Highly fluorinated ketones

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UNIVERSITY OF DURHAM

A THESIS

entitled

HIGHLY FLUORINATED KETONES

submitted by

MICHAEL CLARK, B.Sc.

A candidate for the degree of Doctor of Philosophy

1971

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MEMORANDUM

The work described in this thesis was carried out in the University of Durham between October 1967 and September 1970. 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 publication:-

R.D. Chambers and M. Clark, Tetrahedron Letters, 1970, 2741.

SUMMARY

Highly Fluorinated Ketones

The reaction of hexafluoroacetone with high test peroxide produced a 1:1 adduct, possessing a polar peroxide bond. Its usefulness as an oxidising agent was investigated in a series of reactions between the adduct and ketones, aromatic amines, and mesitylene. Some success was obtained with all three groups of compounds, and the adduct was shown to be of the same order of reactivity as peracetic acid, but much less reactive than trifluoroperacetic acid.

The reaction between dimethyl or diethyl oxalate and pentafluorophenyl-lithium was found to be a useful route to the α-diketone, decafluorobenzil. Low temperature hydrolysis of the reaction was shown to be important as decafluorobenzil rearranges much more readily than benzil in the presence of hydroxide or alkoxide ions. This increased rate of rearrangement is due to the greater electron-withdrawing ability of pentafluorophenyl as compared with phenyl. The reaction mechanism for the formation of decafluorobenzil involves an initial dialkyl oxalate-pentafluorophenyl-lithium complex which is stable in solution at low temperatures. This has been demonstrated by reaction of the complex with phenyl-lithium to give 2,3,4,5,6-pentafluorobenzil.

Extension of the dimethyl oxalate reaction to pentachlorophenyl-lithium gave decachlorobenzil, but attempts to prepare octafluoro-9,10-phenanthraquinone from octafluoro-2,2'-dilithiobiphenyl and diethyl

oxalate by a similar route were unsuccessful; the products obtained were the mono-addition compound, ethyl 2-(2',3',4',5'-tetrafluorophenyl)-tetrafluorobenzoylformate, and the cyclised compound, 9-carbethoxyoctafluorofluoren-9-ol.

Pentachlorophenyl-lithium was found to attack the ketone carbonyl carbon of methyl pentafluorobenzoylformate giving the hydroxy-ester, methyl 2,3,4,5,6-pentachloropentafluorobenzilate, whereas pentafluorophenyl-lithium attacked the ester carbonyl carbon of methyl pentachlorobenzoylformate to yield the α-diketone, 2,3,4,5,6-pentachloropentafluorobenzil. This difference in position of attack is attributed to steric effects due to the pentachlorophenyl group.

Several differences were found in the reactions of benzil and decafluorobenzil with alkyl- and aryl-lithiums. Thus the addition of butyl-lithium to decafluorobenzil was found to proceed with migration of pentafluorophenyl, whereas migration of phenyl in the reaction between butyl-lithium and benzil was only observed at a higher temperature. This easier migration of pentafluorophenyl is attributed to its greater ability to stabilise a partial negative charge during migration.

With pentafluorophenyl-lithium, benzil gave α-pentafluorophenylbenzoin, but decafluorobenzil gave two compounds; perfluoro-α-phenylbenzoin, and perfluoro-2,2-diphenylbenzofuran-3-one, a cyclised product involving displacement of an ortho fluorine by an oxygen anion. The addition of pentachlorophenyl-lithium to benzil gave either an initial addition product, α-pentachlorophenylbenzoin, or a product resulting from phenyl migration and cyclisation, tetrachloro-2,2-diphenylbenzofuran-3-one, depending on the hydrolysis temperature. With decafluorobenzil however, rearrangement via an epoxide was observed, resulting in the formation of an ester, bis(pentafluorophenyl)methyl pentachlorobenzoate.

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General Introduction

The chemistry of fluorocarbon compounds has, over the last two decades, expanded to become an important field of organic chemistry research. This has been possible because fluorine is unique in that, in a hydrocarbon system, extensive and complete replacement of hydrogen by fluorine can occur to produce a completely new chemistry of fluorocarbon compounds, which are based on carbon and fluorine rather than carbon and hydrogen. Despite the slightly larger size of the fluorine atom, distortion of the geometry of the system is not a major feature affecting the chemistry of fluorocarbons, in contrast to chlorocarbon chemistry.

The main differences in the properties of fluorocarbons as compared with hydrocarbons stems from the different electronic environment in which functional groups are found. Extensive replacement of hydrogen by fluorine tends to produce electron-deficient systems which can have a profound effect on the reactivity of a functional group. Also, this change in electronic environment means that hydrocarbons and fluorocarbons often complement each other in the mechanism of their reactions. In unsaturated hydrocarbon systems, reactions often involve the proton and the carbonium ion, whereas in unsaturated fluorocarbon systems, it is the fluoride ion, F^-, and the carbanion which play an important role. The chemistry of carbanions has been investigated to a lesser extent than that of carbonium ions, and so this new area of chemistry provides an excellent opportunity for examining mechanisms and reaction processes involving carbanions.

However, fluorocarbon chemistry is not restricted to academic investigation. The slightly larger fluorine atom tends to protect the carbon chain more than hydrogen, and this, coupled with the high strength of the carbon-fluorine bond, promotes greater stability in the molecule. In the field of aliphatic compounds, such fluorocarbons have found industrial applications as inert polymers, aerosol sprays, refrigerants, and lubricants of high thermal stability. The chemistry of polyfluoroaromatic compounds developed later than that of the polyfluoroaliphatics, and although no commercial outlets have as yet been found, considerable research is at present being directed towards such areas as pharmaceuticals and agricultural chemistry.

The work in this thesis is divided into two parts, both of which are concerned with the difference in reactivity of functional groups in non-fluorinated and fully-fluorinated systems. In the first part, an attempt is made to exploit the extremely reactive nature of the carbonyl group in hexafluoroacetone, which enables it to form an adduct with hydrogen peroxide, and a study is made of the efficiency of the adduct as an oxidising agent. The second part is concerned with the synthesis of some halogenated benzils, and compares and contrasts the reactions of benzil and the fully-fluorinated compound, decafluorobenzil, with hydroxide ion, alkoxide ion, and some alkyl- and aryl-lithiums.

CHAPTER 1

Organic peracids

1.1. Introduction.

Organic peracids were first discovered at the beginning of the century and their preparation, properties, and uses have since been the subject of extensive investigation. Although many other peracids have been studied,[1] the most widely used have been performic, perbenzoic, peracetic, and, more recently, trifluoroperacetic acids. This chapter is intended as a brief summary of the methods of preparation of the more important acids, and as an outline of their main areas of application.

1.2. Preparation.

A general method for the preparation of peracids is the equilibration reaction between a carboxylic acid and hydrogen peroxide in the presence

$$\mathrm{RCOOH} + \mathrm{H_2O_2} \rightleftharpoons \mathrm{RCOOOH} + \mathrm{H_2O} \qquad \text{(I)}$$

$$(\mathrm{R} = \mathrm{H}, \mathrm{CH_3}, \mathrm{C_6H_5}, \mathrm{CF_3})$$

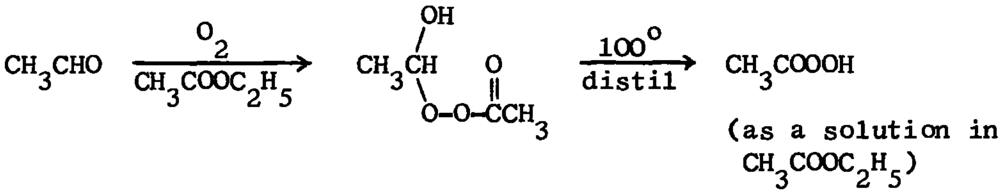
of a strong acid as catalyst.[2] Solutions of up to 90% performic acid have been prepared from 90% hydrogen peroxide and formic acid by this method (I, R = H),[3] although they are not very stable, losing 25% of the active oxygen on standing at 0°C for 24 hrs.,[3] and even dilute solutions should be used immediately after preparation.

Peracetic acid can be obtained in a similar manner as a 45-50% solution (I, R = $\mathrm{CH_3}$). A better way however, is by the reaction of hydrogen peroxide with acetic anhydride[4] (II, R = CH_3), this method

$$(RCO)_2O + H_2O_2 \longrightarrow RCOOOH + RCOOH \qquad (II)$$
$$(R = CH_3,\ CF_3)$$

having the advantage that peracid formation occurs more rapidly. Trifluoroperacetic acid, the most powerful of the peracids discussed, is also best prepared from the corresponding anhydride (II, R = CF_3),[5] in a reaction conveniently conducted in methylene chloride solution.

Solutions of peracids without carboxylic or strong acids present are sometimes desired and here specific routes to the appropriate peracids must be used. Thus anhydrous peracetic acid can be obtained by air oxidation of acetaldehyde in ethyl acetate, followed by thermal



$$CH_3CHO \xrightarrow[CH_3COOC_2H_5]{O_2} CH_3CH(OH){-}O{-}O{-}C(=O)CH_3 \xrightarrow[distil]{100^\circ} CH_3COOOH$$

(as a solution in $CH_3COOC_2H_5$)

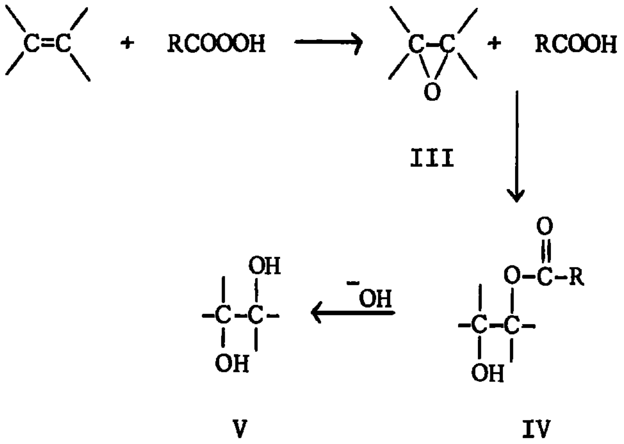
decomposition of the intermediate.[6] The peracid loses oxygen only slowly on standing[7] and, unlike performic acid, has been obtained pure.

The most convenient preparation of perbenzoic acid is the equilibration reaction (I, R = C_6H_5) with methanesulphonic acid acting as solvent and catalyst.[8] This peracid is a stable solid and only slightly soluble in water, and so can be obtained free from the sulphonic acid by dilution of the reaction mixture with water, followed by filtration or extraction.

1.3. Reactions with olefins.

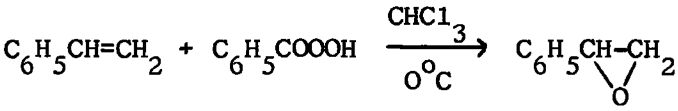
Olefin oxidation by peracids can lead either to epoxide formation

(III) or, by further reaction involving ring cleavage by the corresponding carboxylic acid, to hydroxy-esters (IV), which on base hydrolysis give

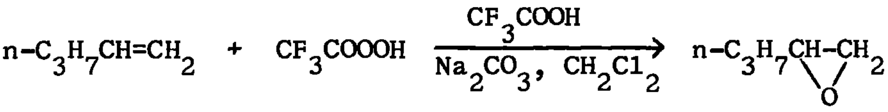


trans-1,2-diols (V).

These reactions do not generally require forcing conditions and most of the common peracids have been used to give good yields of products, e.g.[9]

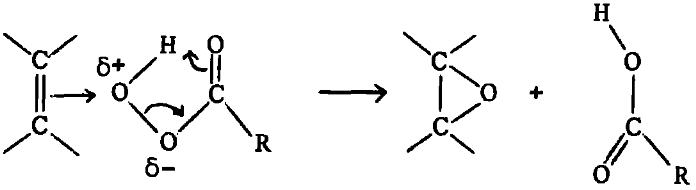

$$C_6H_5CH{=}CH_2 + C_6H_5COOOH \xrightarrow[0^\circ C]{CHCl_3} C_6H_5\underset{\diagdown O \diagup}{CH{-}CH_2} \qquad (70\%)$$

Epoxide ring opening is acid-catalysed[2] and in order to prevent cleavage, the peracid must either be free from strong acids such as trifluoroacetic or mineral acids, or be used with a suitable salt to act as a buffer. Thus epoxidation can be successfully carried out using trifluoroperacetic


$$n{-}C_3H_7CH{=}CH_2 + CF_3COOOH \xrightarrow[Na_2CO_3,\ CH_2Cl_2]{CF_3COOH} n{-}C_3H_7\underset{\diagdown O \diagup}{CH{-}CH_2} \qquad (81\%)$$

acid provided sodium carbonate or disodium hydrogen phosphate is added to react with the trifluoroacetic acid present.[10] The reactivity of this peracid makes it particularly suitable for the oxidation of olefins which are only slowly attacked by perbenzoic or peracetic acids.

The present accepted mechanism for epoxidation involves electrophilic attack by oxygen at the less hindered side of the olefin. Support for this comes from observations that electron-donating substituents on the



olefin (e.g. alkyl) increase the rate of epoxidation,[11] while the presence of a strongly electron-withdrawing group in the peracid also increases the rate[2] by increasing the polarity of the oxygen-oxygen bond and hence the electrophilic nature of the attacking oxygen. This agrees with the observed high reactivity of trifluoroperacetic acid as compared with peracetic acid.

Oxidation of olefins with peracids in the presence of strong acids as catalysts leads directly to the trans-hydroxy-esters,[12] which are easily hydrolysed with retention of configuration to the trans-diols. Most peracids have been used, but trifluoroperacetic acid is again particularly effective, giving excellent yields of α-glycols from a variety of olefins[12] (see Table 1).

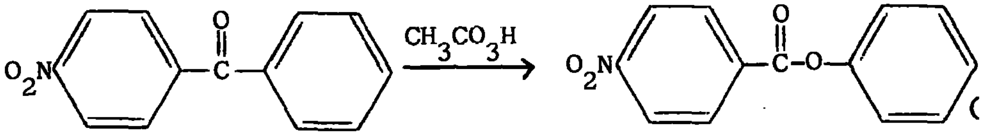
Table 1

Oxidation of olefins with CF_3COOOH

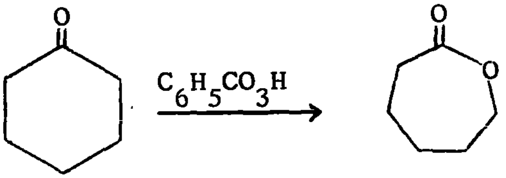
Olefin	Glycol	Yield %
Cyclohexene	trans-1,2-cyclohexanediol	82
Allyl chloride	3-chloro-1,2-propanediol	70
Oleic acid	9,10-dihydroxystearic acid	80
Oct-1-ene	1,2-octanediol	92

1.4. Reaction with ketones.

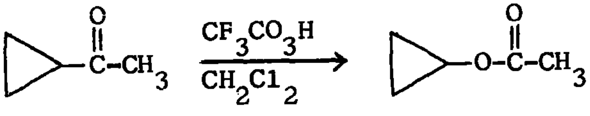
The oxidation of ketones to esters (the Baeyer-Villiger reaction) is generally effected with the more reactive peracids, as reaction proceeds more slowly than in the epoxidation of olefins. Thus, while other acids have been used (see examples), elimination of long reaction times requires the use of trifluoroperacetic acid. Reaction can be



95%
(Ref. 15)

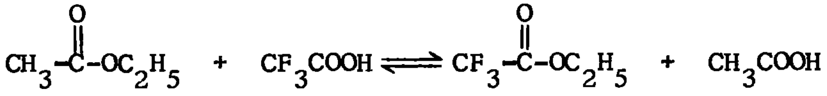


71%
(Ref. 2)



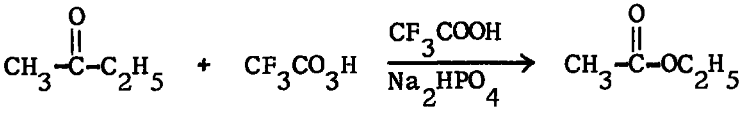
53%
(Ref. 14)

complicated however by products resulting from transesterification, i.e. reaction between trifluoroacetic acid and the ester product. Addition



$$CH_3-\overset{O}{\overset{\|}{C}}-OC_2H_5 + CF_3COOH \rightleftharpoons CF_3-\overset{O}{\overset{\|}{C}}-OC_2H_5 + CH_3COOH$$

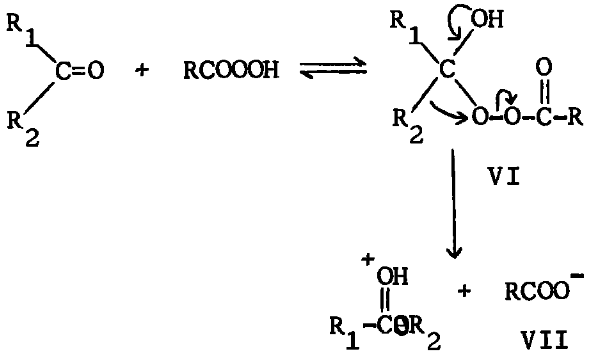
of a buffer minimises this by reacting with the trifluoroacetic acid to form a salt.[14]



$$CH_3-\overset{O}{\overset{\|}{C}}-C_2H_5 + CF_3CO_3H \xrightarrow[Na_2HPO_4]{CF_3COOH} CH_3-\overset{O}{\overset{\|}{C}}-OC_2H_5 \quad 72\%$$

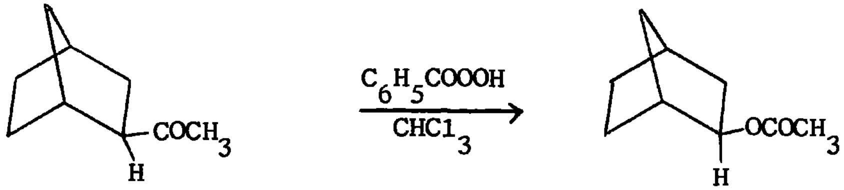
(Ref. 14)

The reaction mechanism has been studied by several groups of workers.[14-19] The peracid first undergoes nucleophilic addition to the carbonyl group to form a peracid-ketone complex VI. This is followed



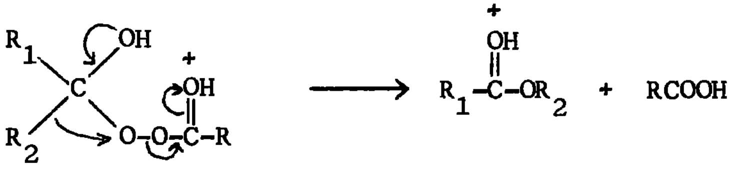
by a concerted process involving loss of the anion VII and migration of a group (R_2) with its electron pair from carbon to electrophilic oxygen. Evidence comes from tracer studies using labelled oxygen in benzophenone,[18] where it was found that all the activity remained in the carbonyl oxygen of the ester. Electron-donating groups in the ketone, and electron-withdrawing groups in the peracid both increase the rate of reaction.

The rearrangement is intramolecular, as shown by several workers who found that migration occurred with retention of configuration,[2] e.g.



(optically active) (optically active)

The reaction is acid-catalysed, and Sauers[22] suggested that with strong acids, VI is probably protonated, thus enabling VII to leave as a neutral species:

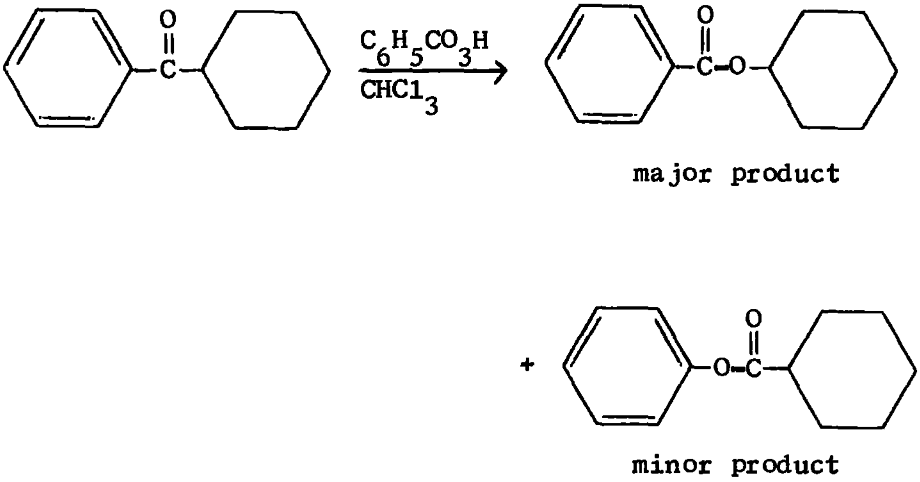


VIII

Support for this comes from kinetic work conducted by Hawthorne and Emmons[17] who found that the oxidation of ketones with trifluoroperacetic acid in the presence of trifluoroacetic acid was third order, suggesting that acid, ketone, and peracid were involved in an intermediate such as VIII in the rate-determining step.

Reactions carried out in the absence of strong acids have been found to show second order kinetics,[19] and this has been explained on the basis of a slow rate-controlling addition of peracid to ketone. In their investigation however, Hawthorne and Emmons[17] concluded that the rate-determining step was the decomposition and not the formation, of the protonated peracid-ketone complex.

The oxidation of unsymmetrical ketones can obviously lead to two possible isomeric esters, e.g.[13]

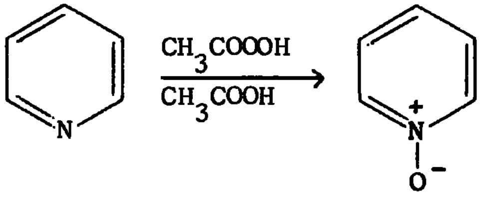


Several workers have studied the relative ease of migration of various groups in a series of ketones,[13-16,20,21] and the following order of migratory aptitudes has been obtained; t-alkyl $>$ cyclohexyl $\sim$ sec-alkyl $\sim$ benzyl $\sim$ phenyl $>$ primary alkyl $>$ cyclopropyl $>$ methyl. Recently, Smissman and co-workers[21] studied the migratory aptitudes in a series of acetophenones, substituted with various electron-withdrawing groups. They observed some methyl migration in most reactions, and found the order methyl $>$ aryl in o-nitroacetophenone.

The observed series is consistent with mechanistic requirements where one would expect the most nucleophilic substituents to migrate most readily, although it has been suggested that steric factors[16] and the nature of the leaving group[23] may also be responsible.

1.5. Oxidation of amines.

Peracetic and trifluoroperacetic acids have been most used for amine oxidations. Thus pyridine, a tertiary amine, has been oxidised

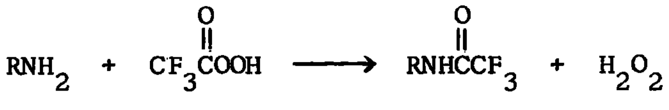


to pyridine N-oxide by peracetic acid.[2]

Primary amines can give a variety of products, depending on the conditions and the peracid used. Using peracetic acid, Emmons oxidised several primary aliphatic amines to nitro-alkanes,[24] e.g.

$$(CH_3)_2CHCH_2NH_2 \xrightarrow[CH_3COOH]{CH_3COOOH} (CH_3)_2CHCH_2NO_2 \qquad 65\%$$

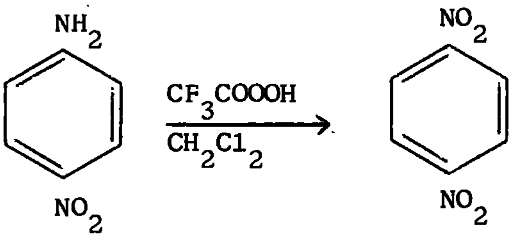
With trifluoroperacetic acid however, the presence of trifluoroacetic acid led to the formation of amine trifluoroacetate salts. When the reaction mixture was buffered with sodium carbonate, N-alkyl trifluoroacetamides were obtained:-



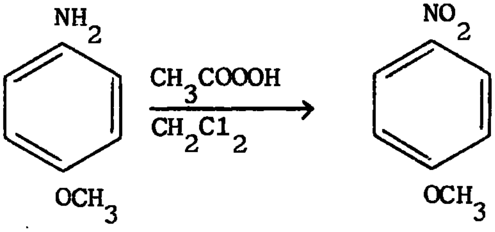
$$RNH_2 + CF_3\overset{O}{\overset{\|}{C}}OOH \longrightarrow RNH\overset{O}{\overset{\|}{C}}CF_3 + H_2O_2$$

Peracetic and trifluoroperacetic acids can also give different results with aromatic primary amines. The oxidation of aniline with peracetic acid has, in one paper, been reported to give mainly azoxybenzene,[25] and in another, to give a mixture of nitrosobenzene and azoxybenzene.[3] In a re-investigation, Emmons found that under anhydrous conditions peracetic acid could successfully be used for the oxidation of several anilines to nitrobenzenes.[24]

Trifluoroperacetic acid has also been used to oxidise a range of aromatic amines,[26] and is superior to peracetic acid in that it gives higher yields and also oxidises weakly basic amines such as



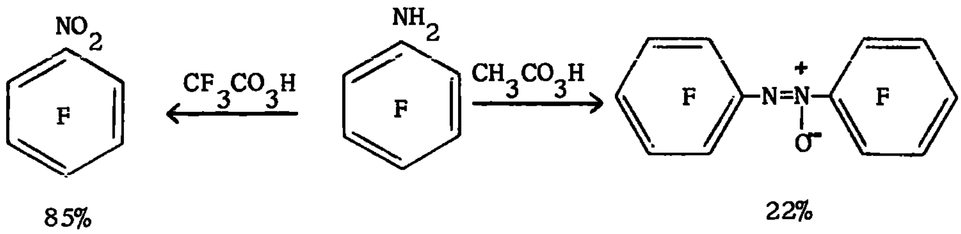
(Ref. 26)



82% (Ref. 24)

p-nitroaniline where peracetic acid fails. With anilines bearing electron-donating substituents however, such as p-anisidine, attack at the benzene nucleus occurs, and the reaction must be carried out with the less reactive peracetic acid.

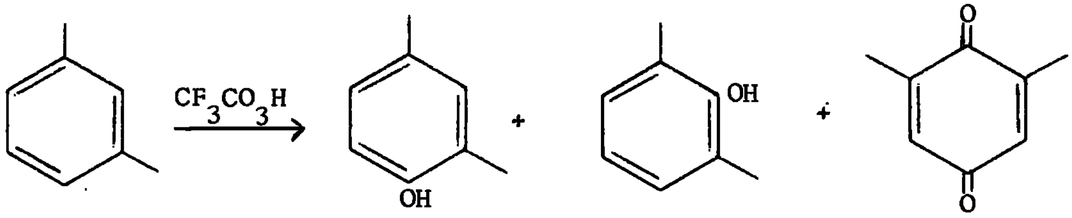
Trifluoroperacetic acid has been successfully used to oxidise

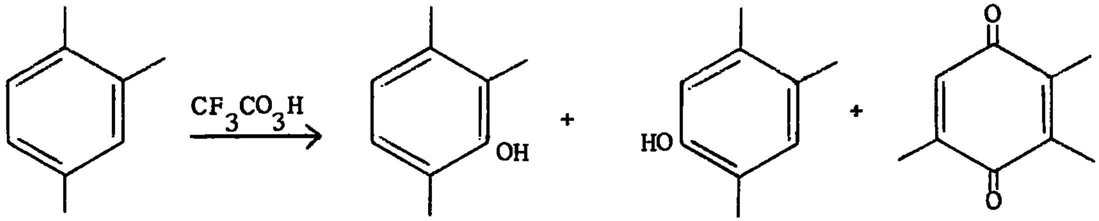


pentafluoroaniline to pentafluoronitrobenzene in good yield.[27] Peracetic acid on the other hand, prepared from 30% hydrogen peroxide, has been reported to give only a low yield of decafluoroazoxybenzene.[28]

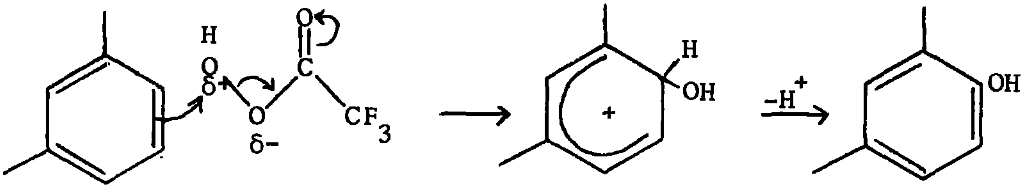
1.6. Electrophilic aromatic hydroxylation.

Early investigations of the reactions between peracids and aromatic hydrocarbons were restricted to perbenzoic acid[29] and hydrogen peroxide and acetic acid,[30] and while reaction did occur, yields were generally low or not reported. The preparation of trifluoroperacetic acid enabled the reaction to be studied more widely. Thus m-xylene was found to give a mixture of 2,4- and 2,6-xylenols and m-xyloquinone, and

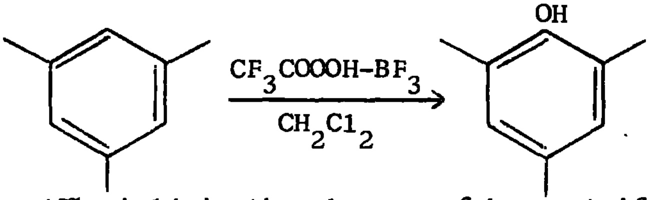




1,2,4-trimethylbenzene gave 2,3,6- and 2,4,5-trimethylphenol and the quinone, although in both cases the percentage conversion was only 30-40%.[31] The orientation of substitution in these products indicated that the mechanism involved electrophilic attack of positive hydroxyl rather than a free radical process, e.g.

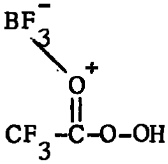


More recently, Hart and Buehler[32] have shown that the addition of boron trifluoride, a Lewis acid, greatly enhances the efficiency of the trifluoroperacetic acid. Using this reagent, they obtained an 88% yield of mesitol from mesitylene, based on peracid consumed,



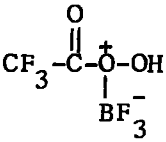
compared to a 45% yield in the absence of boron trifluoride. Other methylbenzenes were also studied and all gave high conversions to mixtures of phenols, quinones, and products involving a Wagner-Meerwein rearrangement.

The added boron trifluoride is able to assist heterolytic cleavage of the polar oxygen-oxygen bond by co-ordinating with either of



$$CF_3-\overset{\overset{BF_3^- \searrow O^+}{\|}}{C}-O-OH$$

or



$$CF_3-\overset{\overset{O}{\|}}{C}-\underset{\underset{BF_3^-}{|}}{\overset{+}{O}}-OH$$

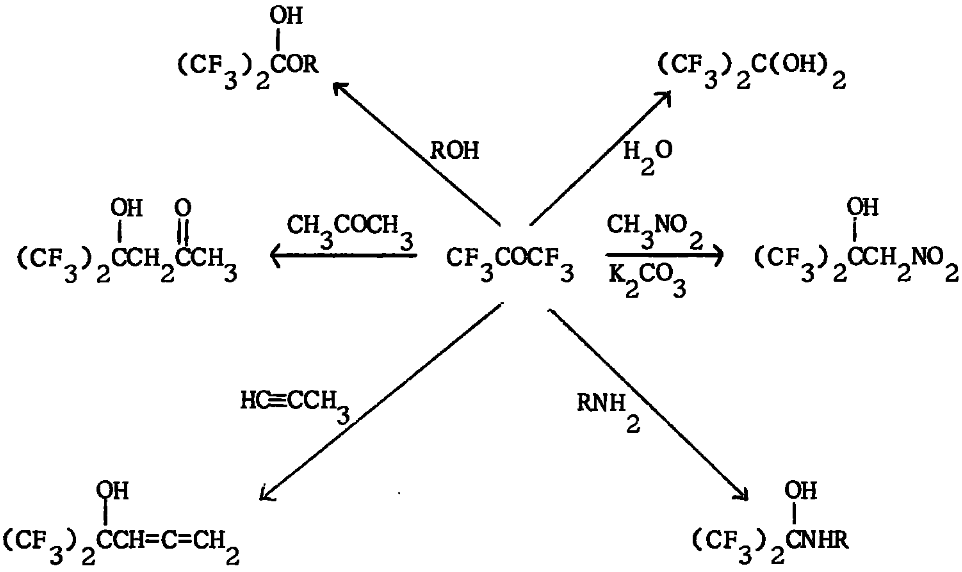
the oxygens attached to carbon, thus enhancing the electrophilicity of the attacking oxygen and increasing the efficiency of the leaving group, although the former is probably the more important effect.

CHAPTER 2

Oxidation reactions of hexafluoroacetone-hydrogen peroxide

2.1. Introduction.

The chemistry of hexafluoroacetone has been extensively studied,[33] and the most interesting feature of the ketone is the extremely electron-deficient nature of the carbonyl carbon atom, arising from the electron withdrawing influence of the trifluoromethyl groups. Thus, as well as undergoing the usual reactions of aliphatic ketones, hexafluoroacetone will readily combine with a wide variety of active hydrogen compounds[33]

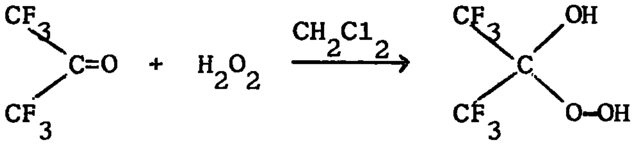


to yield substituted hydroxyl compounds, which are generally stable with respect to dehydration or regeneration of the ketone.

From this knowledge of the chemistry of hexafluoroacetone, it seemed possible that hydrogen peroxide might also react with the ketone, to form an adduct with a polar peroxide bond. This was in fact found to be the case, and reactions of this adduct as an oxidising agent have been investigated.

2.2. Preparation of the adduct.

Two methods were used for the preparation of the adduct. Initially, hexafluoroacetone was bubbled into a vigorously stirred suspension of 90% hydrogen peroxide in methylene chloride, cooled in an ice-bath. A single phase was obtained after addition of about half the hexafluoroacetone, and uptake of gas dropped noticeably when a roughly 1:1 molar ratio of hydrogen peroxide to hexafluoroacetone was reached.



As hexafluoroacetone boils at -28°, it can easily be handled in a vacuum system, and a simpler preparation of the adduct was to allow the hydrogen peroxide in methylene chloride to stir under an atmosphere of the gas. Again, cooling the reaction flask accelerated the rate at which the gas dissolved. It was found that the adduct evolved hexafluoroacetone if left standing at room temperature, and so it was generally used immediately after preparation.

2.3. Aim of investigation.

The greater reactivity of trifluoroperacetic acid as compared with peracetic acid is attributed to the strong electron-withdrawing effect of the trifluoromethyl group,[33] which increases the polarity of the oxygen-oxygen bond. Hexafluoroacetone-hydrogen peroxide possesses two trifluoromethyl groups and although the carbonyl group is now saturated, the peroxide bond should similarly be highly polarised, thus enhancing the electrophilic nature of the hydroxonium oxygen to give a more reactive peracid. Consequently the reactions studied were those which for good results have previously required the use of the more reactive peracids.

2.4. Oxidation of ketones.

A. Experimental method.

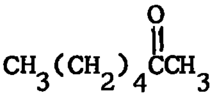
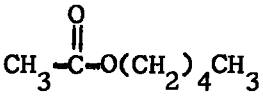
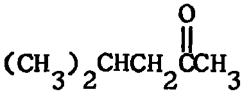
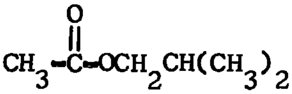
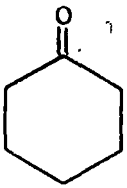
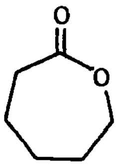
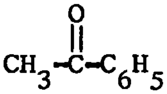
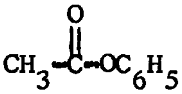
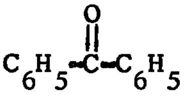
For this series of experiments, the ketone in methylene chloride solution was added dropwise to a stirred solution of excess peroxide adduct in methylene chloride. After a period at reflux the reaction mixture was stirred at room temperature before being diluted with solvent and washed first with water to remove most of the acidic hexafluoroacetone hydrate (hexafluoropropane-2,2-diol) formed during the reaction, then with sodium carbonate solution, and finally with ferrous sulphate solution to ensure complete removal of any remaining peroxide. Removal of solvent and distillation of the residue gave the ester products.

B. Discussion of results.

Several ketones were treated with hexafluoroacetone-hydrogen peroxide (2-hydroperoxyhexafluoropropan-2-ol) - the results are summarised in the following table:-

Table II

Oxidation reactions with $(CF_3)_2C(OH)OOH$

Ketone	Ester	Yield %
 $CH_3(CH_2)_4\overset{\overset{O}{\|}}{C}CH_3$ n-amyl methyl ketone	 $CH_3-\overset{\overset{O}{\|}}{C}-O(CH_2)_4CH_3$ n-amyl acetate	81
 $(CH_3)_2CHCH_2\overset{\overset{O}{\|}}{C}CH_3$ isobutyl methyl ketone	 $CH_3-\overset{\overset{O}{\|}}{C}-OCH_2CH(CH_3)_2$ isobutyl acetate	73
 cyclohexanone	 caprolactone	50
 $CH_3-\overset{\overset{O}{\|}}{C}-C_6H_5$ acetophenone	 $CH_3-\overset{\overset{O}{\|}}{C}-OC_6H_5$ phenyl acetate	34
 $C_6H_5-\overset{\overset{O}{\|}}{C}-C_6H_5$ benzophenone	-	-

The aliphatic ketones, isobutyl methyl ketone and n-amyl methyl ketone were oxidised smoothly to the corresponding esters in relatively clean reactions. Reflux was essential to ensure complete conversion of the ketone, and as distillation did not yield completely pure ester, the yields were determined by saponification of the reaction product. The yields are ~10% lower than those obtained by Emmons and Lucas[14] using trifluoroperacetic acid, but are an improvement on results from the more hazardous route of McLure and Williams[34] using hydrogen peroxide-boron trifluoride etherate.

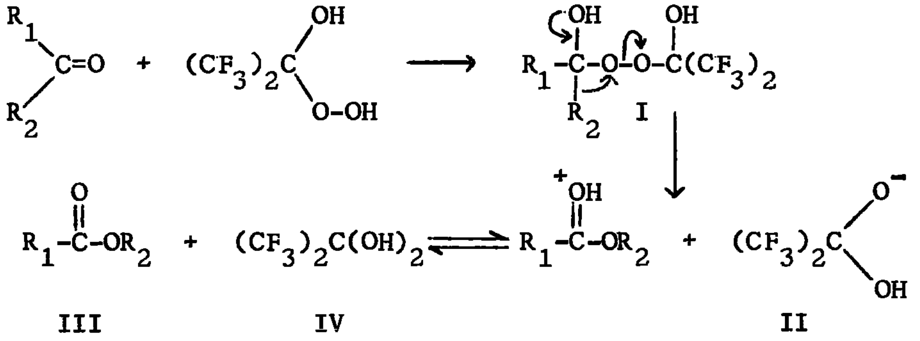
Cyclohexanone was oxidised to caprolactone in fair yield. This reaction had previously been carried out using trifluoroperacetic acid by Sager and Duckworth,[35] who obtained the lactone in excellent yield (81%).

Poor results were obtained when the reaction was extended to aryl and aralkyl ketones. Thus the attempted oxidation of benzophenone gave an 80% recovery of starting material, while the oxidation of acetophenone gave a mixture of products including phenyl acetate, recovered ketone, and a tarry residue. This, coupled with the low recovery of material, suggests that side reaction involving electrophilic attack in the aromatic ring of the ester also occurs, leading either to base-soluble products which would be lost on work-up, or to intractable material. Ring attack has been observed with trifluoroperacetic acid during certain amine oxidations.[26]

Reaction at room temperature minimised side reaction and gave the best recovery of material, but even so the overall yield of phenyl acetate was only 34%. This is in contrast to the highly efficient way in which trifluoroperacetic acid oxidises alkyl, aryl, and aralkyl ketones smoothly to the corresponding esters.[14]

Since acetophenone is oxidised to the ester, albeit in low yield, one might expect benzophenone to react also, as the inductive effect should make the diaryl ketone slightly more susceptible to nucleophilic attack. The fact that no reaction is observed is a reflection on the steric hindrance around the carbonyl group caused by the two phenyl groups, preventing the initial attack of the peracid.

It is probable that the mechanism for these oxidations is similar to that accepted for other examples of the Baeyer-Villiger reaction with peracids. Addition of the hexafluoroacetone-hydrogen peroxide



adduct to the ketone gives the complex (I) which, by loss of the anion (II), the conjugate base of hexafluoroacetone hydrate, and concerted migration of the most nucleophilic group (R_2), yields the ester (III). The diol (IV) is a much weaker acid ($pK_a = 6{\cdot}6$)[36] than trifluoroacetic acid (pK_a = 0·3), and also weaker than benzoic acid (pK_a = 4·2) or acetic acid (pK_a = 4·7), so the mechanism is unlikely to involve a protonated intermediate complex.

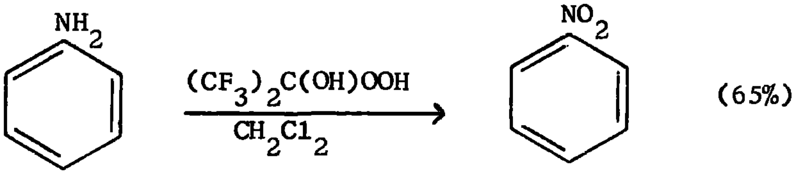
2.5. Oxidation of aromatic amines.

A. Experimental method.

These reactions, unlike those involving ketones,were carried out without reflux. This was in order to minimise side reactions - the reaction mixture darkened rapidly during addition of the oxidising agent even at room temperature. Work up followed the same lines as for ketones, distillation or sublimation finally yielding the oxidation products.

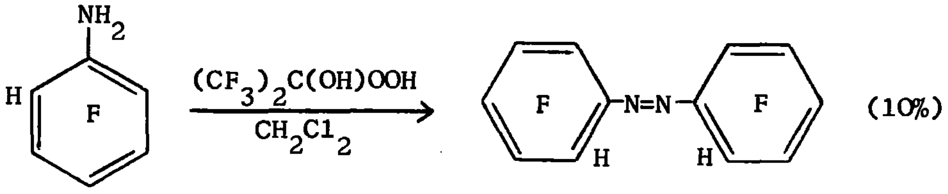
B. Discussion of results.

The oxidation of aniline with hexafluoroacetone-hydrogen peroxide gave nitrobenzene as the only product, apart from intractable



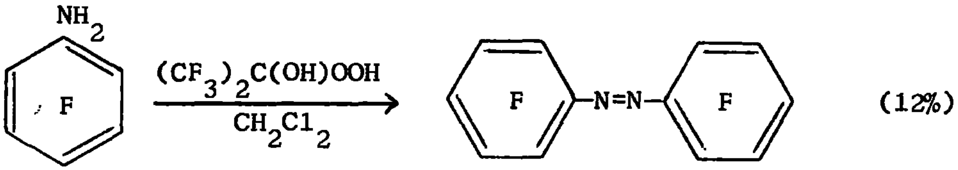
material, in 65% yield. This conversion of an aromatic amine to a nitro compound has been achieved with only a few other reagents - Caro's acid, anhydrous peracetic acid, and trifluoroperacetic acid, the latter being the most effective. While the yield obtained above is lower than with the other organic peracids previously mentioned, it does show that hexafluoroacetone-hydrogen peroxide is a fairly reactive oxidising agent.

Unfortunately, it was not found possible to extend this reaction to the polyfluoroanilines, as the oxidation of 2,3,4,5-tetrafluoroaniline gave a tarry residue which gave nothing on attempted distillation,

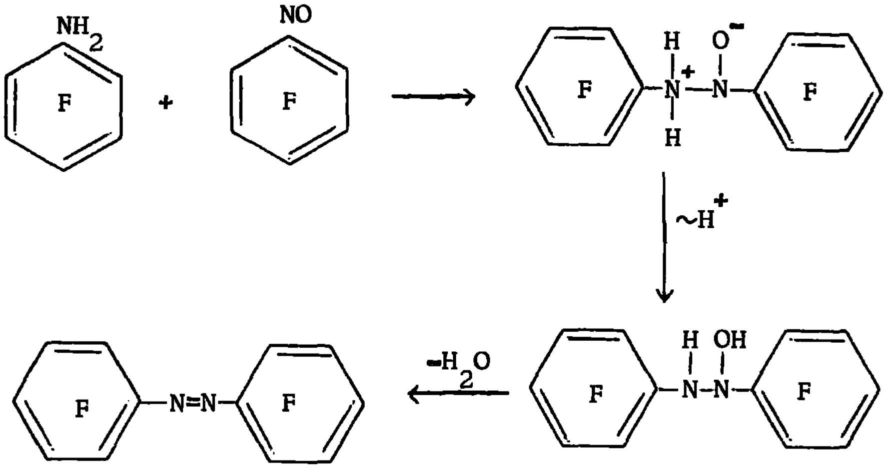


but from which 2,2',3,3',4,4',5,5'-octafluoroazobenzene was sublimed in 10% yield. This compound has been prepared previously in much higher yield by the oxidation of 2,3,4,5-tetrafluoroaniline with bleaching powder.[37]

Suspecting that the poor results might in part be due to the peracid attacking the aromatic proton as well as the amine group, the oxidation was repeated using pentafluoroaniline, but a very similar reaction occurred, giving only a 12% yield of the orange decafluoroazobenzene.

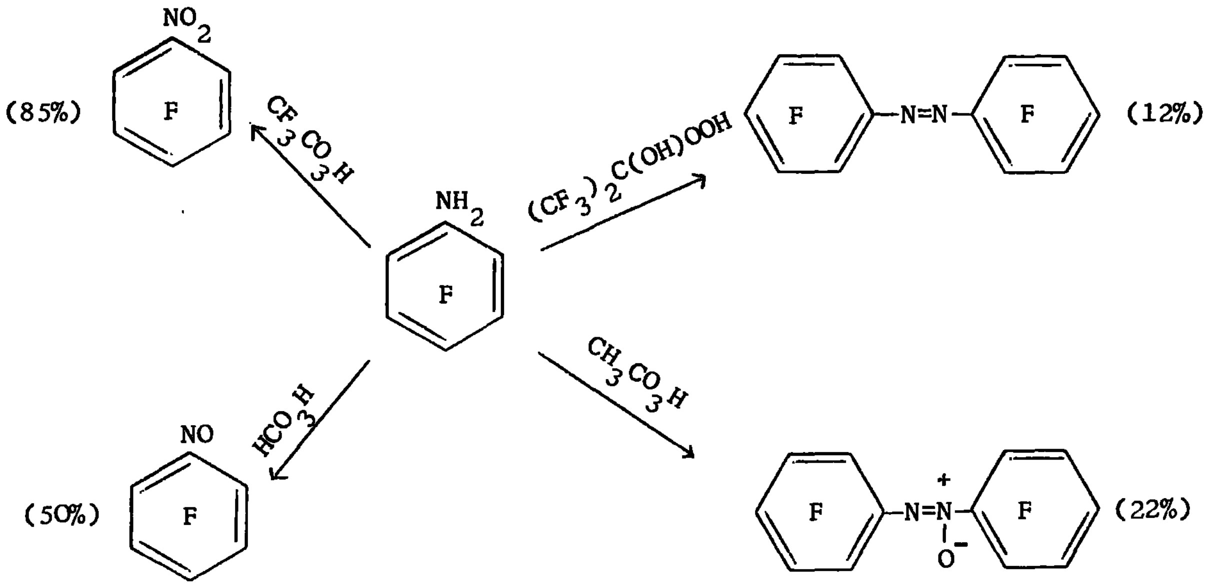


The mechanism for formation of the azobenzene may involve condensation between pentafluoronitrosobenzene, an initial oxidation product, and pentafluoroaniline, although, starting from these compounds



Burdon and co-workers[38] obtained a multi-component mixture, and suggested that nucleophilic displacement of fluorine was also taking place. A similar reaction here would explain the low recovery of tractable material. However, the recent preparation of the octafluoro- and decafluoro-azobenzenes from the appropriate anilines in reasonable yield[37] suggests that another mechanism may possibly be involved.

2,3,4,5-Tetrafluoroaniline and pentafluoroaniline are less basic than aniline itself, and so would be expected to be more resistant to oxidation. Hexafluoroacetone hydrogen-peroxide appears to be less able than other peracids to overcome this decrease in amine reactivity. Thus, trifluoroperacetic acid[27] and performic acid[39] can be used to give useful oxidation products in good yields, and peracetic acid prepared from only 30% hydrogen peroxide, which is much less efficient than that prepared from 90% hydrogen peroxide, gave decafluoroazoxybenzene, although only in low yield.[28] Hexafluoroacetone-hydrogen peroxide on the other hand oxidised pentafluoroaniline only to the azobenzene in low



yield, a reaction which can be carried out more effectively with other reagents.[37]

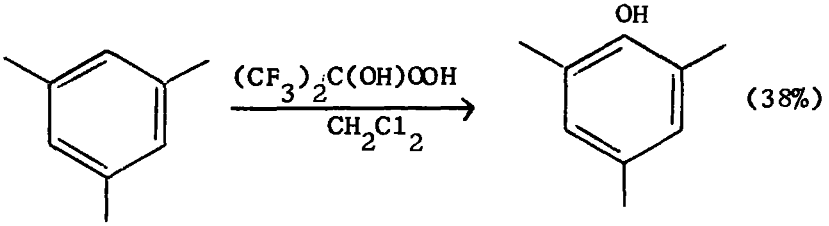
2.6. Oxidation of mesitylene.

A. Experimental method.

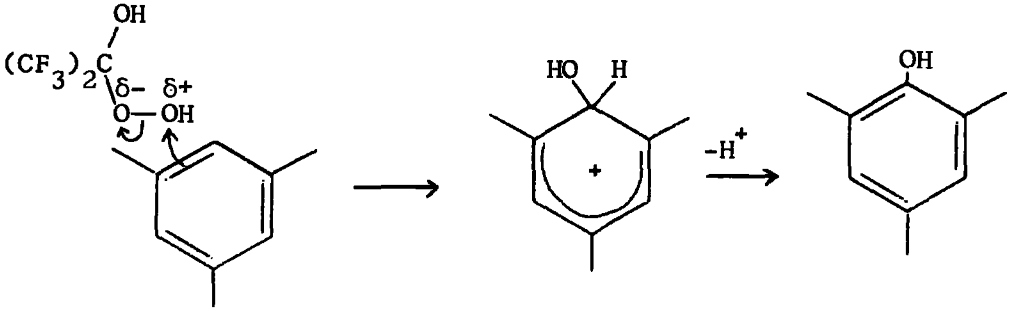
Mesitol, the expected oxidation product from this reaction, is more susceptible to electrophilic attack than mesitylene, and in order to minimise further attack on the phenol, a large excess of arene was used. This is in contrast to previous experiments where an excess of oxidising agent was employed. Further oxidation of the product was also restricted by adding the oxidising agent dropwise to the mesitylene rather than in the reverse order, and by conducting the experiments at or below room temperature.

