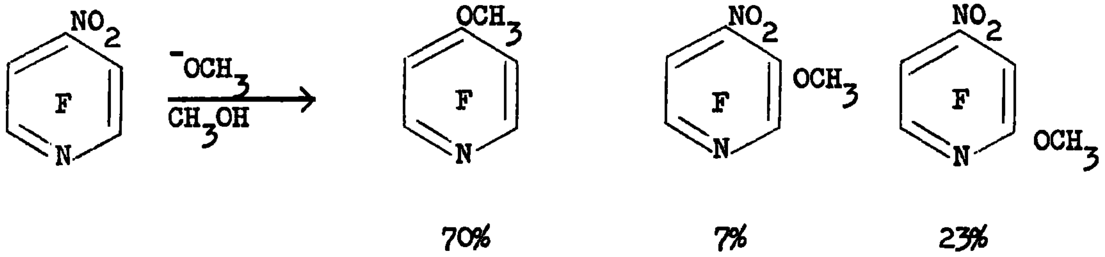
Similar interactions can be used to rationalise the observed orientation of nucleophilic substitution in certain C_6F_5X compounds, where X = $N(CH_3)_2$,[44] $NHCH_3$,[44] and OCH_3.[43] On the basis of $I\pi$ repulsions (N $>$ O $>$ F), meta substitution would be expected to predominate; however steric interaction, between the group X and the ortho fluorine atoms, tends to twist the nodal plane of the p orbitals on X out of the plane of the ring, thus reducing the $I\pi$ repulsions between the two sets of electrons,[51] and accounting for the observed para attack.

3.2. Nucleophilic Substitution in Polyfluoroheterocyclic Systems.

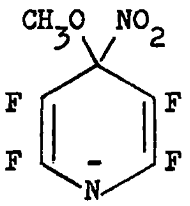
Compared with the homocyclic systems, relatively much less work has been done on the polyfluoroheterocyclic compounds, since they have only recently become available; the systems most studied being the nitrogen heterocycles.

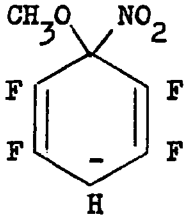
Pentafluoropyridine was the first fluorinated heterocyclic compound to be made, and consequently, has been studied in greatest detail. A wide variety of nucleophiles will react with this to give 4-substituted tetrafluoropyridines,[56,57] under conditions that are much milder than for the corresponding reactions of hexafluorobenzene.

A number of nucleophilic substitution reactions of these 4-substituted tetrafluoropyridines have been carried out. When the substituent is OCH_3[57] and Br[58], replacement of the 2-fluorine occurs, and with excess methoxide a 2,6-dimethoxy compound can be obtained. However reaction of 4-nitrotetrafluoropyridine gives a mixture of products.



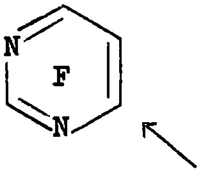
These results were rationalised by assuming that the ring nitrogen is the greatest single factor in determining the orientation of substitution, with the $I\pi$ effect of fluorine of only minor significance. The stabilisation accruing to the transition state from the localisation of the negative charge on the nitrogen far outweighs any absence of a destabilisation due to localisation of the charge adjacent to a fluorine. That this effect is important is indicated by the displacement of a nitro group from 4-nitrotetrafluoropyridine. Such an occurrence is not observed in the reaction of 2,3,5,6-tetrafluoronitrobenzene,[59] since on the basis of the $I\pi$ effect alone this compound should be analogous to 4-nitrotetrafluoropyridine, with the negative charge being localised on a ring atom which does not carry a fluorine atom. In fact this compound undergoes substitution ortho to the nitro group. This decreased importance of $I\pi$ effect is easily understood, since localisation of the negative charge preferentially on the ring nitrogen atom must mean a reduced charge density on the ring carbon atoms compared with the polyfluorobenzene case, hence $I\pi$ repulsions are reduced. The fact that pentafluoropyridine is much more reactive than pentafluorobenzene (which is not very much different in its reactivity from hexafluorobenzene) indicates that the presence of

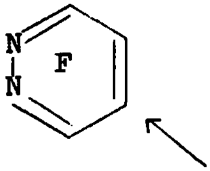


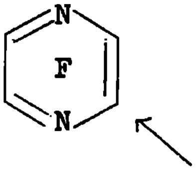


a ring nitrogen is very much more activating than a mere absence of fluorine would be.

Further evidence on this point is provided by the substitution reactions of the three tetrafluorodiazines, which react at the positions indicated.

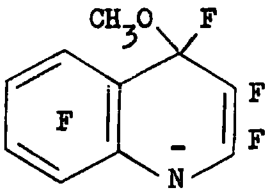


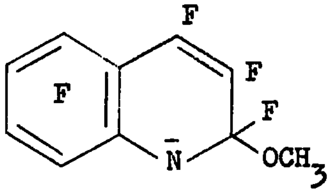




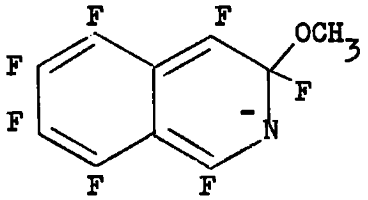
All three compounds were found to be more reactive than pentafluoropyridine, but tetrafluoropyrimidine[60] and tetrafluoropyridazine[61] were more reactive than tetrafluoropyrazine.[62] This is readily understood since in the case of the pyrimidine and pyridazine the transition state is such that the negative charge can be localised onto the nitrogen via a type II canonical, whereas in the pyrazine case only a type III canonical is possible.

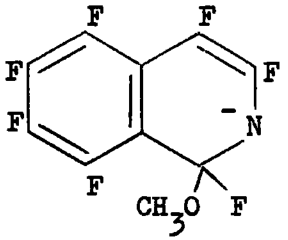
Heptafluoroquinoline reacts with methoxide in methanol[63] to give a mixture of 2-methoxy and 4-methoxyhexafluoroquinoline in the ratio 3·4:1, while heptafluoroisoquinoline yields only 1-methoxyhexafluoroisoquinoline.[63] In the case of the quinoline, the orientations can be rationalised in terms of localisation of the negative charge onto the nitrogen atom.





That 2-substitution predominates indicates that the nitrogen is having considerable effect in distorting the relative energies of the canonicals of type II and III. On the basis of the observed orientation of substitution in heptafluoroquinoline and octafluoronaphthalene, one would predict that nucleophilic attack should occur at the 3-position in heptafluoroisoquinoline.



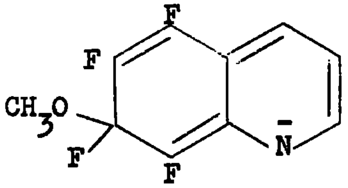


The observed 1-substitution would appear to be taking place preferentially at a position para to a fluorine substituent, in apparent violation of the Iπ effect, but in reality the charge is most likely localised on the nitrogen atom; and 1-substitution occurs because it disturbs the aromaticity of the carbocyclic ring least of all.

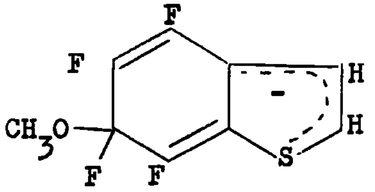
It is worth noting that an examination of the rates of nucleophilic substitution of the monohalo quinolines and isoquinolines shows that the 2-halo and 4-halo derivatives of the former are the most reactive (and of roughly equal reactivity), and that the 1-halo derivative of the latter is also the most reactive. Thus the observed orientation of nucleophilic substitution, in heptafluoroquinoline and isoquinoline, is further confirmation for the fact that orientation of substitution in these systems is dependent mainly on the ring nitrogen atom, and not on any effects of the fluorine atoms.

The other polyfluoroheterocyclic systems whose nucleophilic reactions have been studied so far are those which do not have hetero atom in the ring undergoing substitution. Thus they are more like 1,2-disubstituted tetrafluorobenzene derivatives than the nitrogen heterocycles just discussed.

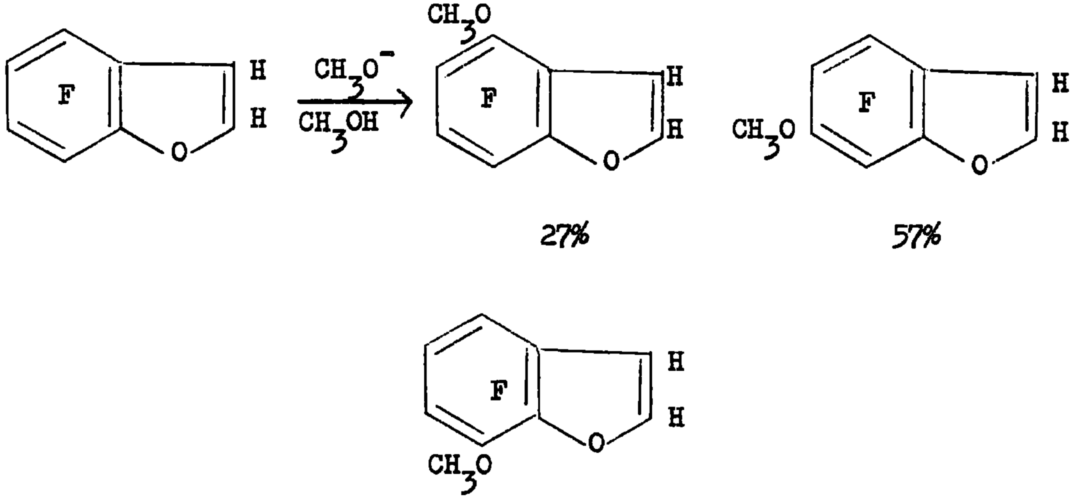
Nucleophilic substitution in 5,6,7,8-tetrafluoroquinoline has been shown to occur at the 7 position,[64] and this has been rationalised as the only position where it is possible to obtain delocalisation of the electron pair onto the nitrogen via a type II canonical.



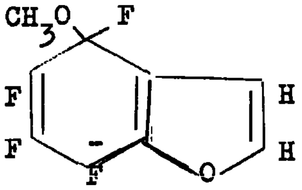
4,5,6,7-Tetrafluorobenzo[b]thiophen reacts with nucleophiles mainly at the 6 position,[65] and this can be rationalised in an analogous way to the tetrafluoroquinoline case, since only with 6 substitution can one get delocalisation of the electrons round the thiophen ring and into sulphur 3d orbitals.



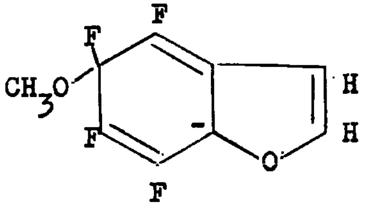
In contrast to the preceeding two cases where only one product was isolated, nucleophilic substitution with methoxide in methanol in 4,5,6,7-tetrafluorobenzo[b]furan yields a mixture of three isomeric monomethoxy derivatives[66].


27%
57%
16%

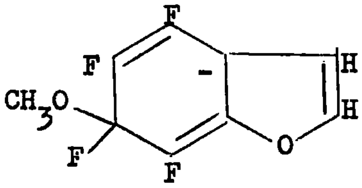
These isomer ratios have been rationalised[67] in terms of Iπ effect by considering first the canonicals of type II .



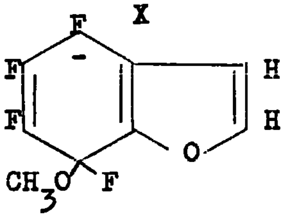
VIII



IX

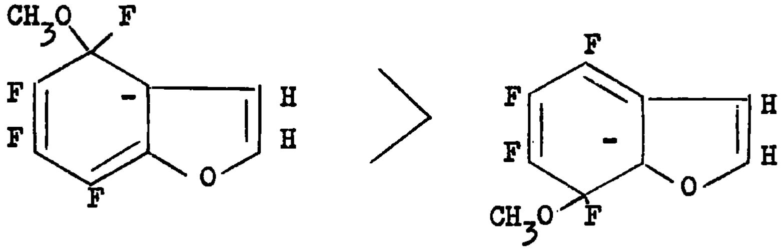


X



XI

Since the order for the $I\pi$ effect will be O > F > ring C, we can see that the order of stability is X > VIII, XI > IX. To understand the fact that more 4 substitution than 7 substitution is observed, a consideration of the relevant type III canonicals is necessary as shown.



In conclusion then, it can be seen that the orientation of nucleophilic substitution in the homocyclic series can, to a great extent, be rationalised in terms of the $I\pi$ effect. However for heterocyclic systems, the results must be treated with greater caution, since the different electronegativities of the ring atoms may favour localisation of the charge, in the transition state, at the hetero-atom, and this in some cases gives rise to orientations which are not in accord with those predicted by the $I\pi$ effect.

DISCUSSION OF EXPERIMENTAL

Chapter 4

Effect of Substituents on Carbanion Stability

As indicated in chapter 2, while a considerable amount of work has been done on the relative ability of the halogens to stabilise an adjacent (i.e. α) carbanion, very little has been done on the effect of β halogens, apart from fluorine. As will have been seen, measurement of the α effect of the halogens has provided much important information on the electronic properties of the halogens, and it is possible that a measurement of the β effect might be similarly valuable. It was thought that this problem could be tackled by a measurement of the kinetic acidities of compounds of the type CH_3SCF_2CFXH and $CH_3SCFXCFXH$ (X = Cl, Br), which could be readily synthesised by a free radical addition of methane-thiol to the appropriate olefins. The method chosen to measure the kinetic acidities was proton n.m.r., and to test the method it was decided to see if Hine's results[17] applied to the series CH_3OCF_2CXYH.

4.1. Experimental Method.

The reaction to be followed was, e.g.

$$\begin{tikzcd} \mathrm{CH_3OCF_2CFClH} + \mathrm{OH^-} \arrow[r, "k"] & \mathrm{CH_3OCF_2\overset{-}{C}FCl} + \mathrm{H_2O} \arrow[d, "\mathrm{fast}"', "\mathrm{CH_3OD}"] \\ & \mathrm{CH_3OCF_2CFClD} \end{tikzcd}$$

The solvent used was CH_3OD, and the base NaOH (for convenience). Since the reaction is one which goes to equilibrium, which is when the statistical percentage of H and D in the solvent is the same as that of the protons undergoing exchange, the first order rate expression used is

$$k = \frac{2\cdot 303}{t} \log_{10} \frac{C_0 - C_\infty}{C - C_\infty}$$

where C_0, C, and C_∞ are the concentrations of undeuterated material at times t = 0, t = t, and $t = \infty$ seconds. A similar expression was used by Andreades in his measurements of kinetic acidity.[29] The rate constant obtained is a pseudo first order, since the concentration of base is assumed to remain steady throughout the reaction.

To measure the concentration of the undeuterated material, proton n.m.r. was used, since it is a convenient and rapid method for following such reactions. The concentration was assumed to be proportional to peak height rather than peak area. That this was justified was demonstrated by making up known mixtures of benzene, CH_3OCF_2CFClH, and methanol and recording their n.m.r. spectra; a plot of peak height against concentration for both benzene and the ether gave a good straight line. To obtain a better average measure of peak height, all the peaks of the multiplet were measured, and their heights summed, and this was used as a measure of concentration (the methine proton of CH_3OCF_2CFClH shows as a doublet of triplets).

Benzene was used as an internal standard to ensure that variations in the height of the peak being followed were due to the exchange reaction and not due to machine factors. If such variations were found to be due to machine factors, then an appropriate correction was made to the measured peak height.

Some difficulty was experienced in measuring the peak height for the ∞ reading, since this was small, and often of comparable magnitude to background noise. Thus calculated C_∞ values were used, assuming a statistical distribution of the protons and deuterons,

$$C_\infty = \frac{n_H}{n_D + n_H} \times C_0$$

where n_H is the number of moles of ether and base put into the tube, and n_D is the number of moles of CH_3OD put into the tube.

The tubes were made up by weighing and the n.m.r. spectrum recorded immediately. They were then placed into a thermostat bath accurate to $\mp 1^\circ$ for a known length of time, when the spectrum was taken again; about 5 or 6 points were taken in this way for each run. The accuracy was not very great, but this does not matter too much since one is really only interested in the large effects.

4.2. α Effect of the Halogens.

The three ethers CH_3OCF_2CFClH, CH_3OCF_2CFBrH, and $CH_3OCF_2CCl_2H$ were made by nucleophilic addition of methanol to the appropriate olefin, and the kinetic acidities were measured at 63°.

	CH_3OCF_2CFClH	CH_3OCF_2CFBrH	$CH_3OCF_2CCl_2H$
10^4k sec.$^{-1}$	0·9	1·4	28
k(rel.)	1·0	1·6	31

Hine[17] observed the following relative rates for replacing F by Cl,

$$\frac{k(CHCl_3)}{k(CHFCl_2)} = 50, \quad \frac{k(CHBrCl_2)}{k(CHBrClF)} = 14, \quad \frac{k(CHBr_2Cl)}{k(CHBr_2F)} = 8$$

and for replacing Cl by Br.[17,18]

$$\frac{k(CHBr_2Cl)}{k(CHBrCl_2)} = 5, \quad \frac{k(CHBr_3)}{k(CHBr_2Cl)} = 4, \quad \frac{k(CF_3CBr_2H)}{k(CF_3CBrClH)} = 1{\cdot}8$$

Thus the results obtained here of 31 and 1·6 respectively correlate with Hine's. It should be noted that the actual magnitude of the acceleration in rate, produced by replacing F by Cl etc., will depend on the other groups present. This is what Hine termed[17] the 'saturation effect'; the more stabilised a carbanion is by its substituents, the less the stabilisation effect produced by replacing one of these by a more stabilising substituent. Thus the difference in rates should be greatest for CHF_3/CHF_2Cl and least for CHI_2F/CHI_2Cl. Steric effects might be important in reducing the stabilisation produced by the bulkier halogens since it could impede the approach of the base in the rate determining proton abstraction step.

The reactions carried out above were complicated by a competing elimination reaction, which would appear to be less affected by the different substituents than is the exchange reaction, since it is most noticeable for CH_3OCF_2CFClH, and hardly noticeable for $CH_3OCF_2CCl_2H$, which exchanges much more rapidly than the former. This elimination reaction has the effect of using up base, hence slowing down the exchange reaction. It is most probably HF which is eliminated, since Hine[69] showed that with the analogous CF_3CCl_2H compound less than 4% of the halide ion liberated was Cl^-. Presumably the initially formed $CH_3OCF{=}CFCl$ reacts further with base.[70]

4.3. β Effect of the Halogens.

The thioether $CH_3SCFClCFClH$ was prepared by free radical addition of CH_3SH to $CFCl{=}CFCl$; however attempts to measure its kinetic acidity failed, since it readily reacted with base in a β elimination reaction.

It was thought that the mechanism of this elimination reaction might be Elcb, since this had been proposed by Hine[69] for the dehydrofluorination reactions of compounds of the type CF_3CXYH (X,Y = Cl, Br, I). If this was in fact the case, it would be possible to obtain some information on the ability of a βCl to stabilise a carbanion from the rate of reaction, since loss of halide ion from the intermediate carbanion was unlikely to be the rate determining step.

However it was necessary to show that the reaction was in fact a simple elimination reaction; this was done as follows,

(i) The thioether was reacted with excess base, and the product isolated was shown to be $CH_3SCF{=}CFCl$.

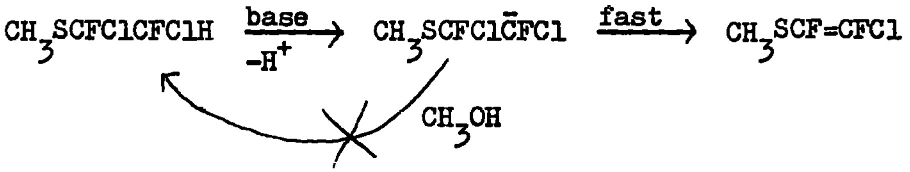
(ii) The reaction with base was run in methanol and, before completion, a sample was analysed by v.p.c., the only components observed were methanol, $CH_3SCF{=}CFCl$, and $CH_3SCFClCFClH$.

Thus the reaction is

$$CH_3SCFClCFClH + OH^- \longrightarrow CH_3SCF{=}CFCl + H_2O + Cl^-$$

and the vinyl thioether does not react further with base, since it can be prepared in the presence of excess base.

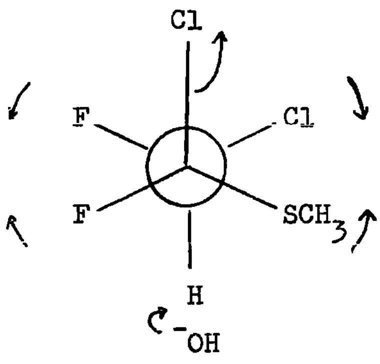
An indication that the reaction could be a concerted process was provided when the reaction was run in CH_3OD and stopped before completion; mass spectrometric analysis of recovered starting material showed no evidence of any significant deuterium incorporation. Hine has argued[69] that such evidence does not rule out initial carbanion formation, since every carbanion, once formed, could eliminate halide ion, rather than abstract a proton from the solvent.



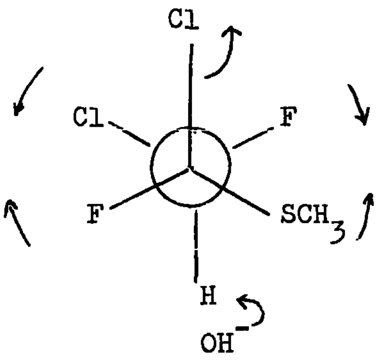
However fairly conclusive proof that the reaction went by a concerted route was provided when the kinetics of the reaction were measured. This was done titrimetrically, by measuring the amount of base left after a given time. It was found that the second order plot changed slope after about 25% reaction. This was attributed to the two diastereomers of $CH_3SCFClCFClH$ reacting at different rates. From the intercepts of the two straight lines on the $^1/C_B$ axis it was possible to estimate the relative amounts of the two diastereomers, and this agreed with that measured by ^1H n.m.r., since the methine multiplet for the minor isomer was situated ~ 0·6 p.p.m. upfield from the same multiplet of the major isomer.

	Relative Amount		
	n.m.r.	kinetics	Rate Constant (26^o)
Isomer A	82%	83%	$(1{\cdot}16 \mp 0{\cdot}02) \times 10^{-4}$ mole^{-1} litre.sec.$^{-1}$
Isomer B	18%	17%	$(2{\cdot}12 \mp 0{\cdot}06) \times 10^{-4}$ mole^{-1} litre.sec.$^{-1}$

This difference of rate can be attributed to steric repulsion of Cl and SCH_3 which are eclipsing in the transition state of A, but not in the case of B.



A



B

The strong conformational dependence of the rate of elimination thus appears to indicate that in the transition state, breaking of the carbon-chlorine bond, and also double bond formation is quite developed, and so the process is not Elcb, and must be a concerted E2 process.

It was thought that substitution of a more electronegative group than CH_3S might hinder departure of Cl^-, and perhaps make the elimination process more Elcb in character. However when the rate of reaction of the sulphone $CH_3SO_2CFClCFClH$ with base was measured it was found to be ~ 0·12 $mole^{-1}$. $litre. sec.^{-1}$ at 26°, a 1000 fold increase compared with $CH_3SCFClCFClH$. Similarly it was found that the rate for $CH_3SO_2CF_2CFClH$, $(1{\cdot}9 \mp 0{\cdot}1) \times 10^{-4}$ $mole^{-1}$. $litre. sec.^{-1}$ was ~1000 times faster than that for CH_3SCF_2CFClH, ~ 2×10^{-7} $mole^{-1}$. $litre. sec.^{-1}$, both at 62°.

Most probably we are getting elimination of $CH_3SO_2^-$ by a bimolecular process.

$$\begin{tikzcd}
CH_3SO_2CFClCFClH \arrow[r, "OH^-"] & CH_3SO_2^- + CFCl{=}CFCl + H_2O \\
& ? \arrow[from=1-2, "base"]
\end{tikzcd}$$

Although elimination of sulphinyl anions is uncommon it is not unknown, and it has been shown[71] that RSO_2^- is eliminated as readily as Br^- from systems of the type

$$XCH(CH_3)_2 \xrightarrow{base} X^- + CH_2{=}CHCH_3 + H^+$$

Thus one would expect elimination of $CH_3SO_2^-$ preferentially to Cl^-. If elimination of $CH_3SO_2^-$ is not taking place, it would be very unusual to find an electron withdrawing group situated at the β carbon atom accelerating an elimination reaction.

In conclusion it would seem that it is impossible to measure the desired effect in the chosen system. In order to measure the carbanion stabilising effect of βCl it will be necessary to choose a system where an elimination reaction is prohibited, perhaps by using a suitable bicyclic system where the acidic proton is at a bridgehead position.

4.4. Effect of βCH_3S and βCH_3SO_2 on Carbanion Stability.

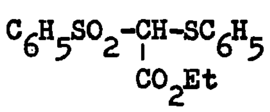
The kinetic acidities of the compounds shown were measured.

$CH_3SCF_2CCl_2H$ $k(34^\circ) = 8 \times 10^{-4}$ sec.$^{-1}$
CH_3SCF_2CFBrH $k(54^\circ) = 3 \times 10^{-4}$ sec.$^{-1}$
$CH_3SO_2CF_2CFBrH$ $k(54^\circ) = 0{\cdot}6 \times 10^{-4}$ sec.$^{-1}$
$CH_3OCF_2CCl_2H$ $k(34^\circ) = 1{\cdot}5 \times 10^{-4}$ sec.$^{-1}$
CH_3OCF_2CFBrH $k(54^\circ) = 0{\cdot}2 \times 10^{-4}$ sec.$^{-1}$

Thus for the XCF_2CFBrH series at 54° we have

	CH_3O	CH_3SO_2	CH_3S
k(rel.)	1	3	15

It should be noted that for the XCF_2CCl_2H series (at 34°) k = 5 for X = CH_3S (relative to X = CH_3O), this would appear to be due to the operation of the 'saturation effect';[17] the greater stabilising ability of αCl_2 compared with αFBr, reduces the need for extra stabilisation from βCH_3S.

From the above results it would appear that a βCH_3S is more effective than a βCH_3SO_2 group in stabilising a carbanion. This is the reverse of their relative effects when in the α position; thus the pKa of $(C_6H_5SO_2)_2CH \cdot CO_2Et$ is 4·6, whereas that of  $C_6H_5SO_2\text{-}\underset{\substack{|\\ CO_2Et}}{CH}\text{-}SC_6H_5$ is 8·9.[72,73]

It is possible that the result for βCH_3S could be rationalised in terms of a 'neighbouring group participation' effect, with partial delocalisation of the electron pair into vacant sulphur 3d orbitals. However one would expect this effect to be even more important in the case of CH_3SO_2, because of the higher electron deficiency of the sulphur atom (as with the α effect of these groups). Perhaps the most satisfactory rationalisation is in terms of an electrostatic polarisability effect,[17] since this might be expected to lie in the order $CH_3O < CH_3SO_2 < CH_3S$.

