Elemental fluorine for selective fluorination

Matthew Edward Sparrowhawk

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Submitted by

Matthew Edward Sparrowhawk B.Sc.(Hons.)
(Hatfield College)

A Candidate for the degree of Doctor of Philosophy
Department of Chemistry
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For Mum, Dad, Laura and Graham for all their support over the last six years.

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Memorandum.

The work described in this thesis was carried out in the University of Durham between the 1st October 1994 and 30th September 1997. This thesis is the work of the author, except where acknowledged by reference, and has not been submitted for any other degree.

The work has been presented by the author, in part, at:

1. *The Use of Acids in the Promotion of the Electrophilic Fluorination of Aromatics Using F_2.* M. E. Sparrowhawk, R. D. Chambers, J. Hutchinson, G. Sandford and J. Thomson. Presented at the 16th International Symposium on Fluorine Chemistry, University of British Colombia, Vancouver, Canada, August 1997.

And in paper form in:

2. *Elemental Fluorine 5. Reactions of 1,3-dithiolanes and thioglycosides with fluorine-iodine mixtures.* R. D. Chambers, G. Sandford, M. E. Sparrowhawk and M. J. Atherton, *J. Chem. Soc., Perkin Trans. 1,* 1996, 1941-1944.

Nomenclature and Abbreviations.

Throughout this work , an 'F' in the centre of a ring denotes that all unmarked bonds are to fluorine. Also the following abbreviations have been employed.

NMR	Nuclear Magnetic Resonance Spectroscopy
GC/MS	Gas Liquid Chromatography-Mass Spectrometry
IR	Infra Red Spectroscopy

Statement of Copyright.

Abstract.

Elemental Fluorine for Selective Fluorination.

M. E. Sparrowhawk, University of Durham, 1998.

This thesis relates an investigation into the use of elemental fluorine in the direct and selective fluorination of organic molecules. The thesis is divided into seven chapters which may be outlined in the following manner.

Chapter One.

This chapter reviews the established background of the project. It discusses the historical background of direct fluorination, the preparation and properties of elemental fluorine, its use as a reagent in selective electrophilic fluorinations in organic synthesis and its use in the generation of other selective electrophilic fluorinating agents.

Chapter Two.

This chapter relates the development of a new methodology for the selective fluorodesulphurisation of 1,3-dithiolanes to generate diaryl geminal difluorides using elemental fluorine. It also details a new, simple deprotection procedure for these dithiolanes discovered in the course of this work.

Chapters Three and Four.

The third chapter details the extension of a previously established method for the direct, selective fluorination of deactivated aromatic compounds using acids as reaction solvents, particularly sulphuric and formic acids. We relate the importance of acid strength and the degree of activation of the substrate. The tolerance of the substrate to highly acidic conditions is also a key factor.

Chapter Four details further investigations of the fluorination of aromatic systems, particularly more highly activated compounds. The fluorination of mesitylene or 1,3,5-trimethylbenzene, in a variety of solvents is outlined, the reaction exhibiting limited success. We contrast the chemistry of the deactivated 4-nitrotoluene and demonstrate that the presence of nitro-additives promotes the electrophilic fluorination of mesitylene.

Chapter Five to Seven.

Experimental details of the work discussed in Chapters Two-Four.

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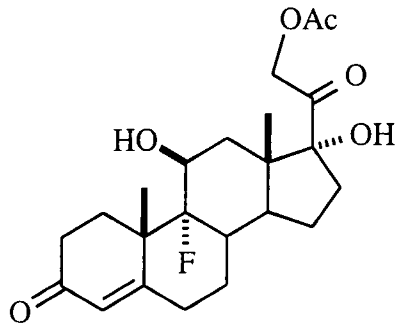
Chapter Seven Experimental to Chapter Four................................ 119

Chapter One. Elemental Fluorine in Organic Chemistry.

1.1 Introduction.

The study of the chemistry of fluorine and its compounds dates back as far as 1771 and the discovery of hydrogen fluoride by Scheele. Elemental fluorine was first prepared in 1886 by Moissan[1] and the history of organofluorine chemistry does not really begin until 1900 with the work of Swarts [2]. As there are very few naturally occurring organofluorine compounds[3], this is a field of predominantly 'man-made' chemistry. Over the course of the last century the field has grown dramatically as the commercial and academic potential of these compounds has been realised. In the 1930's Midgely and Henne demonstrated that fluoromethanes could be used as effective refrigerants[4] while in 1937 Simons prepared and isolated the first range of perfluorocarbons[5], compounds of extreme chemical and thermal stability which were utilised during the Manhattan project of World War II. These discoveries generated an intense wave of interest and research into fluorine chemistry.

This fascination with organofluorine chemistry stems from the extreme and often unusual properties displayed by compounds containing fluorine. Some exhibit great thermal and oxidative stability, while others demonstrate enhanced lipophilicity. Such properties make organofluorine compounds potentially useful materials for commercial applications. Fluorocarbons have been used extensively as lubricants[6], polymers[7], refrigerants[8] and dyes.[9] Organofluorine compounds may also have great biological significance. Replacing a hydrogen atom by fluorine has a dramatic effect on the electronic properties of a compound while leaving its molecular geometry relatively unchanged.[10] Fried demonstrated that 9α-fluorohydrocortisone acetate **(1)** had a biological activity 10.7 times greater than that of the non-fluorinated analogue.[11] This triggered a surge of interest in the effect of incorporation of fluorine into biologically active species. In addition, some of these compounds exhibit an enhanced lipophilicity which may facilitate passage across cell membranes and organofluorine molecules have wide application in the pharmaceutical and agrochemical industries[12, 13].



(1)

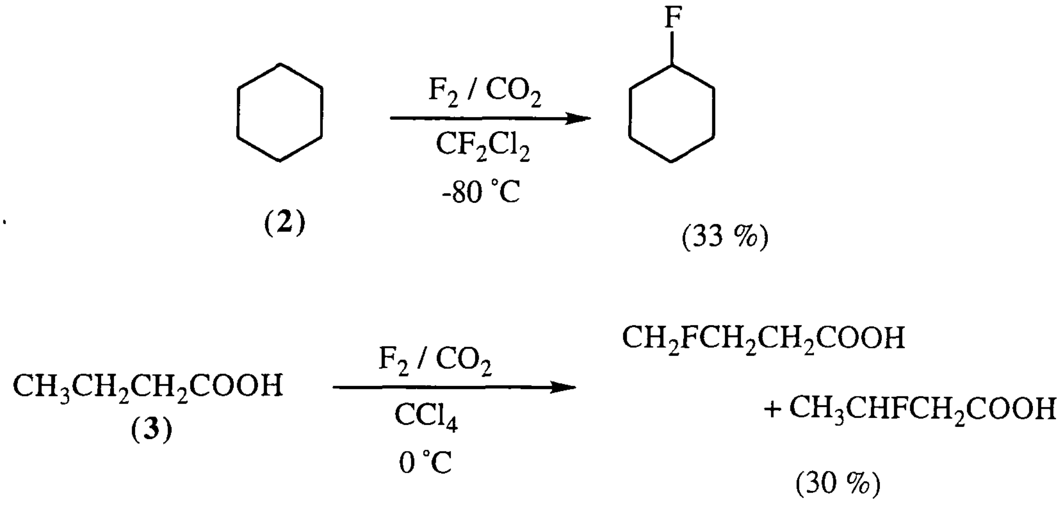
Despite this great interest in organofluorine chemistry there is not a very wide range of reagents and techniques for the incorporation of fluorine into organic molecules. Elemental fluorine has long been considered too reactive and dangerous for practical use in organic chemistry right up to the late 1960's.[14] Even today, many prejudices still pervade against its application. Fluorine is a strong oxidising agent which reacts with most organic molecules, often exothermically and even explosively on occasion. In order to increase control of these reactions it is necessary to slow the rate of reaction. The most popular method is to use fluorine as a dilute solution with an inert gas, e.g. nitrogen or argon. This approach was used by Bockemüller as early as 1933[15], but has only come into general usage in the last thirty years. This procedure is generally very effective and has led to a steady increase in the investigation of elemental fluorination as a genuine synthetic technique.

1.2 The History of Elemental Fluorination.

Elemental fluorine was first prepared in 1886 by Moissan as the product of the electrolysis of anhydrous hydrogen fluoride containing a little potassium hydrogen fluoride[1]. During investigations of his new halogen, he observed the effect of reacting neat fluorine with a range of organic compounds, including CH_4, $CHCl_3$ and CCl_4, quoting that the reaction resulted in 'burning' of the substrate with frequent explosions.[16] In 1890, he reported the reaction of carbon and fluorine, claiming he had prepared CF_4, but his reported boiling point is grossly incorrect (-15 °C c.f. -129 °C for CF_4) and his results were later to be shown in error by Swarts.[2] His last attempts at direct fluorination with Chavanne appear to have involved the use of liquid fluorine and solid methane at liquid air temperatures.[17, 18] The resulting explosion pulverised the glass apparatus.

No significant progress in direct fluorination was made until the 1930's. This situation contrasts dramatically with that of the other halogens, especially chlorine the next in series. Chlorine is much easier to obtain, manipulate and react with organic compounds. By the time Moissan had isolated fluorine, processes like the chlorination of acetic acid were routine procedures and vast quantities of chloral hydrate were being manufactured by reaction of chlorine and ethanol. Under similar conditions fluorine reacts fiercely leading to fires and explosions[16]. Such unfavourable comparisons did little to encourage work in this area.

The fluorine-ignition problem could be understood by thermochemical considerations, first suggested by Bockemüller in 1933.[15] The heat generated by incorporation of fluorine is ample to disrupt adjacent C-C bonds, and so this heat must be dissipated for successful fluorination. More recent reviews suggest that initiation of radical processes may also play a role.[8, 19, 20] To this end, he moderated his reactions by using fluorine diluted in an essentially inert gas, e.g. nitrogen or carbon dioxide, and dilute solutions of the organic substrate in an inert solvent, e.g. CF_2Cl_2 and CCl_4. In this manner Bockemüller studied the fluorination of a range of compounds including cyclohexane (**2**) and n-butyric acid (**3**) (Fig 1.1)[15].



$$\underset{(\mathbf{3})}{CH_3CH_2CH_2COOH} \xrightarrow[CCl_4,\ 0\ ^\circ C]{F_2 / CO_2} CH_2FCH_2CH_2COOH + CH_3CHFCH_2COOH \quad (30\ \%)$$

Fig 1.1

Similar work was carried out by Bigelow dealing with the liquid phase fluorination of aromatics dissolved or suspended in cold CCl_4 (0 °C)[21, 22]. No synthetically viable results were obtained but the experiments confirmed Bockemüller's theory that addition leading to saturated products rather than electrophilic substitution would occur.

Another method for controlling direct fluorinations was to react fluorine gas with organic vapours within meshes of copper gauze, the so-called vapour phase fluorination process. This approach was developed by Fredenhagen and Cadenbach in the early 30's[23] but many of their reactions must have involved liquid films of the organic material. It was Bigelow and Calfee who applied the principle to fluorinations completely in the vapour phase[24], and achieved further success by diluting fluorine with nitrogen. Through this approach they demonstrated the fluorination of hydrocarbons and chlorocarbons, e.g. ethane and tetrachloroethene, to produce fluorocarbons (Fig. 1.2).

$$C_2H_6 \xrightarrow[\text{copper gauze}]{F_2 /N_2} C_2F_6 + CF_3CHF_2 + CHF_2\,CHF_2 + CHF_2CH_2F + \text{some impurites from C-C bond fisson.}$$

$$Cl_2C{=}CCl_2\ (\text{or}\ CCl_3CCl_3) \xrightarrow[\text{copper gauze},\ 125\text{-}160\ ^\circ C]{F_2 /N_2} CFCl_2\,CFCl_2 \quad (> 20\%)$$

Fig. 1.2

Musgrave and co-workers extended this approach using a variety of packed reactors[25], including silver, copper, nickel and even gold gauze, but this methodology was eventually replaced by the cobalt trifluoride process.

Solid phase fluorination was another area explored. Through this approach a major advance was achieved reacting elemental fluorine with organic compounds to yield a product which could be isolated in a pure form. Fluorine was passed over a mixture of the solid substrate and an inert dilutent, e.g. fluorite or nickel shot, or a catalyst where appropriate, at a temperature chosen to afford a controlled reaction. The most significant reaction observed in this manner was the fluorination of carbon itself. In 1930, Ruff and Keim reported the isolation of CF_4 from the fluorination of wood charcoal in a glass tube[26], and later, Simons and Block reported the reaction of carbon and fluorine using mercuric chloride as a catalyst[5, 27]. This reaction produced a mixture consisting of C_3F_8, C_4F_{10}, C_6F_{14} and cyclo-C_6F_{12}, in addition to CF_4. These products exhibited high chemical and thermal stability including resistance to UF_6 leading to their exploitation by the Manhattan project.

In spite of these advances and the likelihood of greater progress to come, at the time it seemed unlikely that large scale syntheses of fluorocarbon compounds, especially highly functionalised ones, would be practically realised in the foreseeable future. It was only the advent of World War II and the Manhattan project with its demands for highly stable materials to be used handling UF_6 that would generate an intense wave of interest in organofluorine chemistry and its compounds. Fluorine was about to come of age.

1.3 The Preparation and Properties of Elemental Fluorine.

1.3.1 Preparation.

a) Electrochemical Preparation of Fluorine.

The earliest known electrochemical preparation of fluorine is the electrolysis of anhydrous hydrogen fluoride containing potassium hydrogen fluoride carried out by Moissan in 1886[1], but modern production of elemental fluorine can be traced back to the development of fused potassium fluoride/anhydrous hydrogen fluoride as the electrolyte.[28] This approach has been extended and is used extensively in the large scale commercial preparation of fluorine[29], most commonly using a mixture of KF.2HF (m.p. 71.7 °C) with the cell heated to around 100 °C.

Contamination of the fluorine produced is difficult to avoid due to the volatility of hydrogen fluoride, however the use of fused potassium fluorides can help by significantly reducing the vapour pressure of HF. Corrosion of reactors is reduced through the use of metals like copper and nickel which soon develop a protective fluoride coating. A typical fluorine cell is shown in Fig. 1.3.

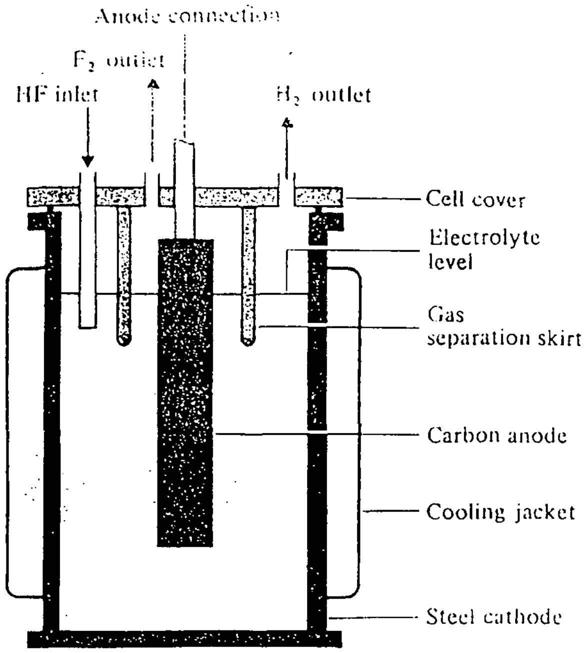


Fig 1.3

b) Chemical Syntheses.

Practical routes to a purely chemical synthesis of elemental fluorine, excluding electrochemical, photochemical and discharge techniques, have been sought for over 184 years by many notable chemists from Davy[30] to Fremy[31], Moissan[32, 33] and Ruff[34, 35]. All their attempts came to nought. The problem lies in the fact that while the decomposition of fluorine compounds to liberate F_2 is sound in theory, in practice the reaction is thermodynamically very unfavourable. Also, the required reaction temperatures are so extreme that rapid reaction between evolved fluorine and the reactor walls precludes any significant isolation of fluorine.

The first real chemical synthesis of fluorine was carried out by Steel[36] in 1959 (Fig 1.4).

$$IF_7AsF_5 + 2\,KF \xrightarrow{>200\,^\circ C} KIF_6 + KAsF_6 + F_2$$

Fig. 1.4

Most approaches to this problem are based upon the formation of unstable high oxidation state transition metal fluorides which can be stabilised by anion formation, e.g. MnF_4 and NiF_4 are stabilised as MF_6^{2-} ions. Furthermore, it has been well established that a weak Lewis acid such as MF_4 can be displaced by a stronger one, e.g. SbF_5, the unstable MF_4 may then decompose liberating F_2[37] (Scheme 1).

$$K_2MF_6 + 2SbF_5 \longrightarrow 2KSbF_6 + [MF_4]$$

$$[MF_4] \longrightarrow MF_3 + F_2$$

Scheme 1

This idea has formed the basis of the first practical synthesis of fluorine demonstrated by Christe[37] (Fig. 1.5), though this method has not been widely exploited.

$$K_2MnF_6 + 2SbF_5 \longrightarrow 2KSbF_6 + MnF_3 + {}^1/_2\,F_2$$

Fig. 1.5

1.3.2 The Properties of Elemental Fluorine.

a) Physical Properties.

Fluorine is more abundant in the earth's crust than chlorine (0.065 % c.f. 0.055%) found in minerals such as fluorospar (CaF_2), cryolite (Na_3AlF_6) and fluoroapatite[38]. In its pure form elemental fluorine exists as a pale green diatomic gas. It is the most electronegative of the elements and is found as a single isotope ^{19}F in nature though ^{18}F is known (half life = 109.7 min) and has been used as a tracer. The physical properties of fluorine, both the diatomic F_2 and some of its atomic properties are listed in Table 1 in comparison to the other halogens.[38, 39]

Property	Fluorine	Chlorine	Bromine	Iodine
Molecular Properties (X_2)				
Melting point (°C)	-218.6	-101	-7.3	114
Boiling point (°C)	-188.1	-34.0	59.5	185
Density of Solid (g/cm^3)	1.3	1.9	3,4	4.9
Heat of Vapourisation (KJ/mol)	6.54	20.41	29.56	41.6
Heat of Dissociation (KJ/mol)	158.8	242.58	192.8	151.1
Atomic Properties (X)				
Covalent Radius (Å)	0.71	0.99	1.14	1.33
Ionisation Potential (KJ/mol)	1681	1250	1139	1007
Electron Affinity (KJ/mol)	-328.0	-348.8	-324.6	-295.3
Electronegativity	4.0	3.0	2.8	2.5

Table 1 Some Physical Properies of the Halogens.

b) Chemical Properties.

Fluorine is the most reactive of all the elements, reacting with all others except nitrogen and the lighter noble gases, often very vigorously. As had already been stated it will also react with many other compounds, especially organics, sometimes causing fires and explosions. This high reactivity may be understood to be due to the low energy of the

F-F bond in contrast to the stronger bonds formed with other elements, e.g. the C-F bond. The low F-F bond energy can be explained by the small size[40] and relatively high nuclear charge of the fluorine atom. This causes a decreased overlap between bonding orbitals which coupled with increased repulsion between the non-bonding orbitals reduces the bond strength between two fluorine atoms. Similar phenomenon is observed for O-O and N-N bonds. Table 2 details the bond strengths of fluorine with some common elements.[41]

Bond	**Bond Strength (KJ/mol)**
C-F	485
Si-F	565
H-F	565
N-F	283
P-F	490
F-F	154.8

Table 2. Bond Strengths of Fluorine with Some Common Elements.

Fluorine reacts with hydrogen with extreme violence to produce HF (Δ H° HF (g) = -271.7 KJ/mol at 25 ° C), while with water it produces oxygen, oxygen difluoride and hydrogen fluoride and sometimes small quantities of ozone and hydrogen peroxides. Fluorine combines with all other halogens in a highly exothermic reaction from which a series of interhalogen compounds are formed, e.g. ClF, ClF_3, BrF_3. It attacks all metals at room temperature, but some metals and alloys, e.g. copper and nickel, form a protective layer of fluoride which prevents further reaction. This is termed passivation and is invaluable in the handling of elemental fluorine.

1.4 The Organic Chemistry of Elemental Fluorine.

Elemental fluorine may react with organic molecules by one of two modes of attack, as a free radical process or as an electrophile, depending on whether the F-F bond undergoes homolytic or heterolytic fission. The balance between these processes determines the degree of selectivity and control in these reactions. Radical reactions are rapid, generally unselective and relatively uncontrolled, while electrophilic processes are slower and more controlled, directed by charge interactions. Promoting the electrophilic mode of attack increases control and selectivity of fluorinations. The bulk of this review will deal with the electrophilic reactions of fluorine, but first we shall touch upon some of its free radical processes.

1.4.1 Radical Fluorinations.

Due to the high bond energies of the C-F and H-F bonds fluorination reactions are extremely exothermic in nature. This, coupled with the low dissociation energy of elemental fluorine suggest that the radical process is the most likely mode of fluorination (Scheme 2).

$$F_2 \longrightarrow 2F^\bullet$$

$$RH + F^\bullet \longrightarrow R^\bullet + HF$$

$$R^\bullet + F_2 \longrightarrow RF + F^\bullet$$

Scheme 2

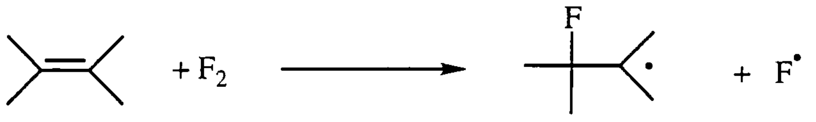
There is some debate about the initiation of radical fluorinations. Quite high temperatures are required for the appreciable dissociation of fluorine ($K \approx 10^{-20}$ atm at room temperature[19]). An alternative mechanism was suggested by Miller involving the reaction of fluorine with a hydrocarbon molecule to generate a radical species (Scheme 3)[42-44]. The radical reactions of fluorine with alkenes would seem to support this theory, an exothermic process generating two radical intermediates.[19]

$$RH + X_2 \longrightarrow R^\bullet + HX + X^\bullet$$

$X = F$ $\Delta H \approx 17$ KJ mol^{-1}

$X = Cl$ $\Delta H \approx 226$ KJ mol^{-1}

$X = Br$ $\Delta H \approx 283$ KJ mol^{-1}



$\Delta H \approx -4.8$ KJ mol^{-1}

Scheme 3.

Radical fluorinations are considerably less selective than chlorination[45], and in contrast to chlorination, these selectivities are unaffected by increases in temperature. The low solubility of fluorine creates problems in the studies of relative selectivities of fluorine radicals but experiments using radicals in the gas phase have yielded results which are compared to several common radical species in Table 3, showing the relative ratios for reaction of the fluorine, chlorine and bromine radicals at primary, secondary and tertiary sites in hydrocarbons[23].

	Relative Selectivities at 300 K		
Radical	$-CH_3$	$>CH_2$	$-\overset{\vert}{\underset{\vert}{C}}H$
$F^\bullet$	1	1.2	1.4
$Cl^\bullet$	1	3.9	5.1
$Br^\bullet$	1	82	1600

Table 3 The Relative Selectivities of Halogen Radicals for Primary, Secondary and Tertiary Hydrogens in Alkanes.

This lack of selectivity is difficult to reconcile with Bockemüller's results[15] with butyric acid (Fig 1.1), and it was found that fluorination is more affected by substitution or polar effects than chlorination or bromination, suggesting the promotion of the electrophilic mode of attack.

1.4.2 Perfluorination.

Perfluorinated compounds have been shown to display an extreme oxidative and thermal stability making them ideal for the manipulation of elemental fluorine and UF_6. Lagow has demonstrated that perfluoro compounds can be produced by the direct fluorination of hydrocarbons. One of the earliest examples of this process was the fluorination of polyethene oxide[46, 47] (Fig 1.6). The reaction is controlled by variation of temperature and dilution. The high solubility of fluorine in fluorocarbons (around 30% by volume) is exploited in this methodology to overcome the problem of removing the last hydrogen atoms from the substrate when provided with sufficient activation, usually in the form of heat. For solid fluorocarbons he found that complete perfluorination could be achieved by carrying out fluorination under increased pressure. These principles have also been applied to the perfluorination of adamantanes[48, 49], crown ethers[50, 51] and orthocarbonates[52].

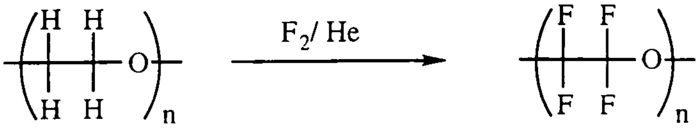


Fig 1.6

1.4.3 Electrophilic Fluorinations.

a) Direct Fluorination of Carbon-Carbon Multiple Bonds.

i) Alkenes.

The beginning of the application of elemental fluorine in modern organic synthesis was Merritt's investigation of the addition of F_2 to alkenes in the 1960's[53-56]. In these experiments, he observed that *cis* stilbene (**4**) was fluorinated by 1 equivalent of F_2 at low temperature and pressure with the products showing predominantly *syn* addition (Fig 1.7).

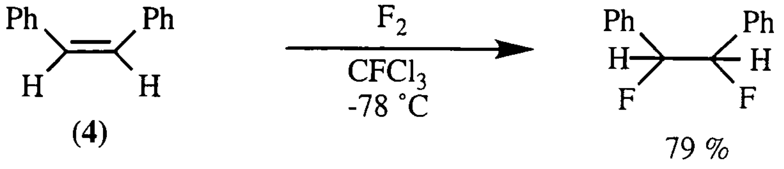


Fig 1.7

Following on from these initial studies, he went on to look at the effect of fluorine on a range of alkenes (Fig 1.8).

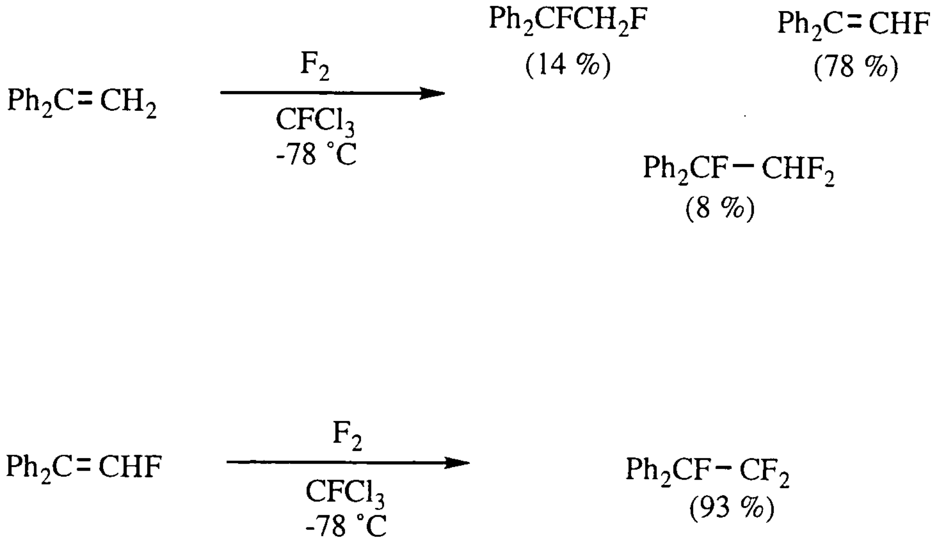


Fig 1.8

These observations seemed to rule out a free radical pathway, the mode of attack is electrophilic[54] leading Merritt to propose that this was a concerted reaction.

More recently this reaction has been further developed by Rozen[57], using more polar solvents and a much lower concentration of fluorine. For example, the fluorination of *trans* 3-hexen-1-ol acetate (**5**) dissolved in a solvent system consisting of a mixture of trichlorofluoromethane, ethanol and chloroform using a 1% fluorine in nitrogen mixture, gave a single difluoro adduct in approximately 55% yield. This product was identified as the *threo* isomer of 3,4-difluorohexan-1-ol acetate, and arises from the *syn* addition of fluorine to the alkene. When the *cis* isomer of the parent alkene **(6)** was fluorinated, again *syn* addition was the sole mode of attack yielding the *erythro* difluoro product in comparable amounts (Fig 1.9). Similar results were obtained for cyclic alkenes and enones.

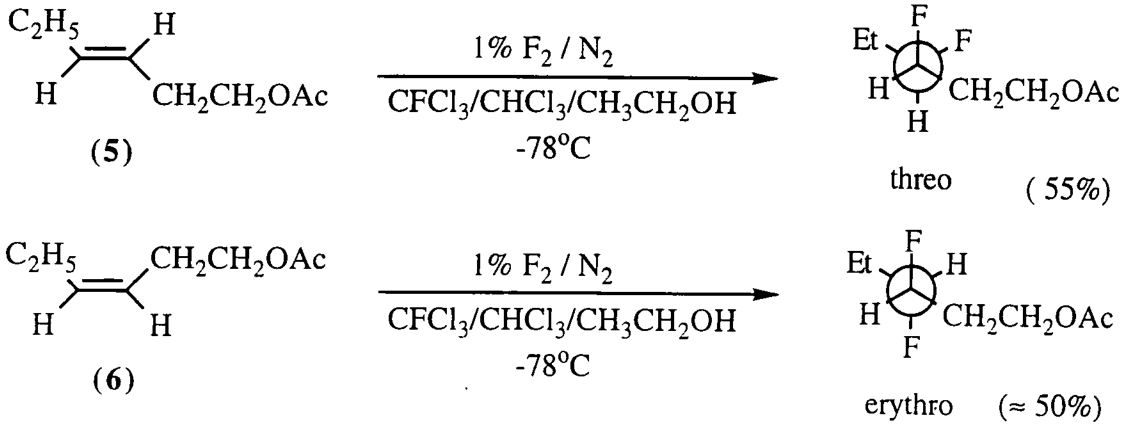
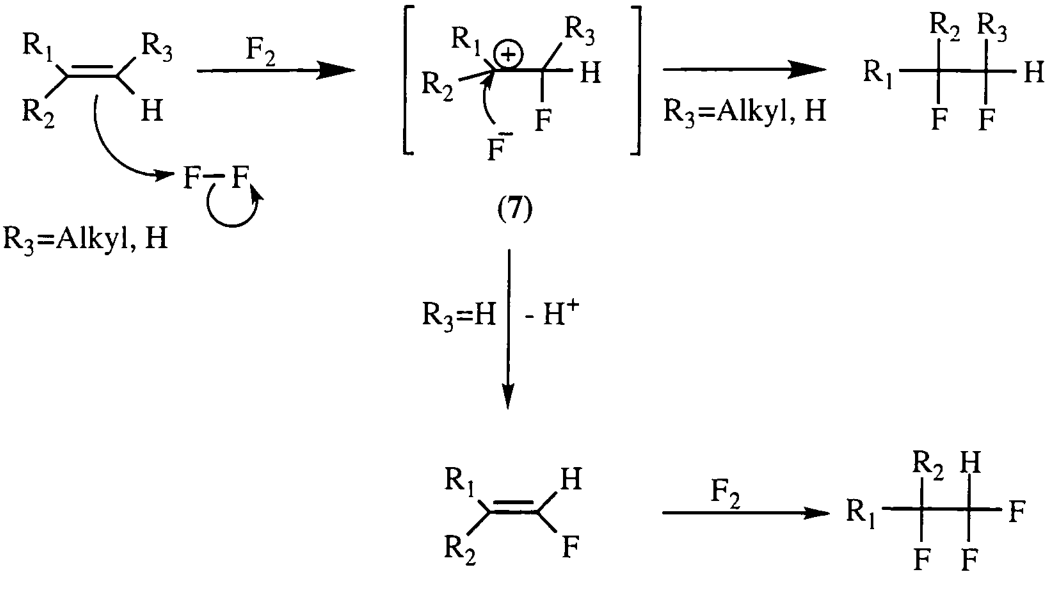


Fig 1.9

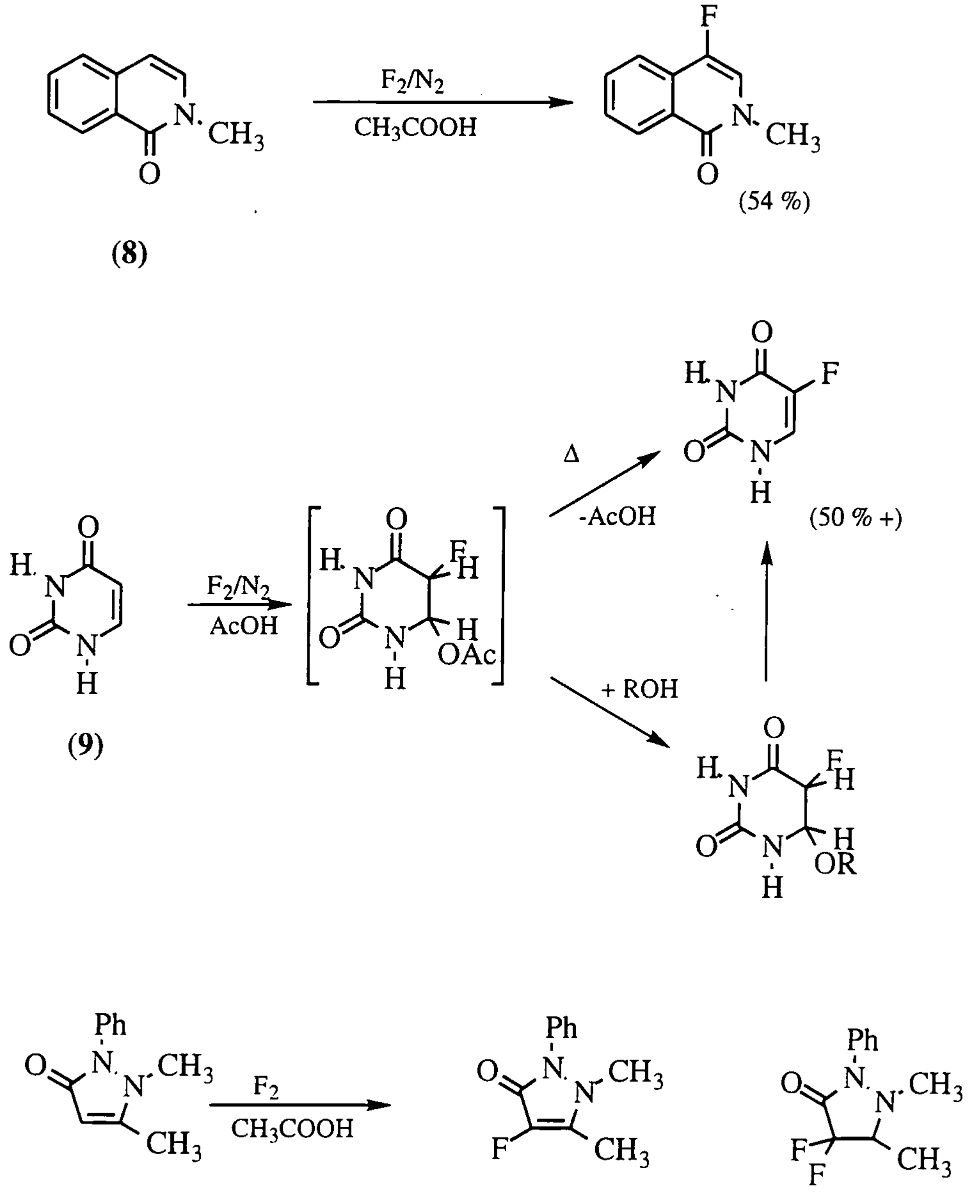
The exclusively *syn* addition supports the observations of Merritt, and is a sharp contrast to the reactions of other halogens. Rozen proposed a mechanism proceeding via a tight ion pair. Initial nucleophilic attack by the double bond on fluorine produces a pair of ions (7) consisting of an unstable α-fluorocarbocation and fluoride. This intermediate collapses before any rotation about the C-C bond occurs and so only one isomer is formed selectively. In the case of terminal double bonds, e.g. 1-octene and 1-dodecene, a significant amount of a trifluoro product was isolated. This was not due to overfluorination since attempts to drive the isolated difluoro products to further fluorination resulted in indiscriminate reaction and C-C bond cleavage. Rather, it was proposed that a fluoroalkene was produced immediately after formation of the α-fluorocarbocation, by ejection of a proton, which can further react with fluorine to give the observed trifluoro products. These mechanisms are outlined in Scheme 4.



Scheme 4

ii). Heterocycles.

A number of unsaturated heterocyclic compounds may be fluorinated using elemental fluorine directly, exhibiting addition across the carbon-carbon double bond in a similar manner to the reactions of alkenes. For example, fluorinations of 2-methylisocarbostyril **(8)**[58], uracil **(9)**[59] and antipurine **(10)**[60] in acetic acid (Fig 1.10) are thought to proceed via *syn* addition of fluorine across the double bond followed by elimination of HF, sometimes assisted by the solvent. For example, in the production of 5-fluorouracil using acetic acid as the solvent, an unstable acetoxy intermediate is formed, which may eliminate a molecule of acetic acid to give the product. In the presence of an alcohol this intermediate may react to produce the alkoxy derivative, but this also may be readily converted to fluorouracil. A more recent study of the fluorination of uracil, suggest that these reactions may involve radical cation intermediates.[61]



(8)

(9)

(10)

Fig 1.10

iii) Enol Derivatives.