B. Discussion of results.

The oxidation of mesitylene with hexafluoroacetone-hydrogen peroxide



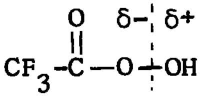
under these conditions gave a 38% yield of mesitol. The mechanism is presumably similar to that accepted for previous examples of electrophilic hydroxylation;



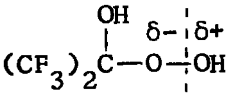
The yield is slightly lower than that obtained with trifluoroperacetic acid alone (45%),[32] but greatly improved results have been reported if boron trifluoride, a Lewis acid, is bubbled through the reaction mixture during addition of the oxidising agent.[32] When this was applied to the hexafluoroacetone-hydrogen peroxide reaction, no mesitol was obtained, the only product, apart from recovered mesitylene, being a mixture of high boiling compounds and polymeric material. Why boron trifluoride should have a different effect on this reaction is by no means clear. Hexafluoroacetone-hydrogen peroxide differs from trifluoroperacetic acid in that it possesses a hydroxyl group instead of a carbonyl and this change from sp^2 to sp^3 hybridisation (i.e. increase in p character) would be expected to encourage co-ordination in the former peracid. On the other hand, the co-ordinated carbonyl oxygen may be better able to partially offset the loss of electrons by further polarisation of the carbon-oxygen π-bond. The recovery of only higher boiling products suggests that the first point may be the more important as boron trifluoride may co-ordinate too effectively, giving rise to rapid further oxidation of any mesitol formed.

2.7. Comparison with other peracids.

Overall, these results indicate that hexafluoroacetone-hydrogen peroxide is less reactive than trifluoroperacetic acid, which gives superior results with all the groups of compounds studied. Although one might expect the polarity of the peroxide bonds in the two peracids to be roughly similar and hence have a similar effect on the electrophilic nature of the attacking oxygen, the difference in reactivity can be rationalised fairly easily. Cleavage of the peroxide bond in trifluoroperacetic acid involves loss of the trifluoroacetate ion which, since it is resonance stabilised, is a much better leaving group than the



$\mathrm{CF_3{-}\overset{O}{\overset{\|}{C}}{-}O}\overset{\delta-\ \delta+}{\vdots}\mathrm{OH}$



$\mathrm{(CF_3)_2\overset{OH}{\overset{|}{C}}{-}O}\overset{\delta-\ \delta+}{\vdots}\mathrm{OH}$

conjugate base of hexafluoropropane-2,2-diol involved in the hexafluoroacetone-hydrogen peroxide oxidations. The former peracid consequently shows the greater reactivity. Also, since the trifluoroacetic acid present with the trifluoroperacetic acid is a much stronger acid than hexafluoroacetone hydrate, which is present with hexafluoroacetone-hydrogen peroxide, reactions involving acid catalysis will again proceed much more readily in the former case.

Comparison with other peracids is more difficult as there is no other peracid whose reactions with all the various substrates have been studied in great detail. Thus peracetic acid shows comparable or greater reactivity with ketones and aromatic amines but little study has been made of its reactions with arenes. The limited work that has been done in this area using peracetic acid and also perbenzoic acid suggests that they are less effective than hexafluoroacetone-hydrogen peroxide. However, while the reactivity of this new peracid is of interest, this survey of reactions indicates that it does not have any particular advantages over reagents already available.

CHAPTER 3

Polyhaloaryl-lithium compounds

3.1. Preparation of polyfluoroaryl-lithiums.

Lithium-halogen and, less frequently, lithium-hydrogen interconversion reactions have been used in organometallic chemistry as convenient routes to aryl-lithium compounds.[40]

$$\mathrm{ArX} + n\text{-}C_4H_9Li \longrightarrow \mathrm{ArLi} + n\text{-}C_4H_9X \quad (X = H,\ Br)$$

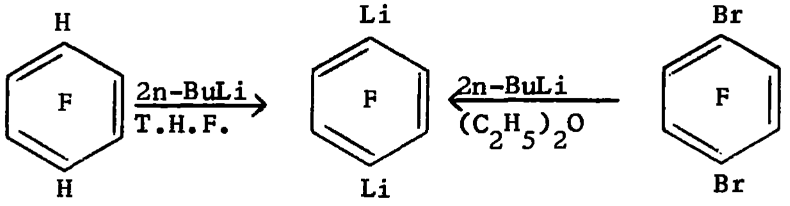
The first application of this method to polyfluoroaryl-lithiums was by Tatlow and co-workers[41] who prepared pentafluorophenyl-lithium by the exchange reaction between bromopentafluorobenzene and butyl-lithium

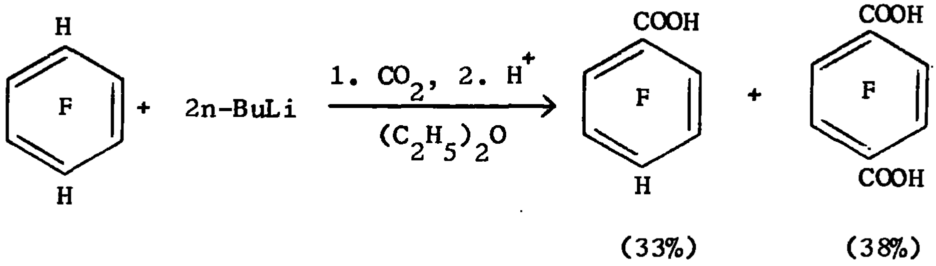
$$C_6F_5Br + n\text{-}C_4H_9Li \xrightarrow[-78^{\circ}C]{} C_6F_5Li + n\text{-}C_4H_9Br$$

in ether solution at -78°C. Tamborski and co-workers[40] later showed that the preparation could also be effected by lithium-hydrogen exchange, and that this lithiation reaction proceeded much more readily in tetrahydrofuran-hexane than in ether-hexane. That lithium-hydrogen exchange is much slower than lithium-bromine[40] was demonstrated by allowing equimolar quantities of butyl-lithium, bromopentafluorobenzene, and pentafluorobenzene to react in tetrahydrofuran. After carbonation and hydrolysis, no bromopentafluorobenzene was detected.

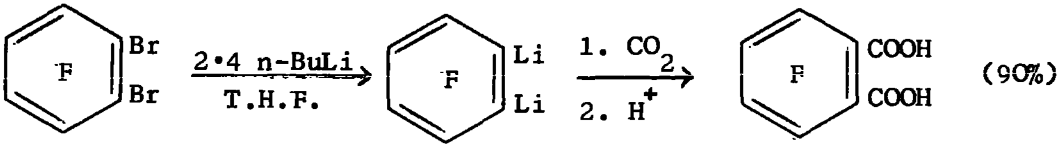
The preparation of mono- and di-lithiotetrafluorobenzenes has received considerable attention, and again choice of solvent is important. Tamborski and Soloski[42] found that for complete di-lithiation of 1,2,4,5-tetrafluorobenzene, tetrahydrofuran was essential as solvent;

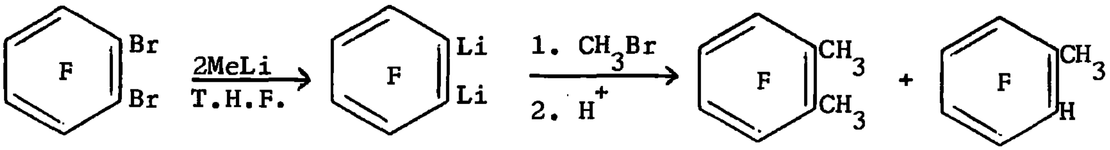
ether giving a mixture of mono- and di-lithiated products. Di-lithiation could be successfully achieved in this solvent however, if 1,4-dibromotetrafluorobenzene was used as starting material,[40] again showing that lithium-bromine exchange occurs more readily than lithium-hydrogen.





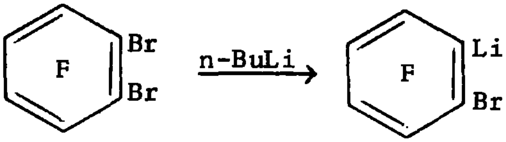
The preparation of tetrafluoro-1,2-dilithiobenzene was found to be much more difficult. Thus the reaction of 1,2,3,4-tetrafluorobenzene with two equivalents of butyl-lithium gave predominantly the mono-lithiated product in ether or tetrahydrofuran,[42] and 1,2-dibromotetrafluorobenzene in tetrahydrofuran only gave full conversion if an excess of butyl-lithium was used.[43] While this latter route was satisfactory for simple reactions such as carbonation, more extensive use was

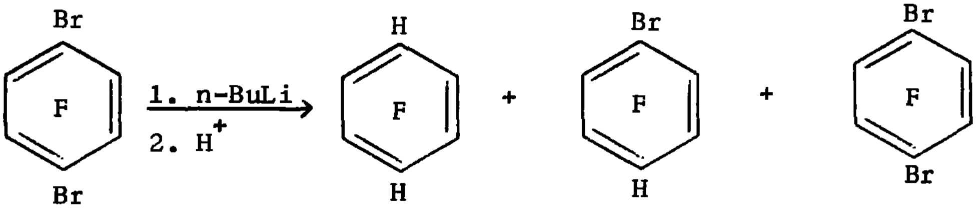




complicated by the excess alkyl-lithium. The use of two equivalents of methyl-lithium did give complete conversion but here the dilithio-compound immediately reacted with the methyl bromide formed to give a mixture of 2,3,4,5-tetrafluorotoluene and 3,4,5,6-tetrafluoro-o-xylene.

The reluctance of 1,2-dibromotetrafluorobenzene to undergo dilithiation is exemplified by the addition of one equivalent of butyl-lithium, which gives the synthetically useful 2-bromotetrafluorophenyl-lithium as the sole product.[44] This is in contrast to the reaction of 1,4-dibromotetrafluorobenzene where, under the same conditions,





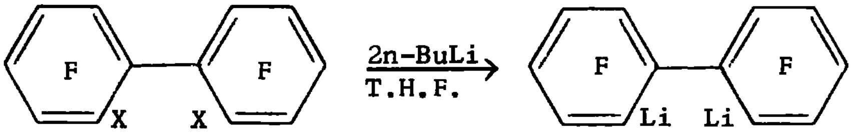
a mixture of products is obtained.

A series of para-substituted tetrafluorophenyl-lithiums have been prepared by lithium-hydrogen interconversion,[45] although where the substituent contains an active hydrogen, an extra equivalent of butyl-

(X = CF_3, CH_3, OH, NH_2, SH, p-HC_6F_4)

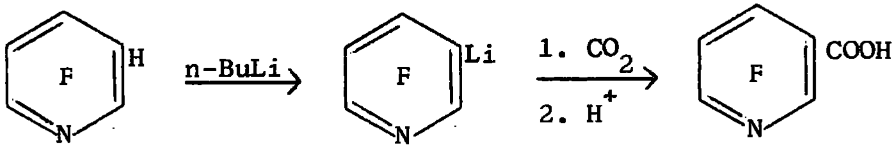
lithium must be employed.

Octafluoro-2,2'-dilithiobiphenyl, a particularly useful compound for further syntheses, has been prepared by both lithium-bromine[44] and lithium-hydrogen exchange.[46]

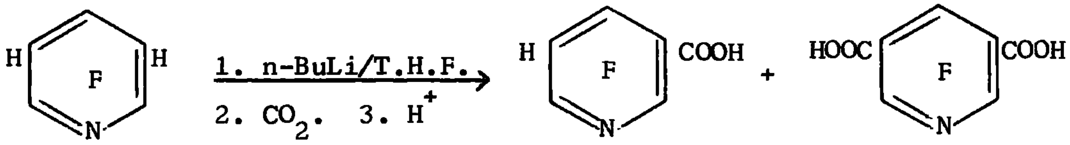


(X = H, Br)

Other polyfluoroaryl-lithiums prepared include tetrafluoro-3-lithio- and tetrafluoro-4-lithio-pyridine[47] which were characterised by carbonation reactions to give tetrafluoronicotinic acid and tetrafluoroisonicotinic acid respectively, e.g.

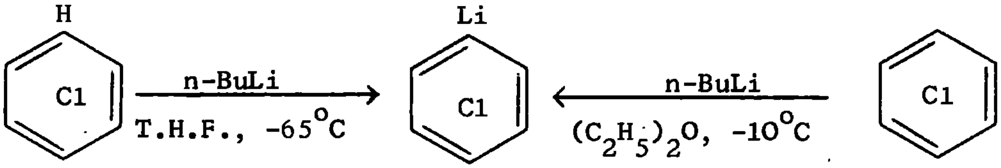


Attempts to dilithiate 2,4,6-trifluoropyridine in hexane were unsuccessful as the monolithiated product was insoluble in the solvent, but using tetrahydrofuran, products resulting from mono- and di-lithiation were obtained on carbonation.



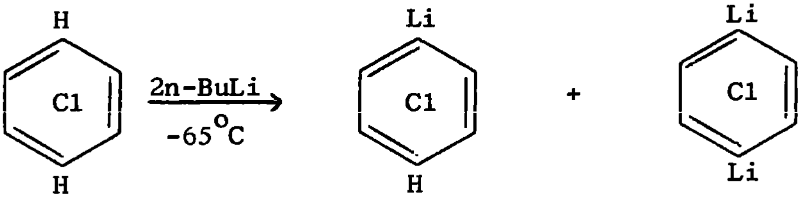
3.2. Preparation of polychloroaryl-lithiums.

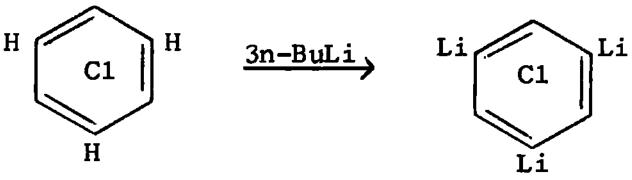
Metallation of highly chlorinated benzenes can be achieved by either halogen-metal or hydrogen-metal exchange. Thus pentachlorophenyl-lithium can be prepared by the reaction of either pentachlorobenzene[48]



or hexachlorobenzene[49] with butyl-lithium. The lithium-chlorine exchange method involves less side reaction, and for this reaction, ether was shown to be a much better solvent than tetrahydrofuran.

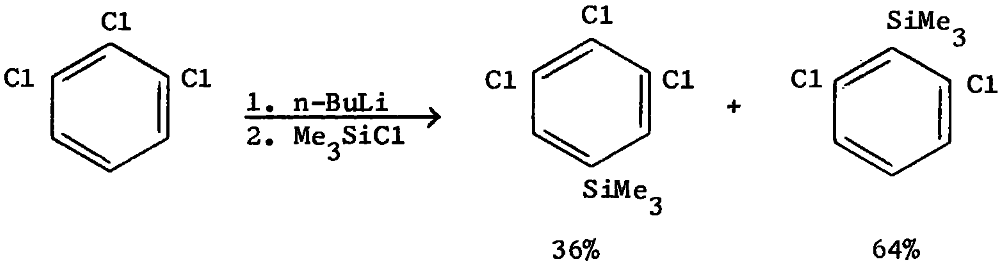
Extension of the study to the tri- and tetra-chlorobenzenes led to interesting results. Of the compounds so far investigated, those possessing a hydrogen atom with two ortho chlorines undergo almost exclusive lithium-hydrogen exchange. Thus, in 1,2,4,5-tetrachloro- and 1,3,5-trichloro-benzene,[50] the hydrogen atoms are progressively

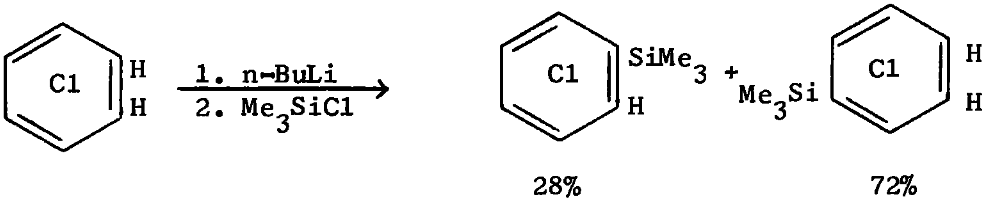




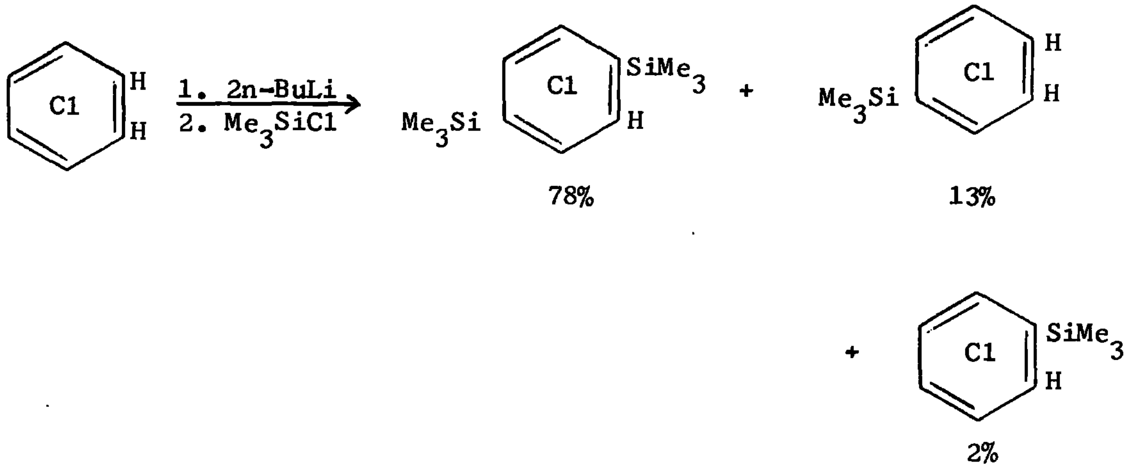
metallated to give the tetrachlorodilithio- and trichlorotrilithiobenzenes respectively.

If the compound does not possess such a hydrogen atom, lithium-halogen exchange will also occur,[51] this time at a position where the chlorine possesses two ortho chlorines. Thus 1,2,3-trichloro- and 1,2,3,4-tetrachloro-benzenes give a mixture of products, as characterised with chlorotrimethylsilane, resulting from both types of exchanges.

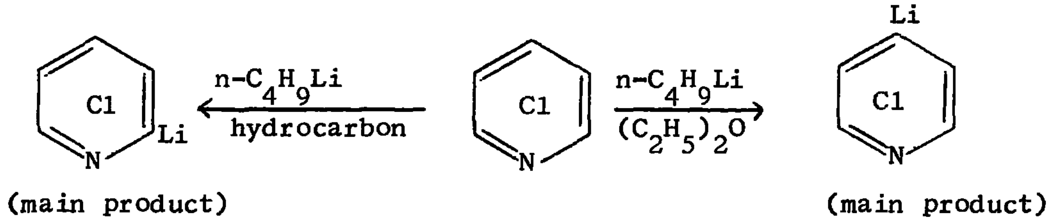




It is noteworthy that when two equivalents of butyl-lithium are reacted with 1,2,3,4-tetrachlorobenzene, the major product characterised with chlorotrimethylsilane is that arising from lithium-chlorine and lithium-hydrogen exchange in the same molecule.[51]

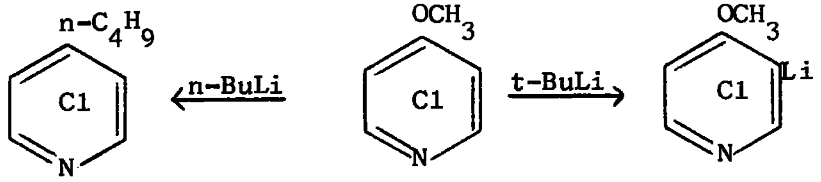


The lithiation of pentachloropyridine was found to give different results depending on the solvent employed.[52] In methylcyclohexane, the major product was 3,4,5,6-tetrachloro-2-pyridyl-lithium, whereas in ether solution, exchange occurred mainly at the 4-position.



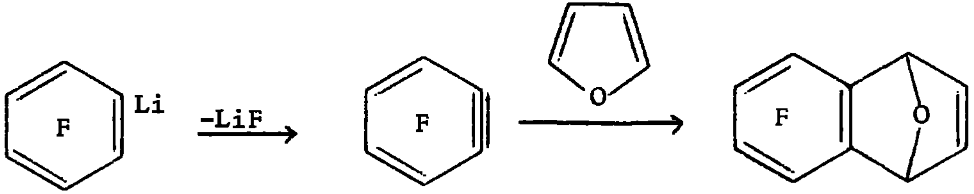
One explanation put forward was that in the hydrocarbon solvent, the pentachloropyridine, a weak base, co-ordinated with the electron deficient butyl-lithium, and thus directed the metallation mainly into the 2-position, whereas in ether solution the nitrogen would be adequately solvated. An additional suggestion was that since butyl-lithium exists as a hexamer in the hydrocarbon rather than the dimer in ether, steric factors may make the less hindered 2-position more favourable.

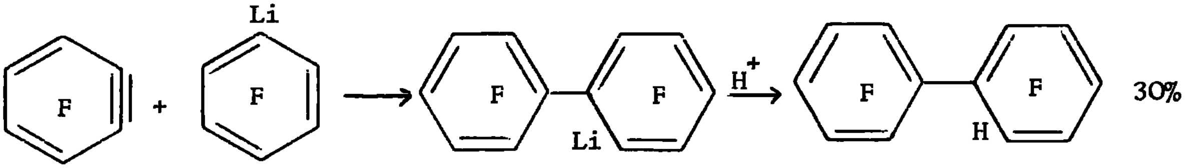
When the lithiation of tetrachloro-4-methoxypyridine was attempted using n-butyl-lithium, substitution took place in the 4-position in preference to lithium-chlorine exchange.[53] However, with the more bulky t-butyl-lithium, metal-halogen interconversion did occur at the 3-position.



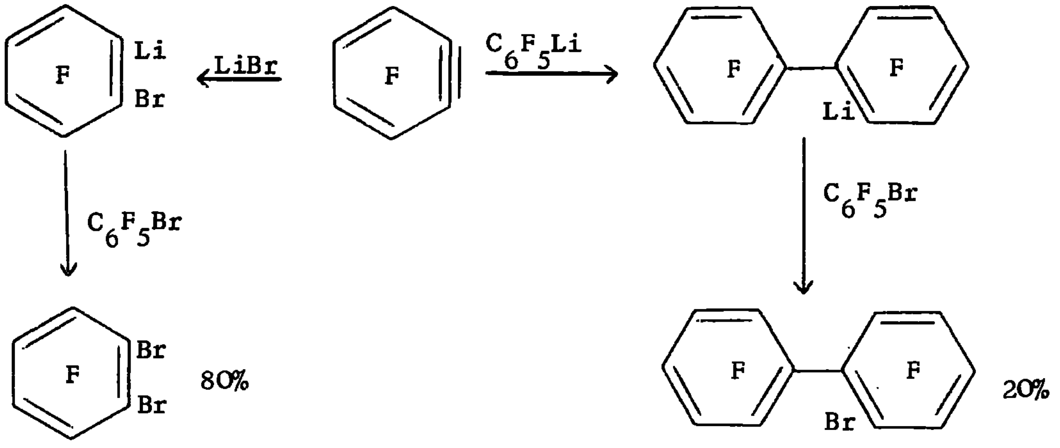
3.3. Polyhalobenzyne formation and reactions.

The ability of o-halogenophenyl-lithiums to eliminate lithium halide to form a benzyne is well known.[41] While polyfluoro- and polychlorophenyl-lithiums are more stable than the mono-o-halogenated compounds with respect to this elimination, benzyne formation still occurs rapidly above 0°C. This was first observed by Tatlow and co-workers[41] who isolated the Diels-Alder adduct from the decomposition of pentafluorophenyl-lithium in the presence of furan. In the absence of a trapping agent, the tetrafluorobenzyne reacts with pentafluorophenyl-lithium to give initially nonafluoro-2-lithiobiphenyl. Although further reaction occurs to give polymeric material, short reaction times give nonafluoro-2-hydrobiphenyl in 30% yield.[54]

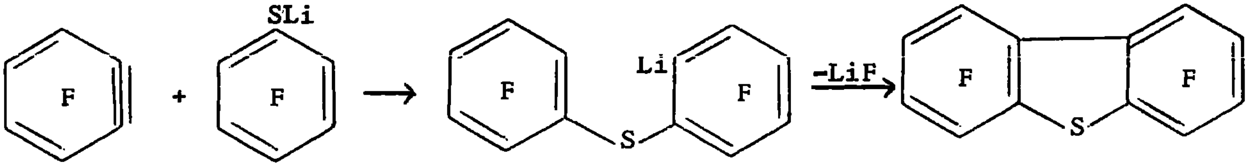




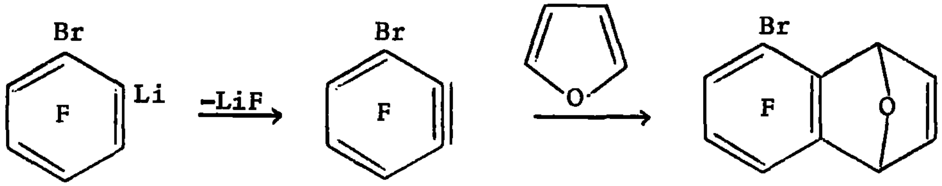
The decomposition of pentafluorophenyl-lithium in the presence of excess bromopentafluorobenzene at 15° has been studied.[55] The reaction products have been explained on the basis of two addition reactions involving tetrafluorobenzyne. Reaction of the benzyne with undecomposed pentafluorophenyl-lithium followed by lithium-bromine exchange gives 2-bromononafluorobiphenyl, while addition of lithium bromide again followed by lithium-bromine exchange yields 1,2-dibromotetrafluorobenzene. This metal-halogen exchange is well known - the addition of bromopentafluorobenzene to 2-lithiononafluorobiphenyl for example gives 2-bromononafluorobiphenyl.[55]



The room temperature reaction of pentafluorophenyl-lithium with lithium pentafluorothiophenate provides an excellent route to the heterocycle, octafluorodibenzothiophen,[56] and is a good example of the synthetic use of tetrafluorobenzyne.

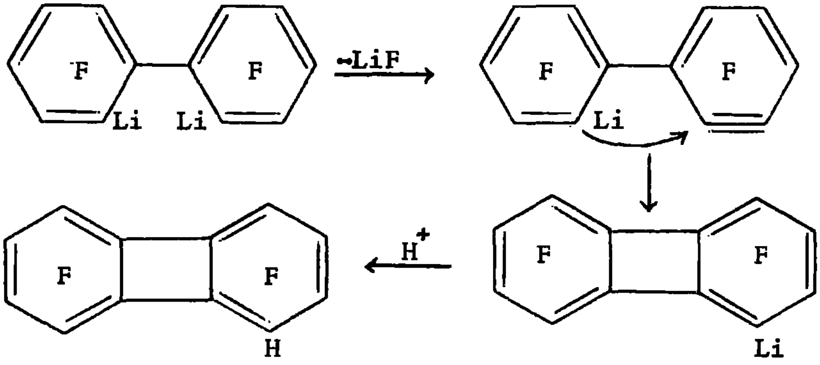


The decomposition of 2-bromotetrafluorophenyl-lithium in furan proceeds via elimination of lithium fluoride, rather than lithium bromide which would be expected in terms of bond strengths.[57] This is attributed to the low solubility of lithium fluoride as compared with lithium bromide



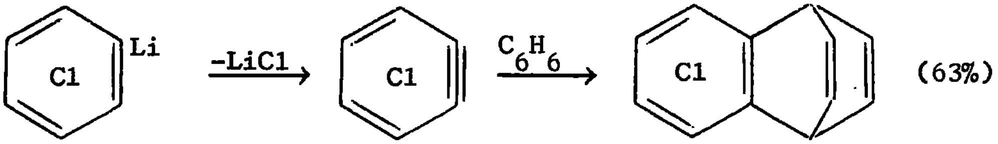
in the solvent used, making the elimination of the bromide reversible, but that of the fluoride irreversible.

Octafluoro-2,2'-dilithiobiphenyl forms benzynes that can be trapped with furan in much the same way as pentafluorophenyl-lithium.[58] In the absence of a trap however, cyclisation occurs to give, after hydrolysis, a 30% yield of heptafluoro-1-hydrobiphenylene.



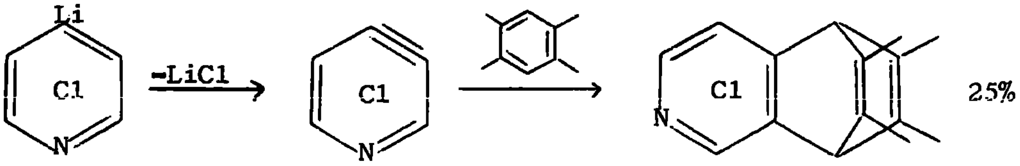
Tetrafluoro-4-lithiopyridine decomposes in the presence of furan to give polymeric material only.[59] Lithium fluoride elimination may well occur, but the reaction of unchanged lithiopyridine with the trifluoropyridyne will produce a bipyridyl system which will be extremely susceptible to further nucleophilic attack.

Benzyne formation from pentachlorophenyl-lithium[60] and two isomeric tetrachloropyridyl-lithiums[61] has been investigated. Heaney and Jablonski found that pentachlorophenyl-lithium was significantly more stable than pentafluorophenyl-lithium[60] - more than half of the pentachloroaryl-lithium was still present after 12 hours in a reaction with benzene at room temperature. Tetrachlorobenzyne formation occurred more rapidly at 50°, and a 63% yield of adduct was isolated.

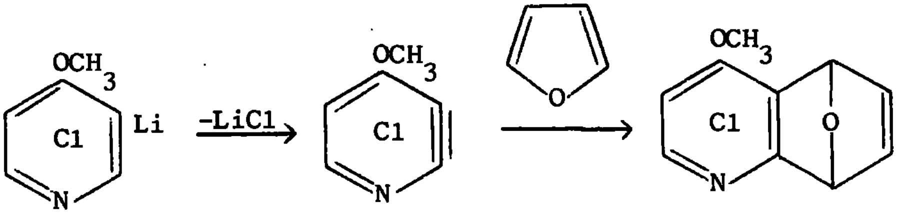


Attempts to obtain an adduct with furan were unsuccessful as metallation of the heterocycle occurred below the temperature required for tetrachlorobenzyne formation. This is further evidence of the increased stability of pentachlorophenyl-lithium, as tetrafluorobenzyne generated from pentafluorophenyl-lithium, can be easily trapped by furan.

Tetrachloro-4-pyridyl-lithium was also found to eliminate lithium chloride only slowly at room temperature,[61] although prolonged heating in a series of aromatic hydrocarbons gave adducts resulting from 1,4-addition of trichloro-3-pyridyne, e.g.

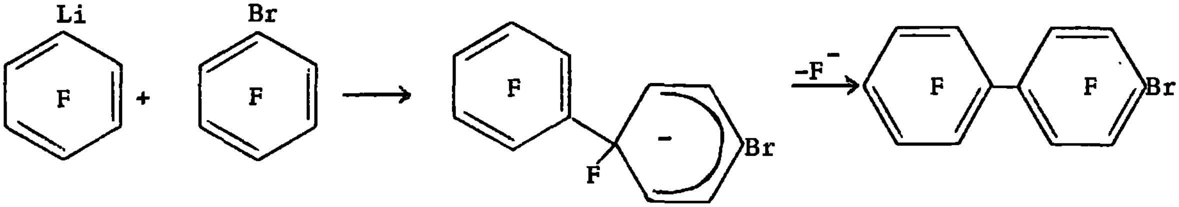


No conclusive evidence for the elimination of lithium chloride from tetrachloro-2-pyridyl-lithium was found, and it was suggested that it may not give a 2-pyridyne since these, once formed, can be trapped as expected, e.g.[53]



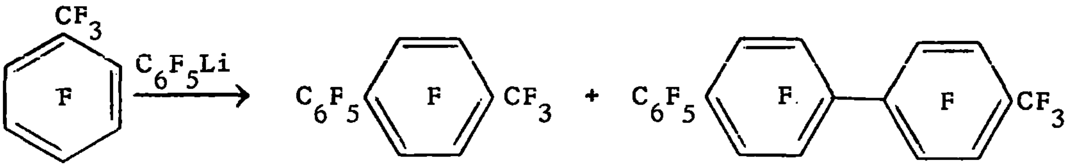
3.4. Nucleophilic reactions of polyfluoroaryl-lithiums.

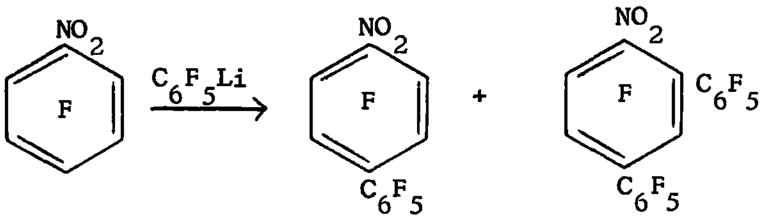
Pentafluorophenyl-lithium can be used successfully as a nucleophile provided the reaction temperature is low enough to prevent benzyne formation. Thus with bromopentafluorobenzene at -40°C, the major product is 4-bromononafluorobiphenyl,[55] in contrast to results obtained via the benzyne route at 15°C (section 3.3). Further attack on the biphenyl can



occur to give considerable amounts of polymeric material.

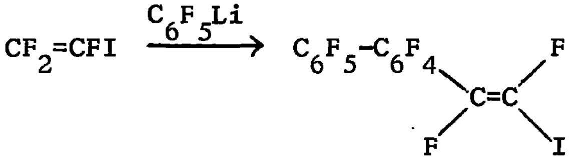
Pentafluorophenyl-lithium also undergoes nucleophilic substitution in octafluorotoluene and pentafluoronitrobenzene.[55]



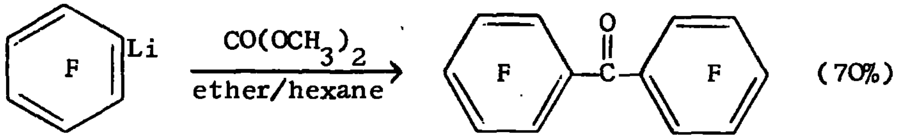


Addition-elimination reactions with olefins have been studied and contrasting products have been obtained with chloro-[55] and iodo-[62] trifluoroethylene. The chloro-olefin on disubstitution with pentafluorophenyl-lithium gives 1,2-bis(pentafluorophenyl)chlorofluoroethylene, but with the iodo compound, although addition of the first molecule of pentafluorophenyl-lithium and lithium fluoride elimination proceed in the same way, the second pentafluorophenyl group attacks the para fluorine in the aromatic ring to yield a substituted biphenyl. Both steric and inductive effects make further attack on the olefin less favourable than in the chloro compound.

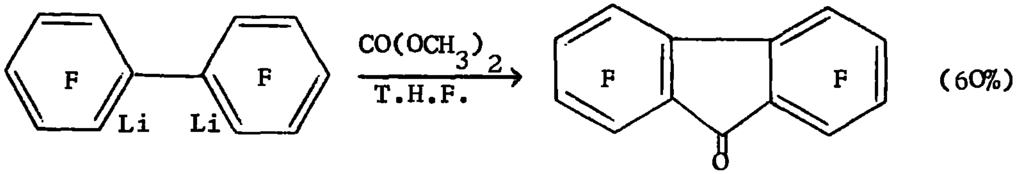
$$CF_2{=}CFCl \xrightarrow{C_6F_5Li} C_6F_5CF{=}CClC_6F_5$$



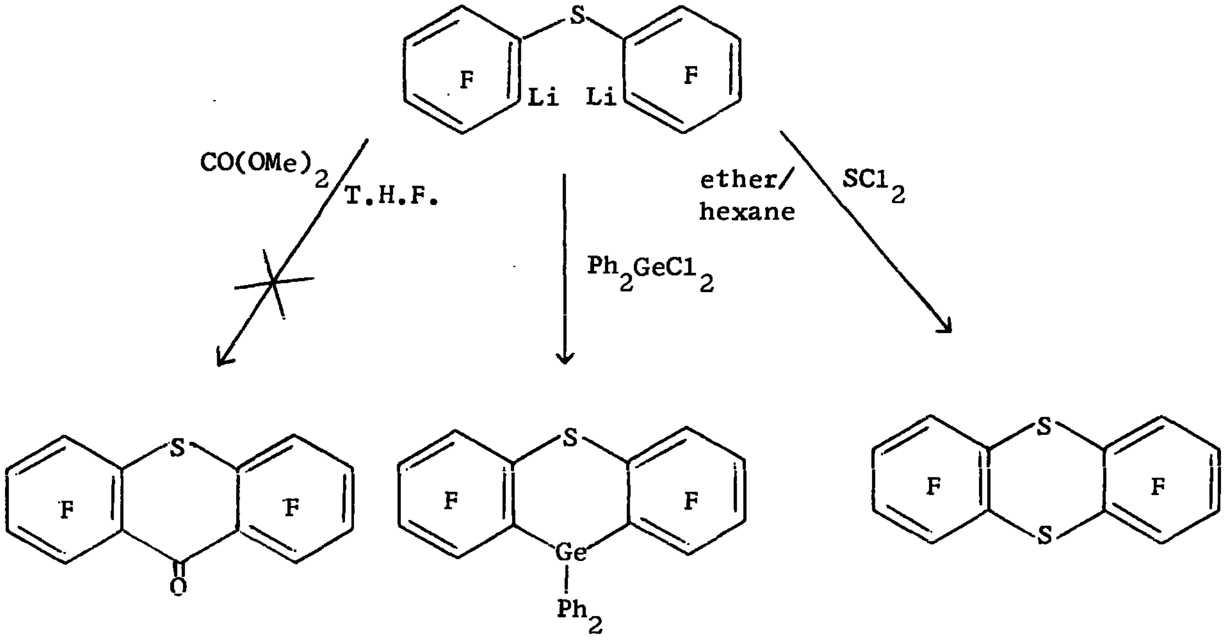
Dimethyl carbonate has been successfully used in the preparation of several fluorinated ketones from polyfluoroaryl-lithiums.[63] With pentafluorophenyl-lithium for example, decafluorobenzophenone is formed in good yield, although precautions must be taken to prevent further reaction to give tris(pentafluorophenyl)methanol. The reaction with



octafluoro-2,2'-dilithiobiphenyl is a good example of the importance of choice of solvent - octafluorofluoren-9-one is formed in only 5% yield in ether/hexane but in tetrahydrofuran the yield is 60%.



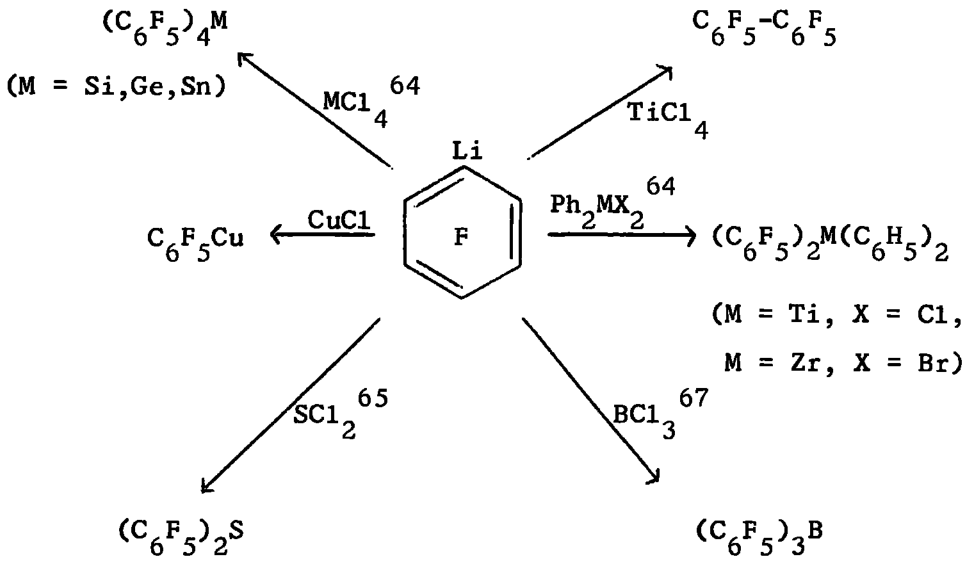
Attempts to prepare octafluorothioxanthone from bis(tetrafluoro-2-lithiophenyl)sulphide by the same method were unsuccessful,[63] although it has been shown that the sulphide does react with sulphur dichloride to yield octafluorothianthren,[65] and with diphenyl germanium dihalide



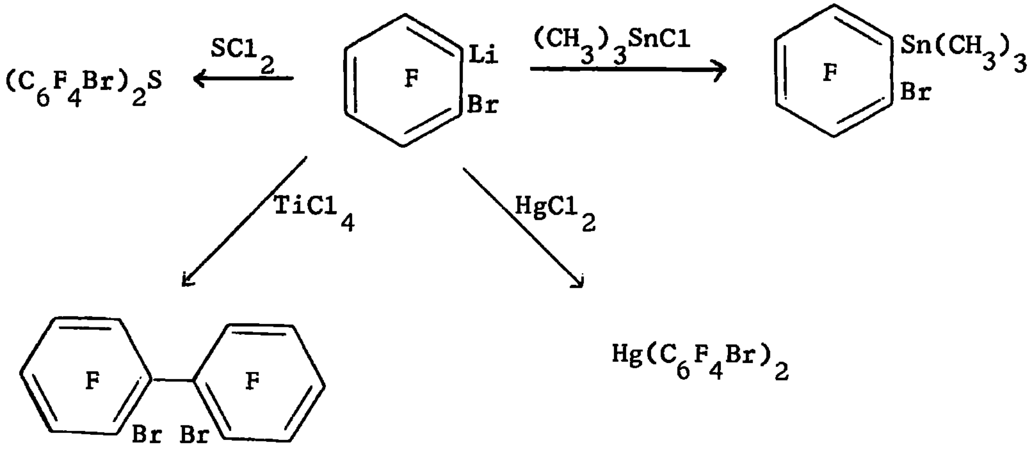
I

to give I.[66]

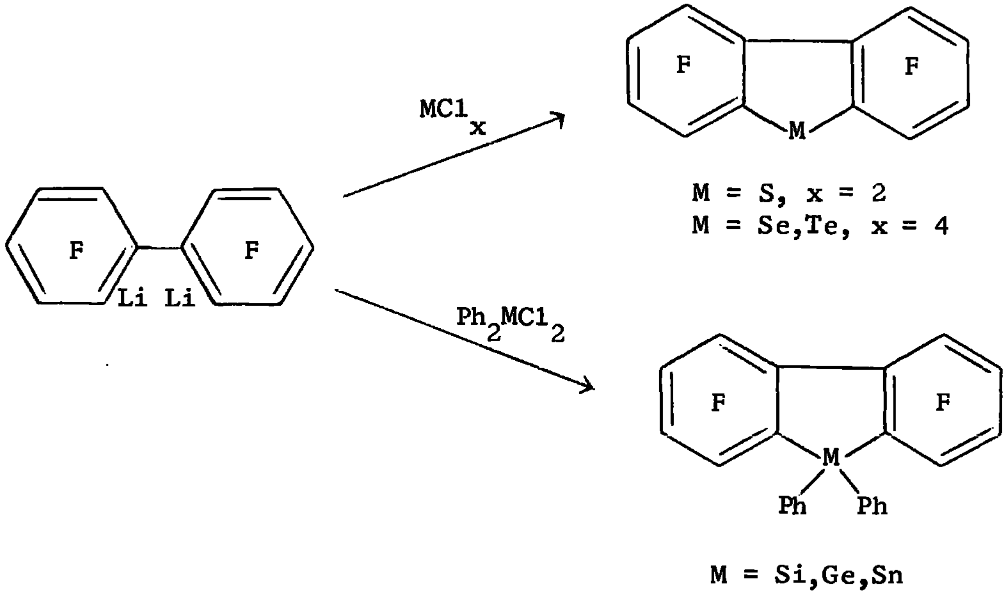
Reactions with metal and non-metal halides have received considerable attention, and a few examples of the reactions of pentafluorophenyl-lithium are shown. Pentafluorophenylcopper is a useful reagent which has been used in the synthesis of octafluorostyrene,[62] polyfluoro-diketones,[68] and polyhaloacetylenes.[69] Of particular interest is the reaction of pentafluorophenyl-lithium with excess titanium tetra-chloride[44,70] to give decafluorobiphenyl in good yield (> 80%). It is believed to involve the intermediate $(C_6F_5)_2TiCl_2$ which decomposes on standing at room temperature to the biaryl and $TiCl_2$.



2-Bromotetrafluorophenyl-lithium also undergoes several reactions involving displacement of halide, e.g.[65]

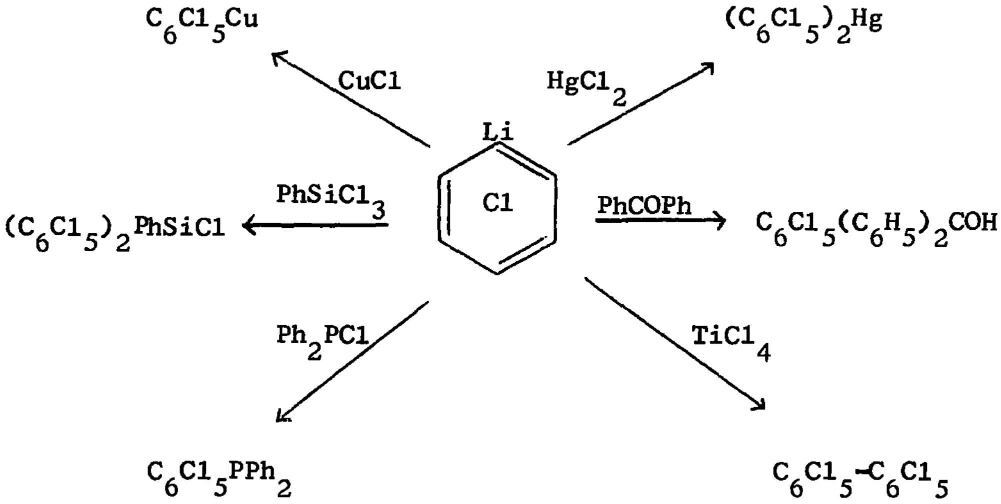


2,2'-Dibromo-octafluorobiphenyl is formed in 92% yield by the titanium tetrachloride coupling reaction, and dilithiation gives octafluoro-2,2'-dilithiobiphenyl, which has been used in routes to fluorinated dibenzo heterocyclic compounds, e.g.[44,71]



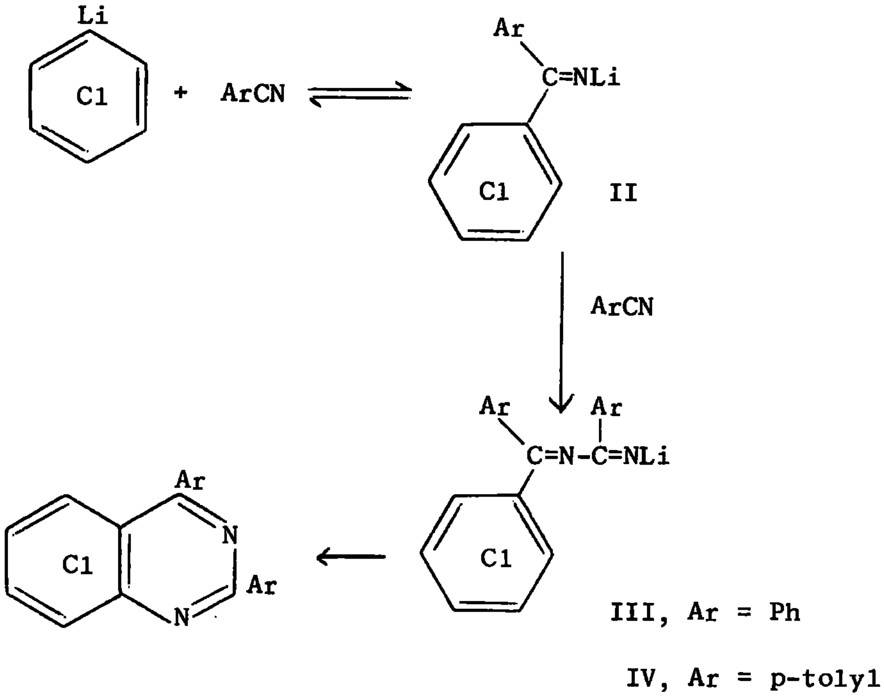
3.5. Nucleophilic reactions of polychloro-aryl lithiums.

Reactions of polychloroaryl-lithiums have been less widely studied although pentachlorophenyl-lithium has been found to undergo several of the reactions of pentafluorophenyl-lithium. Thus it reacts with titanium tetrachloride to give decachlorobiphenyl,[72] although only in low yield, and with cuprous chloride to form pentachlorophenylcopper.[69]



Its reactions with benzophenone, diphenylchlorophosphine, and mercuric chloride have also been investigated,[49] while Gilman has prepared a series of pentachlorophenyl-substituted silicon compounds,[73] and discussed the steric effects involved in their preparation and reactions.

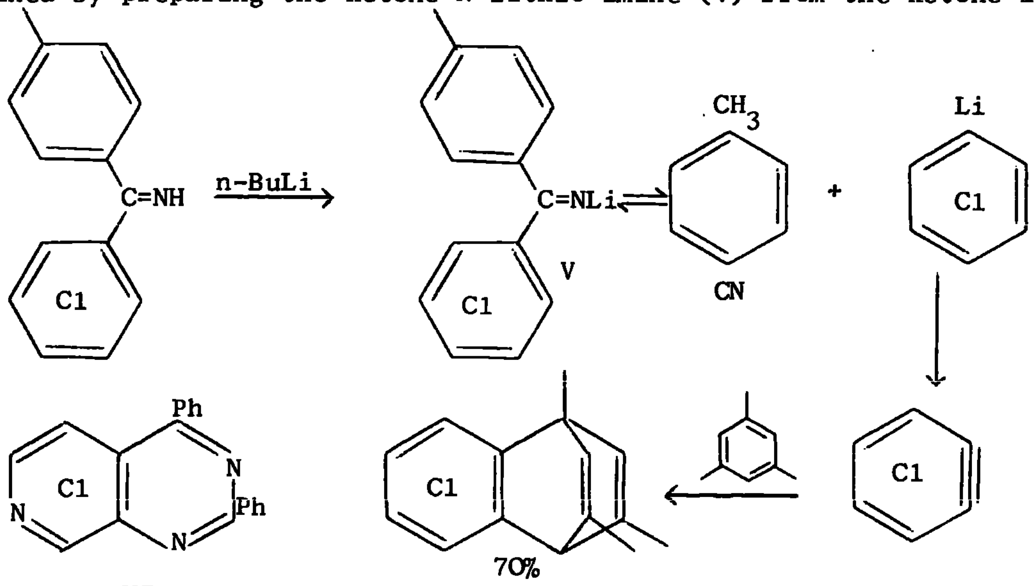
Cook and Wakefield have studied the reactions between pentachlorophenyl-lithium and benzonitrile[74] and found that addition of the aryl-lithium proceeds reversibly. Reaction with two molecular proportions of benzonitrile occurs as shown to give 5,6,7,8-tetrachloro-2,4-diphenylquinazoline(III) in 43% yield. When one equivalent of benzonitrile was added to give the N-lithio imine (II, Ar = Ph), then followed by one equivalent of p-tolunitrile, the products obtained included 5,6,7,8-tetrachloro-2,4-di-p-tolylquinazoline (IV). This suggested that the addition of pentachlorophenyl-lithium was reversible and confirmation was obtained by preparing the ketone N-lithio imine (V) from the ketone imine



II

III, Ar = Ph

IV, Ar = p-tolyl



V

VI

and heating it in the presence of mesitylene, when the tetrachlorobenzyne adduct was isolated in 70% yield together with p-tolunitrile.