Chapter 5

Reaction of Polyfluoroaryl-lithiums with Dimethylcarbonate

5.1. Introduction.

Dialkylcarbonates have found fairly extensive use in organic chemistry as versatile reagents for the preparation of esters, ketones, and tertiary alcohols. Thus diethylcarbonate was shown to react with Grignard reagents in three stages[74].

$$RMgX + CO(OEt)_2 \longrightarrow R{\cdot}COOEt + EtOMgX$$

$$RMgX + R{\cdot}COOEt \longrightarrow R{\cdot}CO{\cdot}R + EtOMgX$$

$$RMgX + R{\cdot}CO{\cdot}R \longrightarrow R_3COMgX \xrightarrow[H_2O]{H^+} R_3COH$$

However they have been most used as carboalkoxylation reagents, e.g.[75]

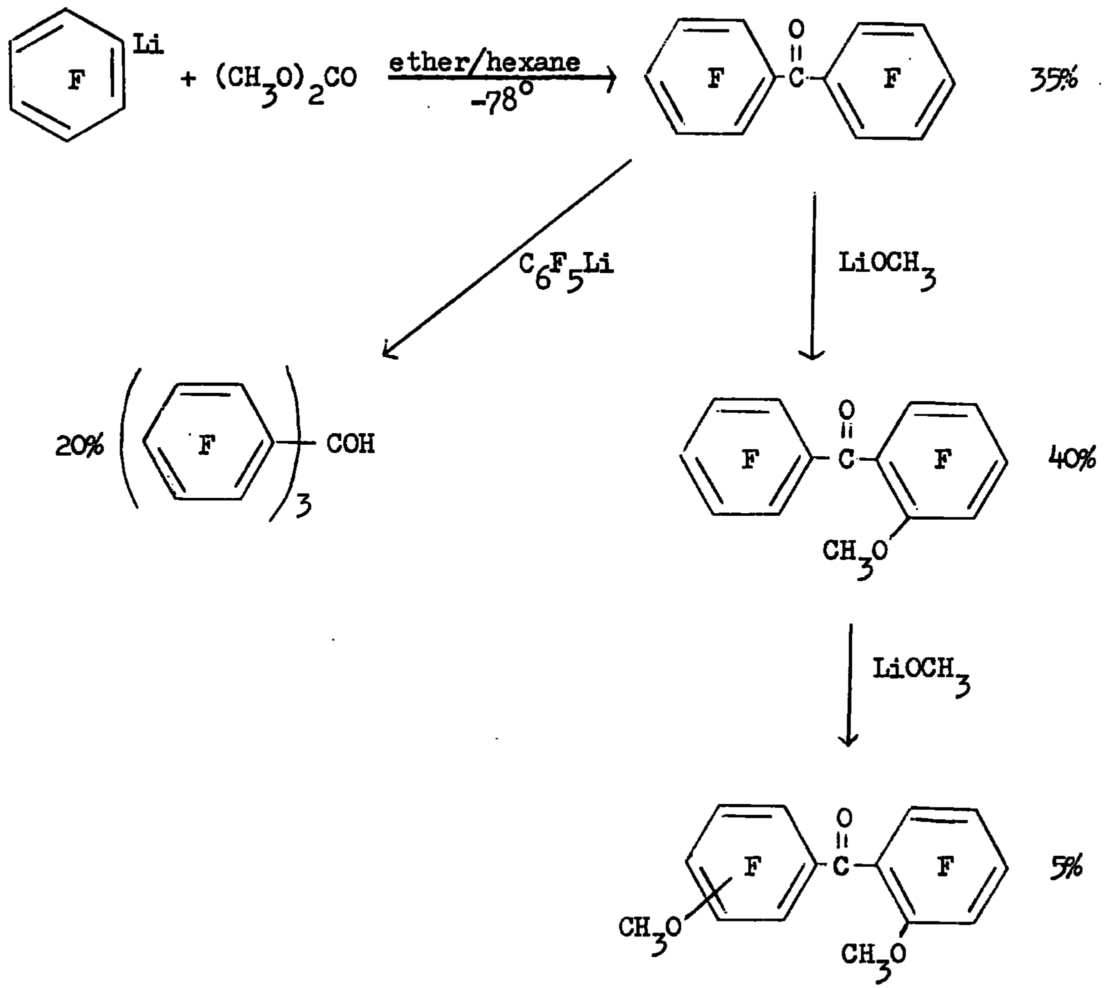
$$PhCH_2{\cdot}COOEt \xrightarrow[NH_3]{NaNH_2} Ph{\cdot}\overset{-}{C}HCOOEt \;\; \overset{+}{Na} \xrightarrow{CO(OEt)_2} Ph{\cdot}CH(COOEt)_2$$

Apart from a brief report[76] of the preparation of $(C_6F_5)_3COH$ by reaction of $(EtO)_2CO$ with 3 equivalents of C_6F_5Li, very little use has been made of these compounds in fluorine chemistry, and consequently it seemed appropriate to investigate their use in the preparation of polyfluoroaryl ketones, especially octafluoro-9-fluorenone.

5.2. Preparation of Decafluorobenzophenone.

First the reaction of dimethylcarbonate with two equivalents of pentafluorophenyl-lithium (prepared from C_6F_5H or C_6F_5Br) was investigated.

The initial attempt was unsuccessful since a mixture of products was obtained as shown.



The mixture was separated by preparative scale v.p.c. and the products characterised, although insufficient of the dimethoxy derivative was obtained for characterisation.

These difficulties were overcome by

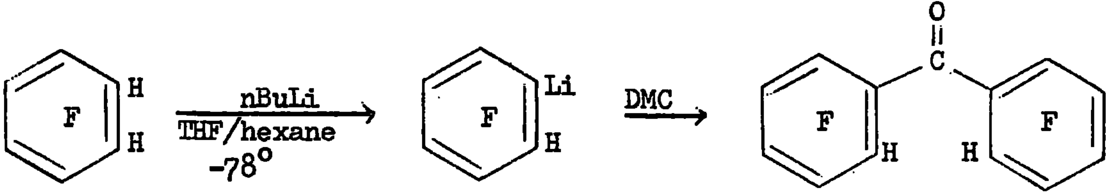
(i) adding the required amount of dimethylcarbonate (DMC) rapidly, thus reducing the length of time for which excess pentafluorophenyl-lithium is present and so inhibiting the formation of tris(pentafluorophenyl)carbinol,

(ii) hydrolysing the reaction mixture at -20° instead of at room temperature and so preventing the formation of methoxy derivatives.

In this way 70% yields of decafluorobenzophenone were obtained, and this method appears to be a more convenient synthesis than the methods used so far, which involve oxidation of bis(pentafluorophenyl)methanol,[77] or pyrolysis of $Si(OCOC_6F_5)_4$.[78]

5.3. Preparation of Octafluoro-2,2'-dihydrobenzophenone.

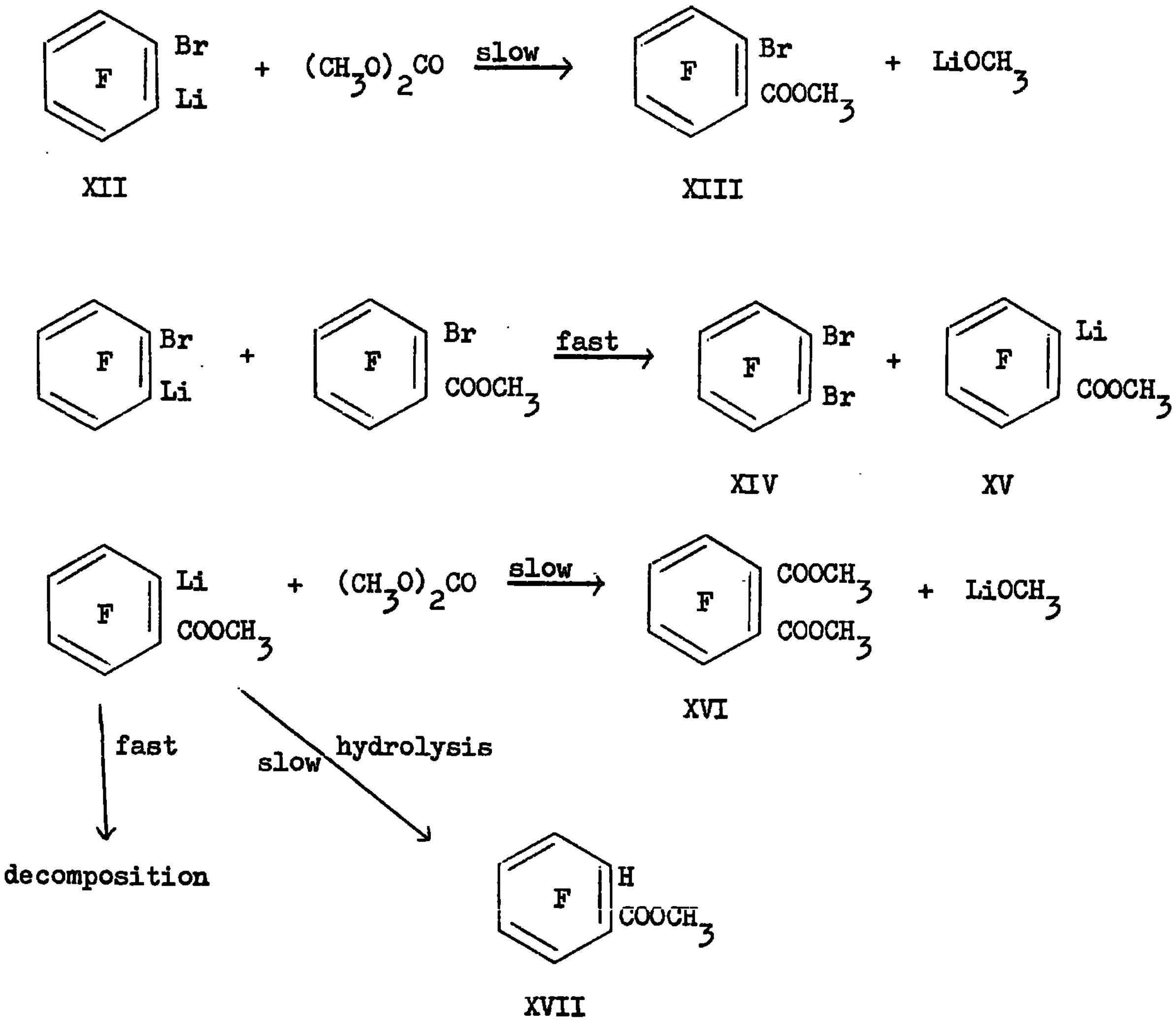
This was accomplished by means of an analogous route



Several methods for the preparation of the tetrafluorophenyl-lithium were tried, the most convenient one being shown. It was found that the use of 1-bromo-2,3,4,5-tetrafluorobenzene resulted in the presence of butyl bromide which impeded the purification of the product, which surprisingly enough is a high boiling liquid. The use of THF as solvent gives the best yields (compared to ether) when it is hydrogen that is being lithiated, as indicated in section 1.1.

5.4. Reaction of 2-Bromotetrafluorophenyl-lithium with Dimethylcarbonate.

Extension of this reaction to 2-bromotetrafluorophenyl-lithium was complicated by an exchange reaction and did not yield the corresponding benzophenone. The reactions which occur are as shown.



Thus when equimolar amounts of XII and DMC are allowed to react at -78° in ether/hexane, then the major products are XIV (~70%) and XIII (~30%), with only minor amounts (< 1%) of XVI and XVII (see Table 7). However the high yield of the dibromo compound XIV does not indicate that the initial exchange reaction has not gone (XII is made by reaction of nBuLi with XIV), since under these conditions the reaction has been shown to be essentially instantaneous.[5,6]

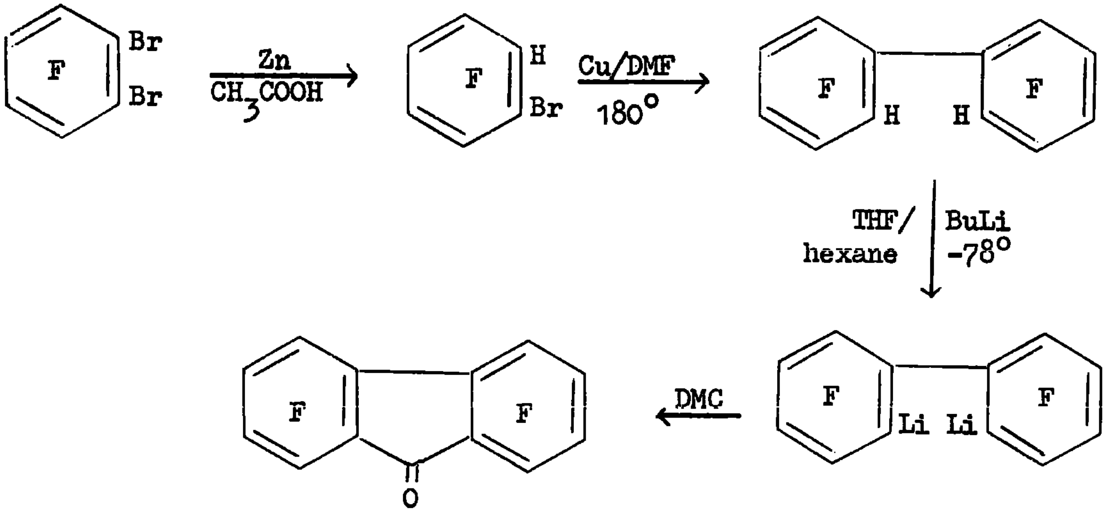
It will have been appreciated from section 1.2. that rapid Li/Br exchange reactions, such as that occurring between XII and XIII are not uncommon. Even when a 10:1 excess of DMC is used, the amount of XIII is still only equal (roughly) to the amount of XII, and this must surely indicate that the exchange reaction is much more rapid than the reaction of the lithium compounds with DMC. It should be noted that since the exchange reaction is essentially an equilibrium process its direction reflects the superior ability of $COOCH_3$ to stabilise the ortho carbanion compared with Br, the extra stabilisation presumably resulting from field effects. Recently Tamborski has proposed[6] a similar exchange reaction to account for the production of XIV and tetrafluorophthalic acid from the reaction of XII and CO_2.

The evidence for the decomposition reaction of XV is really only negative at present, since no decomposition products have been isolated; and from their non-isolation it would appear that they are either water soluble or polymeric. Whatever the nature of this reaction it would appear to be very rapid, since when gaseous HCl was passed through the reaction mixture (at -78°) 15 minutes after adding the DMC, only 28% of the product was XVII, thus indicating that about half of the XV had decomposed (since in the absence of decomposition one would expect about half the product to be XVII). This is also supported by the low yields of XVI, even when a 10:1 excess of DMC is used.

Thus the synthesis of 2,2'-dibromo-octafluorobenzophenone does not appear to be possible by this route, since even changing the solvent to hexane alone did not stop the exchange reactions. As a result the preparation of octafluoro-9-fluorenone by an analogous route to that used to prepare octafluorodibenzothiophen[13] is also prevented.

5.5. Preparation of Octafluoro-9-fluorenone.

A synthesis of this compound was however developed from the commercially available 1,2-dibromotetrafluorobenzene as shown.



The zinc/acetic acid reduction is that used by Tilney-Bassett,[79,80] as is the Ullmann coupling reaction.[80]

The choice of solvent for the cyclisation stage is extremely important, since if ether/hexane is used the product is very complicated with ~12 components showing on v.p.c. analysis, although octafluoro-9-fluorenone can be obtained from this mixture by recrystallisation from hexane. However it appears that the fluorenone is only present to the extent of 5% in the reaction product mixture. On changing the solvent to THF/hexane it was found that the product was practically pure octafluoro-9-fluorenone in ~60% yield (the remainder was an unsublimable tar).

5.6. Pyrolysis of Octafluoro-9-fluorenone.

The mass spectrum of octafluorodibenzothiophen-5,5-dioxide showed an abundant peak at M312 corresponding to SO loss, and when subsequently pyrolysis was attempted octafluorodibenzofuran was obtained.[81] Consequently when the mass spectrum of octafluoro-9-fluorenone showed an abundant peak at M296, and a metastable peak at ~M270 corresponding to the transition

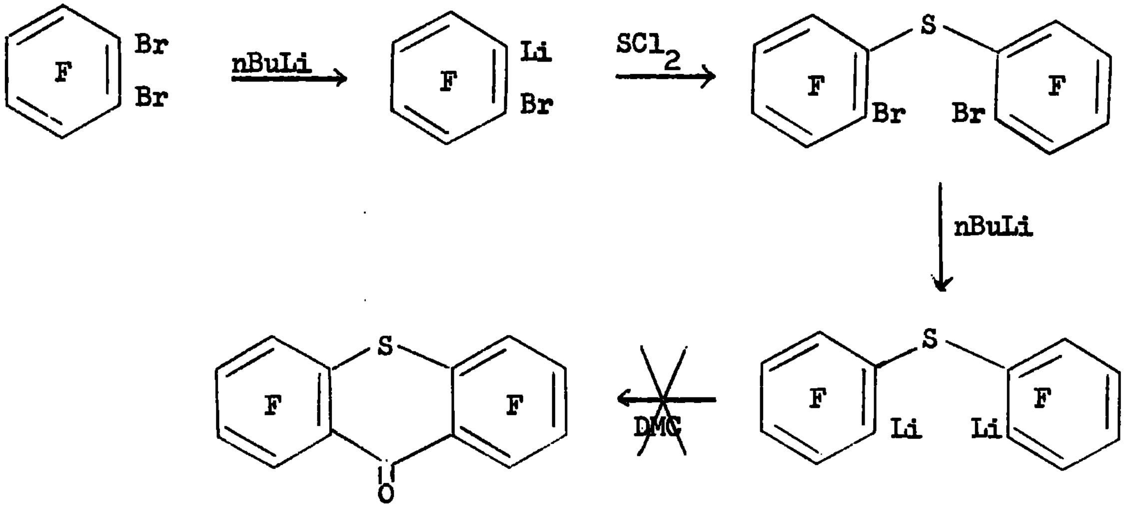
$$324^{+} \longrightarrow 296^{+} + 28,$$

it was thought that pyrolysis of the fluorenone would lead to octafluorobiphenylene. Unfortunately pyrolysis (at 10^{-2} mm.) did not yield the desired biphenylene; the fluorenone was recovered unchanged at temperatures up to 800°, where extensive blackening of the tube occurred, but no other products were obtained.

It should be noted that the hydrocarbon fluorenone shows a similar CO-loss peak in the mass spectrum.[82]

5.7. Attempted Preparation of Octafluorothioxanthone.

The route used in this attempt was as shown below.



Bis(2-bromotetrafluorophenyl)sulphide was prepared by the standard route,[5,13] and the lithiation reaction of this, and reaction with DMC were carried out in THF/hexane at -78°. However only a semicrystalline yellow polymer was obtained, which appeared to have involved solvent in some way since its infra-red showed strong C-H stretching peaks. That this reaction did not work is surprising since the dilithio compound is known to react readily with SCl_2 to yield octafluorothianthren.[5]

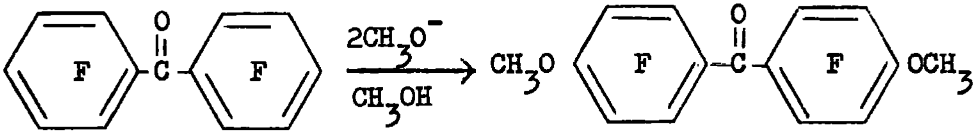
Chapter 6

Orientation of Nucleophilic Substitution in Some Polyfluoroaromatic Systems.

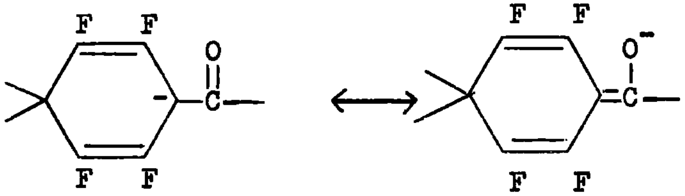
The orientation of nucleophilic substitution can yield valuable information on the mechanism of such reactions, and the effect of substituents on the mechanism. The orientations discussed in this chapter were determined by n.m.r. (^{19}F and ^{1}H) and in some cases by chemical means; and the next chapter contains an account of the proof of these orientations.

6.1. Decafluorobenzophenone.

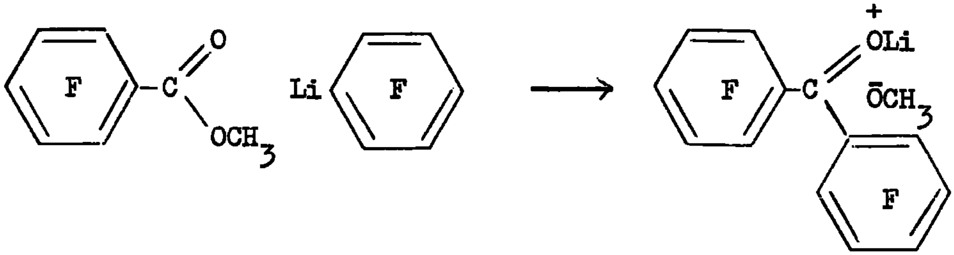
In methanol solution, decafluorobenzophenone will react with two equivalents of sodium methoxide to yield octafluoro-4,4'-dimethoxybenzophenone.



This orientation can be rationalised in terms of the Iπ effect, since one would expect a lower p electron density on the carbonyl carbon atom than on a fluorine atom, and also the fact that the rings and the carbonyl group are not coplanar will reduce overlap and hence the Iπ effect of the carbonyl group. The mesomeric effect also would account for 4-substitution since this allows delocalisation of the electron pair onto the carbonyl oxygen atom via a Type II canonical (see 3.1).



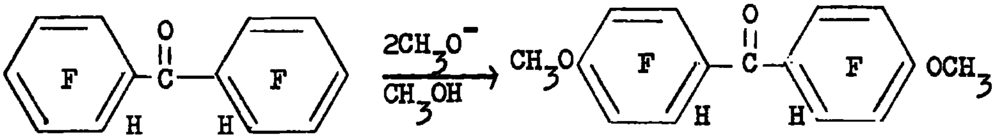
However it was mentioned in section 5.2., that decafluorobenzophenone will react with $LiOCH_3$ in ether/hexane to yield nonafluoro-2-methoxybenzophenone. This is interesting since it suggests the operation of a solvent effect. It should be noted that it would be difficult to do this reaction in the normal way, since $LiOCH_3$ would be insoluble in ether/hexane because of the high lattice energy of the salt, and the low solvation energy associated with solvents of this type. In fact the most probable explanation is that because of the low dielectric constant of the medium, the $LiOCH_3$ is not separated from the benzophenone after formation, and the two remain in the same solvent



shell, with the lithium cation co-ordinated by the carbonyl oxygen atom, thus the CH_3O^- will be held by electrostatic forces in a favourable position to substitute into one of the ring ortho positions. Ortho substitution will be favoured over meta substitution, by the possibility, in the former of delocalisation of the electron pair onto the carbonyl oxygen.

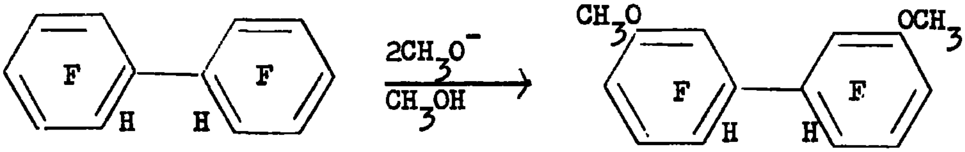
6.2. Octafluoro-2,2'-dihydrobenzophenone.

This compound will react with two equivalents of methoxide in methanol to yield hexafluoro-2,2'-dihydro-4,4'-dimethoxybenzophenone.



XVIII

That this compound (XVIII) should undergo substitution para to the carbonyl, while the analogous octafluoro-2,2'-dihydrobiphenyl XIX



XIX

undergoes substitution para to hydrogen[83] is very intriguing. The observed orientation in XIX may be rationalised in terms of the Iπ effect since this would be in the order F 〉 ring C 〉 H, and so one would predict a similar orientation in the case of the benzophenone XVIII, since the expected order of Iπ effect should be F 〉 carbonyl C 〉 H.

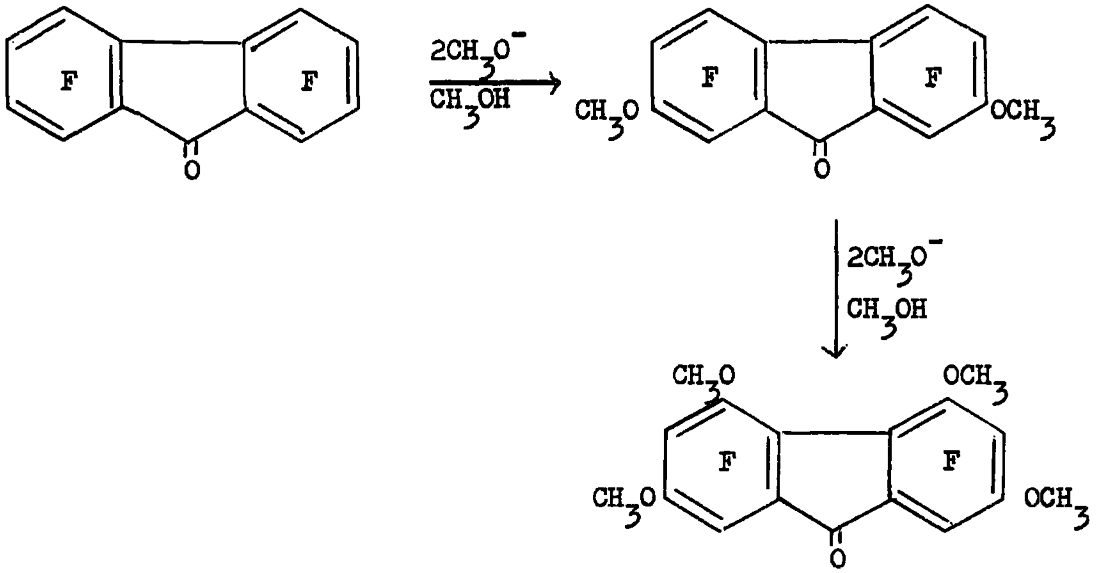
This prediction is not verified, and this would suggest that mesomeric and field effects in XVIII are sufficiently important to overcome the Iπ directive effects, these mesomeric effects directing the substitution para to the carbonyl group.

Thus these results are best rationalised in terms of a competition between Iπ effect and mesomeric effect, the stronger one controlling the orientation. The Iπ effect of a carbonyl carbon atom is probably less than that of a ring carbon atom, because of the effect of the electronegative carbonyl oxygen atom in reducing the p electron density at the carbon atom. Also the mesomeric effect of the carbonyl group is stronger than that of the phenyl group; this is indicated by their respective σ_p[84] values, $\sigma_p\ (C_6H_5CO) = 0{\cdot}46$, $\sigma_p\ (C_6H_5) = -0{\cdot}01$. This difference in orientation is then determined by a strong mesomeric effect and weak Iπ effect in the case of XVIII, and a weaker mesomeric effect and stronger Iπ effect in the case of XIX.

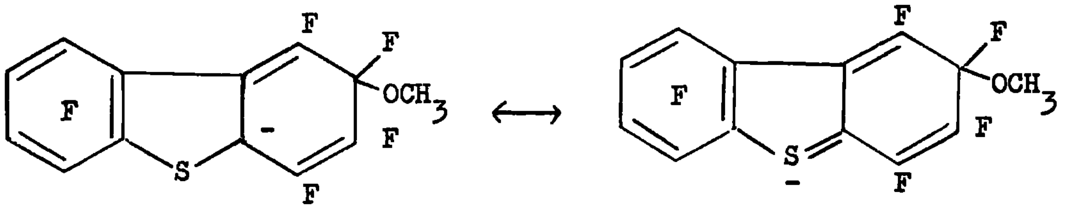
This appears to be the first time such an effect has been noted. The other tetrafluorobenzenes studied have been the tetrafluorohalobenzenes,[54] where the halogen (Cl, Br, I) has only a weak mesomeric effect, and the Iπ effects are dominant in determining the orientation of substitution, or as in the case of some 2-substituted tetrafluoronitrobenzenes[86] (the 2-substituents are NH_2, NHMe, NMe_2, and OMe) where considerations of relative Iπ effects and relative mesomeric effects both predict the same orientation.