In an attempt to prepare α-fluorocarbonyl compounds, the reaction of F_2 with the enol derivatives of ketones and aldehydes have been studied. For example, many enolised 3-substituted pyruvate esters have been efficiently fluorinated in good yields, using F_2 in N_2 (Fig 1.11).[62]

$$RCH{=}C(OH)CO_2R' \xrightarrow[\substack{CFCl_3 \\ -78\ ^{\circ}C}]{F_2} RCHF(CO)CO_2R'$$

i) R'= Me, R= Ph (50-60 %)

ii) R'= Me, R= p-PhCl (65 %)

iii) R'= Et, R= n- PrCO (70 %)

Fig 1.11

Similarly, Purrington was able to prepare a number of α-fluoroaldehydes and ketones from trimethylsilyl derivatives (Fig 1.12). These reactions were carried out at -78 °C in $CFCl_3$, over a relatively short time (approx. 3 1/2 hours). The silylated enol is readily lost as the volatile trimethylsilyl fluoride leaving the α-substituted product. The mechanism was thought to proceed via a six membered transition state (Scheme 5).

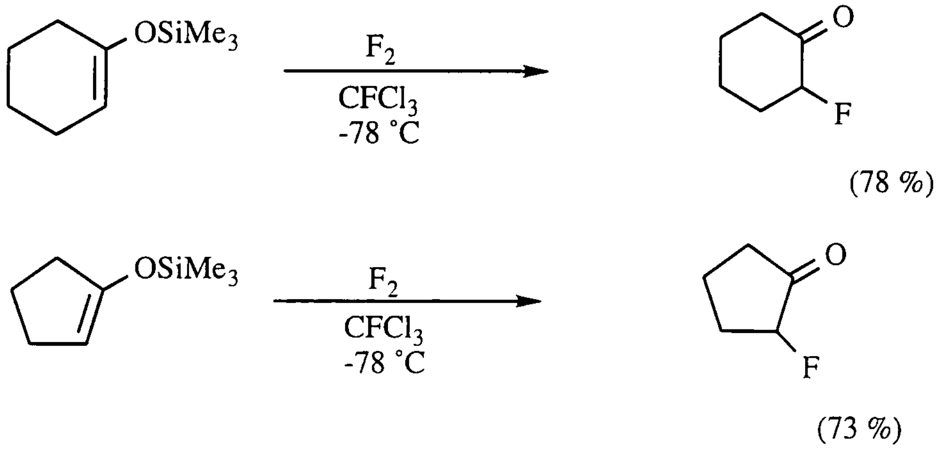
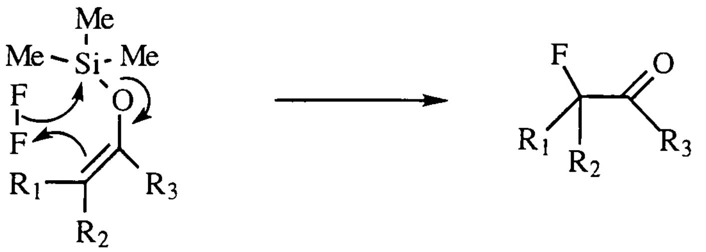


Fig 1.12



Scheme 5.

Rozen has claimed that the direct fluorination of enol acetates was not an effective route to α-fluorocarbonyls. He reported these reactions as giving complex mixtures with no definite isolatable products, the only exception being the simplest case, vinyl acetate

(Fig 1.13).[63]

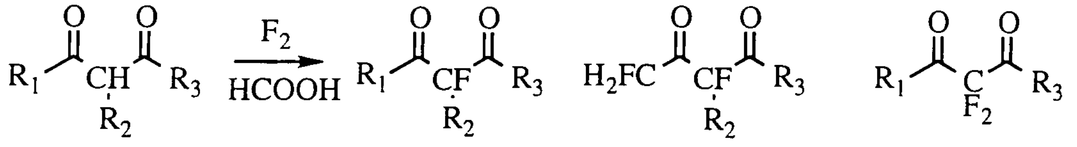
$$H_2C{=}CHOCOCH_3 \xrightarrow[CFCl_3]{F_2} CH_2FCHO$$

(12.5 %)

Fig 1.13

A recent development has been the fluorination of 1,3-dicarbonyl compounds.[64] Fluorination of these compounds had previously been carried out using electrophilic fluorinating agents or via silyl enol ether derivatives, direct fluorination was thought to be too reactive and non-selective. However, it has now been observed that some 1,3-dicarbonyls will react directly with fluorine, giving the selectively fluorinated product in high yields.

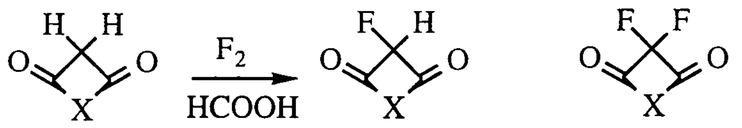
In this reaction, fluorine diluted to 10 % with nitrogen was passed through vigorously stirred solutions of 1,3-dicarbonyls in a solvent of formic acid. This reaction was studied for a range of dicarbonyls where the major product was observed to be due to monofluorination at the 2 position with traces of isomers of the difluorinated dicarbonyl species (Fig 1.14).



i) R_1, R_3= Me; R_2 = H.	(70 %)	(11 %)	(3 %)
ii) i) R_1, R_2, R_3= Me.	(76 %)	(9 %)	------
iii) R_1= Me; R_2 = Cl; R_3= OEt.	(85 %)	(5 %)	

Fig 1.14

Examples of the fluorination of cyclic 1,3-dicarbonyls were also studied. For these compounds, the cyclic products seem to be more reactive to additional fluorine and more difluorination is observed(Fig 1.15).



			Conversion.
i) X= $-CH_2CMe_2CH_2-$	(10 %)	(50 %)	>95 %
ii) X= -NHCONH-	(50 %)	(30 %)	>80 %
iii) X= -NMeCONMe-	(70 %)	(15 %)	25 %

Fig 1.15

1,3-Diketones were seen to be more reactive than the corresponding keto-esters, while diesters like diethylmalonate were unreactive. The reaction was also seen to occur when using acetonitrile as a solvent.

The mechanism of this reaction was established by NMR studies, measuring the rate at which hydrogen is displaced from the 2-position in a series of ketoesters dissolved in DCO_2D. At the same time, the enol content of these solutions was also established. From these observations it was concluded that mechanism was similar to that for the reaction of dicarbonyls with other halogens going via the enol derivatives. Initially, fluorine reacts rapidly with any enol present in solution thereafter the rate of reaction is governed by the rate of enol formation.

iv) Alkynes.

A variation on the reaction of alkenes, it was observed that the products of the fluorination of alkynes varied according to the solvents used.[53-55] With $CFCl_3$, acetylenes were seen to be tetra fluorinated. Reducing the amount of fluorine used had no effect on this phenomenon. However, the reaction of substituted tolanes produced a complex mixture of products, including *cis* and *trans* stilbenes and some rearrangement products, such as 1,2,2-trifluoro-1,2-diaryl and 1,2,2,2-tetra fluoro-1,1-diaryl ethanes. This reaction is thought to proceed via a fluorovinyl radical with a partial positive charge, borne out by observations of selectivity, small negative ρ value and the inhibition of fluorination by oxygen.[65] Merritt observed a number of products from solvent incorporation when working in methanol. This is further evidence of the electrophilic nature of fluorine in the reaction, the alkoxy ion attacking the site of developing positive charge (Fig 1.16).[66]

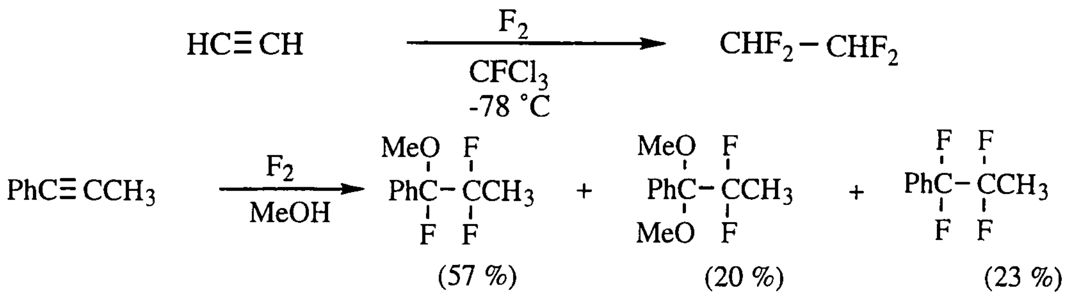


Fig 1.16

b) Fluorinations of Carbon-Nitrogen Bonds and Derivatives.

i). Imines

The low temperature fluorination of benzaldehyde imines with F_2 was seen to give a mixture of α,α-difluoro secondary fluoramines and α-fluoramines.[67] This reaction, again, is an electrophilic process, proceeding via an intermediate vicinal difluoride. The driving force of this reaction is a combination of the weak N-F bond (272 kJ/mol) and the relative acidity of the benzylic proton and as a consequence, the difluoride readily undergoes dehydrofluorination, yielding the α-fluoramine, which may react with a further molecule of F_2 to give the trifluoro adduct (Fig 1.17).

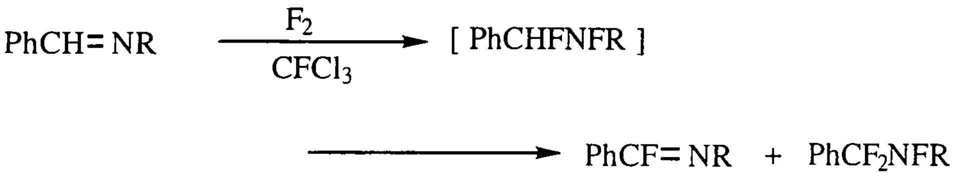


Fig 1.17

This α,α-difluorofluoramine may further undergo conversion to *N*- fluoroimine on dried silica gel at 160 °C or hydrolysis to give *N*- fluoro-*N*- alkylbenzamides.

ii). Diazo compounds.

Geminal difluorides have been easily prepared from diazo compounds by direct fluorination (Fig 1.18). [68]

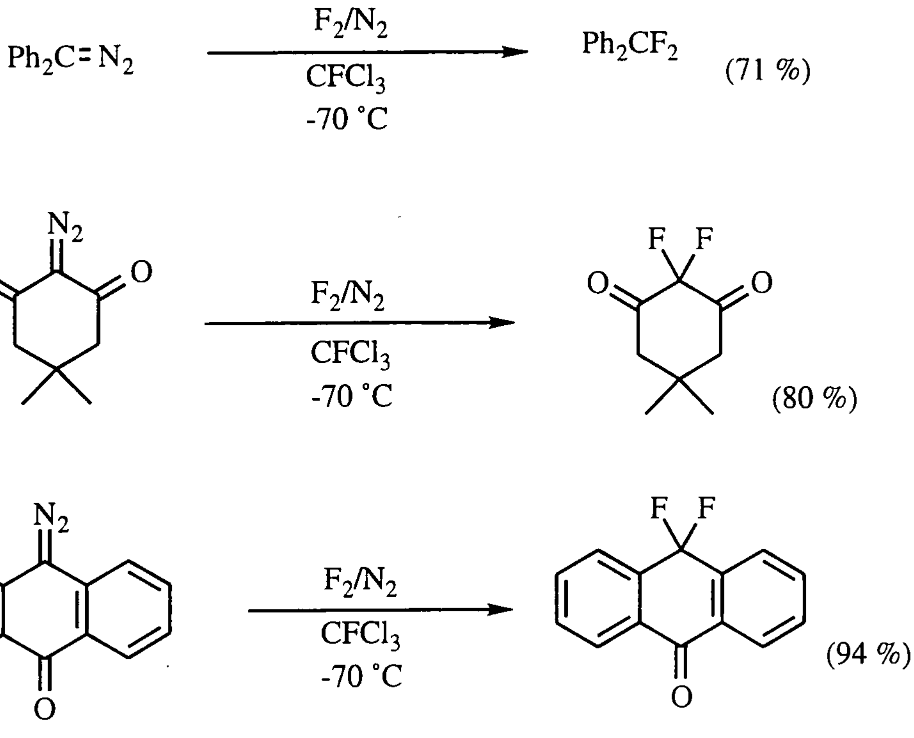
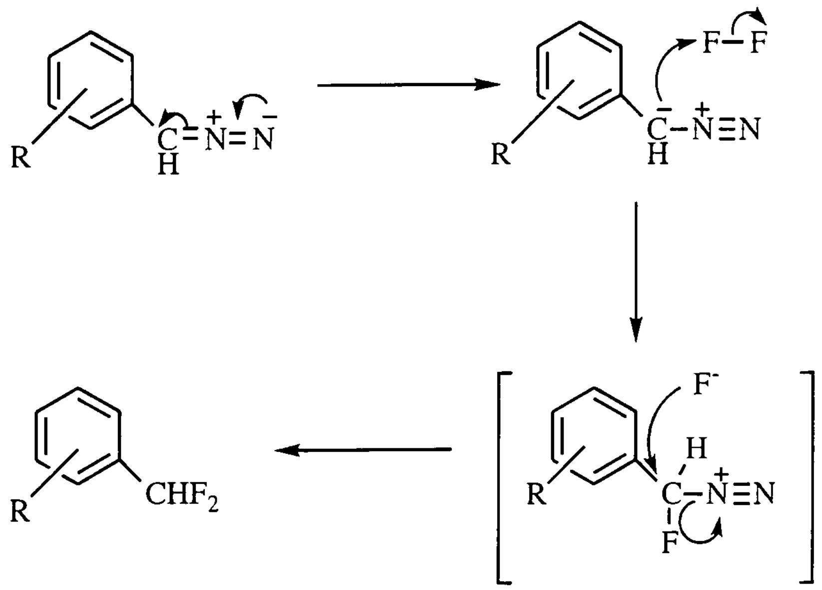


Fig 1.18

Fluorination occurs at sites adjacent to an aromatic or a carbonyl group. Also, neither the carbonyl or C-H functionalities are affected by the reaction.[68-70] These observations tend to discount the possibility of a free radical pathway, suggesting a mechanism where F_2 acts as an electrophile (Scheme 6).



Scheme 6

Aryl ketone hydrazones undergo fluorination in a similar fashion (Fig 1.19).[71] Oxidation of the hydrazone gave a diazo intermediate which reacted with either HF, generated in the reaction, to give monofluorinated products or elemental fluorine yielding the geminal difluoride.

$$\mathrm{Ph_2C{=}NNH_2} \xrightarrow[\mathrm{CFCl_3}]{\mathrm{F_2}} \underset{(11\ \%)}{\mathrm{Ph_2CHF}} + \underset{(69\ \%)}{\mathrm{Ph_2CF_2}}$$

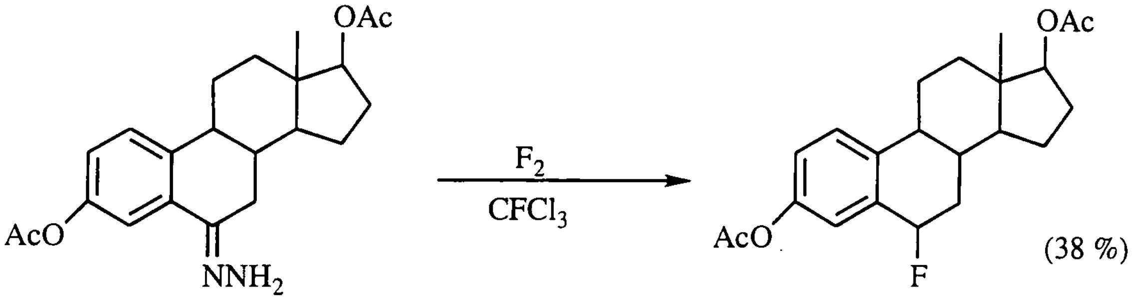


Fig 1.19

The hydrazones of benzaldyde, cyclohexanone and cyclopentanone did not undergo fluorination.

iii) Isocyanates.

Merritt observed that alkyl isocyanates do not undergo fluorination across the double bond. Instead, side chain fluorinations occurred, rapidly followed by fluorination at the nitrogen with loss of fluorophosgene, COF_2.[72] The reaction was complicated by the action of HF on the isocyanate, leading to the formation of *N*- carbamyl fluorides (Fig 1.20).

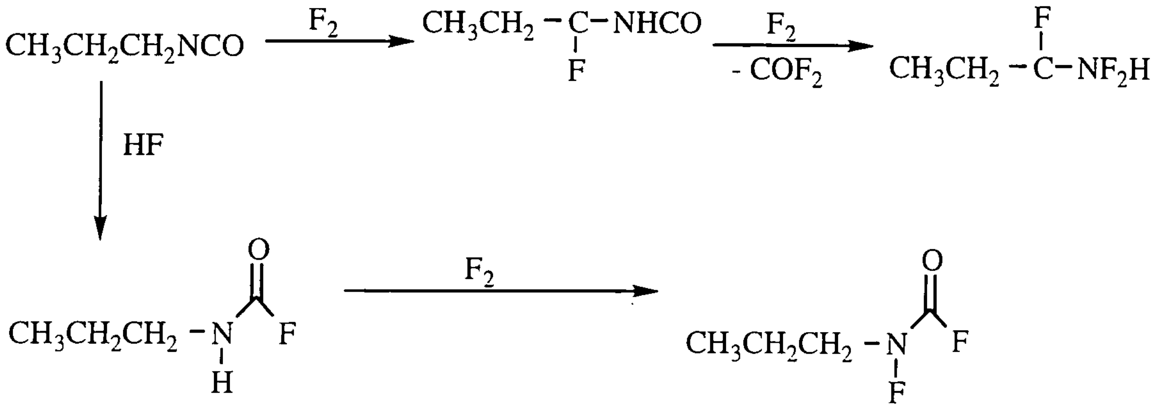


Fig 1.20

iv) Isonitriles.

Fluorination of isonitriles was shown to give primarily the aza analogues of fluorophosgene. However, traces of HF in the system also may lead to some addition and dimerised products (Fig 1.21).[73]

$$RN{\equiv}C \xrightarrow{F_2} [RN{=}CF_2]$$

$$\longrightarrow RNHCF_3 + RN{=}CFNRCF_3$$

Fig 1.21

v) Amides.

Amides are another nitrogen containing species which may be fluorinated directly.[74] Difluoroaminocarboxylic acids have been prepared from their corresponding lactams using elemental fluorine (Fig 1.22).

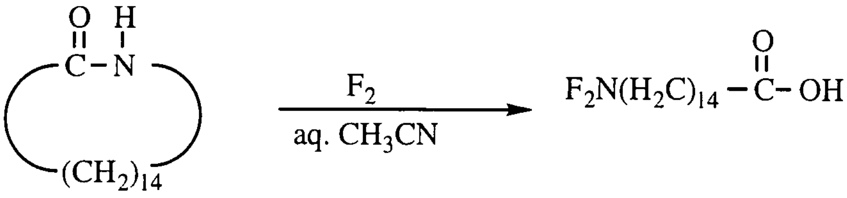
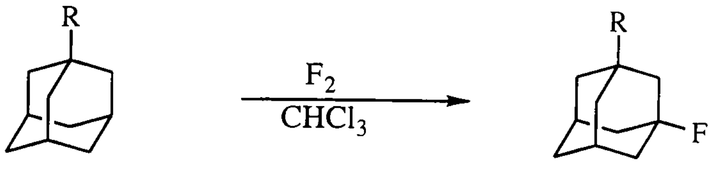


Fig 1.22

The NF_2 group is thought to be a closer isostere for CH_3 than CH_2F, as it introduces less polarity into the chain.

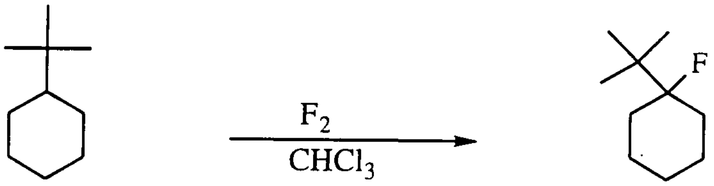
c) Fluorination of Tertiary Carbon Sites.

Elemental fluorine has also been shown to replace tertiary hydrogens, which is claimed by Rozen to exhibit a retention of configuration, for a number of unactivated substrates (Fig 1.23).[75-80]



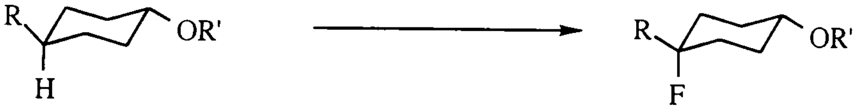
(11)

i) R = H (71-90 %)
ii) R = OH (70 %)
iii) R = p-$O_2CC_6H_4NO_2$ (90 %)
iv) R = $NHCOCF_3$ (83 %)



(70 %)

(12)



(13)

Fig 1.23

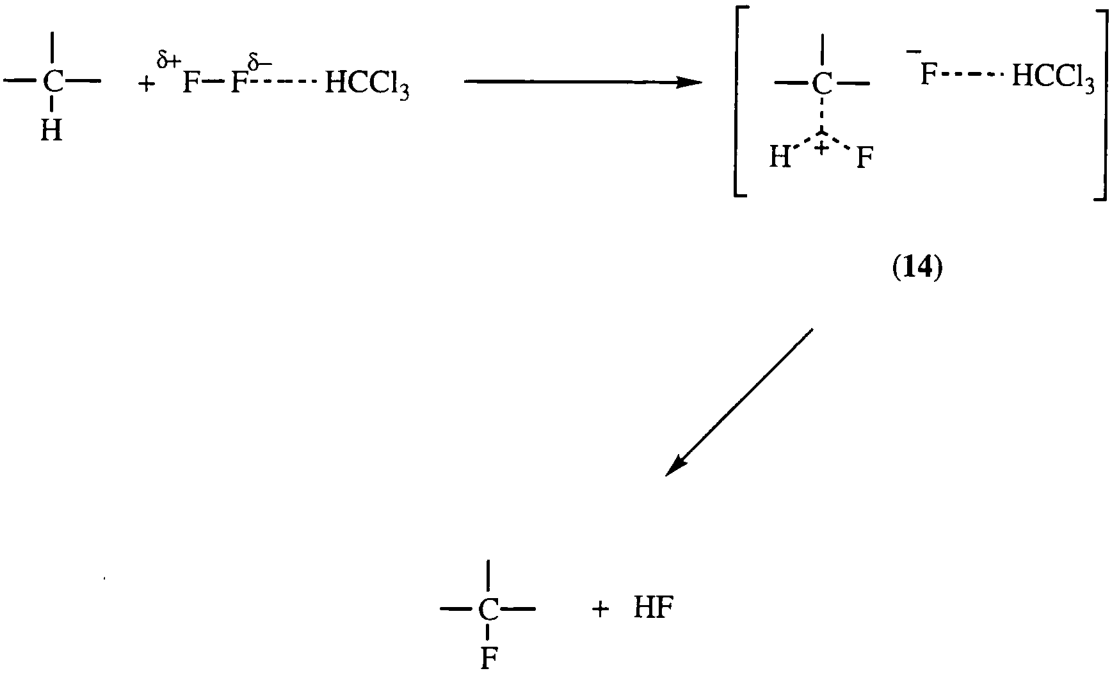
Rozen has studied the fluorination of various cycloalkanes[81]. These reactions were carried out a low temperature in a polar solvent, typically a 1:1 mixture of trichlorofluoromethane and chloroform, using 4-6% fluorine in nitrogen. Electron density is key to this reaction. Electron rich C-H bonds react preferentially compared to poorer ones and where the hydrogen is adjacent or close to an electron withdrawing group very little fluorination is observed. For example, when C-H is β to an ester, the yield of fluorinated product was about half that when it was γ (Fig 1.24). As a result, incorporation of one fluorine atom in the molecule has an inhibiting effect on further fluorination.

$$(CH_3)_2CHR \xrightarrow[CHCl_3]{F_2} (CH_3)_2CFR$$

i) R = $CH_2CO_2CH_2CCl_3$ (25-30 %)
ii) R = $(CH_2)_2\ CO_2CH_2CCl_3$ (55 %)

Fig 1.24

It was also suggested that the retention of configuration shown in these reactions demonstrated that these substitutions occurred via a non-classical pentaco-ordinated fluorocarbocation **(14)** (Scheme 7). The polar solvent fulfils several functions, it promotes the polarisation of F_2 and then acts as an acceptor for the fluoride ion produced in the reaction. Chloroform may also act as a radical scavenger. In non-polar solvents, e.g. pure $CFCl_3$ or pentane, an indiscriminate radical fluorination is the predominant process.



Scheme 7

This mechanism requires an attraction of the positive end of the fluorine dipole to hydrogen followed by electrophilic attack. Therefore, the reaction is facilitated by conditions which promote ionic processes and will favour C-H bonds with a high p-orbital character. Consequently, tertiary hydrogens react preferably to primary and secondary ones. For cyclic substrates ring strain also plays a role. Reactivity of C-H bonds was observed to increase with increasing ring size for the same reason (Fig 1.25).

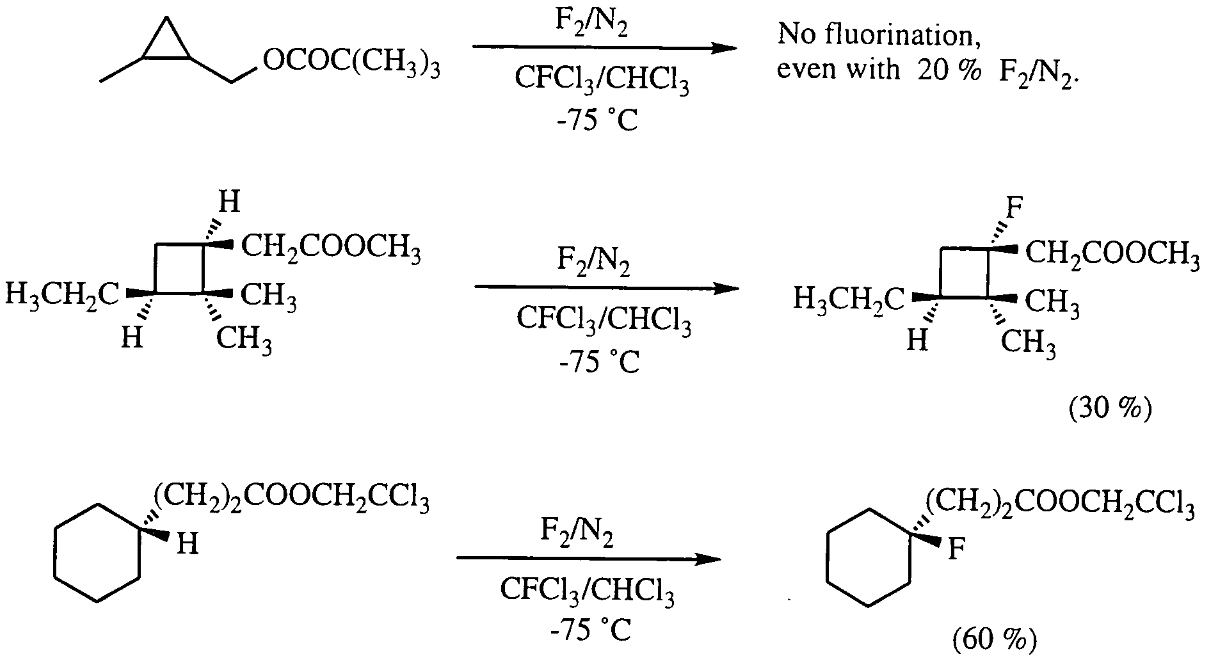
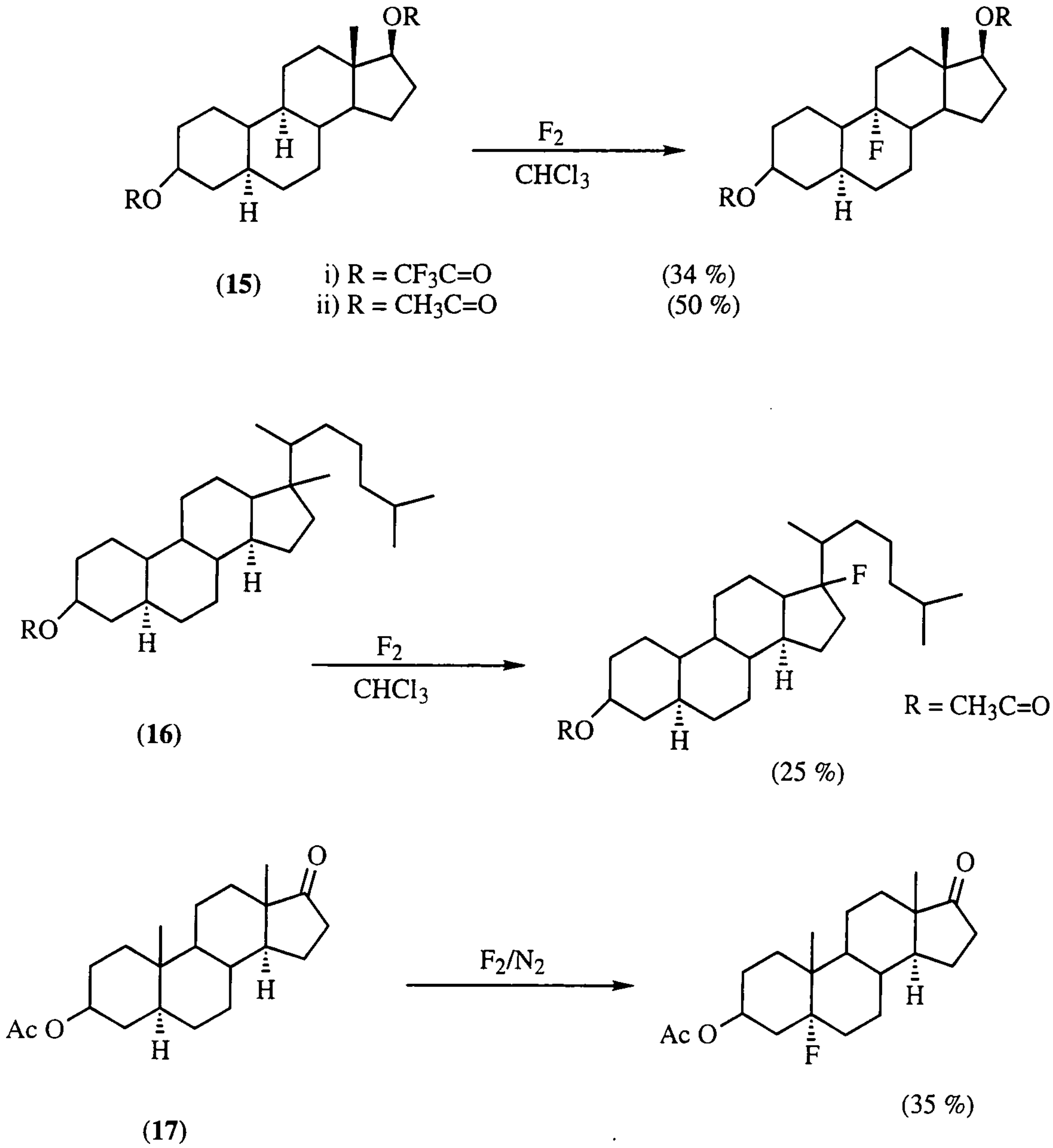


Fig 1.25

Even when conditions favour electrophilic fluorination the radical process is not completely suppressed. Fluorine radicals are always present albeit in low concentration and with substrates which are suitable for the electrophilic reactions, e.g. small rings or even the monofluoro products, these highly reactive species will eventually react with any unreacted materials. Double bonds may be introduced by acidic or basic dehydrofluorination of these monofluoro products, thus giving rise to an excellent route for further chemical transformations at previously unreactive sites of organic molecules.[82]

An interesting application of this methodology is in the fluorination of steroids. This approach can be of biological significance since selectively fluorinated compounds, particularly steroids, have potential applications in pharmacology and radiodiagnostic studies. Barton[75] has carried out fluorinations of many common steroids **(15, 16)**, while Rozen has reported the reactions of the less common 5β- and 3α- sterols[83], e.g. 17-oxo-5β-androstan-3α-ol acetate **(17)** (Fig 1.26).



(15)

(16)

(17)

Fig 1.26

The chemistry of tertiary halides has also been investigated, notably the production of fluoroadamantanes by the fluorination of their iodo- and bromo-analogues.[84] Nucleophilic substitution of an organic halide by another halogen is a well established procedure but there are very few examples of this reaction at a saturated carbon centred where electrophilic attack is involved. Rozen investigated the reaction of fluorine with some bromo- and iodo- adamantanes in various solvents (Fig 1.27). If the reaction was not carried out under strictly anhydrous conditions or in the presence of ethanol, some formation of the corresponding alcohols or ethoxy compounds was observed (2-5% for bromo-, up to 20% for iodo-analogues). Starting materials did not react with water or ethanol. 1:1 Trichlorofluoromethane/chloroform was seen to be the solvent of choice, requiring only 1 mol. equivalent of F_2 for complete conversion.

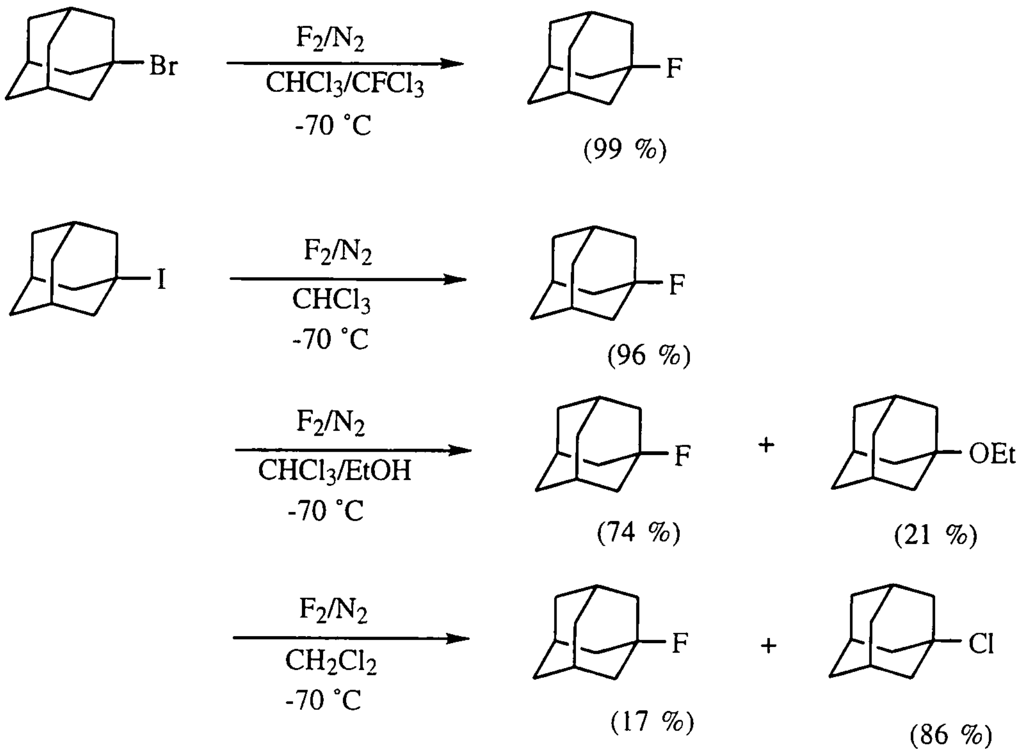
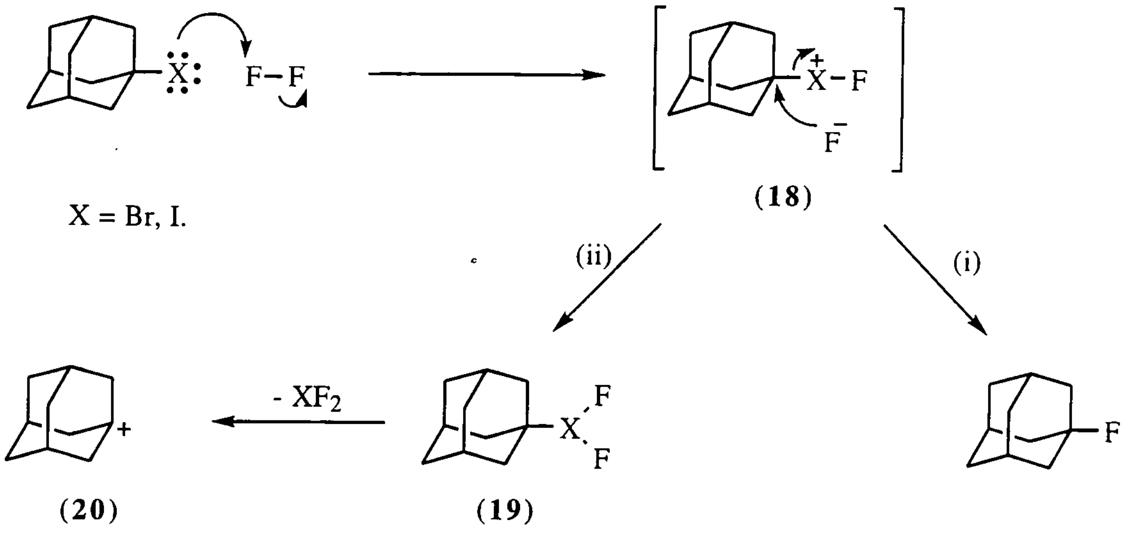


Fig 1.27

These observations led the researchers to postulate the mechanism outlined in Scheme 8, in which fluorine acts as an electrophile. For the bromo derivative, the reaction rapidly follows path (i) since bromine is a strongly electronegative atom and the positive charge is centred mainly on the carbon. Intermediate **(18)** collapses on attack by fluoride to give the product. When X=I the reaction may also proceed along path (ii) simultaneous with (i). Positive iodine is more stable than bromine and the larger atom may accommodate several fluorine atoms. Compounds such as **(19)** are known in aromatic chemistry[85] but here it decomposes generating the stable carbocation **(20)** which may further react with fluoride, water, ethanol or any other nucleophilic species present.