Tetrachloro-4-pyridyl-lithium also reacts with benzonitrile to give the cyclised product 5,6,8-trichloro-2,4-diphenyl-1,3,7-triazanaphthalene (VI) but in much lower yield.[75]

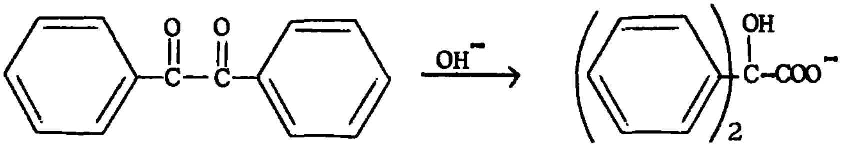
CHAPTER 4

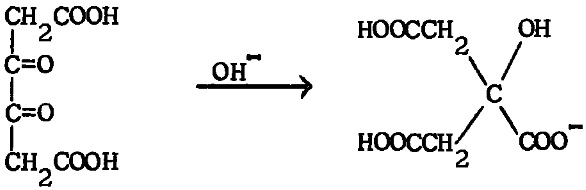
The benzilic acid and related rearrangements

4.1. The benzil-benzilic acid rearrangement.

A. Introduction.

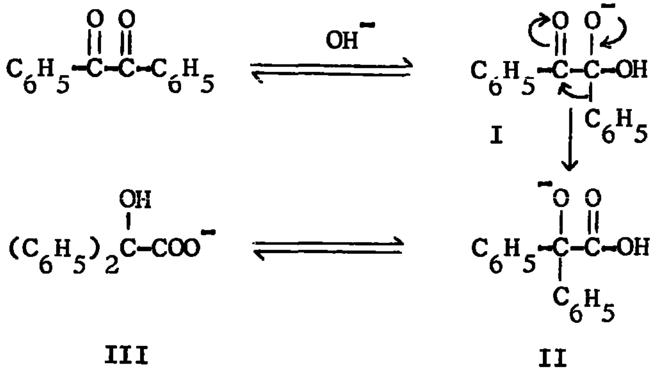
The benzilic acid rearrangement was discovered in 1838 by von Liebig.[76] It has since been the subject of extensive synthetic and kinetic study, and has been shown to be one of a group of base-induced molecular rearrangements. Examples of the rearrangement, which involves the transformation of an α-diketone into the salt of an α-hydroxy acid in the presence of base, are found in both aromatic and aliphatic systems,[77] e.g.





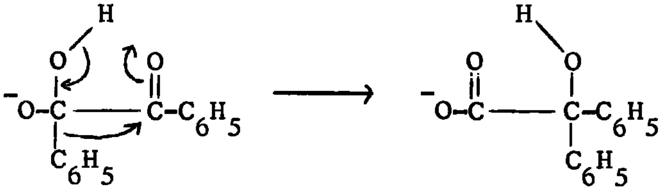
B. Mechanism of the rearrangement.

The currently accepted mechanism was first proposed by Ingold in 1928.[78] It involves initial reversible addition of hydroxide ion to the



carbonyl of the α-diketone, followed by a rate-determining intramolecular rearrangement to the intermediate II, which undergoes proton transfer to give the benzilate anion III. Support for the initial addition step comes from work[79] which showed that in pyridine solution, potassium hydroxide and benzil form a 1:1 adduct which on heating rearranges to give potassium benzilate. Evidence for the reversibility of the reaction was obtained by Roberts and Urey[80] who found that in O^{18}-enriched water, the carbonyl oxygens underwent base-catalysed exchange at a much faster rate than rearrangement occurred.

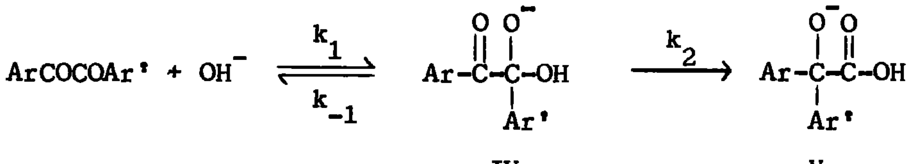
It was suggested that the intermediate I might rearrange to the benzilate anion by a concerted process[81,82] and not via the intermediate II.



This mechanism could only occur with specific hydroxide ion catalysis and the later discovery that the rearrangement could be effected with certain alkoxide ions[83] suggested Ingold's original mechanism to be the correct one. Also Hine and Haworth[84] found the rearrangement of benzil to sodium benzilate was ~85% faster in D_2O/dioxan than in H_2O/dioxan, contrary to what would be expected if the proton transfer was part of the rate-determining step. They attributed this difference in rate to the greater basicity of deuteroxide ion in heavy water than of hydroxide ion in ordinary water.

C. The nature of the transition state in the rate-determining step.

The rate-determining step of the benzilic acid rearrangement is accepted as involving the transformation of the anion IV into V by



$$\mathrm{ArCOCOAr' + OH^-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{Ar{-}\overset{\overset{O}{\|}}{C}{-}\underset{\underset{Ar'}{|}}{\overset{\overset{O^-}{|}}{C}}{-}OH} \xrightarrow{k_2} \mathrm{Ar{-}\underset{\underset{Ar'}{|}}{\overset{\overset{O^-}{|}}{C}}{-}\overset{\overset{O}{\|}}{C}{-}OH}$$

IV V

migration of Ar'. The rate of reaction can be written as,[77]

$$v = k_2 [IV]$$

and since it has been shown that the reversible addition reaction occurs much more rapidly than rearrangement to V,[80] as an approximation one can write

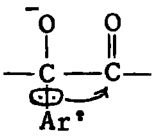
$$K = \frac{k_1}{k_{-1}} = \frac{[IV]}{[\mathrm{ArCOCOAr'}][\mathrm{OH^-}]} ,$$

thus $$v = k_2 K[\mathrm{ArCOCOAr'}][\mathrm{OH^-}] .$$

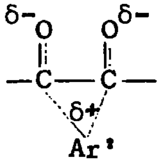
From this equation and the mechanism presented, there are several factors which might be expected to affect the rate of rearrangement:-

a) Substituents in the benzil system which hinder base attack at the carbonyl by electron donation or steric effects might lower K, the equilibrium constant, and hence lower the overall rate. Conversely, electron-withdrawing groups might be expected to increase the rate.

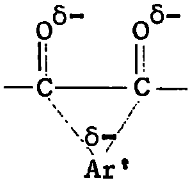
b) The rearrangement involves migration of a group with its pair of electrons (VI), and this could take place in several ways depending on the bonding in the transition state. Thus if attack occurs at the carbonyl group such that bond formation preceeds bond cleavage (VII),



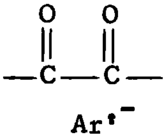
VI



VII



VIII



IX

electron-donating groups might increase k_2. Conversely, electron-withdrawing substituents might increase k_2 in a looser transition state such as VIII or even IX where ion pairs are involved.

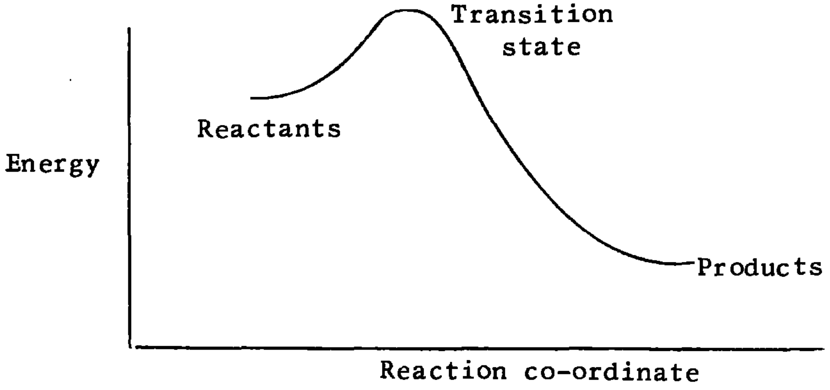
c) Substituents which would make the migrating terminus more susceptible to nucleophilic attack might also be expected to increase the rate of rearrangement.

In order to decide on the importance of each of these effects and to correlate them with experimental results on the rearrangement of some substituted benzils, it is essential to have some knowledge of the nature of the transition state in this rate-determining step.

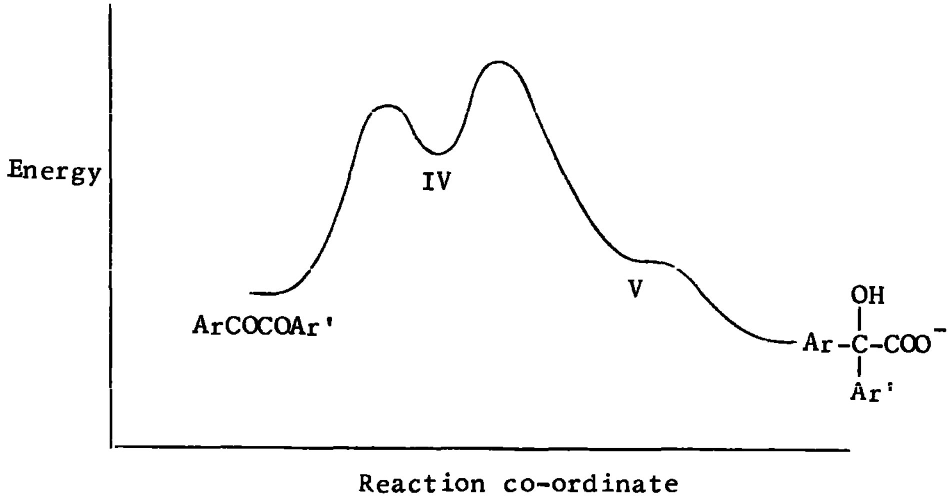
In a study of the correlation between the rates and free energies of chemical reactions, Hammond put forward the following postulate as an aid in estimating the structure of the transition states for the reactions:[85]

> "If two states, as for example, a transition state and an unstable intermediate occur consecutively during a reaction process and have nearly the same energy content, their interconversion will involve only a small reorganization of the molecular structures."

Thus in a fast highly exothermic reaction the activation energy will be small compared to the energy difference between the reactants and products, and the transition state should therefore closely resemble the reactants. If for example, the rate-determining step involves breaking a bond which is nearly covalent in the reactants, it will be only slightly altered in going to the transition state.

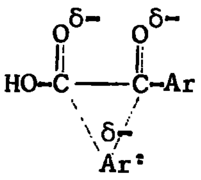


Hammond applied the postulate to the benzilic acid rearrangement of an unsymmetrical α-diketone.[85] He considered the adduct IV to be an unstable intermediate, and therefore suggested that the structure of the transition state would be closely related to it. On this basis, factors



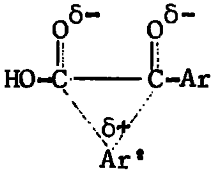
which lowered the energy of the intermediate IV would also lower the energy of the transition state.

While this application does suggest a transition state which has been used to successfully explain the experimental data covering the rates of rearrangement of substituted benzils and the migratory aptitudes of the substituted groups, it gives little information on how migration takes place; whether for instance, the migrating species is electron-rich or -deficient. Two of Hammond's conditions for the best application of the postulate were that the reaction should be fast and highly exothermic, neither of which is fully satisfied in this example. This implies that, while the transition state may well be nearer IV than V in molecular structure, it need not necessarily be very closely related to IV. It is thus possible that considerable bond breaking may have taken place to give a transition state such as X. The migrating group will carry some of the negative charge provided bond breaking has proceeded more than bond making. A transition state like this will also satisfy the Hammond postulate in a general sense in that it will resemble reactants more than products provided the new bond is formed to a lesser extent than the bond being broken.



X

Alternatively, a transition state could be envisaged where bond making has gone further than bond breaking (XI). In this case, the migrating group will be electron deficient, and would thus be stabilised by electron-donating substituents (e.g. CH_3, p-OCH_3), the opposite to the previously mentioned transition state. This too could satisfy the Hammond postulate provided the bond being broken is still stronger than the bond being formed.

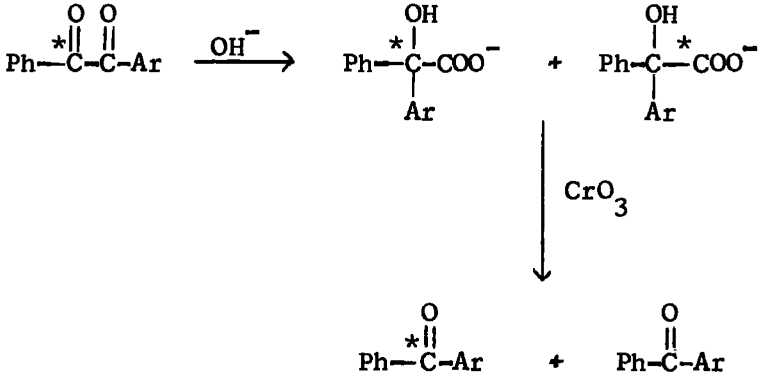


XI

D. <u>Experimental evidence.</u>

Considerable study has been made of both the rates of rearrangement of benzils and the migratory aptitudes of the substituted groups.[77] It has been found that for symmetrically substituted benzils, electron-donating substituents such as p-methoxy, p-amino, and methyl slow down the rate of rearrangement relative to benzil, while electron-withdrawing groups in the meta- and para-positions such as chlorine increase the rate. Steric effects are observed with ortho-substituted benzils - thus 2,2'-dichlorobenzil rearranges more slowly than its meta- or para-disubstituted isomers, the overall order being meta > para > ortho rather than ortho > meta > para which would be expected in terms of the inductive effect alone. Similarly 2,2'-dimethylbenzil rearranges considerably more slowly than the 3,3'- and 4,4'-dimethylbenzils.

Similar steric and electronic effects are also observed in the rearrangement of unsymmetrical benzils. Obviously, the same product will be obtained whichever group migrates, and to determine the migratory aptitudes of each group, isotopic labelling with C^{14} must be used.[86] Measurement of the remaining activity after oxidation of the products to the substituted benzophenones enabled the percentage migration of the substituted phenyl groups to be determined. The results in Table III[82,86-88] show that, apart from the ortho-substituted compounds where steric effects



<u>Table III</u>

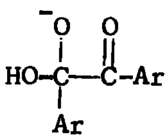
<u>Migration in the system ArCOCOPh</u>

Ar	% migration of Ar
p-Tolyl	38·8
o-Tolyl	2·7
o-Chlorophenyl	31·2
m-Chlorophenyl	81·2
p-Chlorophenyl	67·2
p-Methoxyphenyl	31·8
Benzoyl	100
3-Pyridyl	76·6

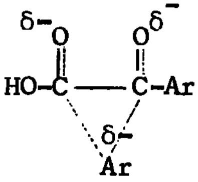
are also involved, the less nucleophilic group has migrated to the greater extent.

E. Interpretation of results.

The transition state for the rate-determining step as suggested by Hammond[85] and used by other workers[86] can be taken as being closely related to the intermediate XII. Thus electron-withdrawing substituents in symmetrical benzils will stabilise the anion and hence lower the energy of the transition state, resulting in the observed increased rate of rearrangement. Bulky groups in the ortho positions will lower the concentration of XII by hindering base attack at the carbonyl group in the initial reversible addition step, and thus lead to a slower rate of rearrangement than might be expected in terms of electronic effects alone. The experimental results also support a transition state such as XIII where substituents able to aid stabilisation of the partial negative charge on the migrating group, will lead to increased rates of rearrangement.

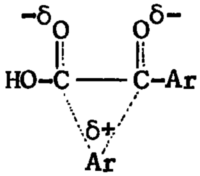


XII



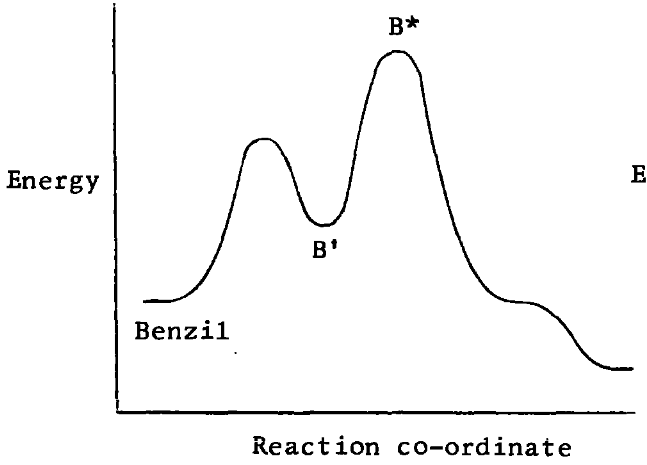
XIII

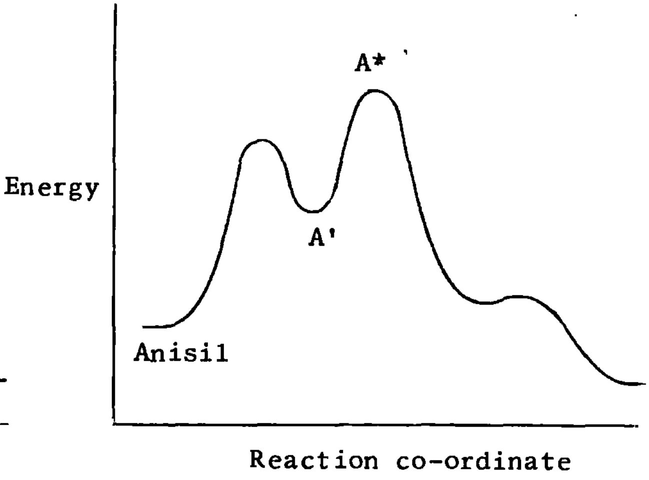
However a transition state such as XIV cannot be ruled out even though the migrating group carries a partial positive charge, since the overall rate of reaction has been shown to be a function of both the specific rate constant (k_2) for the rate-determing step and the equilibrium constant (K)



XIV

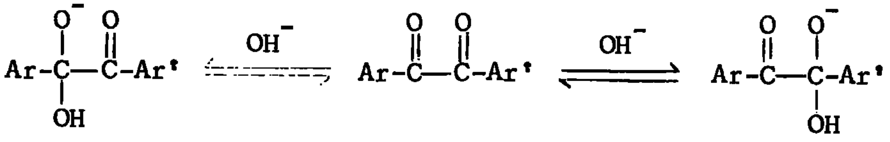
for the formation of the intermediate ion. Thus electron-donating substituents (e.g. p-methoxy) may, in fact, increase the rate of migration but result in a slower overall reaction by lowering K, as the intermediate XII will be destabilised by the substituents. This can be demonstrated by comparing the following possible energy diagrams for the rearrangement of benzil and anisil;





It can be seen that the transition state energy for anisil, A*, is lower than for benzil (B*), but that the concentration of the intermediate, B', will be greater than for A'. The combined effect may then be a slower rate of rearrangement for anisil.

In the case of unsymmetrically substituted benzils it was found that, with the exception of ortho-substituted compounds, the more electron-withdrawing group migrated to the greater extent. These results can be explained quite easily, bearing in mind the dependence of the rate of reaction on both K and k_2. For an unsymmetrical α-diketone, nucleophilic attack will occur at the more electron-deficient carbonyl carbon atom to give an intermediate which will be stabilised by electron-withdrawing substituents. Thus if Ar' is more electron-withdrawing than Ar,



XV XVI

the concentration of XVI will be greater than that of XV. If the rearrangement involves migration of a group carrying a partial negative charge (X) then obviously XVI will rearrange faster than XV and Ar' will migrate to the greater extent. If however, the migrating group in the transition state carries a partial positive charge, as in XI, and XV rearranges faster than XVI, a greater proportion of the product may still result from Ar' migration, because of the greater concentration of XVI.

Application of the Hammond postulate suggests that as XVI is a close approximation to the transition state and of lower energy than XV, then Ar', the more electron-withdrawing group, should migrate to the greater extent.

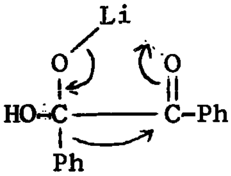
Thus all three representations of the transition state could be used to explain the experimental results. However of these three possibilities, the most likely representation is probably XIII where the migrating species carries some negative charge. The possibility of the group migrating with a partial positive charge, i.e. where bond formation has proceeded more than bond breaking, is less likely as charge separation is involved and this production of positive charge in a system which, overall, is electron rich might be expected to result in a higher transition state energy than one not involving charge separation.

A Hammond reaction constant, ρ, has been obtained from a plot of migration ratios of meta- and para-substituted benzils against the σ values of the respective substituents.[77] The value, 1·43, confirms the influence of electron-withdrawing groups on the overall reaction rate, but unfortunately does not give any information on the charge developed on the migrating group. It is thus not possible to rule out a positively charged migrating group - only to suggest that it is less likely.

The other suggestion, that the transition state is closely related to the intermediate XII, may also be considered less likely than XIII on the grounds discussed earlier in section 4.1.C.; namely, that the benzilic acid rearrangement does not closely follow the conditions of the Hammond postulate. The successful use of XII to explain the experimental results may account for the lack of attempts to create a more accurate representation of the transition state. In this rearrangement, all that can be deduced from the Hammond postulate is that the transition state resembles reactants more than products. It thus seems reasonable that a better representation of the transition state may be XIII, where bond breaking has gone further than bond making, and, if the Hammond postulate is to be satisfied, where the bond being formed is weaker than the bond being broken. This is probably a more accurate representation of the charge distribution in the transition state, although it should be stressed that other structures cannot be ruled out.

F. Effect of the cation.

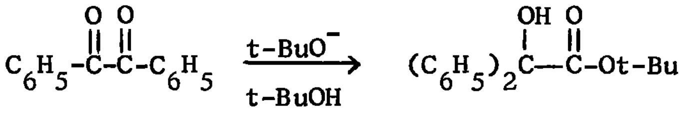
Another factor which has been found to affect the rate of reaction is the nature of the cation involved. In a study of the effect of alkali cations, Puterbaugh and Gaugh[89] found that in 2:1 dioxan-water, lithium hydroxide brought about rearrangement of benzil between three and four times faster than the other alkali hydroxides. This is attributed to the greater effectiveness with which the metal cation co-ordinates with the intermediate during the migration step, possibly in a ring mechanism as shown:



Pfeil[90] noticed that in 50% aqueous dioxan, barium hydroxide brought about rearrangement of 2,2'-dichlorobenzil fifteen times more rapidly, and thallium hydroxide seventy-five times more rapidly, than sodium hydroxide. He also found that the reaction with thallium hydroxide was of the third order, and presumably, in these examples the rearrangement must involve a different mechanism.

4.2. The benzilic ester rearrangement.

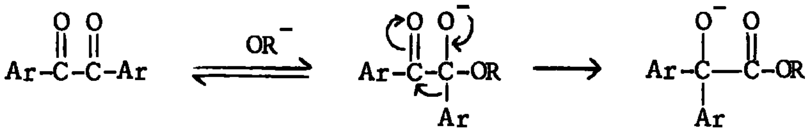
Several groups of workers tried unsuccessfully to bring about the rearrangement of benzil with alkoxides. Reaction with either sodium methoxide or sodium ethoxide[77] gave adducts, but on decomposition with water no benzilate esters were isolated, and it was not until 1956 that Doering and Urban[83] showed that the reaction of benzil with potassium t-butoxide in t-butanol gave t-butyl benzilate. Reaction also occurred with sodium methoxide in methanol to give a slightly lower yield of ester,



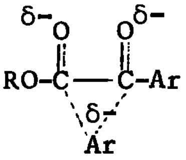
$$C_6H_5\text{-}\overset{\overset{O}{\|}}{C}\text{-}\overset{\overset{O}{\|}}{C}\text{-}C_6H_5 \xrightarrow[t\text{-}BuOH]{t\text{-}BuO^-} (C_6H_5)_2\overset{\overset{OH}{|}}{C}\text{—}\overset{\overset{O}{\|}}{C}\text{-}Ot\text{-}Bu$$

but attempts to bring about the rearrangement with ethoxide or isopropoxide ion were complicated by reduction of the benzil to benzoin by hydride ion transfer from the alkoxide. The rearrangement also failed with phenoxide and substituted phenoxide ion,[91] presumably because the phenoxides were too weak as nucleophiles to attack the carbonyl group.

Doering and Urban found that the reaction was second order,[83] first order each in benzil and alkoxide ion, and put forward a mechanism which is basically the same as for the benzilic acid rearrangement, i.e. initial reversible alkoxide ion attack at the carbonyl group followed by a rate determining migration step.

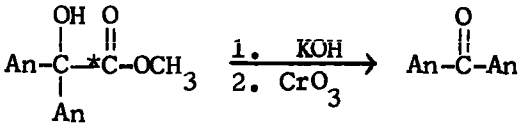


As the mechanisms are very similar, much of the discussion of transition states, rates of rearrangement, and migratory aptitudes in the benzilic acid rearrangement should apply equally well to the benzilic ester rearrangement. Thus a similar transition state can be envisaged for the migration step, the only difference being the replacement of the



hydroxyl group by an alkoxy group. Electron-withdrawing substituents would thus be expected to increase the rate of rearrangement although it should be borne in mind that much less work has been done on this rearrangement, and consequently any predictions from this transition state should be treated with caution.

Eastham and Selman[92] investigated the reversibility of the migration step by preparing the isotopically labelled methyl anisilate (XVII) and subjecting it to the conditions of the ester rearrangement. If the migration step were reversible, activity should be found in the hydroxyl carbon atom. Degradation of the product at 97° gave

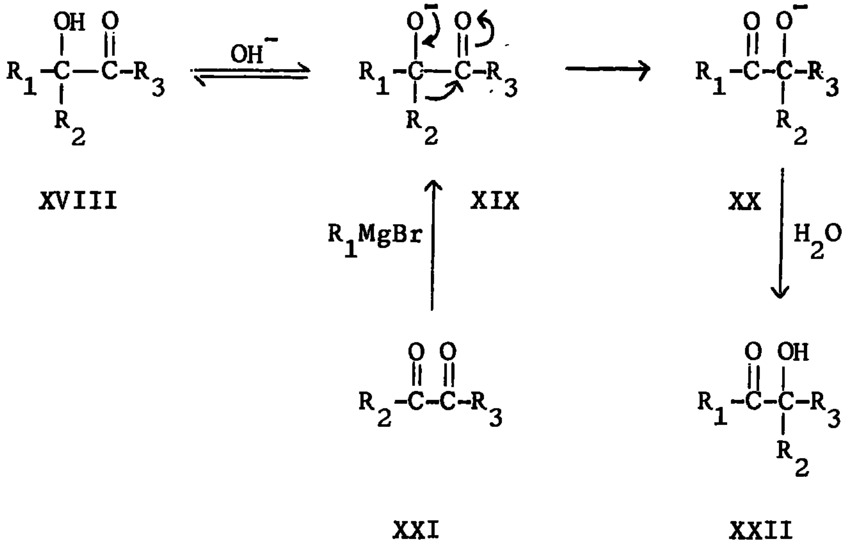


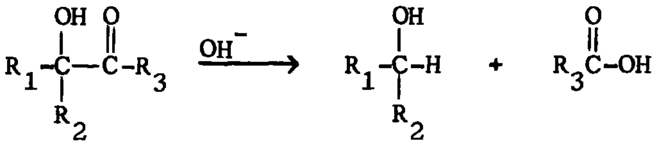
XVII (An = p-$CH_3O{\cdot}C_6H_4$)

4,4'-dimethoxybenzophenone which showed no radioactivity. Increasing the reaction temperature to 200° still gave no evidence for anisyl migration, indicating that the migration step was not reversible. This implies that the energy difference between the transition state and the ester must be much greater than that between the transition state and the anisil.

4.3. The tertiary ketol rearrangement.

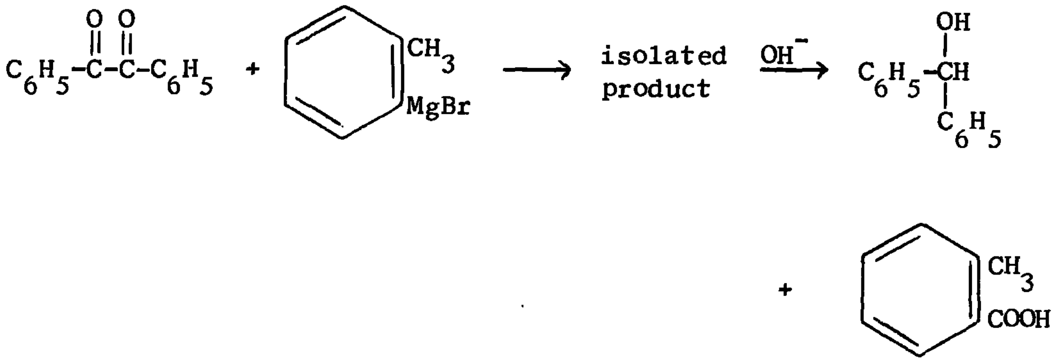
The tertiary ketol rearrangement involves the transformation of an α-keto-alcohol (XVIII) in the presence of base to the isomeric product, XXII. Since this reaction proceeds via the conjugate bases (XIX and XX) of the keto-alcohols, the rearrangement can also arise from the reaction of an α-diketone (XXI) with a Grignard reagent or aryl-lithium.[77] Confusing results were obtained from initial work on this reaction as base was employed to cleave the products resulting from addition of the Grignard.



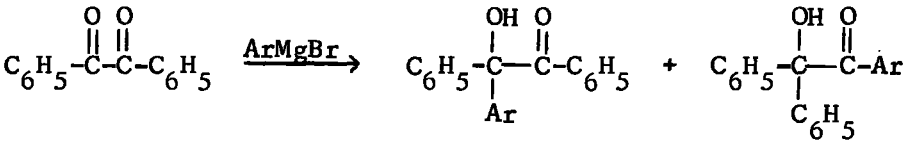


$$R_1-\overset{\overset{OH}{|}}{\underset{\underset{R_2}{|}}{C}}-\overset{\overset{O}{\|}}{C}-R_3 \xrightarrow{OH^-} R_1-\overset{\overset{OH}{|}}{\underset{\underset{R_2}{|}}{C}}-H + R_3\overset{\overset{O}{\|}}{C}-OH$$

Thus Roger and McGregor,[93] studying the reaction between o-tolyl magnesium bromide and benzil, isolated a product which they cleaved with base to give o-toluic acid and diphenylmethanol, but they were uncertain whether aryl migration took place before or after the addition of base.



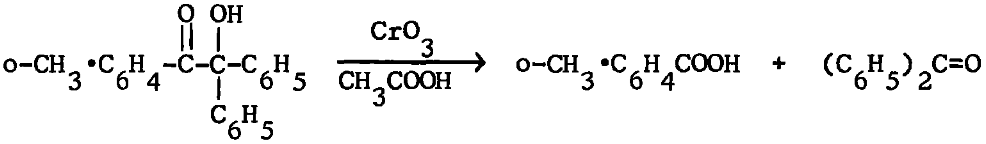
In a re-investigation of the reaction, Eastham and co-workers[94] found that a mixture of keto-alcohols was obtained, resulting from straightforward addition of the Grignard reagent and also from rearrangement (Equation 1, Ar = o-tolyl), and that the product characterised by Roger and McGregor was the rearranged compound, 2-methyl-α-phenylbenzoin



$$C_6H_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-C_6H_5 \xrightarrow{ArMgBr} C_6H_5-\overset{\overset{OH}{|}}{\underset{\underset{Ar}{|}}{C}}-\overset{\overset{O}{\|}}{C}-C_6H_5 + C_6H_5-\overset{\overset{OH}{|}}{\underset{\underset{C_6H_5}{|}}{C}}-\overset{\overset{O}{\|}}{C}-Ar \quad \text{(Equation 1)}$$

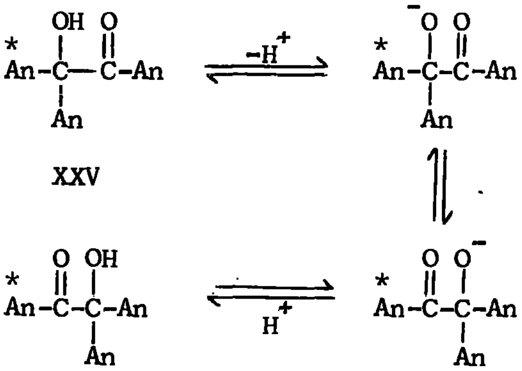
XXIII XXIV

(XXIV, Ar = o-tolyl). They also found that α-tolylbenzoin (XXIII, Ar = o-tolyl) rearranges in presence of base to XXIV (Ar = o-tolyl). The use of chromic acid rather than base to identify the α-keto-alcohols from their cleavage products, eliminated any possibility of further rearrangement occurring, e.g.



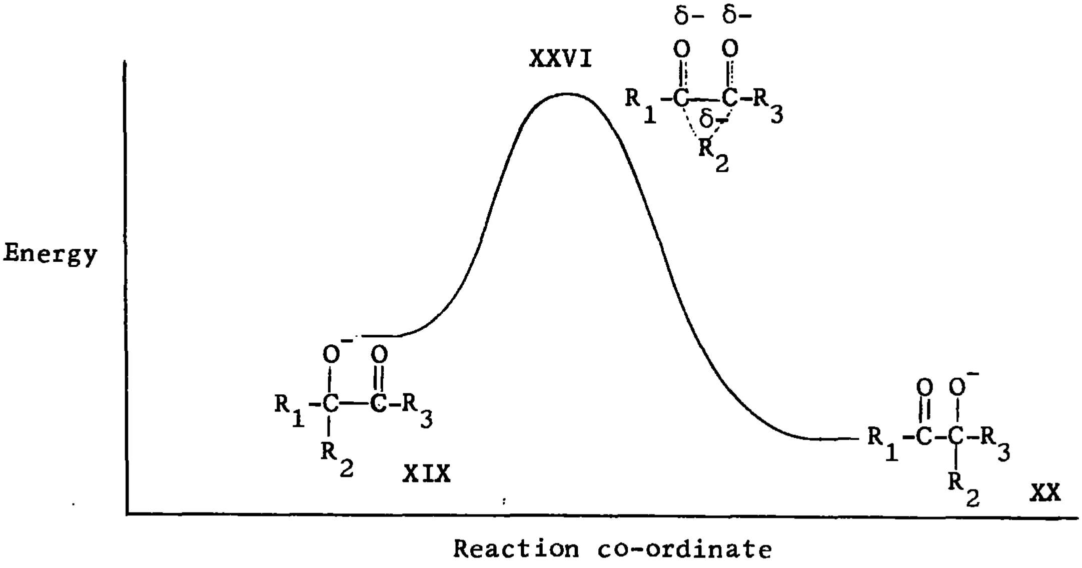
$$o\text{-}CH_3\cdot C_6H_4\text{-}\overset{O}{\overset{\|}{C}}\text{-}\underset{\underset{C_6H_5}{|}}{\overset{OH}{\overset{|}{C}}}\text{-}C_6H_5 \xrightarrow[CH_3COOH]{CrO_3} o\text{-}CH_3\cdot C_6H_4COOH + (C_6H_5)_2C{=}O$$

Several other examples of the rearrangement are known. Migration has been shown to occur in the reactions of meta- and para-tolyl magnesium bromide with benzil (Equation 1, Ar = m- and p-tolyl) to give mixtures of products.[94] Doering and Urban found that the addition of mesityl magnesium bromide to benzil gave 2,4,6-trimethyl-α-phenylbenzoin,[83] the rearranged product, and tentatively suggested that migration only occurred if it relieved steric strain. However, it was shown using C^{14} labelling that rearrangement occurs in α-anisylanisoin (XXV) where no relief of steric strain is involved.[94]



XXV

It is more probable that a combination of electronic and steric effects will determine whether migration is favourable. The ratio of products from a reaction between a Grignard reagent and benzil will be determined by the relative energies of the intermediates XIX and XX, and the rate of rearrangement by the energy of the transition state. The intermediates will be stabilised by electron-withdrawing groups on the carbon attached to the oxygen bearing the negative charge, and will be destabilised by either bulky or electron-donating groups. Thus rearrangement may be expected to occur to produce an anion where the least stabilising group is attached to the carbonyl carbon atom, as is in fact observed in the previous examples. Of course, migration may not take place if the activation energy is too high. However, from the previous discussion on the benzilic acid rearrangement, a reasonable representation of the transition state might be XXVI, and on this basis, one would expect rearrangement to proceed most easily if the migrating group was efficient at stabilising a partial negative charge.



CHAPTER 5

Reactions of aryl-lithiums with dialkyl oxalates and keto-esters

5.1. Introduction.

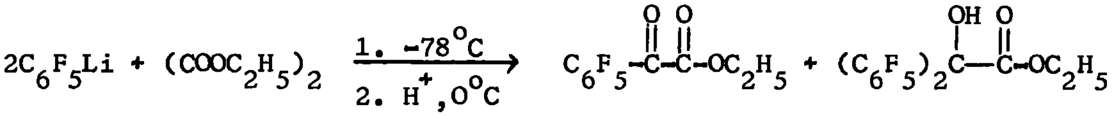
The reaction of various polyfluoroaryl-lithiums with dimethyl-carbonate has been demonstrated to be of considerable synthetic utility in the development of polyfluoroaromatic chemistry; in particular, it allows the ready synthesis of decafluorobenzophenone and octafluorofluoren-9-one.[63] It seemed possible that dialkyl oxalates would react in a similar way to dimethylcarbonate with aryl-lithiums and provide a useful route to α-diketones such as decafluorobenzil and octafluoro-9,10-phenanthraquinone. The results of these and other experiments involving dialkyl oxalates in the preparation of α-diketones are discussed in this chapter.

5.2. The preparation and rearrangement of decafluorobenzil.

A. Effect of change of hydrolysis temperature on the reaction between pentafluorophenyl-lithium and dialkyl oxalates.

While this work was in progress, a synthesis of decafluorobenzil was reported in a communication by Gilman et al.[68] who prepared the diketone from pentafluorophenylcopper and oxalyl chloride, although no experimental details or yields have as yet been published.

The author's first attempt to prepare decafluorobenzil involved the reaction of two equivalents of pentafluorophenyl-lithium (prepared by lithium-hydrogen exchange between pentafluorobenzene and butyl-lithium in ether/hexane at -78°C) with diethyl oxalate at -78°C. The reaction mixture was allowed to warm only to 0°C rather than room temperature in order to prevent nucleophilic substitution by ethoxide ion,[63] before hydrolysis with dilute HCl. The reaction yielded two major and several minor products, none of which was decafluorobenzil. The two major components were separated by distillation and identified as ethyl pentafluorobenzoylformate(I) and ethyl decafluorobenzilate(II). Ethyl pentafluorobenzoylformate is obviously formed by reaction of diethyl oxalate with only one equivalent of pentafluorophenyl-lithium, but the benzilate ester could be envisaged to arise by two possible routes. These are: i) attack by two molecular proportions of pentafluorophenyl-lithium at the same carbon in the diethyloxalate (Route A), and ii) initial formation of decafluorobenzil, followed by a benzilic ester rearrangement during the warm up period (Route B). In order to discover which of the two possible routes was correct, the reaction was



$$2C_6F_5Li + (COOC_2H_5)_2 \xrightarrow[2.\ H^+,0^\circ C]{1.\ -78^\circ C} C_6F_5-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-OC_2H_5 + (C_6F_5)_2\overset{OH}{\overset{|}{C}}-\overset{O}{\overset{\|}{C}}-OC_2H_5$$

I 43% II 46%

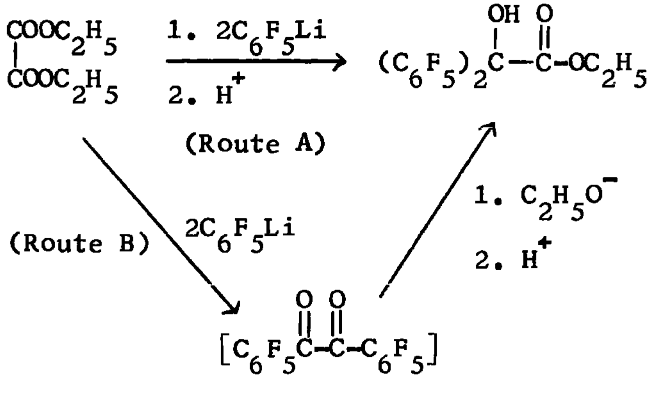
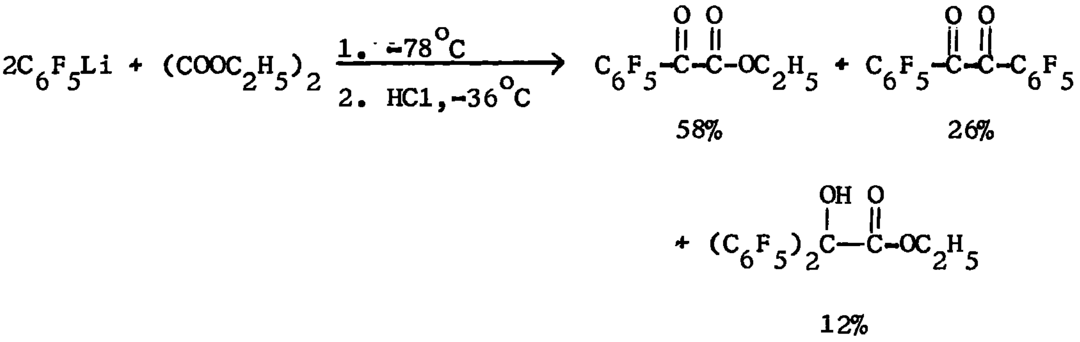


Figure 1

repeated and hydrolysed at a lower temperature (-36°C) in an attempt to trap any of the α-diketone before rearrangement occurred. From this reaction decafluorobenzil was obtained in low yield together with the two previously mentioned products, suggesting Route B to be correct.

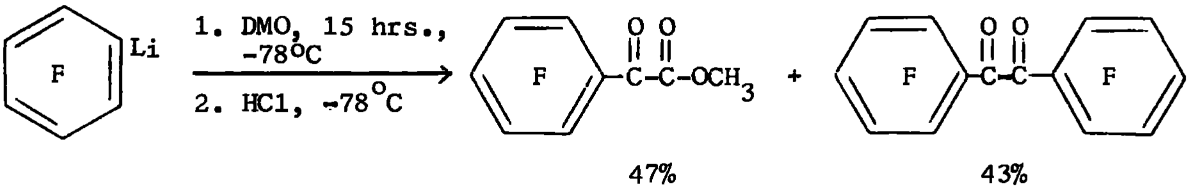


$$2C_6F_5Li + (COOC_2H_5)_2 \xrightarrow[2.\ HCl,-36^{\circ}C]{1.\ -78^{\circ}C} \underset{58\%}{C_6F_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-OC_2H_5} + \underset{26\%}{C_6F_5-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-C_6F_5}$$

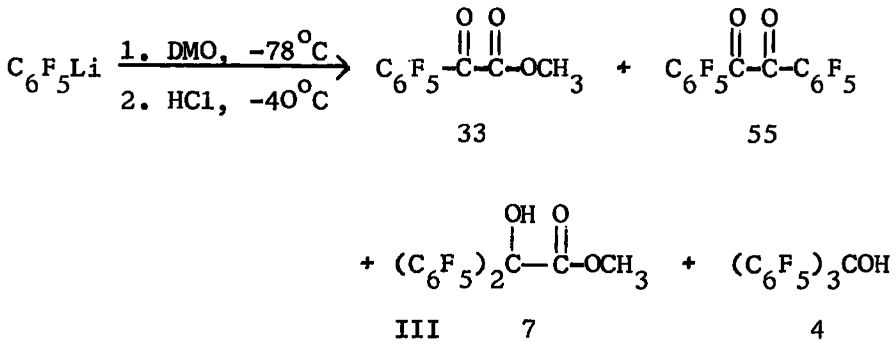
$$+ \underset{12\%}{(C_6F_5)_2\overset{\overset{OH}{|}}{C}-\overset{\overset{O}{\|}}{C}-OC_2H_5}$$

The rearrangement and its mechanism will be discussed later in Section 5.2.C.

Several reactions of pentafluorophenyl-lithium with diethyl and also dimethyl oxalate were performed in order to optimise the yield of decafluorobenzil. Reaction with dimethyl oxalate (DMO) gave slightly better results although long reaction times were still essential to obtain reasonable yields of product. Probably the best conditions involved reaction for ~15 hours or longer at -78°C followed by hydrolysis at -78°C with gaseous HCl. After work up, methyl penta-



fluorobenzoylformate was obtained in 47% yield and decafluorobenzil in 43% yield, based on dimethyl oxalate. Allowing the reaction mixture to warm to -40°C over a period of about half an hour before hydrolysis, increased the percentage of decafluorobenzil in the reaction product, but

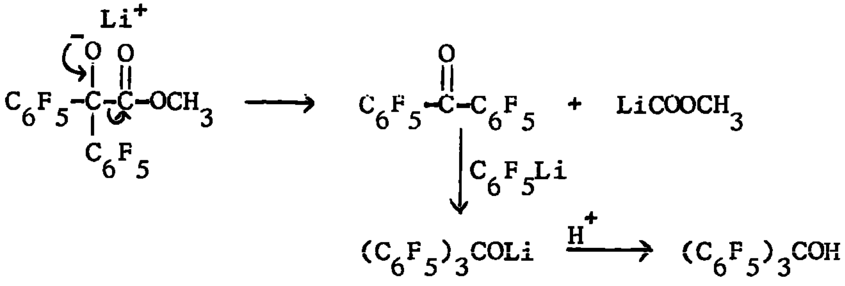


$$C_6F_5Li \xrightarrow[\text{2. HCl, }-40^{\circ}\text{C}]{\text{1. DMO, }-78^{\circ}\text{C}} \underset{33}{C_6F_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}OCH_3} + \underset{55}{C_6F_5\overset{O}{\overset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}C_6F_5}$$

$$+ \underset{\text{III}\quad 7}{(C_6F_5)_2\overset{OH}{\overset{|}{C}}\text{—}\overset{O}{\overset{\|}{C}}\text{-}OCH_3} + \underset{4}{(C_6F_5)_3COH}$$

(figures as % total reaction product)

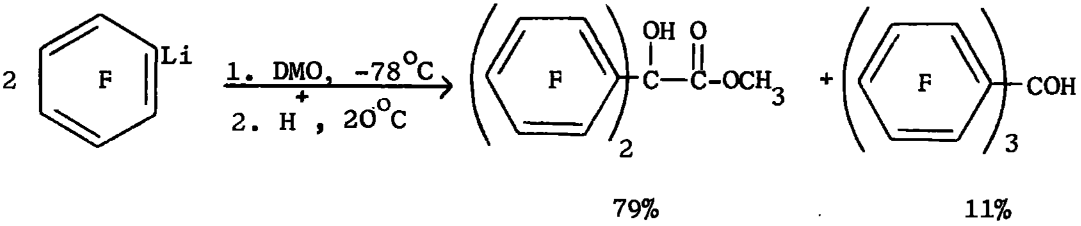
the formation of side products, later shown to be methyl decafluorobenzilate(III) and tris(pentafluorophenyl)methanol made product separation more difficult and did not necessarily result in a higher isolated yield. The tris(pentafluorophenyl)methanol may possibly be formed by elimination of $LiCOOCH_3$ from the conjugate base of methyl decafluorobenzilate, followed by further reaction with pentafluorophenyl-lithium.



$$\overset{Li^+}{C_6F_5\text{-}\overset{^-O}{\overset{|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}OCH_3} \atop {\quad |\atop C_6F_5} \longrightarrow C_6F_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}C_6F_5 + LiCOOCH_3$$

$$\begin{tikzcd} C_6F_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}C_6F_5 \arrow[d, "C_6F_5Li"] & \\ (C_6F_5)_3COLi \arrow[r, "H^+"] & (C_6F_5)_3COH \end{tikzcd}$$

The carbinol was also observed in slightly higher yield as a minor product from the reaction between pentafluorophenyl-lithium and dimethyl oxalate when hydrolysis was effected at room temperature. The major product, methyl decafluorobenzilate, was obtained pure by column chromatography and, unlike the ethyl ester, is a solid.

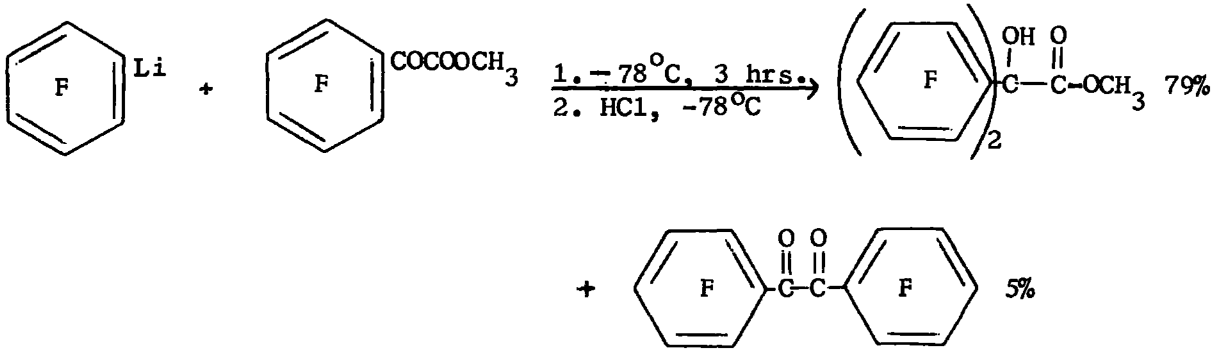


From this last reaction, it seems that room temperature hydrolysis is essential for complete consumption of the pentafluorophenyl-lithium. For instance, in the preparation of decafluorobenzil which involves hydrolysis at lower temperatures, even after reaction times of 15 hours, a significant amount of the aryl-lithium remained. With shorter reaction times (~30 mins.) a good yield of methyl pentafluorobenzoylformate with a little decafluorobenzil was obtained, indicating that addition of the first molecule of pentafluorophenyl-lithium to the oxalic ester occurs fairly rapidly, to be followed by a much slower addition of the second.

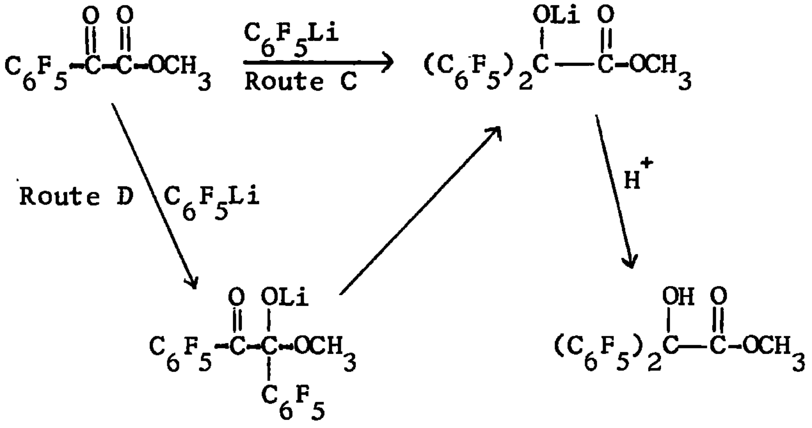
This reluctance of pentafluorophenyl-lithium to react completely with diethyl oxalate is in marked contrast to its reaction with dimethylcarbonate[63] where under similar conditions in the preparation of decafluorobenzophenone, precautions had to be taken to prevent the rapid formation of tris(pentafluorophenyl)methanol when the stoichiometric amounts of reagents were used.