6.3. Octafluoro-9-fluorenone.

Substitution of fluoride by methoxide in this system occurs first at the 2 (and 7) positions and then at the 4 (and 5) positions.

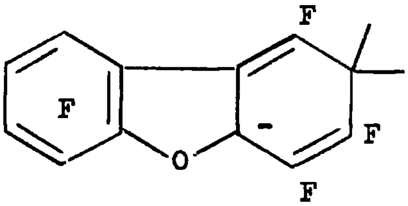


This orientation of substitution with the methoxide substituting at positions meta to the carbonyl group appears to be highly anomalous, since one would predict para substitution (i.e. at the 3 and 6 positions) as in decafluorobenzophenone and octafluoro-2,2'-dihydrobenzophenone. Such differences between the diphenyl system and the dibenzo system are not observed in the case of the sulphides and sulphones. Thus decafluorodiphenyl sulphide (see section 6.4) and octafluorodibenzothiophen[13,83] both undergo substitution para to sulphur, and in the latter case this was attributed to the possibility of delocalisation of the electron pair into vacant sulphur 3d orbitals via the preferred type II canonical.

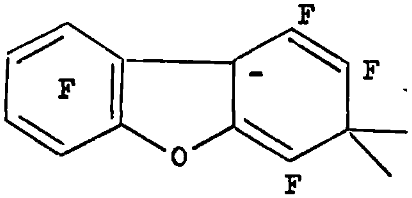


Similarly one can account for substitution para to sulphonyl in decafluorodiphenyl sulphone (see section 6.6) and octafluorodibenzothiophen-5,5-dioxide (section 6.7).

It is unlikely that octafluoro-9-fluorenone is analogous to octafluorodibenzofuran[85] or 1,2,3,4-tetrafluorodibenzofuran[87] both of which undergo substitution meta to the oxygen. This orientation was attributed to the Iπ effect of oxygen being greater than that of a ring carbon atom, i.e.



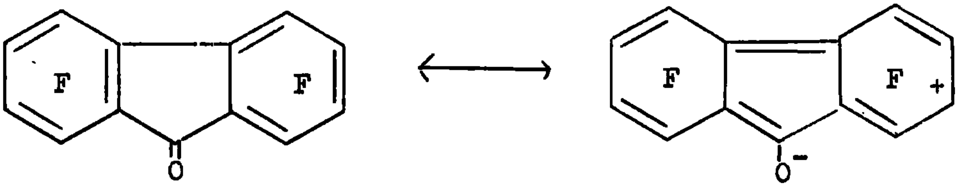
less stable than



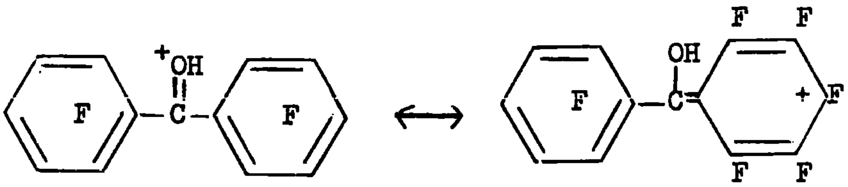
However as has been seen, a carbonyl group appears to have a weaker Iπ effect than a ring carbon atom, and a stronger mesomeric effect than a phenyl group. Admittedly in the case of the fluorenone the system is planar, whereas in the benzophenone there will be a considerable dihedral angle between the plane of the ring and the plane of the carbonyl group. Reducing this dihedral angle should increase the effectiveness of the mesomeric effect, and also the Iπ effect of the carbonyl group. But since both depend on p orbital overlap, they both might be affected to the same extent. However it should be noted that a good part of the stabilisation effect of carbonyl can be attributed to the field effect of the carbon-oxygen bond dipole which should not be dependent on angle.

Thus the conclusion is that there is something rather peculiar about the fluorenone system. This has in fact been noted before. Measurement of the effect of various substituents in 2, 3, and 4 positions on the rate of $NaBH_4$ reduction of fluorenone,[88,89,90] showed that substituents in the 2 and 4 positions exerted extraordinary mesomeric effects as if they were in direct conjugation with the reaction centre (the rate determining step is attack by H^- on the carbonyl carbon atom). This was attributed to conjugation across the central ring and through the other ring.

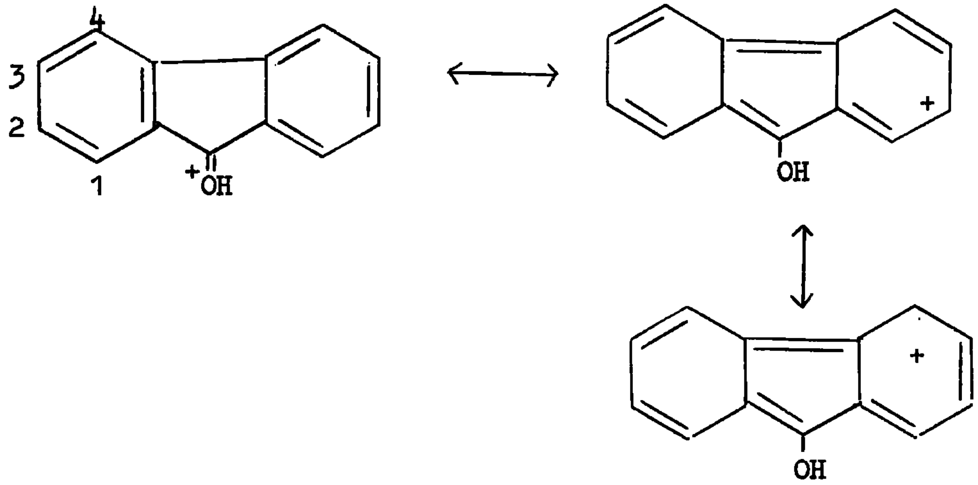
Further evidence is provided by the ^{19}F spectrum of octafluoro-9 fluorenone itself, especially the shifts at the 2 and 3 positions. Fluorine chemical shifts have been used before as a measure of substituent effects,[91,11] electron withdrawing groups causing deshielding of the fluorine, and electron donating groups causing shielding. Previously such effects when operating by mesomeric effects occurred to the greatest extent at the para position. Thus in octafluorodibenzothiophen the shifts are -8·1 (para to S) and -5·9 (meta to S) p.p.m. from C_6F_6, and in octafluorodibenzothiophen-5,5-dioxide -19·9 (para to SO_2) and -15·6 (meta to SO_2). The observed order of the shifts is that expected since S and SO_2 appear to exert a stronger electron withdrawing mesomeric effect than the ring linkage. In the case of octafluorodibenzofuran it is the other way round and the shifts parallel the orientation -2·0 (para to O) and -8·8 (meta to O). However in the case of octafluoro-9-fluorenone the shifts are -11·9 (para to CO) and -19·6 (meta to CO), in spite of the fact that carbonyl exerts the strongest mesomeric effect. They would be consistent with mesomeric withdrawal by the carbonyl via the other two rings.



This is also indicated by the ^{19}F n.m.r. spectra of the protonated species, which were recorded in concentrated H_2SO_4 solution. The spectrum of decafluorobenzophenone by comparison with the unprotonated molecule showed that the shifts of the various fluorine atoms were ortho -1·9, meta -2·5, and para -5·1 p.p.m. The greater deshielding of the para position is indicative of the more effective conjugation with the carbonyl group from this position.



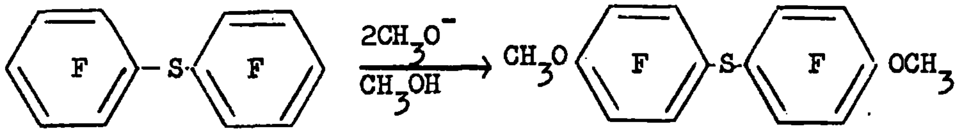
In the case of octafluoro-9-fluorenone the shifts for the various positions are 1, -1·9; 2, -5·4; 3, -0·9; and 4, -4·0 p.p.m. This again indicates that in the fluorenone system electron withdrawal by the carbonyl group is more effective at the 2 and 4 positions, positions meta to the carbonyl group.



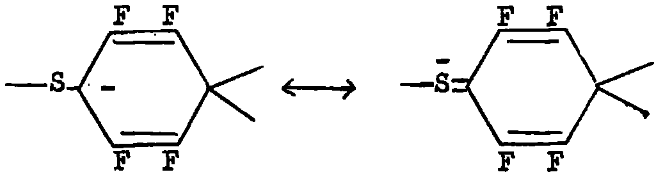
In conclusion then, octafluoro-9-fluorenone undergoes substitution at the 2 position, meta to the carbonyl group. This is contrary to all predictions based on a simple consideration of the relative effects of the carbonyl group and the ring linkage, which treat the system as a 1,2-disubstituted tetrafluorobenzene. The available evidence suggests that this is a peculiarity of the fluorenone system, whereby the carbonyl group appears to be in direct conjugation with the meta positions via the other two rings. The reason for this behaviour is at the moment somewhat obscure. This now suggests that extreme caution should be used in applying the simple qualitative arguments used previously for rationalising the observed orientation of substitution in the dibenzoheterocycles.

6.4. Decafluorodiphenyl Sulphide.

Reaction of this compound with two equivalents of methoxide in methanol yields octafluoro-4,4'-dimethoxydiphenyl sulphide.

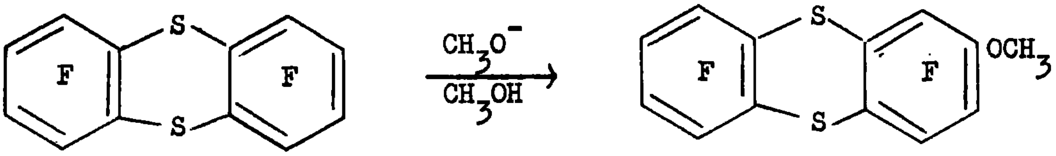


This orientation is the same as that found[92] for the attack of hydride ion on this compound and for the attack of methoxide on $C_6F_5SCH_3$.[93] It can be rationalised in terms of the Iπ effect (F > S) or in terms of the mesomeric effect of sulphur, whereby the electron pair is delocalised into vacant sulphur 3d orbitals (see section 2.4).



6.5. Octafluorothianthren.

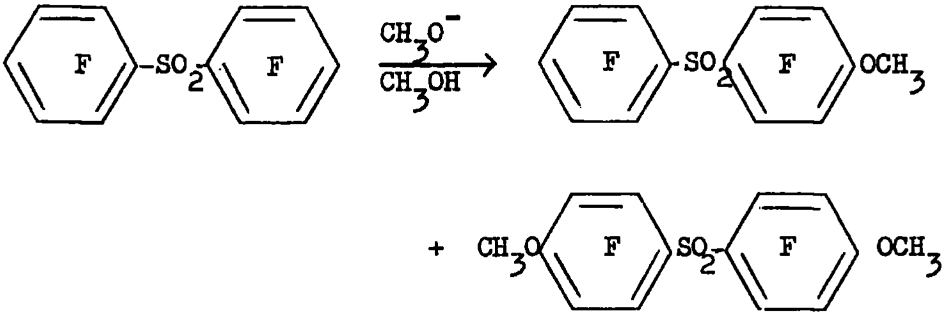
This compound reacts with one equivalent of methoxide in methanol to yield a mixture of starting material, heptafluoro-2-methoxythianthren, and a dimethoxy derivative of unknown orientation(s). The mixture



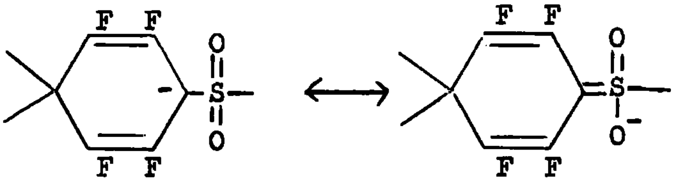
was separated by preparative scale v.p.c. Again this orientation can be rationalised in terms of Iπ effect (F > S) or in terms of mesomeric effect as in 6.4.

6.6. Decafluorodiphenyl Sulphone.

Reaction of this compound with one equivalent of methoxide in methanol yielded a mixture of starting material, nonafluoro-4-methoxydiphenyl sulphone and octafluoro-4,4'-dimethoxydiphenyl sulphone.

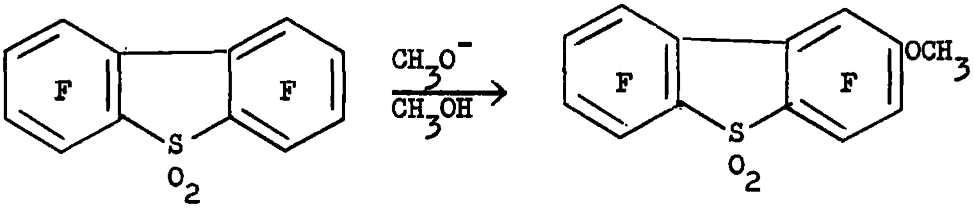


This orientation of substitution is the same as that determined[93] for $C_6F_5SO_2CH_3$, and is probably best rationalised in terms of the mesomeric effect of the sulphonyl group (see section 2.4).



6.7. Octafluorodibenzothiophen-5,5-dioxide.

This compound reacts with an equal amount of methoxide in methanol to yield a mixture of starting material and heptafluoro-2-methoxy dibenzothiophen-5,5-dioxide.



This orientation can be rationalised as in 6.6, though bearing in mind that the situation could be more complicated, as with octafluoro-9-fluorenone.

Chapter 7

Determination of Orientation of Nucleophilic Substitution

7.1. N.M.R. Methods.

The use of n.m.r., both ^{19}F and ^{1}H is an invaluable technique in the determination of orientation of nucleophilic substitution in polyfluoroaromatic compounds, and the following spectral features have been used consistently as valuable probes in determining the orientation.

a) When considering substitution by methoxyl, which is the case in question, the most useful guide is the change in the chemical shifts of the ring fluorines, relative to the unsubstituted compound. For methoxyl these changes in the shifts are very characteristic, ortho fluorines being invariably shifted downfield and meta and para fluorines being shifted upfield, this is shown in Table 1. Thus a comparison of the ^{19}F shifts of the parent compound with those of the methoxy derivative will show which fluorines have been shifted downfield and which upfield, and hence the orientation is often indicated.

b) Examination of the F-F coupling constants can be of use in determining the relative orientation of the fluorine atoms. The available evidence from various substituted polyfluorobenzenes[94] and biphenyls[96] suggests that J_{FF} values lie in the following ranges:-

J_{FF}^{ortho} , 18 - 22 c/s

J_{FF}^{meta} , 0 - 8 c/s

J_{FF}^{para} , 7 - 12 c/s

Table 1

Substituent Effects for the Introduction of CH_3O into Polyfluoroaromatic Systems.

Compound	ortho	meta p.p.m.	para	Ref.
pentafluoroanisole	-4·4	+2·0	+1·7	94
heptafluoro-2-methoxydibenzothiophen	-7, -5	+2	-	95
hexafluoro-2,2'-dihydro-5,5'-dimethoxybiphenyl	-5, -6	+2	-	95
hexafluoro-3,7-dimethoxydibenzofuran	-2·9, -3·3	+3·2	-	85
5,6,8-trifluoro-7-methoxyquinoline	-3·0, -4·7	+1·5	-	66
1,2,4-trifluoro-3-methoxynaphthalene	-4·9, -5·7	+1·9	-	66

The actual value of the coupling constant, especially J_{FF}^{meta} and J_{FF}^{para}, depends strongly on the substituents present,[97] but the values quoted seem to be a fairly reliable guide in most cases.

c) Coupling between the methoxyl protons and the adjacent ortho fluorines of the ring, for which these is considerable evidence,[98] can be used as a guide to orientation. Thus if the methoxyl protons are split into a triplet or doublet of doublets with a coupling constant in the range 0·5 - 3·5 c/s, then it indicates that the methoxyl has two ortho fluorine neighbours. If only a doublet is observed, then this is indicative of only one ortho fluorine neighbour.

d) When the molecule contains aromatic protons, a measurement of the H-F coupling constants from the ^{1}H spectrum is a good guide to orientation. The available data[54,96,99] suggests that J_{HF} values lie in the following ranges:-

J_{HF}^{ortho}, 9 - 12 c/s

J_{HF}^{meta}, 5 - 8 c/s

J_{HF}^{para}, 2 - 3 c/s.

7.2. Decafluorobenzophenone.

The observed ^{19}F resonances in the spectrum of octafluoro-4,4'-dimethoxybenzophenone are at -19·0 and -5·0 p.p.m. from C_6F_6, each of the peaks being a doublet of splitting ~18 c/s (the smaller splittings were not resolvable). The number of peaks can only mean that the methoxyls have entered at the 4-position, since only this orientation would give a product with only two different fluorine environments. Substitution at the 2 or 3 positions would require the presence of 4 peaks in the spectrum. When the observed shifts are compared with those of decafluorobenzophenone (in $CHCl_3$), -21·4 (2), -2·7 (3), and -16·5 p.p.m. (4), then it is observed that the fluorines ortho to the CH_3O have been shifted downfield by 2·3 p.p.m., and those meta to the CH_3O have been shifted upfield by 2·4 p.p.m., and this is consistent with what is observed above. The observed coupling constants are J_{FF}^{ortho} .

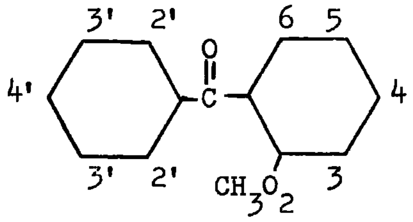
The ^{19}F spectrum of nonafluoro-2-methoxybenzophenone shows 7 peaks and the details are given in Table 2.

Table 2

^{19}F spectrum of Nonafluoro-2-methoxybenzophenone (in CH_2Cl_2)

shift p.p.m.	Relative Intensity	Fine Structure	Coupling Constants c/s
-20·9	2	DT	20·2, 5·6
-19·4	1	DDD	22·1, 9·7, 4·3
-14·5	1	TT	20·8, 4·0
-12·9	1	TD	20·3, 4·1
-7·7	1	DDD	19·6, 8·8, ∼2
-1·8	2	Complex	-
∼0	1	?	-

D = Doublet, T = Triplet

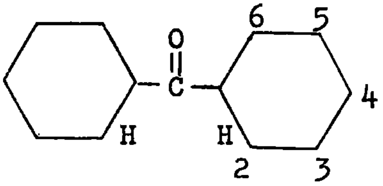


The peaks at -20·9, -14·5, and -1·8 p.p.m. can be assigned to the 2', 4', and 3' fluorines respectively of the unsubstituted ring. The remaining resonances must belong to the substituted ring; that there are four resonances indicates that the methoxyl has entered either ortho or meta to the carbonyl group. However since there is no resonance to lower field than that of the 2' fluorine it would appear that the methoxyl has entered ortho to the carbonyl group; since if it had entered meta it would have caused a significant downfield shift of one of the ortho fluorines. Thus the assignments are -19·4(6), -12·9(4), -7·7(3), and 0·0(5), and the observed CH_3O substituent shifts are ortho -6·1, meta +1·8, +3·2, and para +1·6 p.p.m., (relative to $(C_6F_5)_2CO$ in CH_2Cl_2), which are consistent with the previously observed values.

The coupling constants are also consistent with this orientation and the values quoted previously, since $J_{34} = 20{\cdot}0$, $J_{35} \sim 2$, $J_{36} = 9{\cdot}3$, $J_{45} = 20{\cdot}3$, $J_{46} = 4{\cdot}2$, and $J_{65} = 22{\cdot}1$ c/s.

7.3. Octafluoro-2,2'-dihydrobenzophenone.

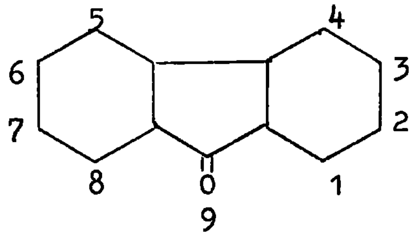
The ^1H n.m.r. of hexafluoro-2,2'-dihydro-4,4'-dimethoxybenzophenone shows two resonances; one (relative intensity 1) at 3·4τ is a doublet of doublets of doublets ($J_1 = 11{\cdot}4$, $J_2 = 6{\cdot}1$, $J_3 = 2{\cdot}3$ c/s), and the other (relative intensity 3) at 6·5 τ is a triplet ($J \sim 1{\cdot}5$ c/s). Thus since the methoxyl protons are split into a triplet, it suggests that they have two ortho fluorine neighbours, and that substitution has occurred at the 4 or 5 positions. The coupling constants of the aromatic protons indicates that $J_1 = J_{HF}^{ortho}$, $J_2 = J_{HF}^{meta}$, and $J_3 = J_{HF}^{para}$ and that the substituent has entered at the 4 or 6 positions. However since the methoxyl splitting is not consistent with 6 substitution the nucleophile must have entered at the 4 position.



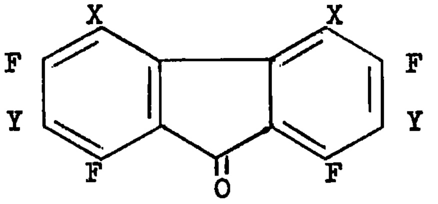
The ^{19}F n.m.r. shifts are consistent with this orientation, since three resonances are observed at -29·9, -22·5, and -11·3 p.p.m. The shifts observed for the parent compound of -25·3 (3), -24·5 (6), -15·2 (4), and -8·7 (5) indicate that in the dimethoxy derivative the fluorine adjacent to the hydrogen has had its resonance shifted downfield, while that of the fluorine adjacent to the carbonyl has been shifted upfield. This gives rise to CH_3O substituent shifts of ortho -4·6, -2·6 and meta +2·0 p.p.m.

7.4. Octafluoro-9-fluorenone.

The ^{19}F n.m.r. spectrum of octafluoro-9-fluorenone itself shows four peaks of equal intensity at -30·3, -24·9, -19·6, and -11·9 p.p.m. The resonance at -24·9 p.p.m. was assigned to fluorine atom 4



since its shift is roughly the same as that observed for the corresponding fluorine in octafluorodibenzothiophen[83] (-22·9 p.p.m.), octafluorodibenzothiophen-5,5-dioxide[85] (-22·9 p.p.m.), and octafluorodibenzofuran[85] (-24·3 p.p.m.). Hence the resonance at -30·3 p.p.m. may be assigned to position 1.



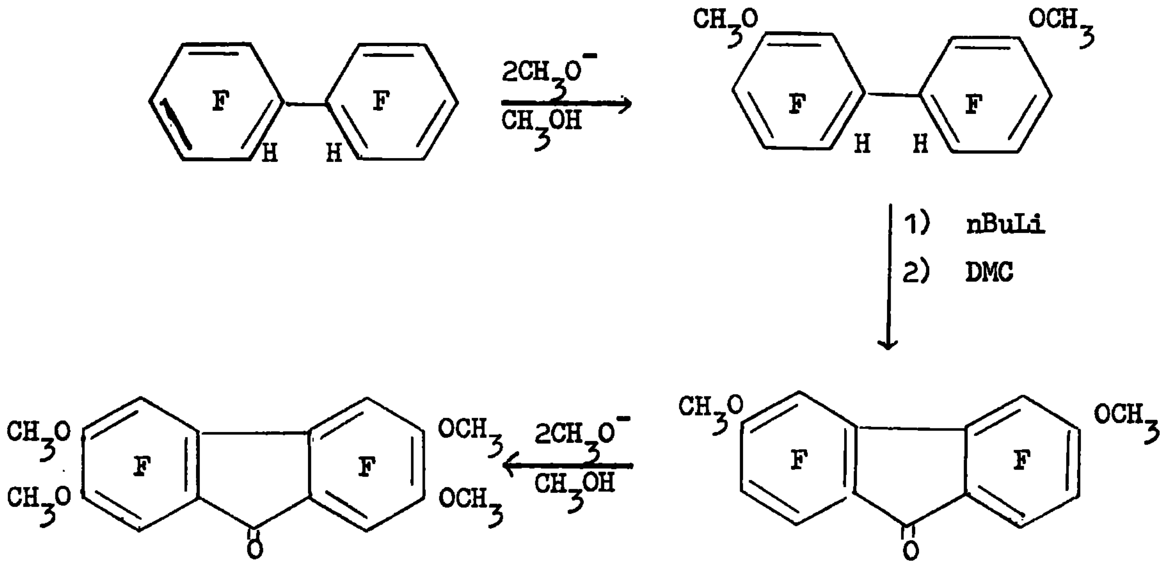
X = F, Y = OCH_3 XX

X = Y = OCH_3 XXI

The ^1H n.m.r. spectrum of hexafluoro-2,7-dimethoxy-9-fluorenone XX shows a doublet of doublets ($J \sim 0{\cdot}5$ and 1·5 c/s) at 5·8 τ, which indicates that the methoxyl is in positions 2 or 3. The ^{19}F n.m.r. shows three equal intensity peaks at -35·4 (unsplit), -22·1 (doublet, $J \sim 20$ c/s), and -13·3 p.p.m. (doublet, $J \sim 20$ c/s). Since the lowest field peak in the parent compound appears to have been shifted downfield in XX, this indicates that the methoxyl has entered at the 2 position. This is also indicated by the coupling constants in that the 1 fluorine does not appear to have an ortho F-F coupling. It should be pointed out, that because of the high molecular weight and low solubility of the fluorenone and its derivatives it was never possible to observe more detailed fine structure than the large ortho F-F couplings. This orientation gives CH_3O substituent shifts of ortho -5·1, -1·4 and meta +2·8 p.p.m.

The ^{19}F n.m.r. of tetrafluoro-2,4,5,7-tetramethoxy-9-fluorenone XXI shows two unsplit peaks at -32·8 and -18·4 p.p.m. Comparison of these shifts with those for XX shows that the lowest field peak in the latter has been shifted upfield, indicating that the methoxyl has entered at either the 3 or 4 positions. The peak at -18·4 p.p.m. can correspond to either a downfield shift of the -13·3 p.p.m. (3) peak in XX or to an upfield shift of the -22·1 p.p.m. (4) peak; however the latter would not be consistent with the data of Table 1, and the conclusion is that the methoxyl has entered at the 4 position. This orientation gives CH_3O substituent shifts of ortho -5·1 and meta +2·6 p.p.m.

This orientation was confirmed chemically by the following route,



XXIII

XXII

which involves cyclisation of the known[83] hexafluoro-2,2'-dihydro-5,5'-dimethoxybiphenyl. The cyclisation reaction appeared to go less readily than with the unsubstituted compound, since when using identical reaction conditions only ~65% conversion was achieved, and only a 15% yield of hexafluoro-3,6-dimethoxy-9-fluorenone (XXII) was obtained. This product was easily separated from unreacted starting material by recrystallisation from hexane. The spectroscopic properties of XXII were completely different to those of XX, thus proving that they are isomeric. The ^{19}F spectrum showed three resonances at -29·8, -26·9, and -22·6 p.p.m., and these are assigned to the 4, 1, and 2 positions respectively, which gives CH_3O substituent shifts of ortho -4·9, -3·0 and meta +3·4 p.p.m.