Scheme 8

d) Fluorination of Aromatic Systems.

i) Benzene and Benzenoid Derivatives.

Early attempts to fluorinate aromatic rings were plagued with problems, but in 1970, Grakauskas demonstrated the fluorination of a 6% solution of benzene in acetonitrile at - 35°C to give predominantly monofluorobenzene, with small amounts of the *o-*,*m-*, and *p* - difluoro products also observed. He then carried out reactions using toluene and nitrobenzene, and on the basis of the isomer distribution of these products (Fig 1.28), he postulated that the fluorination was an electrophilic substitution analogous to that observed for the other halogens.

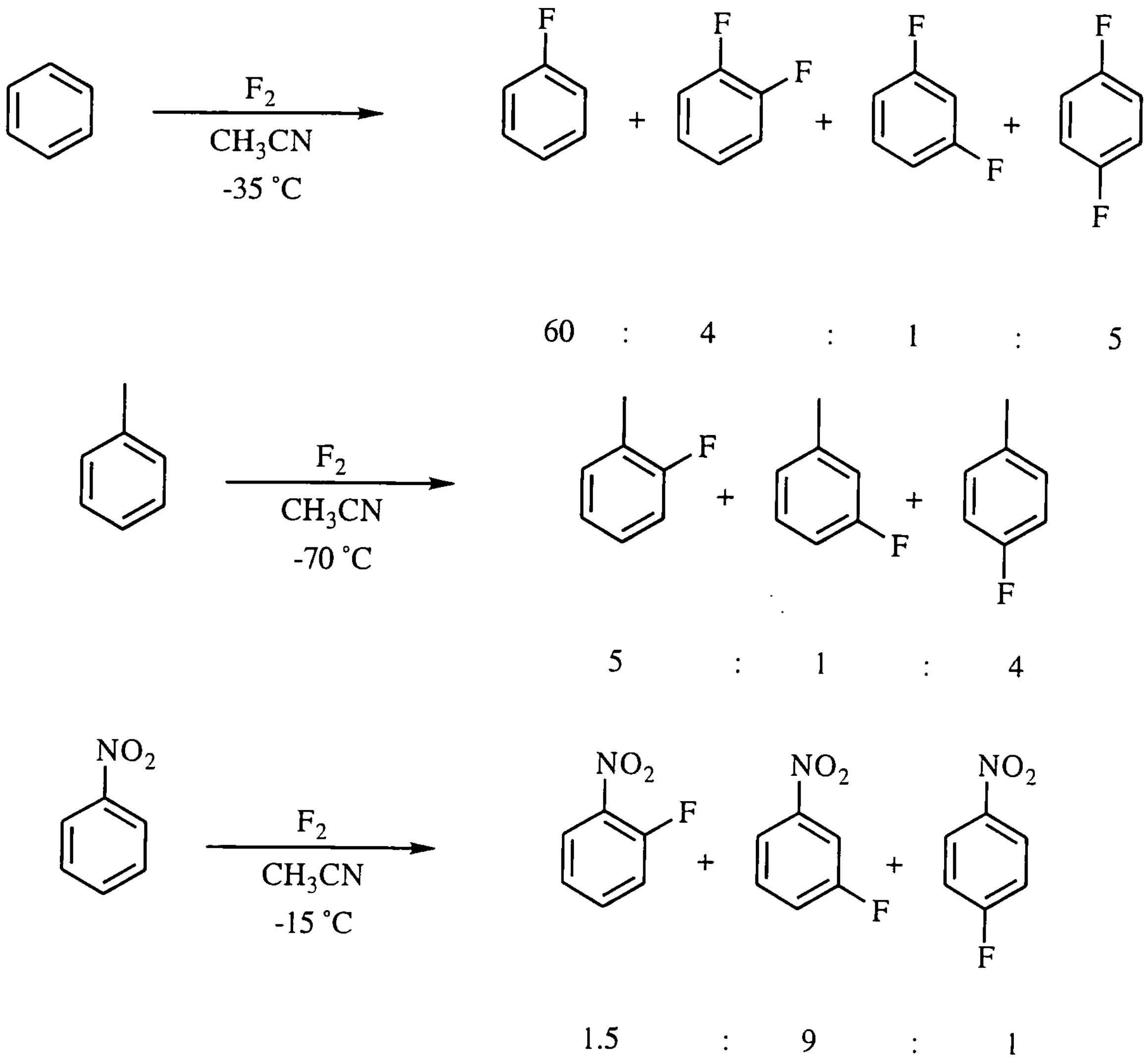
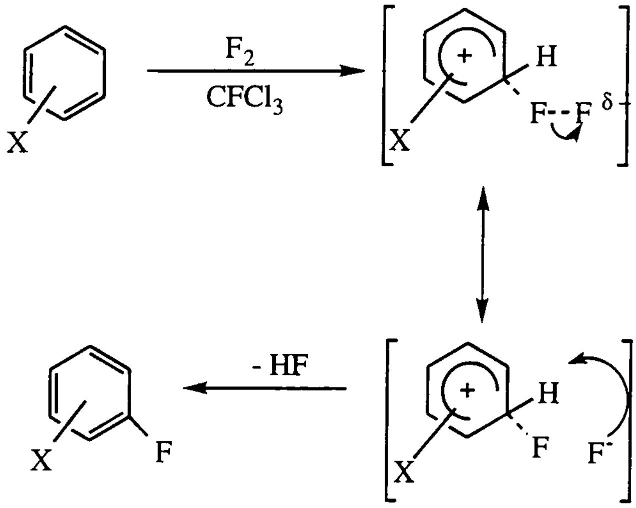


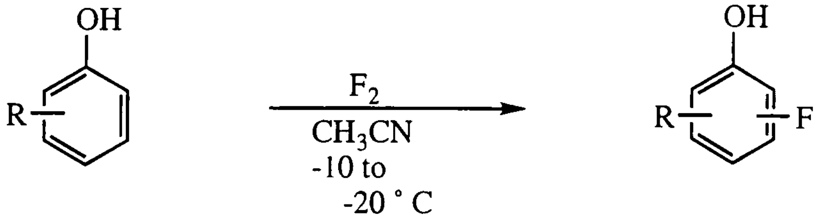
Fig 1.28

The introduction of dilute solutions of F_2 has greatly enhanced the control of these reactions. Cacace has performed substitutions on a variety of aromatic rings using elemental fluorine (< 0.76 % in N_2).[86] These reactions were carried out in $CFCl_3$ at -78 °C, and showed first order kinetics dependant only on substrate concentration.[86,87] Plotting σ_+ values for aromatic substitution gave a ρ value of -2.45, supporting the supposed electrophilic mechanism (Scheme 9).



Scheme 9

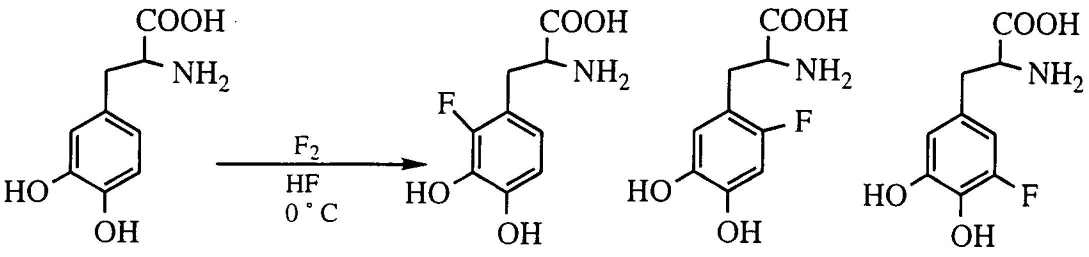
Misaki has investigated the fluorination of various substituted phenols in acetonitrile (Fig 1.29).[88]



	Conversion
i) R = 2-CH_3	(70.8 %)
ii) R = 3-CH_3	(67.7 %)
iii) R = 2-COOH	(79.0 %)
iv) R =2-CHO	(63.0 %)

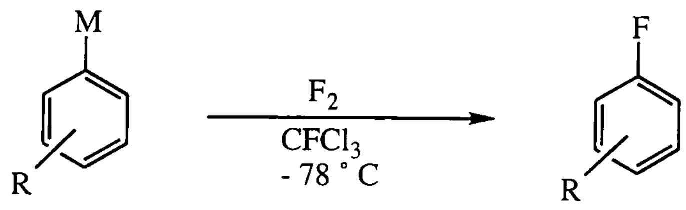
Fig 1.29

He has also used anhydrous HF as a solvent for some of these fluorinations, notably L-DOPA **(21)**, where it minimises the oxidation which is usually caused by the deprotonation of the hydroxyl group (Fig 1.30).[89]



(21) (5.8 %) (12.0 %) (1.7 %)

Fluorine has also been used in the cleavage of several metal-aryl and silyl-aryl bonds (Fig 1.31).[90, 91]



i) R = 4-(OCH_3), M = Sn (n-Bu)$_3$ (72 %)
ii) R = 4-CH_3, M = Sn (n-Bu)$_3$ (82 %)
iii) R = 4-F, M = Sn (n-Bu)$_3$ (>95 %)
iv) R = 4-CH_3, M = $SiMe_3$ (28 %)
v) R = H, M = HgPh (40 %)

Fig 1.31

Recently, an extensive study of the liquid-phase fluorinations of aromatics has been carried out by Conte *et al* at the University of Padua.[92] In this work a number of substrates and solvents have been considered in order to establish the ideal conditions for this reaction, e.g. benzene in $CFCl_3$, chloroform and methanol among others.

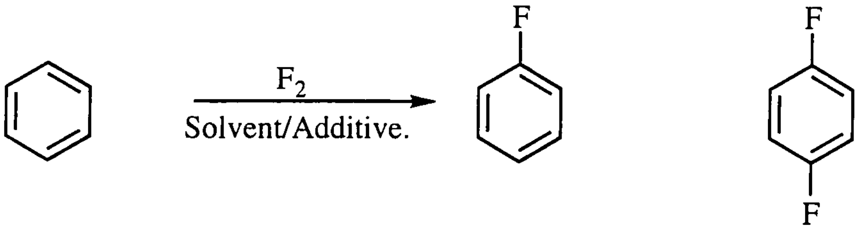
They established that the key factor in these fluorinations is the solubility of fluorine in the solvent. For most organic solvents this solubility is poor, and this gave rise to the problematical reactions at the gas/liquid phase boundary. Therefore increasing the solubility of fluorine would make direct fluorination of aromatic compounds possible under less drastic conditions.

It was observed that the use of solvents or additives containing an OH group led to a greatly increased reactivity of F_2. Under these conditions the acidic hydrogen can react with fluorine giving HF and the hypofluorite -OF. This lends credence to the suggested ionic mechanism of liquid phase electrophilic substitution, with OF acting as an analogue of F^+.

These results are best demonstrated by the reaction of benzene (Fig 1.32). When the fluorination is carried out in $CFCl_3$, the reaction was seen to occur with low conversions giving the mono- and disubstituted products in low yields with extensive formation of black tars. With the addition of varying amounts of trifluoroacetic acid, conversion of starting material was greatly improved with high yields of fluorobenzene formed along with some traces of 1,4 difluorobenzene. A similar trend was observed for chloroform, but this reaction was complicated by interactions between the solvent and the acid. Trifluoroacetic acid on its own, was seen to be ineffective as a solvent as the benzene substrate was separated from the solution at temperatures below 7 °C.

This enhanced reaction in the presence of trifluoroacetic acid was ascribed to either the change in polarity of the system with addition of acid or to the possible formation of a hypofluorite, CF_3OOF. Both of these phenomena would be capable of promoting electrophilic fluorination.

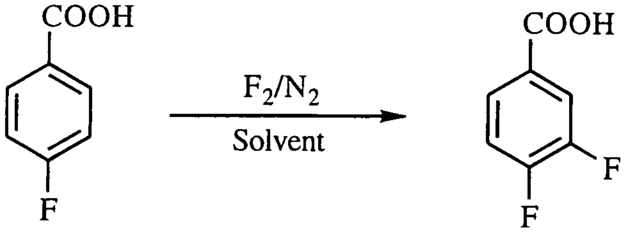
Similarly, the use of methanol as a solvent produced greater yields of fluorobenzene, largely unaffected by the presence of additives. In contrast, 2, 2, 2-trifluoroethanol was a rather ineffective solvent, giving poor conversions and yields.



			Conversions.
i) Solvent = $CFCl_3$ / -30 ^{0}C Additive = CF_3COOH	(79.4 %)	(10.1 %)	(32.8 %)
ii) Solvent = $CHCl_3$ / -30 ^{0}C Additive = CF_3COOH	(43.5 %)	(10.9 %)	(69.3 %)
iii) Solvent = CH_3OH/ -40 ^{0}C			
a) Solvent only	(52.0 %)	---------	(40.1 %)
b) Additive = 5% NaOH	(39.5 %)	---------	(44.9 %)
c) Additive = 9.8% KOH	(39.5 %)	---------	(14.1 %)
iv) Solvent = CF_3CH_2OH	(36.3 %)	---------	(28.3 %)

Fig 1.32

Chambers and co-workers have extended this idea of using polar and acidic solvents to promote electrophilic fluorination[93-95] to far more acidic systems. Using 4-fluorobenzoic acid (**22**) as a model substrate, the fluorination reaction was studied using a range of solvents (Fig 1.33).

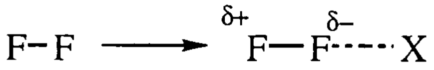


(22)

Solvent	Conversion (%)
$CF_2ClCFCl_2$	0
CH_3CN	53
CF_3COOH	56
HCOOH	65
conc. H_2SO_4	84

Fig 1.33

These observations showed that conversion to product increased with increasing acidity of the solvent media. On the grounds of these results it was suggested that the mechanism involved some degree of interaction between the solvent and fluorine, for example between F_2 and the proton of sulphuric acid (Scheme 10).



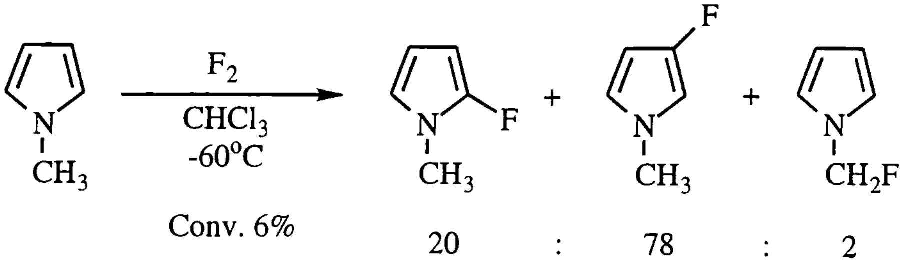
$$\text{F–F} \longrightarrow \overset{\delta+}{\text{F}}\text{—}\overset{\delta-}{\text{F}}\cdots\text{X}$$

(X = solvent, or H^+ for acids)

Scheme 10

ii) Heteroaromatic Systems.

There are few examples of the direct fluorination of heteroaromatic systems in the literature when compared to the analogous reactions of the other halogens.[96-98] Simons reported the fluorination of pyridine to give 2-fluoropyridine in 1948 and the reaction of elemental fluorine with quinolines and isoquinoline have also been outlined. *N*-methylpyrrole and thiophene have been shown to react with fluorine yielding mixtures of mono-fluorinated isomers[99, 100], consistent with an electrophilic process, in contrast furan gave a mixture of products largely resulting from addition of fluorine to the ring (Fig 1.34). Conversions of these reactions were kept low to avoid substrate degradation and polymerisation.



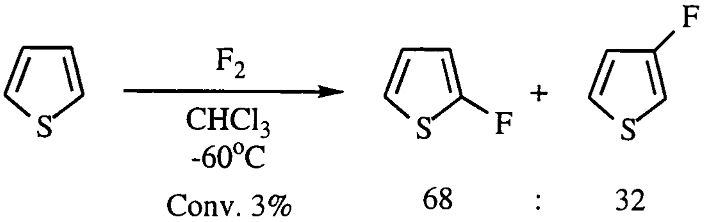


Fig 1.34

Recent work in the Chambers group has suggested that the addition of iodine to the reaction mixture can be used to modify the reactivity of fluorine and using mixtures of F_2/I_2 the fluorination of some pyridine derivatives has been investigated (Fig 1.35)[95].

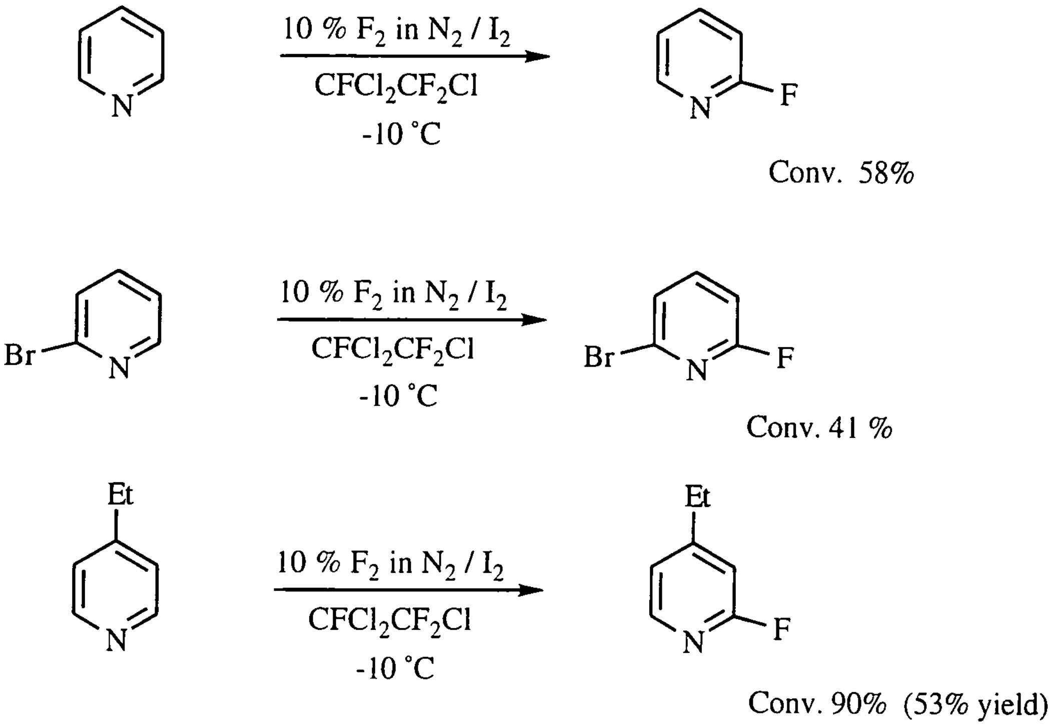
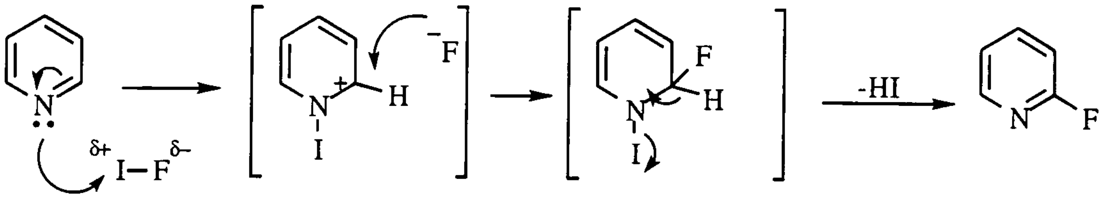


Fig 1.35

The mechanism of this reaction is thought to proceed via electrophilic attack by I^+

on nitrogen, promoted by interaction between fluorine and iodine, perhaps forming some 'I-F' species, although the exact nature of this compex is unknown. This is rapidly followed by nucleophilic reaction with fluoride ion (Scheme 11).

$$F_2 + I_2 \longrightarrow \overset{\delta+}{I}-\overset{\delta-}{F}$$



Scheme 11

This methodology has been further extended to benzofused pyridines[101] (Fig 1.36).

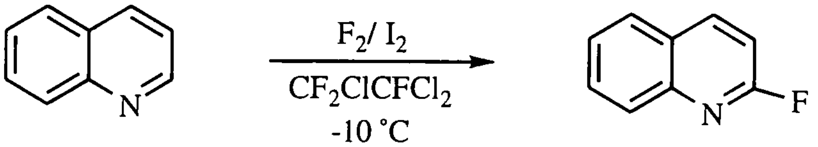


Fig 1.36

e) Fluorine as an Enabler for Other Synthetic Transformations.

In addition to direct fluorinations, elemental fluorine has also been used to promote other synthetic transformations. The high oxidising power of fluorine allows its use in oxidation reactions, and as has already been mentioned the fluorination of tertiary hydrogens coupled with dehydrofluorination has been used to incorporate double bonds into otherwise unactivated molecules.[82] In this section we shall detail a few examples of this sort of chemistry.

i) The Iodination and Bromination of Aromatics.

Previously, the fluorination of pyridines using F_2/I_2 mixtures has shown that this system is a possible source of electrophilic iodine.[95] Chambers and co-workers have applied this system as potential methodology for the iodination of aromatic systems. It is thought that some form of 'I-F' species is produced which coupled with an acid solvent provides a source of I^+. This species has been shown to react with a range of benzenoid compounds by means of electrophilic aromatic substitution. A similar process can be observed for mixtures containing bromine, and is seen to more reactive, facilitating bromination of highly deactivated aromatics, where attempts at iodination had proved unsucessful, e.g. 1-fluoro-2,4-dinitrobenzene (**24**) (Fig 1.37).

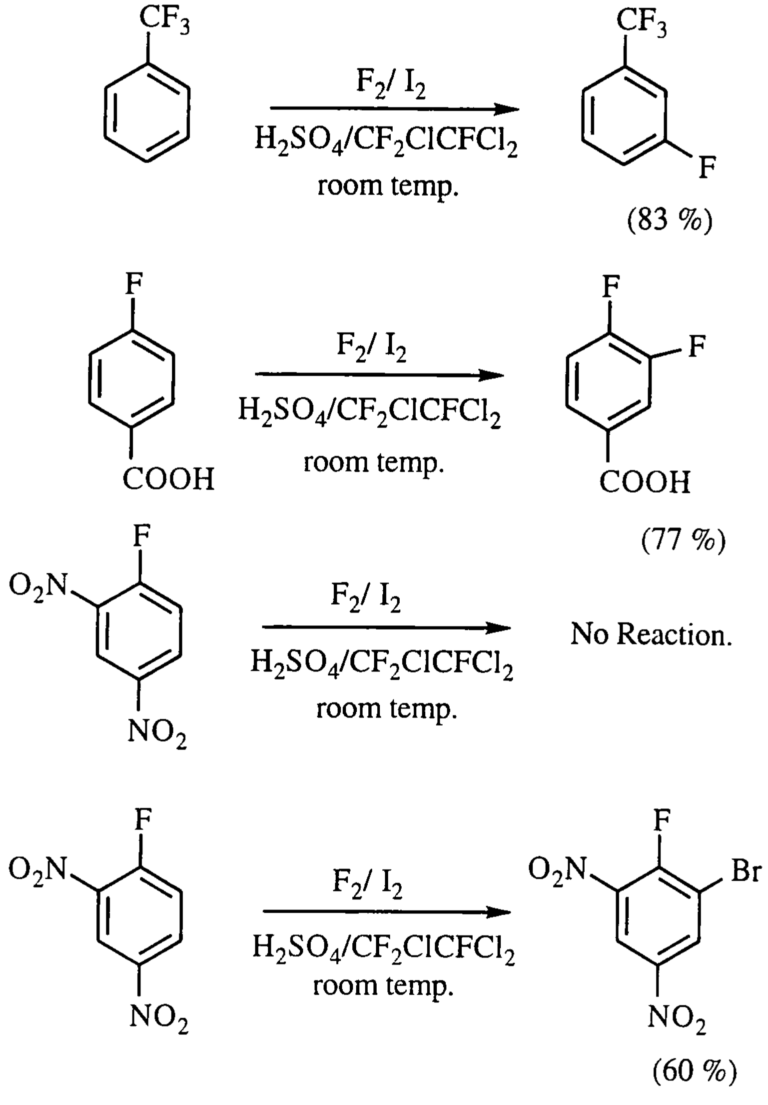


Fig 1.37

ii) Electrophilic Methoxylations and Hydroxylations.

The methoxide ion is a very common tool in organic synthesis, but reactions of the analogous electrophilic "MeO^+" species are relatively unknown. Such a reactive intermediate would have great synthetic and theoretical potential. Rozen *et al* have suggested that elemental fluorine can be used in the production of the previously unreported MeOF, a source of positive methoxylium[102]. Earlier work observing the reaction of water and fluorine in acetonitrile showed the formation of HOF-CH_3CN, which could be used as a reagent in hydroxylation reactions[103] (Fig 1.38). The HOF molecule is polarised such that the partial negative charge falls on fluorine, providing a which could be used as a reagent in hydroxylation reactions[103] (Fig 1.38). The HOF molecule is polarised such that the partial negative charge falls on fluorine, providing a source of hydroxylium "$HO^{\delta+}$" moiety. Pure hypofluorous acid is very unstable, so CH_3CN fulfils a stabilising role in the complex, creating a reagent stable at 0 °C for several hours.

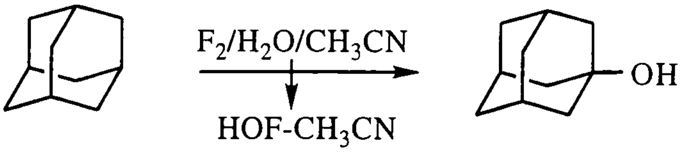


Fig 1.38

This principle was extended in the search for a route to MeOF. Methanol was treated with elemental fluorine in acetonitrile, generating the methyl hypofluorite *in situ*, which further reacted with a range of enol derivatives to yield α-methoxy ketones. These compounds are usually prepared by a multistep synthesis involving a nucleophilic displacement of an appropriately placed leaving group by methoxide, typically in poor yields[104, 105]. The reaction of MeOF offers a single step route by attack of MeO^+ at the electron rich end of the carbonyl's enol form. Methyl enol ethers were seen to react best, but the process also worked with silyl enol ethers and enol acetates with some limited success (Fig 1.39). Enol acetates, other than benzylic, were generally poor substrates tending to produce tars and low yield of the desired products.

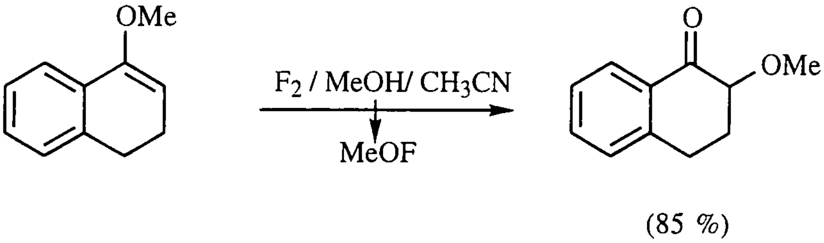
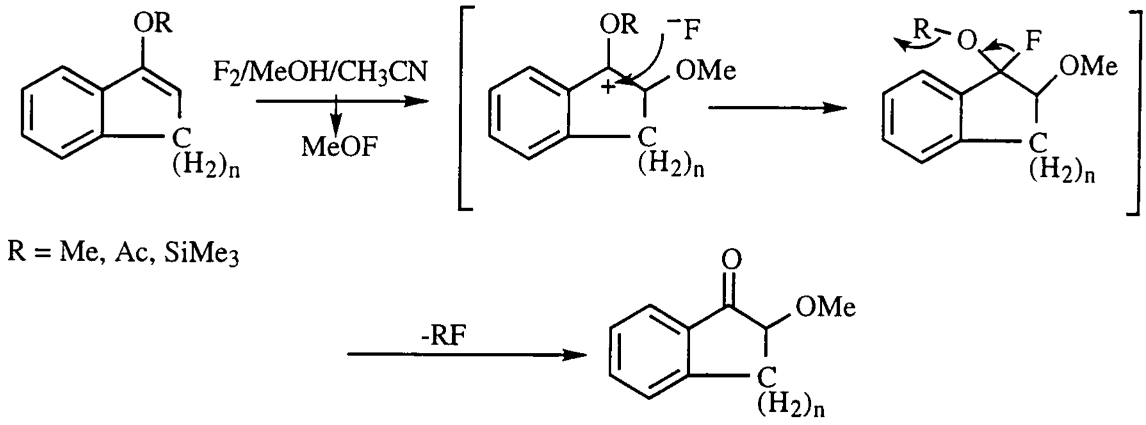


Fig 1.39

The reaction is thought to proceed via a addition/elimination mechanism, similar of that of fluorinations carried out using CF_3OF (Scheme 12).[106]



Scheme 12

This theory was supported by the reaction of terminal enols, e.g. methyl ether and enol acetates of acetophenone, from which the adduct of MeOF across the double bond is the only isolated product. These adducts may be hydrolysed to the desired α-methoxy ketones (Fig 1.40).

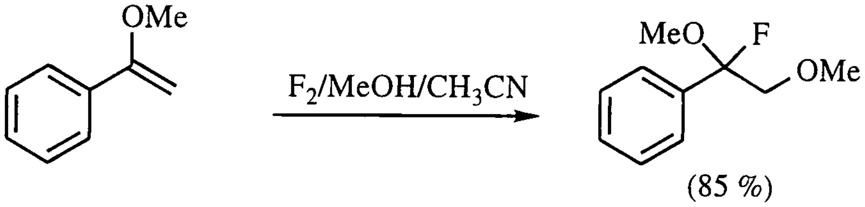


Fig 1.40

iii) Oxidations and Epoxidations.

The HOF-CH_3CN complex prepared by Rozen is an extremely versatile reagent. In addition to hydroxylation reactions, it has also found application in a host of oxidation and epoxidation reactions. Using fluorine and water in acetonitrile to generate HOF-CH_3CN *in situ*, Rozen has been able to produce epoxides of almost any type of double bond at room temperature (Fig 1.41). Regular alkenes are observed to react in a matter of seconds[107], while enones[108] and perfluoroalkylethenes[109, 110], which are usually cannot be oxidised by orthodox procedures, require somewhat longer reaction times. Free hydroxyl or carboxylic acid groups do not interfere with this process[111], in contrast to other direct epoxidation methods[112].

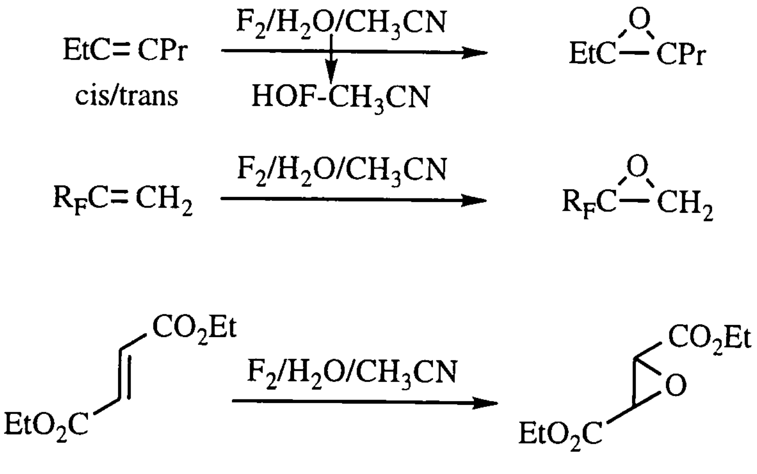


Fig 1.41

The reagent has also been used as a conventional oxidising agent. Secondary alcohols have been oxidised to ketones in high yields in only a few minutes, by abstraction of α-hydrogens[107]. Even acid sensitive systems such as 3-pinol have been observed to react well[113]. Prolonged reaction has been shown to produce good yields of the respective esters via a Baeyer-Villager oxidation of the intermediate ketone[107]. Secondary and primary methyl ethers react in a similar manner[114]. Some of these reactions are shown in Fig 1.42.

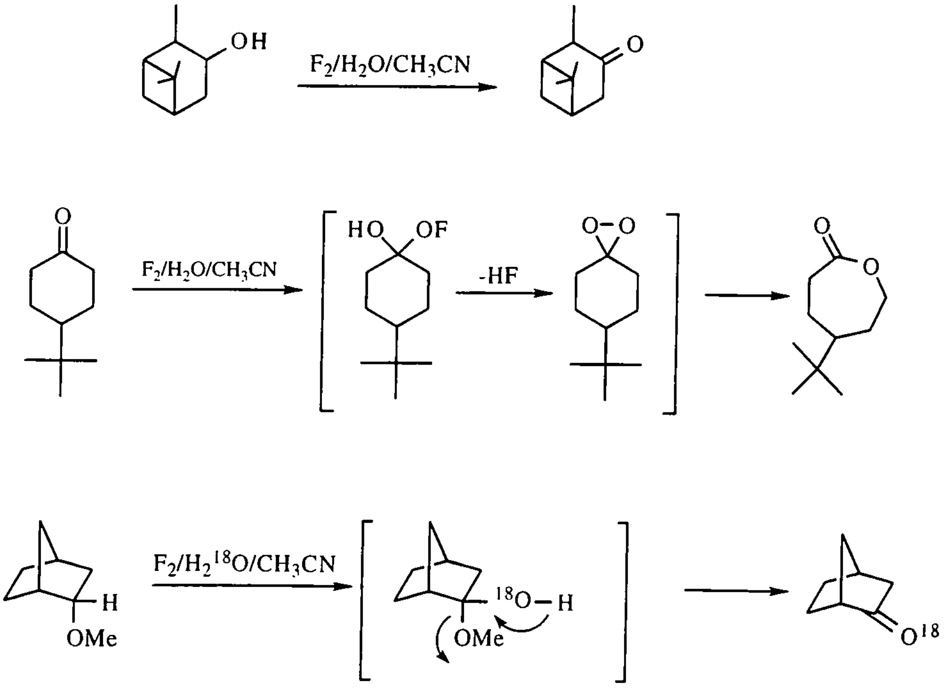
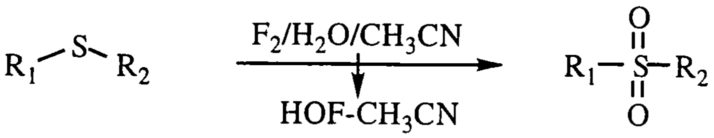


Fig 1.42

The oxidation of sulphides to sulphones is another reaction which may be carried out using HOF-CH_3CN. This procedure usually requires prolonged treatment with oxidants containing heavy metals such as $KMnO_4$[115] or osmium tetroxide[116], but hypofluorous-acetonitrile may this transformation quantitatively at 0 °C on a time scale of a couple of minutes (Fig 1.43). This methodology is cleaner, with no toxic waste products to dispose of and has been seen to be effective for a range of sulphides with alkyl[117], aryl[118] and even fluoroalkyl[118] substituents, often giving yields in excess of 90 %.



R_1, R_2 = Alkyl, Aryl, R_F etc.

Fig 1.43

1.5 Electrophilic Fluorinating Agents Derived from Elemental Fluorine.

At present elemental fluorine is not a widespread reagent used in organic synthesis. Due to the great academic and industrial interest in incorporating fluorine selectively in organic molecules, there have been several attempts to develop viable electrophilic fluorinating reagents for use in organofluorine research. Many of these compounds involve the direct use of elemental fluorine in their preparation. Typically these reagents fall into two major classes; O-F and N-F fluorinating agents; both of which have been extensively reviewed in the recent literature.[119, 120]

The OF class of fluorinating agents were devised as a substitute for elemental fluorine and perchloryl fluoride ($FClO_3$) in electrophilic fluorination which were disfavoured because of their high reactivity and the potential for explosions. Fluoroxy reagents such as CF_3OF (**25**) and $CsSO_4F$ (**27**), are safer to handle and can be easily used to selectively fluorinate organic molecules. Typically, with the exception of CF_3OF, these reagents are not particularly stable at room temperature and are usually prepared *in situ* by direct fluorination and are not isolated or purified before reaction with the substrate. For example, caesium fluoroxysulphate may prepared by bubbling fluorine through a solution of caesium sulphate in deionised water (Fig 1.44), however care had to be taken since this reagent had been known to detonate occasionally on contact with metal surfaces. A recent review by Rozen has covered this area in much greater detail.[119] A few examples of fluoroxy fluorinating agents are given in Table 4.

$$Cs_2SO_4 \xrightarrow[H_2O]{F_2} \underset{\mathbf{(27)}}{CsSO_4F} + CsF$$

Fig 1.44

The second major group of electrophilic fluorinating agents are the NF-compounds. Again, it is claimed that these are safer and easier to handle than elemental fluorine. These compounds can be further subdivided into two types, neutral R_2NF compounds, e.g. $(CF_3SO_2)_2NF$ **(28)** and quarternary R_3N^+F A^- salts, such as N-fluoropyridinium triflate **(30)**. The R_2N- and R_3N^+ fragments are chosen so that they form good leaving groups, promoting the reactivity of the electrophilic fluorine with nucleophiles. These reagents are typically prepared by direct reaction of the R_2NH and R_3N precursors with elemental fluorine, e.g. the preparation of N- fluoroquinuclidium fluoride **(32)** (Fig 1.45) [121, 122] There are now a large range of known NF reagents which demonstate varying degrees of oxidising and fluorinating power toward nucleophiles, and many have recently been reviewed in the literature.[120] Some NF-reagents have been shown to be quite stable compounds, able to be stored for some time without degrading, which, coupled with their ease of use, has led to their application as commercial reagents, e.g. Selectfluor™ **(31)**. Some examples of NF-reagents and their application are given in Table 4.