B. Further mechanistic evidence.

Evidence for the mechanism of the reactions involving the preparation and rearrangement of decafluorobenzil was obtained from an interesting reaction between pentafluorophenyl-lithium and methyl pentafluorobenzoylformate. It was hoped to use the keto-ester recovered from the incomplete reaction of pentafluorophenyl-lithium with dimethyl oxalate to prepare decafluorobenzil, but hydrolysis of the reaction mixture at -78° after only three hours gave methyl decafluorobenzilate as the major product, with only traces of decafluorobenzil and unreacted keto-ester. This is in contrast to the reaction of pentafluorophenyl-lithium with dimethyl oxalate where, under similar conditions, addition of the second molecular proportion of pentafluorophenyl-lithium occurs at a much slower rate to yield the α-diketone, decafluorobenzil.



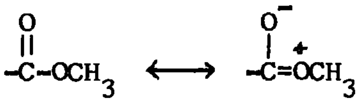
Although at first the formation of different reaction products may seem surprising, the presence of methyl decafluorobenzilate as the major product from the keto-ester reaction can be rationalised quite easily. The product could have arisen either by direct attack of pentafluorophenyl-lithium at the carbonyl carbon (Route C), or by attack at the ester carbon to give the adduct IV (Route D), which could then undergo the benzilic ester rearrangement to give methyl decafluorobenzilate.



IV III

Figure 2

The former route seems the more likely as the carbonyl carbon atom will be more electrophilic than the ester carbon atom. Pentafluorophenyl is a good electron withdrawing group[95] whereas methoxide will tend to decrease the double bond character of the carbonyl by resonance stabilisation.



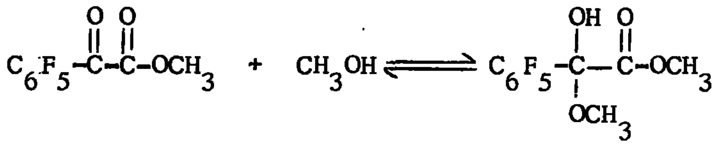
$$-\overset{\overset{O}{\|}}{C}-OCH_3 \longleftrightarrow -\overset{\overset{O^-}{|}}{C}=\overset{+}{O}CH_3$$

This is found in the previously mentioned reaction between dimethylcarbonate and two equivalents of pentafluorophenyl-lithium.[63] Aryllithium attack at the carbonyl group of decafluorobenzophenone occurs to a considerable extent while the methyl pentafluorobenzoate is still present in the reaction mixture, indicating that the ketone is more susceptible to nucleophilic attack than the ester.

C. Discussion of the reaction mechanism.

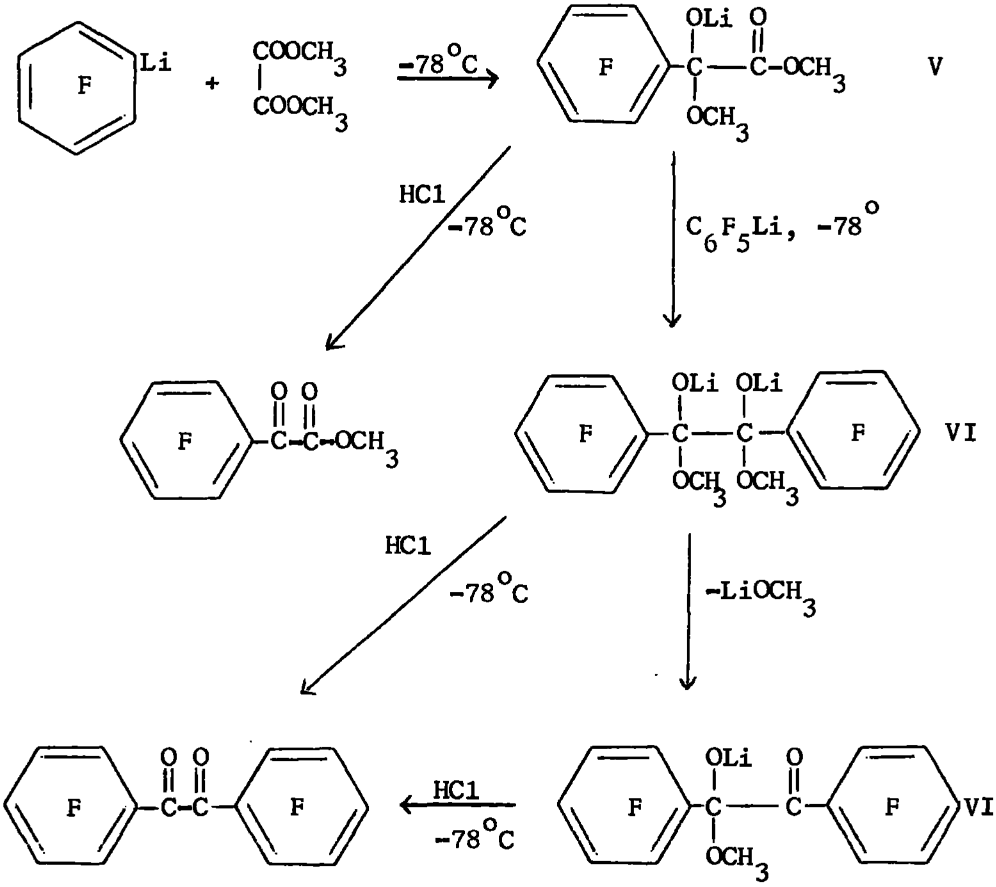
It has been shown so far that the reaction of dialkyl oxalates with two equivalents of pentafluorophenyl-lithium yields alkyl decafluorobenzilates if hydrolysed at room temperature, and decafluorobenzil if hydrolysed at -78°C, the latter preparation requiring long reaction times in order to obtain reasonable yields. It has also been shown that pentafluorophenyl-lithium reacts with methyl pentafluorobenzoylformate at -78°C to give methyl decafluorobenzilate in a reaction which proceeds much faster than the preparation of decafluorobenzil.

This last reaction indicates that methyl pentafluorobenzoylformate cannot be an intermediate in the preparation of decafluorobenzil at -78°C, as the hydroxy-ester III would then be expected to be the major product. It is more probable that reaction occurs between the first equivalent of pentafluorophenyl-lithium and dimethyl oxalate to give an adduct V which does not eliminate alkoxide ion. Hemiketals are easily hydrolysed by mineral acids, and so hydrolysis of V would give the observed methyl pentafluorobenzoylformate. Support for such an intermediate comes from ^{19}F n.m.r. studies which indicate that in methanol solution at 40°C, an equilibrium exists between the benzoylformate and its methanol adduct.



$$C_6F_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}\overset{O}{\overset{\|}{C}}\text{-}OCH_3 + CH_3OH \rightleftharpoons C_6F_5\text{-}\underset{OCH_3}{\overset{OH}{\overset{|}{C}}}\text{—}\overset{O}{\overset{\|}{C}}\text{-}OCH_3$$

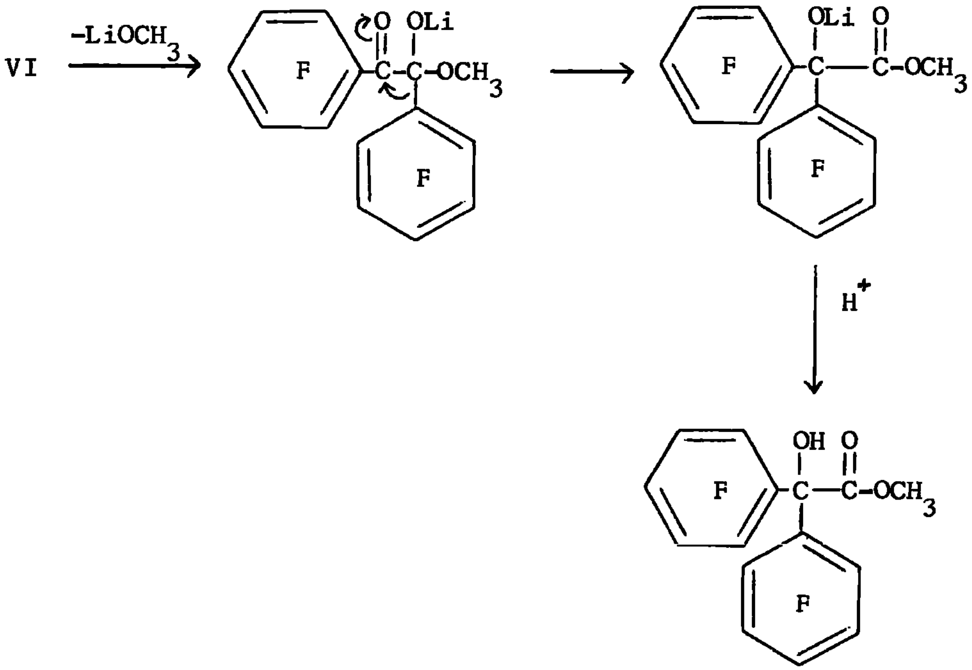
Attack on the intermediate V at the same carbon atom by the second equivalent of pentafluorophenyl-lithium is now prevented, and instead a slower addition occurs at the less electrophilic ester carbon atom.



This may result in the di-addition product (VI) or elimination of lithium methoxide from VI may occur to give VII; the latter would involve less steric crowding, and the lithium atom may be able to stabilise the molecule by co-ordinating with the carbonyl oxygen. On the other hand, it has previously been rationalised (Section 5.2.B) that C_6F_5CO- should be more susceptible to nucleophilic attack than CH_3OCO- and since V slowly reacts with pentafluorophenyl-lithium, one might expect

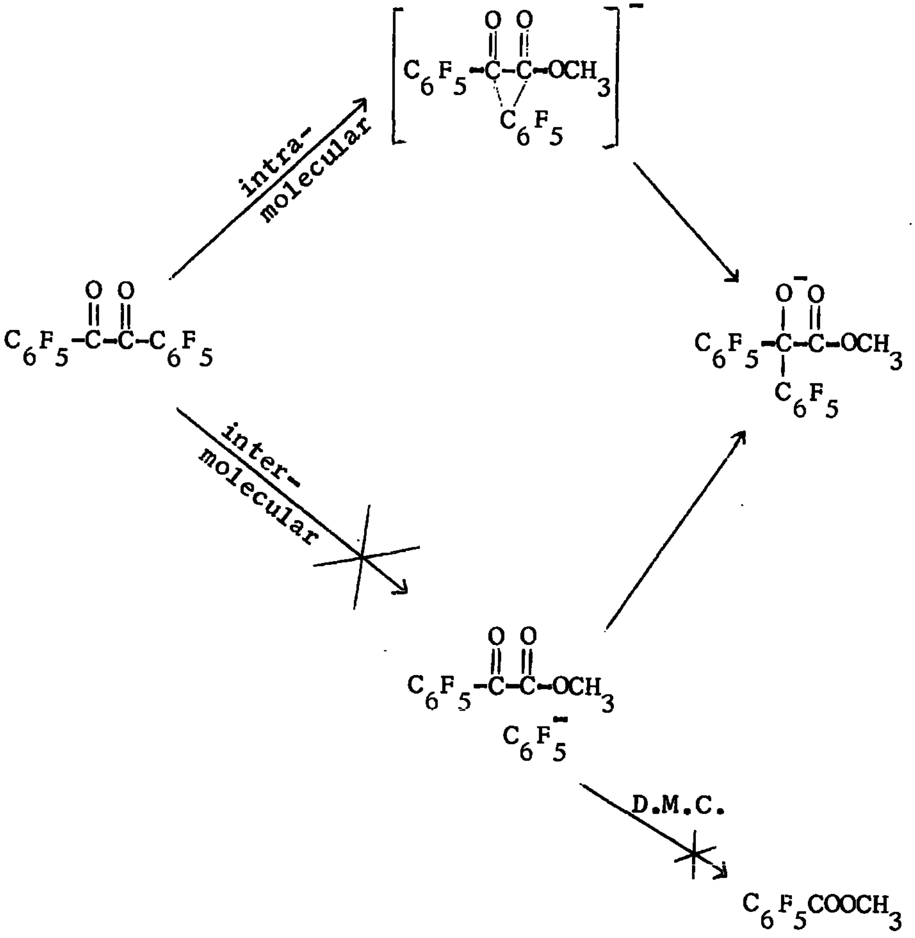
VII to do so also. However, in a reaction employing three equivalents of pentafluorophenyl-lithium with dimethyl oxalate, no perfluoro-α-phenylbenzoin was obtained on hydrolysis. Thus the evidence perhaps favours VI although the structure VII cannot be entirely ruled out as the bulky groups around the carbonyl may prevent attack of the aryl-lithium. Either compound, VI or VII, will give decafluorobenzil on hydrolysis at -78°C.

If the reaction mixture is allowed to warm to room temperature before hydrolysis, the intermediate VII will gain sufficient energy to undergo a benzilic ester rearrangement (- if VI is the intermediate, loss of lithium methoxide will first occur to give VII). There seems no



reason why migration should not proceed in the same way as for other examples of the rearrangement.

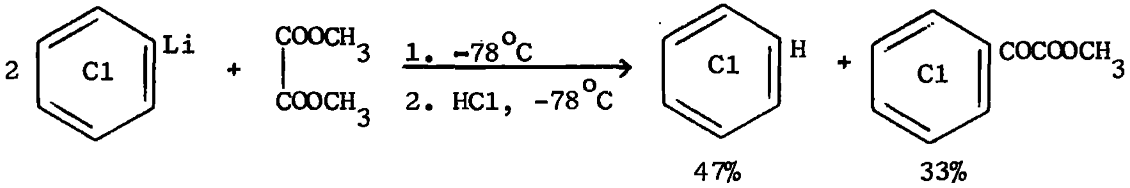
It has been suggested that the migration step might involve ion pairs or even discrete anions.[99] The possibility of an intermolecular rearrangement occurring was investigated by conducting the rearrangement of decafluorobenzil with methoxide ion in dimethylcarbonate in the hope that the solvent would trap any free pentafluorophenyl anions to give methyl pentafluorobenzoate. However, after careful removal of solvent, the only product was methyl decafluorobenzilate, indicating that the



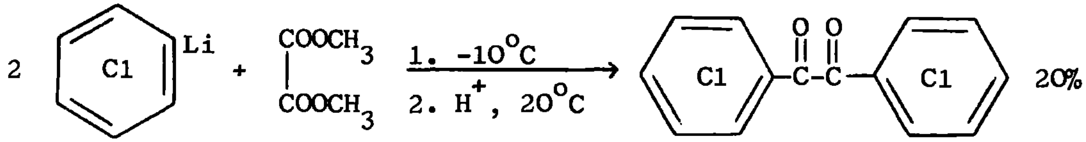
rearrangement is most probably an intramolecular process.

5.3. Preparation of decachlorobenzil.

Pentachlorophenyl-lithium has been prepared from a suspension of hexachlorobenzene in ether by lithium-chlorine exchange with butyl-lithium at -10°C,[49] and its reactions with dimethyloxalate have been investigated as a route to decachlorobenzil. In order to prevent the occurrence of a benzilic ester rearrangement as in the pentafluorophenyl-lithium reactions, the pentachlorophenyl-lithium solution in the first reaction was cooled to -78°C before the addition of dimethyloxalate. After hydrolysis at -78°C, the reaction product was found to be a two-component mixture which was separated easily by fractional sublimation

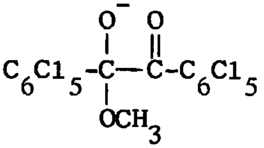


into pentachlorobenzene (47%) and methyl pentachlorobenzoylformate (33%). Despite the 2:1 ratio in favour of the aryl-lithium over the alkyl oxalate, there was no evidence for decachlorobenzil, and the keto-ester was obtained only in moderate yield. This suggests that pentachlorophenyl-lithium is much less reactive than pentafluorophenyl-lithium towards dimethyloxalate and in view of this, the reaction was repeated under different conditions. The di-ester was added to the pentachlorophenyl-lithium at -10°C, and after warming to room temperature, the reaction mixture was stirred for a further 12 hours. In this way, a fairly involatile product was obtained which included some polymeric material which may have arisen from the decomposition of pentachlorophenyl-lithium via tetrachlorobenzyne. Sublimation gave a material which on recrystallisation from nitrobenzene gave decachlorobenzil



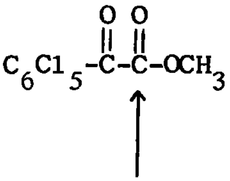
in 20% yield. A second crop of crystals was obtained which analysed correctly for methyl decachlorobenzilate. The infra-red spectrum supported this structure but confirmation from mass spectroscopic evidence was lacking. Attempts to oxidise the material to decachlorobenzophenone with chromium trioxide in acetic acid gave only recovered starting material.

The mechanism of formation of decachlorobenzil may not be the same as for decafluorobenzil as there is no evidence to show the existence of an intermediate such as VIII. Indeed it has been found (see section 5.7) that in methyl pentachlorobenzoylformate, nucleophilic attack by



$$\mathrm{C_6Cl_5{-}\overset{O^-}{\underset{OCH_3}{C}}{-}\overset{O}{\overset{\|}{C}}{-}C_6Cl_5}$$

VIII



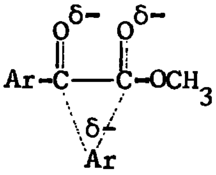
$$\mathrm{C_6Cl_5{-}\overset{O}{\overset{\|}{C}}{-}\underset{\uparrow}{\overset{O}{\overset{\|}{C}}}{-}OCH_3}$$

pentafluorophenyl-lithium occurs at the ester carbonyl carbon atom, so decachlorobenzil may well be formed simply by attack of pentachlorophenyl-lithium at the more reactive carbonyl carbon atom of the benzoylformate.

5.4. Effect of halogen on the rate of the benzilic ester rearrangement.

The effect of halogens on the rate of rearrangement of benzils has been studied to a limited extent in the benzilic acid rearrangement, where the following order was obtained; 3,3'-dichloro- > 4,4'-dichloro- > benzil > 2,2'-dichloro-benzil.[77] The observation that the ortho-disubstituted compound rearranged more slowly than benzil, while the meta and para compounds rearranged faster, was attributed to steric effects hindering initial base attack at the carbonyl carbon, and thus leading to a slower overall rate of rearrangement. No work has been reported on highly halogenated benzils in either the benzilic acid or ester rearrangement, and some discussion therefore seems appropriate on the reactions of decafluoro- and decachloro-benzil with alkoxide ion.

The observation that methyl decafluorobenzilate has been obtained, although in low yield, from reactions between pentafluorophenyl-lithium and dimethyl oxalate hydrolysed as low as -40°C, indicates that the ester rearrangement occurs much more readily than that of benzil with methoxide ion where formation of methyl benzilate requires refluxing in methanol. This is best explained using the transition state model discussed in section 4.1.E.:



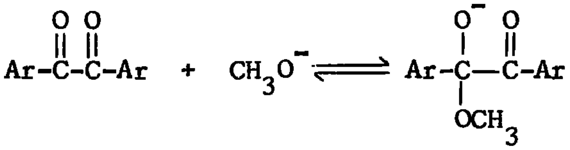
Pentafluorophenyl has been shown to be a much better electron-withdrawing group than phenyl; this is demonstrated by comparing the acidities of the phenols and the benzoic acids.

Table IV

Ionisation constants of phenols[96] and benzoic acids.[47]

	pKa
C_6H_5OH	9•9
C_6F_5OH	5•5
C_6H_5COOH	4•21
C_6F_5COOH	3•38

Thus the equilibrium constant for the alkoxide addition reaction (Equation 2) will be greater for Ar = C_6F_5 than Ar = C_6H_5, resulting in a greater concentration of intermediate available for rearrangement in the former case.



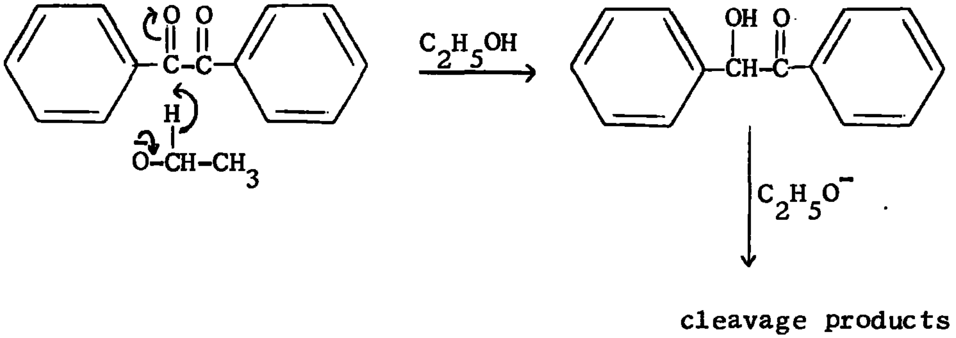
$$\mathrm{Ar{-}\overset{\overset{O}{\|}}{C}{-}\overset{\overset{O}{\|}}{C}{-}Ar} + CH_3O^- \rightleftharpoons \mathrm{Ar{-}\underset{\underset{OCH_3}{|}}{\overset{\overset{O^-}{|}}{C}}{-}\overset{\overset{O}{\|}}{C}{-}Ar}$$

(Equation 2)

Since the transition state indicates that the migrating group in the rearrangement carries a partial negative charge, the rate will depend on the groups ability to stabilise the charge and hence lower the transition state energy. That pentafluorobenzene is more acidic than benzene, i.e. $C_6F_5^-$ a more stable anion than $C_6H_5^-$, is shown by the metal-hydrogen exchange which occurs between butyl-lithium and pentafluorobenzene, and also from the rates of tritium exchange on a series of fluorinated benzenes[97] which indicated that fluorine in all positions in the ring stabilizes a negative charge relative to hydrogen, but that the effect falls off in the order ortho > meta > para. Thus for pentafluorophenyl, the combined effects of ortho, meta, and para fluorines would be expected to have a significant effect on the rate of rearrangement, and this is borne out by the experimental results. It is unfortunately not possible to obtain a calculated rate of rearrangement from the Hammet equation as ortho substituents in the phenyl ring are involved.

In contrast to the preparation of decafluorobenzil, decachlorobenzil was obtained from a reaction between pentachlorophenyl-lithium and dimethyl oxalate which was hydrolysed at room temperature. It has been shown[95] that the electron-withdrawing ability of pentachlorophenyl is almost identical with pentafluorophenyl, and so at first this result seems surprising. However, it must be remembered that 2,2'-dichlorobenzil was found to rearrange not only more slowly than 3,3'- and 4,4'-dichloro-benzils, but also more slowly than benzil itself.[77] Thus the steric effect of two ortho chlorine substituents on each phenyl would be expected to reduce the rate of rearrangement considerably relative to benzil, and even possibly cancel out the inductive effect of the other chlorine substituents in decachlorobenzil.

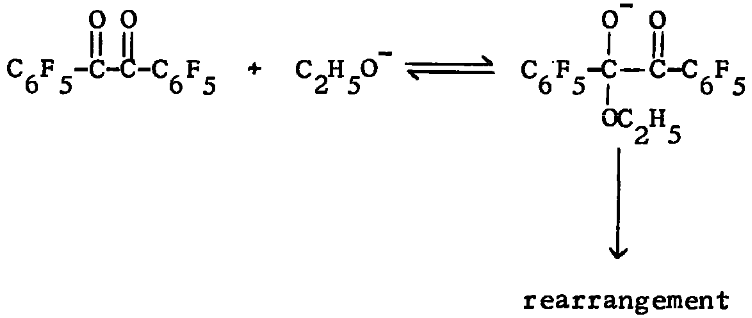
Doering and Urban[83] noted that reaction of benzil with ethoxide ion in ethanol gave no ethyl benzilate. Instead, a mixture of products was obtained arising from the reduction of benzil to benzoin by hydride ion transfer from the alkoxide, followed by subsequent cleavage of the benzoin.



Other primary and secondary alkoxides gave mixtures of the corresponding alkyl benzilate and products resulting from reduction and cleavage.

In the case of decafluorobenzil, rearrangement has been found to occur successfully with ethoxide ion in ethanol. At reflux temperatures, where any competing reduction reaction should be most apparent, ethyl decafluorobenzilate was obtained in quantitative yield in a few seconds, using only a few per cent of the stoichiometric equivalent of alkoxide ion.

The initial attack of alkoxide ion on the α-diketone is reversible, and, as has already been discussed, the effect of the pentafluorophenyl group is to make the α-diketone more susceptible to nucleophilic attack

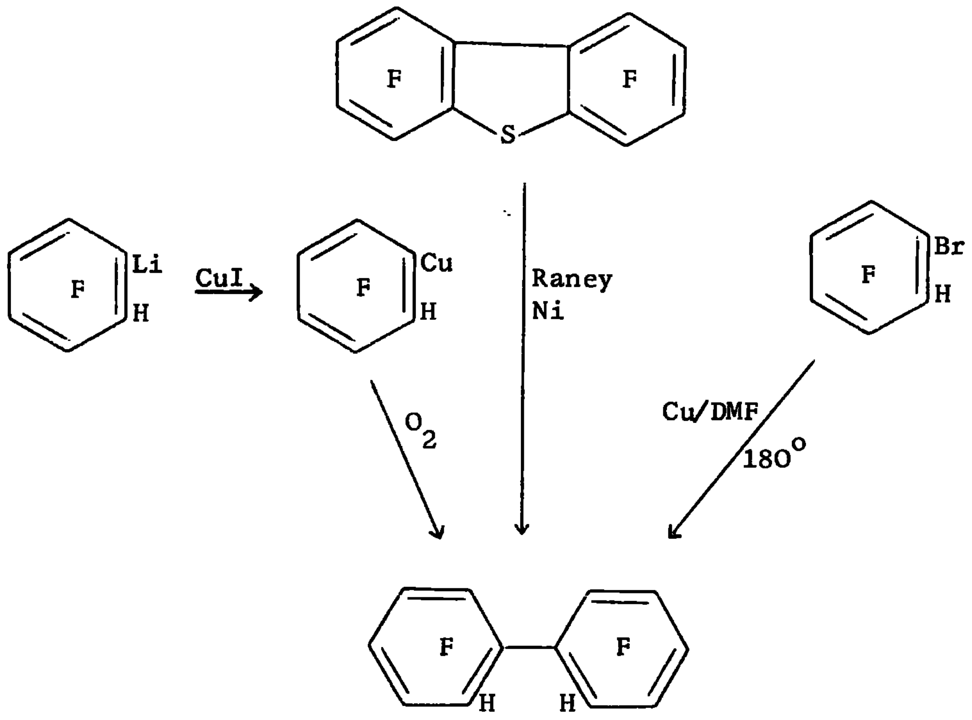


$$C_6F_5-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-C_6F_5 + C_2H_5O^- \rightleftharpoons C_6F_5-\underset{OC_2H_5}{\overset{O^-}{\overset{|}{C}}}-\overset{O}{\overset{\|}{C}}-C_6F_5$$

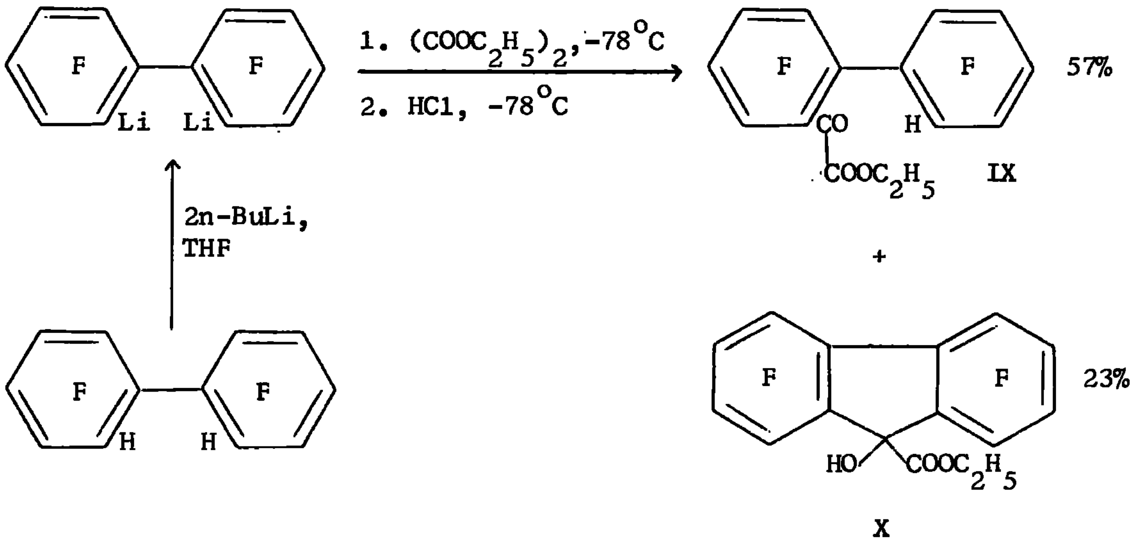
compared with benzil itself, thus shifting the above equilibrium to the right. Rearrangement will then become more favourable than the reduction reaction which depends more on the ability of the alkoxide to furnish hydride ion.

5.5. Reactions of octafluoro-2,2'-dilithiobiphenyl with dialkyl oxalates.

Several routes to octafluoro-2,2'-dihydrobiphenyl, the precursor of the dilithio-compound, were studied. These included the cleavage of octafluorodibenzothiophen with Raney nickel,[46] and an Ullmann coupling reaction with 1-bromo-2,3,4,5-tetrafluorobenzene.[98] The preferred route however was the oxidation of 2,3,4,5-tetrafluorophenylcopper with oxygen,[107] which gave the biphenyl in 70% yield.



The reaction of octafluoro-2,2'-dilithiobiphenyl with diethyl oxalate in tetrahydrofuran was investigated with various reaction times and hydrolysis temperatures, but no octafluorophenanthraquinone was obtained under any conditions. The product in a typical reaction at -78°C was a mixture with two major components which were separated by column chromatography and identified as ethyl tetrafluoro-2-(2',3',4',5'-tetrafluorophenyl)benzoylformate (IX) and 9-carbethoxyoctafluorofluoren-9-ol (X).



The products may well arise by the same mechanism as discussed for the reaction between pentafluorophenyl-lithium and the dialkyl oxalates (Route E). However, since no octafluorophenanthraquinone was obtained, it is possible that either rearrangement took place much more rapidly than in the case of decafluorobenzil, or that cyclisation to the five-membered ring proceeded directly (Route F). The immediate elimination of lithium ethoxide is more likely here than in the decafluorobenzil case, as there is more steric crowding in the intermediate XI, and nucleophilic attack could then occur at the more reactive ketone carbonyl group, rather than at the ester carbonyl.

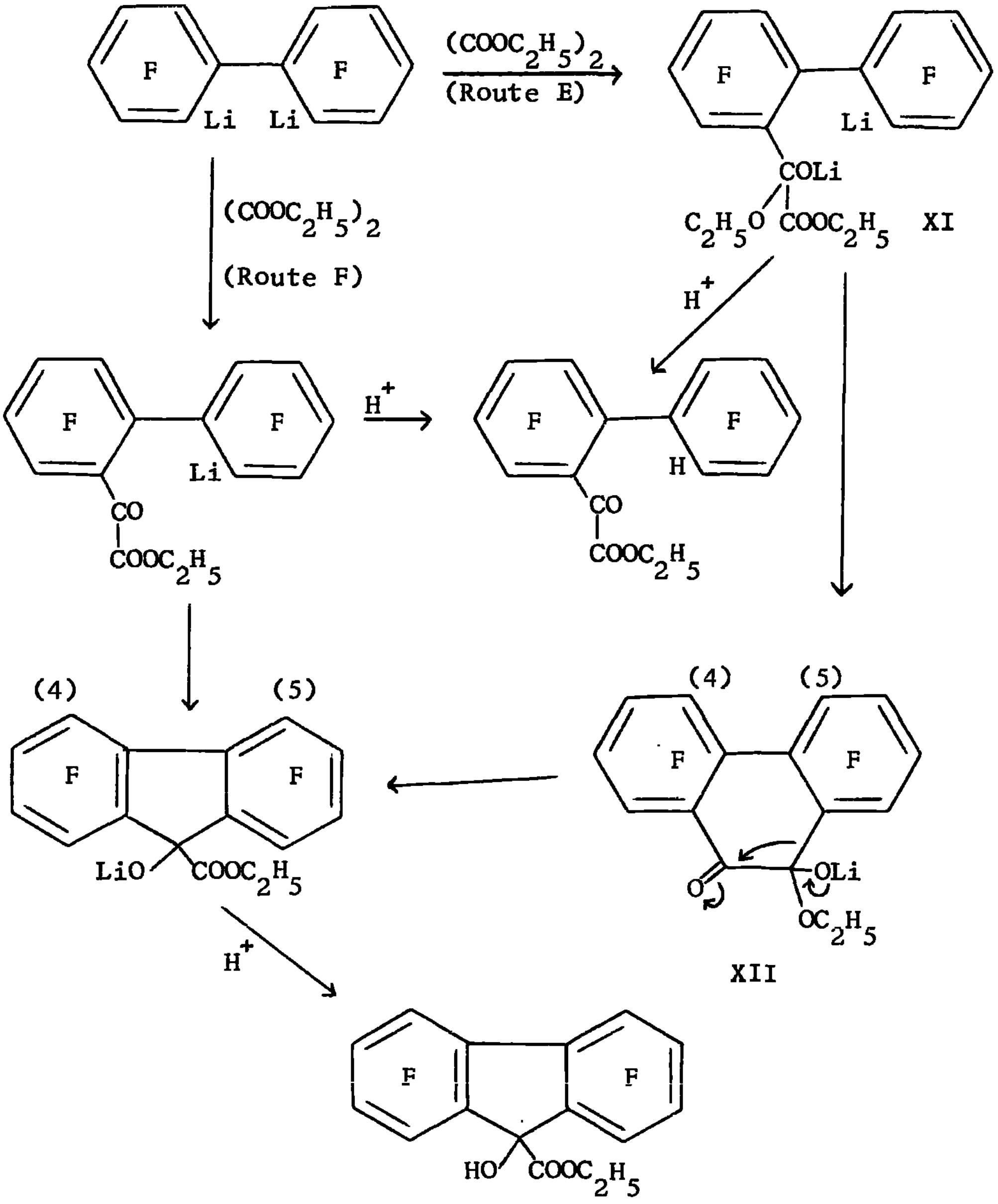
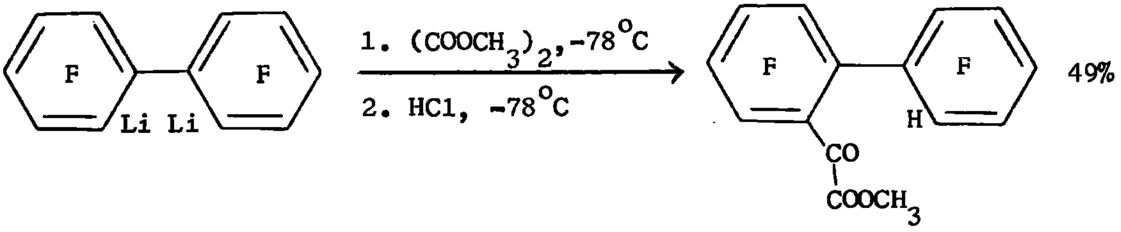


Figure 3

However, the low yield of cyclised product favours Route E since attack at the ester carbonyl has already been shown to be a slow reaction (section 5.2.C). If this is the correct route, it is not clear why the intermediate XII should rearrange so much faster than the intermediate in the rearrangement of decafluorobenzil. One difference is that the two aryl substituents are now joined together and this may lead to better solvation of the intermediate, and also enable the lithium atom to co-ordinate efficiently with the carbonyl oxygen, thus lowering the energy of the transition state. A second factor is that relief of steric strain between the 4- and 5-fluorines (Figure 3) would also occur with rearrangement. While these suggestions are feasible explanations, they do not represent conclusive evidence for Route E.

Attempts to prepare the phenanthraquinone using dimethyl rather than diethyl oxalate were also unsuccessful. Rather surprisingly,

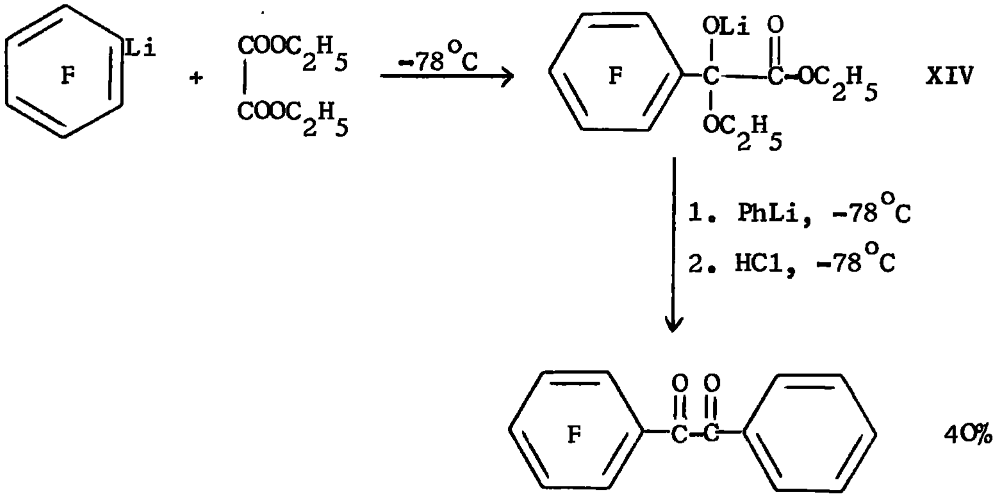


XIII

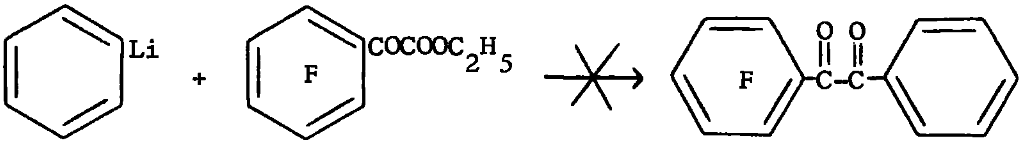
no cyclised product at all was detected, and the only compound isolated was the methyl keto-ester (XIII).

5.6. Preparation of 2,3,4,5,6-pentafluorobenzil.

In section 5.2.C. it was suggested that the reaction between pentafluorophenyl-lithium and either dimethyl or diethyl oxalate involved the initial formation of an adduct (e.g. XIV), which prevented further attack of pentafluorophenyl-lithium at the same carbon atom. Further evidence for this mechanism comes from the following α-diketone preparation. Reaction of pentafluorophenyl-lithium with diethyl oxalate at -78°C produced the adduct XIV and to it was added a solution of phenyl-lithium (prepared by an exchange reaction between iodobenzene and butyl-lithium at -15°C) precooled to -78°C. As in the preparation



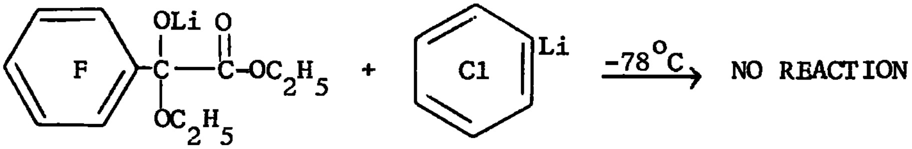
of decafluorobenzil, addition of the second aryl-lithium occurred slowly and a long reaction time (35 hours) was required to produce a reasonable yield of 2,3,4,5,6-pentafluorobenzil. The only other product was unreacted ethyl pentafluorobenzoylformate which was easily removed by distillation. These results are in contrast to the reaction between ethyl pentafluorobenzoylformate and phenyl-lithium at -78°C where,after hydrolysis,no keto-ester was recovered, and no evidence was found for the



pentafluorobenzil. Evidence from ^{19}F n.m.r. spectra indicated that the mixture of products obtained arose from nucleophilic attack at the ketone carbonyl group (as opposed to the ester carbonyl)of the benzoylformate. This is in agreement with observations from the reaction between pentafluorophenyl-lithium and ethyl pentafluorobenzoylformate where attack also occurred at the ketone carbonyl.

5.7. Preparation of 2,3,4,5,6-pentachloropentafluorobenzil.

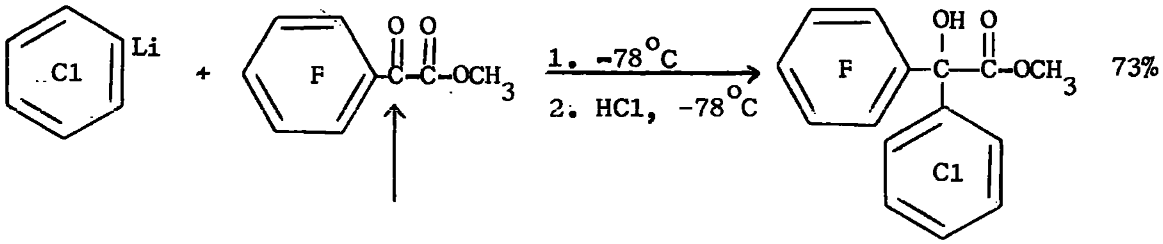
In an examination of the generality of the previous reaction as a route for the preparation of unsymmetrical α-diketones, the synthesis of 2,3,4,5,6-pentachloropentafluorobenzil was attempted from pentafluorophenyl-lithium, diethyl oxalate, and pentachlorophenyl-lithium at -78°C. However, the only products isolated from the reaction were ethyl pentafluorobenzoylformate and pentachlorobenzene, indicating that,

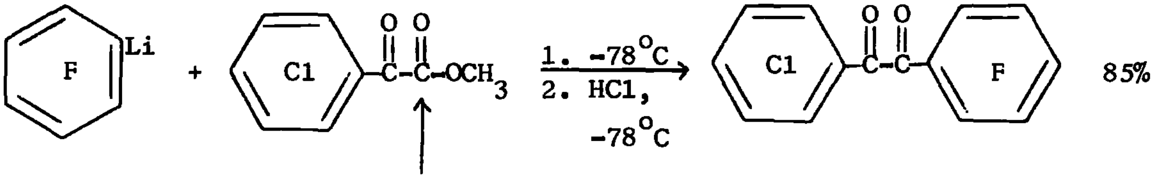


under these conditions, pentachlorophenyl-lithium was too weak a nucleophile to attack the ester carbonyl group of the intermediate XIV. Thus the reactivity of the aryl-lithiums so far studied in reactions with the alkoxide adducts is in the order $C_6F_5 \sim C_6H_5 > C_6Cl_5$.

In terms of the inductive effect alone, one would expect the order of reactivity to be $C_6H_5 > C_6Cl_5 \sim C_6F_5$. However, in the case of the bulky pentachlorophenyl group, attack will be restricted by steric factors, especially due to the ortho chlorines, making the molecule less nucleophilic than would be expected in terms of electronic effects alone. Conversely, pentafluorophenyl-lithium appears to be more reactive than one would predict. It is known that alkyl- and aryl-lithiums exist as dimers, tetramers, hexamers etc., depending on the particular lithio-derivative and the solvent employed. It is thus possible that the particular aggregates of molecules in which phenyl- and pentafluorophenyl-lithium exist, make their reactivities fairly similar.

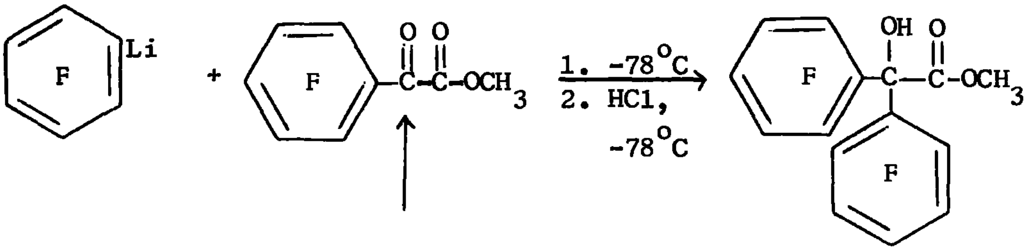
Although pentachlorophenyl-lithium does not attack the ester group in XIV, it is sufficiently reactive to attack the pentafluorophenyl carbonyl group of methyl pentafluorobenzoylformate at -78°C, giving methyl 2,3,4,5,6-pentachloropentafluorobenzilate in good yield. In contrast to this, it was found that pentafluorophenyl-lithium reacted





with methyl pentachlorobenzoylformate under the same conditions to give the yellow crystalline 2,3,4,5,6-pentachloropentafluorobenzil in 85% yield.

Bearing in mind the reaction between pentafluorophenyl-lithium and methyl pentafluorobenzoylformate at -78°C which gives the hydroxy-



ester, methyl decafluorobenzilate (section 5.2.B), it can be seen that the ability of a substituent to activate an adjacent carbonyl group to nucleophilic attack lies in the order $C_6F_5 > OCH_3 > C_6Cl_5$. Since the inductive effect of pentachloro- and pentafluoro-phenyl have been found to be of the same order,[95] it is presumably steric hindrance on the part of the pentachlorophenyl group which directs attack to the ester carbonyl rather than to the more electron-deficient ketone carbonyl group.

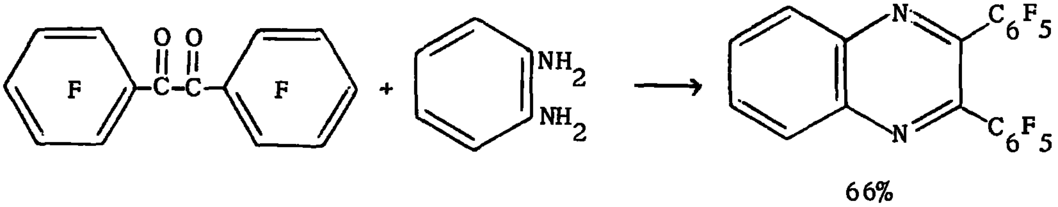
CHAPTER 6

Reactions of Benzils with Nucleophiles

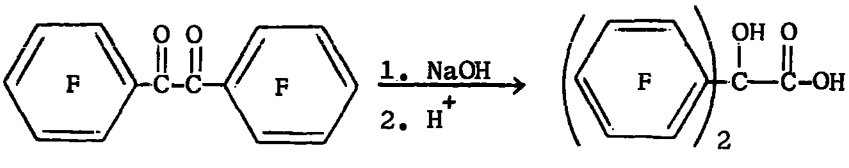
This chapter describes some general reactions of decafluorobenzil, and compares and discusses the reactions of benzil and decafluorobenzil with aryl- and alkyl-lithiums.

6.1. General reactions of decafluorobenzil.

Decafluorobenzil behaves as a typical α-diketone in that it reacts with o-phenylenediamine on warming to 100°C for a few minutes. Recrystallisation of the reaction product from methanol yields pure 2,3-bis(pentafluorophenyl)quinoxaline.

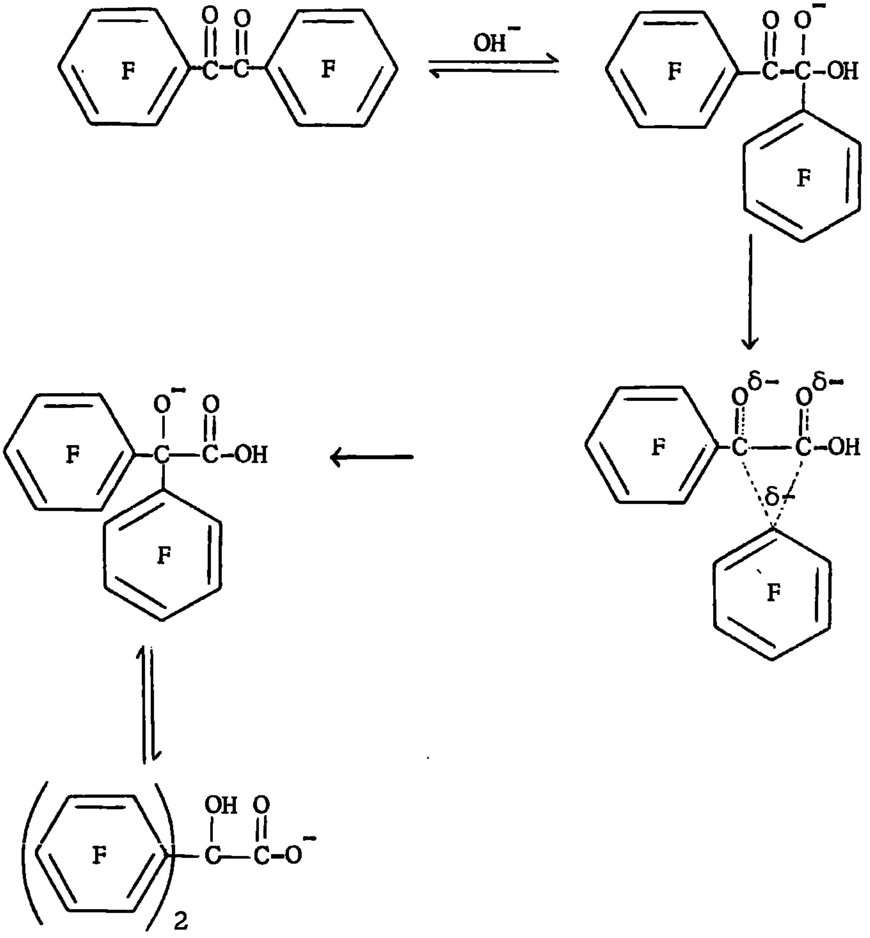


It also reacts in ether solution at room temperature with an aqueous solution of sodium hydroxide to give, on acidification and extraction, decafluorobenzilic acid as the only product. This is



another excellent example of the difference in reactivity between the non-fluorinated and fully-fluorinated benzils. Whereas decafluorobenzil undergoes rearrangement at room temperature in a heterogeneous system in a few minutes, benzil requires refluxing with potassium hydroxide in aqueous dioxan.