Tetrafluoro-2,3,6,7-tetramethoxy-9-fluorenone (XXIII), made from XXII, showed two ^{19}F resonances at -33•5 and -28•3 p.p.m. Comparison with XXII shows that the lowest field peak (4) has moved upfield, and the next lowest peak (1) downfield, thus indicating that the substituent has entered at the 2 position. This orientation yields CH_3O substituent shifts of ortho -6•6 and meta +1•5 p.p.m. which are consistent with the previously obtained values.

7.5. Decafluorodiphenyl Sulphide.

The observed ^{19}F spectrum of octafluoro-4,4'-dimethoxydiphenyl sulphide showed just two resonances at -27•5 and -5•5 p.p.m., and as in 7.2 this can only indicate that the methoxyl has entered at the 4 position. Comparison with the parent compound indicates CH_3O substituent shifts of ortho -3•5 and meta +2•5 p.p.m. The coupling constants support this orientation since the highfield peak is a doublet of doublets of doublets with coupling constants 19•3, 8•9, and 5•1 c/s, which can be assigned to J_{23}, J_{25}, and J_{26} respectively. The low-field peak shows only a doublet of splitting ~20 c/s, the other couplings being unobservable.

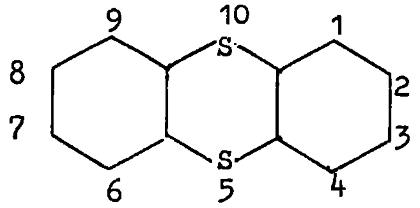
7.6. Octafluorothianthren.

The ^{1}H n.m.r. of heptafluoro-2-methoxythianthren shows a triplet ($J \sim 1$ c/s) at 6•1 τ , thus indicating that the nucleophile has entered at the 2-position. This orientation is confirmed by the ^{19}F n.m.r. spectrum, shown in Table 3.

Table 3.

^{19}F n.m.r. of Heptafluoro-2-methoxythianthren

shift p.p.m.	relative intensity	Fine Structure	Coupling Constants (c/s)
-34·3	1	DD	~12, ~3
-28·8	2	D	~20
-26·6	1	DD	~20, ~12
-13·1	1	DD	~20, ~3
-8·3	2	D	~20



The peaks at -28·8 and -8·3 p.p.m. can be assigned to the 6,9 and 7,8 fluorines respectively, by comparison with the shifts observed in the parent compound (-29·4 and -9·2 p.p.m.). Of the other three peaks it is to be noted that one is to lower field than -28·8 and one just to higher field, which again indicates that the methoxyl has entered at the 2 position. Thus the peaks at -34·3, -26·6, and -13·1 p.p.m. are assigned to the 1,4,and 3 positions respectively, giving CH_3O substituent shifts of ortho -4·9, -3·9 and meta +2·8 p.p.m.

7.7. Decafluorodiphenyl Sulphone.

The ^{19}F n.m.r. of octafluoro-4,4'-dimethoxydiphenyl sulphone shows just two peaks, each a doublet (J ~ 19 c/s), at -23·9 and -6·2 p.p.m. Again this indicates 4 substitution with CH_3O substituent shifts of ortho -1·6 and meta +2·6 p.p.m.

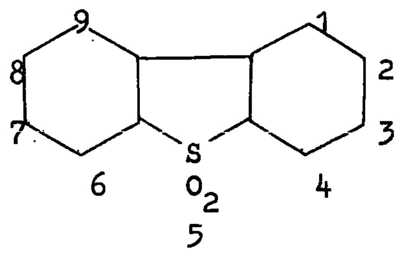
7.8. Octafluorodibenzothiophen-5,5-dioxide.

The ^{19}F n.m.r. of heptafluoro-2-methoxydibenzothiophen-5,5-dioxide is given in Table 4.

Table 4

^{19}F n.m.r. of Heptafluoro-2-methoxydibenzothiophen-5,5-dioxide

Shift p.p.m.	Relative Intensity
-32·3	2
-27·2	1
-22·8	1
-22·1	1
-19·0	1
-13·8	1



The fine structure for this compound appeared to be complex, and probably 2nd order. The resonances at -32·3, -22·8, -22·1, and -13·8 p.p.m. may be assigned to the 6, 9, 8, and 7 positions by comparison with the shifts observed in the parent compound (-34·5, -22·9, -19·9, -15·5 p.p.m.). Thus the shifts for the substituted ring are -32·3, -27·2, and -19·0 p.p.m., and it is seen that the lowest field peak (4) in the parent compound has moved upfield and that the next lowest (1) has moved downfield, thus indicating that the methoxyl has entered at the 2 position. This gives CH_3O substituent shifts of ortho -4·3, -3·5 and meta +2·2 p.p.m.

This orientation was confirmed when it was found that the compound made by oxidation of heptafluoro-2-methoxydibenzothiophen had the same ^{19}F n.m.r.[85]

Chapter 8

Relative Rates of Nucleophilic Substitution in Some Polyfluoroaromatic Systems.

Since nucleophilic aromatic substitution may be considered as proceeding via carbanionic intermediates, a knowledge of the relative rates of nucleophilic substitution can yield information on the relative stability of the intermediates concerned, and hence give information on substituent effects on carbanion stability. Since very little work had been done on the systems studied, it was thought that measurement of the relative rates of these reactions by means of competition reactions would be sufficiently accurate for an initial survey of the general trends of reactivity in this field. This would allow a more detailed kinetic investigation later of any points which appeared to be sufficiently important to warrant such treatment.

8.1. General Theory of the Method.

If two reactants A and B are competing for a deficiency of a third reactant X

$$A + X \xrightarrow{k_A} \text{products}$$

$$B + X \xrightarrow{k_B} \text{products}$$

then the rate constant ratio k_A/k_B is given by the expression[100]

$$\frac{k_A}{k_B} = \frac{\log_{10} C_A/C_A^o}{\log_{10} C_B/C_B^o}$$

where C_A^o and C_B^o are the initial concentrations of A and B, and C_A and C_B are the concentrations at any given time. Since the volume is effectively constant throughout the reaction, the concentrations can be treated as amounts (i.e. number of moles). Thus providing these quantities can be measured, k_A/k_B can be determined.

For example this method has been used before to determine the relative reactivities of various olefins to free radicals,[100] and the concentrations of the olefins were determined by v.p.c. using a Griffin and George, D6 Gas Density Balance Chromatograph. The advantage of this machine is that it needs no prior calibration, and the number of moles of any compound present in the mixture is directly proportional to its peak area,[100] thus

$$n_i \propto \frac{A_i}{M_i - m}$$

where n_i, A_i, and M_i are the number of moles, peak area, and molecular weight of the i th component, and m is the molecular weight of the carrier gas. Thus if a known amount of a standard s is introduced into the reaction product mixture, then

$$\frac{n_i}{n_s} = \frac{A_i}{A_s} \frac{(M_s - m)}{(M_i - m)}$$

and n_i can be calculated when A_i and A_s have been measured.[100]

Since n_i^o will be known (this is the amount of the substance put into the reaction), the rate constant ratio may be calculated.

8.2. Experimental Method and Results.

The procedure was to weigh out 50-100 mg. of each of the two reactants (in roughly equimolar amounts since this minimises the errors), and these were then quantitatively transferred to the reaction flask and dissolved in 30 ml. of dry methanol. The mixture was heated to reflux and left to stir for a period to ensure thorough mixing of the two components, and then a known volume of a previously standardised solution of sodium methoxide in methanol was added. The amount of methoxide added was such as have a deficiency of between 30% and 70%, depending on how close the peaks of the methoxy derivatives were to the peaks of interest on the chromatogram (see below). It appears that when reactant analysis is used,[100] the higher the conversion then the more reliable are the rate constant ratios so obtained. After work up a known amount of one of the other compounds used in this survey was added, and the mixture analysed on the Gas Density Balance.

Two methods were used for measuring peak areas, first cutting out the peaks from the chromatograph and weighing the pieces of paper so obtained, and later a Honeywell Precision Integrator. However there seemed to be no essential difference between the results obtained by the two methods since when one mixture was analysed by both methods, the same rate constant ratio was obtained. Usually about ten chromatograms were taken for each mixture and the rate constant ratios calculated from each of these were then averaged.

As a check on the method a mixture was made up and put through the usual procedure, but without the methoxide, and the mole ratio was measured to be 0·95, whereas from the initial weights of the two components it would appear to be 0·97, and this difference (~2%) is about the same as that quoted previously[100] for this method.

Considerable care had to be exercised in the choice of the two reactants and in the choice of the standard to avoid retention times being the same as that of the methoxy derivatives, since when two peaks overlapped closely it was difficult, if not impossible, to measure peak area for the desired component reliably. Thus it was impossible to compete octafluorodibenzothiophen and decafluorobenzophenone directly since nonafluoro-4-methoxybenzophenone had the same retention time as the dibenzothiophen.

In order to improve the reliability of the results, some reactions were repeated, and the results were found to agree within experimental error; or triangular series of reactions were performed (i.e. competing A with B, then B with C, and C with A) and the results of these were also consistent within experimental error. The results are much more reliable when the difference in reactivity is not very large, here the rate constant ratio is probably reliable to 5-10%, but when the reactivity difference is much larger (> 10), the reliability is less, probably 15-20%. This is because when reactivity differences are large the amount of the least reactive component that has reacted is about the same order of magnitude as the error in the determination of the amount of each component in the mixture.[100]

The reactivities have been ordered (Table 5) on a scale assuming that the rate for octafluorodibenzothiophen is 1·0. This compound was used as a reference because it is roughly in the middle of the scale of reactivities and, because it was readily available, many of the competition reactions were competitions between this compound and one of the others.

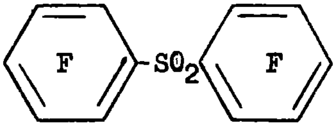
It should be noted that for compounds (5) and (8) the observed relative rate has been doubled to put them onto the same scale of reactivity of the other compounds which each have two replaceable fluorine atoms. Similarly the observed rate for (12) has been halved, since it has four replaceable fluorine atoms.

8.3. The $(C_6F_5)_2X$ Series.

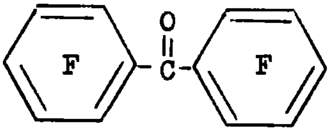
If $\log_{10}$(k rel.) is plotted against σ_p (for CH_3X)[84] for the four compounds in this series ((1), (2), (9), and (13)), a reasonable straight line is produced, although the point for X = O lies off the line more than the others. Ideally σ_p^- values should have been used

Table 5

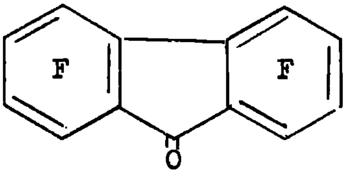
Relative Reactivities to Methoxide in Methanol at 65°

(1) 

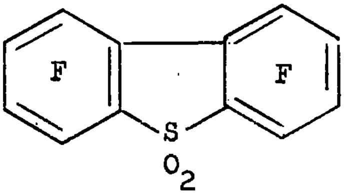
15·2 ∓ 0·7

(2) 

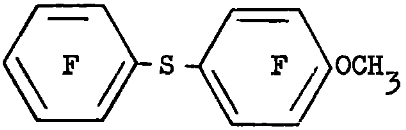
7·5 ∓ 0·4

(3) 

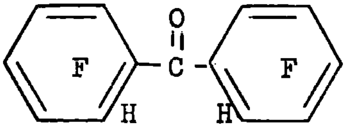
6·6 ∓ 0·9

(4) 

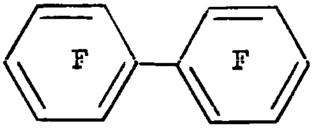
6·1 ∓ 0·3

(5) 

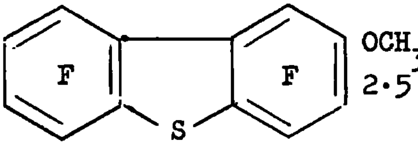
4·0 ∓ 0·2

(6) 

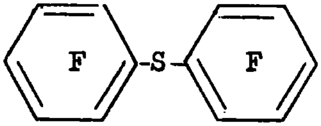
2·8 ∓ 0·3

(7) 

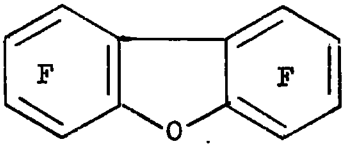
2·7 ∓ 0·1

(8) 

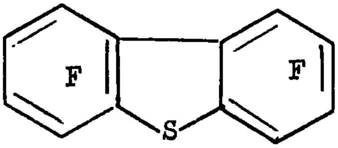
2·5 ∓ 0·5

(9) 

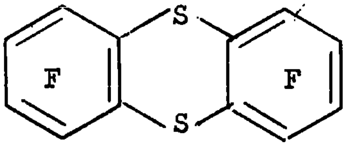
1·6 ∓ 0·2

(10) 

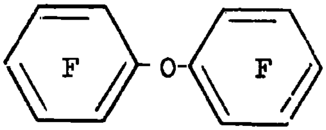
1·1 ∓ 0·1

(11) 

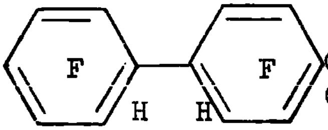
1·0

(12) 

0·35 ∓ 0·02

(13) 

0·24 ∓ 0·01

(14) 

0·088 ∓ 0·005

since we are considering carbanionic species, but this constant for CH_3S does not seem to have been measured. Similar Hammett plots have been obtained when accurate rate constants were measured for the C_6F_5X compounds,[101, 102] and it would appear to indicate that the reactivities parallel the ability of X to stabilise an adjacent carbanion whether by inductive, field, or mesomeric effects. It should be pointed out that reactivity depends on both transition state stability and ground state stability[51] and this can often complicate matters.

8.4. The Dibenzo Series $(C_6F_4)_2X$

Since these four compounds (3), (4), (10), and (11) do not show the same orientation of nucleophilic substitution it is not really possible to attempt any sort of correlation as in 8.3. However it can be seen that the observed order of reactivity $(3) \sim (4) > (10) \sim (11)$ parallels in a qualitative sense the fact that SO_2 and CO are good carbanion stabilising groups while S and O are much poorer.

One of the reasons for undertaking this study of competition reactions was to determine whether the ability of groups, like SO_2, to stabilise an adjacent carbanion had any conformational dependence, since in the dibenzo series the system is completely planar whereas for the diphenyl series this is not the case. Using sulphur as a reference, since its carbanion stabilising ability does not appear to have any conformational dependence, it can be seen that $k_1/k_9 = 9{\cdot}5$ and

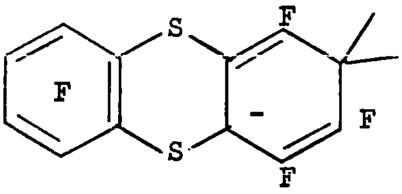
$k_4/k_{11} = 6{\cdot}1$. Thus no large effects appear to be involved, and the carbanion stabilising ability of sulphonyl appears to have little or no conformational dependence.

Another point of interest is that for X = SO_2, S, and CO the dibenzo compound appears to be less reactive than the diphenyl compound, but for that for X = O the position is reversed, and $k_{10}/k_{13} = 4{\cdot}6$. As was mentioned in Chapter 6, the orientation of substitution has been rationalised, for the dibenzofuran, in terms of the greater Iπ effect of oxygen compared with ring carbon. Similarly the relative reactivity of these two compounds can be rationalised in terms of oxygen being destabilising to α carbanions but stabilising to β carbanions by a field effect, as with fluorine. Thus in (13) the carbanion is destabilised by an α oxygen, but in (11) it is stabilised by a β oxygen.

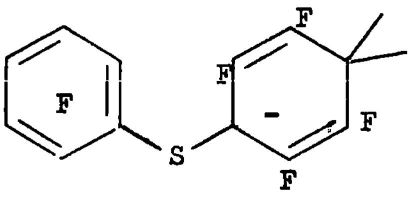
8.5. Octafluorothianthren.

It is seen that this compound is much less reactive than decafluorodiphenyl sulphide (9) this is probably caused by two effects; the first is probably best attributed to the loss of a stabilising β fluorine atom in the transition state.

i.e.



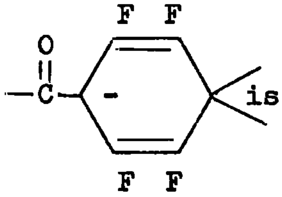
less stable than



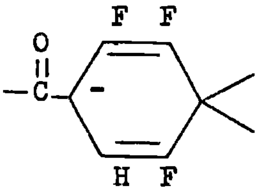
Fluorine is known to be stabilising from the β position due to a powerful field effect, whereas stabilisation due to a β sulphur is probably best attributed to an electrostatic polarisability effect (see section 4.4.). The second effect is that octafluorothianthren probably has the higher ground state stability of the two, since it has two less fluorine atoms which have been replaced by the weakly electronegative sulphur.[51] The combination of these two effects ensures that octafluorothianthren is less reactive than decafluorodiphenyl sulphide.

8.6. Effect of Ring Hydrogen.

From the results it can be seen that $k_2/k_6 = 2{\cdot}7$, which presumably indicates that



is more stable than



though bearing in mind that part of this reactivity difference will be caused by the higher ground state stability of (6) compared with (2), because the latter has two extra fluorine atoms.[51] However it is presumably an indication of the greater carbanion stabilising ability of a β fluorine compared with a β hydrogen, due to the powerful field effect of the former (see section 2.3.). A similar order has been noted before, thus pentafluorobenzene (two β fluorines) is about 120 times more reactive (per replaceable fluorine atom) than 1,2,3,4-tetrafluorobenzene[103] which has only one β fluorine to stabilise the transition state. By comparison the reverse order is observed for α effects since $k(C_6F_6)/k(C_6F_5H) = 0{\cdot}9$.[101]

Also Table 5 shows that $k_7/k_{14} = 31$, but considering that (14) substitutes para to hydrogen, whereas (7) substitutes para to the C_6F_5 group, it can be seen that for para substitution in (14) the rate difference must be very much greater, i.e. $(k_7/k_{14})_p \gg 31$, and yet $k_2/k_6 \sim 3$. This difference in the two rate constant ratios cannot be due to differences in ground state stabilities, since the increase in stability caused by replacing fluorine by hydrogen should be about the same for both sets of compounds.

It is perhaps best accounted for in terms of the 'saturation effect'.[17] In the case of the two benzophenones, (2) and (6), the carbanion is well stabilised by the carbonyl group, and the electron pair is probably considerably delocalised onto the carbonyl oxygen atom, and in this situation replacing one of the β fluorines by hydrogen is not too important, and the observed rate drops by about a factor of 3. However in the case of the biphenyls, (7) and (14), the C_6F_5 is not such a good carbanion stabilising group as carbonyl, and so a more considerable part of the total stabilisation of the carbanion will be due to the field effects of the two β fluorines, in this case replacement of one of these by hydrogen, will have a much more serious effect, as is observed. In fact the orientation changes.

8.7. Effect of Methoxyl.

The results show that $k_5/k_9 = 2{\cdot}5$ and $k_8/k_{11} = 2{\cdot}5$, i.e. that for decafluorodiphenyl sulphide and octafluorodibenzothiophen the second methoxyl substitutes into the molecule at a faster rate than the first. This suggests that the methoxyl and the reaction centre are interacting in some way presumably via the sulphur. The nature of this effect is somewhat obscure since pentafluoroanisole is reported[102] to be less reactive than hexafluorobenzene, and one would perhaps expect a similar order to apply in the present case.

EXPERIMENTAL

Chapter 9

Experimental for Chapter 4

The olefins $CF_2=CFBr$, $CF_2=CCl_2$, and CFCl=CFCl were obtained from Peninsular Chemical Research Inc., Gainesville, Florida, U.S.A., and $CF_2=CFCl$ was prepared by the standard zinc dechlorination of $CF_2Cl.CFCl_2$. Proton n.m.r. were recorded in CCl_4 solution, with benzene or T.M.S. as internal references, on a Perkin-Elmer R.10 Spectrometer. Mass spectra were recorded on an A.E.I. M.S.9 mass spectrometer, and a Perkin Elmer 'Fractometer' was used for v.p.c. work.

9.1. Preparation of 2-Chloro-1,1,2-trifluoro-1-methoxyethane.

A steel autoclave (500 ml.) was charged with dry methanol (130 ml.), sodium (3 g.) and, when hydrogen evolution had ceased, chlorotrifluoroethylene (107 g., 0·92 moles). It was then sealed, and left to stand overnight. On opening volatile material (2 g.) was vented, the residual liquid was poured into water (1000 ml.), the heavy organic layer separated, washed with more water, and dried ($MgSO_4$). This was then distilled through a 10 in. column packed with glass helices, to yield two fractions, (i) mainly methanol, and (ii) 2-chloro-1,1,2-trifluoro-1-methoxyethane (116 g., 85%) b.pt. 68-69°/743 mm. (lit.[104,105] 70·6° and 64·4°/630 mm.). The ^1H n.m.r. showed two resonances, one at 6·3 τ (relative intensity 3) was assigned to the CH_3O group, and the other (relative intensity 1) at 3·9 τ was a doublet of triplets with coupling constants 47·8 and 4·0 c/s (lit.[106] J_{HF} (geminal) = 48·8 c/s, J_{HF} (vicinal) = 4·0 c/s). The mass spectrum showed no parent ion, but peaks corresponding to P^+-F (relative abundance, 7%), P^+-CH_3O (11%), $CH_3OCF_2^+$ (100%), and $\overset{+}{C}FClH$ (30%) were visible.

9.2. Preparation of 2-Bromo-1,1,2-trifluoro-1-methoxyethane.

Procedure as in 9.1. Bromotrifluoroethylene (80 g., 0·5 moles) yielded 2-bromo-1,1,2-trifluoro-1-methoxyethane (92 g., 95%) b.pt. 85-87° (lit.[107] 89°/760 mm.). The ^1H n.m.r. showed two resonances, one at 6·3 τ may be assigned to the CH_3O protons, and the other at 3·7τ was a doublet of triplets (J_{HF} (geminal) = 47·8 c/s, J_{HF} (vicinal) = 4·4 c/s). The mass spectrum showed peaks corresponding to the parent ion (relative abundance 2%), P^+-F (2%), P^+-CH_3O (7%), $\overset{+}{C}FBrH$ (17%), and $CH_3O\overset{+}{C}F_2$ (100%).

9.3. Preparation of 2,2-Dichloro-1,1-difluoro-1-methoxyethane.

Procedure as in 9.1. 1,1-Dichloro-2,2-difluoroethylene (70 g., 0·53 moles) yielded 2,2-dichloro-1,1-difluoro-1-methoxyethane (80 g., 94%), b.pt. 103-104° (lit.[105] 105°). The ^1H n.m.r. showed two resonances, one at 6·3τ may be assigned to the CH_3O protons, and the other at 4·3τ was a triplet (J_{HF} (vicinal) = 4·4 c/s) and is consistent with the above structure. The mass spectrum showed no peak corresponding to the parent ion, but peaks corresponding to P^+-F (2%), P^+-CH_3O (7%), $\overset{+}{C}Cl_2H$ (18%), and $CH_3O\overset{+}{C}F_2$ (100%) were visible.

9.4. Preparation of 2-Chloro-1,1,2-trifluoroethyl methyl sulphide.

This was prepared after the u.v. initiation method of Harris.[108]

A Carius tube was charged with methanethiol (5·5 g., 0·11 moles) and chlorotrifluoroethylene (20 g., 0·17 moles) and irradiated with u.v. from a Hanovia lamp (750 watts) for 19 hours. On opening volatile material (2 g.) was vented, and the residual mixture (considerable decomposition appeared to have occurred) was dried ($CaCl_2$) and distilled to yield 2-chloro-1,1,2-trifluoroethyl methyl sulphide (9·6 g., 40%) b.pt. 40-50°/40 mm. (lit.[109] 104°). The ^1H n.m.r. showed two resonances, one at 7·7 τ (relative intensity 3) was assigned to the CH_3S protons, and the other at 4·0 τ (relative intensity 1) was a doublet of doublets of doublets (J_1 = 49·4, J_2 = 6·2, J_3 = 4·9 c/s), thus J_{HF} (geminal) = 49·4 c/s and J_{HF} (vicinal) = 6·2 and 4·9 c/s; there are two J_{HF} (vicinal) couplings since restricted rotation[110] makes the two vicinal fluorines non-equivalent (lit.[106] quotes J_{HF} (geminal) = 49·0 c/s, and J_{HF} (vicinal) = 6·6 and 5·1 c/s). The mass spectrum showed a parent peak (relative abundance 42%), and peaks corresponding to P^+-F (5%), P^+-Cl (5%), P^+-SCH_3 (8%), $CH_3S\overset{+}{C}F_2$ (100%), and $\overset{+}{C}FClH$ (13%).

9.5. Preparation of 2-Bromo-1,1,2-trifluoroethyl methyl sulphide.

A Carius tube was charged with methanethiol (6·5 g., 0·14 moles) and bromotrifluoroethylene (23 g., 0·14 moles), and irradiated with γ rays from a 250 curie ^{60}Co source for 87 hours. On opening volatile material (0·5 g.) was vented, and the residual liquid dried ($CaCl_2$), and distilled to yield 2-bromo-1,1,2-trifluoroethyl methyl sulphide (23 g., 85%) b.pt. 40-50°/30 mm. (lit.[109] 52°/50 mm.). The ^{1}H n.m.r. showed two resonances, one at 7·8 τ (CH_3S protons) and the other at 3·7 τ, a doublet of doublets with J_{HF} (geminal) = 47·8 c/s and J_{HF} (vicinal) = 8·0 and 5·5 c/s. The mass spectrum shows a parent peak (28%), and peaks corresponding to P^+-Br (7%), P^+-CH_3S (7%), $\overset{+}{C}FBrH$ (10%), and $CH_3S\overset{+}{C}F_2$ (100%).

9.6. Preparation of 2,2-Dichloro-1,1-difluoroethyl methyl sulphide.

Procedure as in 9.5. 1,1-Dichloro-2,2-difluoroethylene (19 g., 0·14 moles) yielded 2,2-dichloro-1,1-difluoroethyl methyl sulphide (24 g., 95%) b.pt. 64-66°/45 mm. (lit.[109] 47°/20 mm.). The ^{1}H n.m.r. showed two resonances, one at 7·7 τ (CH_3S protons), and the other at 4·2 τ a triplet with J_{HF} (vicinal) = 6·6 c/s. The mass spectrum showed a parent ion (32%) and peaks corresponding to P^+-Cl (7%), P^+-CH_3S (7%), $CH_3S\overset{+}{C}F_2$ (100%), and $\overset{+}{C}Cl_2H$ (45%).

9.7. Preparation of 1,2-Dichloro-1,2-difluoroethyl methyl sulphide.

Procedure as in 9.5. 1,2-Dichloro-1,2-difluoroethylene (21 g., 0·16 moles) yielded 1,2-dichloro-1,2-difluoroethyl methyl sulphide (16·5 g., 65%) b.pt. 30-32°/10 mm. (lit.[111] 58·5°/15 mm.). The ^1H n.m.r. indicated it to be a mixture of two diastereomers, the major one (82%) showed a resonance at 7·5τ (CH_3S protons) and a doublet of doublets at 3·5τ (J_{HF} (geminal) = 49·3 c/s, J_{HF} (vicinal) = 5·3 c/s), the minor isomer (18%) also showed a resonance at 7·5τ, and a doublet of doublets at 4·1τ (J_{HF} (geminal) = 51·2 c/s, J_{HF} (vicinal) = 7·7 c/s). The mass spectrum showed a parent peak (50%), and peaks corresponding to P^+-Cl (30%), P^+-HCl (12%), P^+-CH_3S (7%), $CH_3\overset{+}{S}CFCl$ (100%), and $\overset{+}{C}FClH$ (16%).