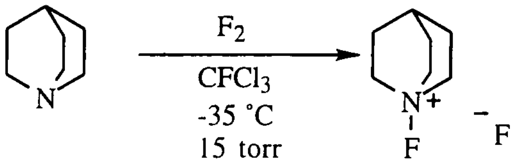


Fig 1.45

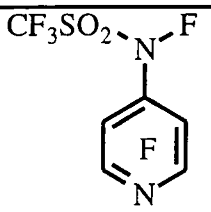
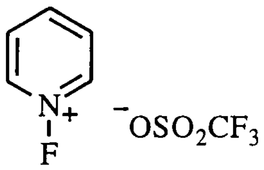
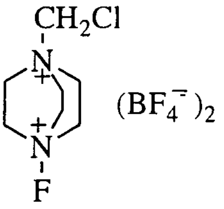
Reagent.	**Application.**
CF_3OF **(25)**	Steroids, alkenes, some aromatics and organometalics
CH_3COOF **(26)**	Alkenes, some heterocycles e.g. Uracil.
$CsSO_4F$ **(27)**	Aromatics, alkenes and enol acetates
$(CF_3SO_2)_2NF$ **(28)**	Aromatics, alkenes, some phosphonates and α-fluorocarbonyls
 **(29)**	Aromatics.
 **(30)**	Aromatics, sulphides, alkenes and β-dicarbonyls
 Selectfluor™ **(31)**	Aromatics, sulphides, alkenes, organometalics and β-dicarbonyls

Table 4 Some Electrophilic Fluorinating Agents.

Results and Discussion.

Chapter Two The Deprotection and Fluorodesulphurisation of 1,3-Dithiolanes.

2.1. Introduction.

The selective fluorination of organic molecules has provoked a great deal of interest in recent years due to the profound effect that incorporation of fluorine or perfluorinated groups can have on the chemical, physical and biological properties of these compounds.[123] The introduction of a CF_2 group into a molecule is an important synthetic target because of a possible relationship between the difluoromethylene moiety and an ether oxygen and many methods for the preparation of this functionality have been outlined in the literature. In particular, the functional group interconversion of carbonyls to difluoromethylene is an oft quoted procedure. This may be achieved either directly, for instance using SF_4, DAST or MoF_6[124], or indirectly by the fluorination of carbonyl derivatives such as hydrazones[125] or diazo-compounds[68] by iodine monofluoride or fluorine (Fig 2.1).

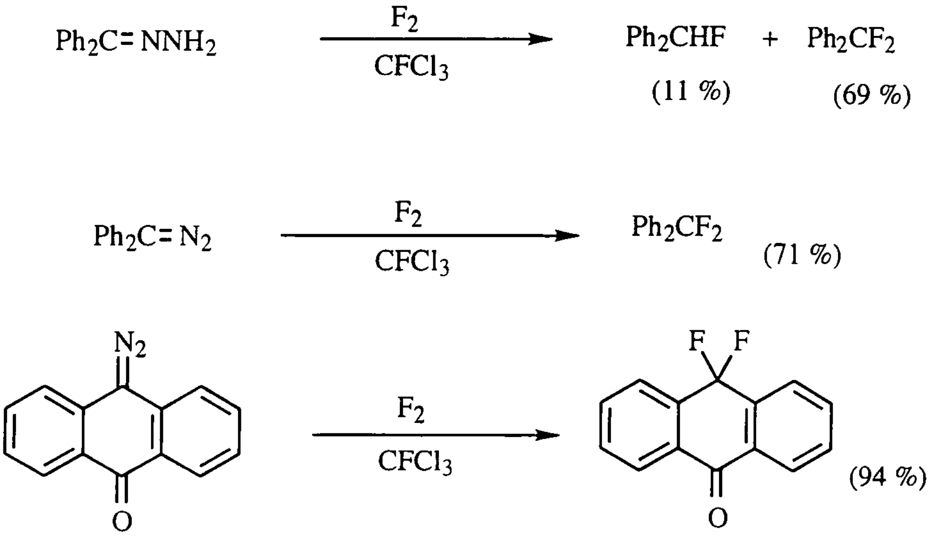


Fig 2.1

An alternative approach is the fluorination of 1,3-dithiolanes, synthetic equivalents of the carbonyl group, using reagents such as SO_2Cl_2/pyridinium polyhydrogen fluoride(PPHF) which consist of a combination of a source of halonium and fluoride ions reported by Prakash (Fig 2.2).[126]

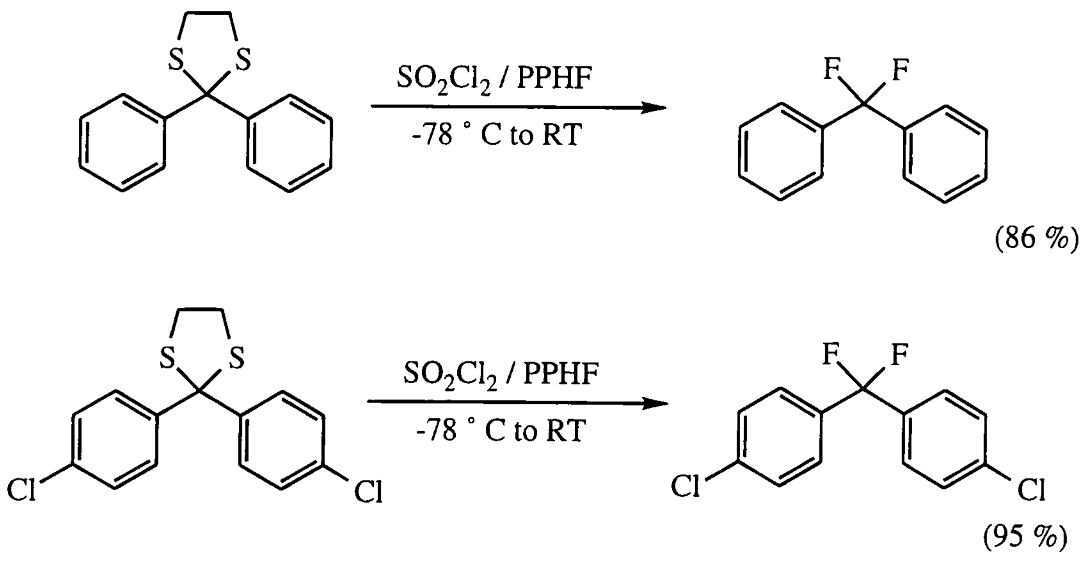
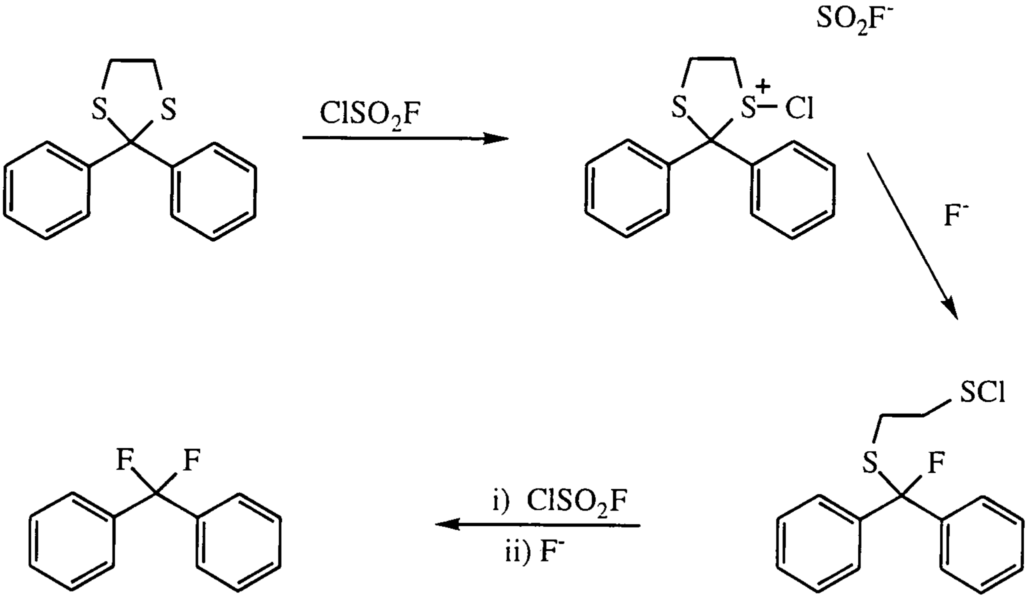


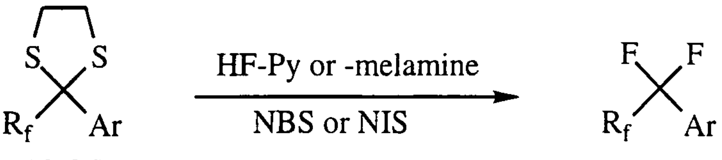
Fig 2.2

The reaction of sulphuryl chloride in pyridinium polyhydrogen fluoride(PPHF) with 1,3-dithiolanes is thought to proceed via electrophilic attack by positive halonium ions at the sulphur sites, followed by nucleophilic displacement of the sulphur group by fluoride ion [126]. This sequence of events was repeated for the second sulphur atom (Scheme 13). The process is believed to involve *in situ* formation of SO_2ClF, and indeed the same result is observed when this reagent is used in place of sulphuryl chloride.



Scheme 13

Similar processes have been observed using NBS/Py-HF [127], $ArIF_2$ [128], following the same type of mechanism. Fluorodesulphurisation has the advantage over the direct reaction of carbonyls to produce the CF_2 moiety using reagents such as SF_4, HF or DAST, since the reagents required are not as highly toxic and have a greater tolerance of acid-sensitive substrates. Kuroboshi has also demonstrated that these methods are effective for 2-perfluoro-2-aryl-1,3-dithiolanes (**33-36**) using HF in complexes with pyridine or melamine in conjunction with *N*- bromo- or *N*-iodosuccinimide (NBS/NIS) (Fig 2.3).



(33-36)

No.	Ar	R_f	Conditions.	Yield (%).
33	4-$^nPrC_6H_4$	CF_3	HF/py, NBS, 10 h	53
34	4-$^nPrC_6H_4$	n-C_3F_7	HF/mel, NBS, 0.25 h	74
35	1-Napthyl	CF_3	HF/py, NIS, 10 h	98
36	4-$^nBuOC_6H_4$	n-C_3F_7	HF/mel, NBS, 0.25 h	79

Fig 2.3

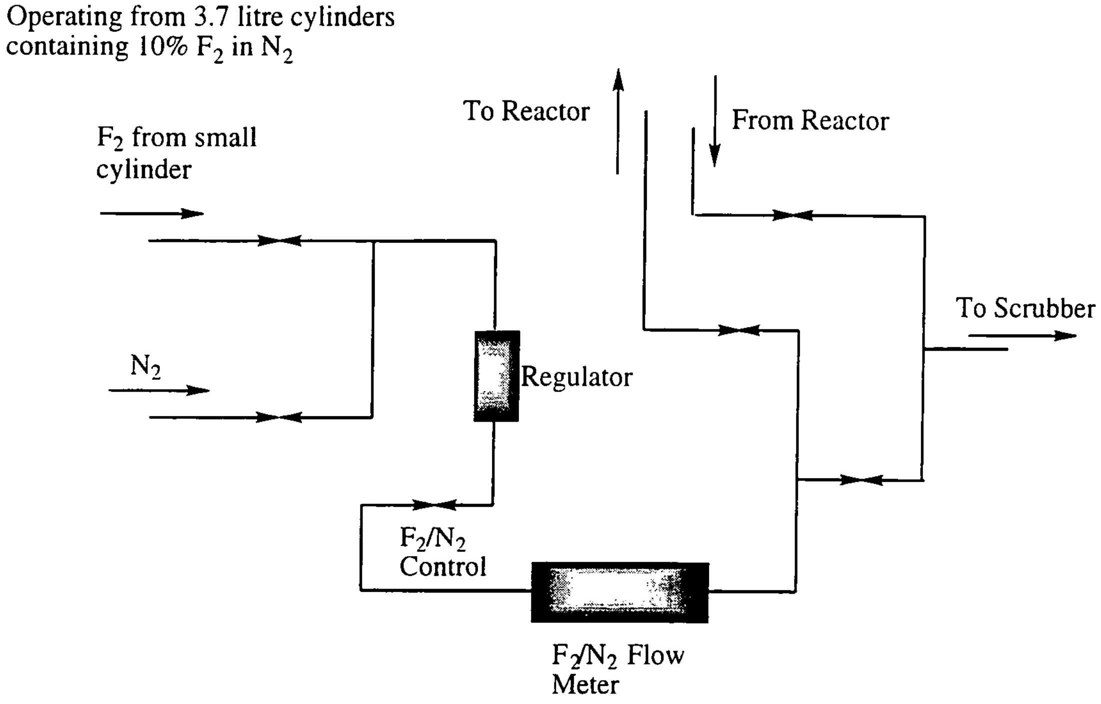
For some time now, our group has been interested in the potential of direct fluorination as a method of synthesising organofluorine compounds. There is some prejudice against the use of elemental fluorine in organic synthesis, principally due to the problems of its intense reactivity, but this may be controlled by judicious use of conditions and reagents. Therefore, we aim to establish the scope and potency of the chemistry of elemental fluorine. To this end, we have looked at a host of reactions involving F_2, many of which have been mentioned in Chapter One. A reaction worth mentioning here is the use of iodine or bromine to moderate the reactivity of fluorine, which in some cases, may have a dramatic effect on the outcome of the reaction. In this manner fluorine has been shown to act as an enabler for a range of synthetic transformations, notably the iodination, bromination and alkoxylation of several aromatic substrates.[95, 129] For example mixtures of elemental fluorine and iodine have been shown to be very effective reagents used in the iodination of benzenoid compounds. Here the reaction is thought to involve the formation of a complex between fluorine and iodine *in situ*, which is polarised to produce a partial positive charge on the iodine providing a source of electrophilic iodonium which may react with aromatic substrates by electrophilic substitution.[95] Extending this principle we wondered if this elecrophilic iodine could be used to react with the sulphur site of 1,3-dithiolanes in the same manner as sulphuryl chloride. Fluoride ion, generated in this reaction, would then attack the developing carbocation displacing the dithiolane moiety to generate the geminal difluoro product. Could we use elemental fluorine, in a mixture with iodine to promote a similar fluorodesulphurisation process to that reported by Prakash ?

This chapter details our attempts to investigate this possibility using 1,3-dithiolanes as substrates and relates a new and easy approach to the deprotection of these systems that was discovered in the course of this work.

2.2 Initial Reactions.

2.2.1 Fluorination Rig and Reactor Design.

All fluorinations were carried out using a 10 % mixture of fluorine in nitrogen prepared in a 3.7 litre passivated stainless steel cylinder. This was connected to the reaction vessel through a small rig of valves containing a regulator and an F_2/N_2 flow meter, to give greater control of the rate of the passage of fluorine (Fig 2.4).



Flow Rate (ml/min).	Fluorine Passed (mmol/hr).
10	2.5
15	3.75
20	5.0

Fig 2.4

The reactions, themselves, were performed in small PTFE reaction vessels (60ml and 120ml). A plan of such a vessel is displayed in Fig 2.5.

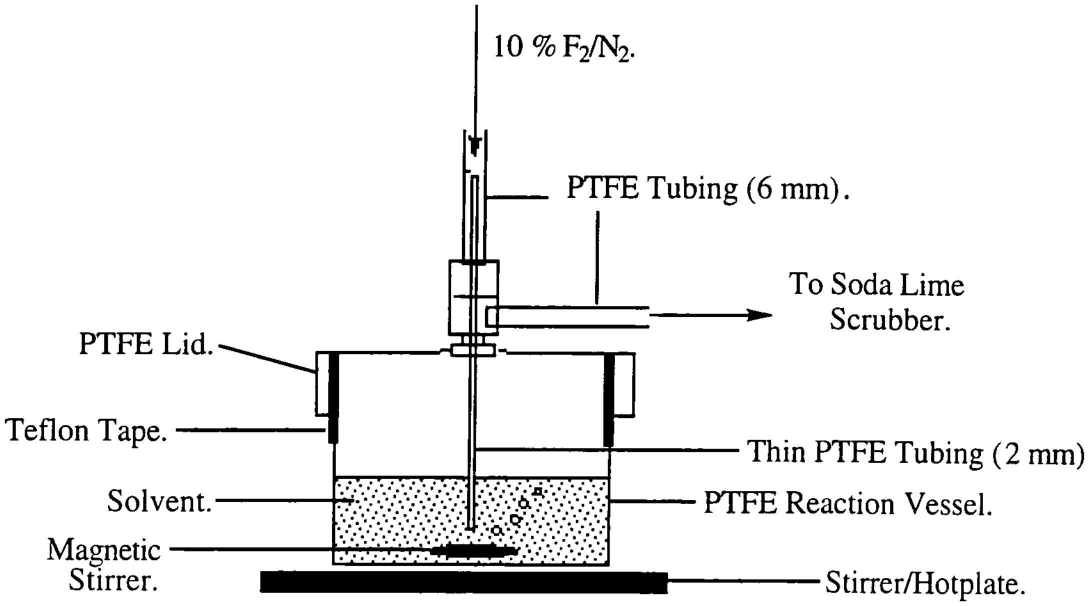
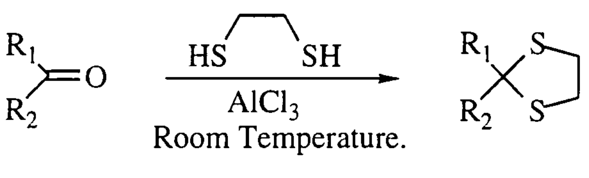


Fig 2.5

The reactor was attached to the fluorination rig by a length of PTFE piping (6mm diam.), inside which a thinner PTFE capillary inlet (2mm diam.) allowed the introduction of fluorine into the system. A solution of the substrate was then prepared such that the reactor was a third full (i.e. 20ml for the 60ml vessel, 40ml for 120 etc.), and stirred continuously using a PTFE magnetic stirrer bar. Waste gas emissions were conveyed to a scrubber column arrangement containing soda lime through a further piece of PTFE tubing (6mm diam.).

2.2.2 Preparation of 1,3 Dithiolanes.

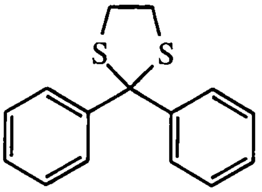
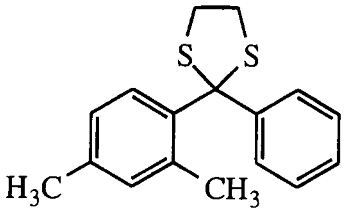
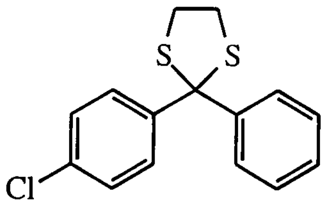
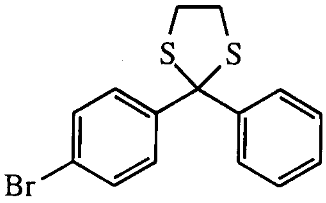
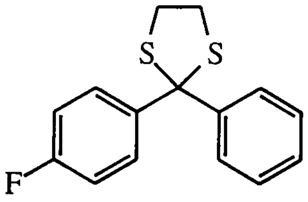
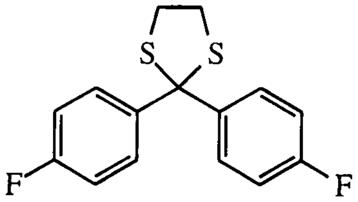
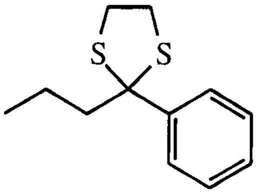
The synthesis of 1,3 dithiolanes may be simply carried out in a one step procedure first reported by B.S. Ong in 1980.[130] In this methodology the dithiolane is produced from the corresponding ketone, e.g. 2,2-diphenyl-1,3-dithiolane (**37**) from benzophenone. The carbonyl group is reacted with 1,2-ethandithiol, in a process analogous to the acetalisation of aldehydes and ketones with diols with a small amount of $AlCl_3$ used as a catalyst (Scheme 14).

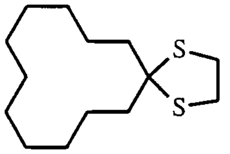
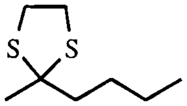
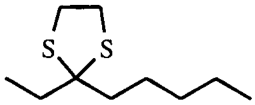
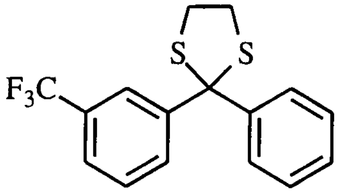
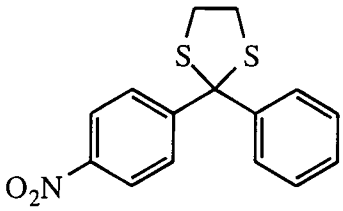


Scheme 14

For this project, the range of 1,3-dithiolanes in Table 5 were prepared by this method.

Table 5 Preparation of 1,3-Dithiolanes.

No.	**Product**	**Yield (%).**
37		74
38		71
39		68
40		75
41		57
42		84
43		78

44		77
45		72
46		77
47		91
48		76

2.2.3 Fluorinations of 2,2-Diphenyl-1,3-Dithiolane.

The initial investigations of the fluorodesulphurisation of 1,3-dithiolanes by elemental fluorine/iodine mixtures were carried out using 2,2-diphenyl-1,3-dithiolane (**37**), the simplest diaryl thiolane. A solution of this substrate was prepared in acetonitrile, to which two equivalents of iodine were added. Through this mixture two equivalents of fluorine, diluted to 10% with nitrogen, were passed at a rate of 10-15 ml/min over the course of 4-5 hours. After this time, the reaction was worked up using a 5% aqueous solution of sodium metabisulphate to remove unreacted iodine then washed with 5% sodium bicarbonate solution to neutralise any HF that had been formed. The products were extracted using dichloromethane and isolated by column chromatography before being analysed by GC/MS and NMR. The reaction went quantitively giving two major products in approximately equal proportions, which were characterised as diphenyldifluoromethylene (**49**) [126] and benzophenone (**58**) by comparison to literature data or existing authentic samples (Fig 2.6).

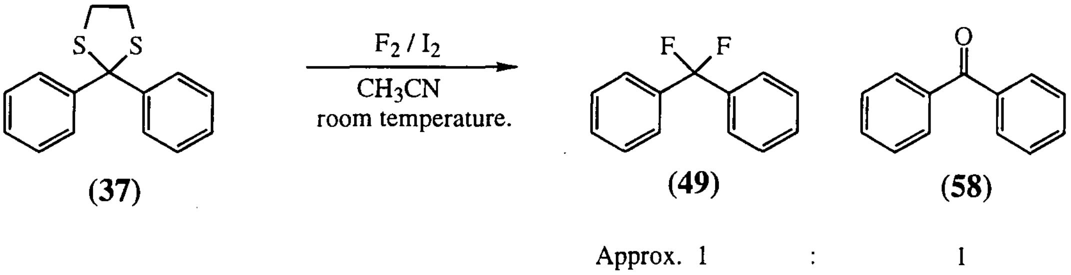


Fig 2.6

The regeneration of benzophenone (**58**), the parent ketone from which the dithiolane had been prepared, in such conspicuous amounts was unexpected and greatly decreased the yield of the desired difluoro product (**49**). Initially, this was ascribed to hydrolysis of the difluoride during the work up. Many difluoromethylenes can be hydrolysed relatively easily and an aqueous work up is employed. To this end, alternative methods were sought using non aqueous media, e.g. copper powder or solid metabisulphate to react with excess iodine. This had little effect on the observed results. It seems that the ketone was formed, not in the work up as first thought, but during the reaction stage itself. This phenomenon could be due to the presence of water in the reaction vessel, probably from the solvent being insufficiently dry. In order to test this theory water (2 ml) was added to the reaction mixture in place of iodine. This had a dramatic effect on the reaction, leading exclusively to the formation of benzophenone (**58**) (Fig 2.7).

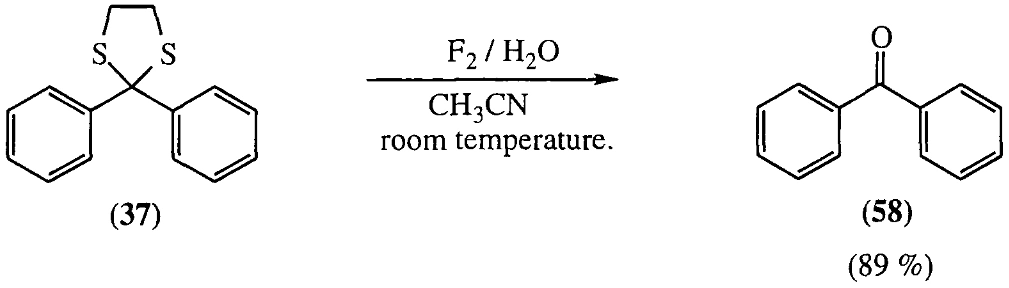


Fig 2.7

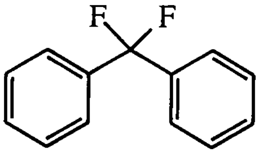
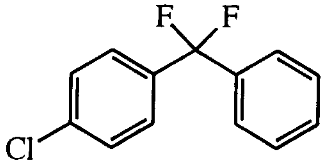
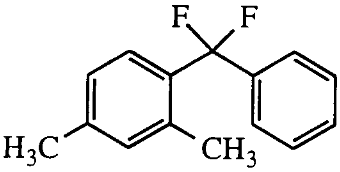
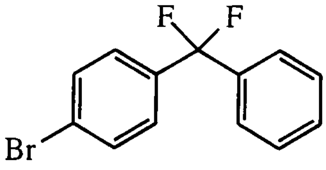
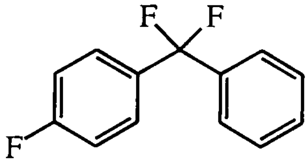
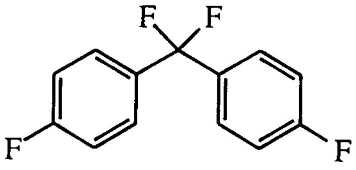
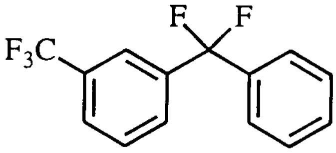
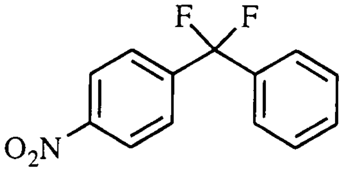
These observations provided a new insight into this reaction system. In our initial experiments, we witnessed the results of two competing processes. The first was the desired fluorodesulphurisation, with I_2/F_2 reacting with the dithiolane to produce the difluoromethylene derivative. Simultaneously, the presence of moisture in the system sets up a secondary reaction by which the 1,3-dithiolane is hydrolysed to its parent ketone, effectively a deprotection reaction. The balance between these two processes determines the mixture of products observed. By varying the reaction conditions it should be possible to exploit these effects to their maximum potential. Adding water leads predominantly to deprotection and so, conversely, scrupulously drying all reagents, solvents and apparatus should promote fluorodesulphurisation. In this manner it became possible for us to fully investigate and develop these two methodologies.

2.3 Fluorodesulphurisations of 1,3-Dithiolanes.

Having established that the presence of moisture in the reaction mixture leads to a competing deprotection process, it became apparent that strictly anhydrous conditions must be employed for efficient fluorodesulphurisation of 1,3-dithiolanes. To this end, all reactants and equipment were scrupulously dried before the reaction was carried out. It was particularly important that the solvent should be completely anhydrous, and so the acetonitrile was dried using phosphorous pentoxide and was distilled prior to use, while the apparatus was kept in an oven before the experiment.

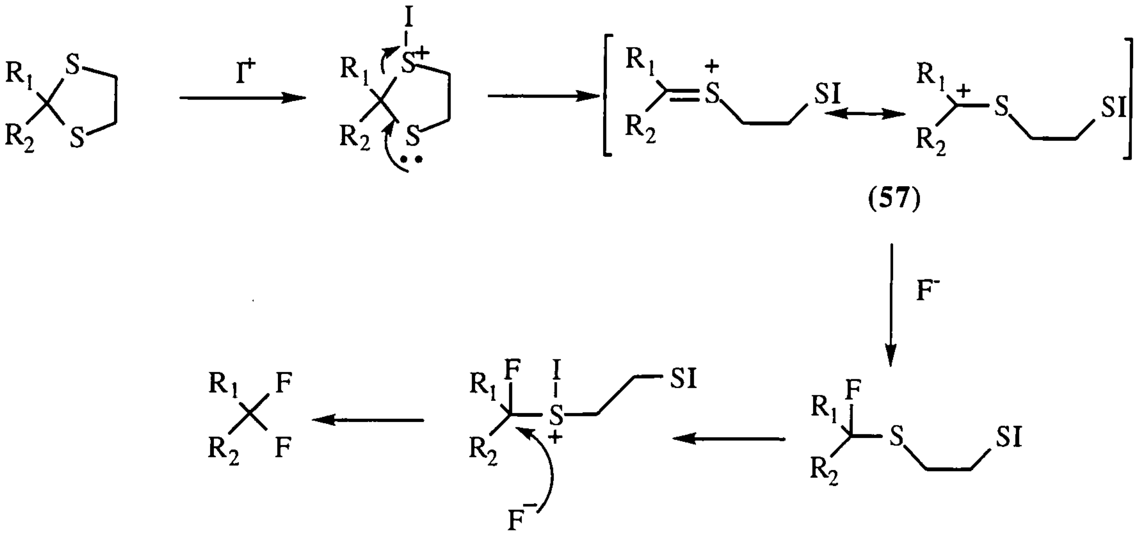
Using these anhydrous conditions, fluorodesulphurisation reactions were carried out for a range of 1,3-dithiolanes (Table 6). The reactions were executed using a solution of the substrate, typically using between 1 and 1.5g (Approx. 5-6mmol), in dry acetonitrile (40ml) in the PTFE reaction vessel. All products were isolated by flash column chromatography using 9:1 hexane/diethyl ether as the eluent and were characterised by NMR and mass spectroscopies. The geminal difluoride products were identified by the chemical shift data, particularly the singlet at -89ppm in the ^{19}F NMR and the large triplet at 120ppm in the carbon spectrum, both characteristic of the central CF_2 group.

Table 6 Fluorinations of 1,3-Dithiolanes.

No.	**Product.**	**Yield (%).**
49		81
50		69
51		81
52		87
53		84
54		74
55		No Apparent Reaction.
56		No Apparent Reaction.

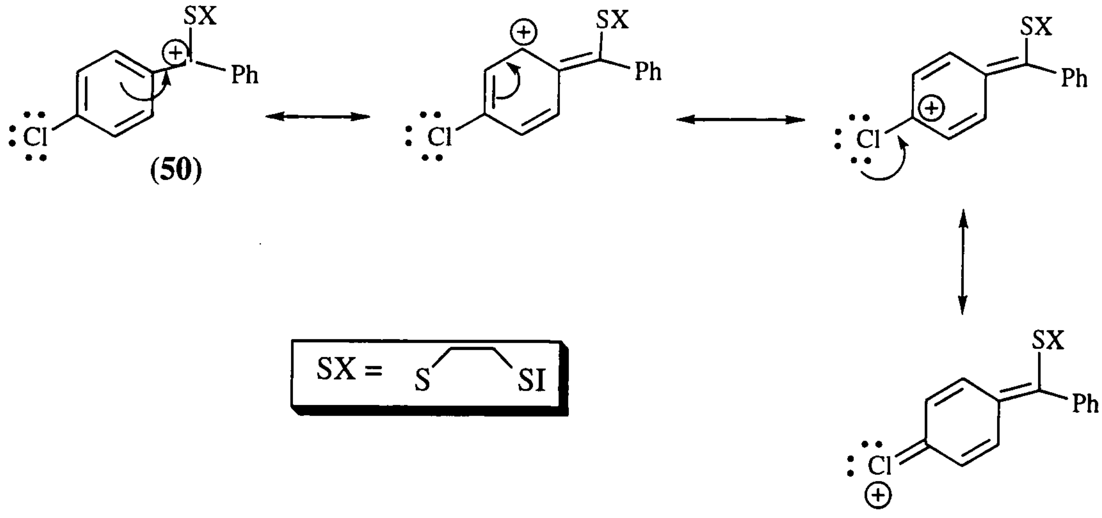
Fluorodesulphurisations were only successful for reactions with diaryl substrates, with no reaction observed with dialkyl or mixed aryl/alkyl substituents. Furthermore, only substrates with substituents capable of stabilising a developing positive charge were shown to react to yield the *gem-* difluoride product, e.g. chloro- or methyl- groups, while others such as the nitro and trifluoromethyl derivatives gave no apparent reaction.

The mechanism is thought to involve the generation of a carbocation intermediate, similar to that observed for Prakash's reactions utilising SO_2Cl_2/PPHF.[126] Mixtures of elemental fluorine and iodine have proved to be a source of electrophilic iodonium and nucleophilic fluoride and the fluorodesulphurisation process is the product of the successive reactions of these two reactive species. First, electrophilic iodine co-ordinates to the sulphur atom of the dithiolane, weakening the C-S bond. As this bond breaks, the carbocation intermediate (**57**) is generated with subsequent attack by fluoride ion. This sequence is then repeated for the second sulphur (Scheme 15).



Scheme 15

Fluorine was only seen to react with substrates that could stabilise the intermediate carbocation (**57**), which is consistent with the mechanism as proposed. No fluorination was obtained with dialkyl substrates, and only diaryl thiolanes gave efficient reaction. Such substrates are able to delocate the developing positive charge about the aromatic ring, stabilising the intermediate carbocation to allow sufficient time to react with fluoride ion. Furthermore, the substituents on the aromatic ring also have a dramatic effect on the reaction, e.g. substrates with methyl- and halo- groups seem to favour fluorination while NO_2 substituents have an inhibiting effect. This may be understood by delocalisation of the intermediate carbocation (Scheme 16).



(50)

Scheme 16

The 2-(2,4-dimethylphenyl)-2-phenyl-1,3-dithiolane **(51)** is a good substrate for fluorodesulphurisation. Here, two of the sites to which the positive charge may be partially delocalised are adjacent to methyl groups. The CH_3 substituent is inductively electron donating and is able to stabilise a neighbouring positive charge. By producing two such stabilised sites, this system creates a fairly stable intermediate that reacts well under these reaction conditions.

Similarly, the 4-chloro- derivative **(50)** allows the intermediate carbocation to be stabilised for this reaction. This substituent has a high electronegativity that makes it inductively electron withdrawing and potentially destabilising to an adjacent partial positive charge. However, this effect is far exceeded by the ability of chlorine to donate lone pairs for resonance, increasing the delocalisation of the charge. This resonance stabilisation produces a more stable intermediate, better in some respects to the simple diphenyl substrate, which may react more readily with free fluoride ion. A similar argument may be made for the 4-bromo **(52)**, 4-fluoro **(53)** and bisfluoro- **(54)** substrates.

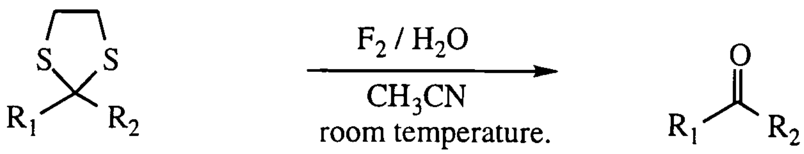
In contrast, the 3-trifluoromethyl and 4-nitro systems **(55-56)** contain highly electron withdrawing substituents. In these substrates, a partial positive charge is developed adjacent to an electron withdrawing group, e.g. NO_2. This draws electrons away from the carbocationic centre, destabilising the system. As a result the reactive intermediate is very unstable and the progress of the reaction is inhibited.

As a final point, it should be noted that many of these products are hydrolytically unstable, particularly (2,4-dimethylphenyl)-phenyl-difluoromethane **(51)** and have a tendency to hydrolyse slowly over time reforming the parent ketone.

2.4 Deprotections of 1,3-Dithiolanes.

Historically, the deprotection of 1,3-dithiolanes to yield their parent carbonyl has been notoriously difficult to achieve. Most of the commonly used procedures tend to require harsh reagents or conditions, e.g. heavy metal derivatives such as HgO[131] or $Tl(NO_3)_3$[132]. Even in the last six years, several papers have been published addressing this very issue, detailing approaches using such diverse agents as DDQ[133], DMSO with high temperature[134] and selenium(IV) oxide[135] but as yet there is no truly general procedure for these deprotections.