The difference in rates of rearrangement of benzil and decafluorobenzil with alkoxide ion has already been discussed (section 5.4), and much of the discussion regarding the stabilisation of the migrating group applies here. Thus it appears that fluorine substituents not only encourage base

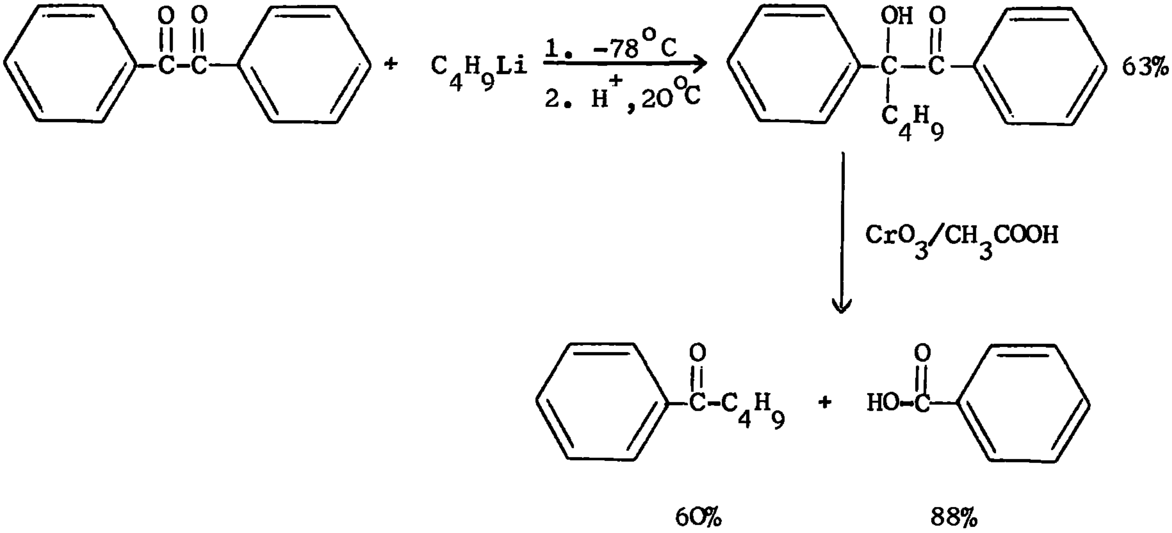


I

attack on the decafluorobenzil to give the intermediate I, but also facilitate rearrangement by stabilising the migrating anionic pentafluorophenyl group. Thus a significant increase in the rate of rearrangement is observed.

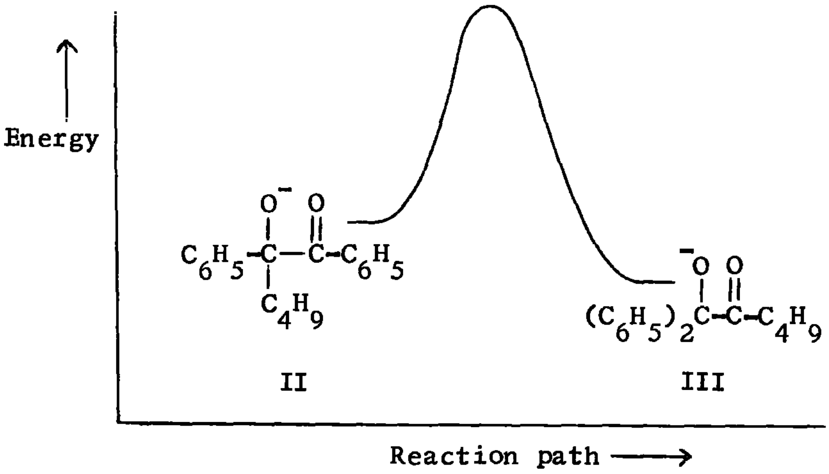
6.2. Reactions of benzil and decafluorobenzil with butyl-lithium.

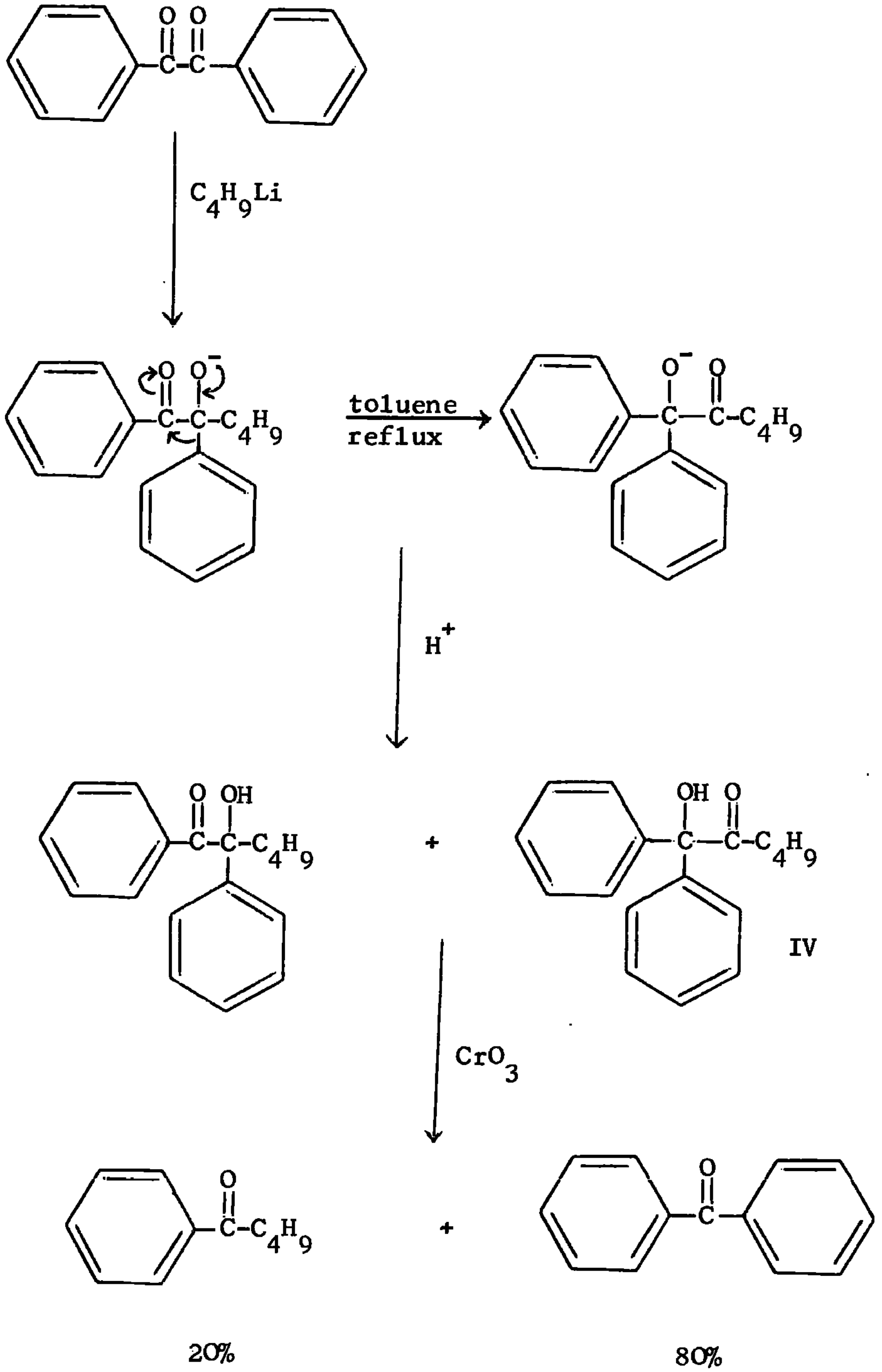
In order to compare the relative migratory aptitude of pentafluorophenyl with other groups, a series of reactions was performed between aryl- and alkyl-lithiums and benzil and decafluorobenzil. The reaction between butyl-lithium and benzil was first investigated. The alkyl-lithium addition was performed at -78°C, and the reaction mixture was allowed to attain room temperature before hydrolysis with dilute acid. From the reaction product, pure α-n-butylbenzoin was isolated in 63% yield. Its structure was deduced by oxidation with chromium trioxide



in glacial acetic acid to give butyl phenyl ketone from the neutral fraction and benzoic acid after acidification of the basic fraction.

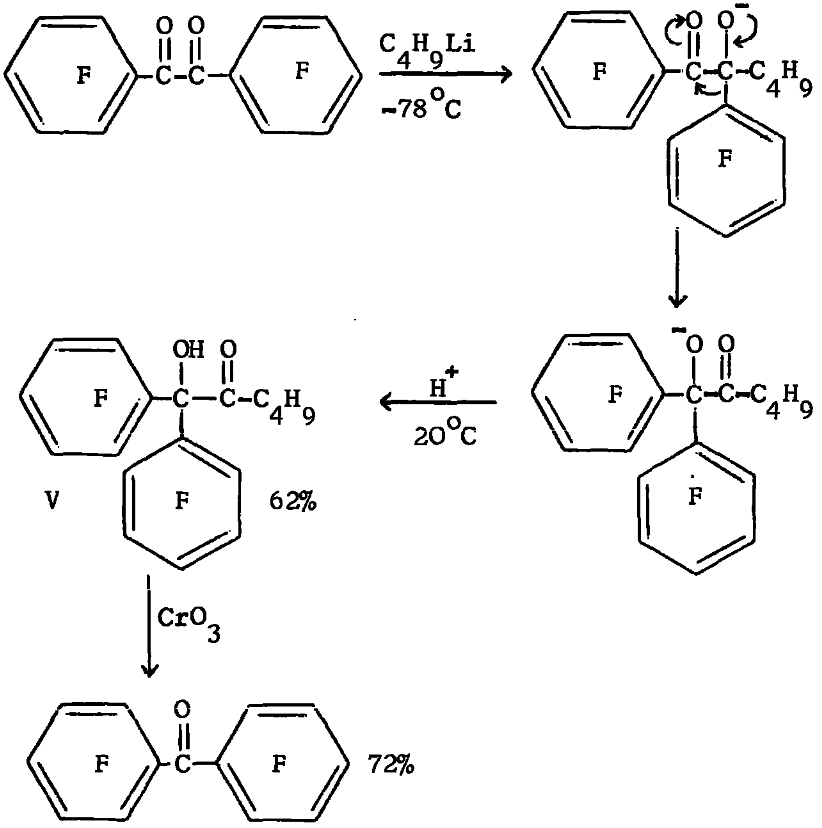
Since phenyl is better able to stabilise a negative charge in a molecule than butyl, one might have expected the reaction product to be 1-hydroxy-1,1-diphenylhexan-2-one (IV) since its conjugate base (III) should be of lower energy than II. That III is in fact the more stable anion was confirmed in a second experiment. The reaction was repeated, but before hydrolysis, most of the ether and hexane was removed by distillation, and the reaction mixture refluxed in toluene, a higher boiling solvent, for three days. A viscous liquid, characteristic of a mixture of isomeric keto-alcohols, was obtained and oxidation as before with chromic acid gave benzophenone and butyl phenyl ketone in the ratio 4:1. If it is assumed that the chromic acid cleaves the two keto-alcohols with approximately equal efficiency, it then follows that the rearranged anion III is the lower energy intermediate. Presumably raising the reaction temperature to 110°C overcomes the rather high activation energy which prevents rearrangement at room temperature.




C4H9Li
toluene
reflux
H+
IV
CrO3
20%
80%

Two reasons may be advanced for the incomplete conversion of II into III. It may be that the difference in their energies is only small, and that an equilibrium is reached with the anions in the ratio 4:1. However, since reflux was carried out over a long period, it is also possible that proton abstraction occurred to give the α-n-butylbenzoin which would then be unable to rearrange.

The reaction of butyl-lithium with decafluorobenzil at -78°C followed by hydrolysis at room temperature, was found to proceed with rearrangement. The product 1-hydroxy-1,1-bis(pentafluorophenyl)hexan-2-one (V) was obtained pure after removal of unidentified minor components by column chromatography. The straightforward addition product, α-butyldecafluorobenzoin, was ruled out from ^{19}F n.m.r. data which showed

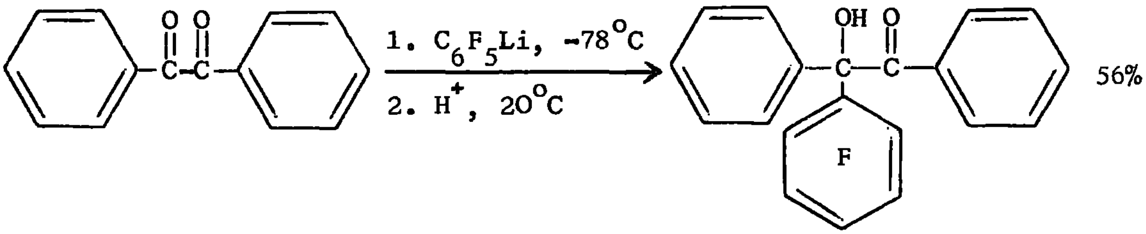


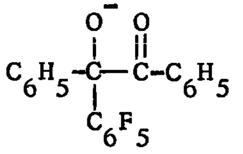
resonances for only one type of pentafluorophenyl group, and further evidence for V as the correct structure came from its oxidation to decafluorobenzophenone.

It thus appears that both phenyl and pentafluorophenyl migrate preferentially to butyl, but that the electron-withdrawing pentafluorophenyl groups are more efficient at lowering the transition state energy in the migration step, and hence migrate at a lower temperature than phenyl.

6.3. Reactions of benzil and decafluorobenzil with pentafluorophenyl-lithium.

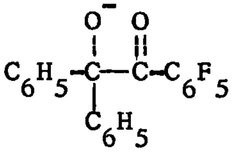
Benzil reacts with pentafluorophenyl-lithium in a straightforward manner to give, after column chromatography and recrystallisation, pure α-pentafluorophenylbenzoin in 56% yield. Refluxing the reaction mixture in toluene before hydrolysis did not affect the reaction product. Although this is negative evidence in the sense that no migration is observed, it does suggest that anion VI is probably of lower energy than VII, which





$C_6H_5-\underset{C_6F_5}{\overset{O^-}{C}}-\overset{O}{\overset{\|}{C}}-C_6H_5$

more stable than

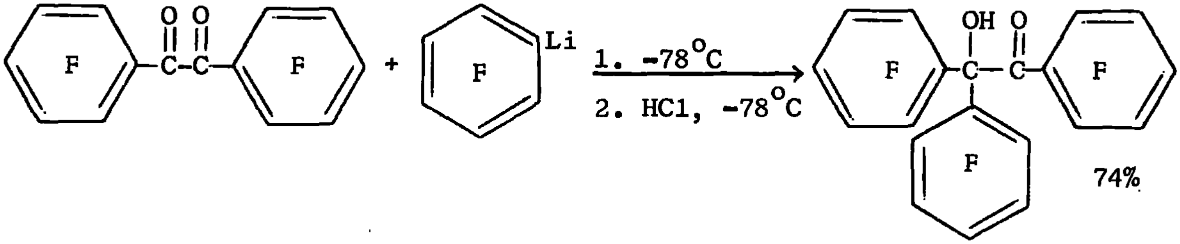


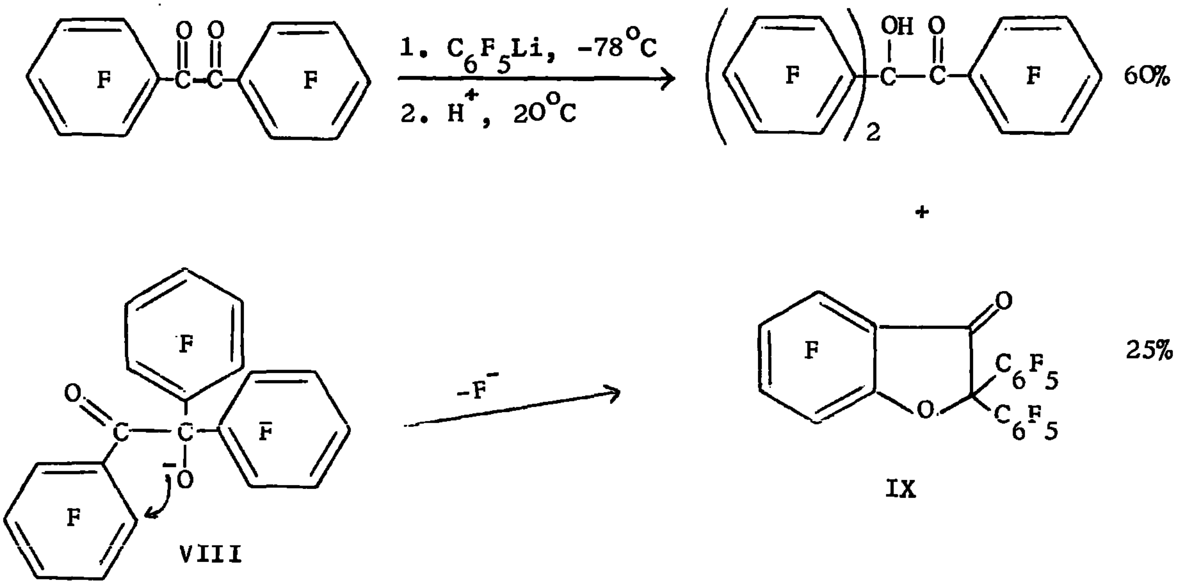
$C_6H_5-\underset{C_6H_5}{\overset{O^-}{C}}-\overset{O}{\overset{\|}{C}}-C_6F_5$

VI VII

is what one would expect from the previous discussion on the anion stabilities.

The products of the reaction between pentafluorophenyl-lithium and decafluorobenzil were found to vary depending on the conditions employed. Hydrolysis at -78°C with gaseous HCl gave the expected product, perfluoro-α-phenylbenzoin, in 74% yield. If, however, the reaction mixture was allowed to attain room temperature before hydrolysis, a second product was also obtained. Separation was achieved by column chromatography and the new compound, the minor component of the mixture, was identified as perfluoro-2,2-diphenylbenzofuran-3-one (IX). It is presumably formed



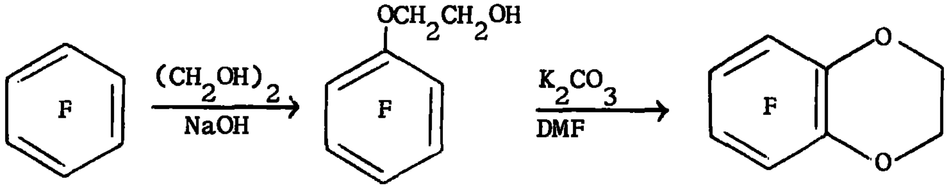


VIII

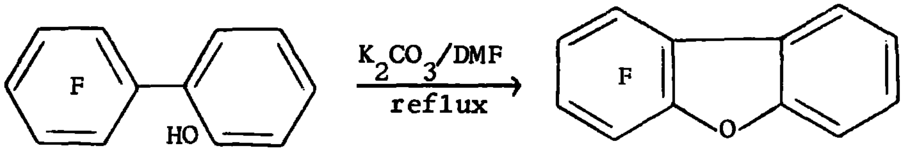
IX

by an intramolecular displacement of ortho-fluorine by the nucleophilic oxygen in VIII, the conjugate base of perfluoro-α-phenylbenzoin. This was shown by the addition of butyl-lithium to the perfluoro-α-phenylbenzoin in ether/hexane which gave, after a period at reflux, the benzofuran-3-one as the major product.

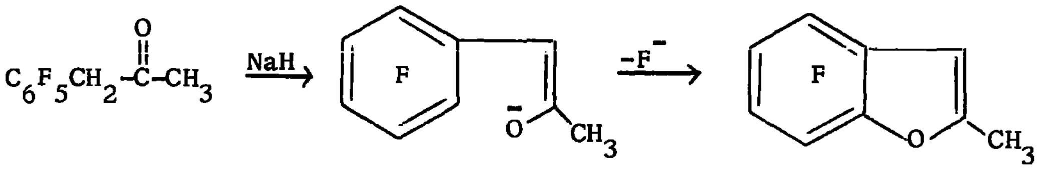
The intramolecular displacement of ortho-fluorine from an aromatic ring has been studied previously as a route to fluorinated oxygen heterocycles. Thus the reaction of hexafluorobenzene with ethylene glycol in the presence of base gave the expected bicyclic compound:[100]



Potassium carbonate in dimethylformamide (DMF) has also been used in the preparation of 1,2,3,4-tetrafluorodibenzofuran from 2,3,4,5,6-pentafluoro-2'-hydroxybiphenyl.[101]

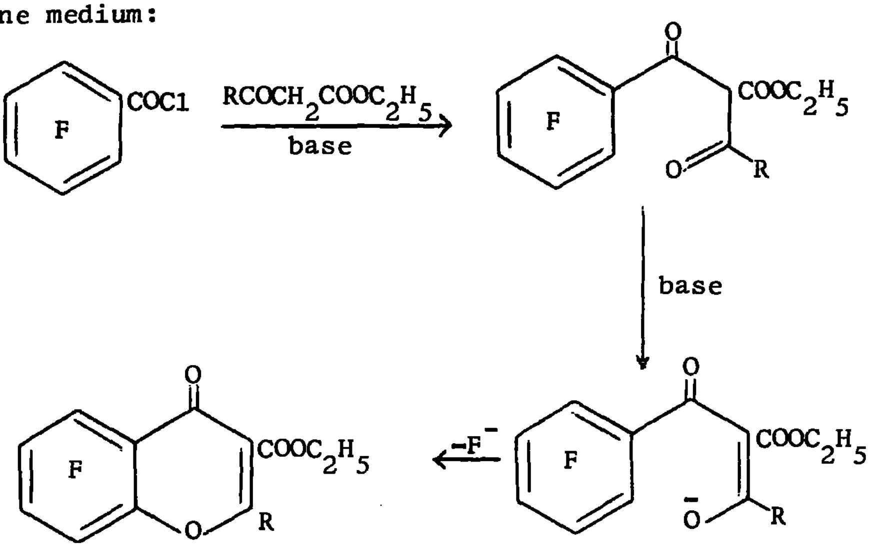


The partially fluorinated benzofuran X has been prepared by treatment of pentafluorophenylpropan-2-one with sodium hydride,[102] the intramolecular enolate anion displacing an ortho fluorine to give 4,5,6,7-tetrafluoro-



X

2-methylbenzo[b]furan (X). In a similar reaction, two groups of workers[103,104] have prepared heterocycles of the type XI starting from pentafluorobenzoyl chloride and the appropriate β-keto-ester, in alkaline medium:



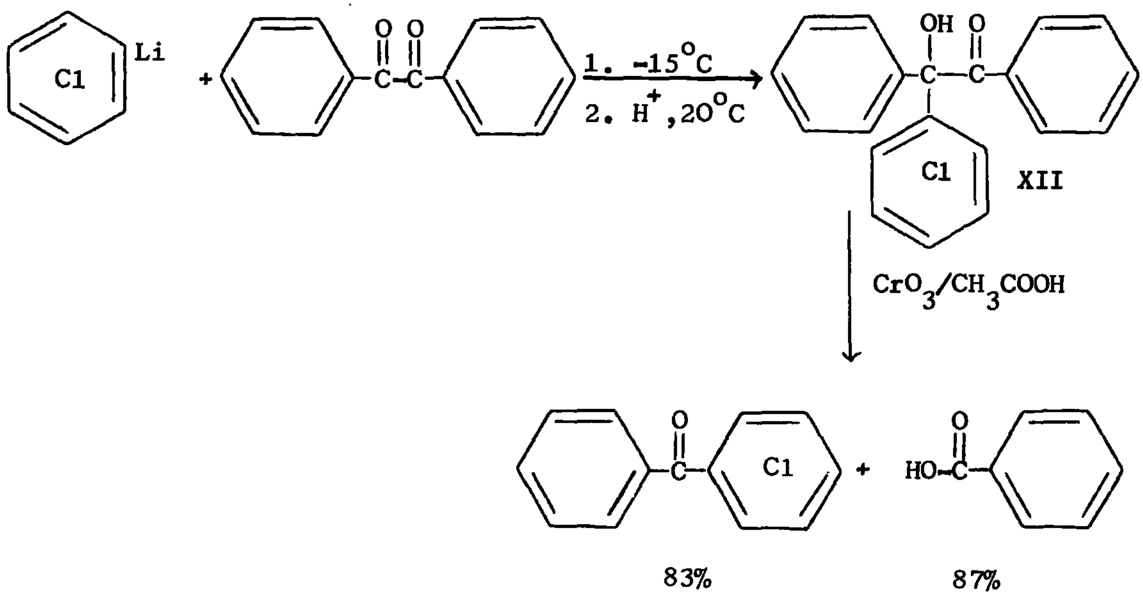
XI

(R = CH_3, C_6H_5, C_6F_5)

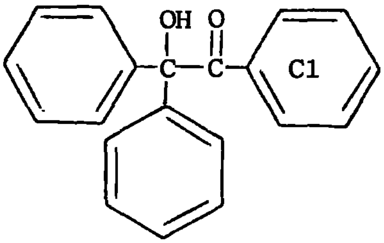
6.4. Reactions of benzil and decafluorobenzil with pentachlorophenyl-lithium.

The reaction between pentachlorophenyl-lithium and benzil at -15°C, hydrolysed at room temperature, yielded the straightforward addition product, α-pentachlorophenylbenzoin, in 75% yield. This compound was characterised from its spectroscopic properties and also from its cleavage on oxidation with chromium trioxide in glacial acetic acid, to give 2,3,4,5,6-pentachlorobenzophenone and benzoic acid.

As in the previous addition reactions of alkyl- and aryl-lithiums to benzil, it was of interest to find out whether α-pentachlorophenylbenzoin

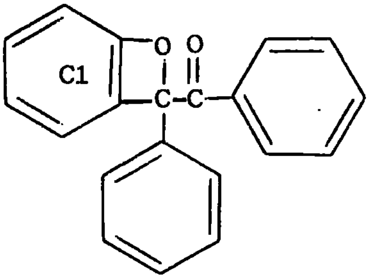


was in fact the most thermodynamically stable product. Consequently, the reaction was repeated and after the formation of the conjugate base of XII at -15°C, most of the solvent was removed and the mixture refluxed in toluene for 89 hours. A single product with different properties to XII was obtained, but was found not to be the rearranged keto-alcohol XIII. The infra-red spectrum indicated absence of -OH, and a strong parent peak

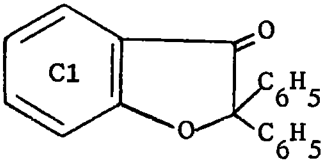


XIII

in the mass spectrum indicated that the period at reflux in toluene had resulted in loss of HCl relative to α-pentachlorophenylbenzoin. Two possible structures, XIV and XV, can be suggested for this compound, depending on whether or not phenyl migration takes place before the

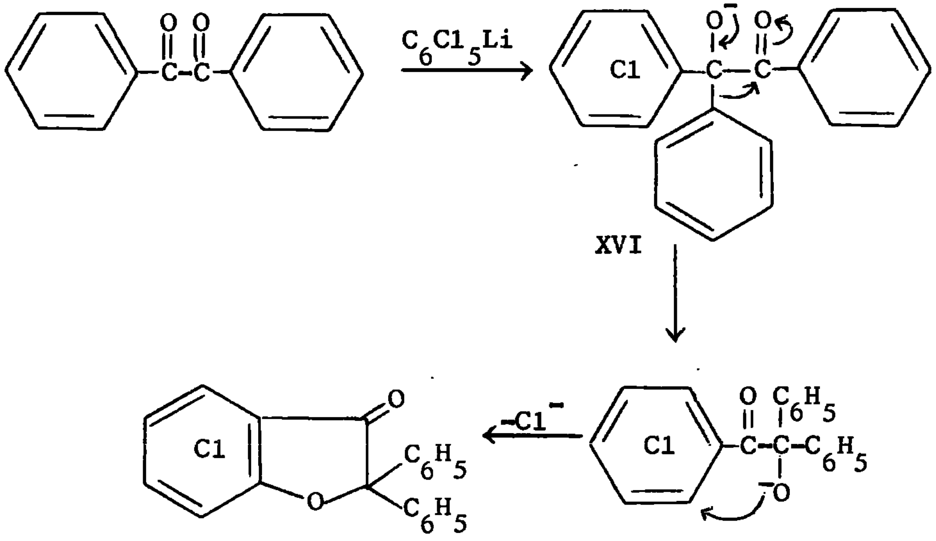


XIV



XV

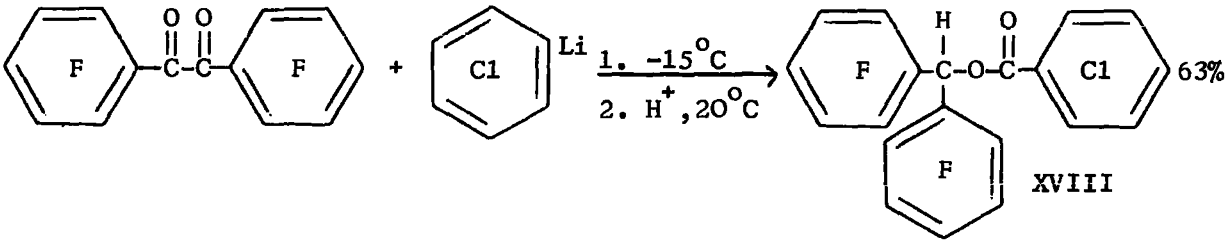
displacement of chloride ion. The position of the C=O stretch in the infrared spectrum, and the breakdown pattern in the mass spectrum, indicated the five-membered ring compound, tetrachloro-2,2-diphenylbenzofuran-3-one (XV), to be the correct structure. The following reaction mechanism can then be written:



It thus appears that phenyl migration occurs, implying that XVI is of higher energy than XVII. This can be explained by taking into account the bulky nature of the pentachlorophenyl group and suggesting that rearrangement takes place to relieve steric strain; this effect over-riding the difference in inductive effects of the two groups which would favour XVI over XVII.

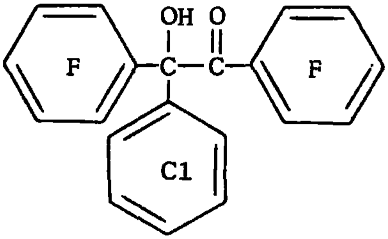
However, a second explanation is possible. Reversibility of the migration step has been observed with α-anisylanisoin (see section 4.3) although the energy of the starting material and products are the same. If the migration step were reversible in this case (i.e. XVI $\rightleftharpoons$ XVII), further reaction of XVII would upset the equilibrium, and XVI could be completely converted into the rearranged product, even though the equilibrium reaction favoured XVI over XVII.

Pentachlorophenyl-lithium also reacts with decafluorobenzil to yield an interesting product. Room temperature hydrolysis of the reaction mixture gave one major and several minor components, the former being obtained pure by recrystallisation from light petroleum, and identified as bis(pentafluorophenyl)methyl pentachlorobenzoate (XVIII). The

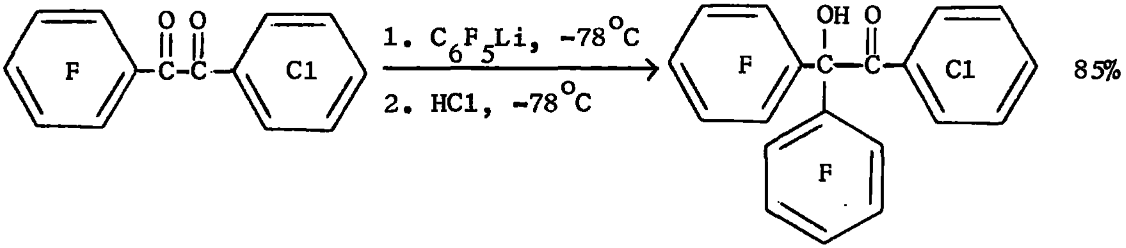


XVIII

absence of a hydroxyl peak in the infra-red spectrum and the presence of a strong parent peak in the mass spectrum ruled out the keto-alcohols XIX and XX (the parent peaks of keto-alcohols are generally absent or very weak). Pentachlorobenzoylbis(pentafluorophenyl)methanol, XX, was in fact prepared by the reaction of 2,3,4,5,6-pentachloropentafluorobenzil



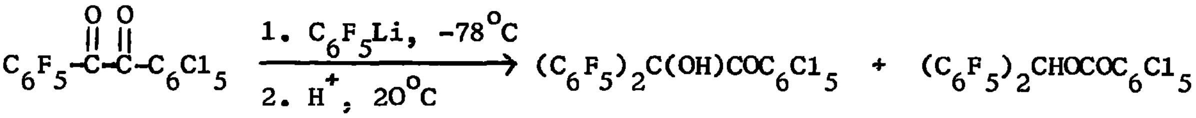
XIX



XX

with pentafluorophenyl-lithium at -78°C, followed by hydrolysis at -78°C, and showed typical properties of a keto-alcohol. ^{19}F N.m.r. confirmed that attack had occurred at the more reactive pentafluorobenzoyl group rather than at the pentachlorobenzoyl group.

Hydrolysis of this last reaction at room temperature gave two products in the ratio 4:1, the minor component being the keto-alcohol XX and the

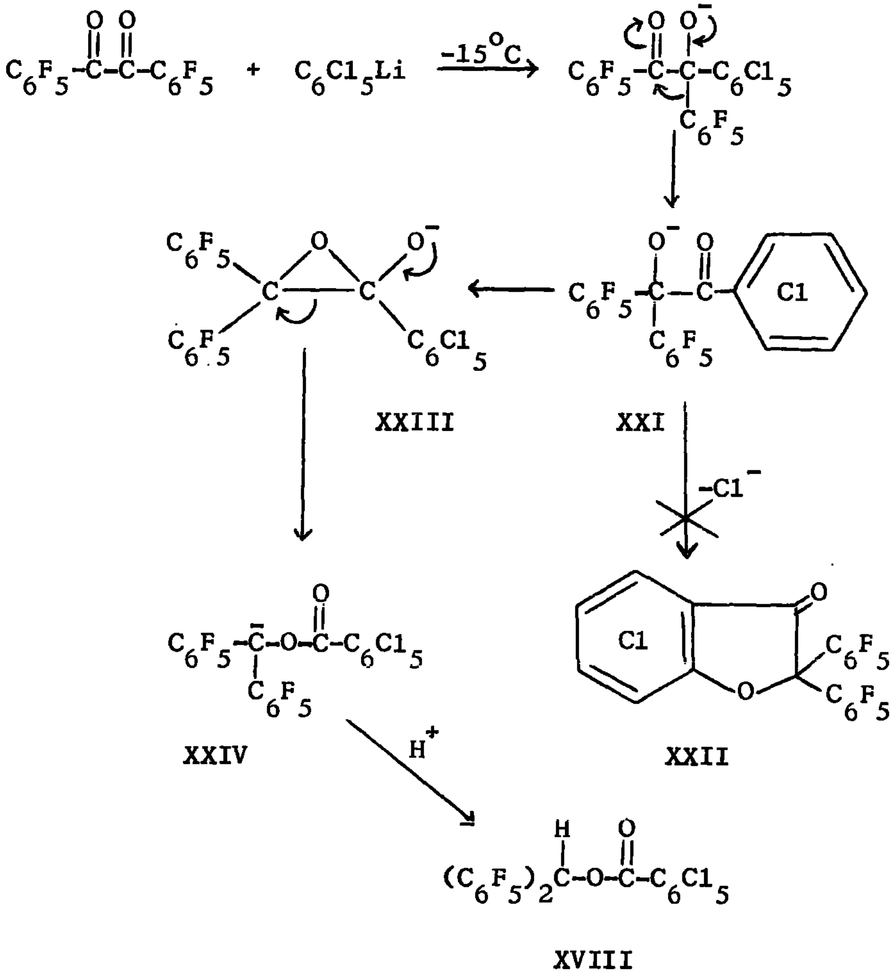


$$C_6F_5-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-C_6Cl_5 \xrightarrow[2.\ H^+,\ 20^\circ C]{1.\ C_6F_5Li,\ -78^\circ C} (C_6F_5)_2C(OH)COC_6Cl_5 + (C_6F_5)_2CHOCOC_6Cl_5$$

XX (20%) XVIII (80%)

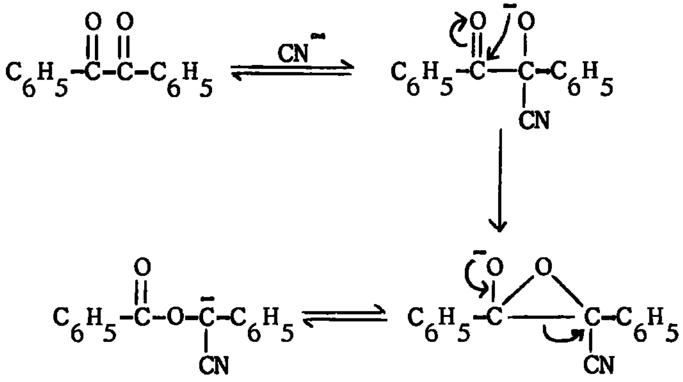
major component being identified as the previously prepared bis(pentafluorophenyl)methyl pentachlorobenzoate,XVIII. This reaction was useful evidence in elucidating the structure of XVIII, as it suggested that its formation must have at sometime involved the conjugate base of XX. The mass spectrum showed no loss of Cl and so ruled out a cyclised structure (i.e. XXI → XXII) of the type obtained in the reaction with benzil.

The mechanism for the formation of XVIII therefore probably involves initial addition of pentachlorophenyl-lithium to decafluorobenzil followed



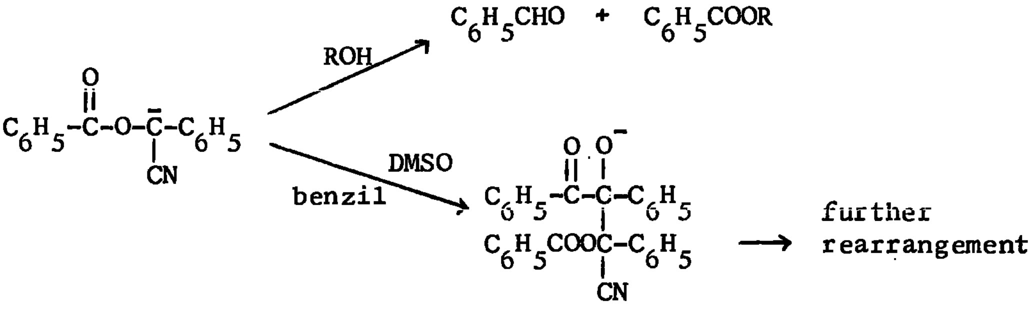
by pentafluorophenyl migration to give the anion XXI. Nucleophilic addition by oxygen at the adjacent carbonyl group gives the epoxide XXIII which by carbon-carbon bond cleavage forms the carbanion XXIV, hydrolysis yielding the benzoate ester XVIII. It is possible, although there is no supporting evidence, that some of these stages (e.g. XXI ⟶ XXIII, XXIII ⟶ XXIV) may be reversible.

Support for such a rearrangement mechanism comes from the reaction between benzil and cyanide ion where the following rearrangement has been shown to occur:[105]



XXV

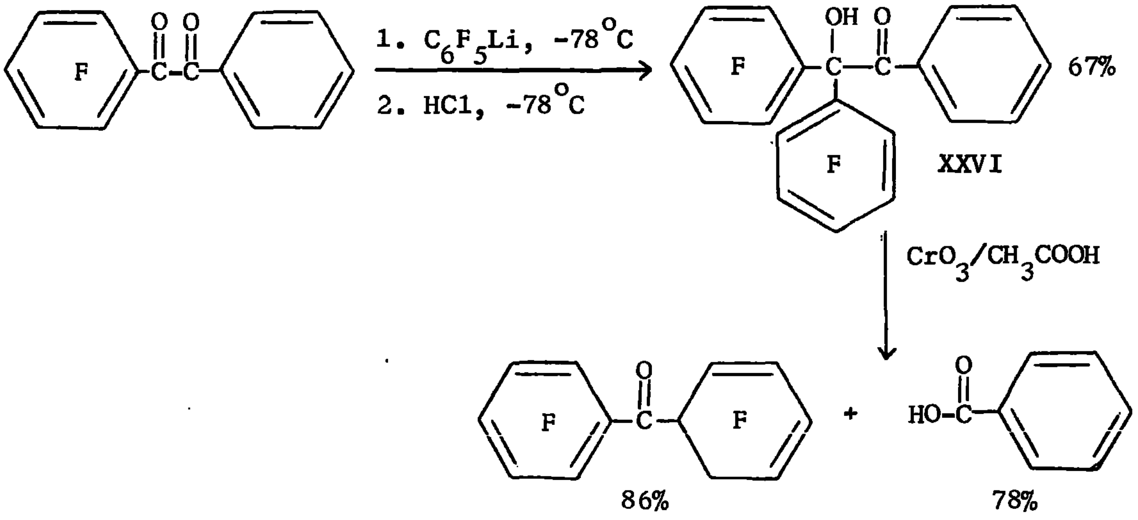
In ethanol, a protic solvent, cleavage of the carbanion XXV then took place to give benzaldehyde and ethyl benzoate, but in an aprotic solvent, dimethylsulphoxide, Trisler and Frye[106] found that further reaction occurred; the carbanion attacking another molecule of benzil



which then underwent further rearrangement. Reaction of the carbanion XXIV would not be expected however as there would be no available α-diketone and attack on a carbonyl group adjacent to the pentachlorophenyl group (e.g. XXI) would also be unlikely.

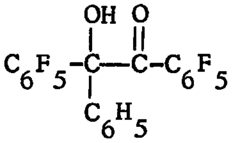
6.5. Reaction of decafluorobenzil with phenyl-lithium.

This reaction was examined under various conditions but always yielded a viscous liquid containing several components, none of which was present as a major product. Separation by column chromatography was unsuccessful as several of the components had similar R_f values. In an attempt to aid identification of the components, benzoylbis(pentafluorophenyl)methanol was prepared from 2,3,4,5,6-pentafluorobenzil and pentafluorophenyl-lithium, and characterised from its cleavage products after oxidation with chromium trioxide in acetic acid.



XXVI

Comparison of this keto-alcohol (XXVI) with the complex reaction mixture by v.p.c. revealed a compound with a similar retention time which was present when the reaction mixture was hydrolysed at -78°C, but absent when hydrolysis was effected at room temperature. Unfortunately, the straightforward addition product XXVII would probably also have a similar retention time, so no firm conclusions can be



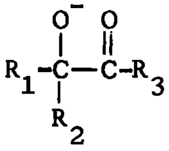
$$C_6F_5-C(OH)(C_6H_5)-C(=O)-C_6F_5$$

XXVII

drawn about the rearrangements taking place. It is possible however to envisage several reactions which may be occurring. Migration of pentafluorophenyl has already been observed in previous reactions, as has cyclisation with elimination of fluoride ion. It is also possible that nucleophilic displacement of ring fluorine by phenyllithium or ester formation as discussed in the last section may be taking place. The occurrence of several of these reactions would help to account for the complex nature of the reaction mixture.

6.6. Migratory aptitudes in the tertiary ketol rearrangement.

In section 4.3., factors affecting the migratory aptitudes and rates of migration of groups in the tertiary ketol rearrangement were discussed. It was suggested that, since bulky and electron-donating groups close to the anion centre will tend to destabilise XXVIII whereas electron-withdrawing groups will lead to stabilisation,

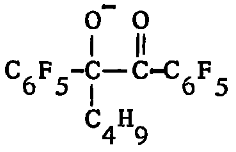


$$R_1-\underset{R_2}{\overset{O^-}{C}}-\overset{O}{\overset{\|}{C}}-R_3$$

XXVIII

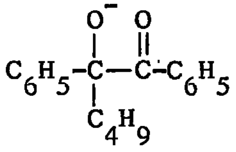
migration should occur to leave the best stabilising groups (e.g. R_1 and R_2) nearest the negative charge. It was also suggested that rearrangement should proceed more easily if the migrating group was able to stabilise a partial negative charge in the transition state.

The results discussed in this chapter are in excellent agreement with these suggestions. Thus in the reactions of butyl-lithium with benzil and decafluorobenzil, migration of phenyl and pentafluorophenyl was observed in preference to butyl. Furthermore, pentafluorophenyl migration in XXIX occurred at a lower temperature than phenyl migration



$$C_6F_5-\underset{C_4H_9}{\overset{O^-}{C}}-\overset{O}{\overset{\|}{C}}-C_6F_5$$

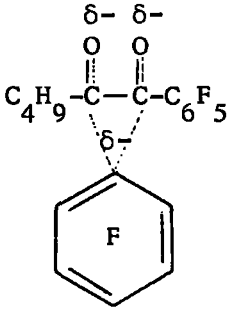
XXIX



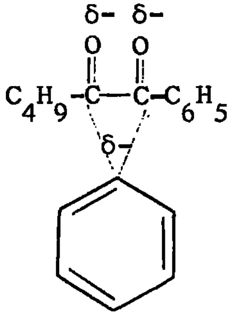
$$C_6H_5-\underset{C_4H_9}{\overset{O^-}{C}}-\overset{O}{\overset{\|}{C}}-C_6H_5$$

XXX

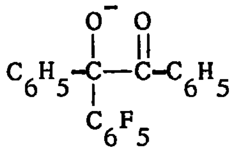
in XXX. Thus the activation energy for the rearrangement of XXIX must be less than for XXX, and this is a reflection of the greater ability of pentafluorophenyl compared to phenyl to stabilise negative charge in the transition state:



results in smaller activation energy than



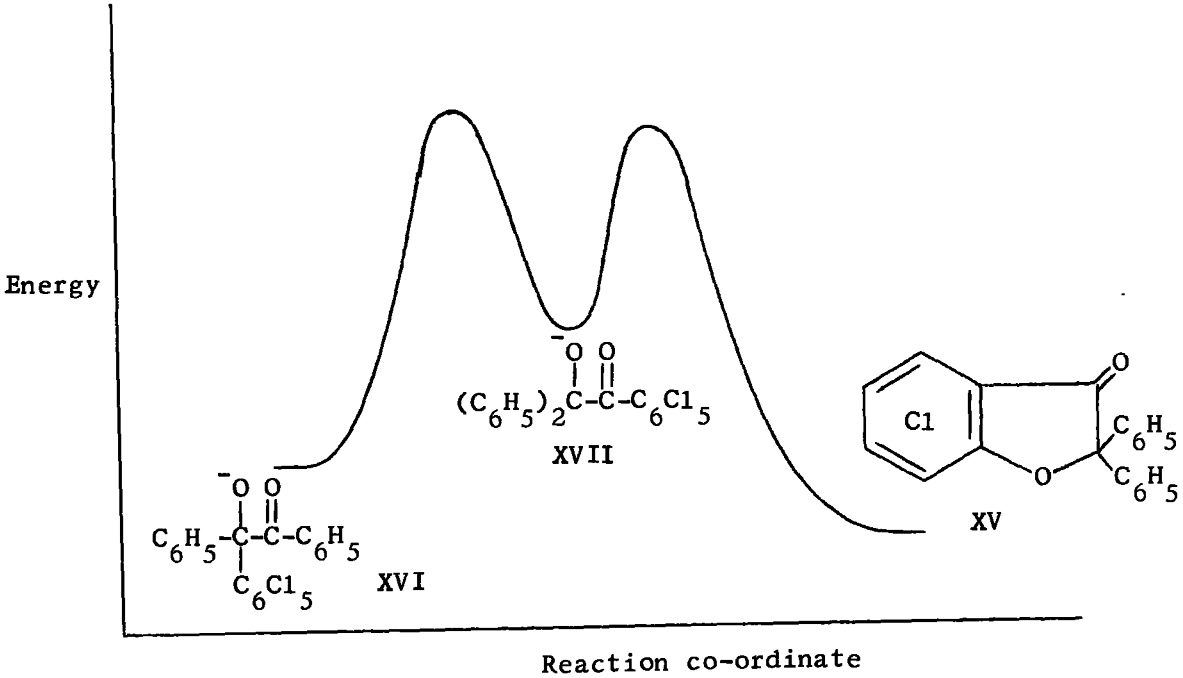
These results suggest the following order of migratory aptitude; $C_6F_5 > C_6H_5 > C_4H_9$, and this is reinforced by the inability to observe phenyl migration in XXXI.



$$C_6H_5-\overset{O^-}{\underset{C_6F_5}{C}}-\overset{O}{\overset{\|}{C}}-C_6H_5$$

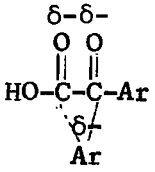
XXXI

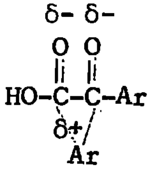
The reactions between pentachlorophenyl-lithium and benzil and decafluorobenzil (section 6.4) suggest that the order of migration for these groups is $C_6F_5 > C_6H_5 > C_6Cl_5$, as pentafluorophenyl migration again occurs more easily than phenyl. Whether in fact phenyl does migrate preferentially to pentachlorophenyl depends on the reversibility of the migration step. It is possible that XVI may be more stable than the rearranged anion XVII (see following diagram), but that in refluxing toluene, sufficient energy is gained for some of the less stable rearranged product to be formed, which can then eliminate chloride ion to give the benzofuran-3-one XV. A similar argument could in fact be applied to the reaction between pentachlorophenyl-lithium and decafluorobenzil, but it is more probable that pentafluorophenyl does



migrate preferentially to pentachlorophenyl as rearrangement occurs without requiring refluxing in toluene.

Finally, as the migration step in the tertiary ketol rearrangement is similar to that in the benzilic acid and ester rearrangements, the observed order of migratory aptitudes gives further support to the structure XXXII put forward earlier as a reasonable representation of


XXXII


XXXIII

the transition state, and makes a structure such as XXXIII seem even less likely.

EXPERIMENTAL

CHAPTER 7

Experimental for Chapter 2

Hexafluoroacetone was obtained from E.I. du Pont de Nemours and Co., and 2,3,4,5-tetrafluoro- and pentafluoro-aniline from Imperial Smelting Corp. Ltd. High test peroxide was obtained from Laporte Chemicals Ltd. and standardised with potassium permanganate.

Proton n.m.r. spectra were recorded on a Perkin-Elmer R.10 Spectrometer and mass spectra on an A.E.I. MS.9 mass spectrometer. V.p.c. work was performed on a Perkin-Elmer Fractometer. Typical examples only of each oxidation reaction are given.

7.1. Baeyer-Villiger oxidation of isobutyl methyl ketone.

Hexafluoroacetone (30·0 g., 0·181 moles) was bubbled into a vigorously stirred suspension of high test hydrogen peroxide (3·7 ml. 87%, 0·131 moles) in methylene chloride (20 ml.) contained in a 100 ml. two-necked flask fitted with a reflux condenser and exit bubbler, and cooled in an ice-bath. A single phase was obtained after addition of the gas, and to this stirred solution was added isobutyl methyl ketone (6·6 g., 0·066 moles) in methylene chloride (20 ml.) over two hours. After a period at reflux (5 hours) the reaction mixture was cooled and poured into water (100 ml.). The aqueous layer was separated and washed with methylene chloride, the washings being added to the original organic fraction. This solution was washed first with 5% sodium bicarbonate solution (2 x 70 ml.) and then with ferrous sulphate solution, and dried ($MgSO_4$). Removal of solvent left a residue (8·3 g.), which was analysed for ester content by saponification. This involved heating a weighed fraction of product with excess methanolic sodium hydroxide, and, after hydrolysis, back titrating the unconsumed base with standard hydrochloric acid. The yield of isobutyl acetate was found to be 73%. A pure sample was obtained by first removing ketone starting material by refluxing a portion of the reaction product (1•5 g.) with Girard's reagent P (5 g.) in methanol (15 ml.) and acetic acid (1 ml.) for 15 hours. On cooling, the reaction mixture was poured into water (100 ml.) and extracted with methylene chloride (2 x 75 ml.). The non-aqueous extracts were dried ($MgSO_4$), and the solvent removed to leave a residue which, after preparative scale v.p.c. (di-n-decylphthalate, 100^o), yielded isobutyl acetate with an infra-red spectrum identical with that of an authentic sample.