9.8. Preparation of 1,2-Dichloro-1,2-difluoroethyl methyl sulphone.

Using an adaptation of the procedure of Barr et al.[112]

1,2-Dichloro-1,2-difluoroethyl methyl sulphide (13·0 g., 0·072 moles) and glacial acetic acid (150 ml.) were placed into a 500 ml. flask, and cooled in an ice/salt bath. Potassium permanganate (16 g.) in hot water (90 ml.) was added slowly at such a rate that the temperature did not rise above 10°. The mixture was allowed to stir at 0° for 3 hours and was then poured into water (1000 ml.). Sodium sulphite was added to destroy the precipitate of MnO_2, followed by sufficient sodium bicarbonate to neutralise the acetic acid. The solution was then extracted with ether, organic layer separated, dried ($CaCl_2$), and solvent removed. The residual liquid was distilled

(75-$85^{\circ}/5$ mm.) to yield 1,2-dichloro-1,2-difluoroethyl methyl sulphone (7·1 g., 50%) (Found: C, 17·5; H, 1·9; Cl, 32·3. $C_3H_4Cl_2F_2O_2S$ requires C, 16·9; H, 1·9; Cl, 33·3%). The ^1H n.m.r. showed it to be a mixture of diastereomers, the major isomer having resonances at 7·0 τ, and a doublet of doublets at 3·4 τ (J_{HF} (geminal) = 48·2 c/s, J_{HF} (vicinal) = 0·9 c/s), and the minor isomer having resonances at 7·0 τ and a doublet at 3·7 τ (J_{HF} (geminal) = 48·2 c/s, J_{HF} (vicinal) $<$ 0·5 c/s). The mass spectrum showed a base peak corresponding to loss of CH_3SO_2.

9.9. Preparation of 2-Chloro-1,1,2-trifluoroethyl methyl sulphone.

Procedure as in 9.8. 2-Chloro-1,1,2-trifluoroethyl methyl sulphide (10·5 g., 0·06 moles) and potassium permanganate (13·5 g.) yielded 2-chloro-1,1,2-trifluoroethyl methyl sulphone (7·3 g., 60%) b.p. $120^{\circ}/100$ mm. (Found: C, 18·5; H, 1·8; Cl, 18·3. Required for $C_3H_4ClF_3O_2S$, C, 18·3; H, 2·0; Cl, 18·1%). The ^1H n.m.r. shows two resonances one at 7·1 τ, and the other is a doublet of doublets of doublets at 3·5 τ with J_{HF} (geminal) = 47·2 c/s and J_{HF} (vicinal) = 13·0 and 3·0 c/s. The mass spectrum shows no parent peak, but peaks corresponding to P^+-CH_3 (9%), $P^+-CH_3SO_2$ (100%), $CH_3\overset{+}{S}O_2$ (27%), $\overset{+}{C}FClH$ (43%), and $CH_3\overset{+}{S}O$ (21%) are observed.

9.10. Preparation of 2-Bromo-1,1,2-trifluoroethyl methyl sulphone.

Procedure as for 9.8. 2-Bromo-1,1,2-trifluoroethyl methyl sulphone, b.p. 70°/5 mm. (Found: C, 15·0; H, 1·7. $C_3H_4BrF_3O_2S$ requires C, 14·9; H, 1·7%). The ^1H n.m.r. shows a peak at 7·1 τ, and a doublet of doublets of doublets at 3·2 τ with J_{HF} (geminal) = 46·6 c/s and J_{HF} (vicinal) = 16·4 and 1·8 c/s. The mass spectrum shows no parent peak, but peaks corresponding to P^+-CH_3 (9%), $P^+-CH_3SO_2$ (100%), $\overset{+}{C}FBrH$ (30%), $CH_3\overset{+}{S}O_2$ (21%), and $CH_3\overset{+}{S}O$ (21%) may be observed.

9.11. Measurement of Kinetic Acidities.

a) e.g. for CH_3OCF_2CFBrH at 63°.

Two solutions were made up first of all, one was a 2·0 mole % solution of NaOH in CH_3OD, and the other was a solution of about 5 mole % benzene in CH_3OCF_2CFBrH (though accurately known). About 0·3 g. of the CH_3OCF_2CFBrH solution was weighed out accurately into an n.m.r. tube, and knowing the concentrations of the two stock solutions, sufficient of the NaOH solution was weighed into the tube so that the mole ratio NaOH: CH_3OCF_2CFBrH = 1:4·0 (this ratio was used for all the reactions). The tube was then well shaken, and the ^1H n.m.r. of the mixture recorded to determine the initial peak heights. The tube was then placed into a thermostat bath at 63 ± 1° for 20 minutes, when the tube was withdrawn and the spectrum recorded again, and so on. For compounds where the reaction was fairly fast, the tubes were cooled in liquid air, since the n.m.r. spectrometer was some distance away from the thermostat bath. Usually the spectrum was recorded several times for each time point to obtain better averages. During the run the observed peak height of the benzene internal reference should remain constant, if it did not, this was presumed to be due to machine factors, and an appropriate correction was made to the measured peak height for the ether.

Time min.	Total Peak Height mm.	k sec.^{-1}
0	124·3, 126·8	-
20	108·8, 108·5	$1{\cdot}4 \times 10^{-4}$
50	87·8, 86·7, 87·8	$1{\cdot}4 \times 10^{-4}$
70	77·7, 80·3	$1{\cdot}3 \times 10^{-4}$
90	66·2, 65·7	$1{\cdot}4 \times 10^{-4}$
	av.	$1{\cdot}4 \times 10^{-4}$

As indicated in section 4.1. the rate expression used to calculate the rate constant was

$$k = \frac{2{\cdot}303}{t} \log_{10} \frac{C_0 - C_\infty}{C - C_\infty}$$

and the C_∞ value was calculated from the statistical proton/deuteron ratio. In this case the calculated peak height at ∞ was 11·2 mm.

The reliability of the result is probably ∓ 10-15%.

b) The results obtained by the above method were

CH_3OCF_2CFClH	$k(63^\circ) = 0{\cdot}9 \times 10^{-4}$ sec.$^{-1}$
$CH_3OCF_2CCl_2H$	$k(63^\circ) = 2{\cdot}8 \times 10^{-3}$ sec.$^{-1}$
	$k(34^\circ) = 1{\cdot}5 \times 10^{-4}$ sec.$^{-1}$
CH_3OCF_2CFBrH	$k(63^\circ) = 1{\cdot}4 \times 10^{-4}$ sec.$^{-1}$
	$k(54^\circ) = 0{\cdot}2 \times 10^{-4}$ sec.$^{-1}$
$CH_3SCF_2CCl_2H$	$k(34^\circ) = 8 \times 10^{-4}$ sec.$^{-1}$
CH_3SCF_2CFBrH	$k(54^\circ) = 3 \times 10^{-4}$ sec.$^{-1}$
$CH_3SO_2CF_2CFBrH$	$k(54^\circ) = 0{\cdot}6 \times 10^{-4}$ sec.$^{-1}$

9.12. Preparation of 2-Chloro-1,2-difluorovinyl methyl sulphide.

a) 1,2-Dichloro-1,2-difluoroethyl methyl sulphide (4•3 g., 0•024 moles), sodium hydroxide (2•0 g., 0•05 moles), and methanol (15 ml.) were placed into a 100 ml. flask and the mixture was left to stir for 15 min. during which time much heat was evolved. The mixture was poured into water, the organic layer separated, dried ($CaCl_2$) and distilled to yield 2-chloro-1,2-difluorovinyl methyl sulphide, b.p. 90-95° (lit.[109,111] 96•5° and 88-89°). (Found: C, 24•7; H, 2•1; F, 26•9. Calc. for $C_3H_3ClF_2S$, C, 24•9; H, 2•1; F, 26•3%). The I.R. showed a sharp peak at $\sim$1670 cm.$^{-1}$, and the ^1H n.m.r. showed only a single peak in the region where SCH_3 resonances occur.

b) A mixture was made up as in (a), but was only allowed to react for 5 min., when a sample of the reaction mixture was withdrawn and analysed by v.p.c. (silicone elastomer, 50^{o}). Only three components were visible, and these had identical retention times to methanol, 2-chloro-1,2-difluorovinyl methyl sulphide (prepared in (a)), and starting material respectively.

c) A mixture was made up as in (a), but using a base: sulphide ratio of 1:4, and using CH_3OD as the solvent. After 1 hour the liquid was decanted off from the precipitated white solid and analysed by mass spectrometry. Examination of the isotope peaks of the parent ion showed that the intensity of the peaks at M181, 183, and 185 relative to those at M180, 182, and 184 was that to be expected in terms of ^{13}C and ^{33}S alone, and that no significant D incorporation had occurred.

9.13. Measurement of Rates of Elimination.

a) e.g. for $CH_3SCFClCFClH$.

A solution of NaOH in dry methanol (50 ml.) was placed into a bath at 26 ∓ 1^{o} and allowed to reach thermal equilibrium. Two 2 ml. titres were withdrawn and titrated with standard HCl, and from this the equivalent quantity of $CH_3SCFClCFClH$ required could be calculated. This amount was weighed out and added to the solution. Further 2 ml. titres were withdrawn at various times and titrated with acid. The results are shown in Table 6.

Table 6

Time min.	Concentration of Base moles litre^{-1}	10^4k mole^{-1} litre sec.$^{-1}$	
2	0·284	3·33	
6	0·278	3·25	
12	0·268	3·43	
16	0·263	3·35	
26	0·251	3·22	
35	0·241	3·19	
50	0·231	2·88	
72	0·214		1·19
87	0·208		1·25
102	0·207		1·13
117	0·204		1·07
145	0·193		1·20
170	0·189		1·12
227	0·172		1·21
260	0·166		1·20
290	0·161		1·18
315	0·156		1·18
365	0·151		1·14
386	0·147		1·14
410	0·144		1·13
430	0·141		1·14
	Mean	3·28 ∓ 0·04	1·16 ∓ 0·02

The rate expression used was the standard one for a second order reaction where there are initially equimolar amounts of the two reactants i.e.

$$^1/C_B - {}^1/C_B^0 = kt$$

A plot of $^1/C_B$ against t is shown in Fig.1. From this graph the two values of $^1/C_B^0$ used to calculate the two rates were obtained, for the initial rate the value used was 3·48 mole^{-1} litre, and for the final rate 4·15 mole^{-1} litre. Thus the rates for the two diastereomers are $(2{\cdot}12 \mp 0{\cdot}06) \times 10^{-4}$ and $(1{\cdot}16 \mp 0{\cdot}02) \times 10^{-4}$ mole^{-1} litre sec.$^{-1}$ From the values of $^1/C_B^0$ it is possible to calculate values for C_B^0, these are 0·287 and 0·241 mole litre^{-1}, thus the %age of the major isomer in the mixture is (0·241/0·287) x 100 = 83%.

b) The other results obtained by the same procedure are

$CH_3SO_2CFClCFClH$	k(25°) $\sim$ 0·12 mole^{-1} litre sec.$^{-1}$
CH_3SCF_2CFClH	k(62°) $\sim 2 \times 10^{-7}$ mole^{-1} litre sec.$^{-1}$
$CH_3SO_2CF_2CFClH$	k(62°) = $(1{\cdot}88 \mp 0{\cdot}03) \times 10^{-4}$ mole^{-1} litre sec.$^{-1}$

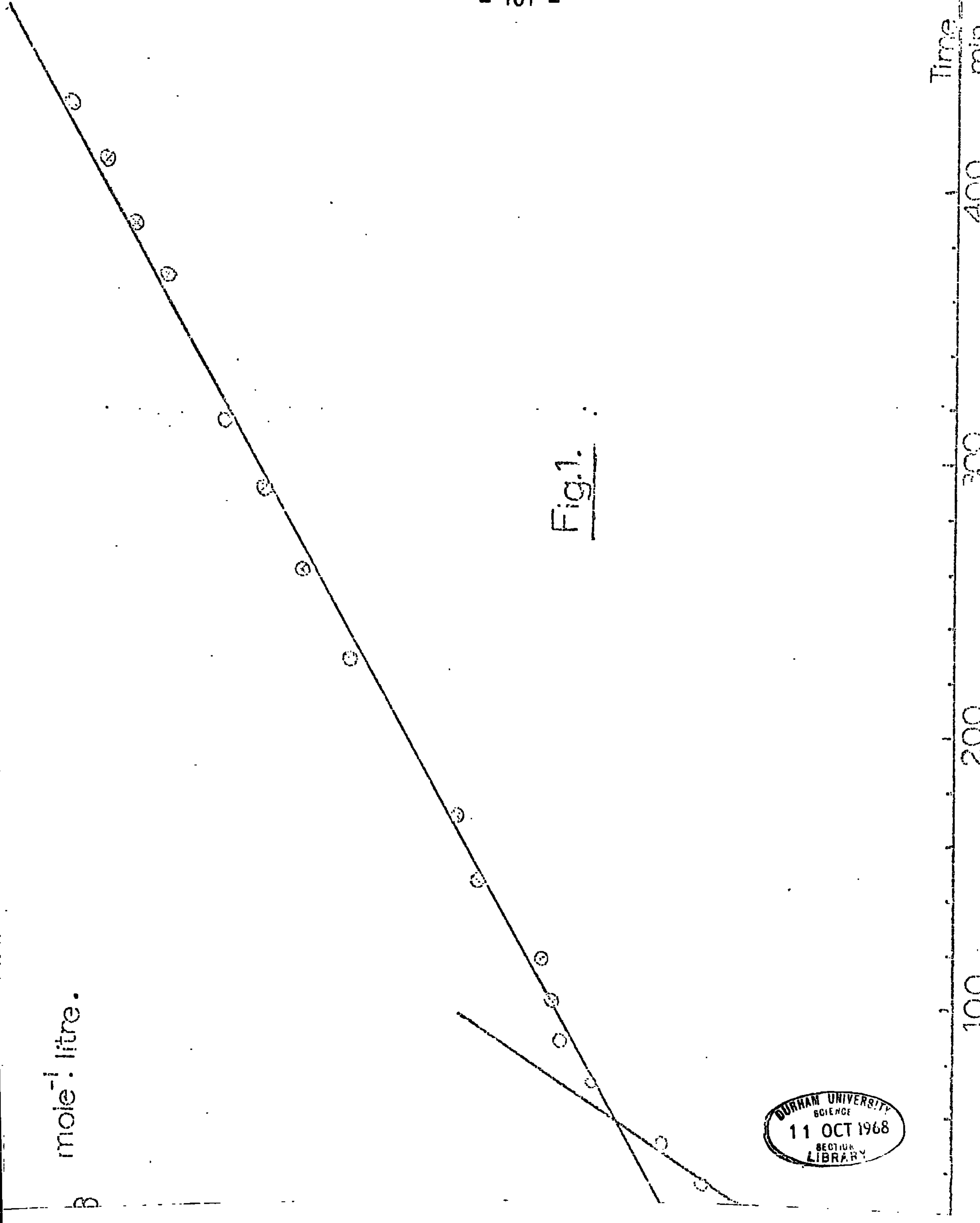


Fig.1.

Chapter 10

Experimental for Chapter 5

Orthodibromotetrafluorobenzene, pentafluorobenzene, bromopentafluorobenzene and 1,2,3,4-tetrafluorobenzene were obtained from the Imperial Smelting Corp. Ltd., and v.p.c. work was done on a Griffin and George, D6 Gas Density Balance Chromatograph.

10.1. Preparation of Decafluorobenzophenone.

a) Butyl-lithium (11·0 ml. of a 2·7M hexane solution, 29·8 m.moles) in dry hexane (20 ml.) was added dropwise to a solution of pentafluorobenzene (5·0 g., 29·8 m.moles) in a mixture of dry ether (60 ml.) and hexane (40 ml.) contained in a 500 ml. flask, which had previously been purged with dry nitrogen, and cooled to -78°. The mixture was allowed to stir at this temperature for 2 hours, and then dimethyl carbonate (1·34 g., 14·9 m.moles), which had been distilled from P_2O_5, was added rapidly, stirring being continued for a further 30 min., during which time a pink-red colour developed. The temperature of the mixture was allowed to rise to -20°, and then hydrolysed with dilute H_2SO_4. The organic layer was separated, dried ($CaCl_2$), and solvent removed; sublimation of the residue ($70^{\circ}/10^{-3}$ mm.) yielded a white solid (4·0 g.). Analytical scale v.p.c. (silicone elastomer, 220°) indicated it to be mainly decafluorobenzophenone, with traces of nonafluoro-2-methoxybenzophenone (1%) and tris(pentafluorophenyl)-

carbinol (5%) (see below). Recrystallisation of the product from a mixture of b.p. 40-60°, petroleum ether/chloroform (4:1, vol:vol) gave pure decafluorobenzophenone (70% yield), m.p. 90-91° (lit.[77] 91-92°), (Found: C, 43·1; F, 52·2. Calc. for $C_{13}F_{10}O$, C, 43·1; F, 52·5%).

(b) Procedure as in (a), except that (i) the stoichiometric quantity of dimethyl carbonate was dissolved in ether (20 ml.) and added dropwise, and (ii) the reaction mixture was allowed to warm to room temperature before hydrolysis with dilute acid. The product was a yellow oil, from which a white solid (3·9 g.) was sublimed ($70^{\circ}/10^{-3}$ mm.). Analytical scale v.p.c. (silicone elastomer, 220°) showed it to be a mixture of four components, and in the ratio 35:40:5:20. This mixture was separated by preparative scale v.p.c. (silicone elastomer, 230°) and shown to be decafluorobenzophenone; <u>nonafluoro-2-methoxybenzophenone</u>, m.p. 77-78°, (Found: C, 45·0; H, 0·8; F, 45·6. $C_{14}H_3F_9O_2$ requires: C, 44·9; H, 0·8; F, 45·7%); an octafluorodimethoxybenzophenone of unknown orientation; and tris(pentafluorophenyl)carbinol, m.p. 115-116° (lit.[76] 116-117°), (Found: C, 43·0; H, 0·4; F, 53·6. Calc. for $C_{19}HF_{15}O$, C, 43·0; H, 0·2; F, 53·8%), in order of increasing retention time.

The mass spectrum of nonafluoro-2-methoxy benzophenone shows a parent ion at M374(80%), and peaks at M207 (100%) assigned to $P^{+}-C_6F_5$, and M195 (70%) assigned to $C_6F_5\overset{+}{C}O$.

The mass spectrum of the tris(pentafluorophenyl)carbinol showed a parent peak (M530) and peaks at M513 (P^+-OH), M363 (P^+-C_6F_5), M195 ($C_6F_5\overset{+}{C}O$), and M167 ($C_6\overset{+}{F_5}$). The ^{19}F n.m.r. shows three resonances; -17·3, -10·3, and -0·8 p.p.m. which are assigned, from the relative intensity and the ortho F-F couplings, to the ortho, para, and meta fluorines respectively.

c) Procedure as in (a), except that bromopentafluorobenzene (10·0 g., 40·4 m.moles) was used, which required n butyl-lithium (19·3 ml., 40·4 m.moles) and dimethyl carbonate (1·8 g., 20·2 m.moles). The product was an oily solid; the oil probably being C_4H_9Br, this was washed with cold 40-60°, petroleum ether and sublimed (100°/10^{-2} mm.) to yield a white solid (4·0 g.). The yield of decafluorobenzophenone was about 55%.

10.2. Preparation of Octafluoro-2,2'-dihydrobenzophenone.

Butyl-lithium (28·0 ml. of a 2·4M solution, 66·7 m.moles) was added dropwise over half an hour to a solution of 1,2,3,4-tetrafluoro benzene (10·0 g., 66·7 m.moles) in dry tetrahydrofuran (100 ml., freshly distilled from potassium) and hexane (45 ml.) contained in a 500 ml. flask, which had previously been purged with dry nitrogen and cooled to -78°. After 2 hours, dimethyl carbonate (3·0 g., 33·3 m.moles) was added rapidly, and after a further hour at -78°, the mixture allowed to warm to -30°. It was then hydrolysed with dilute acid;

the organic layer was separated, dried ($CaCl_2$), and solvent removed by distillation through a short packed column. The residue was distilled (76-80°/10^{-2} mm.) to yield octafluoro-2,2'-dihydrobenzophenone (6·0 g., 55%) (Found: C, 47·6; H, 1·0; F, 46·6. $C_{13}H_2F_8O$ requires C, 47·8; H, 0·6; F, 46·7%), as a colourless liquid. 2,4-Dinitrophenylhydrazone, m.p. 144-145° (Found: C, 45·2; H, 1·3; F, 30·6. $C_{19}H_6F_8N_4O_4$ requires C, 45·0; H, 1·2; F, 30·1%).

The infra-red spectrum shows a C=O stretching frequency of ~1680 $cm.^{-1}$, to be compared with that of decafluorobenzophenone (~1715 $cm.^{-1}$).

The ^1H n.m.r. shows a doublet of doublets of doublets of doublets at 3·3τ, with coupling constants 9·7, 8·2, 5·9, and 2·4 c/s, which correspond to J_{H3}, J_{H4}, J_{H6}, and J_{H5} respectively. The ^{19}F spectrum shows four resonances at -25·3 (3), -24·5 (6), -15·2 (4), and -8·7 (5) and the observed F-F coupling constants are J_{34} = 19·3, J_{35} = 3·1, J_{36} = 13·1, J_{45} = 18·8, J_{46} = 7·6, and J_{56} ~19 c/s, and this is consistent with the assigned structure.

The mass spectrum shows a parent ion at M326 (relative abundance 30%), and peaks corresponding to $C_6F_4H\overset{+}{C}O$ (100%) at M177, and $C_6F_4H^+$ (35%) at M149, together with the metastables for the two transitions between these three ions.

10.3. Reactions of 2-Bromotetrafluorophenyl-lithium with Dimethyl Carbonate

(a) e.g. Reaction of 2-bromotetrafluorophenyl-lithium with a 10:1 excess of dimethyl carbonate.

Butyl-lithium (6·5 ml. of a 2·5M solution, 16·2 m.moles) in dry hexane (20 ml.) was added dropwise, over half an hour, to a solution of 1,2-dibromotetrafluorobenzene (5·0 g., 16·2 m.moles) in dry ether (60 ml.) and hexane (40 ml.) contained in a 500 ml. flask, which had previously been purged with dry nitrogen and cooled to -78°. After 2 hours stirring at this temperature, dimethyl carbonate (14·6 g., 162 m.moles) was added rapidly, and after a further hour at -78°, the mixture was allowed to warm to -20°. It was then hydrolysed with dilute acid, the organic layer was separated, dried ($CaCl_2$), and solvent removed by distillation through a short packed column. The residue was distilled (80-100°/1 mm.) to yield a colourless liquid (3 g.), and a tarry residue remained. Analytical scale v.p.c. (silicone elastomer, 140°) indicated the presence of four components, in the ratio 3:44:45:8, and these were separated by preparative scale v.p.c. (silicone elastomer, 180°) to yield carbomethoxy -2,3,4,5-tetrafluorobenzene (Found: C, 45·7; H, 1·6. $C_8H_4F_4O_2$ requires C, 46·1; H, 1·9%); 1,2-dibromotetrafluorobenzene, identified by retention time and spectroscopically; 1-bromo-2-carbomethoxy-3,4,5,6-tetrafluorobenzene, (Found: C, 33·3. $C_8H_3BrF_4O_2$ requires

C, 33·5%); and 3,4,5,6-tetrafluorodimethylphthalate (Found: C, 45·7; H, 2·2. $C_{10}H_6F_4O_4$ requires, C, 45·1; H, 2·3%) in order of increasing retention time.

The ^{19}F n.m.r. spectrum of 1-bromo-2-carbomethoxy-3,4,5,6-tetrafluorobenzene showed four resonances, assigned as -24·2 (3), -8·3 (4), -12·1 (5), and -34·4 (6) p.p.m., and the following coupling constants were extracted, J_{34} = 20·8, J_{35} = 4·4, J_{36} = 10·2, J_{45} = 19·5, J_{46} = 4·5, and J_{56} = 21·0 c/s. The mass spectrum showed a parent peak at M286/288 (relative abundance, 40%) and peaks corresponding to P^+-CH_3O (100%) at M255/257, P^+-CH_3O-CO (17%) at M227/229, and C_6F_4 (15%) at M148. Metastables could be observed for the consecutive loss of OCH_3, CO, and Br from the parent ion.

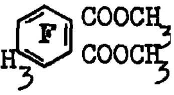
The ^{19}F n.m.r. of carbomethoxy-2,3,4,5-tetrafluorobenzene showed four resonances, which were assigned as follows -24·1 (2), -14·2 (3), -8·3 (4), and -28·0 (5) p.p.m. The mass spectrum showed a parent ion at M208 (41%) and peaks corresponding to P^+-OCH_3 (100%) at M177, and P^+-OCH_3-CO (38%) at M149. Metastables could be observed for the consecutive loss of OCH_3 and CO from the parent ion.

The ^{19}F n.m.r. of 3,4,5,6-tetrafluorodimethylphthalate shows two resonances at -25·3 and -13·0 p.p.m., assigned to the 3,6 and 4,5 fluorines respectively. The mass spectrum shows a parent ion (54%) at M266 and a peak corresponding to P^+-OCH_3 (100%) at M235.

b) This reaction was varied in several ways as shown in Table 7, but the general procedure, and the quantities of 1,2-dibromotetrafluorobenzene and butyl-lithium were the same for all.

Table 7

Reaction of 2-Bromotetrafluorophenyl-lithium with Dimethyl Carbonate

Reagents	Hydrolysis		Products %			
C_6F_4BrLi:DMC	Temp.(°)	Agent				
2:1	+20	dil.H_2SO_4	3	78	19	-
1:1	-20	dil.H_2SO_4	< 1	70	30	-
1:1[a]	-20	dil.H_2SO_4	< 1	73	27	-
1:10	-20	dil.H_2SO_4	3	44	45	8
1:35[b]	-20	dil.H_2SO_4	28	51	17	4
1:1	-20	CH_3OH[c]	3	55	36	6
1:1	-75	HCl[d]	28	52	15	5

(a) Hexane used as solvent (in all other cases it was ether/hexane).

(b) The lithio compound was poured onto $(CH_3O)_2CO$ slush at -78°; the carbonate may not have been completely dry in this experiment.

(c) 5 ml. CH_3OH added, followed by dil.HCl after a few minutes.

(d) Anhydrous HCl bubbled through the mixture at -78°.

10.4. Preparation of 1-Bromo-2,3,4,5-tetrafluorobenzene.

The procedure is essentially that used by Tilney-Bassett,[79,80] except that certain modification is necessary for the smaller scale.

1,2-Dibromotetrafluorobenzene (15·0 g., 48·7 m.moles) was added to zinc dust (3·5 g., 55·2 m.moles) in glacial acetic acid (80 ml.), and the mixture was refluxed for 2 hours, during which time the zinc dissolved. The mixture was then steam distilled, and the distillate extracted with methylene dichloride. The extracts were washed with sodium bicarbonate solution until CO_2 evolution ceased, then dried ($CaCl_2$), solvent removed by distillation through a short packed column, and the residue distilled to yield 1-bromo-2,3,4,5-tetrafluorobenzene, b.p. 138-140° (lit.[80] 140-142°), (9·2 g., 83%), which had the correct[99] ^1H n.m.r.