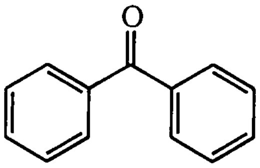
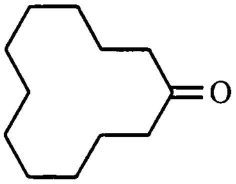
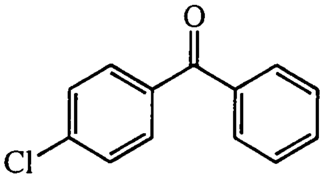
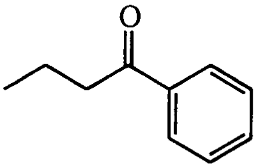
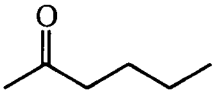
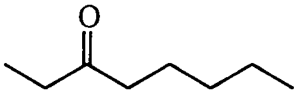
In the course of studying the fluorodesulphurisation if 1,3-dithiolanes using I_2/F_2 mixtures it was observed that there was a significant degree of deprotection to form the parent ketone. This was finally attributed to the interaction of fluorine with moisture in the reaction system. This reaction was carried out under relatively mild conditions and with an excess of water gave the ketone as the sole product in very high yields (Scheme 17). In this manner, fluorine may be considered as a remarkably mild and efficient deprotecting agent.



Scheme 17

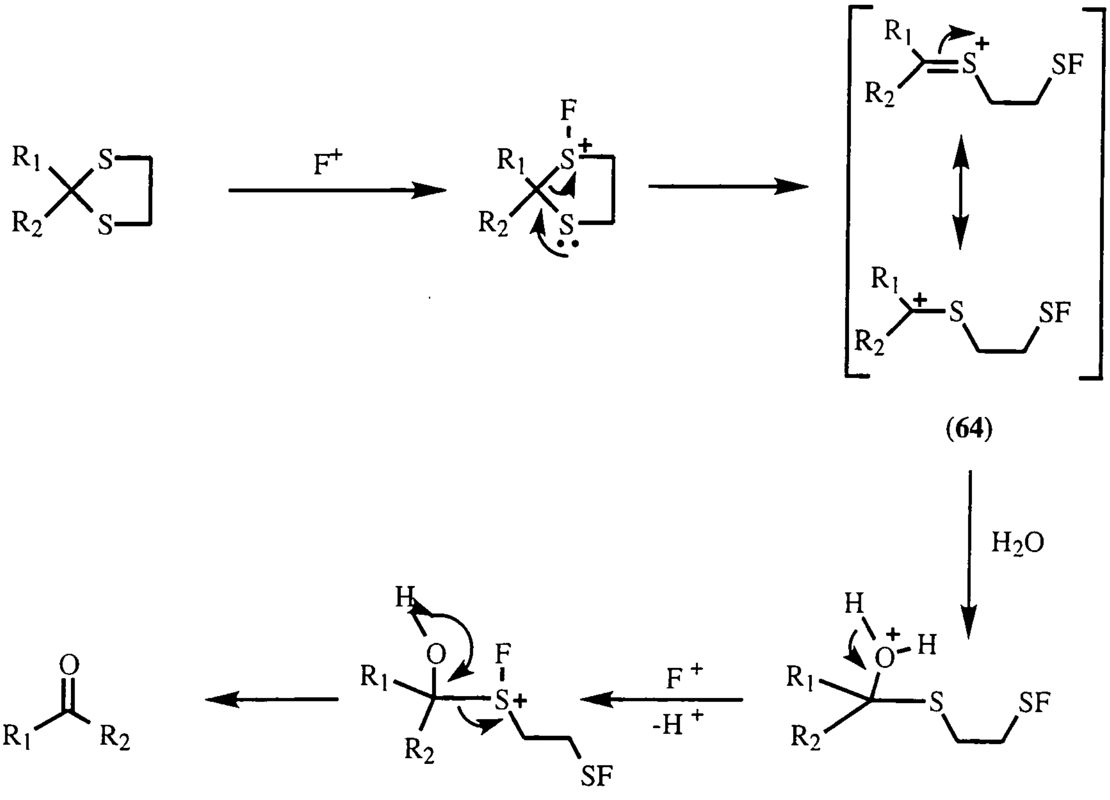
Consequently, it was decided to explore this potential use of fluorine by passing F_2 through solutions of a range of substituted dithiolanes in aqueous acetonitrile, the results of which are collated in Table 7. All products were purified by column chromatography and characterised by NMR, IR and mass spectrometry and confirmed as the parent ketones by reference to existing samples.

Table 7 Deprotections of 1,3-Dithiolanes.

No.	Product.	Yield (%).
58		89
59		87
60		85
61		70
62		79
63		81

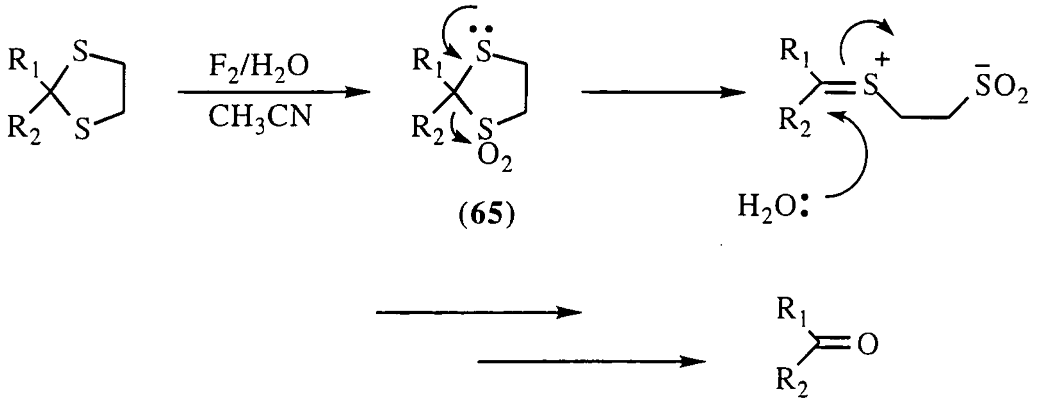
This deprotection methodology was shown to be very effective for a wide range of 1,3-dithiolanes. Diaryl, dialkyl and mixed alkyl/aryl substrates were easily transformed into their parent ketones in excellent yields under relatively mild conditions. Another benefit of this approach is that no toxic residues are produced, e.g. the heavy metal derivatives such as mercury formed in other procedures, and which removes the problem of waste product disposal usually associated with these deprotections.

There are a couple of mechanisms which may possibly account for this reaction. The first is analogous to the mechanism of fluorodesulphurisation. In this rationale, elemental fluorine acts as an electrophile that attacks the sulphur moiety of the dithiolane molecule. In this manner, the carbon-sulphur bond is weakened leading to generation of a carbocation intermediate (**64**) which is vulnerable to nucleophilic reaction with water or any free hydroxyl ions present. Further reaction with fluorine on the second sulphur atom leads to the formation of the parent ketone (Scheme 18).



Scheme 18

An alternate mechanism involves the oxidation of the thiolane to a sulphoxide (**65**). Rozen has reported the formation of a stable HOF-CH_3CN complex[136], produced by passing elemental fluorine through aqueous acetonitrile, which has proved to be a very versatile reagent suitable for hydroxylation, epoxidation and oxidation reactions, e.g. the oxidation of sulphides to sulphones.[137] In this deprotection reaction, HOF-CH_3CN may be generated *in situ* promoting the oxidation of the dithiolane with subsequent ring opening. Again, nucleophilic attack by water leads to the production of the desired ketone (Scheme 19).



Scheme 19

The deprotection procedure is more generally applicable than the fluorodesulphurisation reaction. A wide range of substrates undergo deprotection to the parent ketone not limited only to those with substituents which stabilise a developing positive charge, i.e. carbocation intermediates do not need to be so highly stabilised. A possible explanation is that this may be due to the relative concentration of the attacking nucleophiles in these reactions. In the fluorodesulphurisation, elemental fluorine, diluted to 10 % in nitrogen, is passed as a stream of gas through a vigorously stirred solution of the substrate in acetonitrile. Consequently, fluorine is always the minor component of the reaction mixture and the intermediate carbocation must be stable enough to allow sufficient time for reaction to occur before the gas passes out of the system. In contrast, in the deprotection methodology, water is deliberately added to the reaction mixture, and is present throughout the process, often in massive excess. In this case, water may react almost immediately with the developing carbocation, and such long lived reactive intermediates are not required.

2.5 Conclusion.

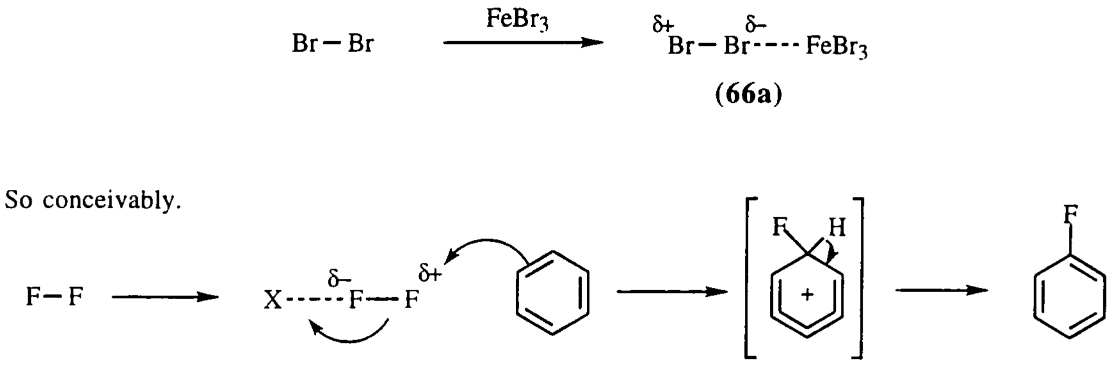
In summary, elemental fluorine may be used in the transformation of 1,3-dithiolanes into geminal difluorides by oxidative fluorodesulphurisation. Using iodine/fluorine mixtures, a range of dithiolanes have been fluorinated though at present this methodology has been limited to diaryl substrates that can stabilise a developing carbocation. Further, in the presence of moisture a competing deprotection reaction occurs, and so strictly anhydrous conditions must be employed for efficient fluorination. This deprotection process has also been investigated and has been shown to regenerate the parent ketone of the dithiolane in excellent yields under relatively mild conditions. This procedure also has no toxic by-products and thus avoids the problem of disposal of waste materials usually associated with deprotections of 1,3-dithiolanes.

The deprotection reaction is a more general procedure than the fluorodesulphurisation, effective for a much wider range of substrates. Deprotections have been carried out for cyclic, dialkyl and mixed alkyl/aryl dithiolanes and is not limited to just diaryl substrates like the fluorination process. This is curious, since both processes are thought to follow similar mechanisms: electrophilic attack by halonium ion followed by reaction with a nucleophile. It has been speculated that this is a concentration effect, water is present in a much greater concentration in deprotection reactions than fluorine in the corresponding fluorodesulphurisation, with the stability of the intermediate carbocation as the limiting factor. This suggests that it should, in theory, be possible to extend our fluorodesulphurisation procedure beyond its current limitations if another method can be discovered to stabilise the intermediate carbocation, e.g. the use of a more polar solvent system. However, a great deal of further study is required to confirm this hypothesis.

Chapter Three The Electrophilic Fluorination of Deactivated Aromatics.

3.1 Introduction.

The direct fluorination of aromatic compounds has not, to date, been employed as a widespread technique for the preparation of fluoroaromatics. However, there have been several attempts to develop this methodology reported in the literature [86-92], which we have outlined in Chapter One. The isomer distribution of the products from these experiments is consistent with an electrophilic process. This contrasts starkly with the situation for other halogens, e.g. chlorine and bromine. Direct chlorinations and brominations are routine procedures, carried out under Friedel-Crafts conditions[138] and the mechanism of this reaction is an electrophilic substitution assisted by a Lewis acid catalyst, e.g. $FeBr_3$. The catalyst polarises the Br_2 molecule to give a much stronger electrophile, $FeBr_4^-\ Br^+$ **(66a)**. This principle can be extended to the reactions of elemental fluorine using a Lewis acid or protonic acid to produce a similar electrophilic species **(66b)** (scheme 20).



(66a)

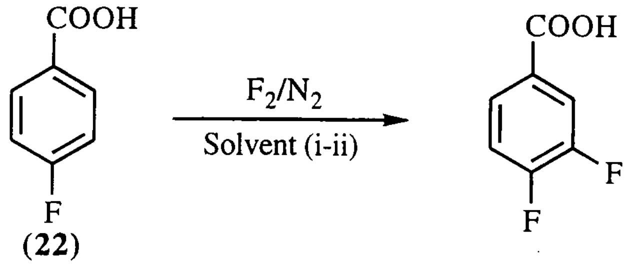
So conceivably.

(66b)

(X = Lewis acid, e.g. BF_3 or H^+)

Scheme 20

In this manner, acid solvents may be used to increase the electrophilic character of fluorine. Previous work carried out by members of the Chambers group has explored the possibility of carrying out direct electrophilic fluorination of aromatic compounds in acidic solvents.[94, 95] The deactivated aromatic, 4-fluorobenzoic acid **(22)**, was chosen as the model substrate and fluorinations were carried out in a range of different solvents of varying acidity and polarity. The products obtained were consistent with an electrophilic process giving selectively reacting at the 3-position, with conversion to 3,4-difluorobenzoic acid seen to increase with increasing acidity of reaction media. In the non-polar solvent $CF_2ClCFCl_2$, no conversion was observed while using strongly acidic solvents, e.g. sulphuric acid, conversion was seen to increase to 84 % (Fig 3.1). A fuller outline of these results may be found in Chapter One (Fig 1.33).



i) $CF_2ClCFCl_2$ Conv. = 0 %
ii) H_2SO_4 Conv. = 84 %

Fig 3.1

The work related in this chapter is a continuation of the investigation of this methodology, expanding the scope of this reaction and considering the effect of the varying characteristics of substituents on the aromatic ring, i.e. the effect of activating vs that of deactivating groups on the reaction and its conditions.

3.2 Development of Fluorination Methodology.

a) The Design of the Fluorination Reactor.

All fluorinations detailed in this chapter were carried out in a glass reaction vessel filled with a solution of the aromatic substrate in 100 ml of solvent. This vessel was shaped to afford a greater degree of contact between fluorine and the substrate than that exhibited by the small PTFE containers previously used in the fluorodesulphurisation reactions, by slowing the passage of the gas through the solution when vigously stirred. For this purpose the reactor was fitted with a rigid stainless steel entrainment stirrer which also allowed the gas inside the vessel to be recirculated. In this manner the time available for reaction to occur is increased and consequently the efficiency of the reaction is enhanced. This stirrer was fitted into a 10mm diam glass locator cap, lined with a PTFE 'O' ring for support, centred in the base of the reactor. The rigid nature of the stirrer allowed the use of an IKAMAG brushless motor, capable of 0-2000 rpm with minimal vibration. Cooling was achieved using a salt water bath and the external coil of a HAAKE cryostat. A diagram of this reactor is shown in Fig 3.2.

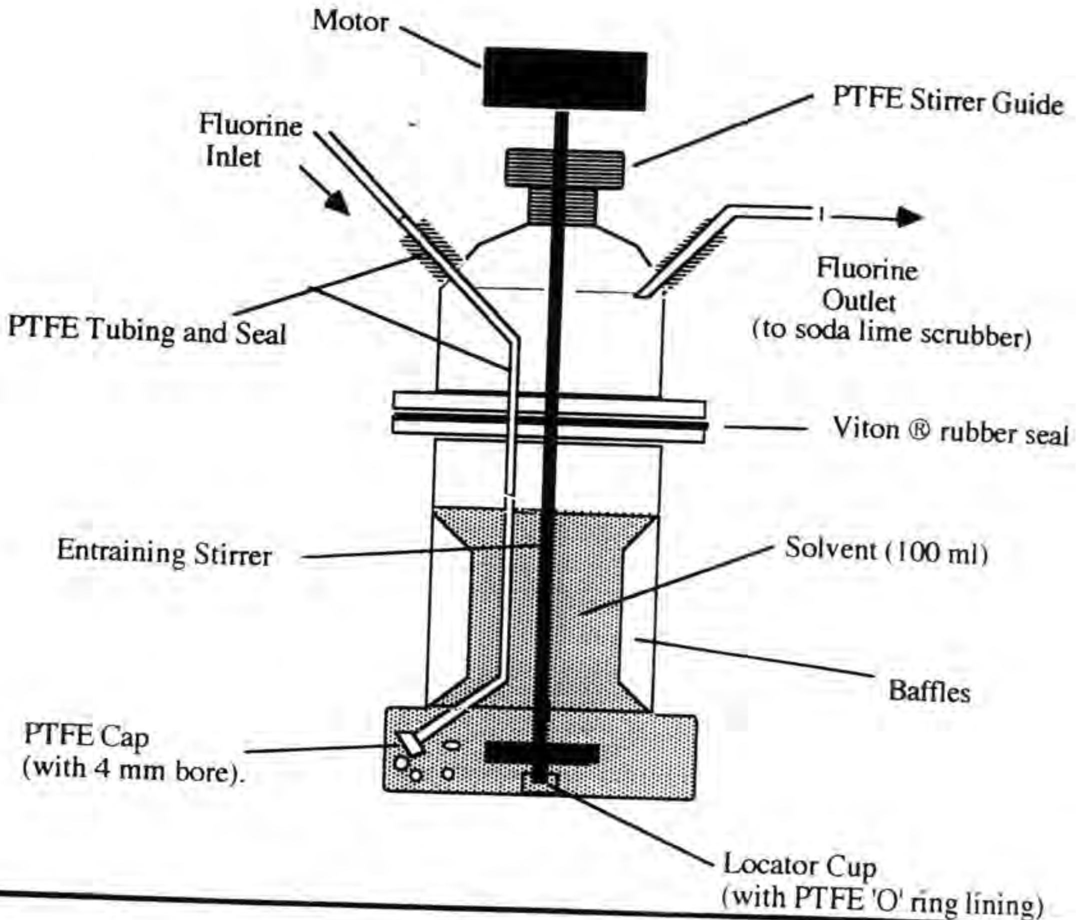
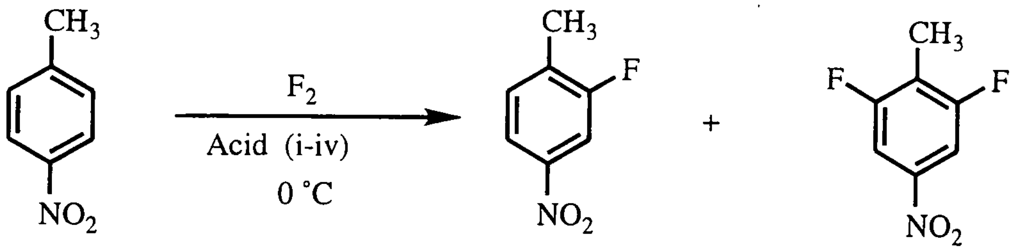


Fig 3.2

b) The Effect of Acid Strength.

Solvent plays a crucial role in the fluorination process. The effect of acid strength on the reaction between fluorine and a model aromatic compound, 4-nitrotoluene,was investigated employing a range of solvent systems of increasing acidity from Lewis acids, such as boron trifluoride, to strong mineral acids, e.g. sulphuric acid (Table 8). Nitrotoluene **(67)** was chosen because a deactivated aromatic would pose a smaller threat of excessive reaction. Also assuming that the reaction is an electrophilic process the 1,4-substituent pattern should lead to the formation of a simple mixture of products since the directing effects of the methyl- and nitro- groups both direct fluorination at the 2-position leading to single isomers of the mono- and difluorinated products, **(68)** and **(69)**.



(67) **(68)** **(69)**

Acid	Conversion (%)	Yield (%)
i) BF_3-OEt_2 / CH_3CN	25	53 (**68**).
ii) CF_3COOH	29	71 (**68**).
iii) HCOOH	46	77 (**68**)..
iv) 98 % H_2SO_4	75	81 (**68**); 2 (**69**).

Table 8

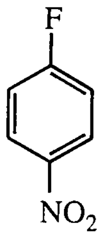
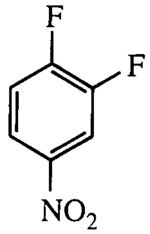
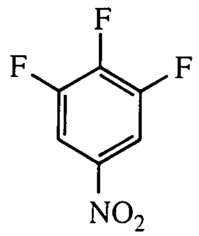
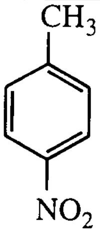
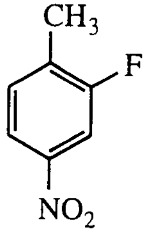
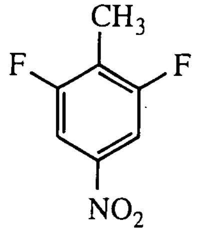
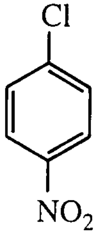
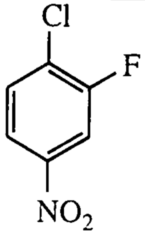
In these experiments, 2-fluoro-4-nitrotoluene (**68**) and 2,6-difluoro-4-nitrotoluene (**69**) were identified by NMR spectroscopy and mass spectrometry, e.g. the ^{19}F NMR spectrum of 2-fluoro-4-nitrotoluene, displays a characteristic singlet at -114.3ppm compared to -119.3ppm for the 3-fluoro- isomer.[139, 140] Products were isolated by column chromatography on silica gel. Conversions were calculated from the amount of starting material remaining at the end of the reaction determined from the mass of product mixture recovered and its composition shown by GC/MS, while the yields relate to the amount of each product isolated. The conversion was observed to increase with increasing acidity of the solvent, in agreement with previous experiments.[94, 95] When using the Lewis acid boron trifluoride, the conversion of nitrotoluene was only around 25 %, while the greatest degree of fluorination was observed in strong sulphuric acid, giving a 75 % conversion to 2-fluoro-4-nitrotoluene (**68**) in 81 % yield. In this example, some degree of difluorination to produce 2,6-difluoro-4-nitrotoluene (**69**) was observed.

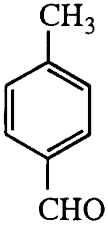
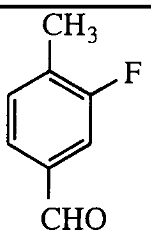
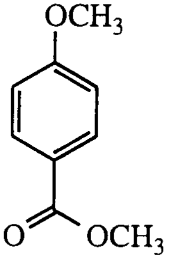
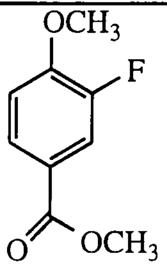
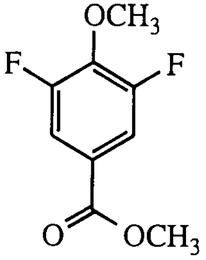
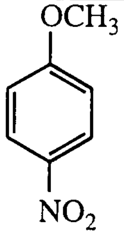
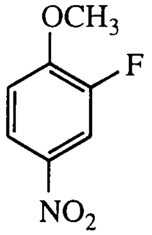
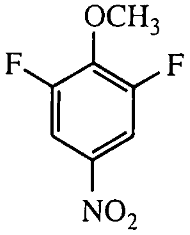
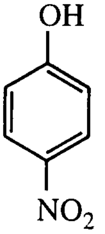
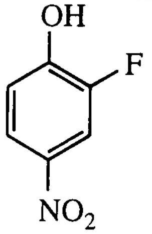
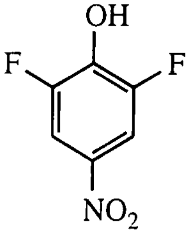
3.3 Fluorinations of Aromatic Compounds in 98 % Sulphuric Acid.

Having established that 98 % sulphuric acid was a good medium for the fluorination of 4-nitrotoluene, we attempted the fluorination of a range of aromatic compounds in this solvent to establish the scope of this reaction (Table 9).

The products were identified by NMR spectroscopy and mass spectrometry, with isomers determined by ^{19}F NMR chemical shift values. For example, it is possible to distinguish 2-fluoro-4-nitrophenol **(84)** (δ_F = -130ppm) from the 3-fluoro isomer (δ_F = -114ppm).[139, 140] The isolated product exhibited a chemical shift of -133.9, characteristic of fluorination at the 2-position. In a similar manner, the difluorinated products could be identified, e.g. the minor product of the reaction of 4-nitroanisole. For this difluorinated product there are three possible isomers, 2,6-difluoro-4-nitroanisole **(82)**, 2,3-difluoro-4-nitroanisole and 2,5-difluoro-4-nitroanisole. For the last two isomers both fluorines and all carbons are inequivalent, thus we would expect to find distinct peaks for each in the respective spectra. The observed ^{19}F NMR spectrum consists of a singlet at -125.1ppm, suggesting that both fluorine atoms are indeed equivalent which is only the case for the 2,6-difluoro isomer. Similarly, only four peaks are observed in the carbon spectra, suggesting that the 2/6 and 3/5 carbons are equivalent which is consistent with this isomer.

Table 9 Fluorinations of Aromatics Compounds in 98 % Sulphuric Acid.

Substrate	**Conversion (%)**	**Products (Yield %)**	
		Monofluorinated	**Difluorinated**
 **(70)**	87	 **(71)** (75 %)	 **(72)** (10 %)
 **(67)**	75	 **(68)** (81 %)	 **(69)** (2 %)
 **(73)**	64	 **(74)** (66 %)	-------------

 **(75)**	74	 **(76)** (60 %)	--------------
 **(77)**	23	 **(78)** (31 %)	 **(79)** (10%)
 **(80)**	63	 **(81)** (50 %)	 **(82)** (11 %)
 **(83)**	30	 **(84)** (24 %)	 **(85)** (8 %)

For highly deactivated substrates, e.g. 4-chloronitrobenzene (**73**), this procedure was very effective giving the monofluorinated products in good conversion and yields. In some cases a degree of difluorination was also observed, e.g. 4-fluoronitrobenzene (**70**) and 4-nitrotoluene (**67**). 4-Fluoronitrobenzene was a particularly good substrate reacting with fluorine to give fluorinated products in 87 % conversion, with the minor product 3,4,5-trifluoronitrobenzene (**72**) obtained in 10 % yield and attempts were made to fluorinate this substrate further to obtain 2,3,4,5,6-pentafluoronitrobenzene. This was attempted by passing a large excess of fluorine, at least 7 molar equivalents, through a solution of the substrate at 0 °C, but this had little effect on the composition of the mixture of products. The experiment was repeated but this time only the first two equivalents of F_2 were passed at 0 °C, after which the temperature was raised to around 30 °C. This increase in temperature was enough to drive the reaction to complete conversion and, while the major component of the product mixture was still 3,4-difluoronitrobenzene **(71)** (66 %), the proportion of the higher fluorinated derivatives also increased. In fact, some degree of trifluorination to produce 2,3,4,5-tetrafluoronitrobenzene **(86)** was observed (Fig 3.4).

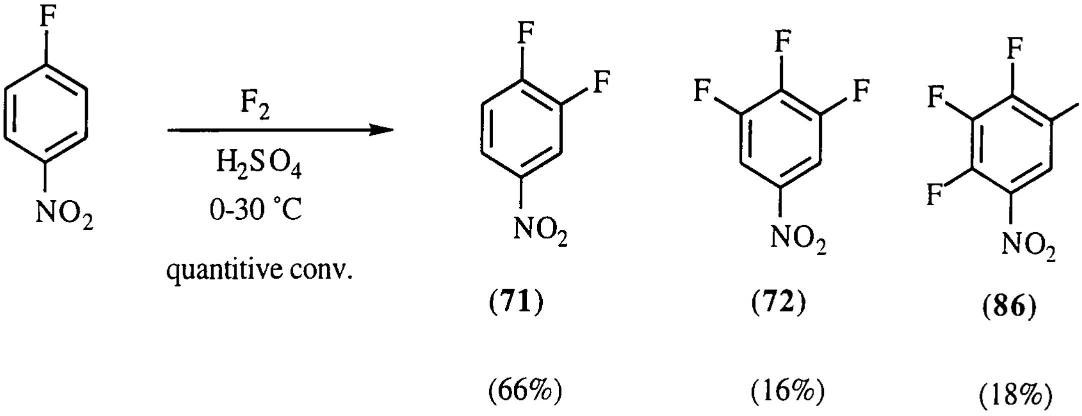
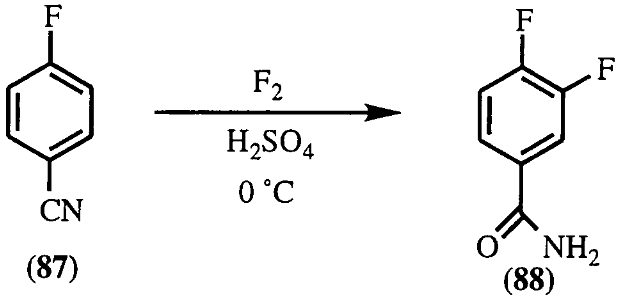


Fig 3.4

For more activated substrates, like 4-nitroanisole and -phenol, the fluorination reaction was less efficient. Yields and conversions were significantly lower and the product mixtures were messy and more tar-like. Recovery of material was poor in these reactions, particularly the fluorination of 4-nitrophenol **(83)**, which would be consistent with sulphonation of the substrate, where sulphonated materials may be retained in the aqueous phase during the work up.

The tolerance of the aromatic substrate to acidic conditions is a crucial factor in this reaction. Some substrates may have substituents that simply will not endure exposure to strong acids. For example, nitrile substituents undergo hydrolysis in sulphuric acid to give an amide derivative. Fluorination of 4-fluorobenzonitrile **(87)** in 98% sulphuric acid produced 3,4-difluoroamidobenzene **(88)** (Fig 3.5), which was very sparingly soluble in most organic solvent making manipulation and isolation difficult but was eventually identified by ^{19}F NMR and GC/MS. It was further determined that fluorine was not involved in this hydrolysis process, demonstrated by treating a sample of the substrate with 98 % sulphuric acid and stirring overnight, leading to hydrolysis of the nitrile to form the amide and even further generating the carboxylic acid.



(87)

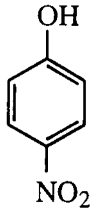
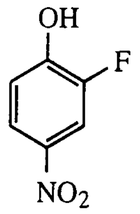
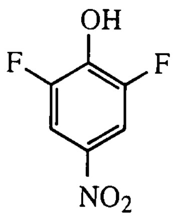
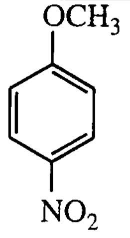
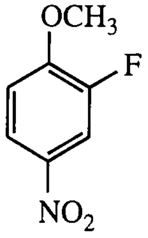
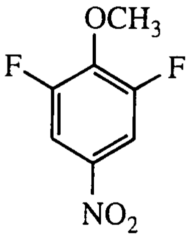
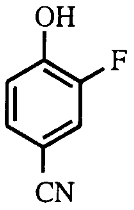
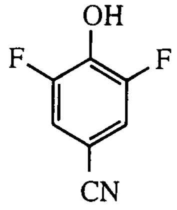
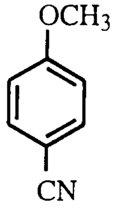
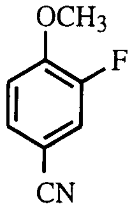
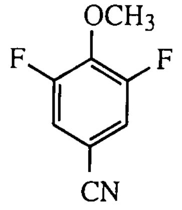
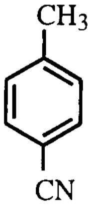
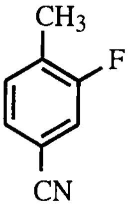
(88)

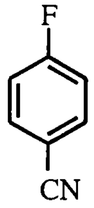
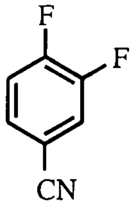
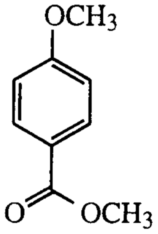
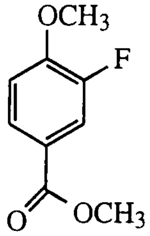
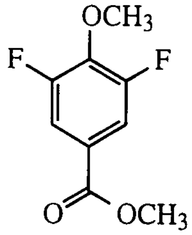
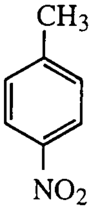
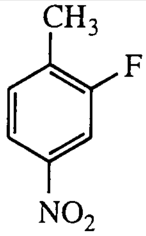
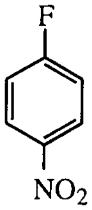
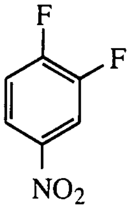
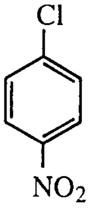
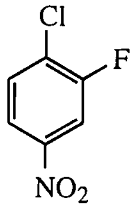
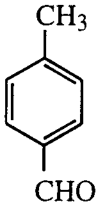
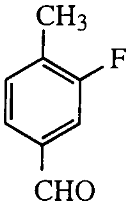
Fig 3.5

3.4 Fluorinations of Aromatic Compounds in Formic Acid.

In the previous section we established that, while very effective for highly deactivated aromatics, the use of 98 % sulphuric acid as a solvent to promote electrophilic fluorinations had many limitations as we move to more activated substrates or those with a higher sensitivity to acidic conditions. The solution to this problem may simply be to use a weaker acid. Formic acid is a milder acid than sulphuric, with a pK_a of +3.75 compared to -3. To investigate this possibility, many of the experiments that had previously been carried out in 98 % sulphuric acid were repeated, especially those reactions involving more activated substrates, e.g. 4-nitrophenol **(83)**, and acid sensitive substrates, such as 4-fluorobenzonitrile **(87)**. The results of these experiments are outlined in Table 10. All products were finally purified by column chromatography using hexane/dichloromethane or hexane/diethyl ether mixtures as the eluting solvent, and were identified with reference to chemical shift and mass spectral data, with further characterisation by elemental analysis and IR spectroscopy.

Table 10 Fluorinations of Deactivated Aromatics in Formic Acid.

Substrate	**Conversion (%)**	**Products (Yield %)**	
		Monofluorinated	**Difluorinated**
 **(83)**	100	 **(84)** (70 %)	 **(85)** (11 %)
 **(80)**	80	 **(81)** (56 %)	 **(82)** (15 %)
 **(89)**	89	 **(90)** (66 %)	 **(91)** (15 %)
 **(92)**	88	 **(93)** (55 %)	 **(94)** (21 %)
 **(95)**	93	 **(96)** (56 %)	-------------

 **(87)**	65	 **(97)** (65 %)	--------------
 **(77)**	66	 **(78)** (54 %)	 **(79)** (17 %)
 **(67)**	46	 **(68)** (77 %)	--------------
§  **(70)**	36	 **(71)** (53 %)	Trace Amounts
§  **(73)**	47	 **(74)** (44 %)	--------------
 **(75)**	32	 **(76)** (34 %)	--------------

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[§] Reactions carried out by Dr J. Thomson, F2 Chemicals Ltd.

Formic acid proved to be far more effective for promoting fluorination of less deactivated aromatic substrates, e.g. 4-nitrophenol (**83**) and 4-nitroanisole (**80**), than sulphuric acid. The reactions are much cleaner, giving crystalline products while yields and conversions are greatly increased. For example, the fluorination of 4-nitrophenol in sulphuric acid gave 2-fluoro-4-nitrophenol (**84**) and 2,6-difluoro-4-nitrophenol (**85**) in yields of 23 % and 8 % respectively, and the recovered material is black, oily and difficult to purify. In contrast, when the reaction was carried out in formic acid, the yields of the mono- (**84**) and difluorinated products (**85**) are significantly increased, to 70 % and 11 %, the products recovered as a slightly orange crystalline mixture which can easily be separated by column chromatography.

Formic acid is also a better solvent for those substrates with a low tolerance to highly acidic conditions. Indeed, a number of nitrile substrates including 4-tolunitrile (**95**) and 4-fluorobenzonitrile (**87**) were reacted with fluorine in formic acid to give their fluorinated derivatives in very good conversion and yields. For nitrile substrates with more strongly activating groups at the 1 position, e.g. 4-cyanophenol and -anisole, significant amounts of difluorination were observed.

For more highly deactivated substrates the fluorination reaction is not as efficient when carried out in formic acid than it is in sulphuric, e.g. 4-fluoronitrobenzene (**70**), because these substrates require a stronger electrophile generated by a greater polarisation of fluorine in sulphuric acid.

From these experiments we can get a much clearer picture of the effect of acid media of the fluorination of aromatic compounds. There is not a general, all-purpose solvent that is effective for all aromatic substrates. The degree of activation of the substrate is the key factor. For highly deactivated substrates a strongly acidic solvent is the media of choice, e.g. sulphuric acid. As the degree of activation of the substrate increases the strength of the acid required for efficient fluorination is reduced, and weaker acids such as formic acid become the preferred solvents (Fig 3.6). The sensitivity of the aromatic substrate to acidic conditions also plays a crucial role in determining which acid should be employed for a given substrate.