7.2. Oxidation of n-amyl methyl ketone.

Hexafluoroacetone (30 g., 0•181 moles) was bubbled into a vigorously stirred suspension of hydrogen peroxide (3•7 ml. 87%, 0•131 moles) in methylene chloride (20 ml.) in a flask cooled in an ice-bath. n-Amyl methyl ketone (7•5 g., 0•066 moles) in methylene chloride (20 ml.) was added dropwise over two hours, and the reaction mixture refluxed for five hours before being cooled and poured into water (100 ml.). After work-up as described in 7.1., a residue (9 g.) was obtained which was analysed for ester content (see 7.1.). The yield of n-amyl acetate was found to be 81%, and preparative scale v.p.c. (di-n-decylphthalate, 100^o) yielded the pure ester with an infra-red spectrum identical with that of an authentic sample.

7.3. Oxidation of cyclohexanone.

Hydrogen peroxide (2 ml. 87%, 0•071 moles) in methylene chloride (4 ml.) was stirred under an atmosphere of hexafluoroacetone (18 g., 0•108 moles) until uptake of gas had practically stopped. Cyclohexanone (3•4 g., 0•035 moles) in methylene chloride (5 ml.) was added dropwise over one hour, and the reaction mixture refluxed for three hours, before being poured into water (100 ml.) and extracted with methylene chloride (3 x 40 ml.). The organic extracts were washed with water, sodium carbonate solution and ferrous sulphate solution, and dried ($MgSO_4$). Removal of solvent left a residue which was distilled at reduced pressure to give a fraction (b.p. $58-60^{\circ}/0{\cdot}002$ mm.) which was shown by a comparison of its spectroscopic properties and v.p.c. retention time with those of an authentic sample to be pure caprolactone (2•0 g., 50%).

7.4. Oxidation of acetophenone.

Hexafluoroacetone (30•0 g., 0•181 moles) was bubbled into a vigorously stirred suspension of hydrogen peroxide (3•86 ml. 87%, 0•135 moles) in methylene chloride (30 ml.) contained in a flask cooled in an ice-bath. After addition of the gas, acetophenone (7•85 g., 0•065 moles) in methylene chloride (20 ml.) was added dropwise over thirty minutes, and the reaction mixture stirred at room temperature for a further five hours. The organic layer was separated, washed with 10% sodium carbonate solution (100 ml.), and dried ($MgSO_4$). Removal of solvent left a residue which on distillation (45-48°/ 0•7 mm.) gave a two-component mixture (5•15 g.). The v.p.c. retention times of the components were identical to those of authentic samples of acetophenone and phenyl acetate, and the percentage of each in the distillate was estimated from an n.m.r. spectrum of the mixture, and also by comparing the areas of v.p.c. peaks produced by known amounts of ester and ketone with those of the reaction product. It was thus estimated that the product contained 1•7 g. phenyl acetate and 3•45 g. recovered acetophenone. The yield of phenyl acetate based on the amount of acetophenone consumed was 34%.

7.5. Attempted oxidation of benzophenone.

Hexafluoroacetone (30•0 g., 0•181 moles) was bubbled into a vigorously stirred suspension of hydrogen peroxide (3•5 ml. 87%, 0•124 moles) in methylene chloride (10 ml.). When the addition of gas was complete, benzophenone (13•7 g., 0•075 moles) in methylene chloride (25 ml.) was added and the reaction mixture refluxed for two hours, before being allowed to stir at room temperature overnight. On addition of ferrous sulphate solution, a vigorous reaction followed, indicating that little oxidising agent had been consumed. The organic layer was separated and extracted with 10% sodium carbonate solution (2 x 50 ml.), the aqueous extracts being washed with methylene chloride. The combined organic extracts were dried ($MgSO_4$), and the solvent removed to leave a dark solid, sublimation of which gave practically pure benzophenone (8•5 g.) and no evidence for any phenyl benzoate.

7.6. Oxidation of aniline to nitrobenzene.

Hexafluoroacetone (32•0 g., 0•193 moles) was bubbled into a vigorously stirred suspension of hydrogen peroxide (3•9 ml. 87%, 0•138 moles) in methylene chloride (20 ml.). Aniline (3•5 g., 0•038 moles) in methylene chloride was added dropwise to the oxidising agent over 1•5 hours, and the reaction mixture stirred overnight, before water (100 ml.) and methylene chloride (40 ml.) were added. The aqueous layer was separated and extracted with methylene chloride, the extracts being added to the original organic layer, which was then washed with 10% sodium carbonate solution. The alkali washings were extracted with methylene chloride and the combined organic extracts dried ($MgSO_4$). Removal of solvent gave a dark product which was distilled (208-210°) to give nitrobenzene (2•9 g., 63%) which possessed the same spectroscopic properties and v.p.c. retention time as an authentic sample.

7.7. Oxidation of 2,3,4,5-tetrafluoroaniline.

Hexafluoroacetone (25•0 g., 0•151 moles) was bubbled into a vigorous stirred suspension of hydrogen peroxide (2•9 ml. 87%, 0•103 moles) in methylene chloride (30 ml.). After the complete addition of the gas, the oxidising agent was transferred under nitrogen to a dropping funnel and added dropwise over two hours to a stirred solution of 2,3,4,5-tetrafluoroaniline (5•1 g., 0•031 moles) in methylene chloride (20 ml.). An immediate dark colouration was obtained, and after stirring for 18 hours, water (90 ml.) and methylene chloride (70 ml.) were added. The aqueous layer was washed with methylene chloride, and the combined organic solutions shaken with 5% sodium bicarbonate solution. The alkaline extracts were washed twice with methylene chloride, and the washings added to the organic solution. The latter was dried ($MgSO_4$) and distilled to give only solvent and traces of green and turquoise liquid on the condenser, possibly due to small amounts of the nitroso compound. Sublimation ($80^{\circ}/10^{-2}$ mm.) of the residue (4•0 g.) gave an orange product (0•5 g., 10%) which was recrystallised from b.p. 40-60° petroleum ether to give octafluoro-2,2'-dihydroazobenzene, m.p. 109-110° (lit.,[37] 111-112°), (Found: C, 44•6; H, 0•55; F, 46•1; N, 9•0. Calc. for $C_{12}H_2F_8N$: C, 44•2; H, 0•6; F, 46•6; N, 8•6%).

The mass spectrum showed a parent peak at M326 (relative abundance 35%), and peaks corresponding to $C_6F_4H\overset{+}{N}_2$ (M177, 35%), $C_6F_4H^+$ (M149, 100%), and $C_5F_2H^+$ (M99, 40%).

7.8. Oxidation of pentafluoroaniline.

Hexafluoroacetone (30•0 g., 0•181 moles) was bubbled into vigorously stirred hydrogen peroxide (3•65 ml. 87%, 0•129 moles) in methylene chloride (20 ml.). Pentafluoroaniline (6•8 g., 0•037 moles) in methylene chloride (20 ml.) was added dropwise over 1•5 hours, after which time a black solution was obtained. Work up as described in 7.7 gave a residue which was sublimed ($80^{\circ}/10^{-2}$ mm.) to give an orange product (0•8 g., 12%), and recrystallisation from ethanol yielded decafluoroazobenzene, m.p. 140-141° (lit.,[38] 142-143°).

The mass spectrum showed a strong parent peak at M362 (100%) and peaks corresponding to $C_6F_5N_2^+$ (M195, 5%), $C_6F_5^+$ (M167, 13%) and $C_5F_3^+$ (M117, 4%).

7.9. Oxidation of mesitylene.

A. Without boron trifluoride.

The oxidising agent, prepared from hexafluoroacetone (30•0 g., 0•181 moles) and hydrogen peroxide (3•2 ml. 87%, 0•113 moles) in methylene chloride (25 ml.), was added dropwise over two hours to a stirred solution of mesitylene (39•7 g., 0•331 moles) in methylene chloride (30 ml.). After stirring for 24 hours, water (100 ml.) was added, and the non-aqueous layer separated and washed with 5% sodium bicarbonate solution (2 x 70 ml.). The aqueous extract was washed with methylene chloride (3 x 30 ml.) and the washings combined with the original organic solution. The latter was dried ($MgSO_4$) and most of the solvent removed by distillation. Further distillation (166-168°) gave recovered mesitylene (26•5 g.), and sublimation of the residual solid yielded practically pure mesitol (5•9 g., 38%), leaving a black residue (3•5 g.). Recrystallisation of the mesitol from aqueous methanol gave white needle crystals, m.p. 69-70° (lit.,[32] 69-70°), with spectroscopic properties and v.p.c. retention time identical with those of an authentic sample.

B. With added boron trifluoride.

The hexafluoroacetone-hydrogen peroxide adduct was prepared from hexafluoroacetone (29•0 g., 0•175 moles) and hydrogen peroxide (3•0 ml. 87%, 0•106 moles) in methylene chloride (7 ml.). It was then transferred to a dropping funnel and added over 1•5 hours to a stirred solution of mesitylene (38 g., 0•317 moles) in methylene chloride (25 ml.) contained in a three-necked flask cooled to -20°. At the same time, boron trifluoride was bubbled through the reaction mixture, which quickly darkened. After being allowed to warm to room temperature, the reaction mixture was poured into water (300 ml.) and methylene chloride (200 ml.). A precipitate which was obtained was filtered off and the organic layer from the filtrate was washed in turn with water, sodium carbonate solution, and ferrous sulphate solution, and dried ($MgSO_4$). Most of the solvent was removed to leave a residue which was shown by v.p.c. to contain mesitylene and at least six other components. The mesitylene was removed by reduced pressure distillation, but it was not possible to separate any of the other components of the mixture (4 g., b.p. 120-150°/0•002 mm.), which showed no evidence for the presence of mesitol. Sublimation of the precipitate (4 g.) obtained earlier gave only a trace of mesitylene, leaving polymeric material.

CHAPTER 8

Experimental for Chapter 5

Pentafluorobenzene and 1,2,3,4-tetrafluorobenzene were obtained from Imperial Smelting Corp. Ltd., and hexachlorobenzene was recrystallised from benzene. V.p.c. work was performed on a Griffin and George D6 Gas Density Balance Chromatograph. ^{1}H N.m.r. spectra were recorded on a Perkin-Elmer R.10 Spectrometer or on a Varian A56/60D Spectrometer in CCl_4 solution with TMS as internal reference, unless otherwise stated.

8.1. Preparation of decafluorobenzil.

Butyl-lithium (31 ml. of a 2•3M hexane solution, 71•5 mmoles) in dry hexane (20 ml.) was added dropwise to a stirred solution of pentafluorobenzene (12 g., 71•5 mmoles) in dry ether (150 ml.) and dry hexane (100 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 dimethyl oxalate (4•2 g., 35•6 mmoles) in dry ether (40 ml.) was added. After stirring at -78° for a further 14 hours, the reaction mixture was hydrolysed at this temperature by passing in HCl gas for ~30 minutes. It was then allowed to attain room temperature and water (100 ml.) was added to dissolve precipitated salts. The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a product which v.p.c. indicated to contain two major components. Distillation at reduced pressure yielded the more volatile compound, methyl pentafluorobenzoylformate (4•3 g., 47%), b.p. 47-48°/0·001 mm., (Found: C, 42·8; H, 0·8; F, 37·8. $C_9H_3F_5O_3$ requires: C, 42·5; H, 1·2; F, 37·4%). The infra-red spectrum exhibited a broad absorption in the region 1700-1740 cm.$^{-1}$ due to the overlap of the ketone C=O stretch with the ester C=O stretch.

Sublimation (80°/0·001 mm.) of the remaining product gave a yellow solid (6 g., 43%) which was recrystallised from b.p. 40-60 petroleum ether to yield pure decafluorobenzil, m.p. 79-80° (other workers[68] who have prepared this compound have quoted m.p. 80-80·5°) (Found: C, 43·3; F, 49·1. $C_{14}F_{10}O_2$ requires: C, 43·2; F, 48·8%). The infra-red spectrum exhibited two absorptions in the C=O stretch region at ~1705 cm.$^{-1}$ and ~1720 cm.$^{-1}$. For benzil itself, the absorptions are observed at ~1660 cm.$^{-1}$ and ~1675 cm.$^{-1}$.

8.2. Preparation of methyl decafluorobenzilate.

Butyl-lithium (10·3 ml. 2·3M solution, 23·8 mmoles) in dry hexane (20 ml.) was added dropwise to a stirred solution of pentafluorobenzene (4 g., 23·8 mmoles) in dry ether (90 ml.) and dry hexane (60 ml.) contained in a 500 ml. flask which had previously been purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for 2 hours, and then dimethyl oxalate (1·4 g., 11·9 mmoles) in dry ether (20 ml.) was added. The reaction mixture was allowed to warm slowly to room temperature overnight and then hydrolysed with dilute HCl (100 ml.). The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a viscous liquid (4·5 g.) which v.p.c.

indicated to contain one major product (~90%) and one minor product (~10%). Although purification by distillation was unsuccessful, separation of the components was achieved by column chromatography using b.p. 40-60 petroleum ether-chloroform (4:1) as eluent on a silica-packed column. The minor product was eluted first, and by comparison of its spectroscopic properties with an authentic sample was shown to be tris(pentafluorophenyl)methanol. Continued elution gave a viscous oil which, on prolonged standing, gave crystals of methyl decafluorobenzilate, m.p. 79-80° (Found: C, 42•4; H, 0•95; F, 45•5. $C_{15}H_4F_{10}O_3$ requires: C, 42•7; H, 0•95; F, 45•0%). V.p.c. analysis on the reaction product indicated that the ester was formed in 79% yield.

8.3. Reaction between pentafluorophenyl-lithium and diethyl oxalate.

A. Hydrolysis at 0°.

Butyl-lithium (15•5 ml. 1•15M solution, 17•8 mmoles) in dry hexane (20 ml.) was added dropwise to a stirred solution of pentafluorobenzene (3•0 g., 17•8 mmoles) in dry ether (60 ml.) and dry hexane (40 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was allowed to stir at this temperature for two hours, and then diethyl oxalate (1•25 g., 8•6 mmoles) was added. After stirring at -78° for a further two hours, the reaction mixture was allowed to warm to 0° over a two-hour period and hydrolysed with dilute HCl (100 ml.). The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a viscous liquid (2•7 g.), shown by v.p.c. to contain two major components. Distillation at reduced pressure gave a fraction which contained a single component, ethyl pentafluorobenzoylformate (0•9 g., 39%), b.p. 58-60°/0•002 mm. (Found: C, 44•7; H, 1•6; F, 35•9. $C_{10}H_5F_5O_3$ requires: C, 44•8; H, 1•9; F, 35•4%). The infra-red spectrum showed C=O stretching frequencies at ~1738 cm.$^{-1}$ (ketone carbonyl) and ~1755 cm.$^{-1}$ (ester carbonyl).

Further distillation (88-90°/0•001 mm.) of the reaction product gave a higher boiling fraction, shown by v.p.c. to be almost pure (1•5 g., 40%), although preparative scale v.p.c. (silicone elastomer, 200°) was necessary to obtain an analytically pure sample of the viscous ethyl decafluorobenzilate (Found: C, 44•2; H, 1•3; F, 44•0. $C_{16}H_6F_{10}O_3$ requires: C, 44•1; H, 1•4; F, 43•6%).

The proton n.m.r. spectrum showed three resonances, a triplet at 8•67τ (relative intensity 3, $-\mathrm{C}\underline{\mathrm{H}}_3$, J = 7•3 Hz), a quartet at 5•68τ (relative intensity 2, $-\mathrm{C}\underline{\mathrm{H}}_2-$), and a single peak at ~4•96τ (relative intensity 1, $-\mathrm{O}\underline{\mathrm{H}}$).

B. Hydrolysis at -36°.

Butyl-lithium (20•7 ml. 1•15M solution, 23•8 mmoles) in hexane (20 ml.) was added dropwise to a stirred solution of pentafluorobenzene (4•0 g., 23•8 mmoles) in ether (90 ml.) and hexane (30 ml.) contained in a flask cooled to -78° and previously purged with dry nitrogen. After stirring at this temperature for two hours, the mixture was allowed to warm to -36°, and diethyloxalate (1•6 g., 11•0 mmoles) was added. The reaction mixture was stirred for 30 minutes and hydrolysed with gaseous HCl. It was then allowed to attain room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a viscous liquid (3•4 g.) which was found by v.p.c. analysis to consist of ethyl pentafluorobenzoylformate (1•7 g., 58% yield), decafluorobenzil (1•1 g., 26%), and ethyl decafluorobenzilate (0•6 g., 12%).

8.4. Reaction between pentafluorophenyl-lithium and methyl pentafluorobenzoylformate - hydrolysis at -78°.

Butyl-lithium (3•4 ml. 2•3M solution, 7•8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (1•3 g., 7•8 mmoles) in dry ether (90 ml.) and dry hexane (60 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was stirred for two hours and methyl pentafluorobenzoylformate (2•0 g., 7•8 mmoles) was added. After a further three hours, the reaction mixture was hydrolysed with gaseous HCl at -78°, then warmed to room temperature and water (100 ml.) added. The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a yellow oil (2•7 g.) which was shown by a comparison of the retention times of the components with those of authentic samples to contain recovered methyl pentafluorobenzoylformate (5%), decafluorobenzil (5%), and methyl decafluorobenzilate (90%). The yield of benzilate ester in the product based on the amount of keto-ester consumed was 79%.

8.5. The rearrangement of decafluorobenzil with methoxide ion in dimethylcarbonate.

Sodium methoxide (2 ml. of a 0•1M solution in methanol, 0•2 mmoles) in dry dimethylcarbonate (5 ml.) was added dropwise to a stirred solution of decafluorobenzil (1 g., 2•56 mmoles) in dimethylcarbonate (50 ml.) at 80°, in a flask previously purged with dry nitrogen. The yellow colour due to the decafluorobenzil was discharged before the addition of the sodium methoxide solution was complete.

The reaction mixture was fractionally distilled, and each fraction analysed by v.p.c. - only methanol and dimethylcarbonate were present. The residue was poured into water (50 ml.) and extracted with ether. The organic extracts were dried ($MgSO_4$), and the solvent again carefully removed by distillation. V.p.c. analysis of the residue did not show any trace of either methyl pentafluorobenzoate or methyl pentafluorobenzoylformate which might have been formed if intermolecular rearrangement took place. The only product obtained was methyl decafluorobenzilate (1 g., 92%).

8.6. The rearrangement of decafluorobenzil in the presence of ethoxide ion.

A solution of sodium ethoxide was prepared from sodium (0•03 g., 1•3 mmoles) and ethanol (10 ml.). After the addition of ~5% of this solution over ~ 2 seconds to a solution of decafluorobenzil (0•5 g., 1•28 mmoles) in ethanol (30 ml.) at 80°, the yellow colour due to the α-diketone was completely discharged. The reaction mixture was poured into water (100 ml.) and extracted with ether (3 x 50 ml.), and the ether extracts dried ($MgSO_4$). Removal of solvent left a single component product (0•5 g.), shown by a comparison of its spectroscopic properties with those of an authentic sample to be ethyl decafluorobenzilate.

8.7. Reaction between pentachlorophenyl-lithium and dimethyl oxalate.

A. Hydrolysis at -78°.

Butyl-lithium (12•2 ml. 2•3M solution, 28 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred suspension of hexachlorobenzene (8 g., 28 mmoles) in dry ether (400 ml.) contained in a flask previously purged with dry nitrogen and cooled to -15°. The resulting pale yellow solution of pentachlorophenyl-lithium was stirred at this temperature for 30 minutes, and then cooled to -78°. Dimethyl oxalate (1•65 g., 14 mmoles) was added and the reaction mixture stirred for a further 8 hours, before hydrolysis at -78° with gaseous HCl. It was then allowed to attain room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a yellow residue (9•4 g.) which v.p.c. indicated to be a two-component mixture. Fractional sublimation (70°/0•001 mm.) gave pentachlorobenzene (3•3 g., 47%) m.p. (recrystallised from methanol) 85-86°, (lit.[49] 87•8-88•6°) showing the correct spectroscopic properties; and (120°/0•001 mm.) <u>methyl pentachlorobenzoylformate</u> (3•1 g., 34%), m.p. 131-2°, (Found: C, 32•8; H, 1•15; Cl, 54•3. $C_9H_3Cl_5O_3$ requires: C, 33•1; H, 0•9; Cl, 54•4%). The residual material did not sublime under conditions up to 200°/0·001 mm.

The infra-red spectrum of the benzoylformate showed C=O stretching frequencies at ~1729 cm.$^{-1}$ (ketone carbonyl) and ~1758 cm.$^{-1}$ (ester carbonyl).

B. Hydrolysis at 20°.

Butyl-lithium (12 ml. 2·35M solution, 28 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred suspension of hexachlorobenzene (8 g., 28 mmoles) in dry ether (400 ml.) contained in a flask previously purged with dry nitrogen and cooled to -15°. A pale yellow solution was obtained, and after stirring for 30 minutes, dimethyl oxalate (1·65 g., 14 mmoles) was added. The reaction mixture was allowed to warm to room temperature overnight and hydrolysed with dilute HCl. After filtering to remove insoluble material, the organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave an orange residue which was combined with the previous precipitate (total, 8·9 g.). Fractional sublimation (120°/0·001 mm.) gave first a mixture (1·2 g.) shown by v.p.c. to contain pentachlorobenzene and methyl pentachlorobenzoylformate, and at a higher temperature (200°/0·001 mm.) a solid (4·7 g.) which was insoluble in most common solvents. Recrystallisation from nitrobenzene however, gave yellow crystals of <u>decachlorobenzil</u> (1·5 g., 20%), m.p. 328-9° (other workers,[68] who have recently prepared this compound have quoted m.p. 320-322°), (Found: C, 30·6; Cl, 64·0. $C_{14}Cl_{10}O_2$ requires: C, 30·3; Cl, 64·0%). The infra-red spectrum showed a C=O stretch at ~1728 cm.$^{-1}$.

On standing, the nitrobenzene filtrate yielded white crystals (1•0 g.) which analysed correctly for methyl decachlorobenzilate m.p. 234-235° (Found: C, 31•0; H, 0•7; Cl, 60•4. $C_{15}H_4C_{10}O_3$ requires: C, 30•7; H, 0•85; Cl, 60•6%). The infra-red spectrum showed an O-H stretch (~3420 $cm.^{-1}$), C-H stetch (~2940 $cm.^{-1}$) and C=O stretch (~1725 $cm.^{-1}$), but the highest observable peak in the mass spectrum corresponded only to $C_6Cl_5CO^+$.

In an attempt to characterise the product further, a portion of the material (0•5 g.) was heated with chromium trioxide (0•2 g., 2•0 mmoles) in acetic acid (15 ml.) and water (0•5 ml.) at 120° for 2 hours. The reaction mixture was cooled, poured into water, and extracted several times with ether. The ether extracts were dried ($MgSO_4$), and the solvent removed to leave a residue (0•45 g.) which t.l.c. indicated to contain, apart from recovered starting material, only a trace of a second component.

8.8. Preparation of octafluoro-2,2'-dihydrobiphenyl.

The method used is that described by Tamborski and Soloski.[107]

Butyl-lithium (87 ml. 2•3M solution, 0•2 moles) was added dropwise to a stirred solution of 1,2,3,4-tetrafluorobenzene (30 g., 0•2 moles) in tetrahydrofuran (150 ml., freshly distilled from lithium aluminium hydride) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for 30 minutes, and cuprous iodide (39 g., 0•2 moles) was added. After stirring for a further 21 hours, the reaction mixture was allowed to warm slowly to room temperature, and oxygen was bubbled through, causing a rise in temperature. Oxidation was continued until the reaction mixture returned to room temperature (~2 hours). The mixture was then hydrolysed with dilute HCl, extracted with ether and dried ($MgSO_4$). Removal of solvent left a dark solid which was dissolved in the minimum volume of b.p. 40-60 petroleum ether, and eluted from a neutral grade alumina column. The product was eluted rapidly, and removal of solvent gave a solid which was recrystallised from ethanol to yield octafluoro-2,2'-dihydrobiphenyl (18 g., 60%) which showed the correct spectroscopic properties.

8.9. Reaction of octafluoro-2,2'-dilithiobiphenyl with diethyl oxalate.

Tetrahydrofuran (150 ml.), which had been freshly distilled from lithium aluminium hydride, was contained in a flask previously purged with dry nitrogen and cooled to -78^{o}. Butyl-lithium (14•6 ml. 1•15M solution, 16•8 mmoles) in dry hexane (10 ml.) was added dropwise, followed by a solution of octafluoro-2,2'-dihydrobiphenyl (2•5 g., 8•4 mmoles) in tetrahydrofuran (30 ml.). The mixture was stirred at -78^{o} for 4 hours, and diethyl oxalate (1•22 g., 8•4 mmoles) added. After stirring for a further 1•5 hours, the reaction mixture was hydrolysed with gaseous HCl. It was then allowed to warm to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a residue which was distilled ($90-120^{o}/0{\cdot}005$ mm.) to give a viscous liquid (2•7 g.), shown by v.p.c. to contain two compounds, a major component (~70%) and a minor component (~30%) with a longer retention time. Separation was effected by elution on a silica-packed column using b.p. 40-60 petroleum ether-benzene (1:1) as eluent. The major product, a viscous liquid was eluted first and identified as ethyl tetrafluoro-2-(2',3',4',5'-tetrafluorophenyl)benzoylformate, b.p. 95-97°/0•005 mm. (Found: C, 48•5; H, 1•5; F, 38•7. $C_{16}H_6F_8O_3$ requires: C, 48•2; H, 1•5; F, 38•2%. The yield of benzoylformate in the distilled product was calculated from v.p.c. analysis to be 57%.

Continued elution yielded, after removal of solvent, a white solid, 9-carbethoxyoctafluorofluoren-9-ol, m.p. 77-78° (Found: C, 48•1; H, 1•6; F, 37•8. $C_{16}H_6F_8O_3$ requires: C, 48•2; H, 1•5; F, 38•2%). The yield of the fluorenol in the distilled product was calculated from v.p.c. analysis to be 23%.

8.10. Reaction of octafluoro-2,2'-dilithiobiphenyl with dimethyl oxalate.

Octafluoro-2,2'-dilithiobiphenyl was prepared by the procedure given in 8.9 from octafluoro-2,2'-dihydrobiphenyl (3 g., 10•1 mmoles) and butyl-lithium (8•8 ml. 2•3M solution, 20•2 mmoles) in tetrahydrofuran (150 ml.). Dimethyl oxalate (1•1 g., 9•35 mmoles) in tetrahydrofuran (25 ml.) was added, and after stirring for 25 minutes, the reaction mixture was hydrolysed at -78° with gaseous HCl. It was then allowed to warm slowly to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left an orange residue (3•6 g.) and careful liquid sublimation (80°/0•005 mm.)

yielded a single component (v.p.c.) which on prolonged standing gave a white solid, methyl tetrafluoro-2-(2',3',4',5'-tetrafluorophenyl)-benzoylformate (1•9 g., 49%) m.p. 47-48°, (Found: C, 47•2; H, 1•2; F, 39•9. $C_{15}H_4F_8O_3$ requires: C, 46•9; H, 1•05; F, 39•6%). Attempts to obtain further fractions by sublimation resulted in decomposition of the residual material.

8.11. Preparation of 2,3,4,5,6-pentafluorobenzil.

Butyl-lithium (12•4 ml. 2•4M solution, 29•8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (5•0 g., 29•8 mmoles) in dry ether (150 ml.) and dry hexane (100 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was allowed to stir at this temperature for two hours, diethyl oxalate (4•35 g., 29•8 mmoles) was added, and the reaction mixture stirred for a further three hours.

Butyl-lithium (12•4 ml. 2•4M solution, 29•8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of iodobenzene (6•07 g., 29•8 mmoles) in dry ether (60 ml.) and dry hexane (35 ml.) contained in a flask previously purged with dry nitrogen and cooled to -10°. The mixture was allowed to stir for 2 hours, cooled to -78°, and transferred under nitrogen to a precooled dropping funnel. The solution of phenyl-lithium at -78° was added dropwise to the pentafluorophenyl-lithium-dimethyl oxalate reaction mixture, which was then stirred for 36 hours, and hydrolysed at -78° with gaseous HCl. The reaction mixture was allowed to warm to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a residue which v.p.c. indicated to contain three main components. The first of these, butyl iodide, was removed by reduced pressure distillation together with iodine crystals which sublimed from the reaction mixture. Further distillation (58°/0•002 mm.) gave ethyl pentafluorobenzoylformate (3 g., 38%), which showed the correct spectroscopic properties, and (110-112°/0•001 mm.) a single component product (3•6 g., 40%) which was recrystallised from b.p. 40-60 petroleum ether to yield 2,3,4,5,6-pentafluorobenzil, m.p. 70-71° (Found: C, 56•2; H, 1•8; F, 31•8. $C_{14}H_5F_5O_2$ requires: C, 56•0; H, 1•7; F, 31•7%) as yellow crystals. At higher temperatures (112-130°/0•001 mm.) a fraction (0•8 g.) containing several unidentified components was obtained, leaving a black residue (1•3 g.).

The infra-red spectrum of 2,3,4,5,6-pentafluorobenzil showed two absorptions in the C=O stretch region at $\sim$1685 $cm.^{-1}$ and $\sim$1715 $cm.^{-1}$

8.12. Reaction between ethyl pentafluorobenzoylformate and phenyl-lithium.

Butyl-lithium (1•88 ml. 2•4M solution, 4•52 mmoles) in dry hexane (10 ml.) was added dropwise to a solution of iodobenzene (0•92 g., 4•52 mmoles) in ether (100 ml.) and hexane (50 ml.) contained in a flask previously purged with dry nitrogen and cooled to -10°. The mixture was stirred at this temperature for two hours, cooled to -78°, and ethyl pentafluorobenzoylformate (1•2 g., 4•52 mmoles) added rapidly. After stirring for a further 4 hours, the reaction mixture was hydrolysed at -78° with gaseous HCl. It was then allowed to warm to room temperature, water (100 ml.) was added, and the organic layer was separated and dried ($MgSO_4$). Removal of solvent left a pale red oil (1·9 g.) which v.p.c. indicated to contain two major components apart from the keto-ester starting material. It was not possible to obtain a separation by distillation but ^{19}F n.m.r. evidence suggested that both compounds resulted from attack at the ketone carbonyl group, and no evidence was found for any of the α-diketone prepared in 8.11.

8.13. Preparation of 2,3,4,5,6-pentachloropentafluorobenzil.

A. Attempted reaction of pentachlorophenyl-lithium with the pentafluorophenyl-lithium-dimethyl oxalate complex.

Butyl-lithium (10·6 ml. 2·24M solution, 23·8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (4·0 g., 23·8 mmoles) in dry ether (150 ml.) and hexane (100 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was stirred for 2 hours, dimethyl oxalate (2·8 g., 23·8 mmoles) added, and the reaction stirred for a further three hours.

Butyl-lithium (10·6 ml. 2·24M solution, 23·8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred suspension of hexachlorobenzene (6·75 g., 23·8 mmoles) in dry ether (100 ml.) contained in a flask previously purged with dry nitrogen and cooled to -10°. The mixture was stirred for 30 minutes at this temperature, cooled to -78°, and transferred under nitrogen to a precooled dropping funnel. The pentachlorophenyl-lithium solution at -78° was added dropwise to the pentafluorophenyl-lithium-dimethyl oxalate complex, which was then stirred for 36 hours, and hydrolysed with gaseous HCl at -78°. The reaction mixture was allowed to warm to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left an orange residue which v.p.c. indicated to be mainly pentachlorobenzene and methyl pentafluorobenzoylformate. No evidence was obtained for any α-diketone from spectroscopic measurements on the residue.

B. Reaction of pentafluorophenyl-lithium with methyl pentachlorobenzoylformate.

Butyl-lithium (3•25 ml. 2•4M solution, 7•8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (1•3 g., 7•8 mmoles) in dry ether (90 ml.) and dry hexane (60 ml.) contained in a flask which had previously been purged with dry nitrogen and cooled to -78°. The mixture was stirred for 2 hours, and methyl pentachlorobenzoylformate (2•6 g., 7•8 mmoles) in dry ether (30 ml.) was added. After stirring for four hours, the reaction mixture was hydrolysed with gaseous HCl. It was then allowed to warm to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a residue indicated by v.p.c. to be a single component (3•2 g., 87%) which was recrystallised from carbon tetrachloride to give yellow crystals of <u>2,3,4,5,6-pentachloropentafluorobenzil,</u> m.p. 132-3° (Found: C, 35•2; Cl, 37•5; F, 20•7. $C_{14}Cl_5F_5O_2$ requires:

C, 35•5; Cl, 37•5; F, 20•1%). The infra-red spectrum showed two absorptions in the C=O stretch region at ~1705 cm.$^{-1}$ and ~1720 cm.$^{-1}$

8.14. Reaction between pentachlorophenyl-lithium and methyl pentafluorobenzoylformate - preparation of methyl 2,3,4,5,6-pentachloropentafluorobenzilate, $C_6Cl_5(C_6F_5)C(OH)COOCH_3$.

Butyl-lithium (4•7 ml. 2•25M solution, 10•5 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred suspension of hexachlorobenzene (3•0 g., 10•5 mmoles) in dry ether (300 ml.) contained in a 500 ml. flask which had previously been purged with dry nitrogen and cooled to -15°. The mixture was allowed to stir at this temperature for 30 minutes, cooled to -78°, and methyl pentafluorobenzoylformate (2•67 g., 10•5 mmoles) was added rapidly. After stirring for a further three hours, the reaction mixture was hydrolysed at -78° with gaseous HCl. It was then warmed to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a residue (5•3 g.) which was washed with cold b.p. 40-60 petroleum ether to give a white solid (4•1 g., 72%) indicated by v.p.c. to be a single component. Recrystallisation from chloroform yielded methyl 2,3,4,5,6-pentachloropentafluorobenzilate, m.p. 161-2° (Found: C, 35•8; H, 0•9; Cl, 34•8; F, 19•2. $C_{15}H_4Cl_5F_5O_3$ requires: C, 35•7; H, 0•8; Cl, 35•2; F, 18•7%). The infra-red spectrum showed a strong ester C=O stretch at 1740 cm.$^{-1}$

CHAPTER 9

Experimental for Chapter 6

9.1. Preparation of 2,3-bis(pentafluorophenyl)quinoxaline.

Decafluorobenzil (0·33 g., 0·85 mmoles) and freshly sublimed o-phenylenediamine (0·088 g., 0·85 mmoles) were heated together at 100° for 10 minutes. On cooling, a brown solid was produced which was dissolved in hot methanol. On standing, a white crystalline precipitate was obtained, identified as 2,3-bis(pentafluorophenyl)quinoxaline (0·25 g., 2 crops, 64%), m.p. 161-3° (Found: C, 52·2; H, 0·85; N, 5·9. $C_{20}H_4F_{10}N_2$ requires: C, 51·9; H, 0·85; N, 6·05%). The ^1H n.m.r. spectrum (CCl_4 solution, TMS internal reference) showed two peaks, one centred at 1·85 τ and the other at 2·0 τ.

9.2. Preparation of decafluorobenzilic acid.

Decafluorobenzil (0·8 g., 2·05 mmoles) in ether (15 ml.) was stirred at room temperature with an aqueous solution of sodium hydroxide (12 ml. 1·5M solution, 18 mmoles) for five minutes, by which time the characteristic yellow colour of the α-diketone had disappeared. The reaction mixture was acidified with dilute HCl and extracted with ether. The ether extracts were dried ($MgSO_4$), and the solvent removed to leave a residue which was recrystallised from carbon tetrachloride to give decafluorobenzilic acid (0·7 g., 83%), m.p. 135-136° (Found: C, 41·0; H, 0·5; F, 46·8. $C_{14}H_2F_{10}O_3$ requires: C, 41·2; H, 0·5; F, 46·6%).

The infra-red spectrum showed a strong hydroxyl O-H stretch at ~3420 cm.$^{-1}$, and a broad carboxylic O-H stretch from ~2850 cm.$^{-1}$ to ~3220 cm.$^{-1}$

9.3. Reaction of benzil with butyl-lithium.

A. Without reflux - preparation of α-n-butylbenzoin.

Butyl-lithium (19·0 ml. 2·3M solution, 42·8 mmoles) in dry hexane (20 ml.) was added dropwise to a stirred solution of benzil (9 g., 42·8 mmoles) in dry ether (250 ml.) contained in a flask which had previously been purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for two hours, then warmed slowly to room temperature overnight and hydrolysed with dilute HCl. The organic layer was separated and dried ($MgSO_4$), and the solvent removed to leave an oily residue. On addition of b.p. 40-60 petroleum ether (40 ml.) a white precipitate (9·8 g.) was obtained which v.p.c. indicated to be principally one component. Recrystallisation from b.p. 40-60 petroleum ether yielded α-n-butylbenzoin (7·1 g., 62%) m.p. 70-71° (Found: C, 80·9; H, 7·2. Calc. for $C_{18}H_{20}O_2$: C, 80·6; H, 7·5%). This melting point differs considerably from that of 124° quoted in the only previous reference[108] to this compound in the literature. This discrepancy cannot be easily explained as both here and in the reference, the reaction product was also characterised by further reaction to give known products.

The infra-red spectrum showed a strong O-H stretch at ~3420 cm.$^{-1}$ and a C=O stretch at ~1680 cm.$^{-1}$ The ^{1}H n.m.r. spectrum (CCl_4 solution, TMS internal reference) showed the following resonances; a triplet (3 protons, $\underline{CH_3}$-CH_2-) at 9•24τ, a broad multiplet (4 protons, CH_3-$\underline{CH_2}$-$\underline{CH_2}$-CH_2-) from ~8•6 to ~8•9τ , a triplet (2 protons, -CH_2-$\underline{CH_2}$-CO-) at 7•79τ, a broad singlet (1 proton, -O-$\underline{H}$) at 5•41τ, and a complex group of peaks (10 protons, 2 x $\underline{C_6H_5}$-) from ~2•15 to ~3•0τ.

As part of its characterisation, the α-n-butylbenzoin was cleaved with chromium trioxide in acetic acid.

Chromium trioxide (0•88 g., 8•8 mmoles) in warm glacial acetic acid (10 ml.) and water (0•5 ml.) was added to a solution of α-n-butylbenzoin (1 g., 3•72 mmoles) in acetic acid (15 ml.) and the reaction mixture heated to ~100° for 2 hours. It was cooled, poured into water (100 ml.) and extracted with ether (3 x 50 ml.). The extracts were washed with water to remove acetic acid, extracted with 2•5N potassium hydroxide solution (4 x 50 ml.), washed once more with water, and dried ($MgSO_4$). Removal of solvent left a product indicated by v.p.c. to be a single component, which was identified from its ^1H n.m.r. spectrum as n-butyl phenyl ketone (0•35 g., 60%).

The basic extracts were acidified, cooled, and extracted with ether. The organic extracts were washed with water, dried ($MgSO_4$), and the solvent removed to leave an oil. Water (20 ml.) was added and a white precipitate was obtained which was filtered off, dried, and shown by a comparison of its spectroscopic properties with those of an authentic sample to be benzoic acid (0•42 g., 88%).

B. With refluxing in toluene.

Butyl-lithium (11•9 ml. 2•4M solution, 28•6 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of benzil (6•0 g., 28•6 mmoles) in dry ether (100 ml.), contained in a flask which had previously been purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for two hours, then warmed to room temperature over four hours and most of the solvent removed by distillation under nitrogen. Dry toluene (200 ml.) was added, the reaction mixture refluxed for 84 hours, cooled, and hydrolysed with dilute HCl (100 ml.). The organic layer was separated, dried ($MgSO_4$), and most of the solvent removed. V.p.c. on the residue showed one minor peak with a relatively short retention time, and a broad peak due to the keto-alcohols. Reduced pressure distillation (~65°/0•002 mm.) removed the more volatile component (1 g.) which was not investigated further. Continued distillation (110-150°/0•002 mm.) gave a mixture (5•8 g.) of two components, the infra-red spectrum of which showed a C=O stretch at 1680 $cm.^{-1}$ and a stronger C=O stretch at ~1715 $cm.^{-1}$, suggesting a mixture of α-keto-alcohols. The mass spectrum of the mixture showed no parent peak but strong fragment ions observed at M183($(C_6H_5)_2\overset{+}{C}OH$, relative abundance 60%), M163 ($C_4H_9(C_6H_5)\overset{+}{C}OH$, 33%), M105 ($C_6H_5\overset{+}{C}O$, 100%), M85 ($C_4H_9\overset{+}{C}O$, 7%), M77 ($C_6H_5^+$, 100%), and M57 ($C_4H_9^+$, 20%), suggested that the mixture contained α-n-butylbenzoin, and also the rearranged product, 1-hydroxy-1,1-diphenylhexan-2-one. Further evidence for the presence of this last compound was obtained by oxidising the reaction product with chromium trioxide in acetic acid.

The reaction product (2 g.) was dissolved in acetic acid (10 ml.) and to it was added a solution of chromic trioxide (1•76 g., 17•6 mmoles) in acetic acid (15 ml.) and water (1 ml.). This mixture was heated to 100° for two hours, cooled, poured into water (150 ml.), and extracted with ether (4 x 50 ml.). The ether extracts were extracted with 2•5N potassium hydroxide solution, washed with water, and dried ($MgSO_4$). Removal of solvent left a viscous liquid (0•95 g.) which v.p.c. indicated to contain benzophenone (80%) and butyl phenyl ketone (20%).

If the oxidising agent is equally effective with both the keto-alcohols, these results suggest that the original mixture contained 1-hydroxy-1,1-diphenylhexan-2-one ($\sim$80%) and α-n-butylbenzoin ($\sim$20%).

9.4. Preparation of 1-hydroxy-1,1-bis(pentafluorophenyl)hexan-2-one.

Butyl-lithium (3•4 ml. 2•3M solution, 7•7 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of decafluorobenzil (3•0 g., 7•7 mmoles) in dry ether (200 ml.) contained in a flask which had previously been purged with dry nitrogen and cooled to -78°. After stirring for two hours at this temperature, the mixture was allowed to warm to room temperature overnight and hydrolysed with dilute HCl. The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a pale yellow viscous liquid (3•1 g.) which v.p.c. indicated to contain one major component and several minor ones. A pure sample of the major product was obtained by dissolving the residue in a minimum volume of b.p. 40-60 petroleum ether and eluting it down a silica-packed column using b.p. 40-60 petroleum ether-chloroform (4:1) as eluent. Several minor components were obtained first, and continued elution gave 1-hydroxy-1,1-bis(pentafluorophenyl)hexan-2-one, b.p. 93-95°/ 0•001 mm. (Found: C, 48•3; H, 2•2; F, 42•8. $C_{18}H_{10}F_{10}O_2$ requires: C, 48•2; H, 2•2; F, 42•4%). The yield of keto-alcohol in the reaction product was calculated from v.p.c. analysis to be 62%. The infra-red spectrum showed an O-H stretch at ~3420 $cm.^{-1}$ and a C=O stretch at ~1735 $cm.^{-1}$ The ^1H n.m.r. spectrum (CCl_4 solution, TMS internal reference) showed the following resonances; a triplet (3 protons, $\underline{CH_3}$-CH_2-) at 9•23τ, a broad multiplet (4 protons, CH_3-$\underline{CH_2}$-$\underline{CH_2}$-) from ~8•4 to ~8•9τ, a triplet (2 protons, CH_2-$\underline{CH_2}$-CO-) at 7•54τ, and a broad singlet (1 proton, O-$\underline{H}$) at 5•87τ.

The observed ^{19}F n.m.r. spectrum (see Appendix) was consistent with this rearranged product, and further evidence was obtained from its oxidation with chromium trioxide.

Chromium trioxide (0•32 g., 3•2 mmoles) in acetic acid (10 ml.) and water (0•5 ml.) was added to a solution of 1-hydroxy-1,1-bis(pentafluorophenyl)hexan-2-one (0•6 g., 1•34 mmoles) in acetic acid (5 ml.), and the reaction mixture heated to 100° for 2 hours. It was cooled, poured into water (100 ml.), and extracted with ether (3 x 50 ml.). The extracts were washed once with water, extracted with potassium hydroxide solution (4 x 50 ml., 2•5N), washed again with water, and dried ($MgSO_4$). Removal of solvent left a white solid which v.p.c. indicated to be a single component, and which was shown by comparison of its spectroscopic properties with those of an authentic sample to be decafluorobenzophenone (0•35 g., 72%).

9.5. Preparation of α-pentafluorophenylbenzoin.

Butyl-lithium (6•2 ml. 2•3M solution, 14•3 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (2•4 g., 14•3 mmoles) in dry ether (90 ml.) and dry hexane (60 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for 2 hours, and benzil (3 g., 14•3 mmoles) in ether (40 ml.) was added. After stirring for a further two hours, the reaction mixture was allowed to warm to 0° over one hour, and hydrolysed with dilute HCl. The non-aqueous layer was separated, dried ($MgSO_4$), and the solvent removed to leave a pale yellow residue, sublimation of which gave a product (5•0 g.) indicated by v.p.c. to be mainly one component. Purification by recrystallisation was not successful, and it was necessary to remove impurities on a silica-packed column using b.p. 40-60 petroleum ether-chloroform (4:1) as eluent. Recrystallisation from b.p. 40-60 petroleum ether of a practically pure fraction eluted from the column yielded α-pentafluorophenylbenzoin, (3 g., 56%) m.p. 112-114° (Found: C, 63•6; H, 3•0; F, 25•5. $C_{20}H_{11}F_5O_2$ requires: C, 63•5; H, 2•9; F, 25•2%).

The infra-red spectrum showed a strong O-H stretch at ~3330 $cm.^{-1}$, and a C=O stretch at ~1687 $cm.^{-1}$ The ^1H n.m.r. spectrum (ether solution, TMS internal reference) showed the following resonances; a broad singlet (O-$\underline{H}$) at 4·42τ, and a complex group of peaks ($\underline{C_6H_5}-\overset{|}{C}=O$, and $\underline{C_6H_5}-\overset{|}{\underset{|}{C}}-OH$) from 2·0 to 2·8$\tau$.

In order to discover whether α-pentafluorophenylbenzoin or a possible rearrangement product was the more thermodynamically stable, the reaction was repeated at a higher temperature.

Butyl-lithium (10 ml. 2·38M solution, 23·8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (4·0 g., 23·8 mmoles) in dry ether (90 ml.) and dry hexane (60 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for two hours, and benzil (5·0 g., 23·8 mmoles) in dry ether (40 ml.) was added. After stirring for a further two hours, the reaction mixture was warmed to room temperature and most of the solvent removed by distillation under nitrogen. Dry toluene (150 ml.) was added, and the reaction mixture refluxed for 3 days. It was cooled, hydrolysed with dilute HCl, and the organic layer separated and dried ($MgSO_4$). Removal of toluene left a semi-solid residue which v.p.c. indicated to contain one major component with a retention time identical to that of α-pentafluorophenylbenzoin prepared earlier in this section. Sublimation and recrystallisation from b.p. 40-60 petroleum ether gave a crystalline solid (4 g.) with the same spectroscopic properties as a characterised sample of α-pentafluorophenylbenzoin.

9.6. Reaction between pentafluorophenyl-lithium and decafluorobenzil.

A. Hydrolysis at -78°.

Butyl-lithium (3•6 ml. 2•25M solution, 7•7 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (1•29 g., 7•7 mmoles) in dry ether (100 ml.) and dry hexane (50 ml.) contained in a flask which had previously been purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for 2 hours, and decafluorobenzil (3 g., 7•7 mmoles) added. After stirring for a further 6 hours, the reaction mixture was hydrolysed at -78° with gaseous HCl. It was then allowed to warm to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a pale yellow solid (3•7 g.) which v.p.c. indicated to contain decafluorobenzil (13%) and an unknown compound with a longer retention time (87%). Washing with cold b.p. 40-60 petroleum ether removed the decafluorobenzil and yielded <u>perfluoro-α-phenylbenzoin</u> (2•8 g., 74% based on consumed decafluorobenzil) m.p. (recrystallised from carbon tetrachloride) 116-117°, (Found: C, 42•8; H, 0•3; F, 51•5. $C_{20}HF_{15}O_2$ requires: C, 43•0; H, 0•2; F, 51•1%). The infra-red spectrum showed an O-H stretch at ~3470 $cm.^{-1}$, and a C=O stretch at ~1720 $cm.^{-1}$

B. Hydrolysis at 20°.

Decafluorobenzil was added to a solution of pentafluorophenyl-lithium exactly as described in 9.6.A. The reaction mixture was stirred at -78°

before being allowed to warm to room temperature overnight, and hydrolysed with dilute HCl. The organic layer was separated, dried ($MgSO_4$) and the solvent removed to leave a white solid (4•1 g.) which, although v.p.c. showed only one peak, t.l.c. indicated to contain two components. Separation was effected on a silica-packed column using carbon tetrachloride as eluent. The first fraction eluted from the column gave a white solid containing no protons and which spectroscopic evidence (see Appendix) indicated to be <u>perfluoro-2,2-diphenylbenzofuran-3-one</u>, m.p. 158-159°, (Found: C, 44•3; F, 49•65. $C_{20}F_{14}O_2$ requires: C, 44•6; F, 49•4%). The infra-red spectrum exhibited a strong C=O stretch at $\sim$1750 $cm.^{-1}$ This value is slightly higher than is normally observed with fluorinated ketones, and is presumably due to the formation of a five-membered ring structure.

Continued elution yielded the major component of the mixture and which, from a comparison of its spectroscopic properties with those of a previously characterised sample, was shown to be perfluoro-α-phenylbenzoin. The yields of each component were determined from a ^{19}F n.m.r. spectrum of the reaction product which indicated that the benzofuran-3-one was formed in $\sim$25% yield and the α-phenylbenzoin in $\sim$ 60% yield.

9.7. <u>Reaction of perfluoro-α-phenylbenzoin with butyl-lithium.</u>

Butyl-lithium (0•85 ml. 2•1M solution, 1•8 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of perfluoro-α-phenylbenzoin

(1 g., 1•8 mmoles) in dry ether (40 ml.) and dry hexane (20 ml.) contained in a flask previously purged with nitrogen. The mixture was refluxed for 12 hours, allowed to cool, and hydrolysed with dilute HCl. The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a yellow oil (0•9 g.) which t.l.c. indicated to contain ~12 components, the major one having an R_f value identical with that of perfluoro-2,2-diphenylbenzofuran-3-one. Elution of the reaction product on a silica-packed column (b.p. 40-60 petroleum ether-chloroform (4:1) eluent) yielded a pure sample of the benzofuranone (0•4 g., 41%).

9.8. Reaction of pentachlorophenyl-lithium with benzil.

A. Without reflux - preparation of α-pentachlorophenylbenzoin.

Butyl-lithium (7•8 ml. 2•25M solution, 17•6 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred suspension of hexachlorobenzene (5•0 g., 17•6 mmoles) in dry ether (500 ml.) contained in a flask previously purged with dry nitrogen and cooled to -15°. The mixture was stirred at this temperature for 30 minutes, and benzil (3•7 g., 17•6 mmoles) in ether (30 ml.) was added. After stirring for a further two hours, the reaction mixture was allowed to warm slowly to room temperature overnight, and hydrolysed with dilute HCl. The organic layer was separated, dried ($MgSO_4$) and the solvent removed to leave an orange residue (7•9 g.), which was shown by t.l.c. to contain one major component. Sublimation, although accompanied by some decomposition yielded a white solid (6•1 g., 75%) which was identified from its spectroscopic properties and cleavage products with chromium trioxide as α-pentachlorophenylbenzoin, m.p. 168-170°, (Found: C, 51·9; H, 2·5; Cl, 38·4. $C_{20}H_{11}Cl_5O_2$ requires: C, 52·1; H, 2·4; Cl, 38·5%). The infra-red spectrum showed an O-H stretch at ~3380 cm.$^{-1}$, and a C=O stretch at ~1657 cm.$^{-1}$ The frequency of the C=O stretch is evidence for $C_6H_5\text{-}\overset{|}{C}{=}O$ rather than $C_6Cl_5\text{-}\overset{|}{C}{=}O$ as the absorption due to the latter group is generally observed at higher frequencies. Further evidence that rearrangement had not taken place was obtained by cleaving the keto-alcohol with chromium trioxide.