10.5. Preparation of Octafluoro-2,2'-dihydrobiphenyl.

Again the procedure used was that described by Tilney-Bassett.[80]

A mixture of dimethylformamide (40 ml.), copper bronze (5 g.) and 1-bromo-2,3,4,5-tetrafluorobenzene (8·0 g., 34·9 m.moles) was heated under reflux for 7 hours. Excess copper and copper bromide produced were removed by filtration; the filtrate was then poured into water and extracted with ether. The ether extracts were combined with the ether used for washing the copper/copper bromide residue, dried ($CaCl_2$), and solvent removed to leave a brown semi-crystalline solid, which on sublimation (70°/10^{-2} mm.) yielded octafluoro-2,2'-dihydrobiphenyl (3·6 g., 70%), which showed the correct spectroscopic properties.[113]

10.6. Preparation of Octafluoro-9-fluorenone.

a) Tetrahydrofuran (60 ml.), which had been freshly distilled from potassium, was contained in a 500 ml. flask which had previously been purged with dry nitrogen and cooled to -78°. Butyl-lithium (5·0 ml. of a 2·4M solution, 12·0 m.moles) in dry hexane (30 ml.) was added dropwise, followed by a solution of octafluoro-2,2'-dihydrobiphenyl (1·8 g., 6·0 m.moles) in tetrahydrofuran (30 ml.). The mixture was stirred at -78° for 4 hours, and then dimethyl carbonate (0·55 g., 6·1 m.moles) was added rapidly. After a further 1·5 hours, the mixture was allowed to warm slowly to 0°, and was then hydrolysed with dilute acid. The organic layer was separated, dried ($CaCl_2$), and solvent removed. Sublimation ($120^{\circ}/10^{-2}$ mm.) of the residue gave an orange solid (1·1 g.), leaving a tarry residue. Analytical scale v.p.c. (silicone elastomer, 220°) indicated it to be a single component (60% yield) of longer retention time than the starting material, and recrystallisation from hexane/methylene dichloride gave <u>octafluoro-9-fluorenone</u>, m.p. 239-241° (sealed tube, since it sublimes readily $\sim 190^{\circ}$) (Found: C, 48·0; F, 46·6. $C_{13}F_8O$ requires, C, 48·2; F, 46·9%) as pale yellow crystals.

The infra-red spectrum showed a strong C=O stretch at 1737 cm.$^{-1}$, and this corresponds to a value of 1720 cm.$^{-1}$ for fluorenone itself,[114] and values in the range 1715-1724 cm.$^{-1}$ for various di, tri, tetra,and pentafluoro-9-fluorenones.[115]

The ultra-violet spectrum of octafluoro-9-fluorenone showed strong absorptions at λ = 207 (ϵ = 19, 200), 240(sh) (ϵ = 44, 400), and 256 (ϵ = 55, 700) m.μ. and numerous weaker absorptions at longer wavelengths (up to 360 m.μ.). In fluorenone itself[116] there are two intense absorptions at λ = 248 (ϵ = 61, 700) and 257 (ϵ = 100,000) m.μ. and these appear to be stronger than in the fluorocarbon. Both compounds appear to show about the same number of long wavelength bands.

b) Butyl-lithium (5·6 ml. of a 2·4M solution, 13·5 m.moles) in dry hexane (20 ml.) was added dropwise to a solution of octafluoro-2,2'-dihydrobiphenyl (2·0 g., 6·7 m.moles) in dry ether (60 ml.) and dry hexane (40 ml.), contained in a 500 ml. flask which had previously been purged with dry nitrogen and cooled to -78°. The mixture was allowed to stir at this temperature for 5 hours before dimethyl carbonate (0·6 g., 6·7 m.moles) was added rapidly. After a further hour at -78°, the mixture was allowed to warm to -20°, when the deep red coloured solution was hydrolysed with dilute sulphuric acid. The organic layer was separated, dried ($CaCl_2$), solvent removed, and the residue sublimed to yield a yellow solid, leaving a black tar. Analytical scale v.p.c. (silicone elastomer, 220°) indicated the solid to be a mixture of about six major components, and about as many minor components. Recrystallisation of the mixture from hexane yielded pure octafluoro-9-fluorenone, though in very low yields. The other components of the mixture, apart from starting material, could not be identified.

10.7. Pyrolysis of Octafluoro-9-fluorenone.

Octafluoro-9-fluorenone was pyrolysed in a flow system, as used previously for the preparation of octafluorodibenzofuran.[85] This was a heated silica tube packed with quartz wool. The compound to be pyrolysed was sublimed slowly into the tube (the whole system being under vacuum, $\sim 10^{-2}$ mm.), and any material issuing from the pyrolysis tube had to pass through a liquid air trap before being pumped away down the vacuum system. The temperature used and recovery obtained for the three runs are shown below.

Temperature (°)	Recovery (%)
550[a]	89
800[a]	91
800[b]	42

At first the pyrolysis tube was only loosely packed with quartz wool[a], but since no reaction appeared to occur, for the final attempt it was packed very tightly[b] in order to increase the mean residence time in the tube. The recovery was determined by weighing the material sublimed in (usually ~ 40 mg.) and the weight of material collected.

In each case v.p.c. and infra-red showed that starting material was the only substance collected.

10.8. Attempted Preparation of Octafluorothioxanthone.

Tetrahydrofuran (50 ml.) and hexane (70 ml.) were contained in a 500 ml. flask which had previously been purged with dry nitrogen and cooled to -78°. Butyl-lithium (15·0 ml. of a 2·1M solution, 31·4 m.moles) was added dropwise, followed by a solution of bis(orthobromotetrafluorophenyl)sulphide (7·5 g., 15·5 m.moles, prepared as in 11·10(a)) in tetrahydrofuran (30 ml.). After 5 hours stirring at -78°, dimethyl carbonate (1·4 g., 15·5 m.moles) was added rapidly, and the mixture left to stir for a further hour, before it was allowed to warm to -20°. The reaction mixture was then hydrolysed with dilute acid; the organic layer separated, dried ($CaCl_2$) and solvent removed. The yellow-brown semi-crystalline residue would not sublime, and its infra-red spectrum indicated strong C-H stretching frequencies.

Chapter 11

Experimental for Chapters 6 and 7

11.1. Preparation of Octafluoro-4,4'-dimethoxybenzophenone.

A solution of sodium (0·065 g., 2·8 m.moles) in dry methanol (10 ml.) was added dropwise to a solution of decafluorobenzophenone (0·50 g., 1·4 m.moles) in dry methanol (40 ml.) contained in a 100 ml. flask which had previously been purged with dry nitrogen. After 15 hours stirring at room temperature, the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$), and solvent removed. Sublimation ($110^{\circ}/10^{-2}$ mm.) of the residue yielded a white solid (0·5 g.), and analytical scale v.p.c. (silicone elastomer, 220°) showed it to consist of a major component ($\sim$90%) and two minor components, one of shorter retention time and the other of longer retention time than the major component. Recrystallisation from b.p. 40-60° petroleum ether yielded pure octafluoro-4,4'-dimethoxybenzophenone, m.p. 82-83°, (Found: C, 46·5; H, 1·4; F, 39·0. $C_{15}H_6F_8O_3$ requires, C, 46·7; H, 1·6; F, 39·4%).

The mass spectrum shows a parent ion at M386 and a base peak at M207 corresponding to $CH_3OC_6F_4\overset{+}{C}O$; a metastable peak ($\sim$ M111) is visible corresponding to the transition $386^{+} \longrightarrow 207^{+}$.

11.2. Preparation of Hexafluoro-2,2'-dihydro-4,4'-dimethoxybenzophenone.

Sodium (0·13 g., 5·7 m.moles) in dry methanol (10 ml.) was added dropwise to a refluxing solution of octafluoro-2,2'-dihydrobenzophenone

(0·79 g., 2·4 m.moles) in dry methanol (30 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen. After refluxing for 49 hours the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$), and solvent removed. Sublimation ($130^{\circ}/10^{-2}$ mm.) of the residue yielded a white solid (0·8 g.), which was shown by analytical scale v.p.c. (silicone elastomer, 220°) to be a mixture of a major component (~85%) and a minor component (~15%) of longer retention time. Recrystallisation from aqueous methanol yielded <u>hexafluoro-2,2'-dihydro-4,4'-dimethoxybenzophenone</u>, m.p. 58-59°, (Found: C, 51·6; H, 2·1; F, 32·3. $C_{15}H_8F_6O_3$ requires, C, 51·4; H, 2·3; F, 32·6%) as white needles.

The mass spectrum showed a parent ion at M350 and a base peak at M189 corresponding to $CH_3OC_6F_3H{\cdot}\overset{+}{CO}$; a metastable for the transition $350^+ \longrightarrow 189^+$ could be observed.

11.3. Preparation of Hexafluoro-2,7-dimethoxy-9-fluorenone.

Sodium (0·042 g., 1·83 m.moles) in dry methanol (10 ml.) was added dropwise to a solution of octafluoro-9-fluorenone (0·29 g., 0·90 m.moles) in dry methanol (40 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen. After stirring for 16 hours at room temperature, the mixture was poured into water, and the yellow precipitate extracted into ether. The extracts were dried ($CaCl_2$) and solvent removed. Sublimation of the residue ($130^{\circ}/10^{-2}$ mm.) yielded a yellow solid (0·3 g.), the mass spectrum of which indicated that it was a mixture of a dimethoxy derivative (~85% , M348) and a trimethoxy derivative (~15%, M360). Recrystallisation from methanol yielded pure <u>hexafluoro-2,7-dimethoxy-9-fluorenone</u>, m.p. 115-117°, (Found: C, 51·9; H, 1·9; F, 32·5. $C_{15}H_6F_6O_3$ requires, C, 51·7; H, 1·7; F, 32·8%) as yellow crystals.

The infra-red spectrum shows a strong C=O stretch at ~ 1722 $cm.^{-1}$ The mass spectrum is not like that of the parent octafluoro-9-fluorenone which fragments by CO loss, here the primary process appears to be CH_3 loss. In this respect it is similar to heptafluoro-2-methoxy-dibenzothiophen-5,5-dioxide which also fragments mainly by CH_3 loss, whereas with the unsubstituted parent compound SO loss is observed.[85] Thus a parent ion (100%) is observed at M348, and also peaks corresponding to P^+-CH_3 (13%) at M333, P^+-CO (2%) at M320, P^+-CH_3-CO (27%) at M305, and $P^+-CH_3-CO-CH_3$ (2%) at M290. Metastable peaks for the transitions $348^+ \rightarrow 333^+$, $333^+ \rightarrow 305^+$, and $305^+ \rightarrow 290^+$ are visible.

11.4. Preparation of Tetrafluoro-2,4,5,7-tetramethoxy-9-fluorenone.

Sodium (0·089 g., 3·9 m.moles) in dry methanol (10 ml.) was added dropwise to a refluxing solution of octafluoro-9-fluorenone (0·34 g., 1·1 m.moles) in dry methanol (40 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen. A bright yellow solid was precipitated out as the methoxide solution was added. After refluxing for 16 hours, the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$) and solvent removed. Sublimation (130°/10^{-2} mm.) yielded a yellow solid (0·35 g.), and the mass spectrum of this indicated it to be a mixture of a tetramethoxy derivative (~90%, M372) and a trimethoxy derivative (~10%, M360). Recrystallisation from methanol/acetone yielded pure tetrafluoro-2,4,5,7-tetramethoxy-9-fluorenone m.p. 191-192° (Found: C, 54·6; H, 3·3; F, 20·1. $C_{17}H_{12}F_4O_5$ requires, C, 54·8; H, 3·2; F, 20·4%).

The infra-red spectrum showed a C=O stretch at 1705 $cm.^{-1}$. The mass spectrum showed a parent ion (80%) and peaks corresponding to P^+-CH_3 (100%) at M357, P^+-2CH_3 (25%) at M242, P^+-3CH_3 (10%) at M327, and P^+-4CH_3 (12%) at M312. Metastable peaks could be observed for the consecutive loss of three CH_3 groups from the parent ion.

11.5. Preparation of Hexafluoro-2,2'-dihydro-5,5'-dimethoxybiphenyl.

Using the method previously used by J.A. Cunningham.[83]

Sodium (0·63 g., 27·4 m.moles) in dry methanol (15 ml.) was added dropwise to a refluxing solution of octafluoro-2,2'-dihydrobiphenyl (3·4 g., 11·4 m.moles) in dry methanol (50 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen. After refluxing for 54 hours, the mixture was poured into water, extracted with ether, the extracts were dried ($CaCl_2$), and solvent removed. Sublimation (110°/10^{-2} mm.) yielded a white solid (3·5 g.). Analytical scale v.p.c. indicated it to consist of a single component (> 97%), and comparison of its spectroscopic properties and retention time with an authentic sample[117] indicated it to be hexafluoro-2,2'-dihydro-5,5'-dimethoxybiphenyl.

11.6. Preparation of Hexafluoro-3,6-dimethoxy-9-fluorenone.

Tetrahydrofuran (90 ml.), which had been freshly distilled from potassium, and dry hexane (50 ml.) were contained in a 500 ml. flask which had previously been purged with dry nitrogen, and cooled to -78°. Butyl-lithium (8·6 ml. of a 2·4M solution, 20·6 m.moles) in hexane (20 ml.) was added dropwise, followed by a solution of hexafluoro-2,2'-dihydro-5,5'-dimethoxybiphenyl (3·3 g., 10·3 m.moles) in tetrahydrofuran (20 ml.). The resulting mixture was left to stir for 4 hours at -78°, before dimethyl carbonate (1·0 g., 11·1 m.moles) was added rapidly, and after a further half an hour at -78°, the mixture was allowed to warm to 0°. It was then hydrolysed with dilute acid, the organic layer separated, dried ($CaCl_2$), and solvent removed to yield an orange solid. Sublimation ($120^{\circ}/10^{-2}$ mm.) yielded a pale yellow solid (1·5 g.),leaving a black tar. Analytical scale v.p.c. (silicone elastomer, 220°) indicated the solid to be a mixture of starting material (∼80%) and another component of longer retention time (∼20%). This second component was separated by recrystallisation from hexane to yield pure hexafluoro-3,6-dimethoxy-9-fluorenone m.p. 152-153°, (Found: C, 51·8; H, 1·5; F, 32·8. $C_{15}H_6F_6O_3$ requires, C, 51·7; H, 1·7; F, 32·8%).

The infra-red spectrum showed a strong C=O stretch at ~1727 $cm.^{-1}$ The mass spectrum showed a parent ion (80%) at M348, and a base peak at M333 corresponding to P^{+}-CH_3; a metastable at ~ M318 corresponds to the transition $348^{+} \longrightarrow 333^{+}$.

11.7. Preparation of Tetrafluoro-2,3,6,7-tetramethoxy-9-fluorenone.

Sodium (0·032 g., 1·39 m.moles) in dry methanol (10 ml.) was added dropwise to a refluxing solution of hexafluoro-3,6-dimethoxy-9-fluorenone (0·20 g., 0·57 m.moles) in dry methanol (40 ml.) contained in a 100 ml. flask, which had previously been purged with dry nitrogen. After refluxing for 26 hours, the mixture was poured into water, extracted with ether, the extracts dried ($CaCl_2$), and solvent removed. Sublimation ($170^{\circ}/10^{-2}$ mm.) yielded a yellow solid (0·2 g.), and the mass spectrum indicated that it was mainly a tetramethoxy derivative (M372), with some pentamethoxy derivative (M384) present. Recrystallisation from aqueous methanol yielded <u>tetrafluoro-2,3,6,7-tetramethoxy-9-fluorenone</u> m.p. 184-185°, (Found: C, 54·9; H, 3·8; F, 20·0. $C_{17}H_{12}F_4O_5$ requires, C, 54·8; H, 3·2; F, 20·4%).

The infra-red spectrum showed a strong C=O stretch at ~1716 $cm.^{-1}$ The mass spectrum showed a parent ion (100%) at M372, and a peak corresponding to P^{+}-CH_3 (40%) at M357.

11.8. Preparation of Decafluorodiphenyl sulphide.[5]

Butyl-lithium (37 ml. of a 2·7M solution, 100 m.moles) was added dropwise to a solution of pentafluorobenzene (16·8 g., 100 m.moles) in dry ether (60 ml.) and hexane (40 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen and cooled to -78°. After stirring for 3 hours at this temperature, freshly distilled sulphur dichloride (5·2 g., 50 m.moles) in dry ether (20 ml.) was added dropwise, and after half an hour, the mixture was allowed to warm slowly to room temperature. It was then hydrolysed with dilute acid, the organic layer was separated, dried ($CaCl_2$), and solvent removed. Sublimation ($90^{o}/10^{-2}$ mm.) yielded a white solid (13·6 g., 74%) which analytical scale v.p.c. (silicone elastomer, 200°) indicated to be a single component. Comparison of retention times and spectroscopic properties with an authentic sample,[117] indicated it to be decafluorodiphenyl sulphide.

11.9. Preparation of Octafluoro-4,4'-dimethoxydiphenyl sulphide.

Sodium (0·042 g., 1·83 m.moles) in dry methanol (10 ml.) was added dropwise to a refluxing solution of decafluorodiphenyl sulphide (0·30 g., 0·82 m.moles) in dry methanol (30 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen. After refluxing for 48 hours, the mixture was poured into water, extracted with ether, the extracts were dried ($CaCl_2$), and solvent removed. Sublimation (120°/10^{-2} mm.) yielded a cream coloured solid (0·3 g.), and analytical scale v.p.c. (silicone elastomer, 220°) indicated this to consist of a major (90%) component, together with one of longer retention time. Recrystallisation from aqueous methanol yielded octafluoro-4,4'-dimethoxydiphenyl sulphide, m.p. 74-75°, (Found: C, 43·4; H, 1·8; F, 39·5. $C_{14}H_6F_8O_2S$ requires, C, 43·1; H, 1·5; F, 39·0%).

11.10. Preparation of Octafluorothianthren.[5]

a) Bis(2-bromotetrafluorophenyl)sulphide.[5]

Butyl-lithium (19·4 ml. of a 2·5M solution, 48·6 m.moles) was added dropwise to a solution of 1,2-dibromotetrafluorobenzene (15·0 g., 48·6 m.moles) in dry ether (60 ml.) and hexane (40 ml.), contained in a 500 ml. flask which had previously been purged with dry nitrogen and cooled to -78°. After stirring at this temperature for 3 hours, freshly distilled sulphur dichloride (2·5 g., 24·3 m.moles) in dry ether (15 ml.) was added dropwise, and the mixture left to stir for half an hour. It was then allowed to warm to room temperature, hydrolysed with dilute acid, the organic layer was separated, dried ($CaCl_2$), and solvent removed to leave an oily orange solid. This was washed on a filter with several small volumes of cold b.p. 40-60° petroleum-ether and then sublimed (110°/10^{-2} mm.) to yield a white solid (7·6 g., 64%). Analytical scale v.p.c. (silicone elastomer, 220°)

indicated it to be a single component, and its retention time and spectroscopic properties were identical with those of an authentic sample[117] of bis(2-bromotetrafluorophenyl)sulphide.

b) Octafluorothianthren.[5]

Bis(2-bromotetrafluorophenyl)sulphide (6·3 g., 12·9 m.moles) in dry ether (30 ml.) was added dropwise to a solution of butyl-lithium (11·5 ml. of a 2·2M solution, 25·8 m.moles) in dry ether (20 ml.) and dry hexane (50 ml.), contained in a 500 ml. flask which had previously been purged with dry nitrogen, and cooled to -78°. After stirring for 2 hours at this temperature, freshly distilled sulphur dichloride (1·4 g., 13·5 m.moles) in dry ether (15 ml.) was added dropwise, and the mixture left to stir for a further half an hour. It was then allowed to warm to room temperature, hydrolysed with dilute acid, the organic layer was separated, dried ($CaCl_2$), and solvent removed. The residue was sublimed ($100^{\circ}/10^{-2}$ mm.) to yield a white solid (3·0 g., 65%). Recrystallisation from ethanol yielded pure octafluorothianthren, which had spectroscopic properties and v.p.c. retention time identical with those of an authentic sample.[117]

11.11. Preparation of Heptafluoro-2-methoxythianthren.

Sodium (0·028 g., 1·2 m.moles) in dry methanol (10 ml.) was added dropwise to a refluxing solution of octafluorothianthren (0·41 g., 1·1 m.moles) in dry methanol (40 ml.) contained in a 100 ml.

flask which had previously been purged with dry nitrogen. After refluxing for 60 hours, the mixture was poured into water, extracted with ether, the extracts were dried ($CaCl_2$), and solvent removed. Sublimation (110^{o}/ 10^{-2} mm.) yielded a white solid (0·4 g.) and analytical scale v.p.c. (silicone elastomer, 220^{o}) indicated it to be a mixture of starting material (18%), and two components of longer retention time (75% and 7% in order of increasing retention time). Separation of the mixture by preparative scale v.p.c. (silicone elastomer, 230^{o}) showed that the major product was heptafluoro-2-methoxythianthren m.p. 70-72°, (Found: C, 41·7. $C_{13}H_3F_7OS_2$ requires, C, 41·9%). The minor product appeared to be a dimethoxy derivative since its mass spectrum showed a parent ion at M384.

The mass spectrum of the monomethoxy compound shows a parent ion (100%) at M372, and a peak corresponding to P^{+}-S (25%) at M340. In this respect it is similar to octafluorothianthren which also shows a peak corresponding to loss of sulphur (at M328).

11.12. Preparation of Decafluorodiphenyl sulphone.

Hydrogen peroxide (10 ml., 90%) was added cautiously to a mixture of methylene dichloride (50 ml.) and trifluoroacetic anhydride (50 ml.), contained in a 500 ml. flask, and the resulting mixture was refluxed for 10 minutes before a solution of decafluorodiphenyl sulphide (11·1 g., 30·3 m.moles) in methylene dichloride

(50 ml.) was added dropwise. After refluxing for 8 hours, a further mixture of hydrogen peroxide (10 ml., 90%), trifluoroacetic anhydride (30 ml.), and methylene dichloride (30 ml.) was added, and the refluxing was continued for a further 16 hours. The mixture was then poured into water (1000 ml.), the organic layer was separated, dried ($CaCl_2$), and solvent removed. Sublimation ($110^o/10^{-2}$ mm.) yielded a white solid which was recrystallised from aqueous ethanol to yield pure decafluorodiphenyl sulphone, m.p. 132^o-133^o, (7·5 g., 65%), (Found: C, 36·1; Calc. for $C_{12}F_{10}O_2S$, C, 36·2%). Spectroscopic properties and v.p.c. retention times were identical with those of an authentic sample.[117]

11.13. Reaction of Decafluorodiphenyl Sulphone with Sodium Methoxide.

Sodium (0·0543 g., 2·37 m.moles) in dry methanol (10 ml.) was added dropwise to a refluxing solution of decafluorodiphenyl sulphone (0·938 g., 2·36 m.moles) in dry methanol (30 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen. After refluxing for 24 hours, the mixture was poured into water, extracted with ether, the extracts were dried ($CaCl_2$), and solvent removed. Sublimation ($100^o/10^{-2}$ mm.) yielded a white solid (0·95 g.), and analytical scale v.p.c. (silicone elastomer, 220^o) indicated it to be a mixture of starting material (30%) and two other components of longer retention time (52% and 18% in order of increasing retention time).

The mixture was separated by preparative scale v.p.c. (silicone elastomer, 230^{o}) to yield nonafluoro-4-methoxydiphenyl sulphone, m.p. 71^{o} (Found: C, 38·5. $C_{13}H_{3}F_{9}O_{3}S$ requires, C, 38·1%), and octafluoro-4,4'-dimethoxydiphenyl sulphone m.p. 147-148^{o} (Found: C, 39·8. $C_{14}H_{6}F_{8}O_{4}S$ requires, C, 40·0%).

The mass spectrum of the monomethoxy compound showed a parent ion (100%) at M410, and peaks corresponding to $CH_3OC_6F_4SO_2^+$ (27%) at M243, $CH_3OC_6F_4SO^+$ (27%) at M227, $CH_3OC_6F_4O^+$ (92%) at M195, $CH_3OC_6F_4^+$ (33%) at M179, and $C_6F_5^+$ (28%) at M167.

The mass spectrum of the dimethoxy derivative showed a parent ion (95%) at M422, and peaks corresponding to P^+-SO_2 (7%) at M358, $P^+-SO_2-CH_3$ (30%) at M343, $CH_3OC_6F_4SO_2^+$ (25%) at M243, $CH_3OC_6F_4SO^+$ (80%) at M227, $CH_3OC_6F_4O^+$ (100%) at M195, and $CH_3OC_6F_4^+$ (40%) at M179.

11.14. Reaction of Octafluorodibenzothiophen-5,5-dioxide with Sodium Methoxide.

Sodium (0·0509 g., 2·21 m.moles) in dry methanol (10 ml.) was added dropwise to a refluxing solution of octafluorodibenzothiophen-5,5-dioxide[118] (0·775 g., 2·15 m.moles) in dry methanol (40 ml.), contained in a 100 ml. flask which had previously been purged with dry nitrogen. After refluxing for 24 hours, the mixture was poured into water, extracted with ether, the extracts were dried ($CaCl_2$), and solvent removed to yield a semi-solid (0·7 g.), which was shown by analytical scale v.p.c. (silicone elastomer, 220°) to be a mixture of starting material and product in the ratio 1:3. The product was identified as heptafluoro-2-methoxydibenzothiophen-5,5-dioxide by comparison of its v.p.c. retention time, ^{19}F n.m.r., and mass spectrum, with those of a sample of the same compound[117] prepared by oxidation of heptafluoro-2-methoxydibenzothiophen.[85]

11.15. Preparation of Octafluorodibenzothiophen.[83]

A small Carius tube was charged with bis(2-bromotetrafluorophenyl)-sulphide (5·5 g., 11·3 m.moles) and copper bronze (4·0 g., 63 m.moles), then sealed under vacuum. It was then heated for 4 days at 200°. On opening the contents of the tube were scraped into ether and well stirred, the insoluble copper/copper bromide residues were removed by filtration, the filtrate then being dried ($CaCl_2$). On removal of the solvent, the residue was sublimed ($70°/10^{-3}$ mm.) to yield a white solid which was recrystallised from ethanol to yield pure octafluorodibenzothiophen (2·6 g., 70%), which had spectroscopic properties and v.p.c. retention time identical with those of an authentic sample.[117]

11.16. Preparation of Decafluorodiphenyl ether.

This preparation was carried out after the method of Wall et al.[119]

A mixture of potassium pentafluorophenoxide (2·0 g., 9·0 m.moles) and hexafluorobenzene (8 g., 43 m.moles) in NN-dimethylformamide

(50 ml.) was heated to reflux for 16 hours. The black mixture was then poured into water, extracted with ether, the extracts were dried ($CaCl_2$), and the solvent removed by distillation leaving a black tar. Sublimation ($40^{o}/10^{-2}$ mm.) yielded a low melting solid (1·3 g.) which was shown by analytical scale v.p.c. (silicone elastomer, 200°) to be a mixture of two components (~1:2 in order of increasing retention time). These were separated by preparative scale v.p.c. (silicone elastomer, 230°) and shown to be $C_6F_5OC_6F_5$ and the diether $C_6F_5OC_6F_4OC_6F_5$ as reported previously.[119]

The ^{19}F n.m.r. of $C_6F_5OC_6F_5$ showed three resonances at -6·2 (ortho), -2·8 (para), and ~ 0 (meta) p.p.m. The mass spectrum showed a parent ion at M350 and peaks corresponding to $C_6F_5O^+$ at M183 and $C_6F_5{}^+$ at M167.