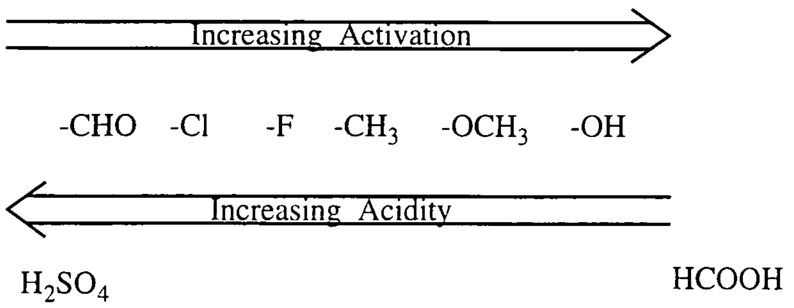
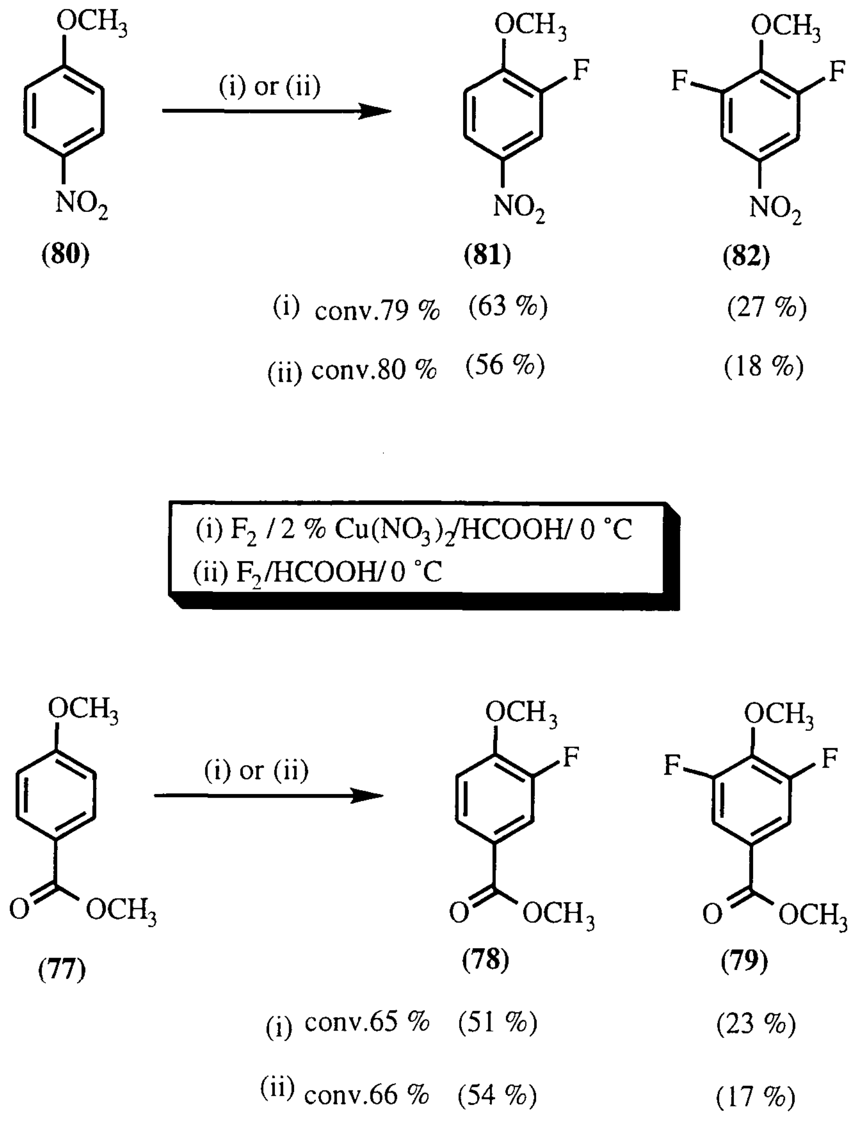


Fig 3.6

3.5 The Investigation of the Effect of Copper(II) Salts as Possible Catalysts for Aromatic Fluorination.

Previously, it was shown that the Lewis acids, e.g. BF_3 etherate were not particularly effective in promoting electrophilic fluorination, however, work carried out on the fluorination of dicarbonyl compounds suggested that copper(II) salts might have such a catalytic effect on fluorination[141], possibly acting like a sort of 'Friedel-Crafts' reagent, co-ordinating to fluorine to increase its electrophilic character. To investigate this hypothesis some fluorinations of aromatic compounds were carried out in formic acid, observing the effect of adding a small amount of copper(II) nitrate (2% by weight) on the reaction and the observed ratio of products. The examples chosen for this study were the reactions of 4-nitroanisole (**80**), which worked particularly well in formic acid, with the aim of increasing the degree of difluorination, and 4-methoxy-methylbenzoate (**77**), fluorination of which had only been moderately successful in both formic and sulphuric acids. The results of these experiments are summarised in Fig 3.7.



(i) F_2 / 2 % $Cu(NO_3)_2$/HCOOH/ 0 °C
(ii) F_2/HCOOH/ 0 °C

Fig 3.7

These experiments showed that the addition of the copper(II) salt had little or no effect on the outcome of the reaction.

3.6 Conclusion.

In conclusion, we have shown that the direct fluorination of aromatic compounds can be a viable synthetic procedure under the correct reaction conditions. By using acid media as a reaction solvent, we have been able to promote the electrophilic fluorination to achieve a selective aromatic substitution reaction yielding the desired fluoroaromatic products. Strong acids, such as sulphuric acid, are required for the efficient fluorination of highly deactivated aromatics, e.g. 4-fluoronitrobenzene (**70**), but as the substrate becomes increasingly activated this solvent becomes less effective. There arises an increasing danger of competing side reactions, e.g. sulphonation, which may have a detrimental effect on the efficiency of the fluorination process. For these substrates, e.g. 4-nitrophenol (**83**), a milder acid like formic acid is the preferred reaction media. Similarly, formic acid is the solvent of choice for substrates which have a low tolerance to highly acidic conditions, e.g. 4-cyanophenol (**90**) where there is a risk of hydrolysis of the nitrile substituent to form an amide. We also investigated the possibility of catalysis by copper(II) salts but found this to be negligible.

Chapter Four The Fluorination of Mesitylene, a Highly Activated Aromatic.

4.1 Introduction.

In the previous chapter we detailed the direct fluorination of some aromatic systems using acid solvents to promote electrophilic fluorination. All the substrates that we have discussed in this thesis so far may be considered as being deactivated toward electrophilic fluorination to some degree, containing such substituents as nitro-, cyano- or ester groups, and for these compounds the reaction is fairly well understood. Conceivably, it should be possible to extend this approach to more highly activated systems. With this aim in mind we have attempted to carry out the fluorination of a highly activated compound chosen as a model substrate, namely 1,3,5-trimethylbenzene or mesitylene (**98**).

In this chapter we relate the results of these investigations into the direct fluorination of mesitylene, which have demonstrated that this reaction is much more complicated than had been expected.

4.2 Development of Reaction Conditions.

4.2.1 Solvent.

The choice of solvent in which the fluorination reaction is to be carried out is crucial. For example, sulphuric acid is not a suitable solvent, its use leading to sulphonation of the aromatic ring prior to fluorination (Fig 4.1).

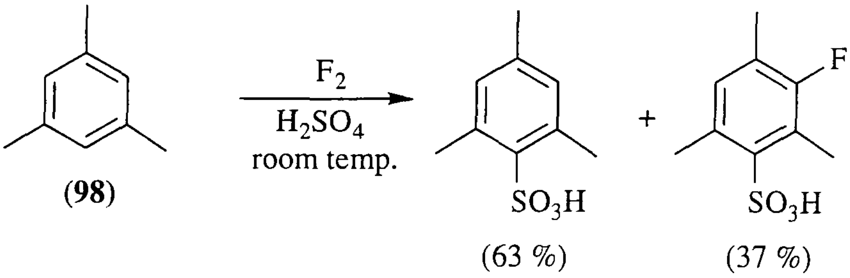


Fig 4.1

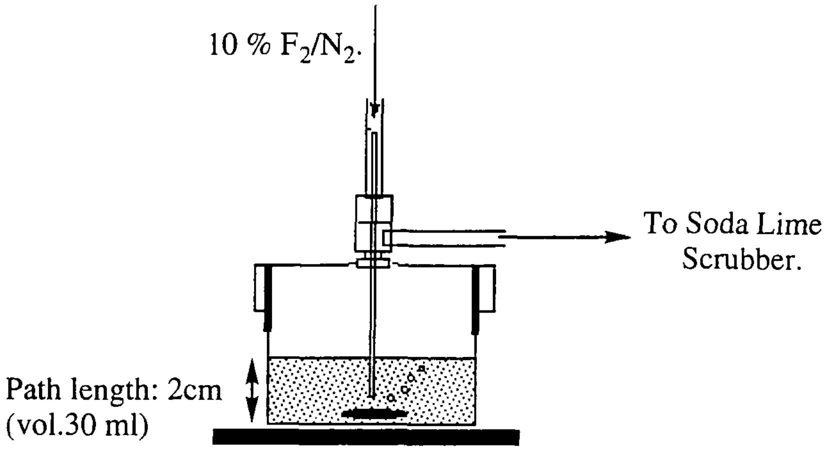
Also, we observed that more highly activated substrates like toluene and mesitylene proved to be insoluble in formic acid, making it an inappropriate media for the fluorination of these compounds. In the search for a more suitable solvent for these reactions, a study was made of the solubilities of activated substrates such as mesitylene and toluene in a range of solvent systems. The results of these experiments are outlined in Table 11. Mesitylene proved to be soluble in acetonitrile, formic acid/acetonitrile mixtures and trifluoroacetic acid, and it was decided to investigate the fluorination of mesitylene in these media.

Solvent	**Toluene**	**Mesitylene**
Acetonitrile	Soluble	Soluble
Formic Acid	Forms Suspension	Insoluble
1:1 CH_3CN/HCOOH	Soluble	Insoluble
4:1 CH_3CN/HCOOH	Soluble	Soluble
3:2 CH_3CN/HCOOH	Soluble	Soluble
Trifluoroacetic Acid	Soluble	Soluble

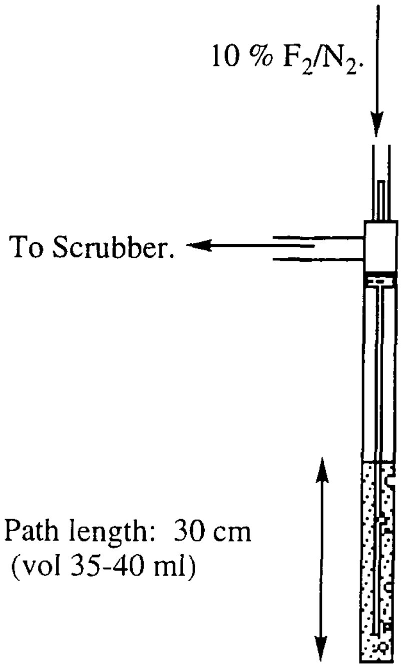
Table 11 Solubility Studies of Activated Aromatic Substrates.

4.2.2 Effect of Reaction Path Length/Contact Time.

The majority of the experiments related in this chapter were carried out in one of two PTFE reactors (Fig 4.2). Reactor A is a short, squat vessel, a more detailed diagram of which may be found in Chapter Two (Fig 2.5) while Reactor B is much taller and narrower.



Reactor A



Reactor B

Fig 4.2

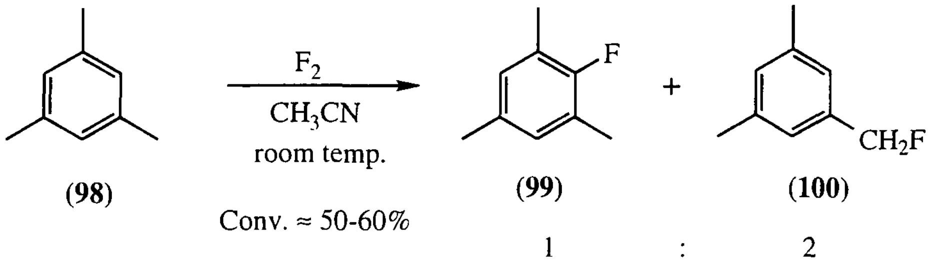
The initial investigations of the fluorination of mesitylene were carried out in acetonitrile. These experiments revealed that the reaction path length was a crucial factor in this process. Reaction path length is defined as the distance that the bubbles of fluorine pass through the solution of the aromatic substrate during fluorination and is consequently a measure of the contact time between F_2 and the substrate. At first the reactions were carried out in Reactor A, similar to that used for the fluorinations of 1,3-dithiolanes but in these experiments the conversion was poor (5%), the bulk of material recovered identified as starting material. Raising the temperature to 40 °C improved this situation slightly, with the total conversion increasing to around 24 %. Similar results were observed for toluene

These observations suggested that the low conversion was due to the rate of this reaction being rather slow and the contact time too short to enable fluorination to occur. Increasing the temperature helps to increase the rate of reaction and would account for the higher conversion observed at 40 °C. A better approach is to increase the contact time between fluorine and in Reactor B, the depth of solution was around 30cm, a significant increase in path length even though the volume of solution is the same as in Reactor A. On repeating the fluorination of mesitylene in acetonitrile at room temperature a substantial increase in conversion was observed (50-60%). Using this reactor we attempted to investigate the fluorination of mesitylene in a range of solvents, which are detailed in the next section.

4.3 The Effect of Solvent on the Fluorination of Mesitylene.

4.3.1 Acetonitrile.

Using Reactor B, the fluorination of mesitylene in acetonitrile at room temperature was carried out and a dramatic improvement in conversion was observed. Fluorinated products were obtained in about 50-60% conversion from starting material compared with 5 % for the corresponding reaction in Reactor A. The products fall into two types arising from either fluorination on the aromatic ring **(99)** or on the methyl substituents to give benzyl fluorides **(100)**. The major products were the monofluorinated derivatives, though there was some indication of di- and trifluorination by GC/MS (Fig 4.3). There were also small traces of some high mass products, possibly from coupling of aromatic rings, e.g. a product with a mass of 238 may be formed by the radical coupling of two mesitylene molecules, the product linked by an ethylene bridge, one with mass 256 could be the product of mesitylene and the fluorinated product and so forth.



(98) **(99)** **(100)**

1 : 2

+ Minute Traces of Other Products
Notably, di- and trifluoro derivatives of each and high mass products (m/z 238, 256, 274)

Fig 4.3

The products were identified by ^{19}F NMR and GC/MS. 1-Fluoromethyl-3,5-dimethyl benzene (**100**) exhibited a distinguishing triplet at -205ppm in the fluorine spectrum[142, 143] while 2-fluoro-1,3,5-trimethyl benzene (**99**) gave a singlet at -128ppm.[139, 140] The mass spectra were also characteristic. The breakdown pattern of the mass spectrum of the benzyl fluoride closely resembles that of mesitylene, as the CH_2F group easily fragments, comparable to CH_3 while a fluorine bound to the ring is not, and so the aromatic fluorides exhibit a very different spectrum. Later, the products were isolated by preparative gas chromatography and further characterised by ^{1}H and ^{13}C NMR confirming these assignments.

This mixture of products can be explained by reference to the two modes of reactivity of elemental fluorine, radical and electrophilic. The fluorination of the aromatic ring can be thought of as the result of electrophilic substitution and indeed, when the fluorination of mesitylene is attempted using a purely electrophilic source of fluorine, e.g. Selectfluor™ (**31**), this is the only product observed (Section 4.3.5). On the other hand, benzyl fluorides are more likely to be the products of a radical reaction. The relative ratio of the two types of products was measured by ^{19}F NMR and GC/MS, revealing that the composition of the product mixture was 2:1 in favour of benzyl fluorides, i.e. the radical reaction is predominant in acetonitrile.

4.3.2 Mixtures of Formic Acid and Acetonitrile as Solvents.

For fluorinations of mesitylene in acetonitrile, the radical mode of reaction is the predominant process involved. Our next step was to try to find some way in which the electrophilic reaction could be promoted e.g. using a mildly acidic solvent, like formic acid, a method which had been successfully employed with the more activated substrates like 4-nitrophenol (**83**) (See Chapter Three). Since mesitylene is insoluble in formic acid, acetonitrile/formic acid mixtures were used as solvents where the increased acidity of the media may favour the electrophilic mode of fluorination. To investigate this possibility we carried out the fluorination of mesitylene in solvent systems composed of 4:1 and 3:2 ratios (by volume) of acetonitrile and formic acid (Fig 4.4)

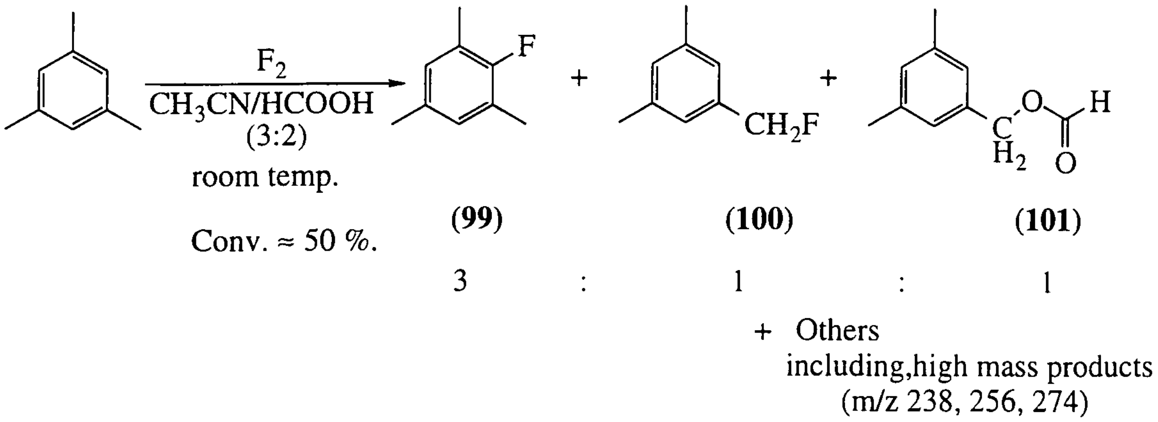


Fig 4.4

The fluorination of mesitylene in 3:2 acetonitrile/formic acid gave a number of products in about 50% conversion from starting material (Fig 4.4). Like the corresponding reaction carried out in acetonitrile, the major products were identified as a series of aromatic and benzyl fluorides, mainly monofluorinated 2-fluoro-1,3,5-trimethylbenzene **(99)** and 1-fluoromethyl-3,5-dimethylbenzene **(100)**, though some evidence of the formation of di- and trifluoro- derivatives was observed. However, a third non-fluorinated product was formed, formic acid-3,5-dimethyl benzyl ester **(101)** which was confirmed by preparative gas chromatography. Characterisation by ^1H and ^{13}C NMR demonstrated that the formate group was bound to the substrate through one of the methyl substituents and not directly to the ring, suggesting that it was the product of a reaction between benzyl fluoride **(100)** and formic acid. For the purposes of estimating the relative amounts of ring to side chain fluorination this ester was treated as a derivative of benzyl fluorides, leading to a ratio of products approx. 2:3, demonstrating that in acetonitrile/formic acid mixtures the electrophilic process is slightly more prevalent.

To confirm that a reaction between formic acid and 1-fluoromethyl-3,5-dimethylbenzene was the source of the formate ester **(101)**, a sequential reaction of fluorination in acetonitrile followed by treatment of the resulting mixture **(102)** with formic acid was carried out (Fig 4.5).

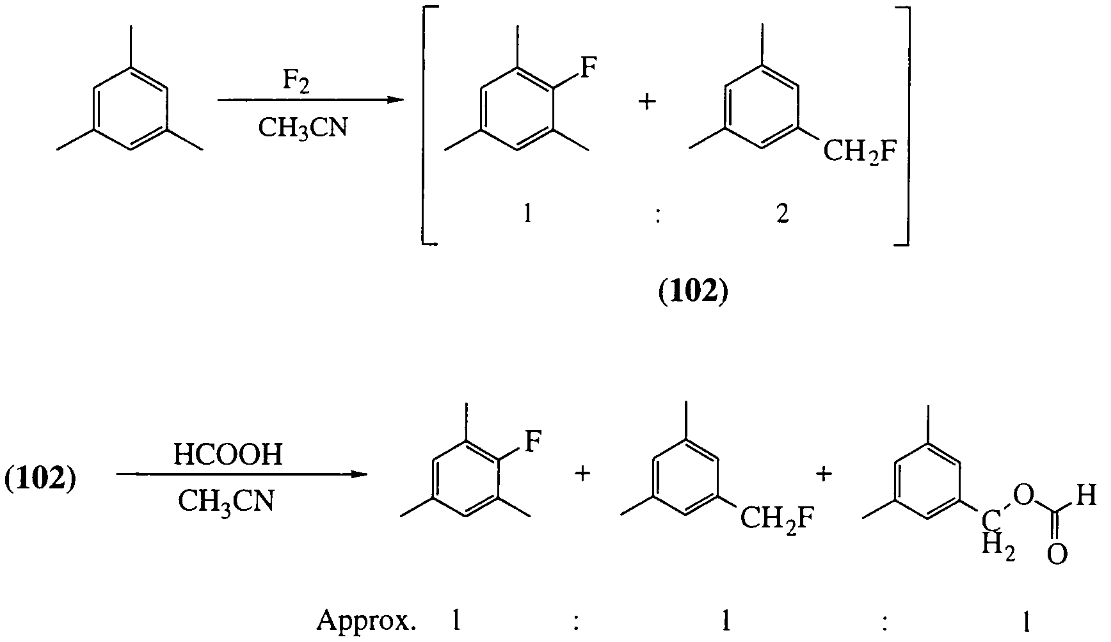
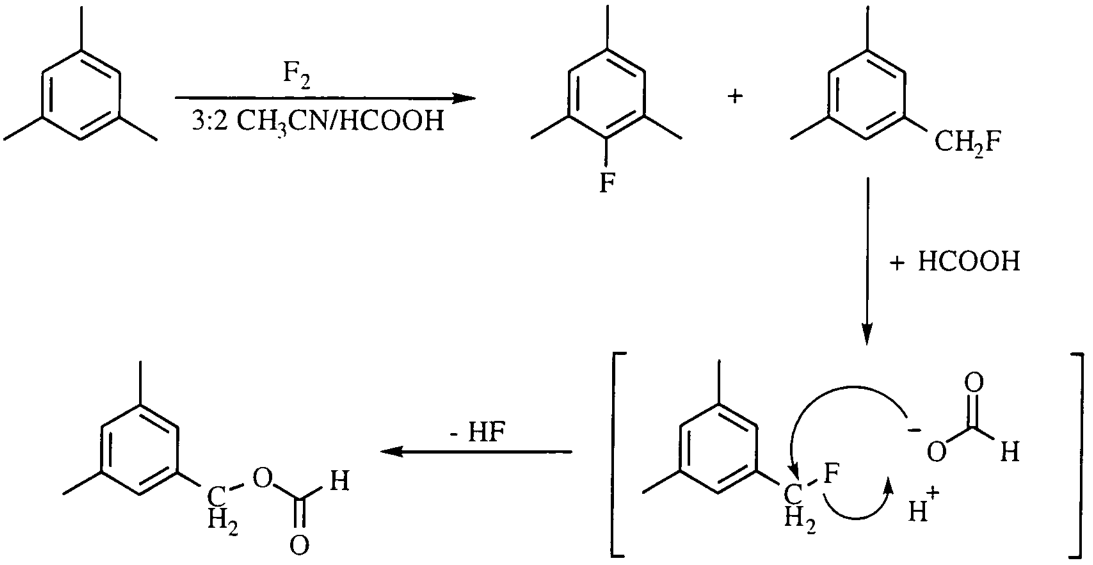


Fig 4.5

In the initial fluorination step, a 2:1 mixture of benzyl and aromatic fluorides was obtained **(102)**, characterised by ^{19}F NMR and GC/MS. No trace of the ester was found. After the reaction of **(102)** with formic acid the amount of benzyl fluoride had been reduced, the ratio of side chain to ring fluorinated products decreased to approx. 1:1. The formate ester was now observed, accounting for the reduction in the amount of free benzyl fluoride and confirmed our view about the source of the formate ester **(101)** (Scheme 21).



Scheme 21

4.3.3 Trifluoroacetic Acid.

The next logical step was to employ an acid in which mesitylene is soluble as the solvent, trifluoroacetic acid (Fig 4.6).

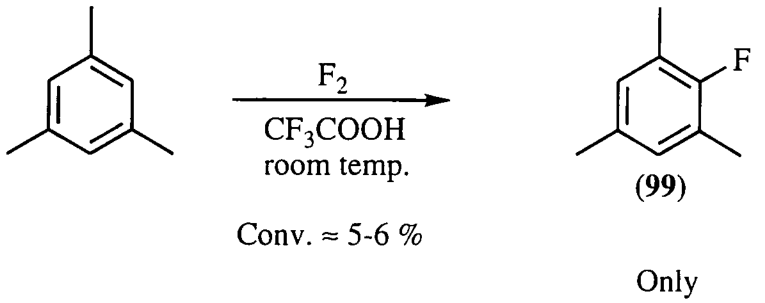
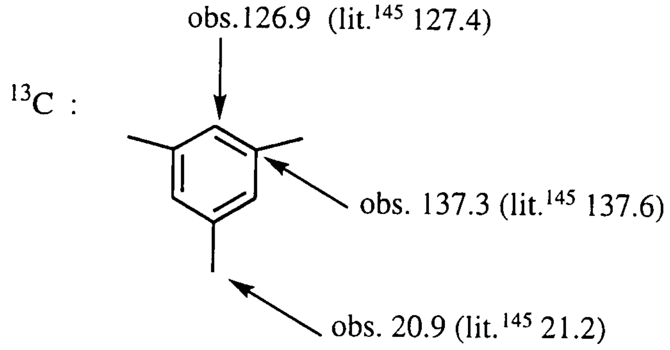


Fig 4.6

The results of this experiment were very interesting. 2-Fluoro-1,3,5-trimethylbenzene (**99**) was the sole product observed, however, the conversion was very low (5-6%). The reaction was repeated several times but the result was entirely reproducible and it appears that trifluoroacetic acid has an inhibiting effect on the reaction. It was suggested was due to a poor solubility of fluorine in trifluoroacetic acid. This idea was not supported by the evidence of the chemical literature where it has been claimed that this solubility is about the same as in $CFCl_3$[144], a common solvent for fluorination reactions. An alternative theory was that since trifluoroacetic acid is a fairly strong acid, its $pK_a \approx 0.23$, maybe protonation of mesitylene had occurred. A comparison was made between the NMR spectra, ^1H and ^{13}C, of mesitylene in deuterated chloroform and trifluoroacetic acid.

In $CDCl_3$ the ^1H spectra consisted of only 2 peaks, at 2.9 (CH_3) and 7.4 ppm (Ar-H), with relative intensities of 9:3. The ^{13}C NMR spectra was composed of 3 peaks, at 20.9 (CH_3), 126.8 (C-H) and 137.3 (C-CH_3) (Fig 4.7).[145]

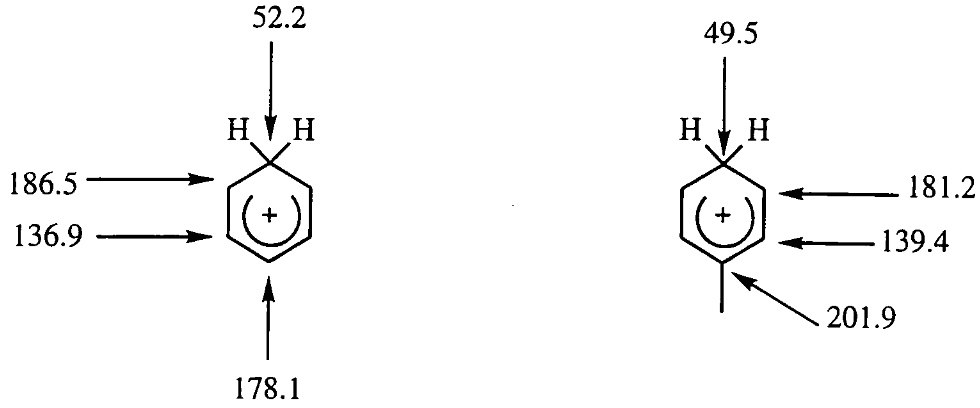


^{1}H : CH_3 2.9
Ring H 7.4

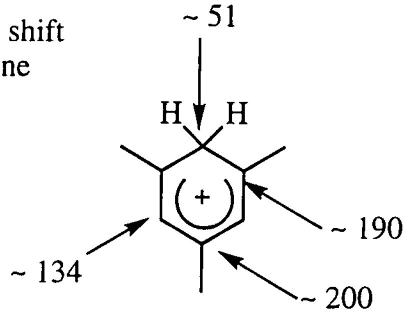
Fig 4.7 NMR values for Mesitylene in deuterated chloroform.

The chemical shift data for the ^{1}H NMR of mesitylene carbocation **(103)** comprises of singlets at 2.8-2.9 (CH_3), 4.5 (CH_2) and 7.6 (Ar-H).[146] These values were recorded by protonation of mesitylene in a mixture of HF and SbF_5. Though the ^{13}C values of this carbocation have not been recorded the ^{13}C NMR spectra of protonated benzene and toluene (para-methylbenzene) are available.[147]. The differences in chemical shift of these spectra are consistent with those expected by the introduction of a methyl group into the para position. Hence, we can extrapolate and estimate the chemical shift values for the protonated mesitylene by calculating the effect of adding two methyl groups in the ortho positions. For this carbocation, we would therefore expect to observe a ^{13}C NMR spectra exhibiting peaks at approx. 51 (CH_2), 134 (meta Ar-C), 190 (ortho Ar-C) and 200ppm (para Ar-C). In this outline, ortho, meta and para are defined relative to the site of protonation (Fig 4.8).

Literature values for ^{13}C NMR of protonated benzene and para-methylbenzene (ref[147]).



Therefore calculated chemical shift values for protonated mesitylene by extrapolation.



(103)

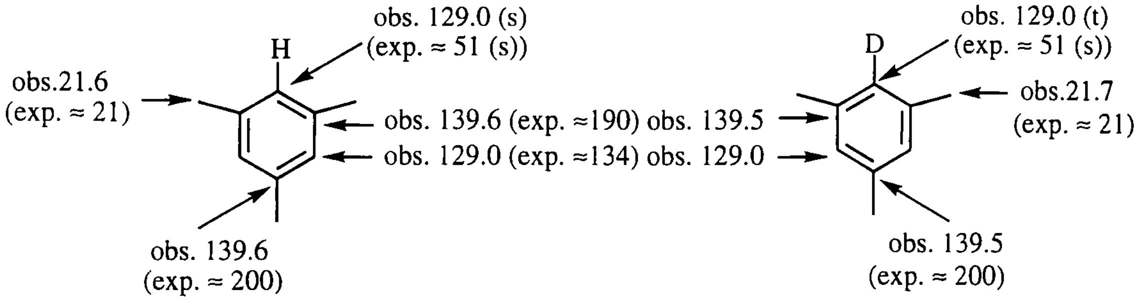
Chemical Shift data of ^1H NMR from Literature (ref.[146]).

CH_3	2.8-2.9
CH_2	4.5
Ring H	7.6

Fig 4.8 Chemical Shift Values for Mesitylene Cation Based on Literature and Calculation.

However, in the ^1H spectrum of mesitylene in trifluoroacetic acid three singlets are observed at 3.1, 7.6 and 11.6. These correspond to CH_3, aromatic and acidic protons respectively, the presence of acidic protons indicating some exchange between hydrogen and deuterium, probably on the aromatic ring. No CH_2 groups are observed which would seem to indicate that the carbocation has not been formed. The ^{13}C NMR is far more interesting. Here, we expect the signals for the para and ortho aromatic carbons to be shifted to much lower field between 190-200 ppm and a CH_2 group at 51. The observed spectrum consists of two sets of three peaks. The first comprises three singlets at 21.7, 129.0 and 139.6 while the second includes a smaller singlet at 22.6, a 1:1:1 triplet overlapping with the singlet at 129.0, and finally a third small singlet at 139.5 (Fig 4.9). The 1:1:1 triplet suggests some incorporation of deuterium on the aromatic ring

(104) but while there is a degree of H/D exchange there is no evidence for protonation or stable carbocation formation in trifluoroacetic acid.



(98) **(104)**

Fig 4.9 Observed NMR Data for Mesitylene in d-Trifluoroacetic Acid (Expected values for Mesitylenium cation in brackets).

In an attempt to improve the degree of fluorination in trifluoroacetic acid we returned to the idea of using acid diluted with acetonitrile. Fluorination of mesitylene in a 1:1 mixture of CH_3CN/CF_3COOH led to an increase in conversion to approx. 50% but gave a complex mixture of products (Fig 4.10).

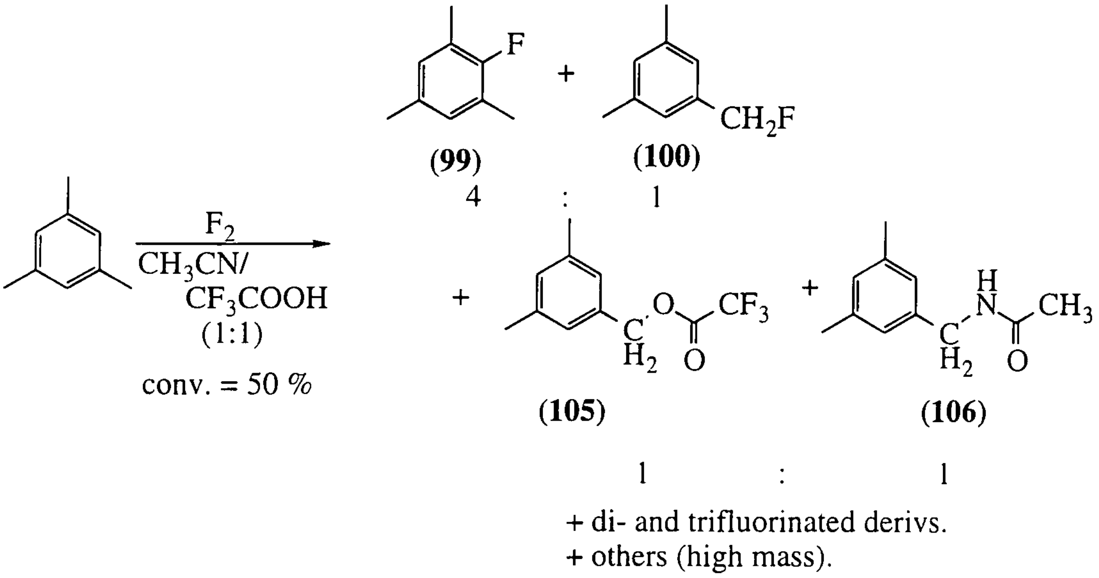
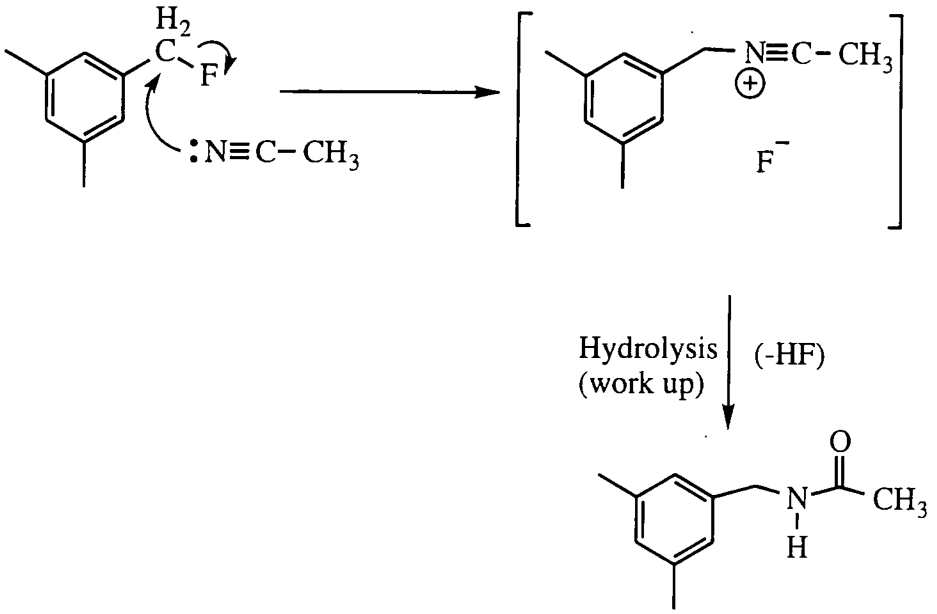


Fig 4.10

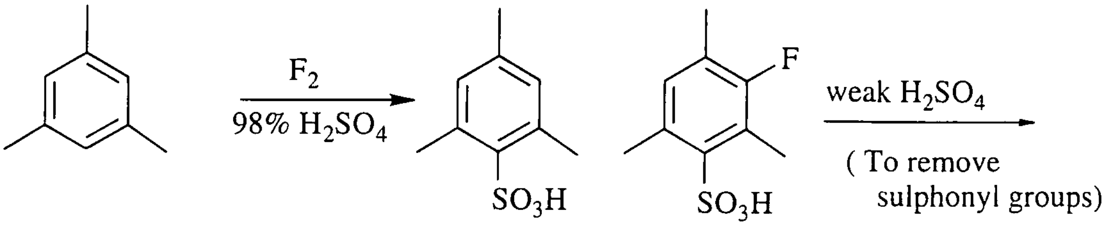
Once more , the major products were due to ring and side chain fluorination to give 2-fluoro-1,3,5-trimethylbenzene **(99)** and 1-fluoromethyl-3,5-dimethylbenzene **(100)** which have been well established, while there also appeared to be a trifluoroacetate ester product **(105)**. A fourth product appeared to be an amide derivative, *N*- (3,5-dimethyl-benzyl)-acetamide **(106)**, which was ascribed to a reaction between the benzyl fluoride **(100)** and acetonitrile. The lone pair of electrons on the nitrogen of the nitrile acts as nucleophile, attacking the CH_2F group displacing fluoride, before undergoing hydrolysis to the amide during the aqueous work up (Scheme 22).