Chromium trioxide (0·75 g., 7·5 mmoles) in acetic acid (10 ml.) and water (0·5 ml.) was added to a solution of the benzoin (1·5 g., 3·26 mmoles) in warm glacial acetic acid, and the mixture warmed to 100° for 1 hour. It was cooled, poured into water, and extracted with ether (4 x 50 ml.). The extracts were washed once with water, extracted with potassium hydroxide solution (4 x 50 ml. 2·5N), washed again with water, and dried ($MgSO_4$). Removal of solvent left a white solid (0·95 g., 83%) shown by v.p.c. to be a single component. Recrystallisation from ethanol yielded 2,3,4,5,6-pentachlorobenzophenone, m.p. 153-154° (lit.[109] 154°), (Found: C, 44·2; H, 1·5; Cl, 49·75. Calc. for $C_{13}H_5Cl_5O$: C, 44·0; H, 1·4; Cl, 50·0%). The infra-red spectrum exhibited a C=O stretch at ~1690 cm.$^{-1}$

The basic extracts were acidified, cooled, and extracted with ether. The organic extracts were washed once with water, dried ($MgSO_4$), and the solvent removed to leave a viscous liquid residue. Water (20 ml.) was added, and the white precipitate which formed was filtered off, dried, and shown by comparison of its spectroscopic properties with those of an authentic sample to be benzoic acid (0•35 g., 87%).

B. With reflux in toluene - preparation of 2,2-diphenyltetrachlorobenzofuran-3-one.

Butyl-lithium (6•7 ml. 2•24M solution, 14•3 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred suspension of hexachlorobenzene (4•07 g., 14•3 mmoles) in ether (200 ml.) contained in flask previously purged with dry nitrogen and cooled to -15°. The mixture was stirred at this temperature for 30 minutes and benzil (3 g., 14•3 mmoles) added. After stirring for a further hour, the reaction mixture was allowed to warm to room temperature, most of the solvent removed by distillation under nitrogen and dry toluene (150 ml.) was added. After refluxing for 89 hours, the reaction mixture was cooled, hydrolysed with dilute HCl, and the organic layer separated and dried ($MgSO_4$). Removal of toluene left a residue (5•5 g.) which was sublimed with some decomposition to give a white solid (2•7 g., 43%) shown by t.l.c. to be a single compound with a different R_f value to α-pentachlorophenylbenzoin, and which was recrystallised from b.p. 40-60 petroleum ether-chloroform to yield tetrachloro-2,2-diphenylbenzofuran-3-one, m.p. 196-7°, (Found: C, 56•9; H, 2•4; Cl, 34•05. $C_{20}H_{10}Cl_4O_2$ requires: C, 56•7; H, 2•35; Cl, 33•6%). The infra-red spectrum showed no O-H stretch and a C=O stretch at ~1730 $cm.^{-1}$

9.9. Reaction of pentachlorophenyl-lithium with decafluorobenzil.

Butyl-lithium (3•4 ml. 2•25M solution, 7•7 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred suspension of hexachlorobenzene (2•2 g., 7•7 mmoles) in dry ether (200 ml.) contained in a flask previously purged with dry nitrogen and cooled to -15°. The pale yellow solution of pentachlorophenyl-lithium was stirred for 30 minutes and decafluorobenzil (3•0 g., 7•7 mmoles) added. The reaction mixture was allowed to warm gradually to room temperature, and after 9•5 hours, hydrolysed with dilute HCl. The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a residue (4•4 g.) which v.p.c. indicated to contain one major component. Recrystallisation from b.p. 40-60 petroleum ether yielded bis(pentafluorophenyl)methyl pentachlorobenzoate (3•1 g., 63%), m.p. 145-147°, (Found: C, 37•4; H, 0•15; Cl, 27•9; F, 30•0. $C_{20}HCl_5F_{10}O_2$ requires: C, 37•4; H, 0•15; Cl, 27•7; F, 29•65%). The infra-red spectrum showed no O-H stretch, but showed an aliphatic C-H stretch at ~ 2980 $cm.^{-1}$, and an absorption in the C=O stretching region at ~1767 $cm.^{-1}$ This last value is consistent with the expected absorption frequency for a halogen-substituted ester. The ^1H n.m.r. spectrum (CCl_4 solution, TMS internal reference) showed only a single peak at 2•4τ.

9.10. Reaction between pentafluorophenyl-lithium and 2,3,4,5,6-pentachloropentafluorobenzil.

A. Hydrolysis at -78°, - preparation of pentachlorobenzoylbis-(pentafluorophenyl)methanol, $(C_6F_5)_2C(OH)COC_6Cl_5$.

Butyl-lithium (1•01 ml. 2•1M solution, 2•12 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (0•356 g., 2•12 mmoles) in dry ether (90 ml.) and dry hexane (60 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for two hours, and 2,3,4,5,6-pentachloropentafluorobenzil (1•0 g., 2•12 mmoles) in dry ether (20 ml.) was added. After stirring for a further three hours, the reaction was hydrolysed at -78° with gaseous HCl. It was allowed to warm to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left a white solid (1•3 g.) which t.l.c. indicated to be practically pure, and recrystallisation from carbon tetrachloride yielded <u>pentachlorobenzoyl-bis(pentafluorophenyl)methanol</u>, (1•15 g., 85%) m.p. 235-237°, (Found: C, 37•6; H, 0•15; Cl, 27•3; F, 29•6. $C_{20}HCl_5F_{10}O_2$ requires: C, 37•4; H, 0•15; Cl, 27•7; F, 29•65%). The infra-red spectrum exhibited an O-H stretch at ~3540 cm.$^{-1}$ and a C=O stretch at ~ 1730 cm.$^{-1}$

B. Hydrolysis at 20°.

Butyl-lithium (1•21 ml. 2•1M solution, 2•54 mmoles) in dry hexane (10 ml.) was added dropwise to a solution of pentafluorobenzene

(0•427 g., 2•54 mmoles) in dry ether (60 ml.) and dry hexane (40 ml.) contained in a flask previously purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for two hours and 2,3,4,5,6-pentachloropentafluorobenzil (1•2 g., 2•54 mmoles) in ether (20 ml.) was added. After stirring at this temperature for a further four hours, the reaction mixture was allowed to warm slowly to room temperature over fourteen hours and hydrolysed with dilute HCl. The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a white solid (1•35 g.) which t.l.c. indicated to contain two components. A comparison of the ^{19}F n.m.r. spectrum of the mixture and the R_f values of the components with those of authentic samples indicated that the product contained bis(pentafluorophenyl)-methyl pentachlorobenzoate (~80%) and pentachlorobenzoylbis(pentafluorophenyl)methanol (~20%).

9.11. Preparation of benzoylbis(pentafluorophenyl)methanol, $(C_6F_5)_2C(OH)COC_6H_5$

Butyl-lithium (2•78 ml. 2•4M solution, 6•67 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of pentafluorobenzene (1•12 g., 6•67 mmoles) in dry ether (60 ml.) and dry hexane (40 ml.) contained in a flask which had previously been purged with dry nitrogen and cooled to -78°. The mixture was stirred at this temperature for 2 hours and 2,3,4,5,6-pentafluorobenzil (2 g., 6•67 mmoles) in dry ether (20 ml.) was added. After stirring for a further three hours, the reaction mixture was hydrolysed at -78° with gaseous HCl. It was then allowed to warm to room temperature, water (100 ml.) was added, and the organic layer separated and dried ($MgSO_4$). Removal of solvent left an oily residue (3•1 g.) which v.p.c. indicated to contain one minor component (~5%) and the major product. Separation was achieved on a silica-packed chromatography column, using b.p. 40-60 petroleum ether-chloroform (4:1) as eluent. The minor component was eluted first, and later fractions yielded a viscous liquid, <u>benzoylbis(pentafluorophenyl)-methanol</u> (2•1 g., 67%), b.p. 124-126°/0•001 mm. (Found: C, 51•6; H, 1•2; F, 40•2. $C_{20}H_6F_{10}O_2$ requires: C, 51•3; H, 1•3; F, 40•6%). The infra-red spectrum showed an O-H stretch at ~3390 $cm.^{-1}$, and a C=O stretch at ~1695 $cm.^{-1}$. The ^1H n.m.r. spectrum (CCl_4 solution, TMS internal reference) showed peaks at 4•45τ (broad singlet, O-$\underline{H}$) and from ~1•9 to ~2•65τ (complex multiplets, $\underline{C_6H_5}$-).

Further characterisation of the product was obtained from its oxidation with chromium trioxide.

Chromium trioxide (0•33 g., 3•3 mmoles) in acetic acid (10 ml.) and water (0•5 ml.) was added to a solution of benzoylbis(pentafluorophenyl)-methanol (0•7 g., 1•5 mmoles) in acetic acid (10 ml.) and the mixture heated to 100° for 2 hours. It was cooled, poured into water (100 ml.), and extracted with ether (4 x 50 ml.). The ether extracts were washed once with water, extracted with potassium hydroxide solution (4 x 50 ml. 2•5M solution), washed again with water, and dried ($MgSO_4$). Removal of solvent left a single component product which by comparison of its spectroscopic properties with those of an authentic sample was shown to be decafluorobenzophenone (0•47 g., 86%).

The basic extracts were acidified, cooled, and extracted with ether. The organic extracts were washed with water, dried ($MgSO_4$) and the solvent removed to leave an oil. Water (10 ml.) was added and a white precipitate was formed which was filtered off, dried, and shown by comparison of its spectroscopic properties with those of an authentic sample to be benzoic acid (0•14 g., 78%).

9.12. Reaction of phenyl-lithium with decafluorobenzil.

Butyl-lithium (1•83 ml. 2•1M solution, 3•85 mmoles) in dry hexane (10 ml.) was added dropwise to a stirred solution of iodobenzene (0•8 g., 3•85 mmoles) in dry ether (90 ml.) and dry hexane (60 ml.) contained in a flask previously purged with dry nitrogen and cooled to -15^{o}. The mixture was stirred at this temperature for two hours, and decafluorobenzil (1•6 g., 3•85 mmoles) was added. After stirring at this temperature for a further two hours, the reaction mixture was allowed to warm slowly to room temperature and hydrolysed with dilute HCl. The organic layer was separated, dried ($MgSO_4$), and the solvent removed to leave a red viscous residue (2•0 g.) which v.p.c. indicated to contain at least ten components with no one peak accounting for a major proportion of the mixture. T.l.c. showed a series of spots with similar R_f values.

APPENDIX

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

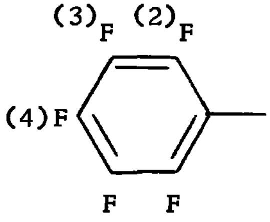
Introduction.

^{19}F N.m.r. spectroscopy has been an invaluable technique in the structure determination of fluorinated compounds, and has been particularly useful as a means for determining the orientation of nucleophilic substitution in polyfluoro-aromatic and -heterocyclic compounds.[110,111] It has been found possible to predict fairly accurately the spectra of substituted aromatic fluorine compounds using substituent shifts. The effect of a particular substituent on the ring fluorines ortho, meta, and para to it can be found by a comparison of the fluorine shifts in the compound with those in the unsubstituted compound. These substituent shifts can then be used to determine the orientation in other compounds containing the same substituent.

Alternatively, the spectrum of a disubstituted compound can be predicted by assuming that the substituent shifts for two groups are additive.[55] A comparison of the actual and predicted spectra is an excellent guide to the assignment of the fluorine resonances in a new compound, as will be demonstrated later.

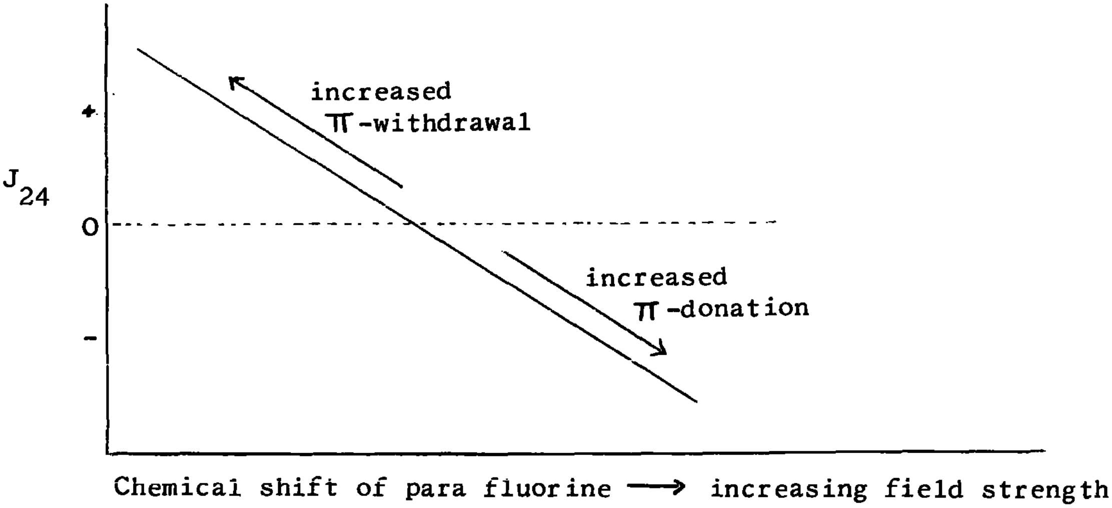
The pentafluorophenyl group.

Most of the compounds whose spectra are recorded in the following pages contain a pentafluorophenyl group. Assignment of the three observed resonances is straightforward as the peak due to the para fluorine is half the intensity of the other two and is also generally found to be a triplet of triplets resulting from coupling with the ortho and meta fluorines. The meta position in a ring is affected only slightly by electronic effects and consequently the meta fluorine is found close to the position of the fluorines in hexafluorobenzene, whereas the ortho fluorine is generally shifted between 20 and 30 p.p.m. downfield from this position. It was only possible to obtain the coupling constants J_{24} and J_{34} as the ortho and meta fluorines involved second order



splittings.

One of the problems in characterising several of these compounds was to decide whether the pentafluorophenyl group was present as $C_6F_5-\overset{|}{C}=O$ or $C_6F_5-\underset{|}{\overset{|}{C}}-OH$. Hogben and Graham,[112] studying a series of substituted



pentafluorophenyl compounds, found a linear relationship between the shift of the para fluorine and J_{24} for the particular compound. They also noted that the greater the ability of the substituent to withdraw π-electrons from the pentafluorophenyl group, then the further downfield the peak appeared. These results can be applied to this problem as the carbonyl group should be better able to withdraw π-electrons than the hydroxyl attached to the carbon atom. Thus one would expect to find the resonance of a para fluorine in a pentafluorophenyl group adjacent to a carbonyl at a lower field than for one in a pentafluorophenyl group adjacent to a hydroxyl-substituted carbon atom.

In the group of compounds studied, the para fluorine was observed in two distinct areas. The shifts due to $C_6F_5-\overset{|}{C}=O$ were found in the region −15·5 to −18·3 p.p.m. (relative to C_6F_6), J_{24}, 5·5 − 6·1 Hz, while those due to $C_6F_5-\underset{|}{\overset{|}{C}}-OH$ were found in the region −8 to −11 p.p.m., J_{24}, 3·0 to 4·0 Hz.

<u>Coupling constants.</u>

Examination of the fluorine-fluorine and fluorine-hydrogen coupling constants can be of use in confirming the correct assignment of peaks in a new compound. Unfortunately, unlike ^1H n.m.r. where the proton-proton ortho, meta, and para coupling constants fall into small characteristic ranges,[113] there is some degree of overlap between the analogous fluorine-fluorine couplings. While J_{FF}^{ortho} values vary only slightly, between 18 and 22 Hz, large variations have been observed with J_{FF}^{meta} (0-12 Hz) and J_{FF}^{para} (6-13 Hz).[113]

These variations have been rationalised in terms of π interactions between the substituent and the aromatic ring.[113] A series of substituent contributions have been drawn up making it possible to calculate values for J_{FF}^{meta} and J_{FF}^{para} which are in good agreement with the observed values, and also enabling coupling constants to be predicted for compounds not yet prepared.

The values of these substituent contributions show a linear dependence on the Hammett σ values of substituents, and consequently one would expect large changes in coupling constants where large σ values are involved. Thus when dealing with fluorines only, or with substituents with small σ values as in the following compounds, the coupling constants are unlikely to lie over such a wide range. A better approximation, taken from more fully fluorinated systems[54,63,114] would be:

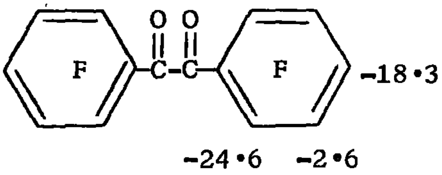
J_{FF}^{ortho}, 18-22 Hz
J_{FF}^{meta}, 0-8 Hz
J_{FF}^{para}, 7-13 Hz.

Characteristic ranges for hydrogen-fluorine coupling constants are:[113]

J_{HF}^{ortho}, 9-12 Hz
J_{HF}^{meta}, 5-8 Hz
J_{HF}^{para}, 2-3 Hz.

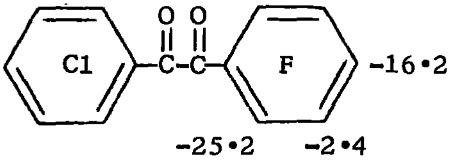
Spectra were recorded on a Perkin-Elmer R.10 Spectrometer or on a Varian A56/60D Spectrometer. Shifts are quoted in p.p.m. from C_6F_6, which was used as internal reference, and coupling constants are given where they could be determined by first order analysis.

1. Decafluorobenzil (CCl_4).



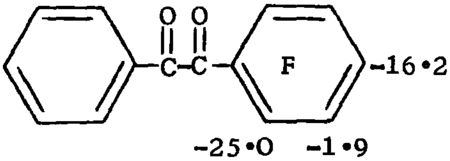
J_{24} = 6·1,
J_{34} = 20·0 Hz

2. 2,3,4,5,6-Pentachloropentafluorobenzil (CCl_4).



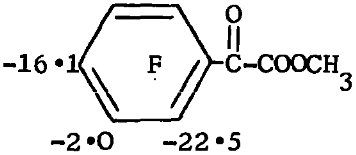
J_{24} = 5·5,
J_{34} = 20·2 Hz

3. 2,3,4,5,6-Pentafluorobenzil (CCl_4).



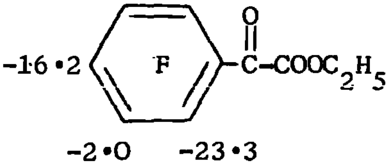
J_{24} = 5·5,
J_{34} = 20·1 Hz

4. Methyl pentafluorobenzoylformate (CCl_4).



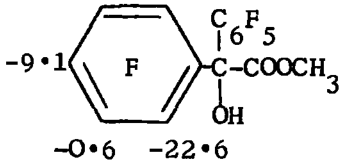
J_{24} = 5·6,
J_{34} = 19·5 Hz

5. Ethyl pentafluorobenzoylformate (neat).



J_{24} = 5·6,
J_{34} = 19·4 Hz

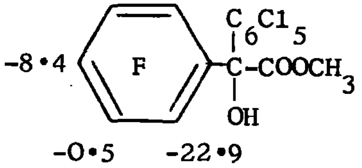
6. Methyl decafluorobenzilate (CCl_4).



J_{24} = 3•5,

J_{34} = 20•2 Hz

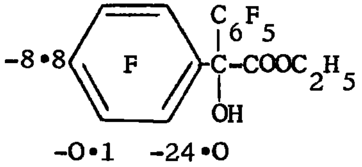
7. Methyl 2,3,4,5,6-pentachloropentafluorobenzilate (CCl_4).



J_{24} = 3•2,

J_{34} = 20•8 Hz

8. Ethyl decafluorobenzilate (ether).



J_{24} = 3•4,

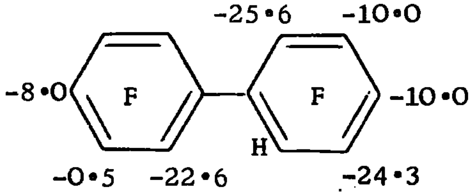
J_{34} = 20•2 Hz

9. Methyl tetrafluoro-2(2',3',4',5'-tetrafluorophenyl)benzoylformate (CCl_4).

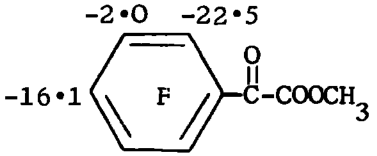
This spectrum showed the following resonances:

Peak No.	Shift (p.p.m.)	Intensity
1	-8•2	1
2	-9•6	1
3	-10•0	1
4	-14•6	1
5	-23•6	1
6,7	-24•0	2
8	-25•1	1

As an aid in assigning the above peaks, a calculated spectrum was constructed from the substituent constants for -o•C_6F_4H[54] and -$COCOOCH_3$ which were obtained from:

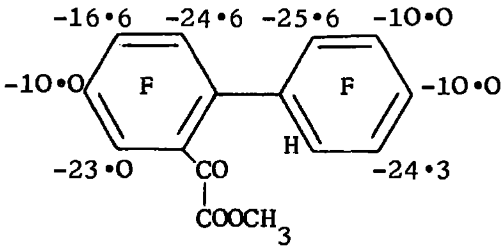


and



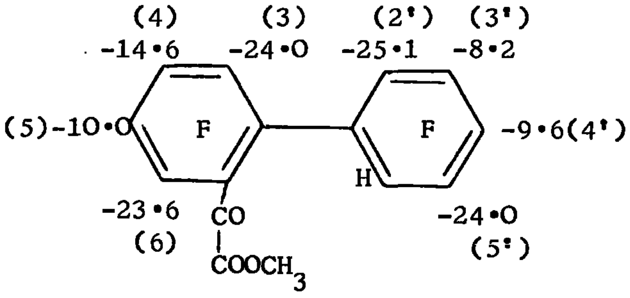
respectively.

Combining these two spectra gives the following calculated spectrum for methyl tetrafluoro-2(2',3',4',5'-tetrafluorophenyl)benzoylformate:



calculated spectrum

This, coupled with the information available on the size of coupling constants, enables the following assignments to be made:



J_{34} = 20•5, J_{35} = 5,
J_{36} = 11•5, J_{45} = 19•3,
J_{46} = 7, J_{56} = 21 Hz.
$J_{2'3'}$ = 20•5, $J_{2'4'}$ = 5•7,
$J_{2'5'}$ = 11•5, $J_{2'H}$ = 5•7,
$J_{3'4'}$ = 19, $J_{3'H}$ = 3 Hz.

Although three peaks have the same calculated shift (-10), these can be assigned unambiguously in the actual spectrum as each peak has characteristic ortho, meta, and para coupling constants, and those peaks in the o-tetrafluorophenyl ring also couple with the ring hydrogen.

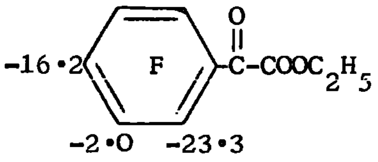
Most of the peaks in this assignment agree with calculated values to ±0·5 p.p.m. although two (peaks 1 and 4) are incorrect by up to 2 p.p.m. Confirmation that the assignments are correct comes from the agreement obtained between the coupling constants for each peak.

10. Ethyl tetrafluoro-2(2',3',4',5'-tetrafluorophenyl)benzoylformate (ether).

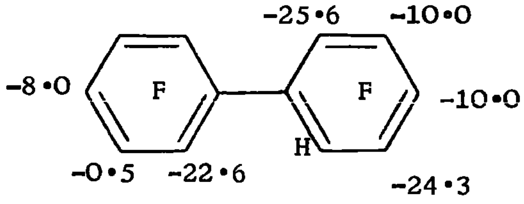
This spectrum showed the following resonances:

Peak	Shift	Intensity
1	-8·0	1
2	-9·8	1
3	-10·2	1
4	-14·8	1
5	-24·5	1
6,7	-25·5	2
8	-26·1	1

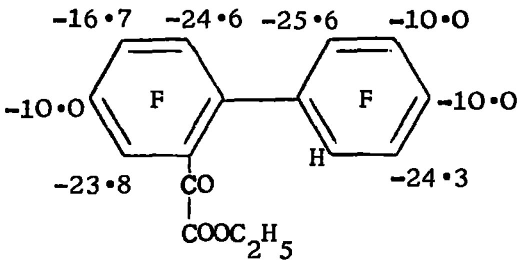
As in the previous example, a spectrum can be constructed for this compound, using the substituent shifts from:



and

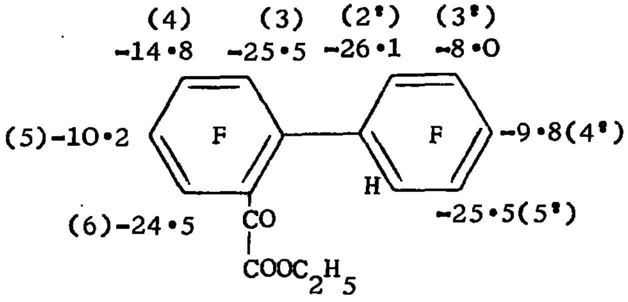


This gives the following calculated spectrum:



calculated spectrum

which, as before, can be used as a guide in making the following assignments from the actual spectrum:



J_{34} = 20, J_{35} = 4·7,

J_{36} = 12·0, J_{45} = 20,

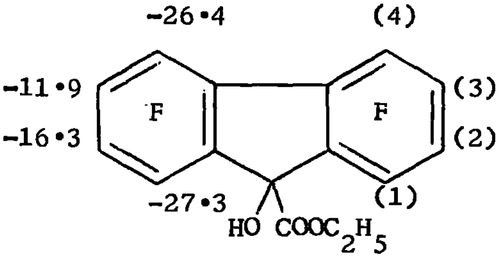
J_{46} = 7·5, J_{56} = 21·5 Hz.

$J_{2'3'}$ = 19, $J_{3'H}$ = 2·4,

$J_{3'4'}$ = 19, $J_{3'5'}$ = 7·5,

$J_{4'H}$ = 4·2, $J_{4'5'}$ = 19 Hz.

11. <u>9-Carboethoxyoctafluorofluoren-9-ol</u> ($CHCl_3$).

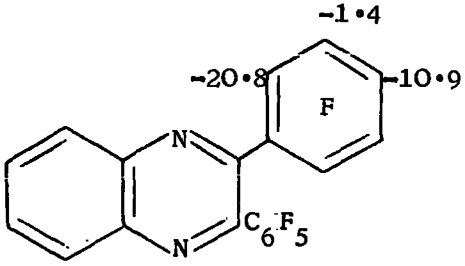


J_{12} = 21·5, J_{13} = 4·7,

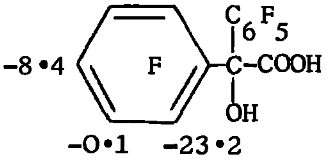
J_{14} = 10·8, J_{23} = 20,

J_{24} = 7·5, J_{34} = 21·5 Hz.

12. <u>2,3-Bis(pentafluorophenyl)quinoxaline</u> (CCl_4).



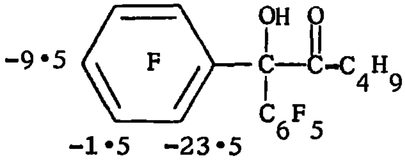
13. Decafluorobenzilic acid (CCl_4).



$J_{24} \sim 3$,

J_{34} = 20·5 Hz.

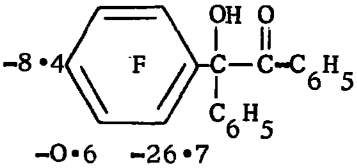
14. 1-Hydroxy-1,1-bis(pentafluorophenyl)hexan-2-one (CCl_4).



J_{24} = 3·4,

J_{34} = 20·4 Hz.

15. α-Pentafluorophenylbenzoin ($CHCl_3$).



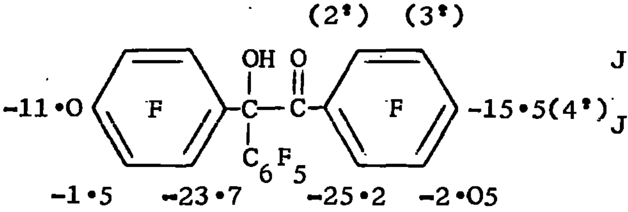
J_{24} = 3·3,

J_{34} = 20·7 Hz.

16. Perfluoro-α-phenylbenzoin (CCl_4).

J_{24} = 4,

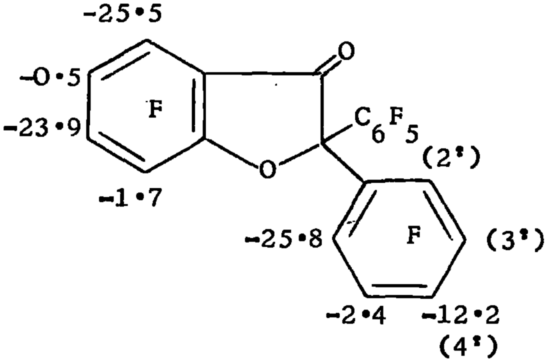
J_{34} = 20 Hz.



$J_{2'4'}$ = 6,

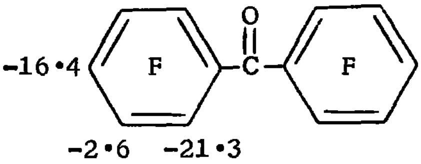
$J_{3'4'}$ = 20 Hz.

17. Perfluoro-2,2-diphenylbenzofuran-3-one (acetone, 60°)

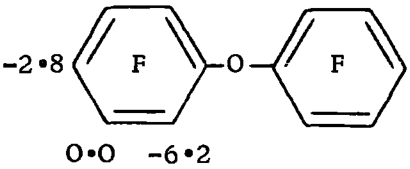


$J_{45} = 20{\cdot}5$, $J_{46} = 9{\cdot}5$,
$J_{47} = 16{\cdot}3$, $J_{56} = 18{\cdot}5$,
$J_{57} = 2$, $J_{67} = 18{\cdot}5$ Hz.
$J_{2'4'} = 4{\cdot}2$, $J_{3'4'} = 20$ Hz.

By comparison with the shifts of the ortho and para fluorines in[63,115]



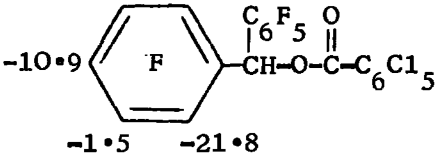
and



,

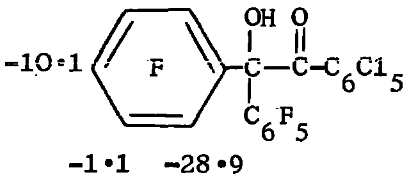
the lowest field peak at -25•5 was assigned to the fluorine ortho to the carbonyl group, and the highest field peak at -0•5 to the fluorine para to the ether linkage.

18. Bis(pentafluorophenyl)methyl pentachlorobenzoate (CCl_4).

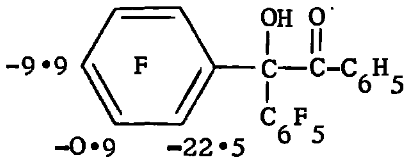


$J_{34} = 20{\cdot}4$ Hz.

19. Pentachlorobenzoylbis(pentafluorophenyl)methanol (acetone).



20. Benzoylbis(pentafluorophenyl)methanol (CCl_4).



J_{24} = 3•8,

J_{34} = 20•4 Hz.

Mass Spectra

Mass spectra were recorded on an A.E.I. MS9 mass spectrometer. All figures quoted are percentages of the base peaks.

1. Decachlorobenzil, 2,3,4,5,6-pentachloropentafluorobenzil and decafluorobenzil.

		Intensity		
Mass No.	Ion	$C_6Cl_5COCOC_6Cl_5$	$C_6Cl_5COCOC_6F_5$	$C_6F_5COCOC_6F_5$
390	P^+			0•5
362	P^+-CO			6
275	$C_6Cl_5CO^+$	100	100	
247	$C_6Cl_5^+$	17	17	
240	$C_6Cl_4CO^+$		2	
212	$C_6Cl_4^+$	8	9	
195	$C_6F_5CO^+$		12	100
177	$C_6Cl_3^+$	3	2	
176	$C_6F_4CO^+$		2	1
167	$C_6F_5^+$		5	20
148	$C_6F_4^+$		2	15
142	$C_6Cl_2^+$	3	3	
117	$C_5F_3^+$		3	12
107	C_6Cl^+	2	1	
98	$C_5F_2^+$			2
93	$C_3F_3^+$		1	3
28	CO^+	25	5	14

2. 2,3,4,5,6-Pentafluorobenzil, $C_6F_5COCOC_6H_5$.

Mass No.	Ion	Intensity
195	$C_6F_5CO^+$	11
167	$C_6F_5^+$	21
148	$C_6F_4^+$	3
117	$C_5F_3^+$	27
105	$C_6H_5CO^+$	63
98	$C_5F_2^+$	7
93	$C_3F_3^+$	8
77	$C_6H_5^+$	100
76	$C_6H_4^+$	7
75	$C_6H_3^+$	7
74	$C_6H_2^+$	11
63	$C_5H_3^+$	2
52	$C_4H_4^+$	4
51	$C_4H_3^+$	75
50	$C_4H_2^+$	31
39	$C_3H_3^+$	6
38	$C_3H_2^+$	3

3. Methyl pentachlorobenzoylformate, $C_6Cl_5COCOOCH_3$.

Mass No.	Ion	Intensity
334	P^+	6
299	P^+-Cl	0·5
275	$C_6Cl_5CO^+$	100
247	$C_6Cl_5^+$	14
240	$C_6Cl_4CO^+$	1
212	$C_6Cl_4^+$	9
177	$C_6Cl_3^+$	7
142	$C_6Cl_2^+$	6
137·5	$C_6Cl_5CO^{++}$	1
118	$C_4Cl_2^+$	2
107	C_6Cl^+	3
106	$C_6Cl_4^{++}$	1
59	$COOCH_3^+$	2
36	HCl^+	6
28	CO^+	5
15	CH_3^+	3

4. Methyl pentafluorobenzoylformate and ethyl pentafluorobenzoylformate.

Mass No.	Ion	Intensity $C_6F_5COCOOCH_3$	Intensity $C_6F_5COCOOC_2H_5$
268	P^+		0•5
254	P^+	3	
224	M268-CO_2		1
210	M254-CO_2	0•5	
195	$C_6F_5CO^+$	100	100
177	$C_6F_4CHO^+$		3
176	$C_6F_4CO^+$	1	
167	$C_6F_5^+$	23	19
148	$C_6F_4^+$	2	2
117	$C_5F_3^+$	14	12
98	$C_5F_2^+$	3	2
97•5	$C_6F_5CO^{++}$	1	0•5
93	$C_3F_3^+$	5	3
79	C_5F^+	2	1
59	$C_2H_3O_2^+$	14	
57	$C_3H_5O^+$		1
45	$C_2H_5O^+$		1
44	$C_2H_4O^+$, CO_2^+	3	2
31	CH_3O^+	2	
29	$C_2H_5^+$		48
28	$C_2H_4^+$, CO^+	7	6
15	CH_3^+	15	

5. Decafluorobenzilic acid, methyl decafluorobenzilate and ethyl decafluorobenzilate

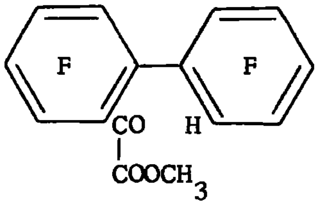
			Intensity	
Mass No.	Ion	RCOOH	$RCOOCH_3$	$RCOOC_2H_5$
			(where R = $(C_6F_5)_2C(OH)$-	
436	P^+			0•5
422	P^+		0•2	
416	M436-HF			3
402	M422-HF		1	
363	$(C_6F_5)_2\overset{+}{C}OH$	45	100	100
362	$(C_6F_5)_2CO^+$	20	4	
347	$(C_6F_5)_2CH^+$			9
346	$(C_6F_5)_2C^+$	12	1	4
344	$(C_6F_5)(C_6F_4)\overset{+}{C}OH$	3	2	1
327	$(C_6F_5)(C_6F_4)C^+$	19	4	6
325	$C_{13}F_8OH^+$	2	9	2
324	$C_{13}F_8O^+$	2	4	2
308	$C_{13}F_8^+$	2		
296	$C_{12}F_8^+$	9	5	5
278	$C_{12}F_7H^+$	3	1	2
277	$C_{12}F_7^+$	3	2	2
265	$C_{11}F_7^+$	4	3	3
258	$C_{12}F_6^+$	2	1	1
247	$C_{11}F_6H^+$	2	1	1

Mass No.	Ion	RCOOH	$RCOOCH_3$	$RCOOC_2H_5$
246	$C_{11}F_6^+$	2	2	1
227	$C_{11}F_5^+$	3	3	2
195	$C_6F_5CO^+$	100	93	70
177	$C_{10}F_3^+$	7	2	2
167	$C_6F_5^+$	54	26	23
148	$C_6F_4^+$	7	5	4
117	$C_5F_3^+$	33	15	12
99	$C_5F_2H^+$	5	2	3
98	$C_5F_2^+$	5	3	2
93	$C_3F_3^+$	9	5	4
59	$C_2H_3O_2^+$		39	
45	CO_2H^+, $C_2H_5O^+$	5		2
44	CO_2^+, $C_2H_4O^+$	13	2	3
31	CH_3O^+		2	
29	$C_2H_5^+$, CHO^+		15	85
28	$C_2H_4^+$, CO^+			15
27	$C_2H_3^+$			16
15	CH_3^+		15	

6. Methyl 2,3,4,5,6-pentachloropentafluorobenzilate, $C_6Cl_5(C_6F_5)C(OH)COOCH_3$

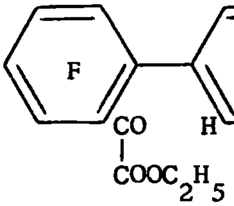
Mass No.	Ion	Intensity
502	P^+	2
467	P^+-Cl	1
443	$C_6Cl_5(C_6F_5)\overset{+}{C}OH$	30
408	$C_6Cl_4(C_6F_5)\overset{+}{C}OH$	1
389	$C_6Cl_4(C_6F_4)\overset{+}{C}OH$	2
275	$C_6Cl_5CO^+$	8
247	$C_6Cl_5^+$	7
212	$C_6Cl_4^+$	8
195	$C_6F_5CO^+$	37
177	$C_6Cl_3^+$	8
167	$C_6F_5^+$	18
148	$C_6F_4^+$	6
142	$C_6Cl_2^+$	12
117	$C_5F_3^+$	18
107	C_6Cl^+	7
98	$C_5F_2^+$	5
93	$C_3F_3^+$	7
69	CF_3^+	7
59	$COOCH_3^+$	100
45	CO_2H^+	8
15	CH_3^+	80

7. Methyl tetrafluoro-2-(2',3',4',5'-tetrafluorophenyl)benzoylformate.



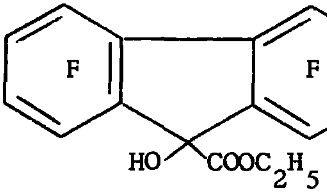
Mass No.	Ion	Intensity
384	P^+	3
325	$P^+ - COOCH_3$	100
324	$C_{13}F_8O^+$	2
305	$C_{13}F_7O^+$	2
297	$C_{12}F_8H^+$	7
296	$C_{12}F_8^+$	4
278	$C_{12}F_7H^+$	20
247	$C_{11}F_6H^+$	17
228	$C_{11}F_5H^+$	3
227	$C_{11}F_5^+$	2
209	$C_{11}F_4H^+$	2
139	$C_{12}F_7H^{++}$	2
123·5	$C_{11}F_6H^{++}$	3
59	$C_2H_3O_2^+$	11
43	$C_2H_3O^+$, C_2F^+	10
41	C_2HO^+	3
29	CHO	7
15	CH_3	12

8. Ethyl tetrafluoro-2-(2',3',4',5'-tetrafluorophenyl)benzoylformate.



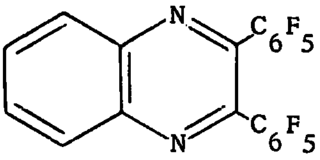
Mass No.	Ion	Intensity
398	P^+	6
325	$C_{13}F_8OH^+$	100
306	$C_{13}F_7OH^+$	2
298	$C_{12}F_8H_2^+$	12
297	$C_{12}F_8H^+$	7
278	$C_{12}F_7H^+$	15
247	$C_{11}F_6H^+$	12
229	$C_{11}F_5H_2^+$	2
228	$C_{11}F_5H^+$	2
209	$C_{11}F_4H^+$	2
162•5	$C_{13}F_8OH^{++}$	3
123•5	$C_{11}F_6H^{++}$	3

9. 9-Carbethoxyoctafluorofluoren-9-ol.



Mass No.	Ion	Intensity
354	$P^{+}-(CO_2,OC_2H_4)$	22
353	$P^{+}-(COOH,OC_2H_5)$	34
325	$C_{13}F_8\overset{+}{O}H$	100
324	$C_{13}F_8\overset{+}{O}$	42
296	$C_{12}F_8^{+}$	25
277	$C_{12}F_7^{+}$	14
265	$C_{11}F_7^{+}$	6
258	$C_{12}F_6^{+}$	4
246	$C_{11}F_6^{+}$	8
227	$C_{11}F_5^{+}$	11
196	$C_{10}F_4^{+}$	3
148	$C_{12}F_8^{++}$	2
57	$COC_2H_5^{+}$	1
44	$CO_2^{+},OC_2H_4^{+}$	3
29	$C_2H_5^{+}$	88

10. 2,3-Bis(pentafluorophenyl)quinoxaline.



Mass No.	Ion	Intensity
462	P^+	69
443	P^+-F	2
295	$P^+-C_6F_5$	2
269	$P^+-C_6F_5CN$	51
250	M269-F	2
231	P^{++}	2
193	$C_6F_5CN^+$	5
117	$C_5F_3^+$	4
102	$C_6H_4CN^+$	9
93	$C_3F_3^+$	4
76	$C_6H_4^+$	100
75	$C_6H_3^+$	13
74	$C_6H_2^+$	6
50	$C_4H_2^+$	40

11. α-Butylbenzoin, $C_6H_5(C_4H_9)C(OH)COC_6H_5$.

Mass No.	Ion	Intensity
183	$(C_6H_5)_2\overset{+}{C}OH$	8
163	$(C_6H_5)(C_4H_9)\overset{+}{C}OH$	100
105	$C_6H_5CO^+$	27
91	$C_6H_3O^+$, $C_7H_7^+$	7
85	$C_4H_9CO^+$	8
79	$C_6H_7^+$	5
78	$C_6H_6^+$	6
77	$C_6H_5^+$	26
71	$C_3H_7CO^+$	4
57	$C_4H_9^+$	16
51	$C_4H_3^+$	7
43	$C_3H_7^+$	7
41	$C_3H_5^+$	7

12. α-Pentachlorophenylbenzoin and α-pentafluorophenylbenzoin.

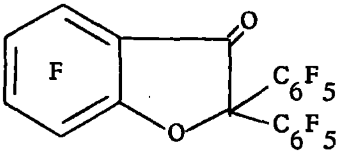
Mass No.	Ion	Intensity $C_6H_5(C_6Cl_5)C(OH)COC_6H_5$	Intensity $C_6H_5(C_6F_5)C(OH)COC_6H_5$
353	$C_6H_5(C_6Cl_5)\overset{+}{C}OH$	33	
317	M353-HCl	2	
275	$C_6Cl_5CO^+$	23	
273	$C_6H_5(C_6F_5)\overset{+}{C}OH$		9
247	$C_6Cl_5^+$	6	
212	$C_6Cl_4^+$	3	
195	$C_6F_5CO^+$		27
183	$(C_6H_5)_2\overset{+}{C}OH$	30	
177	$C_6Cl_3^+$	1	
167	$C_6F_5^+$		7
142	$C_6Cl_2^+$	2	
105	$C_6H_5CO^+$	100	100
77	$C_6H_5^+$	46	43
76	$C_6H_4^+$	2	1
51	$C_4H_3^+$	13	12
50	$C_4H_2^+$	3	2
39	$C_3H_3^+$		1

13. 1-Hydroxy-1,1-bis(pentafluorophenyl)hexan-2-one, $(C_6F_5)_2C(OH)COC_4H_9$.

Mass No.	Ion	Intensity
363	$(C_6F_5)_2\overset{+}{C}OH$	17
253	$C_6F_5(C_4H_9)\overset{+}{C}OH$	8
195	$C_6F_5CO^+$	100
168	$C_6F_5H^+$	25
167	$C_6F_5^+$	24
149	$C_6F_4H^+$	2
148	$C_6F_4^+$	3
137	$C_5F_4H^+$	3
117	$C_5F_3^+$	14
99	$C_5F_2H^+$	8
93	$C_3F_3^+$	6
85	$C_4H_9CO^+$	25
73	$C_4H_9O^+$	3
57	$C_4H_9^+$	25
56	$C_4H_8^+$	33
55	$C_4H_7^+$	6
44	CO_2^+	29
43	$C_3H_7^+$	12
41	$C_3H_5^+$	26

14. Perfluoro-α-phenylbenzoin and perfluoro-2,2-diphenylbenzofuran-3-one.

$(C_6F_5)_2C(OH)COC_6F_5$ = A

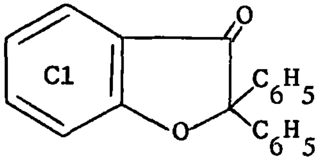


= B

Mass No.	Ion	Intensity	
		A	B
558	P_A^{+}	0•1	
538	P_A^{+}-HF, P_B^{+}	0•5	50
519	P_B^{+}-F		2
510	P_B^{+}-CO		4
491	P_B^{+}-COF		16
460	P_B^{+}-CO-CF_2		10
371	P_B^{+}-C_6F_5		6
363	$(C_6F_5)_2\overset{+}{C}OH$	53	
362	$(C_6F_5)_2CO^{+}$	2	
347	$(C_6F_5)_2CH^{+}$	2	
346	$(C_6F_5)_2C^{+}$	0•5	24
344	$C_6F_5(C_6F_4)\overset{+}{C}OH$	1	
343	$C_6F_5(C_6F_4)\overset{+}{C}O$	1	14
327	$C_6F_5(C_6F_4)C^{+}$	3	35
296	$C_{12}F_8^{+}$	3	12
277	$C_{12}F_7^{+}$	1	2
265	$C_{11}F_7^{+}$	2	3
258	$C_{12}F_6^{+}$	1	3

Mass No.	Ion	A	B
246	$C_{11}F_6^+$	1	2
227	$C_{11}F_5^+$	1	3
195	$C_6F_5CO^+$	100	83
192	$C_6F_4COO^+$		2
176	$C_6F_4CO^+$	2	100
167	$C_6F_5^+$	36	19
164	$C_6F_4O^+$		2
148	$C_6F_4^+$	4	45
136	$C_5F_4^+$		3
129	$C_6F_3^+$		2
117	$C_5F_3^+$	18	12
105	$C_4F_3^+$		14
99	$C_5F_2H^+$	3	
98	$C_5F_2^+$	3	4
93	$C_3F_3^+$	5	5

15. Tetrachloro-2,2-diphenylbenzofuran-3-one.



Mass No.	Ion	Intensity
422	P^+	1
393	$P^+ - CHO$	0·5
256	$C_6Cl_4COO^+$	16
228	$C_6Cl_4O^+$	14
221	$C_6Cl_3COO^+$	3
212	$C_6Cl_4^+$	8
200	$C_5Cl_4^+$	7
193	$C_6Cl_3O^+$	4
177	$C_6Cl_3^+$	6
166	$(C_6H_5)_2C^+$	24
165	$C_6H_5(C_6H_4)C^+$	57
165	$C_5Cl_3^+$	26
158	$C_6Cl_2O^+$	3
152	$C_{12}H_8^+$	3
142	$C_6Cl_2^+$	10
139	$C_{11}H_7^+$	24
130	$C_5Cl_2^+$	24
127	$C_{10}H_7^+$	5

Mass No.	Ion	Intensity
105	$C_6H_5CO^+$	33
95	C_5Cl^+	18
77	$C_6H_5^+$	100
76	$C_6H_4^+$	14
63	$C_5H_3^+$	30
51	$C_4H_3^+$	65
50	$C_4H_2^+$	14
39	$C_3H_3^+$	42

16. Pentachlorobenzoylbis(pentafluorophenyl)methanol and bis(pentafluorophenyl)methyl pentachlorobenzoate.

Mass No.	Ion	Intensity	
		$(C_6F_5)_2C(OH)COC_6Cl_5$	$(C_6F_5)_2CHOCOC_6Cl_5$
638	P^+		19
618	P^+-HF		2
443	$C_6Cl_5(C_6F_5)\overset{+}{C}OH$	0·3	5
363	$(C_6F_5)_2\overset{+}{C}OH$	6	
347	$(C_6F_5)_2\overset{+}{C}H$	1	100
346	$(C_6F_5)_2C^+$		31
327	$C_6F_5(C_6F_4)\overset{+}{C}$	1	9
309	$C_{13}F_8H^+$		4
297	$C_{12}F_8H^+$		5
296	$C_{12}F_8^+$	2	2
278	$C_{12}F_7H^+$		15
275	$C_6Cl_5CO^+$	100	15
265	$C_{11}F_7^+$	2	
247	$C_6Cl_5^+$	20	12
212	$C_6Cl_4^+$	18	9
195	$C_6F_5CO^+$	26	10
177	$C_6Cl_3^+$	5	4
167	$C_6F_5^+$	11	4
148	$C_6F_4^+$	12	1
142	$C_6Cl_2^+$	6	5
117	$C_5F_3^+$	5	3
107	C_6Cl^+	2	1
93	$C_5F_2^+$	2	1

Index to Infra-red Spectra

Solid samples were recorded as KBr discs and liquid samples as contact films.