The ^{19}F n.m.r. spectrum of $C_6F_5OC_6F_4OC_6F_5$ showed four resonances at -6·5 (ortho), -1·3 (para), -0·6 (C_6F_4 fluorines), and +0·5 (meta) p.p.m. For the fluorines of the C_6F_5 rings the following coupling constants were extracted, $J_{23} = 20{\cdot}3$, $J_{24} = 2{\cdot}4$, $J_{25} = 9{\cdot}2$, $J_{26} = 4{\cdot}4$, $J_{45} = J_{43} = 20{\cdot}2$ c/s. The mass spectrum showed a parent ion at M514, and peaks corresponding to $C_6F_5O^+$ and $C_6F_5{}^+$ at M183 and M167 respectively.

Chapter 12

Experimental for Chapter 8, Competition Reactions

A sample of decafluorobiphenyl was provided by Dr. G.M. Brooke, and samples of octafluorodibenzofuran, octafluorodibenzothiophen-5,5-dioxide, and heptafluoro-2-methoxydibenzothiophen by Dr. J.A. Cunningham. The remaining compounds used in this study were synthesised by the routes indicated in the preceding chapters.

12.1. General Method.

e.g. Competition between Octafluorodibenzothiophen and Decafluorodiphenyl ether.

The apparatus used, which was a 100 ml. two-necked flask fitted with dropping funnel/dry nitrogen inlet, magnetic stirrer, reflux condenser, and dry nitrogen outlet, was well purged with dry nitrogen. Octafluorodibenzothiophen (0·0522 g., 0·149 m.moles) and decafluorodiphenyl ether (0·0484 g., 0·148 m.moles) were transferred quantitatively to the flask, and dissolved in dry methanol (30 ml.). The mixture was heated to reflux and a solution of sodium methoxide in methanol (0·9 ml. of a 0·108M solution, 0·098 m.moles) was added, and the mixture was left to reflux for 24 hours. At the end of this time ether was added, and the mixture poured into water; the organic layer was separated, dried ($CaCl_2$) and the solvent removed by distillation. Decafluorodiphenyl sulphone (0·0316 g., 0·0794 m.moles) was added, and the mixture dissolved in $CHCl_3$. This solution was then analysed on the Griffin and George, D6 Gas Density Balance Chromatograph. The areas of the peaks due to decafluorodiphenyl ether, decafluorodiphenyl sulphone, and octafluorodibenzothiophen (in order of increasing retention time) were determined by cutting out the peaks and weighing the pieces of paper so obtained, for the nine chromatographs taken of this mixture.

Using the formula previously given (section 8.1), the number of moles of the two reactants present at the end of the reaction could be determined from these area measurements.

$$n_i = n_s \cdot \frac{A_i}{A_s} \cdot \frac{(M_s - m)}{(M_i - m)}$$

For the present case the carrier gas was nitrogen so m = 28, n_s = 0·0794 m.moles, $M_s = 398$, $M_{11} = 328$, and $M_{13} = 350$. The numbers refer to the numbers given to the compounds in Table 5 , thus octafluorodibenzothiophen is 11 and decafluorodiphenyl ether is 13.

Once n_{11} and n_{13} have been determined for each chromatograph, the rate constant ratio k_{13}/k_{11} may be calculated using the expression (see section 8.1),

$$\frac{k_{13}}{k_{11}} = \frac{\log_{10}(n_{13}/n^{o}_{13})}{\log_{10}(n_{11}/n^{o}_{11})}$$

these results are shown in Table 8.

Table 8

Competition between Octafluorodibenzothiophen and Decafluorodiphenyl Ether.

A_{13}	A_1 (units 10^{-4} g.)	A_{11}	n_{13}	n_{11} (units m.moles)	$\frac{k_{13}}{k_{11}}$
183	136	91	0·123	0·0656	0·23
206	153	108	0·123	0·0690	0·25
187	135	100	0·126	0·0723	0·23
191	138	100	0·126	0·0708	0·23
191	139	94	0·125	0·0662	0·22
186	141	93	0·120	0·0645	0·26
210	157	111	0·122	0·0692	0·26
216	157	111	0·126	0·0692	0·25
194	141	96	0·125	0·0667	0·22
					0·24 ± 0·01

12.2. Results.

The other results obtained in this way are given below, the numbers refer to the compounds in Table 5; the standard used in each reaction is given by the number in parentheses.

$k_{11}/k_9 = 0{\cdot}67 \mp 0{\cdot}04$ (1)

$k_{12}/k_{11} = 0{\cdot}69 \mp 0{\cdot}03$ (9)

$k_{11}/k_{10} = 0{\cdot}88 \mp 0{\cdot}02$ (1)

$k_{13}/k_{11} = 0{\cdot}24 \mp 0{\cdot}01$ (1)

$k_1/k_{11} = 15{\cdot}2 \mp 0{\cdot}7$ (9)

$k_4/k_{11} = 6{\cdot}1 \mp 0{\cdot}3$ (9)

$k_7/k_{11} = 2{\cdot}7 \mp 0{\cdot}1$ (1)

$k_{11}/k_{14} = 11{\cdot}4 \mp 0{\cdot}7$ (1)

$k_4/k_1 = 0{\cdot}47 \mp 0{\cdot}03$ (9)

$k_2/k_1 = 0{\cdot}49 \mp 0{\cdot}01$ (11)

$k_1/k_3 = 2{\cdot}6 \mp 0{\cdot}2,\ 2{\cdot}3 \mp 0{\cdot}1$ (9)

$k_1/k_6 = 5{\cdot}0 \mp 0{\cdot}5,\ 5{\cdot}6 \mp 0{\cdot}2$ (7)

$k_1/k_7 = 6{\cdot}3 \mp 0{\cdot}8$ (11)

$k_9/k_{12} = 2{\cdot}3 \mp 0{\cdot}2$ (1)

$k_9/k_8 = 1{\cdot}38 \mp 0{\cdot}06,\ 1{\cdot}31 \mp 0{\cdot}08$ (1)

$k_7/k_5 = 1{\cdot}35 \mp 0{\cdot}04$ (1)

Within these results, it can be seen that there are three 'triangular' reaction series (see section 8.2):-

(i) $k_1/k_{11} = 15{\cdot}2 \mp 0{\cdot}7$, $k_4/k_{11} = 6{\cdot}1 \mp 0{\cdot}3$, $k_4/k_1 = 0{\cdot}47 \mp 0{\cdot}03$

thus $\dfrac{k_1}{k_{11}} \cdot \dfrac{k_4}{k_1} = \dfrac{k_4}{k_{11}} = 7{\cdot}1 \mp 0{\cdot}8$

which agrees with the observed value within the limits of experimental error.

(ii) $k_{11}/k_9 = 0{\cdot}67 \mp 0{\cdot}04$, $k_{12}/k_{11} = 0{\cdot}69 \mp 0{\cdot}03$, $k_9/k_{12} = 2{\cdot}3 \mp 0{\cdot}2$

thus $\dfrac{k_{11}}{k_9} \cdot \dfrac{k_{12}}{k_{11}} = \dfrac{k_{12}}{k_9} = 0{\cdot}46 \mp 0{\cdot}05$

i.e. $\dfrac{k_9}{k_{12}} = 2{\cdot}2 \mp 0{\cdot}2$ which agrees with the observed value within the limits of experimental error.

(iii) $k_1/k_{11} = 15{\cdot}2 \mp 0{\cdot}7$, $k_{11}/k_7 = 0{\cdot}37 \mp 0{\cdot}01$, $k_1/k_7 = 6{\cdot}3 \mp 0{\cdot}8$

$$\frac{k_1}{k_{11}} \cdot \frac{k_{11}}{k_7} = \frac{k_1}{k_7} = 5{\cdot}6 \mp 0{\cdot}4$$

which agrees with the observed value within the limits of experimental error.

As a check on the method a mixture of decafluorodiphenyl sulphone (0·0751 g., 0·188 m.moles) and decafluorodiphenyl sulphide (0·0667 g., 0·182 m.moles) was made up and put through the above procedure, though without the methoxide. The mole ratio was measured by v.p.c. analysis to be $0{\cdot}95 \mp 0{\cdot}01$, whereas from the initial amounts of the two components it was 0·97.

These results were then used to draw up Table 5 by assuming that $k_{11} = 1{\cdot}0$.

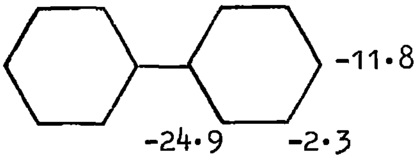
Appendix

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

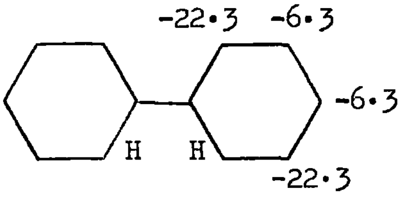
Shifts are quoted from C_6F_6, which was used as an internal reference.

Spectra were recorded on a Perkin-Elmer R.10 Spectrometer. Coupling constants are given where these could be determined, in the other cases either the splitting was too complex to analyse (i.e. by assuming first order splitting), or else the solubility of the compound was too low to observe any fine structure apart from the large ortho F-F couplings.

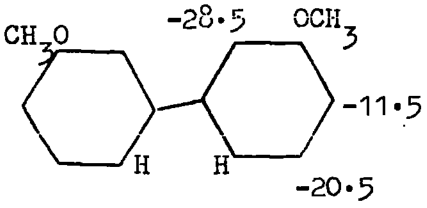
1. Decafluorobiphenyl (CH_2Cl_2)



2. Octafluoro-2,2'-dihydrobiphenyl (acetone)[120]

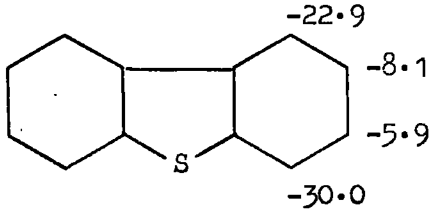


3. Hexafluoro-2,2'-dihydro-5,5'-dimethoxybiphenyl (acetone)[120]

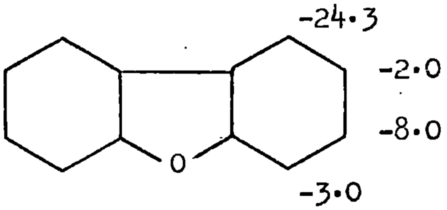


J_{34} = 19•8, J_{35} = 12•4, J_{3H} = 10•0,
J_{46} = J_{4H} = 7•6 c/s

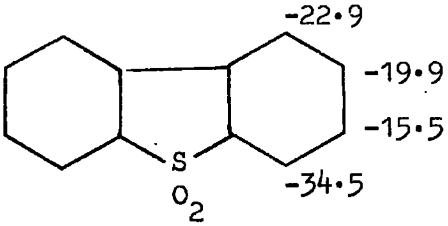
4. Octafluorodibenzothiophen (CH_2Cl_2)



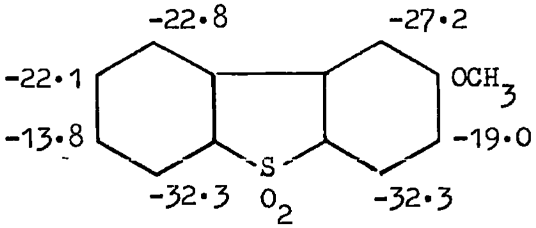
5. Octafluorodibenzofuran (acetone)[120]



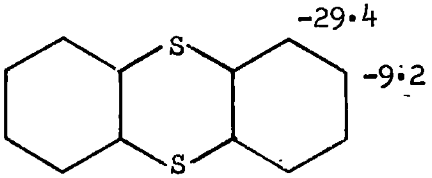
6. Octafluorodibenzothiophen-5,5-dioxide (CH_2Cl_2)



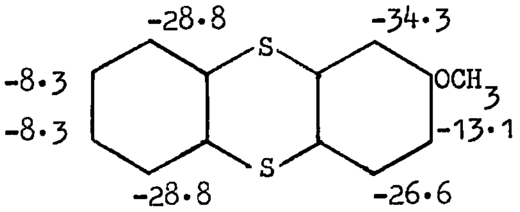
7. Heptafluoro-2-methoxydibenzothiophen-5,5-dioxide (CH_2Cl_2)



8. Octafluorothianthren ($CHCl_3$)



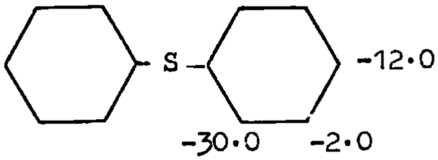
9. Heptafluoro-2-methoxythianthren ($CHCl_3$)



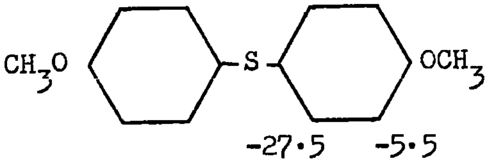
$J_{34} = J_{67} = J_{78} \sim 20$ c/s

$J_{14} \sim 12$ c/s, $J_{13} \sim 3$ c/s

10. Decafluorodiphenyl Sulphide ($CHCl_3$)



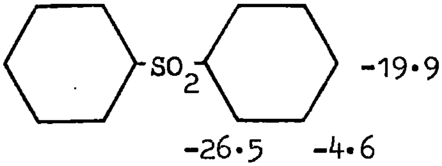
11. Octafluoro-4,4'-dimethoxydiphenyl Sulphide (CH_2Cl_2)



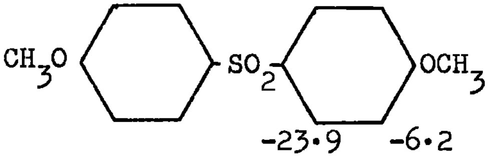
$J_{23} = 19·3$, $J_{25} = 8·9$,

$J_{26} = 5·1$ c/s.

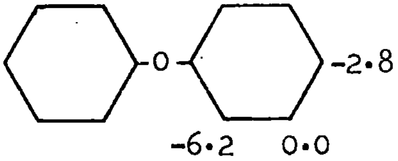
12. Decafluorodiphenyl Sulphone ($CHCl_3$)



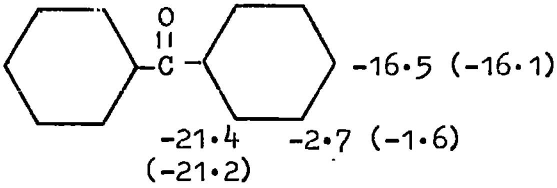
13. Octafluoro-4,4'-dimethoxydiphenyl Sulphone ($CHCl_3$)



14. Decafluorodiphenyl Ether



15. Decafluorobenzophenone ($CHCl_3$)



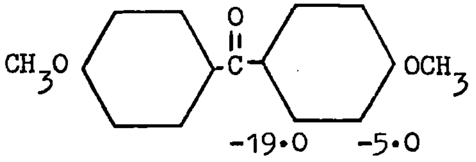
$J_{23} = 24{\cdot}7$, $J_{25} = 10{\cdot}9$,

$J_{24} = 5{\cdot}0$, $J_{26} < 1$ c/s.

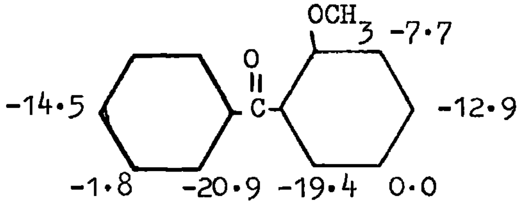
$J_{43} = 19{\cdot}7$ c/s.

Shifts in parentheses are for CH_2Cl_2 solvent.

16. Octafluoro-2,2'-dimethoxybenzophenone ($CHCl_3$)



17. Nonafluoro-2-methoxybenzophenone (CH_2Cl_2)

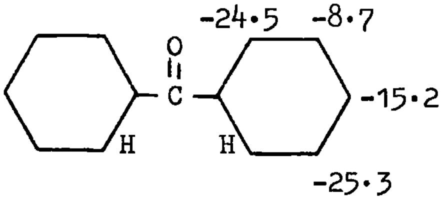


J_{34} = 20·0, J_{35} ~ 2

J_{36} = 9·3, J_{45} = 20·3

J_{46} = 4·2, J_{65} = 22·1

18. Octafluoro-2,2'-dihydrobenzophenone (CH_2Cl_2)



J_{3H} = 9·9, J_{34} = 19·3,

J_{35} = 3·1, J_{36} = 13·1 c/s.

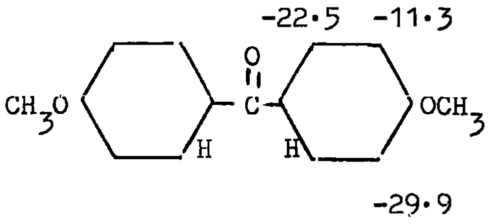
J_{4H} = 7·9, J_{45} = 18·8,

J_{46} = 7·6 c/s.

J_{5H} = 2·4, J_{56} = 19,

J_{6H} = 5·9 c/s.

19. Hexafluoro-2,2'-dihydro-4,4'-dimethoxybenzophenone (CH_2Cl_2)

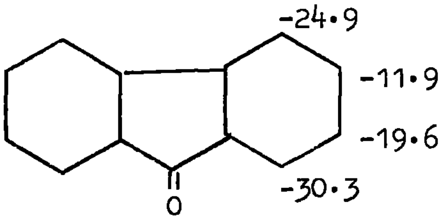


J_{H3} = 11·4, J_{H6} = 6·1 c/s.

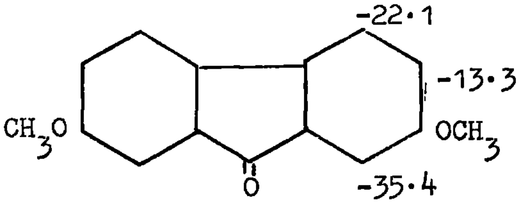
J_{5H} = 2·3, J_{56} = 21·4,

J_{53} = 4·8 c/s.

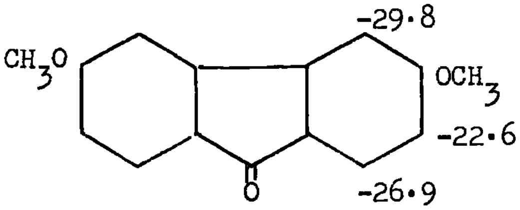
20. Octafluoro-9-fluorenone (CH_2Cl_2)



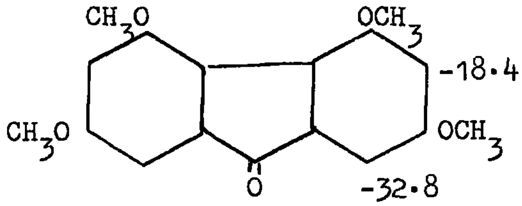
21. Hexafluoro-2,7-dimethoxy-9-fluorenone (CH_2Cl_2)



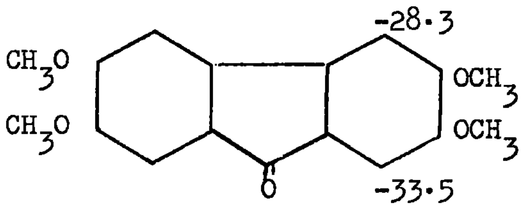
22. Hexafluoro-3,6-dimethoxy-9-fluorenone (CH_2Cl_2)



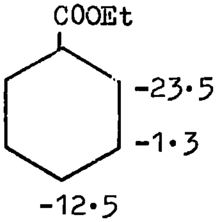
23. Tetrafluoro-2,4,5,7-tetramethoxy-9-fluorenone (CH_2Cl_2)



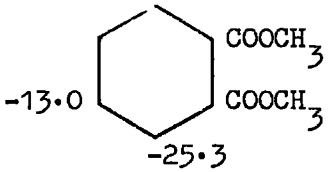
24. Tetrafluoro-2,3,6,7-tetramethoxy-9-fluorenone (CH_2Cl_2)



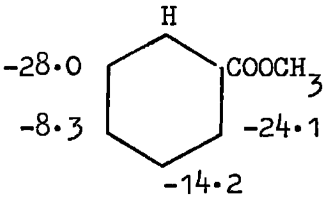
25. Ethyl pentafluorobenzoate.[121] ($CHCl_3$)



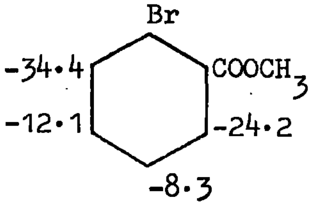
26. 3,4,5,6-Tetrafluorodimethylphthalate ($CHCl_3$)



27. Carbomethoxy-2,3,4,5-tetrafluorobenzene ($CHCl_3$)



28. Bromo-2-carbomethoxy-3,4,5,6-tetrafluorobenzene ($CHCl_3$)

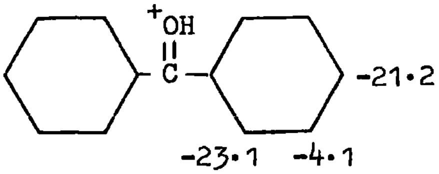


J_{34} = 20·8, J_{35} = 4·4, J_{36} = 10·2 c/s.

J_{45} = 19·5, J_{46} = 4·5, J_{56} = 21·0 c/s.

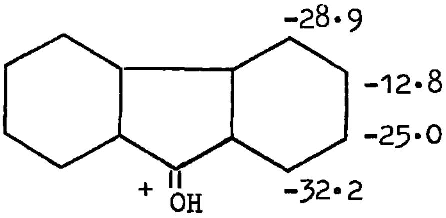
29. Decafluorobenzophenone in conc. H_2SO_4.

The low solubility of this compound is this solvent, together with the high noise which seems to be associated with the latter, meant that the resonances were hardly observable. This situation was improved by using a Digico, Time Averaging Computer and with this the spectra were recorded by Mr. J.D. Dyson under the supervision of Dr. D.T. Clark. After 15 sweeps, the peaks were clearly visible together with the major fine structure (i.e. ortho F-F couplings), and this together with the relative intensities of the peaks enabled the resonances to be assigned as shown.



30. Octafluoro-9-fluorenone in conc. H_2SO_4.

This spectrum was recorded as above, but it required 30 sweeps, since the signal was below the noise level. The observed spectrum showed four peaks of equal intensity at -32·2 (complex), -28·9 (doublet), J ~ 20 c/s), -25·0 (complex), and -12·8 p.p.m. (triplet, J ~ 20 c/s). In order to obtain deshielding of all the fluorines (as is observed for the decafluorobenzophenone case), there is only one possible assignment of these four resonances, and this is shown below.



Any other assignment would imply shielding of some of the fluorines, and this is unlikely.

INFRA-RED SPECTRA

Index of Infra-Red Spectra

1. Decafluorobenzophenone
2. Nonafluoro-2-methoxybenzophenone
3. Octafluoro-4,4'-dimethoxybenzophenone
4. Tris(pentafluorophenyl)carbinol
5. Octafluoro-2,2'-dihydrobenzophenone
6. Hexafluoro-2,2'-dihydro-4,4'-dimethoxybenzophenone
7. Carbomethoxy-2,3,4,5-tetrafluorobenzene
8. Bromo-2-carbomethoxy-3,4,5,6-tetrafluorobenzene
9. 3,4,5,6-Tetrafluorodimethylphthalate
10. Octafluoro-9-fluorenone
11. Hexafluoro-2,7-dimethoxy-9-fluorenone
12. Tetrafluoro-2,4,5,7-tetramethoxy-9-fluorenone
13. Hexafluoro-3,6-dimethoxy-9-fluorenone
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16. Octafluoro-4,4'-dimethoxydiphenyl sulphide
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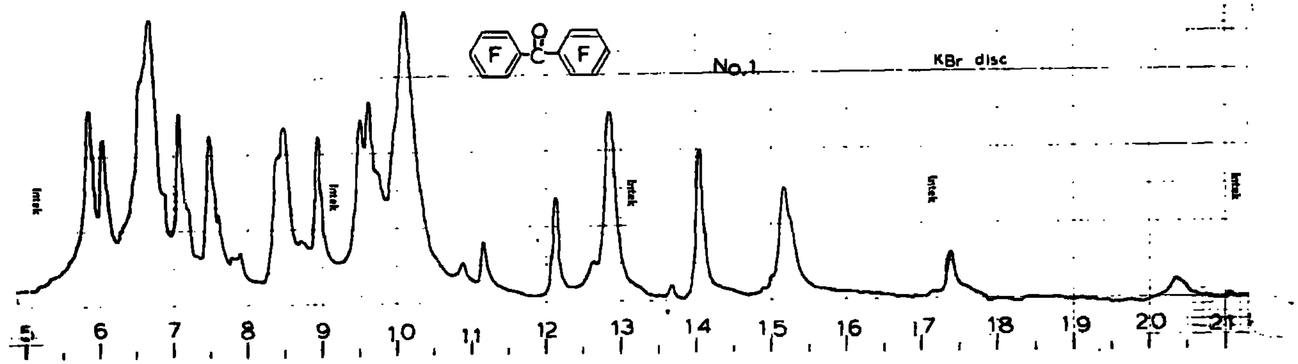
18. Heptafluoro-2-methoxythianthren
19. Decafluorodiphenyl sulphone
20. Nonafluoro-4-methoxydiphenyl sulphone
21. Octafluoro-4,4'-dimethoxydiphenyl sulphone