Scheme 22

4.3.4 Other Acids as Solvents.

An alternative approach to the problems of fluorinating activated aromatics like mesitylene could be to introduce a deactivating group into the molecule which could subsequently be removed after fluorination. This would allow the reaction to be carried out in strong acid as in Chapter Three. Sulphonation is a reversible process and the sulphonyl group is sufficiently deactivating for these purposes, and so, despite previous concerns, sulphuric acid may be a suitable solvent for these reactions after all (Fig 4.11).



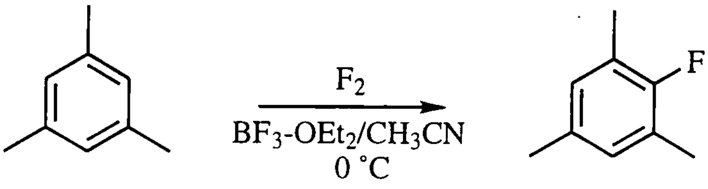
(107) **(108)**

(63 %) (37 %)

Fig 4.11

In practice, mesitylene was completely sulphonated with a subsequent conversion of around 37 % to the fluorinated derivative (**108**). However, the resulting mixture was messy and recovery of products was poor, sulphonated products being more easily retained in the aqueous phase during work up, so the approach was not pursued any further.

Until this point, all work had concentrated on the use of protonic acids as solvents. If such conditions cannot be tolerated by the activated aromatics then the use of Lewis acids, e.g. BF_3, might present an viable alternative. To test this conjecture, a number of experiments were carried out using BF_3-OEt_2 in acetonitrile as the acid solvent (Fig 4.12). When using equal amounts of fluorine and BF_3-etherate relative to the substrate, only the ring monofluorinated product (**99**) was observed in 15 % conversion.



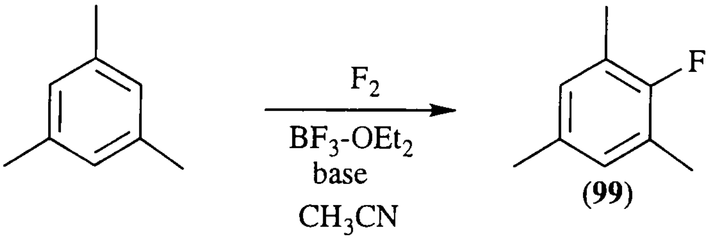
(99)

(Conv. ≈ 15%)

Fig 4.12

If the conversion of this reaction could be improved this process would provide a viable route to 2-fluoro-1,3,5-trimethylbenzene (**99**). Unfortunately all attempts in this direction proved unsuccessful. For example using excess fluorine gave a viscous black mixture which consisted mainly of high molecular weight products (m/z 238, 256).

The low conversion may be due to the production of a superacid, HBF_4, from reaction between BF_3-OEt_2 and any HF produced. This may protonate mesitylene and have an inhibiting effect on fluorination. Fluorinations were attempted using base to neutralise any hydrogen fluoride produced but these met with little success (Fig 4.13).

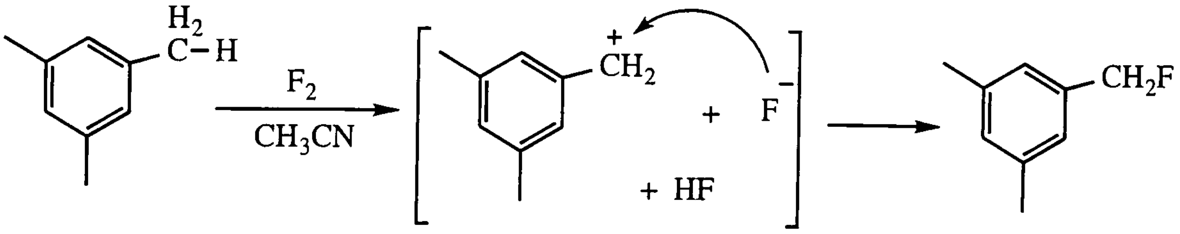


i) base= Et_3N	Conversion = 3 %
ii) base= K_2CO_3	Conversion = 2 %

Fig 4.13

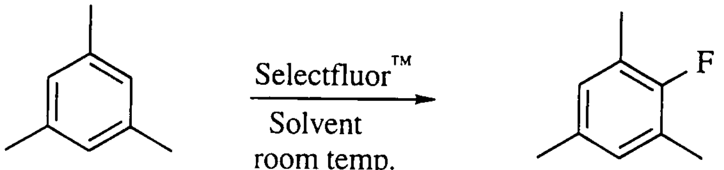
4.3.5 Fluorinations of Mesitylene Using Selectfluor.™

In all of the direct fluorinations of mesitylene studied so far a competition has been observed between electrophilic fluorination on the aromatic ring and the reaction of fluorine with methyl side chains, thought to be a radical process. But is this the true situation or could the side chain fluorination also be an electrophilic process, F_2 reacting with the CH_3 moiety eliminating a hydrogen atom as HF and producing a positively charged $-CH_2^+$ that can undergo further reaction with free fluoride ion (Scheme 23) ?



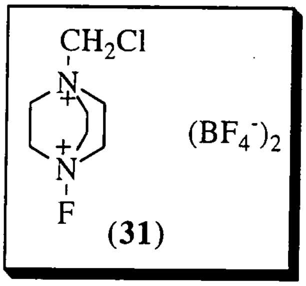
Scheme 23

To investigate this hypothesis, fluorinations were carried out using a purely electrophilic source of fluorine, Selectfluor™ (**31**). These experiments were executed using a solution of mesitylene in either acetonitrile or trifluoroacetic acid to which Selectfluor™ was added (Fig 4.14).



(99)

Solvent :- i) CH_3CN Conversion = 50%
ii) CF_3COOH Conversion = 75%



(31)

Fig 4.14

In these experiments electrophilic fluorination of the aromatic ring was the only reaction observed and furthermore, only monofluorination occurs with no evidence of di- or trisubstitution or any by-products. The conversions of these reactions are very favourable. In acetonitrile, 2-fluoro-1,3,5-trimethylbenzene (**99**) is produced in about 50 % conversion from starting material, while in trifluoroacetic acid this increases to 75 %. These results confirmed our view that side chain fluorination was not an electrophilic process.

On the surface this would appear to be a superior process to direct fluorination, but the two processes can not be compared so easily since the Selectfluor™ reaction was carried out in a sealed system over a much longer time period. The reagents remain in contact for the duration of the reaction, in contrast to elemental fluorination where fluorine is continuously passing through and out of the reaction vessel. In this manner much of the fluorine is lost before it has time to react and as such the process is rather inefficient. The major drawback of these fluorinations is the high cost of the Selectfluor™ reagent making larger scale reactions prohibitively expensive and industrially uneconomical. For industrial purposes an effective direct fluorination procedure is much more desirable.

4.4 The Effect of Nitro-Aromatics and -Alkanes on the Fluorination of Mesitylene.

4.4.1 The Reactions of 4-Nitrotoluene.

4-Nitrotoluene (**67**) was fluorinated quite easily under acidic conditions (Chapter Three). Consider the reactions of nitrotoluene with fluorine in trifluoroacetic acid and acetonitrile or with Selectfluor (Fig 4.15). These reactions were carried out under identical conditions to the corresponding fluorinations of mesitylene.

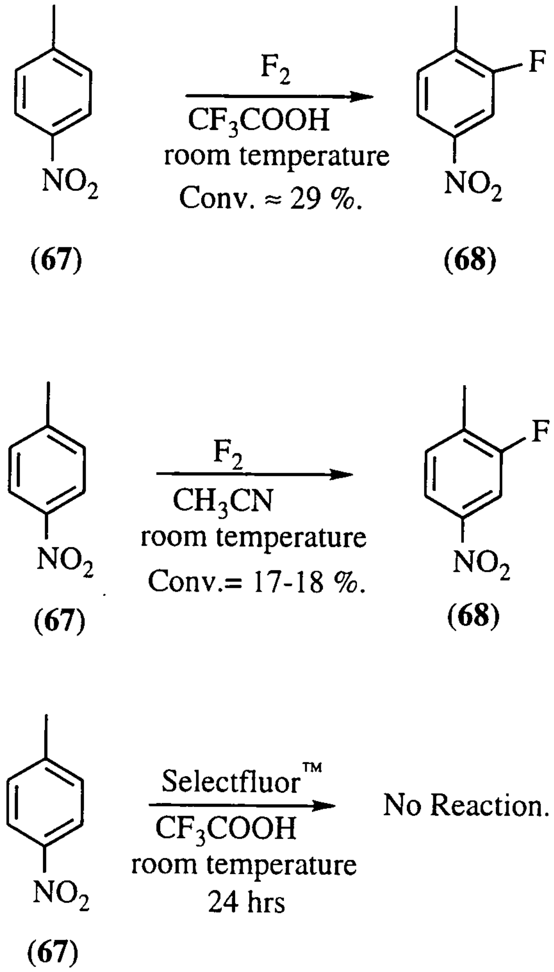
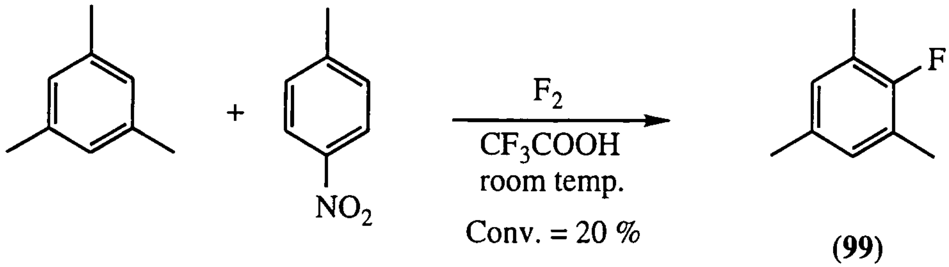


Fig 4.15

Compare, the fluorination of nitrotoluene in trifluoroacetic acid with that of mesitylene under these conditions (Fig 4.6). The fluorination of mesitylene in this solvent is rather poor, selectively giving one product, 2-fluoro-1,3,5-trimethylbenzene **(99)**, but in very low conversion (5%). For 4-nitrotoluene, the conversion is significantly improved, around 29-30% of the starting material undergoes reaction, with the ring fluorinated 2-fluoro-4-nitrotoluene **(68)** the favoured product. In acetonitrile, this selectivity for the electrophilic product is still observed but conversion is reduced relative to the reaction in acid, to around 17-18%. This is consistent with the idea of acid promoting the electrophilic reaction with deactivated aromatics since acetonitrile is the less acidic solvent but contrasts starkly with the results observed for the fluorination of mesitylene in acetonitrile where the conversion is higher and the selectivity greatly reduced as the radical reaction becomes predominant. Further, nitrotoluene does not react with Selectfluor™, even in acid, understandable since this is a deactivated system but again very different to observed reactions of mesitylene.

4.4.2 Competition Reactions Between Mesitylene and Nitrotoluene.

From the observed results of the fluorinations of mesitylene and nitrotoluene in trifluoroacetic acid, it would appear that nitrotoluene is the more reactive substrate, which seems unlikely for an electrophilic process. To compare the reactivities of the two substrates a competition reaction was carried out (Fig 4.16).

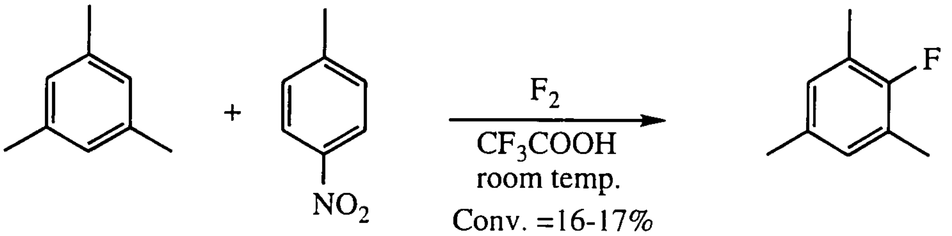


(98) **(67)** **(99)**

1 : 1

Fig 4.16

In this experiment, only mesitylene was fluorinated to give 2-fluoro-1,3,5-trimethylbenzene (**99**). Furthermore, the degree of conversion was increased four fold relative to the reaction in the absence of nitrotoluene, to around 20 %. This result was unexpected based on the previous experiments, and suggests that nitrotoluene has a catalytic effect on the fluorination of mesitylene. A similar reaction was observed when only a small amount of nitrotoluene (1:5 nitrotoluene:mesitylene) was added (Fig 4.17).



5 : 1

Fig 4.17

We wanted to know if this effect was exclusive to nitrotoluene or a function of the nitro group. Experiments were carried out using different nitro-compounds, firstly nitrobenzene (**109**) and then the alkyl nitromethane (**110**) (Fig 4.18). In both these cases, similar results were recorded compared to those already outlined for nitrotoluene. When nitromethane (**110**) was used as a solvent the system proved to be very reactive, the degree of conversion was greatly increased, up to around 75 %. However, corresponding with this rise was an almost total loss of selectivity, leading to the formation of a complex mixture of products suggesting that both the electrophilic and radical processes were at work.

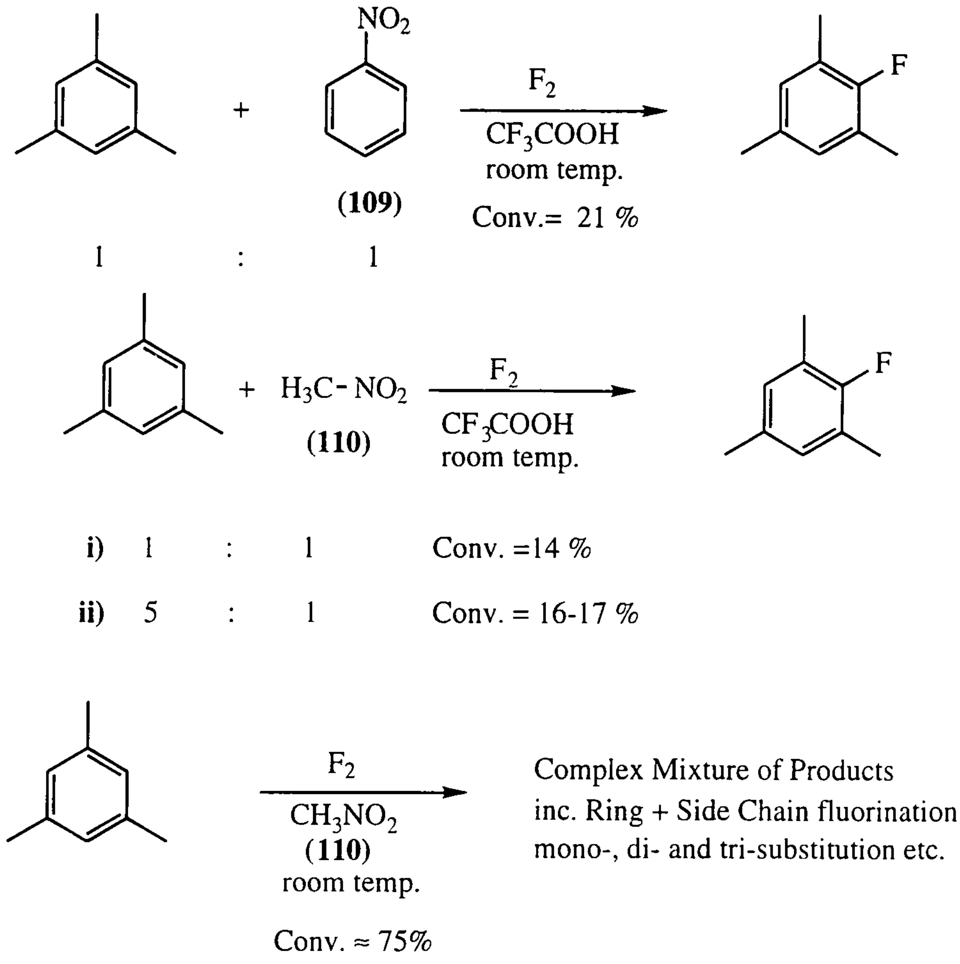
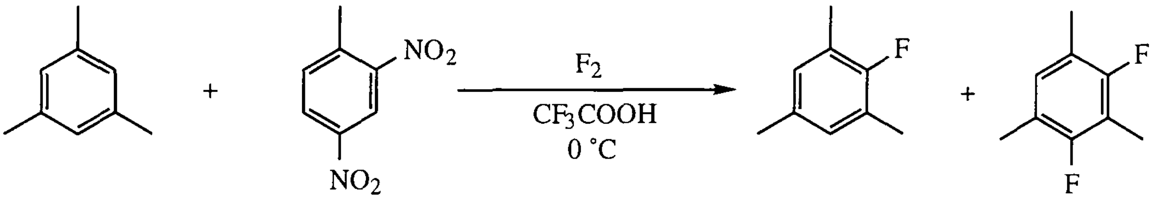


Fig 4.18

Would the use of dinitro-compounds as additives be more beneficial to the reaction ? Fluorinations of mesitylene were carried out using varying amounts of 2,4-dinitrotoluene (**111**) and the results of these experiments are outlined in Table 12.*



(**98**) (**111**) (**99**) (**112**)

& some coupling products (m/z 238, 256, 274)

Ratio of Reactants			Conversion (%).		
Mesitylene (**98**)	Dinitrotoluene (**111**)	Fluorine	Monofluoro (**99**)	Difluoro (**112**)	Total
1	1	1	21	10	31
1	1/5	1	19	6	30
1	2	1	20	5	25

Table 12 Fluorinations of Mesitylene in Trifluoroacetic Acid with Added 2,4-Dinitrotoluene.

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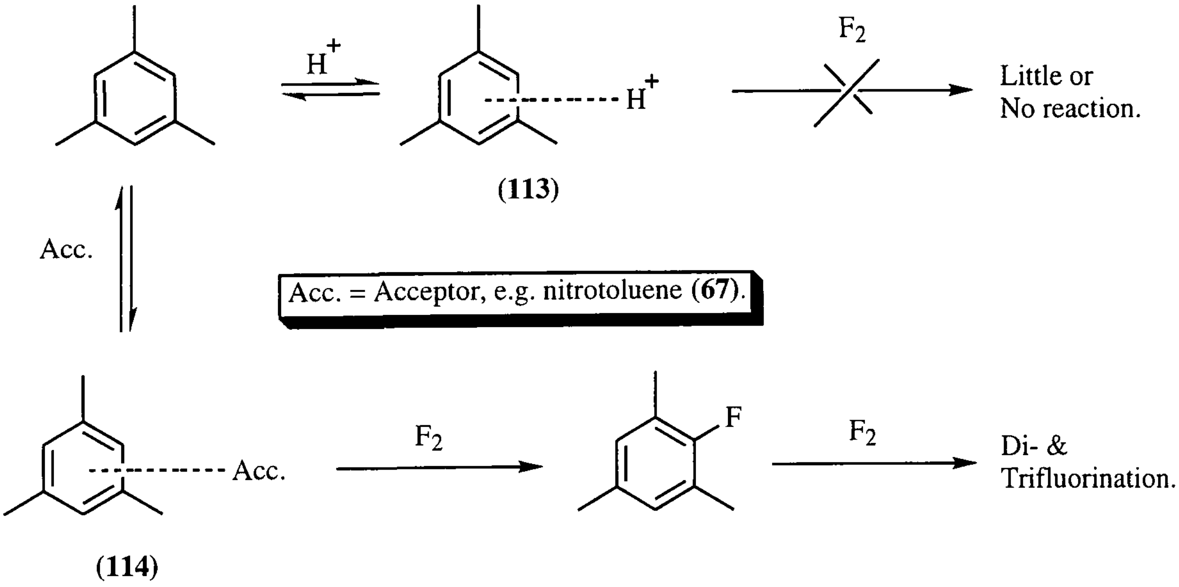
* These experiments were performed using the glass reactor which had been employed in the fluorinations of deactivated aromatics. See Chapter Three (fig 3.2)

4.5 Possible Mechanisms for the Fluorination of Mesitylene.

From the results of our investigations into the fluorination of mesitylene it has become increasingly apparent that the reaction is not as straight forward as had been first thought. It is not a simple case of electrophilic aromatic substitution, there must be some radical component to the reaction, while the apparent catalytic effect of nitro-additives is another unusual factor. However, we have been able to draw some conclusions from these results which has led us to suggest a few possible mechanisms for this reaction.

4.5.1 The Formation of Π-Complexes with Mesitylene.

It has already been established that protonation of mesitylene by trifluoroacetic acid is not the cause of its reduced reactivity in this solvent, so what other possibilities does this leave open ? The aromatic ring of mesitylene is very electron rich and it is possible that this gives rise to some weak interaction between the aromatic substrate and the acidic proton, e.g. the formation of a π-complex **(113)**, which while not strong enough to be observed in NMR spectra nevertheless has an inhibiting effect on the fluorination reaction. Similarly, species such as 4-nitrotoluene **(67)** and 2,4-dinitrotoluene **(111)** may be considered as electron poor, with the nitro- substituents acting as electron withdrawing groups and may also act as an acceptor molecule for an electron rich donor like mesitylene. This could lead to the formation of a different π-complex **(114)** which is more susceptible to fluorination than **(113)**. These interactions are summarised in Scheme 24.

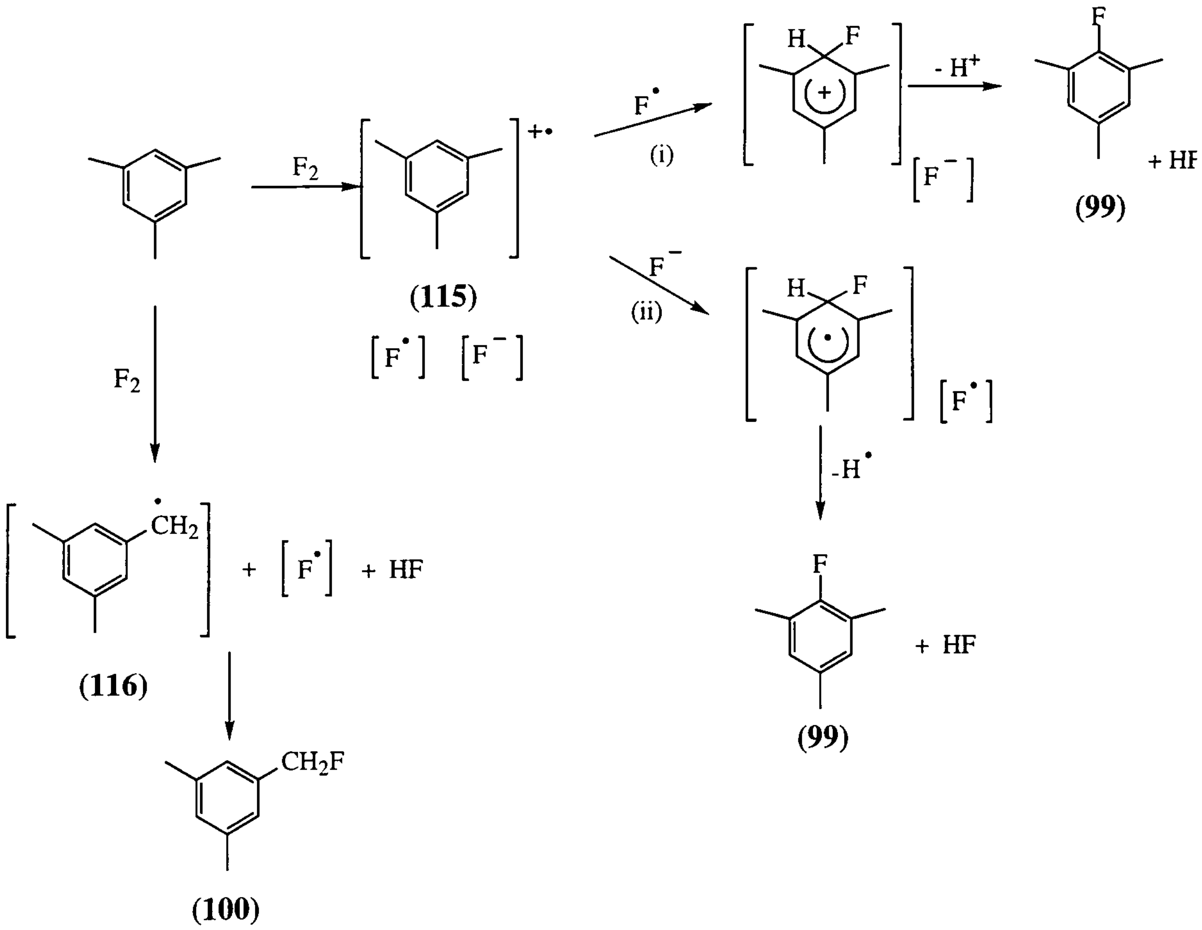


Scheme 24

This theory was investigated through cyclic voltametry experiments carried out by Dr Maurice Medebielle at the Université Denis Diderot in Paris, reporting the following results. Mesitylene was prepared in trifluoroacetic acid-trifluoroacetic anhydride with 0.5M tetrabutylammonium perchlorate added. The compound gave a clear orange solution in this solvent, which had not been observed in our reactions. Using a platinum electrode as the cathode, mesitylene was oxidised by trifluoroacetic acid in a single one-irreversible wave with a potential of +2.10v against Ag. Addition of 1 equivalent of 2,4-dinitrotoluene resulted in no change in either colouration or oxidation potential, only a slight increase of current was observed. These results do not support the proposed π-complex mechanism as we would expect the oxidation potential to decrease in the presence of the additive.

4.5.2 The Formation of Stable Radical Cations.

An alternative mechanism for this fluorination reaction involves the oxidation of mesitylene, which in trifluoroacetic acid may generate a stable radical cation through a series of single electron transfers between fluorine and the aromatic substrate. Electrophilic substitution may be considered as two consecutive single electron transfers between mesitylene and F_2, the first producing a radical cation **(115)** along with fluoride ion and the fluorine radical which may subsequently attack the radical cation to yield the fluorinated product (Scheme 25). Attack by a fluorine atom yields a Wheland intermediate and if sufficiently rapid this reaction is indistinguishable from the established mechanism of aromatic substitution (Path (i)), otherwise the radical cation intermediate plays a more significant role, e.g. the reaction with fluoride ion (Path (ii)). Alternatively, fluorine may react to abstract a hydrogen atom from the methyl group of mesitylene to produce the $CH_2^{\bullet}$ group **(116)** which may undergo radical fluorination to form the CH_2F group **(100)** or coupling reactions giving rise to the high mass products observed. There are precedents for the formation of radical cations in aromatic substitutions in the literature, notably in aromatic nitration reactions[148, 149], while radical cations have been observed in the reactions of aromatics with other halogen including bromine, chlorine and iodine monochloride in 1,1,1,3,3,3-hexafluoropropan-2-ol.[150]



Scheme 25

The solvent has a crucial effect on the course of this reaction. In acetonitrile, the reaction proceeds unimpeded and the radical cation **(115)** reacts to give the observed products. In trifluoroacetic acid, the situation may be quite different. There is evidence in the literature that trifluoroacetic acid may be used to stabilise aromatic radical cations and prevent further reaction of the substrate.[151] It acts by suppressing subsequent reactions by protonation of any potentially reactive species like F^+ and $F^\bullet$, e.g. the reaction of DDQ with an aromatic substrate, initiated thermally or by UV detailed in the literature by Davies (Fig 4.19).[152]

$$\mathrm{ArH} + \mathrm{DDQ} \rightleftharpoons \mathrm{ArH}\cdots\cdots\mathrm{DDQ} \xrightleftharpoons{h\nu \text{ or } \Delta} \mathrm{ArH}^{+\bullet}\ \mathrm{DDQ}^{-\bullet}$$

$$\xrightarrow{H^+} \mathrm{ArH}^{+\bullet}\ \mathrm{HDDQ}^{\bullet}$$

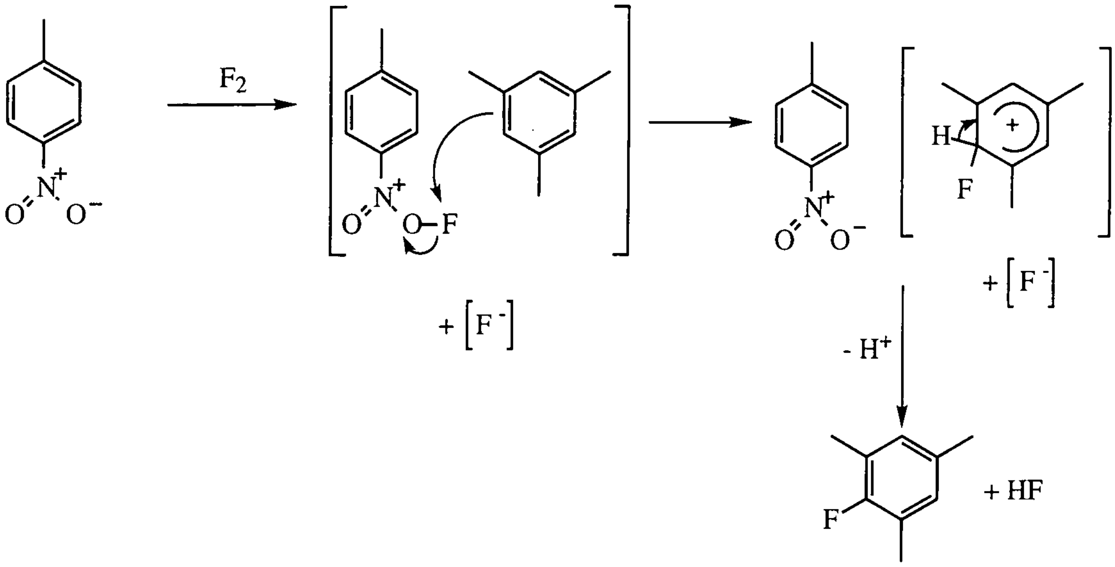
Fig 4.19

In this manner non-acidic oxidants, similar to fluorine, have been used to produce stable radical cations on reaction with aromatic compounds in trifluoroacetic acid. Furthermore, it has been observed that on the addition of acetonitrile to the reaction mixture, trifluoroacetic acid is not strong enough to effectively protonate the attacking species and so the reaction proceeds normally.[153] This tallies with our observations of the fluorination of mesitylene in a 1:1 acetonitrile : trifluoroacetic acid mixture which gave a wide range of products in good conversion, including both electrophilic and radical fluorination and by-products, such as ester and amide derivatives of CH_2F, while in pure trifluoroacetic very little reaction is observed. The effect of nitro-additives on this mechanism is not fully understood, but it may simply be the suppression of radical reactions.

This mechanism would seem to explain most of the observed phenomena but if a stable radical cation species we would expect this to disrupt the NMR spectra of the reaction mixture and no spectrum would be observed. An experiment to investigate this possibility was carried out recording the NMR spectra of a solution of mesitylene in trifluoroacetic acid taken before and immediately after the passage of elemental fluorine. In both cases, the acid component dominated both the ^1H and ^{19}F spectra, with the signals of the acidic proton and CF_3 groups at approx. 11 and -75 ppm respectively, but no interference was observed which does not support the presence of radical cations.

4.5.3 The Reaction of an N-O-F Intermediate

The radical cation mechanism does not fully account for the apparent increase in reactivity observed on the addition of nitrotoluene or similar additive, particularly in trifluoroacetic acid. This leads us to a third possible mechanism in which the nitro species is fluorinated first to produce a reactive N-O-F intermediate. This N-O-F species may then react as an electrophile with mesitylene, producing the observed fluorinated product (Scheme 27).



Scheme 26

Compare the results using nitromethane as an additive and as solvent. If the nitro species is responsible for determining the reaction pathway as this mechanism suggests these reactions should give the same results. In fact, the reactions are very different with nitromethane giving a complex mixture of products in high conversion when used as a solvent, which does not lend support to this hypothesis.

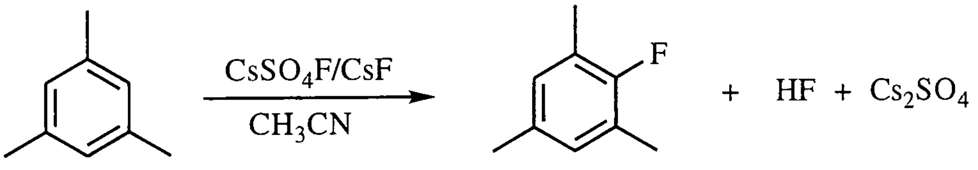
4.6 The Use of Elemental Fluorine for the *In Situ* Formation of Electrophilic Fluorinating Reagents.

It has already been stated that electrophilic fluorinating reagents such as Selectfluor^{TM} can be used to fluorinate mesitylene easily, under conditions where attempts at direct fluorination were unsuccessful. These reagents themselves are generally manufactured using elemental fluorine and so if electrophilic reagents could be generated *in situ* by direct fluorination, these intermediates might subsequently react with mesitylene to produce the desired product, 2-fluoro-1,3,5-trimethylbenzene (**99**).

4.6.1 Caesium Fluoroxysulphate.

It has been well established that bubbling fluorine through aqueous sodium sulphate gives an oxidising solution.[154] In 1981, Appelman discovered that caesium sulphate reacts with fluorine to produce the fluoroxysulphate derivative.[155] The initial chemistry of $CsSO_4F$ (**27**) demonstrated it had some application as a fluorinating reagent for aromatic compounds.[155, 156] If caesium fluoroxysulphate could be generated *in situ* by direct fluorination, this reagent might be used for the consequent fluorination of mesitylene. Initially we attempted this reaction as a two step process, first producing the fluoroxysulphate by passing elemental fluorine through a concentrated solution of caesium sulphate in deionised water. It should be noted that metal ions, other than Cs^+, must be excluded during this reaction because the fluoroxysulphate tends to react explosively. As the fluoroxysulphate is produced it precipitates out of solution as a white solid. On completion of this reaction, a solution of mesitylene in acetonitrile was introduced into the reaction vessel and the mixture was stirred overnight. As the reaction proceeded the white solid dissolved. This experiment was repeated using an excess of caesium sulphate, and the results are outlined in Table 13.

$$Cs_2SO_4 \xrightarrow[H_2O,\ 0\,^{\circ}C]{F_2} \underset{\textbf{(27)}}{CsSO_4F} + CsF$$



(98) **(99)**

Ratio of Cs_2SO_4 : Mesitylene		Conversion of Mesitylene.(%)
1	1	12
2	1	20

Table 13 The Fluorination of Mesitylene Using Caesium Fluoroxysulphate

In these reactions only the ring fluorinated products were observed, albeit in low conversion (10-20%). Increasing the amount of caesium sulphate used was seen to increase the conversion, which led us to assume that formation of the fluoroxysulphate was the limiting factor. The next step was to attempt the fluorination reaction as a 'one pot' synthesis of 2-fluoro-1,3,5-trimethylbenzene. Here, we encountered a problem as mesitylene is immiscible in water while caesium sulphate does not dissolve in acetonitrile. In an attempt to overcome this obstacle we carried out two experiments; one using a concentrated solution of caesium sulphate in water to which mesitylene was added to form a suspension, the other involving a mixture of acetonitrile and water (1:1) (Fig 4.20). However, both experiments proved unsuccessful (conv. less trhan 1%) and this approach was not continued.