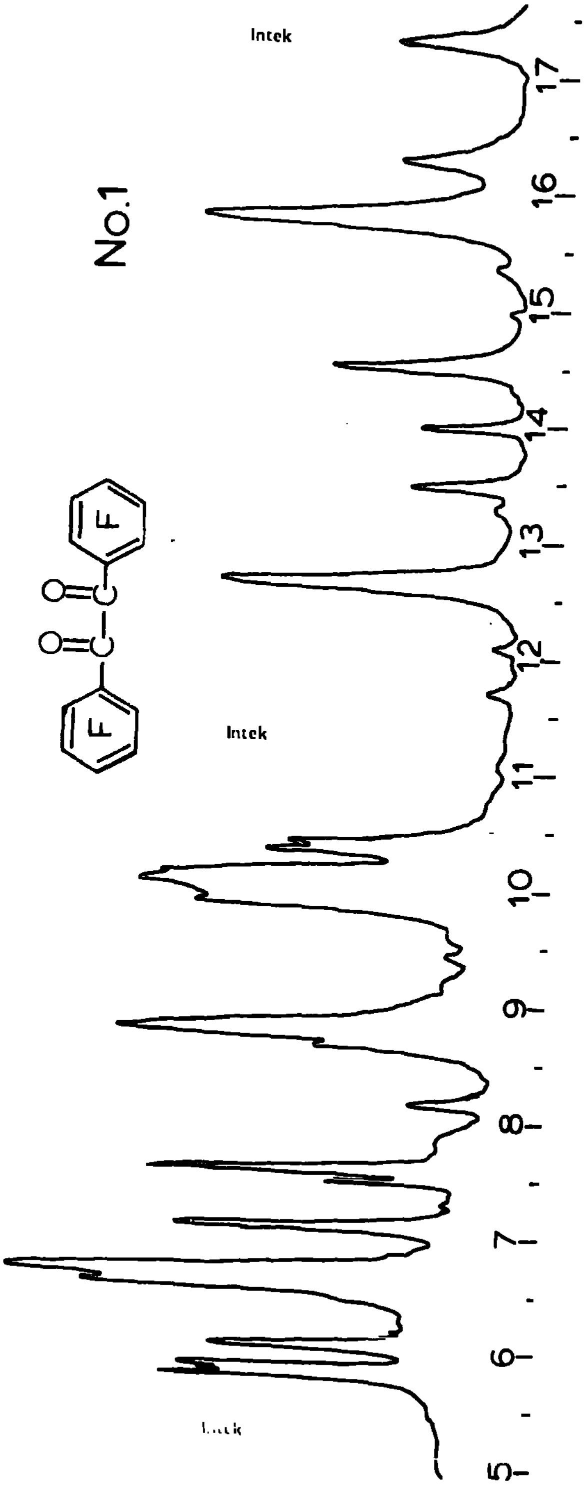
1. Decafluorobenzil (s)
2. 2,3,4,5,6-Pentachloropentafluorobenzil (s)
3. Decachlorobenzil (s)
4. 2,3,4,5,6-Pentafluorobenzil (s)
5. Methyl pentachlorobenzoylformate (s)
6. Methyl pentafluorobenzoylformate (l)
7. Ethyl pentafluorobenzoylformate (l)
8. Methyl 2,3,4,5,6-pentachloropentafluorobenzilate (s)
9. Methyl decafluorobenzilate (s)
10. Ethyl decafluorobenzilate (l)
11. Methyl tetrafluoro-2-(2',3',4',5'-tetrafluorophenyl)benzoylformate (s)
12. Ethyl tetrafluoro-2-(2',3',4',5'-tetrafluorophenyl)benzoylformate (l)
13. 9-Carbethoxyoctafluorofluoren-9-ol (s)
14. 2,3-Bis(pentafluorophenyl)quinoxaline (s)
15. Decafluorobenzilic acid (s)
16. 1-Hydroxy-1,1-bis(pentafluorophenyl)hexan-2-one (l)
17. α-n-Butylbenzoin (s)
18. α-Pentafluorophenylbenzoin (s)
19. Perfluoro-α-phenylbenzoin (s)
20. Perfluoro-2,2-diphenylbenzofuran-3-one (s)
21. α-Pentachlorophenylbenzoin (s)

22. Tetrachloro-2,2-diphenylbenzofuran-3-one (s)

23. Pentachlorobenzoylbis(pentafluorophenyl)methanol (s)

24. Bis(pentafluorophenyl)methyl pentachlorobenzoate (s)

25. Benzoylbis(pentafluorophenyl)methanol (1)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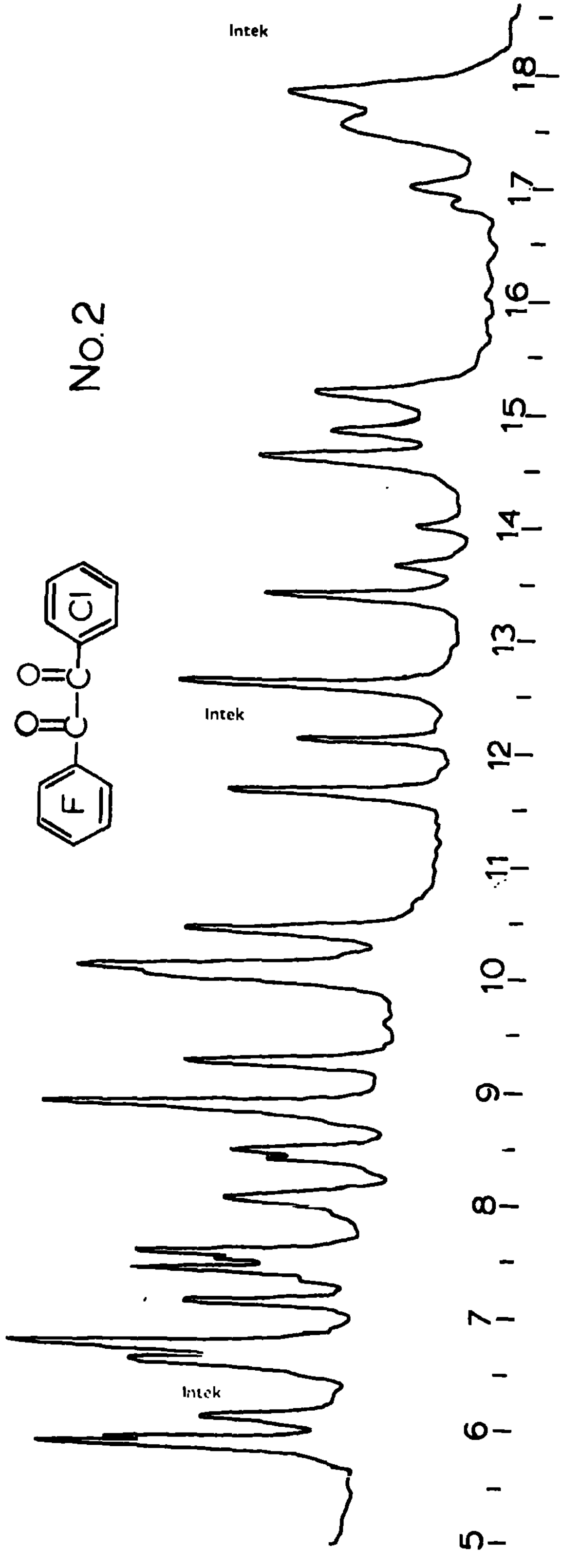
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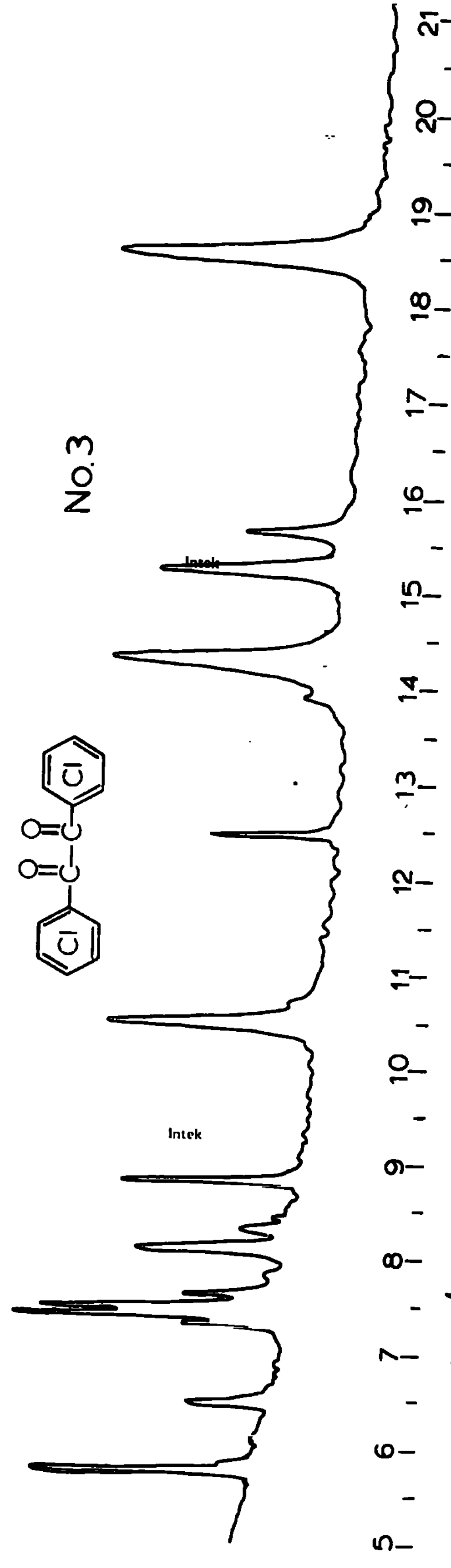
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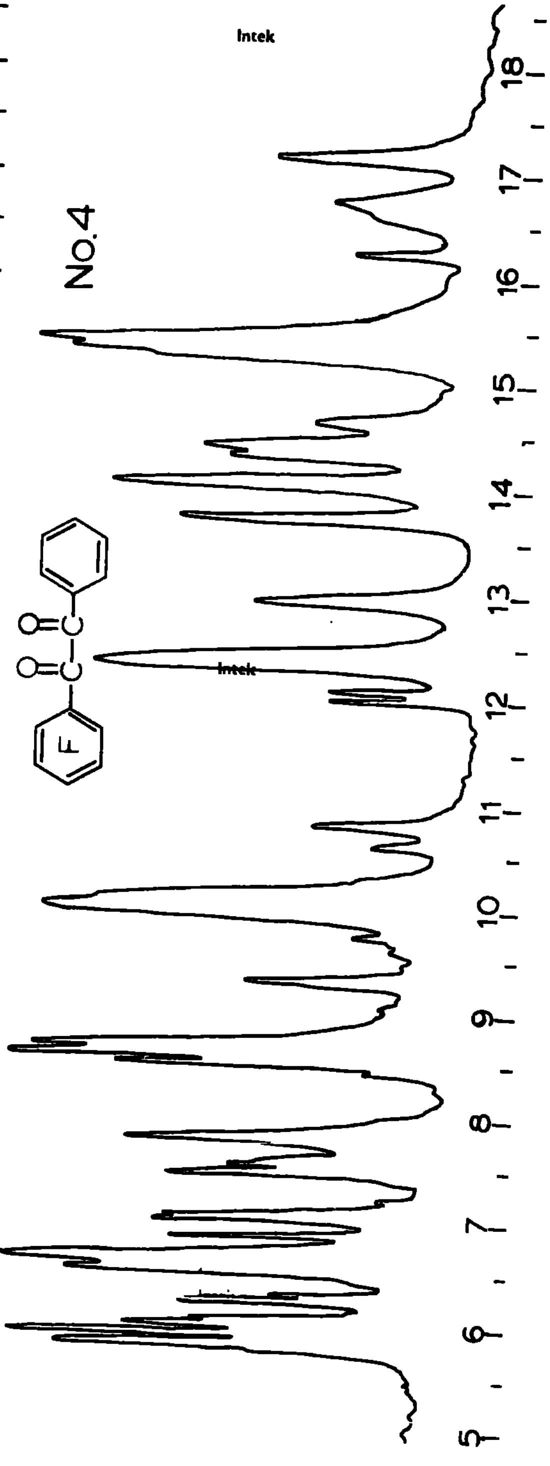
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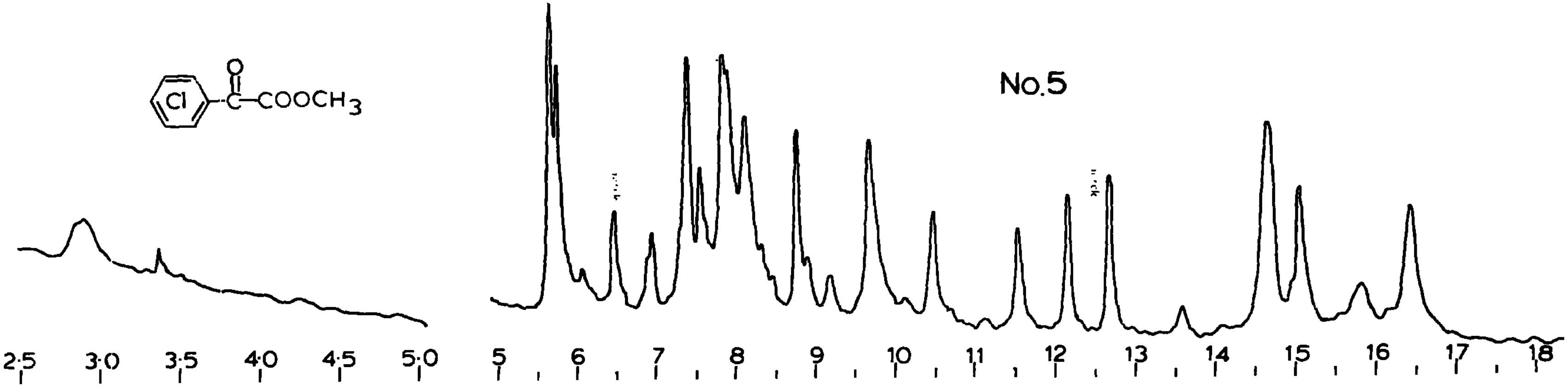
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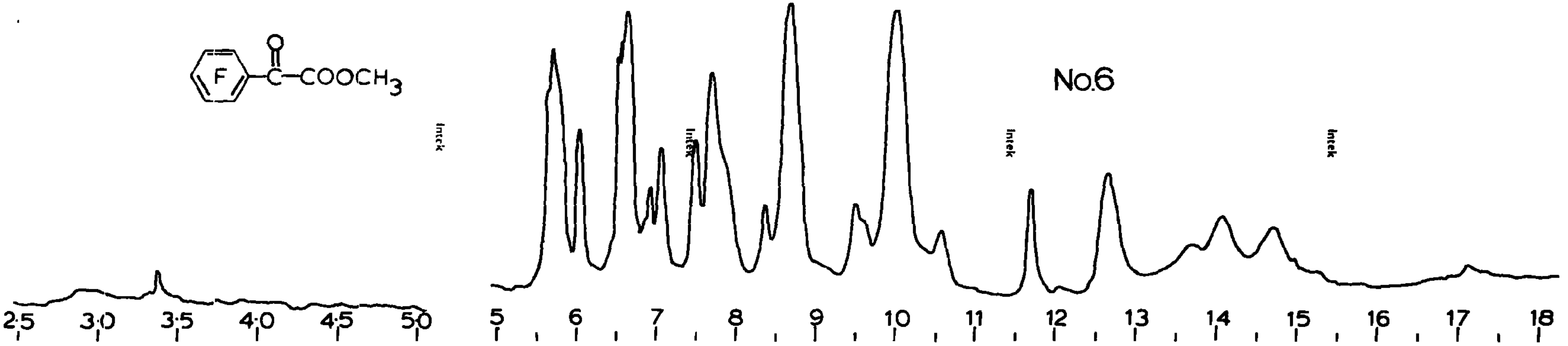
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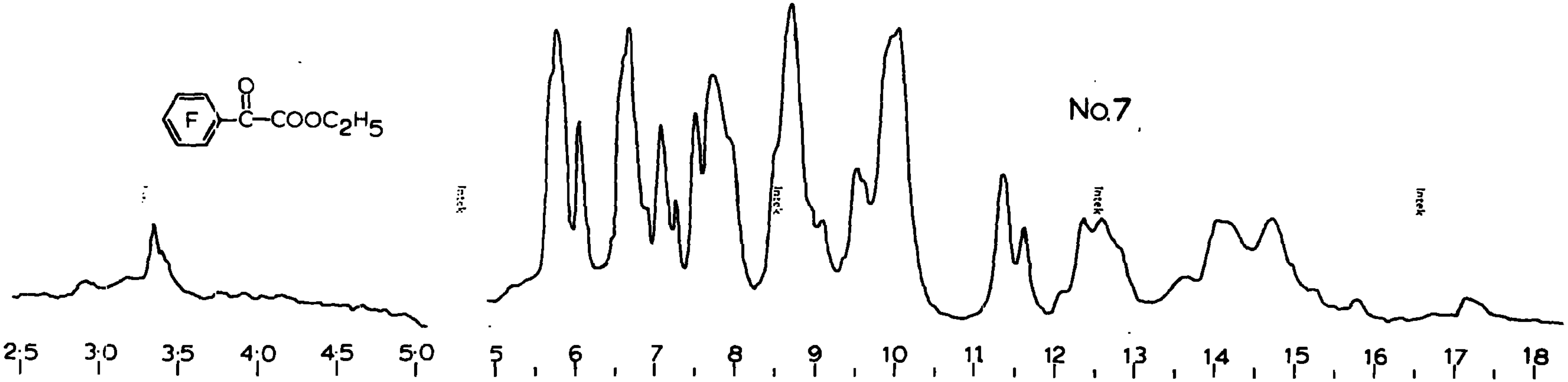
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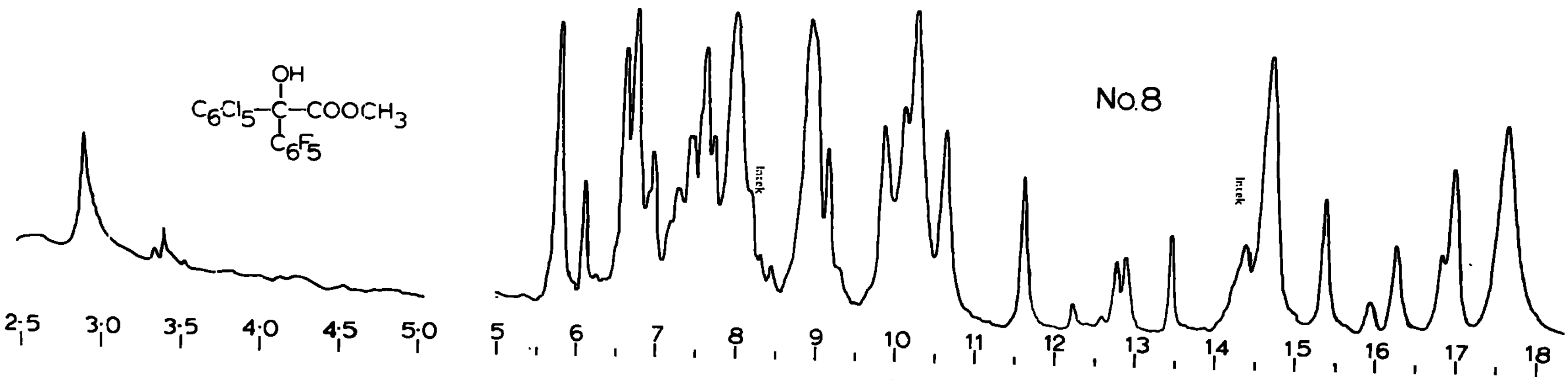
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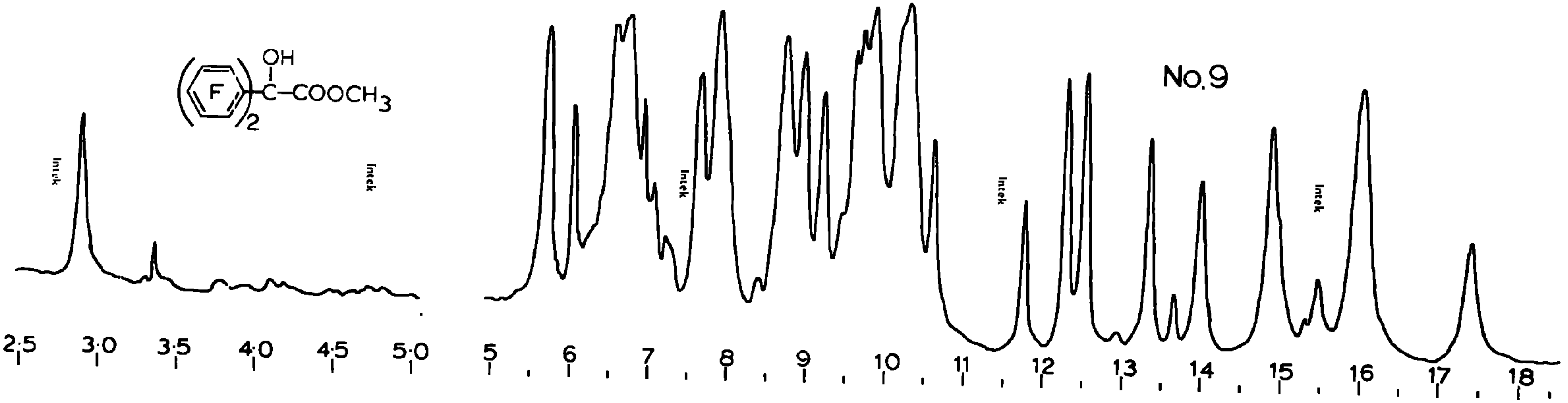
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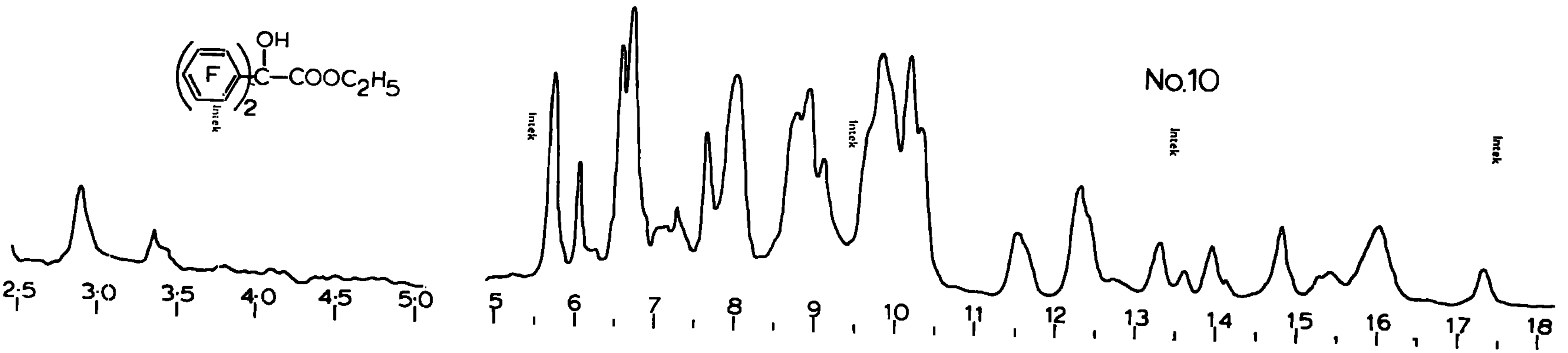
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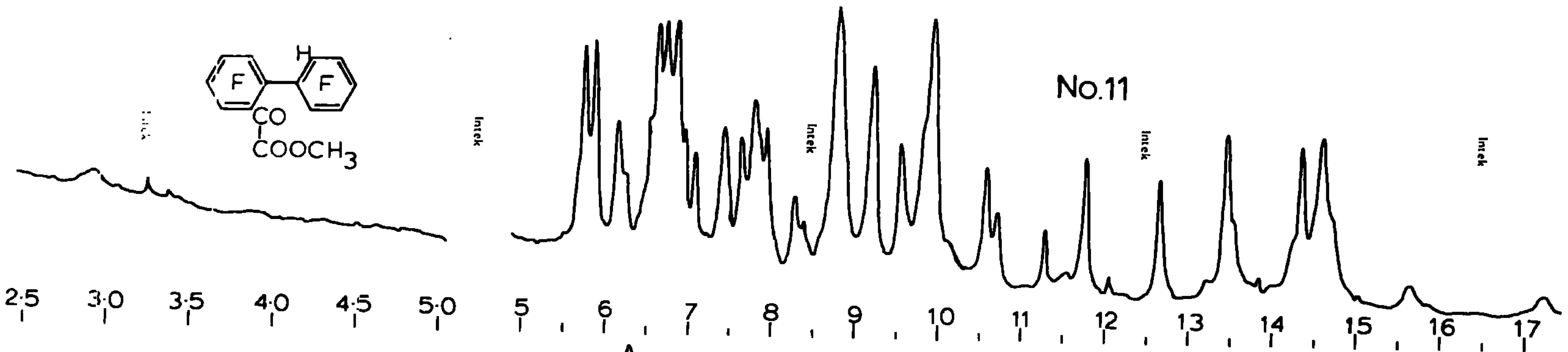
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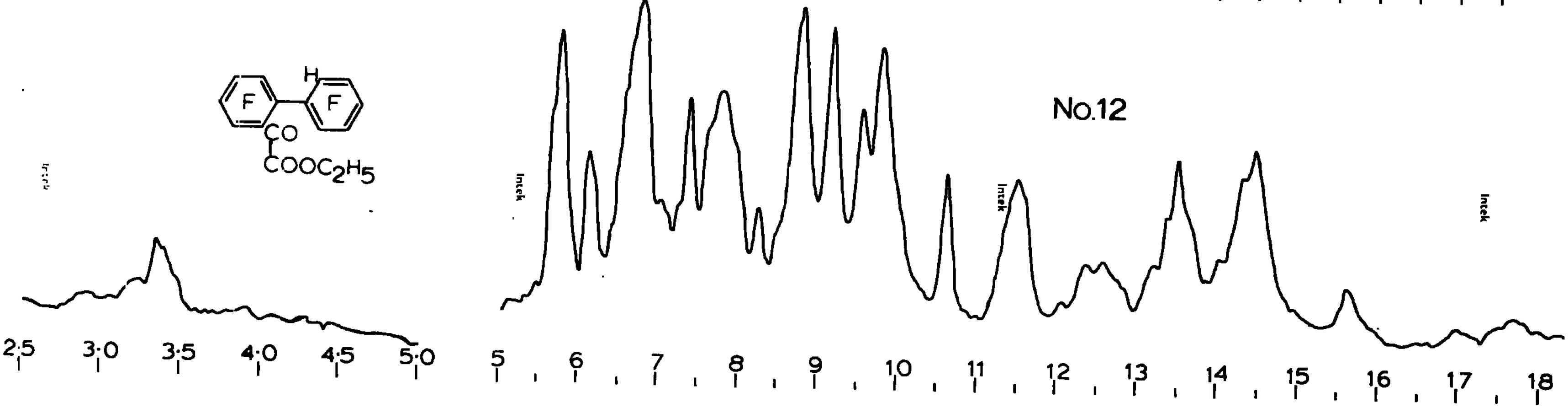
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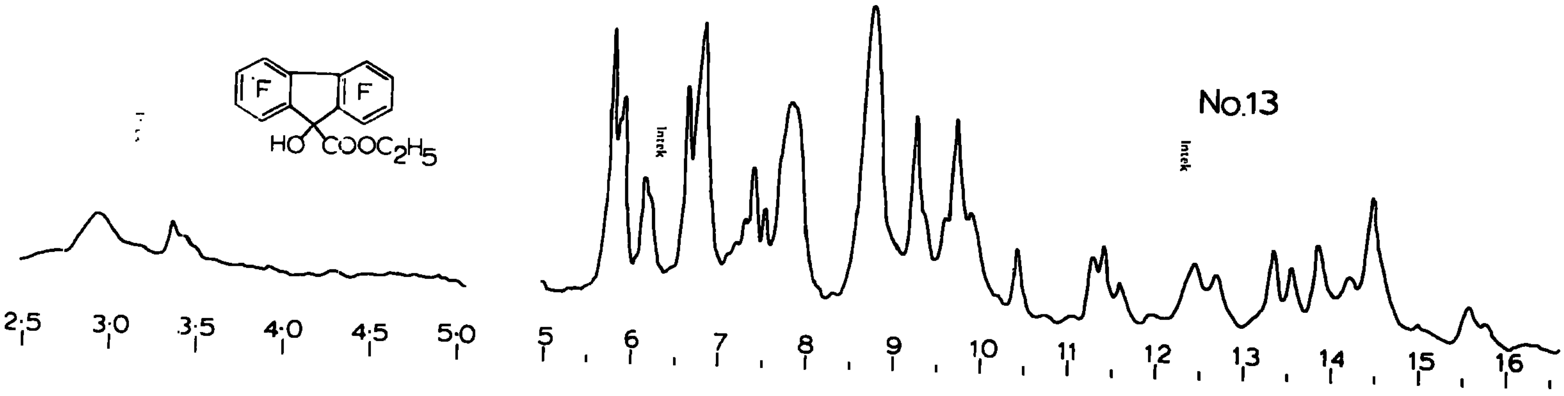
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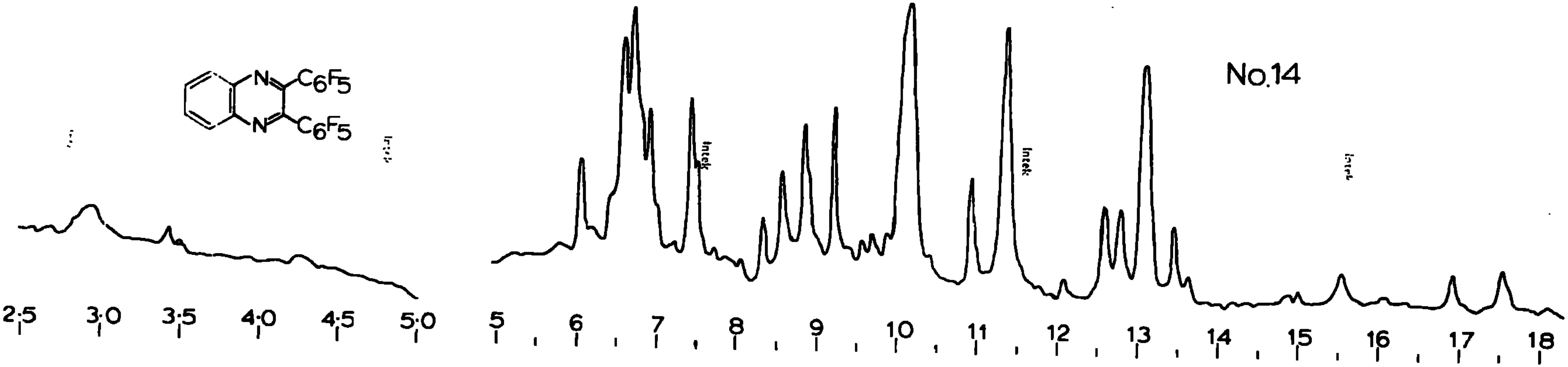
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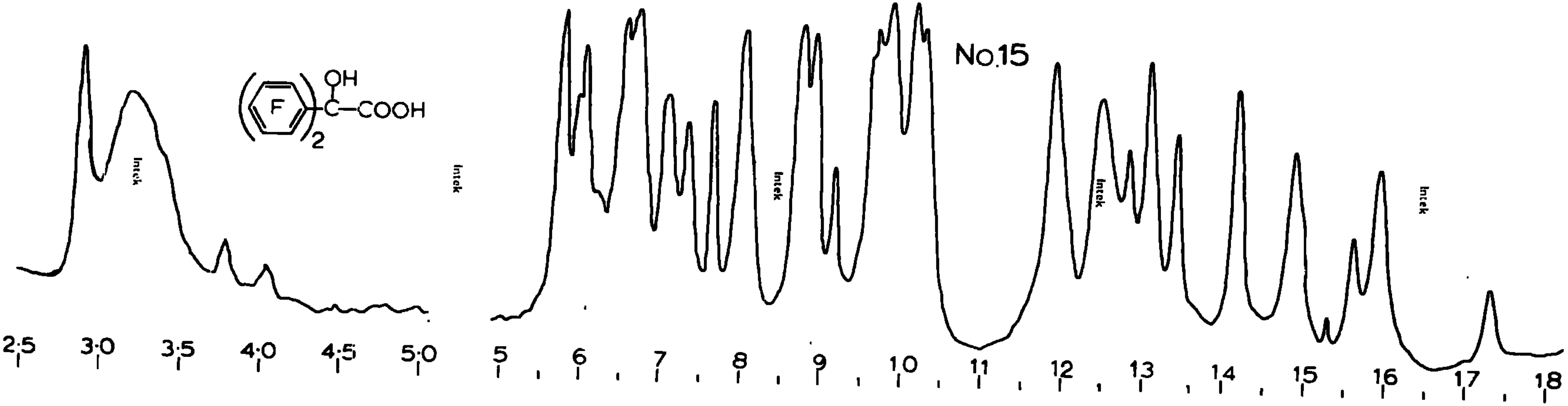
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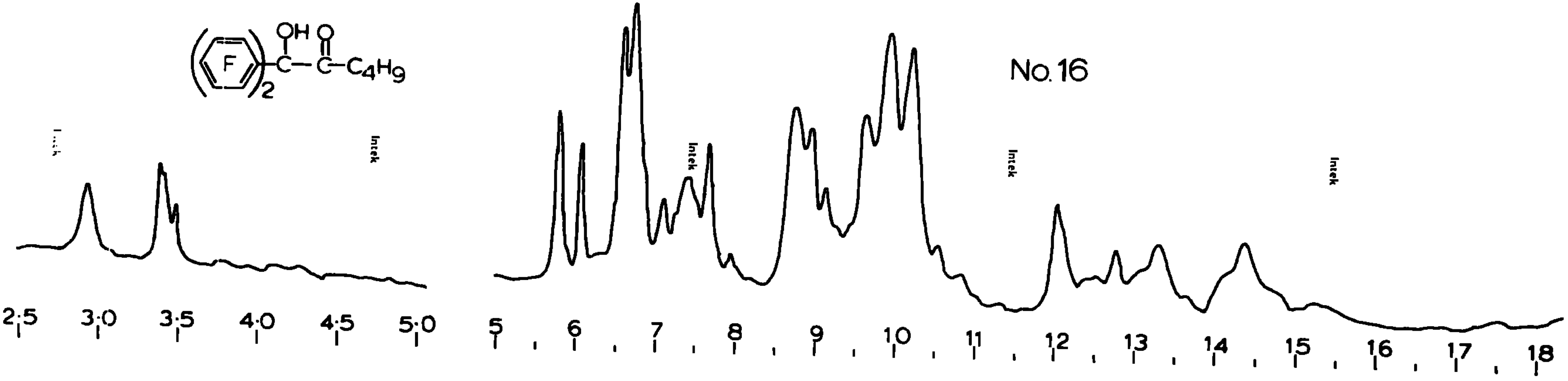
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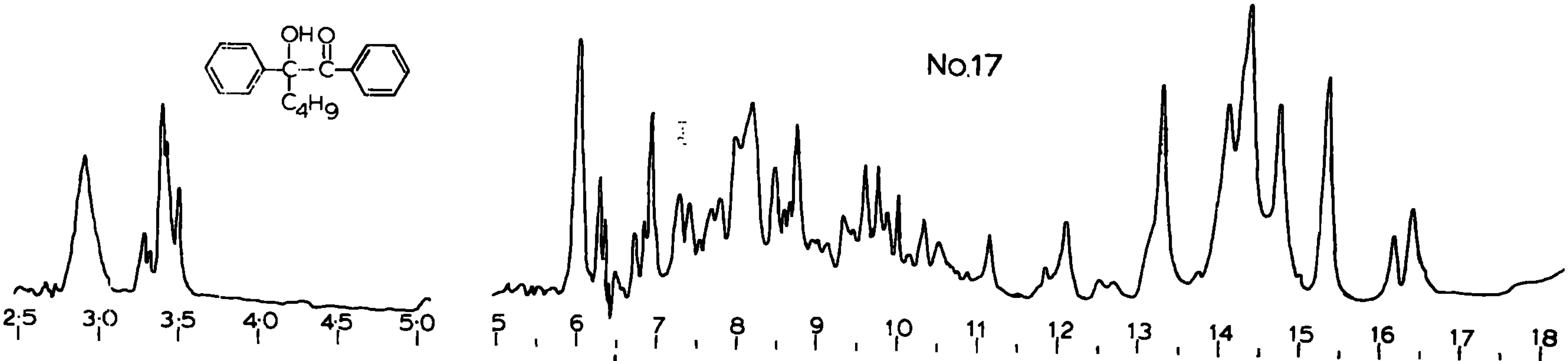
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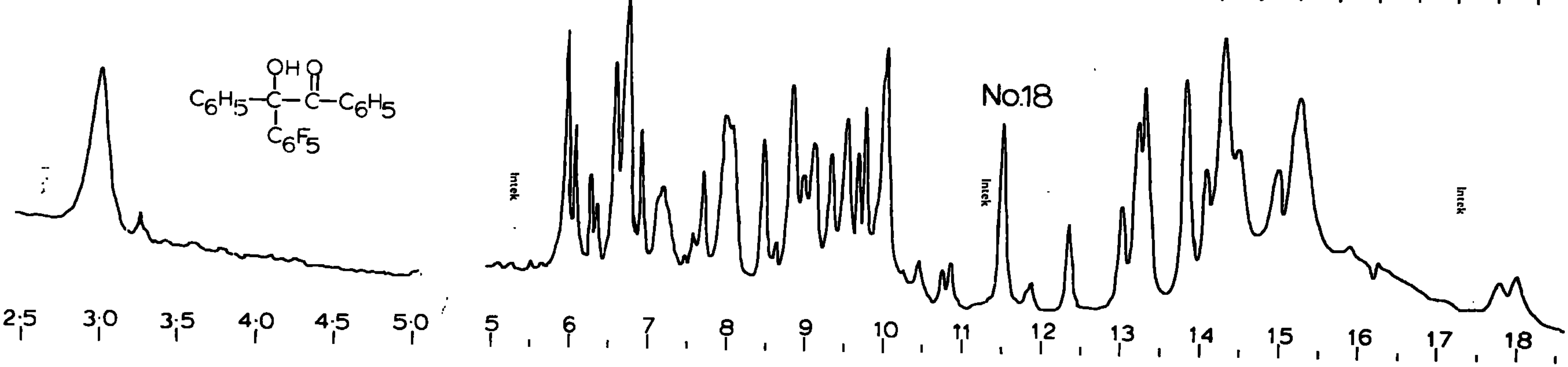
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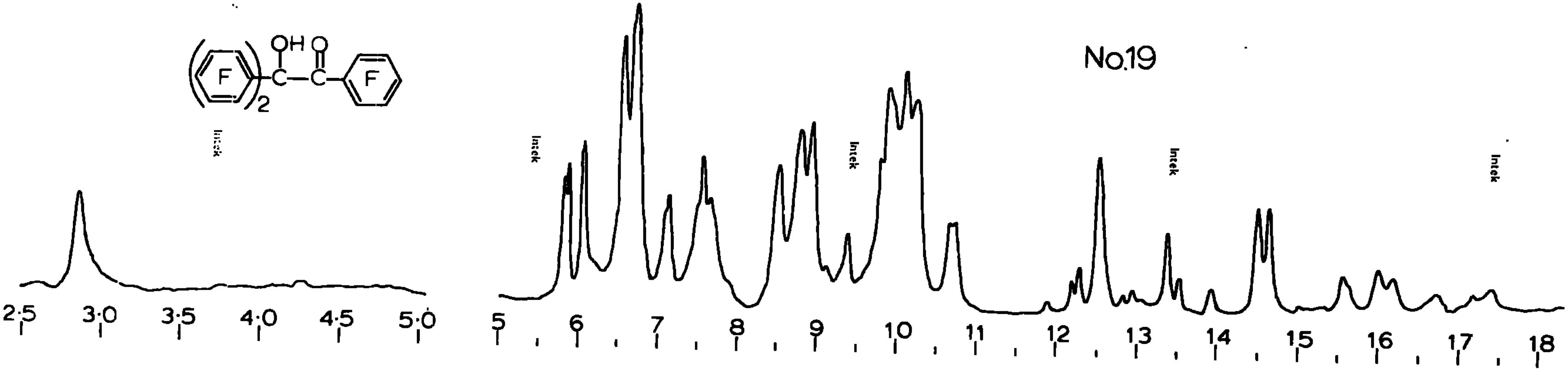
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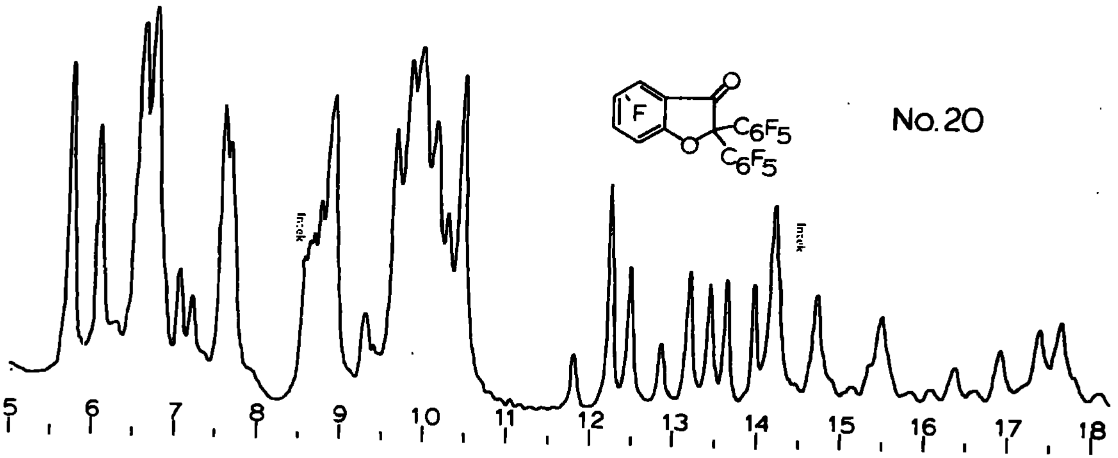
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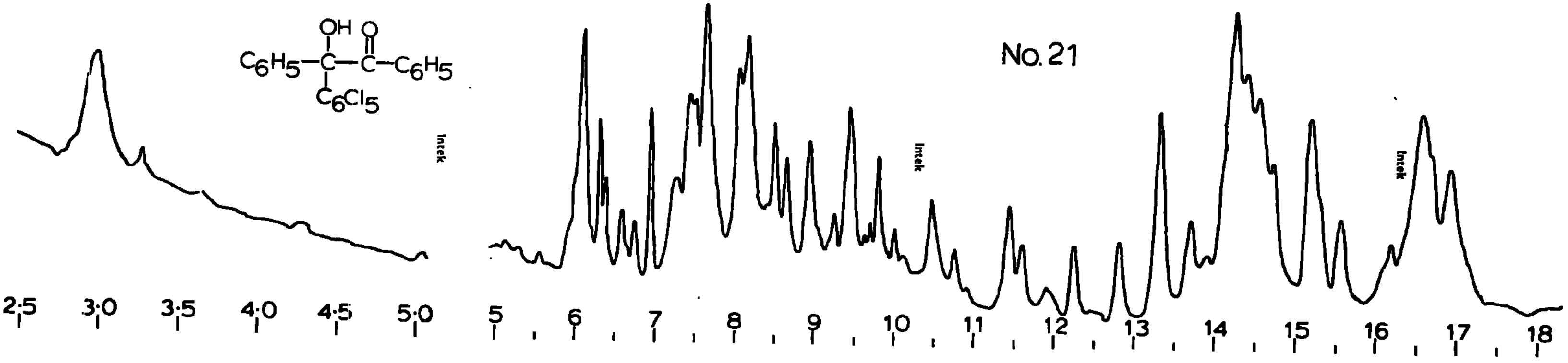
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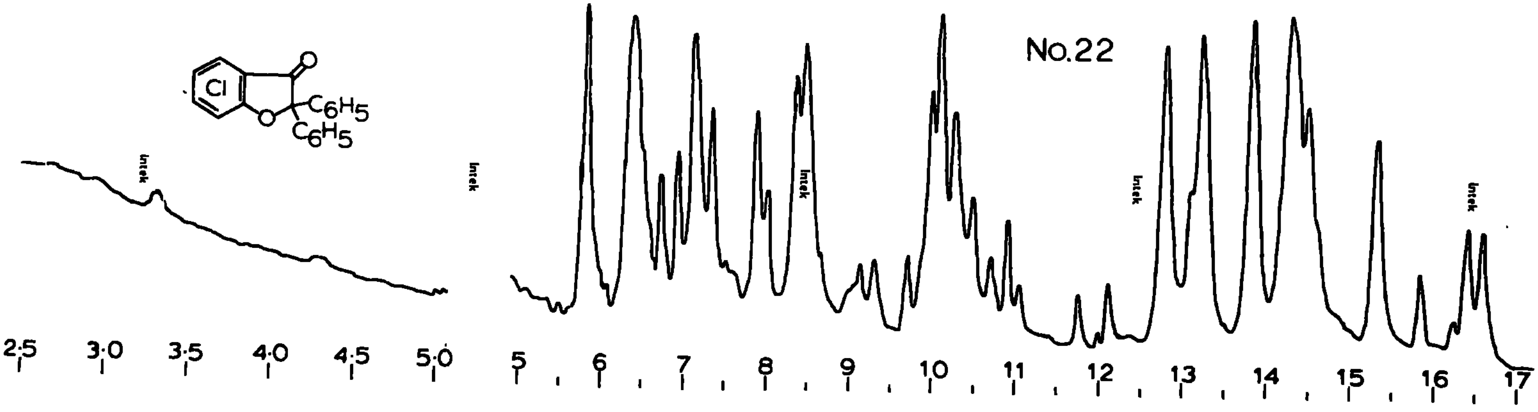
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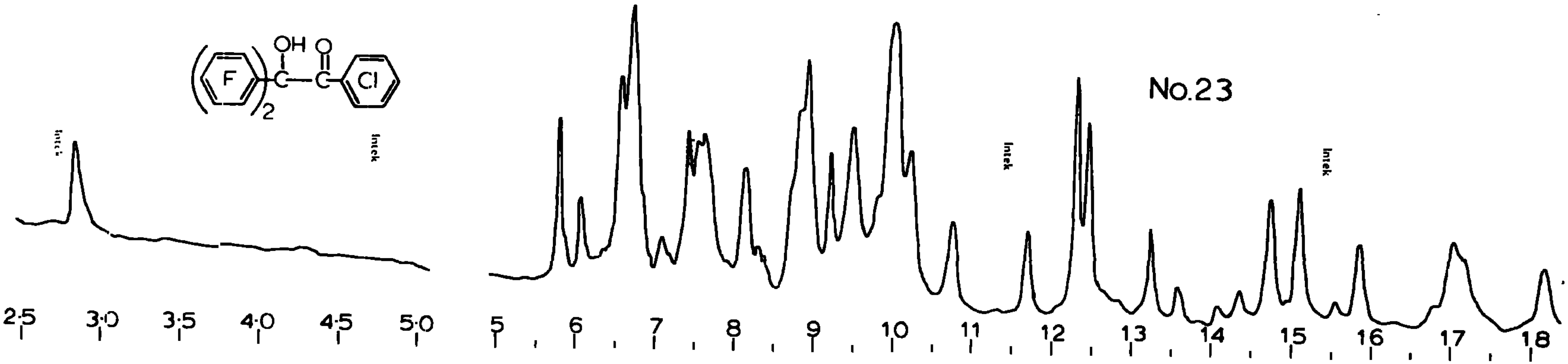

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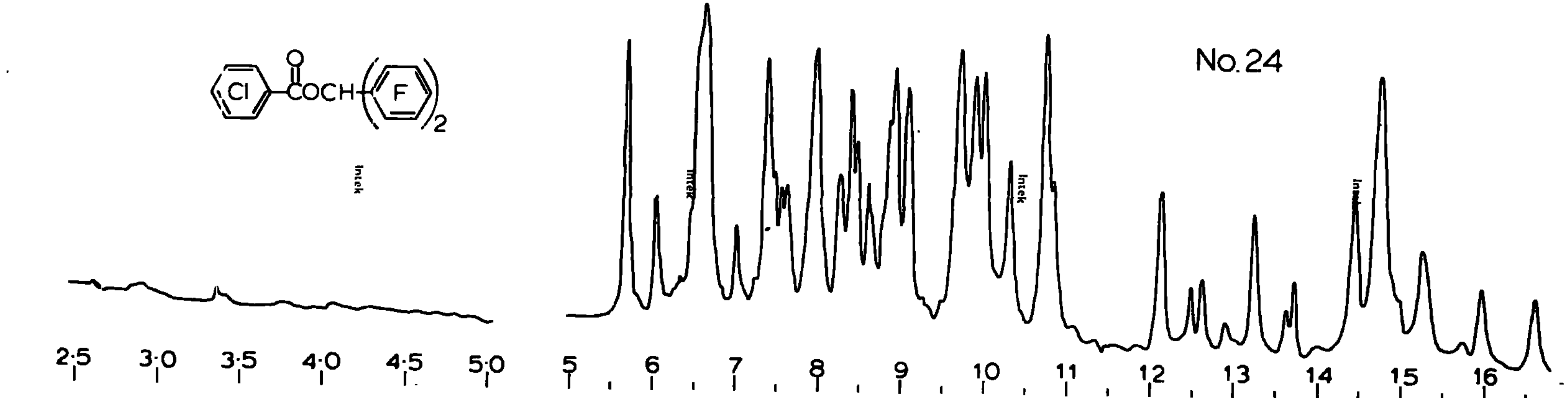

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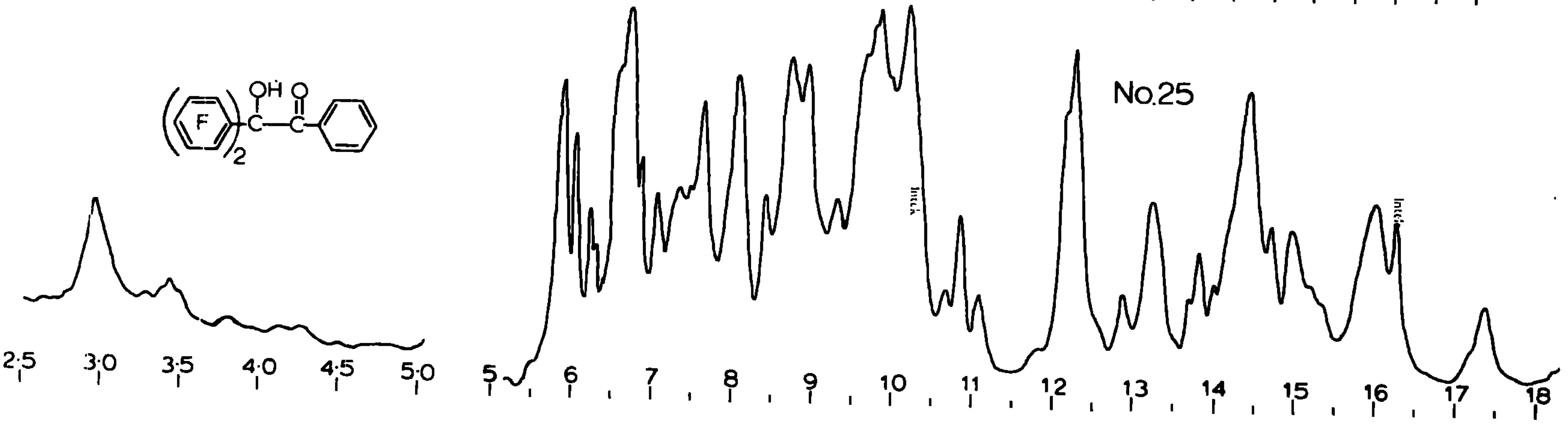

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