No. 1
KBr disc
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Intek
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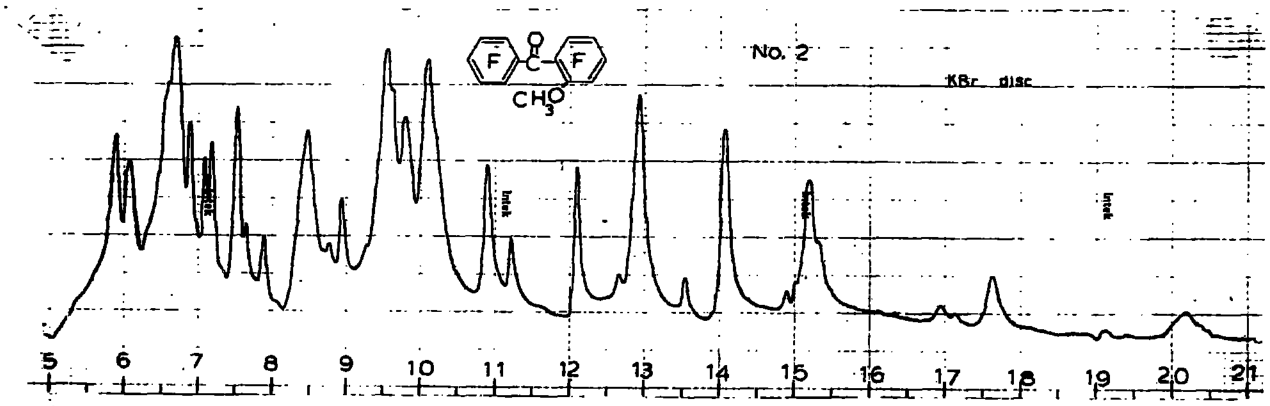
No. 2
KBr disc
F
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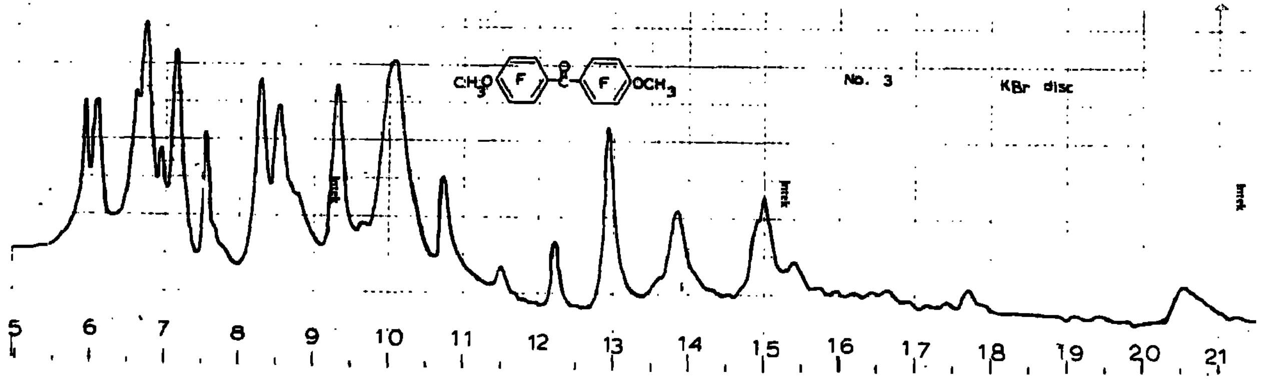
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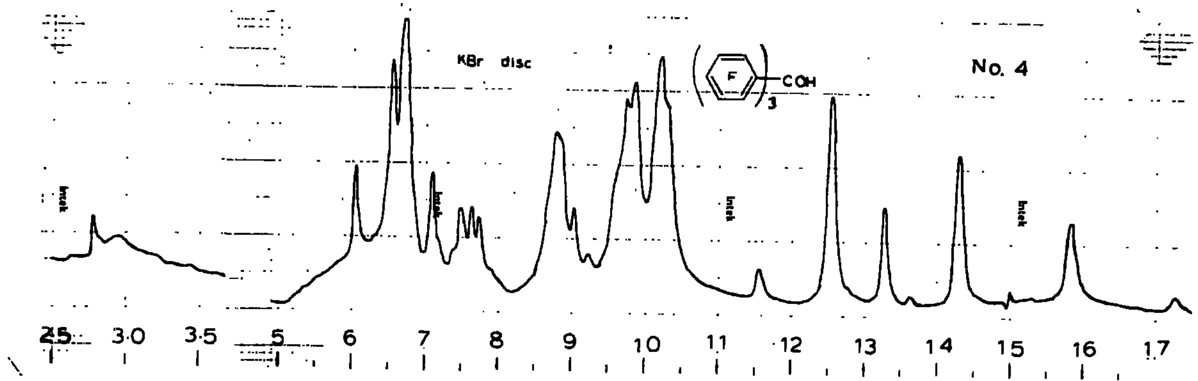
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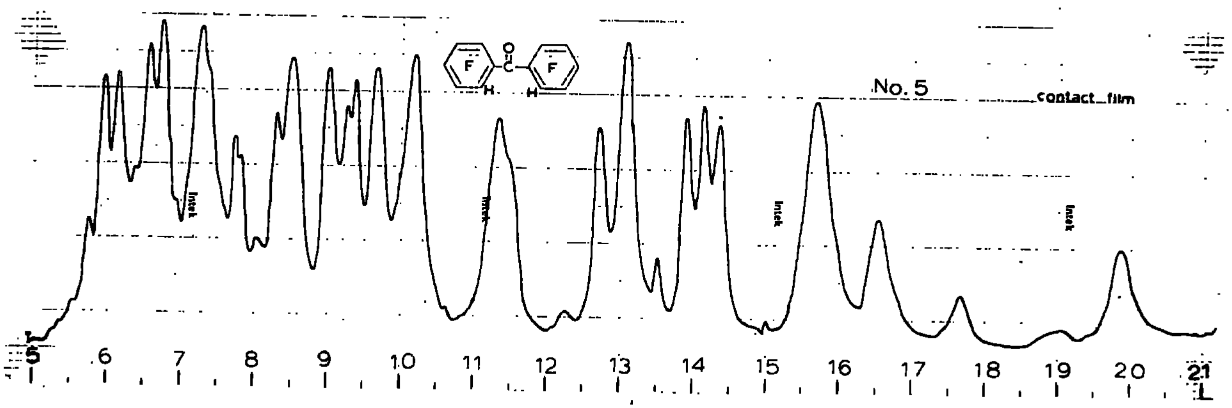
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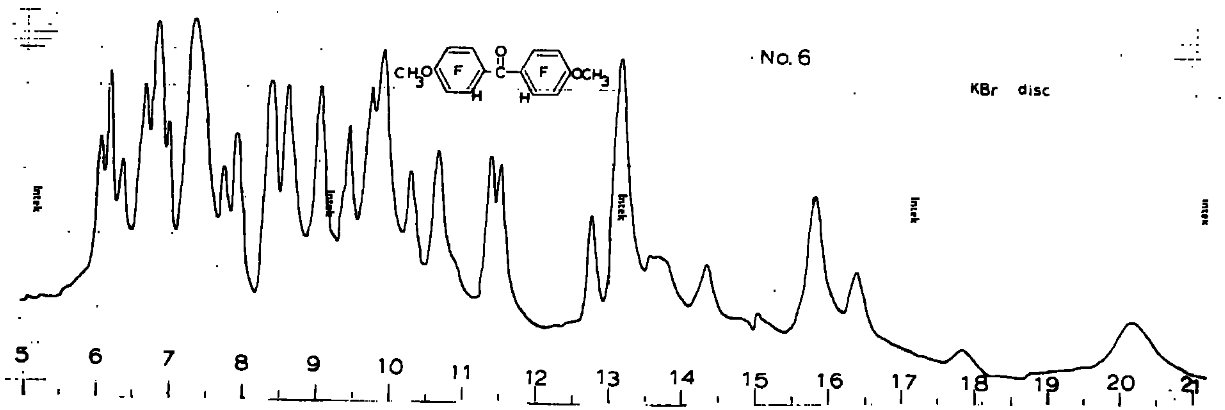
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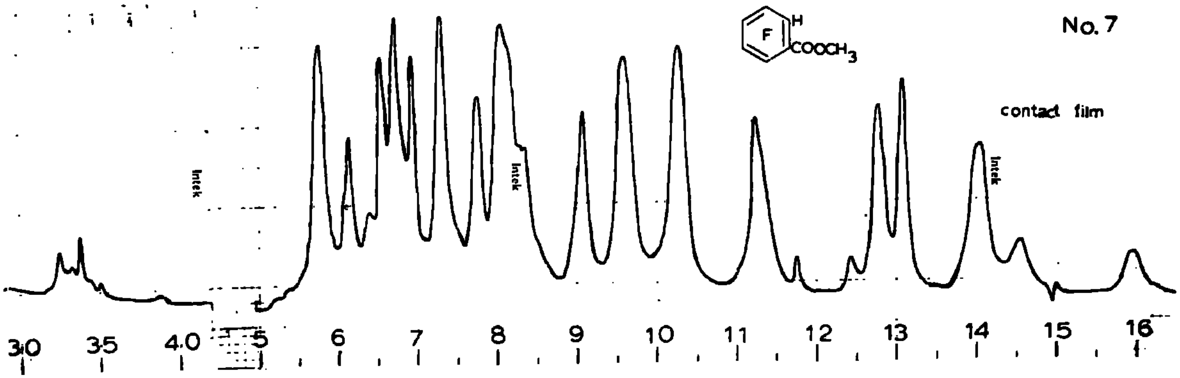
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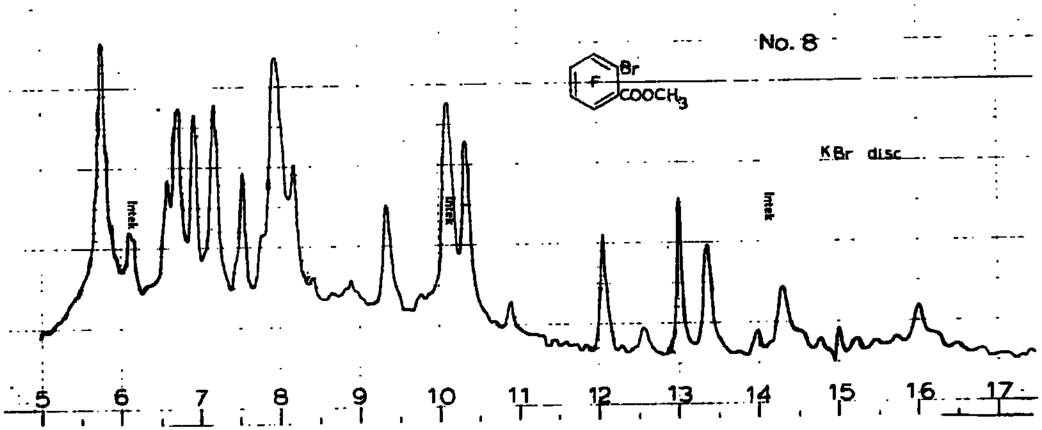
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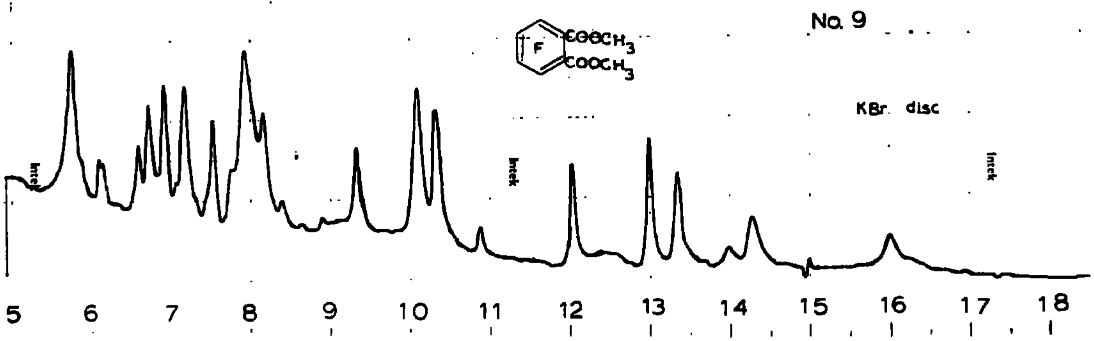
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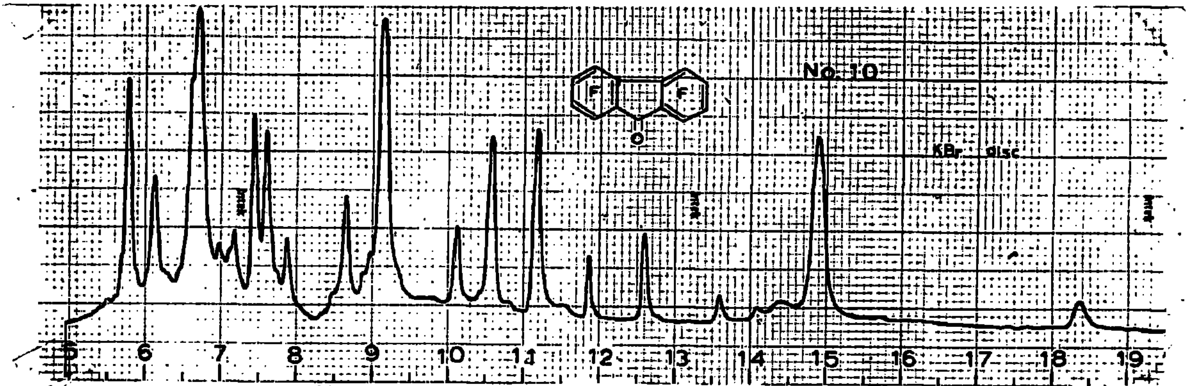
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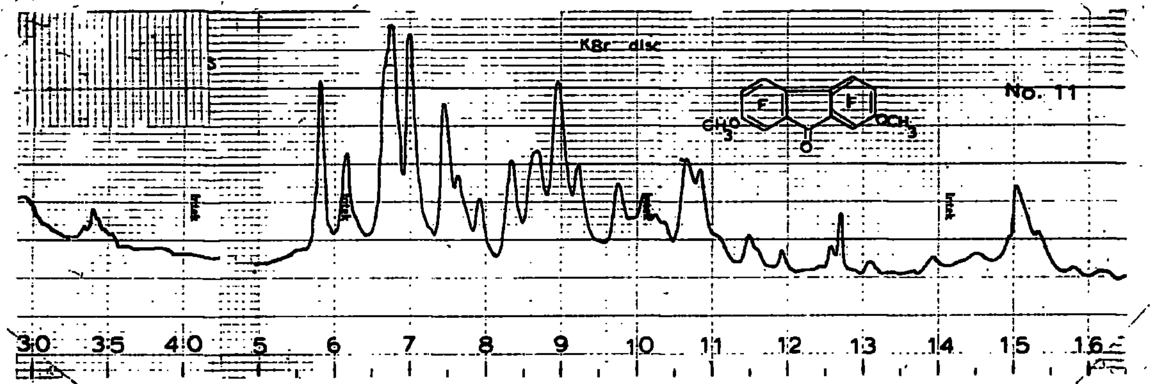
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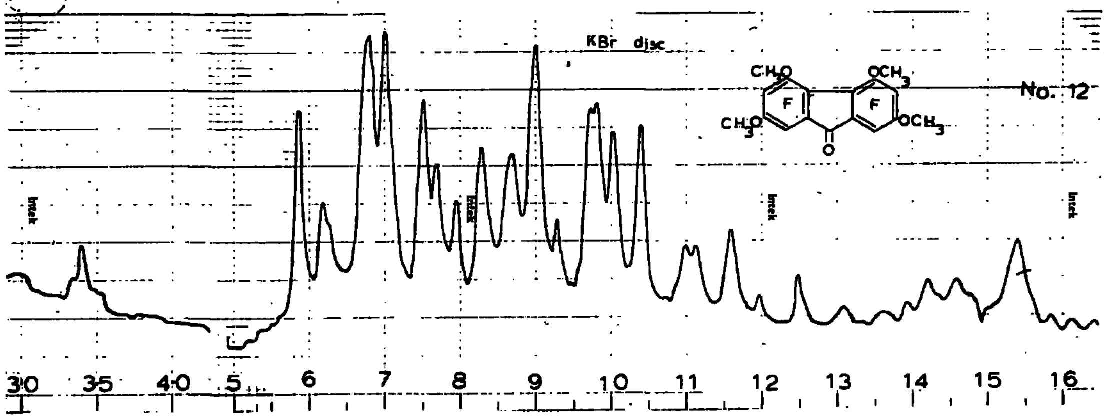
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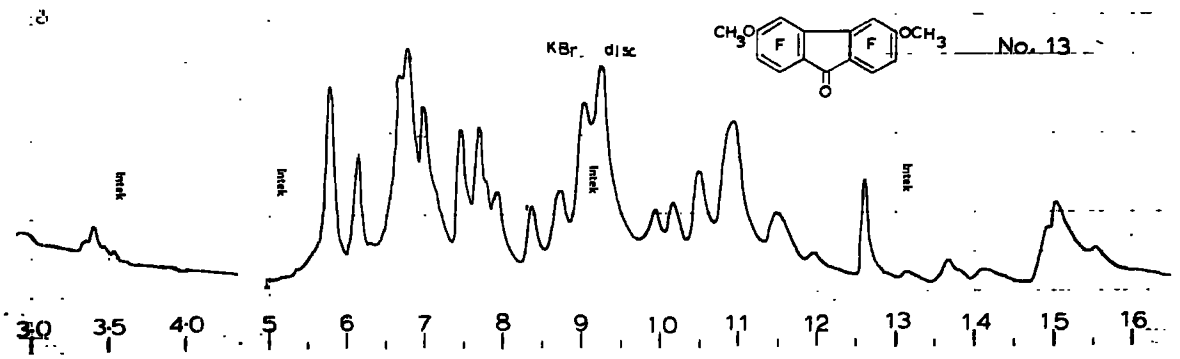

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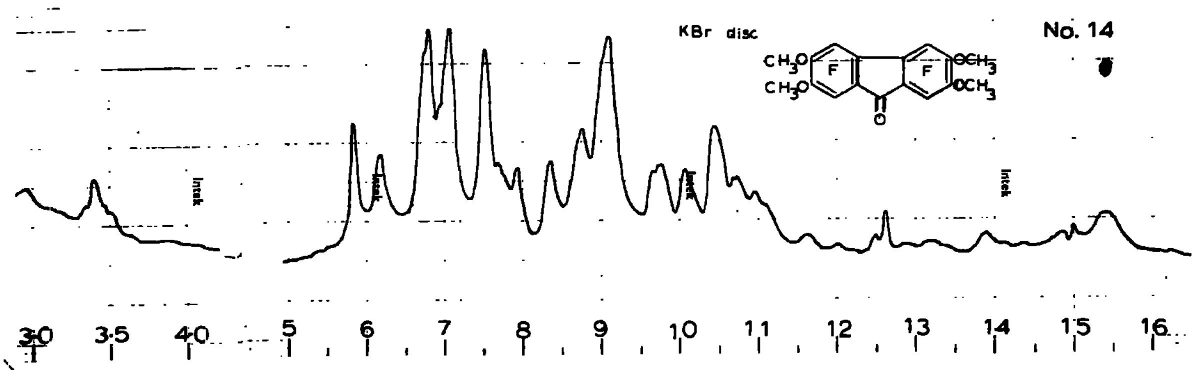

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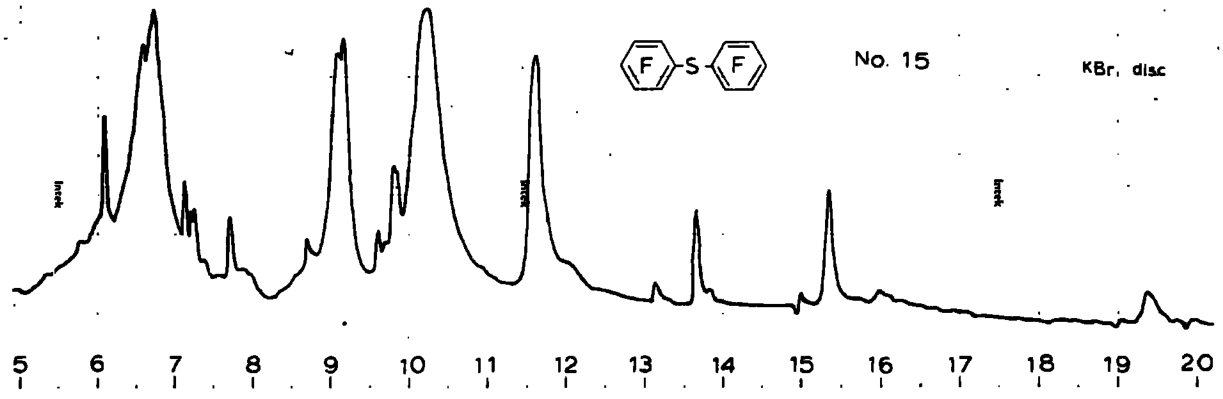

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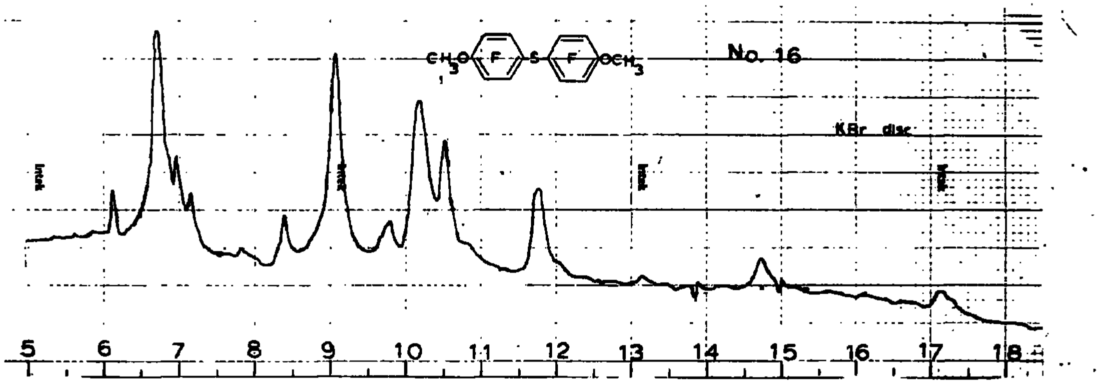

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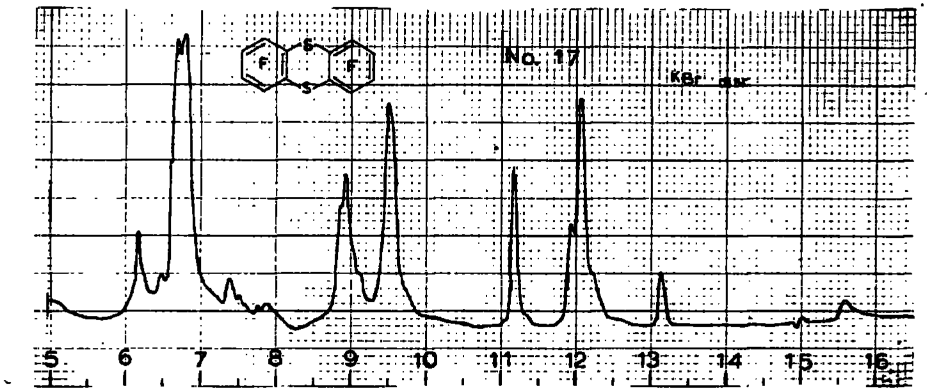

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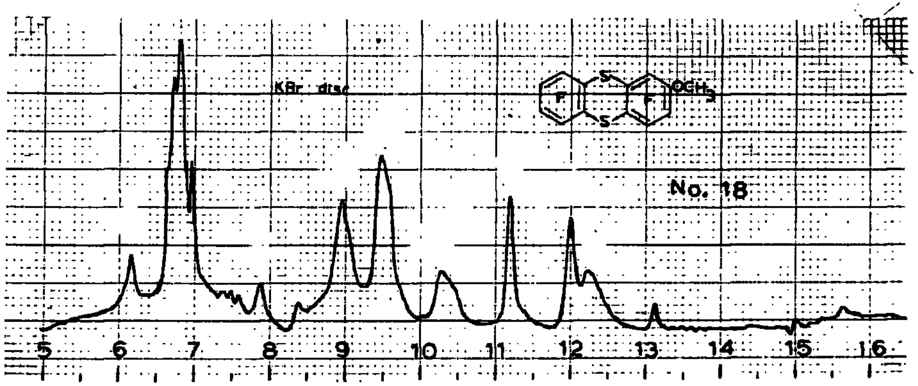

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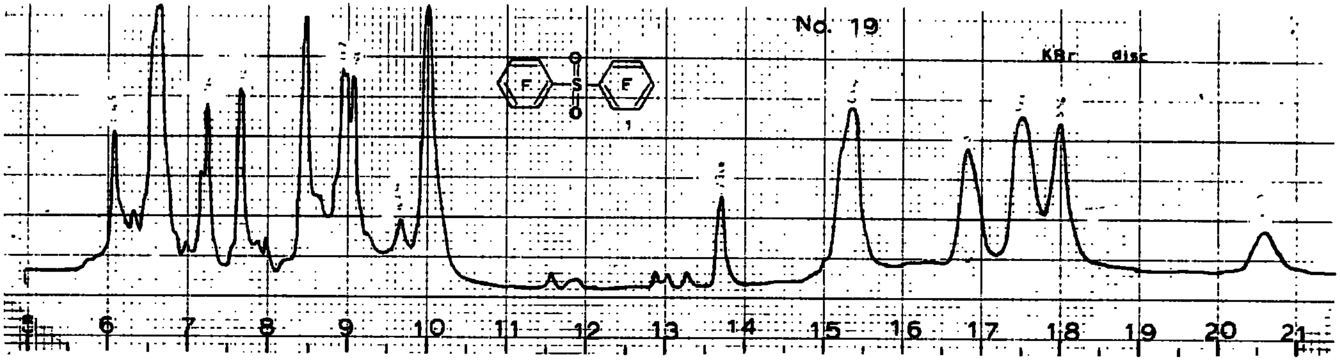

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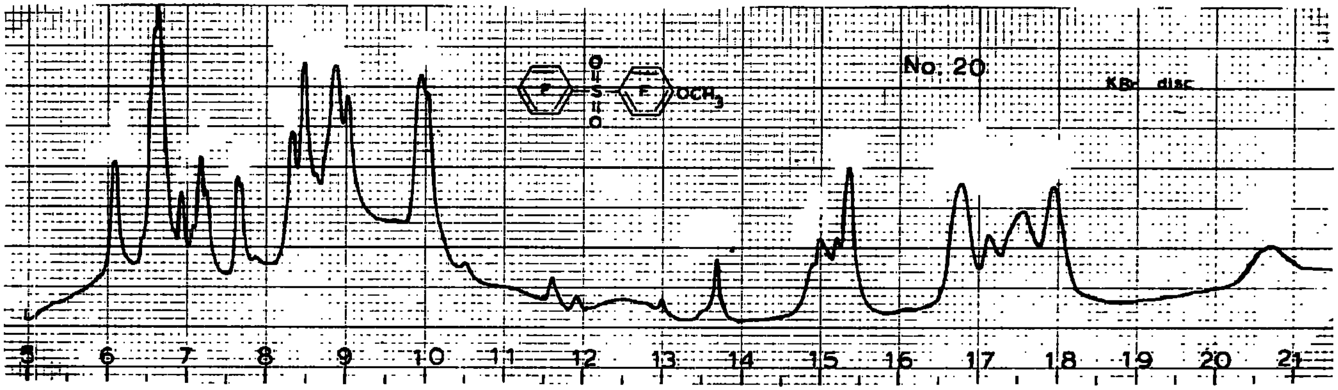

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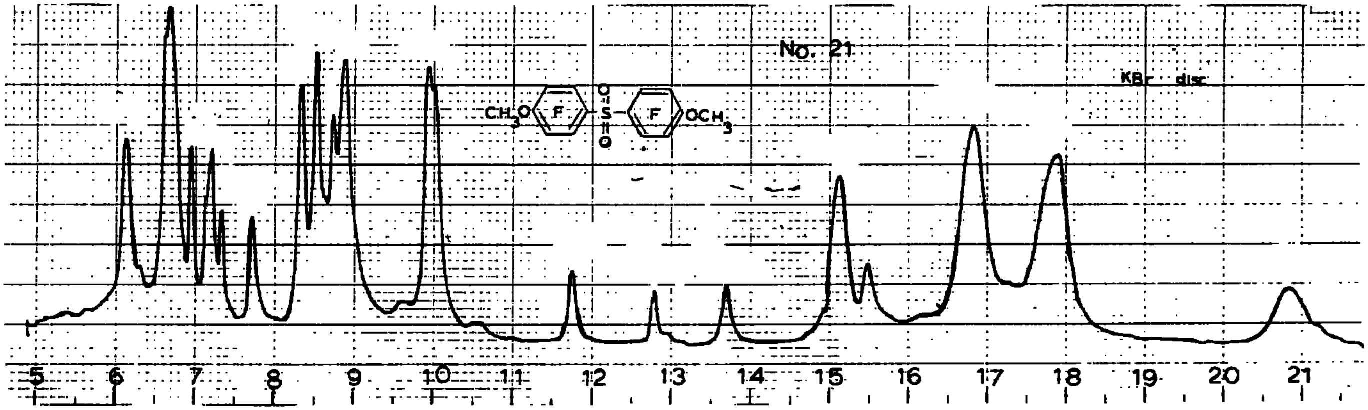

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