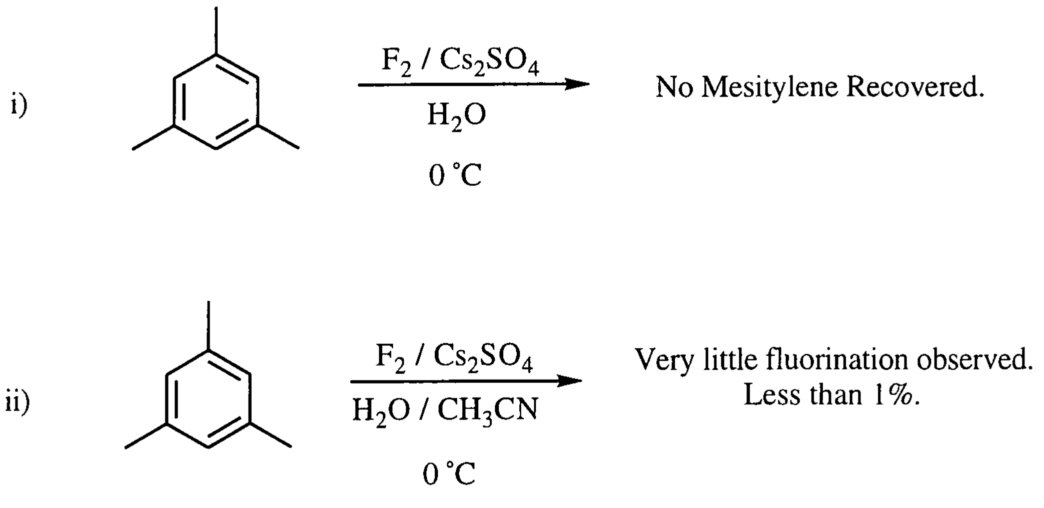
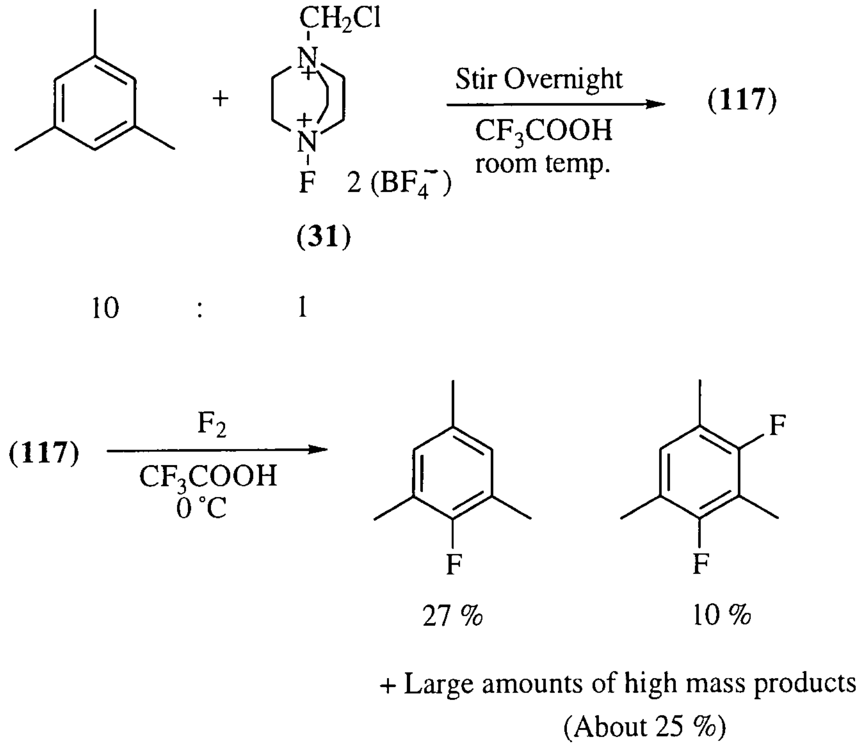


Fig 4.20

4.6.2 The Attempted Regeneration of Selectfluor.™

In an attempt to regenerate the fluorinating reagent Selectfluor™ **(31)** *in situ* a solution of mesitylene and Selectfluor™ was prepared in trifluoroacetic acid, where mesitylene was present in a ten fold excess and Selectfluor™ was allowed to react completely. Next, the resulting mixture **(117)** was transferred to the glass fluorination vessel and an excess of elemental fluorine passed at 0°C over several hours (Fig 4.21).



Total Conversion ≈ 69 %

Fig 4.21

If fluorination is solely due to the reaction of the initial amount of Selectfluor^{TM} **(31)** then the highest conversion we can expect is 10 %, since mesitylene is present in a ten fold excess and, in the absence of all additives, the fluorination of mesitylene in trifluoroacetic acid is poor (conv. 5-6%). In this experiment, a much higher conversion than anticipated was achieved in the order of 69 %. The main products are the mono- and difluorinated derivatives (27 and 10 % respectively) however a large amount of high mass products (m/z 238, 256 , 274) around 25% in total, are found as well, complicating the reaction mixture. These by-products may be due to coupling between aromatic molecules, as we have previously suggested (Section 4.3.1). The reaction appears to be more than simple electrophilic fluorination by regenerated Selectfluor^{TM} **(31)**, and is more reminiscent of a direct reaction of fluorine. This being the case this methodology was not pursued any further.

4.7 Conclusion.

In conclusion, the fluorination of mesitylene is not as straight forward as we might have anticipated from the previous results observed for deactivated aromatic systems. It is not a simple matter of using an acid solvent like sulphuric or formic acids to promote the electrophilic reaction of fluorine. Sulphuric acid cannot be used because of competing sulphonation while the substrate is insoluble in formic. Meanwhile, trifluoroacetic acid appears to have an inhibiting effect on the reaction which is not fully understood. It should also be noted that the radical mode of fluorination has a greater influence in these reactions. It has been further demonstrated that the use of nitro compounds promotes the fluorination of mesitylene. Finally we have detailed several possible mechanisms for this fluorination reaction. So far, the fluorination of mesitylene has proved to be an interesting problem and more work is required to evaluate the mechanism satisfactorily.

Experimental.

The Use of Pressurised Fluorine in the Laboratory.

Elemental fluorine is an extremely reactive reagent and great care must be taken when working with it in the laboratory environment, since there is a risk of fire or explosion caused on the escape of fluorine. Fluorine is also toxic by inhalation, similar to other halogens, e.g. chlorine. Apparatus containing elemental fluorine must be maintained in a well ventilated area, while operators should wear nitrile rubber gloves and a face shield since fluorine can burn skin in a manner akin to hydrogen fluoride. The treatment of fluorine burns is similar to that of HF.

The collaboration of the Chambers group and F2 Chemicals Ltd (formerly BNFL Fluorochemicals) has led to the development of safe techniques for the handling of elemental fluorine. Fluorine is furnished by pressurised cylinder as a 50% mixture diluted with nitrogen, which is housed in its own extracted cabinet. The apparatus is fitted with a pnuematic valve which can be used to shut down the flow of fluorine in emergencies. The pressure of fluorine is also controlled by a fluorine resistant regulator, so that the maximum pressure achieved is around 3 atm. This arrangement is illustrated in fig 5.1

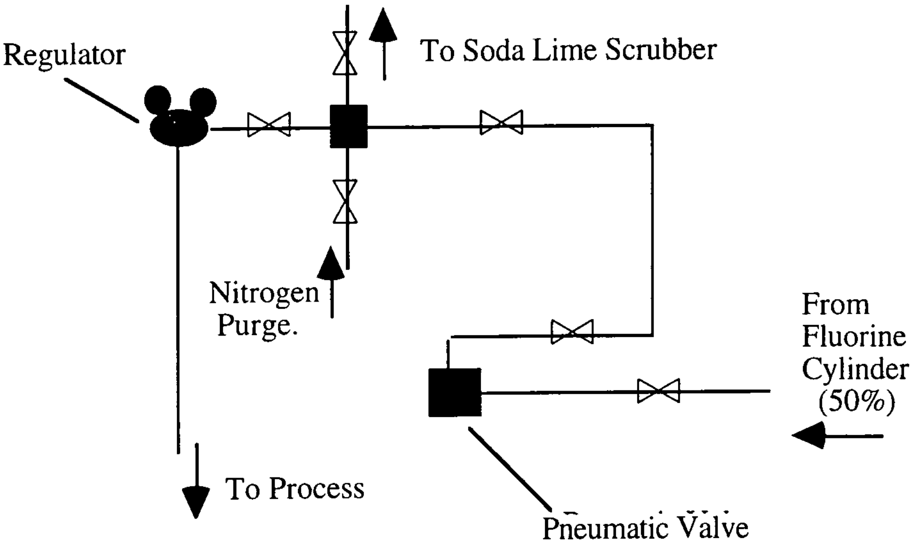


Fig 5.1

For fluorination experiments, elemental fluorine is used as a 10% mixture in nitrogen prepared in 3.7 litre passivated stainless steel cylinders. In the preparation of these mixtures, fluorine is delivered by a passivated $^1/_4$" stainless steel pipe to a passivated pipework rig fitted with Monel® valves (fig 5.2), housed in a stainless steel fumes cupboard which is used to fill the smaller cylinders which may then be transferred to smaller rigs (see fig 2.4). All operations are carried out in the presence of at least two trained members of the group. The large rig is also fitted with with a 4.5 litre cylinder which may be filled with 50% fluorine/nitrogen allowing large scale reactions to be run. A fluorine resistant control valve and flow meter are used to facilitate accurate control of the flow of gas during these large scale fluorinations.

N.B Fluorination Reactions Must Never Be Run Directly From The Large 50% Fluorine/Nitrogen Cylinder.

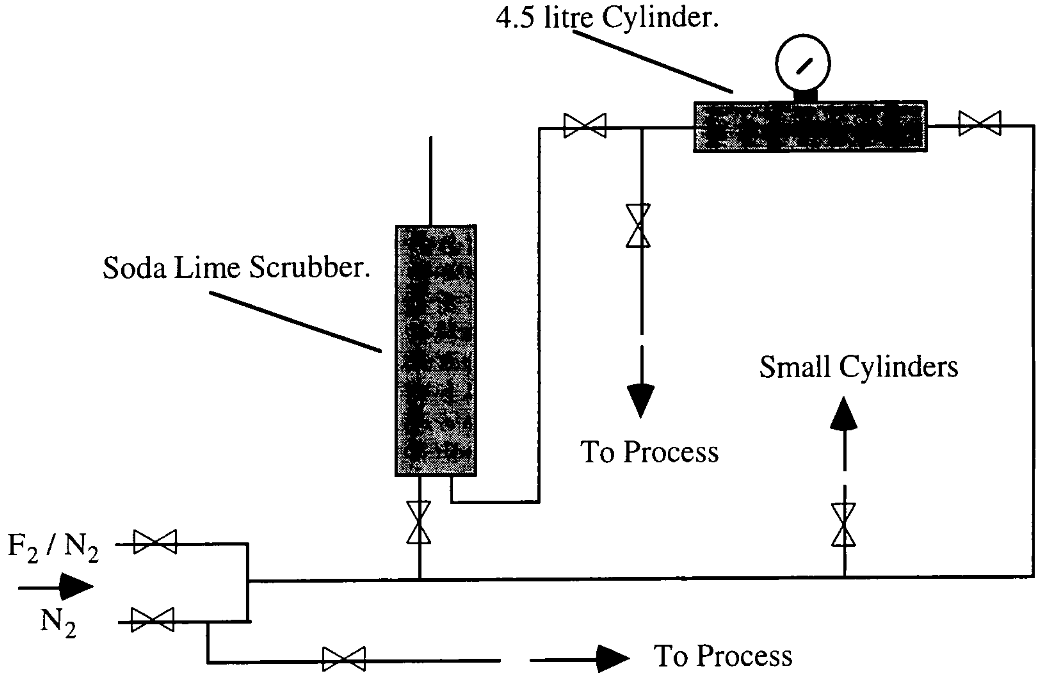


Fig 5.2.

Instrumentation and Reagents.

Reagents and Solvents.

All materials were either obtained commercially (Aldrich, Fluorochem, BDH, Lancaster) or prepared by literature procedures[130]. All solvents were dried before use by literature procedures and stored over molecular sieve.

Gas Liquid Chromatographic Analysis.

Analyses were carried out using a Hewlett Packard 5890A gas liquid chromatograph equiped with a 20m cross-linked methyl silicone capillary column. Preparative scale GC was was performed on a Varian Aerograph Model 920 (catharometer detector) gas chromatograph, fitted with a 3m 10% *SE30* packed column.

Elemental Analysis.

Carbon, hydrogen and nitrogen elemental analyses were obtained on either a Perkin-Elmer 240 or a Carlo Erba Elemental Analyser.

NMR Spectra.

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on either a Varian Gemini 200, a Varian VXR 400S or a Bruker AC250 spectrometer. In ^{19}F NMR spectra, upfield shifts are quoted as negative. J values are given in Hz.

Mass Spectra.

Mass spectra were recorded on either a VG 7070E spectrometer (for solid samples) or a Fissons VG Trio 1000 spectrometer coupled with a Hewlett Packard 5890 series II gas chromatograph (Liquid and Volatile samples).

FT/IR Spectra.

Infra red spectra were recorded on a Perkin-Elmer 1600 FT IR spectrometer using KBr discs (solid samples) or as thin films between two KBr plates (liquids).

Melting Points.

Melting points were recorded at atmospheric pressure and are uncorrected.

Chapter Five Experimental to Chapter Two.

5.1 Preparation of 1,3-Dithiolanes.

General Procedure.

A solution containing a ketone, 1,2-ethanedithiol and aluminium trichloride in dichloromethane (50ml) was stirred at room temperature in a 250 ml round bottom flask for thirty minutes. After this time, water (50ml) was added to quench the reaction. The organic layer was separated off, and the aqueous layer further extracted using dichloromethane (3x50ml). The extract was washed with brine, dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. Purification was achieved by either recrystallisation or distillation. All yields are quoted for pure, isolated products.

a) 2,2-Diphenyl-1,3-dithiolane (37).

Benzophenone (9.1g, 50mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave pure fine white crystalline needles of 2,2-diphenyl 1,3- dithiolane **(37)** (4.95g, 38%); mp 102-104 °C (lit.[130], 105 °C); (Found: C, 69.38 ; H, 5.15. Calc. for $C_{13}H_{10}S_2$: C, 69.76; H, 5.43 %); m/z (EI^+) 258 (M^+, 31%), 230 (100), 198 (28), 165 (92), 121 (90), 77 (32); m/z(CI^+, NH_3) 259 (M^{++} 1, 100%), 230 (19). NMR Spectrum No. 1; Mass Spectrum No. 1; IR Spectrum No. 1.

b) 2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane (39).

4-Chlorobenzophenone (10.79g, 49.95mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave pure off-white crystalline 2-(4-chlorophenyl)-2-phenyl-1,3-dithiolane **(39)** (9.87g, 68%); mp 44-46 °C ; (Found: C, 61.72; H, 4.38. Calc. for $C_{13}H_9S_2Cl$: C, 61.64; H 4.79 %); m/z (EI^+) 292 (M^+, 24%), 263 (100), 232 (29), 229 (45), 199 (27), 197 (25), 155 (47), 121 (38), 77 (14), 43 (49). NMR Spectrum No. 2; Mass Spectrum No. 2; IR Spectrum No. 2.

c) 2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane (40).

4-Bromobenzophenone (13,1g, 50mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a white crystalline solid, 2-(4-bromophenyl)-2-phenyl-1,3-dithiolane **(40)** (12.6g, 75%); m.p. 59-60°C; m/z (CI^+,

NH_3) 337 (M^++1, 91%), 339 (M^++3, 100%). NMR Spectrum No. 3; Mass Spectrum No. 3; IR Spectrum No. 3.

d) 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane (41).

4-Fluorobenzophenone (5.0g, 25mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a pure yellow oil, 2-(4-fluorophenyl)-2-phenyl-1,3-dithiolane **(41)** (3.9g, 57%); m/z (EI^+) 276 (M^+, 23%), 247 (99), 183 (100), 139 (49), 121 (34), 95 (9), 77 (11). NMR Spectrum No. 4; Mass Spectrum No. 4.

e) Bis(4-fluorophenyl)-1,3-dithiolane (42).

Bis(4-fluoro)benzophenone (13.1g, 50mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a white solid, bis(4-fluorophenyl)-1,3-dithiolane **(42)** (12.4g, 84%); m/z (EI^+) 294 (M^+, 25%), 266 (100), 234 (27), 201 (93), 139 (79), 95 (13); (CI^+) 295 (M^+ + 1, 100%), 266 (10), 235 (11), 201 (5), 139 (5). NMR Spectrum No. 5; Mass Spectrum No. 5; IR Spectrum No. 4.

f) 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane (37).

2,4-Dimethylbenzophenone (10.5g, 50mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a white crystalline solid, 2-phenyl-2-(2,4-dimethylphenyl)-1,3-dithiolane **(37)** (10.2g, 71%); m.p. 116-117°C; m/z (CI^+, NH_3) 287 (M^++ 1, 100%). NMR Spectrum No. 6; Mass Spectrum No. 6; IR Spectrum No. 5.

g) 2-(4-Nitrophenyl)-2-phenyl-1,3-dithiolane (48).

4-Nitrobenzophenone (11.3g, 49.8mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave 2-(4-nitrophenyl)-2-phenyl-1,3-dithiolane as a fine white powder **(48)**(11.54g, 76%); m/z (EI^+) 303 (M^+, 28%), 277 (11), 276 (22), 275 (100), 258 (13), 243 (25), 228 (37), 196 (22) 180 (37), 164 (43), 152 (46) 121 (68), 77 (22), 59 (13) 45 (22), 28 (45). NMR Spectrum No. 7; Mass Spectrum No. 7.

h) 2-(3-Trifluoromethylphenyl)-2-phenyl-1,3-dithiolane (47).

3-Trifluoromethylbenzophenone (5.25g, 21mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a pure yellow oil, 2-(3-trifluoromethylphenyl)-2-phenyl-1,3-dithiolane **(47)** (6.2g, 91%); m/z (EI^+) 326 (M^+, 19%), 297 (100), 266 (27), 233 (77), 189 (57), 165 (30), 121 (56), 77 (13). NMR Spectrum No. 8; Mass Spectrum No. 8.

i) 2-Butyl-2-phenyl-1,3-dithiolane (43).

Butyrophenone (7.4g, 50mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a pure yellow oil, 2-phenyl-2-butyl-1,3-dithiolane **(43)** (3.88g, 35%); m/z (EI^+) 224 (M^+, 6%), 181(100), 121(33), 91(12), 77(16). NMR Spectrum No. 9; Mass Spectrum No. 9; IR Spectrum No. 6.

j) 2-Butyl-2-methyl-1,3-dithiolane (45).

2-Hexanone (5.14g, 51.4mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a pure yellow oil, 2-butyl-2-methyl-1,3-dithiolane **(45)** (3.04g, 39%); m/z (EI^+) 176 (M^+, 20%), 119(100), 74(14), 59(29). NMR Spectrum No. 10; Mass Spectrum No. 10; IR Spectrum No. 7.

k) 2-Ethyl-2-pentyl-1,3-dithiolane (46).

3-Octanone (6.35g, 49.6mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave a pure yellow oil, 2-Ethyl-2-pentyl-1,3-dithiolane **(46)** (3.78g, 37%); m/z (EI^+) 204 (M^+, 9%), 174 (20), 133 (33), 105 (15). NMR Spectrum No. 11; Mass Spectrum No. 11; IR Spectrum No. 8.

l) Cyclododecan-1,3-dithiolane (44).

Cyclododecanone (9.0g, 50 mmol), 1,2-ethanedithiol (5.64g, 60mmol) and aluminium trichloride (1g, 7.4mmol) gave pure white crystalline cyclododecan-1,3-dithiolane **(44)** (4.99g, 39%); mp 58-60 °C (cf lit.[127] 59-60 °C); m/z (EI^+) 258 (M^+, 48%), 197 (60), 131 (100). NMR Spectrum No. 12; Mass Spectrum No. 12; IR Spectrum No. 9.

5.2 Fluorodesulphurisations of 1,3-dithiolanes.

General Procedure.

A solution containing a 1,3 dithiolane and iodine in acetonitrile (40ml) was placed in a PTFE reaction vessel*. Elemental fluorine in 10 % dilution with nitrogen (800ml, 17 mmol) was then passed through the solution at a rate of 10 ml/min. over the course of 5-6 hours. The reaction mixture was poured into a solution of 5% aqueous sodium metabisulphate (50ml), and then extracted with dichloromethane (3x50ml). This extract was washed sequentially with sodium bicarbonate solution and water then dried($MgSO_4$). Excess solvent was removed under reduced pressure. The pure geminal difluoro- product was isolated by flash column chromatography using 9:1 hexane/ether as elutant. All yields are quoted for pure, isolated products.

a) 2,2- Diphenyl 1,3-dithiolane (37) to give Diphenyldifluoromethane (49).

i) Using the Iodine/Fluorine system.

2,2-Diphenyl 1,3- dithiolane (1.5g, 5.8mmol), iodine (4.3g, 17mmol) and fluorine (800ml, 17mmol) gave a colourless liquid, difluorodiphenylmethane **(49)** (0.95g, 81 %); m/z (EI^+) 204(M^+, 91.61%), 183(31), 127(100), 77(16), 51(10). NMR Spectrum No. 19; Mass Spectrum No. 19.

ii) Using Fluorine alone.

2,2-Diphenyl 1,3-dithiolane (1.0g, 3.9mmol) and fluorine (12mmol) were seen to produce a complex mixture of black tars.

b) 2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane (39) to give 1-Chlorophenyl-1-phenyldifluoromethane (50).

2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane(1.7g, 5.8mmol), iodine (5.2g, 20.6mmol) and fluorine (800ml, 17mmol) gave a colourless liquid, 1-chlorophenyl-1-phenyldifluoromethane **(50)** (0.94g, 69 %); m/z (EI^+) 240 (M^+, 20%), 238 (M^+, 56),

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*See Chapter Two, fig 2.5

203 (31), 183 (47), 163 (34), 161 (89), 127 (100), 77 (30). NMR Spectrum No. 20; Mass Spectrum No. 20.

c) 2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane (40) to give 1-(4-Bromophenyl)-1-phenyldifluoromethane (52).

2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane (1.0g, 2.9mmol), iodine (2.8g, 11.1mmol) and fluorine (800ml, 17mmol) gave a colourless liquid, 1-(4-bromophenyl)-1-phenyldifluoromethane (**52**) (0.71g, 86.5%); m/z (EI^+) 284(M^+, 63.71%), 282(M^+, 74.19%), 207(43), 205(47), 203(100), 183(77), 127(81), 77(8), 75(12). NMR Spectrum No. 21; Mass Spectrum No. 21.

d) 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane (41) to give 1-(4-Fluorophenyl)-1-phenyldifluoromethane (53).

2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane (1.2g, 4.3mmol), iodine (4.6g, 21mmol) and fluorine (800ml, 17mmol) gave a colourless liquid, 1-(4-fluorophenyl)-1-phenyldifluoromethane (**53**) (0.8g, 83.7%); m/z (EI^+) 222 (M^+, 100%), 201 (29), 183(11), 145 (80), 127 (43), 95 (12), 51 (11). NMR Spectrum No. 22; Mass Spectrum No. 22.

e) Bis(4-fluorophenyl)-1,3-dithiolane (42) to give Bis(4-fluorophenyl)-difluoromethane (54).

Bis(4-fluorophenyl)-1,3-dithiolane (1.6g, 5.4mmol), iodine (4.6g, 21mmol) and fluorine (800ml, 17mmol) gave a colourless liquid, Bis(4-fluorophenyl)-difluoromethane (**54**) (0.96g, 74%); m/z (EI^+) 240 (M^+, 69%), 221 (30), 201 (14), 145 (100), 126 (19), 95 (12), 75 (10). NMR Spectrum No. 23; Mass Spectrum No. 23.

f) 2-Dimethylphenyl-2-phenyl 1,3-dithiolane (38) to give 1-Dimethylphenyl-1-phenyldifluoromethane (51).

2-Dimethylphenyl-2-phenyl 1,3- dithiolane (1.5g,5.8 mmol), iodine (4.3g,17 mmol) and fluorine (800ml, 17 mmol) gave a colourless liquid, 1-dimethylphenyl-1-phenyldifluoromethane (**51**) (0.95g, 81 %); m/z (EI^+) 232 (M^+, 84%), 197(34), 154(100), 127(36), 105(18), 77 (13). NMR Spectrum No. 24; Mass Spectrum No. 24.

g) 2-(4-Nitrophenyl)-2-phenyl 1,3-dithiolane (47).

2-(4-Nitrophenyl)-2-phenyl 1,3-dithiolane (1.5g, 5.0mmol), iodine (6.1g, 24mmol) and fluorine (800ml, 17mmol) gave no apparent reaction.

h) 2-(4-Trifluoromethylphenyl)-2-phenyl-1,3-dithiolane (48).

2-(4-Trifluoromethylphenyl)-2-phenyl-1,3-dithiolane (1.0g, 3.1mmol), iodine (4.0g, 15mmol) and fluorine (800ml, 17mmol) gave no apparent reaction.

5.3 Deprotections of 1,3-dithiolanes.

General Procedure.

A solution containing a 1,3-dithiolane and water (2ml) in acetonitrile (35 ml) was prepared in a PTFE reaction vessel. Elemental fluorine (12mmol) as a 10 % dilution in nitrogen was passed through the solution, at a rate of 10 ml/min over 4-5 hours. The reaction mixture was poured into 10% sodium bicarbonate solution and extracted with dichloromethane. The extract was washed sequentially with water and brine, dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The product was purified by flash column chromatography using a 9:1 hexane/ether system as elutant. All yields are quoted for pure, isolated products.

a) Diphenyl-1,3-dithiolane (38) to give benzophenone (58).

Diphenyl 1,3 dithiolane (1.5g, 5.8mmol) and water (2ml) in acetonitrile (35 ml) gave benzophenone (**58**) as a fine white crystalline solid (0.95g, 89%); m.p 47-49 °C (cf. lit [157] 48-49 °C); m/z (EI$^+$) 182 (M$^+$, 53%) 105 (100) 77 (85) 51 (48). NMR Spectrum No. 13; Mass Spectrum No. 13; IR Spectrum No. 10.

b) Cyclododecan-1,3-dithiolane (44) to give Cyclododecanone (59).

Cyclododecan 1,3 dithiolane (1.0g, 3.9mmol) and water (2ml) in acetonitrile (35ml) gave cyclododecanone (**59**) (0.95g, 87%); m.p 57-58 °C (cf. lit.[157] 58-59 °C); m/z (EI$^+$) 182 (M$^+$, 21%),125 (33), 111 (51), 98 (67), 83 (35), 71 (59), 55 (82), 41 (100), 28 (29). NMR Spectrum No. 14; Mass Spectrum No. 14; IR Spectrum No. 11.

c) 2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane (39) to give Chlorobenzophenone (60).

2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane (1.77g, 6.1mmol) and water (2 ml) in acetonitrile (35ml) gave brown crystalline chlorobenzophenone (**60**) (1.17g, 85%); m.p 73-74 °C (cf. lit.[157] 76-77 °C); m/z (EI+) 218 (M+, 25%), 216 (M+, 72%), 181(24), 141 (33), 139(100), 113 (9), 111 (26), 105(80), 77(39), 51 (34). NMR Spectrum No. 14; Mass Spectrum No. 14; IR Spectrum No. 12.

d) 2-Butyl-2-phenyl-1,3-dithiolane(43) to give Butyrophenone (61).

2-Butyl-2-phenyl-1,3-dithiolane (1.64g, 7.3mmol) and water (2ml) in acetonitrile (35 ml) gave a pure yellow oil, butyrophenone (**61**) (0.76g, 70%); m/z (EI+) 148 (M+, 36.78 %), 120(19), 105(100),77(96), 51(48). NMR Spectrum No. 16; Mass Spectrum No. 16.

e) 2-Butyl-2-methyl-1,3-dithiolane (45) to give 2-Hexanone (62).

2-Butyl-2 methyl-1,3-dithiolane (1.14g, 6.5mmol) and water (2ml) in acetonitrile (35 ml) gave a pure yellow oil, 2-hexanone (**62**)(0.51g, 79%); m/z (EI+) 100 (M+, 5.24%), 85(6), 58(42), 43(100),29(21). NMR Spectrum No. 17; Mass Spectrum No. 17; IR Spectrum No. 13.

f) 2-Ethyl-2-pentyl-1,3-dithiolane (46) to give 3-Octanone (63).

2-Ethyl-2-pentyl-1,3-dithiolane (0.91g, 4.1mmol) and water (2ml) in acetonitrile (35 ml) gave a pure yellow oil, 3-octanone (**63**) (0.49g, 81%); m/z (EI+) 128 (M+, 9.09 %), 99(59), 72(56), 57(85), 43(100), 29(40). NMR Spectrum No. 18; Mass Spectrum No. 18; IR Spectrum No. 14.

Chapter Six Experimental to Chapter Three.

6.1 The Effect of Acid on the Fluorination of Nitrotoluene (67).

General Procedure.

A solution consisting of 4-nitrotoluene (15-20mmol) and an acid (100ml) was prepared in a glass reaction vessel fitted with overhead stirrer.* The solution was cooled to 0 °C in a salt water bath using a HAAKE cryostat. Elemental fluorine (30mmol) in 10 % dilution with nitrogen was then passed through the solution at a rate of 10 ml/min. over the course of 4-5 hours. The reaction mixture was poured into ice/water (400ml) and extracted with dichloromethane (3x100ml). This extract was washed with 10% sodium bicarbonate solution (2x50ml) then dried ($MgSO_4$). Excess solvent was removed under reduced pressure. Crude yields and conversions were calculated from the composition of the product mixture derived from the relative intensities of the gas chromatogram and related to the mass of recovered material. Conversion is defined as the amount of starting material transformed to product while the yield is based on the amount of this product isolated. The monofluorinated 2-fluoro-4-nitrotoluene was isolated by column chromatography on silica gel using hexane/dichloromethane (3:1) as elutant

a). Boron Trifluoride-Etherate/Acetonitrile.

4-Nitrotoluene **(67)** (2.0g,14.6mmol) and boron trifluoride-etherate (5.0g, 35.4mmol) in acetonitrile (100ml) reacted with fluorine (15mmol) gave 2-fluoro-4-nitrotoluene **(68)** (0.3g, conv. 25%, yield 53 %) as a pale yellow crystalline solid (Found: C, 53.9; H, 3.8; N, 8.9. Calc. for $C_7H_6NO_2F$: C, 54.2; H, 3.9; N, 9.0 %); mp. 33.0-34.3 °C (from ethanol) (lit.[158] 34-35 °C); Rf 0.48; υ_{max}/cm^{-1} 1523 (NO_2); m/z (EI^+) 155 (M^+, 100%), 125(20), 109(77), 83(56). NMR Spectrum No. 25; Mass Spectrum No. 25; IR Spectrum No 15.

b). Trifluoroacetic acid.

4-Nitrotoluene **(67)** (2.0g, 14.6mmol) and fluorine (15mmol) in trifluoroacetic acid (100ml) gave 2-fluoro-4-nitrotoluene **(68)** (0.47g, conv. 29 %, yield 71 %); data as above.

c). Formic acid.

4-Nitrotoluene **(67)** (2.0g, 14.6mmol) and fluorine (15mmol) in formic acid

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* See Chapter Three, fig 3.2

(100ml) gave a single fluorinated product, 2-fluoro-4-nitrotoluene **(68)** (0.88g, conv. 46% , yield 53%); data as above.

d). 98 % Sulphuric acid.

4-Nitrotoluene **(67)** (2.0g, 14.6mmol) and fluorine (15mmol) in 98 % sulphuric acid (100ml) gave two fluorinated products (conversion 75 %), 2-fluoro-4-nitrotoluene **(68)** (1.37g, 81 %); data as above; and 2,6-difluoro-4-nitrotoluene **(69)** (0.04g, 2%); δ_F (235 MHz, $CDCl_3$) -111.0 (s); m/z (EI^+) 173 (M^+, 64%), 143(44), 142(48), 127(60), 101(56), 57(50), 30 (100).

6.2. Fluorinations of a Range of Aromatic Substrates in 98% Sulphuric Acid.

General Procedure.

A solution consisting of a 1,4-disubstituted aromatic (15-20mmol) and 98 % sulphuric acid (100ml) was prepared in a glass reaction vessel fitted with overhead stirrer. The solution was cooled to 0 °C. Elemental fluorine in 10 % dilution with nitrogen (30mmol) was then passed through the solution at a rate of 10 ml/min. over the course of 4-5 hours. The reaction mix was poured into ice/water (400ml) then extracted with dichloromethane (3x100ml). This extract was washed with 10% sodium bicarbonate solution (2x50ml) then dried ($MgSO_4$). Excess solvent was removed under reduced pressure. Crude yields were calculated from ^{19}F NMR integrated against a known quantity of a reference, benzotrifluoride (2.5-3mmol). All products were isolated by column chromatography on silica gel using hexane/dichloromethane or hexane/diethyl ether solvent mixtures as the elutant.

a). 1-Fluoro-4-Nitrobenzene (70) to give 1,2,-Difluoro-4-nitrobenzene (71) and 1,2,6-Trifluoro-4-nitrobenzene (72).

i) Using 2 Equivalents of Fluorine.

1-Fluoro-4-nitrobenzene **(70)** (3.3g, 23.6 mmol) and fluorine (30mmol) in sulphuric acid (100ml) gave two fluorinated products (conversion 87%) isolated using 2:1 hexane/dichloromethane. 1,2,-Difluoro-4-nitrobenzene **(71)**(2.4g, 75 %) was obtained as yellow oil (Found: C, 45.36; H, 1.79; N, 8.62. Calc. for $C_7H_3NO_2F_2$: C, 45.3; H, 1.89; N, 8.8 %); m/z (EI^+) 159 (M^+, 86%), 129(28), 113(100), 101(26), 63(77). NMR Spectrum No. 30; Mass Spectrum No. 30. The minor product was identified by ^{19}F NMR and mass spectrometry as 1,2,6-trifluoro-4-nitrobenzene **(72)** (0.4g, 10 %); δ_F (235 MHz, $CDCl_3$) -117.1 (1F, m) -129.6 (2F, d, ^3J 19.6); m/z (EI^+)

177 (M^+, 96%), 147(24), 131(59), 119(37), 81(100), 30 (72).

ii) Using Excess Fluorine.

1-Fluoro-4-nitrobenzene **(70)** (2.5g, 17.7 mmol) and fluorine (120mmol) in 98% sulphuric acid (100ml) gave two fluorinated products (conversion 87%), 1,2,-difluoro-4-nitrobenzene **(71)**(2.2g, 78 %) and 1,2,6-trifluoro-4-nitrobenzene **(72)** (0.41g, 13 %); data as above.

iii) Using Excess Fluorine with Increasing Temperature.

1-Fluoro-4-nitrobenzene (2.4g, 17.0mmol) and fluorine (120mmol) in 98% sulphuric acid (100ml). The first 40mmol of fluorine were passed at 0 °C after which time the temperature was raised to 30 °C. The reaction gave three fluorinated products quantitatively; 1,2,-difluoro-4-nitrobenzene (66%), 1,2,6-trifluoro-4-nitrobenzene **(86)** (16%); data as above and 1,2,3,6-tetrafluoro-4-nitrobenzene (18%); δ_F (235 MHz, $CDCl_3$) -111.0 ; m/z (EI^+) 195 (M^+, 19%), 177 (34), 149 (18), 131 (45), 99 (74), 81 (100), 30 (33).

b) 1-Chloro-4-Nitrobenzene (73) to give 1-Chloro-2-fluoro-4-nitrobenzene (74).

1-Chloro-4-nitrobenzene **(73)** (2.5g, 15.8 mmol) and fluorine (30mmol) in 98% sulphuric acid (100ml) gave 1-chloro-2-fluoro-4-nitrobenzene **(74)** (1.16g, conv. 64 %, yield 65%) isolated using hexane/dichloromethane (2:1) as pale yellow crystals (Found: C, 40.9; H, 1.6; N, 7.7. Calc. for $C_6H_3NO_2ClF$: C, 41.0; H, 1.7; N, 8.0 %); mp. 55.4-56.5 °C (from ethanol) (lit.[159] 63-64 °C); R_f 0.58 ; υ_{max}/cm^{-1} 1533 (NO_2), 3102 (CH); m/z (EI^+) 177 (M^+, 32.3%), 175 (M^+, 100), 147(11), 145(33), 131(24), 129(76), 117(27), 109(21), 93(19), 74(14). NMR Spectrum No. 26; Mass Spectrum No. 26; IR Spectrum No. 16.

c) 4-Tolualdehyde (75) to give 2-fluoro-4-Tolualdehyde (76).

4-Tolualdehyde (2.5g, 20.8mmol) and fluorine (40mmol) in 98% sulphuric acid (100ml) gave 2-fluoro-4-tolualdehyde **(76)** (1.2g, conv. 74 %, yield 64%); δ_F (235 MHz, $CDCl_3$) -116.1; m/z (EI^+) 138 (M^+, 58%), 137(100), 109(98), 83(58), 63(30). 57(39). Mass Spectrum No. 38.

d) Methyl-4-Methoxy-benzoate (77) to give 2-Fluoro-methyl-4-methoxybenzoate (78) and 2,6-Difluoro-methyl-4-methoxybenzoate (79).

Methyl-4-methoxybenzoate (**77**) (2.5g, 15.1mmol) and fluorine (30mmol) in 98% sulphuric acid (100ml) gave two fluorinated products (conv. 23 %) which were isolated using hexane/diethyl ether (2:1) as elutant; 2-fluoro-methyl-4-methoxybenzoate (**78**) (0.19g, 31%) as white crystalline solid; mp. 36.5-37.8 °C (lit.[160] 37.5°C); m/z (EI$^+$) 184 (M$^+$, 36%), 153(100), 125(15), 110(20), 82(30). NMR Spectrum No. 36; Mass Spectrum No. 36; 2,6-difluoro-methyl-4-methoxybenzoate (**79**) (0.07g, 10%) as white crystalline solid; mp. 69.8-70.9 °C (lit.[160] 70-71°C); m/z (EI$^+$) 202 (M$^+$, 57%), 171(100), 143(20), 128(22), 100(48). NMR Spectrum No. 37; Mass Spectrum No. 37; IR Spectrum No. 24.

e). 4-Nitroanisole (80) to give 2-Fluoro-4-nitroanisole (81) and 2,6-Difluoro-4-nitroanisole (82).

4-Nitroanisole (**80**) (2.44g, 15.9mmol) and fluorine (30mmol) in 98% sulphuric acid (100ml) gave two products (conv. 63%) . The resulting product mixture (2.3g) was dark and oily and was seen to consist of 2-fluoro-4-nitroanisole (**81**) (1.14g, 50%); δ_F (235 MHz, $CDCl_3$) -131.4 (s); m/z (EI$^+$) 171 (M$^+$, 100%), 141(38), 125(9), 110(20); and 2,6-difluoro-4-nitroanisole (**82**)(0.26g, 11%); δ_F (235 MHz, $CDCl_3$) -125.1 (2F, s); m/z (EI$^+$) 189 (M$^+$, 100%), 159(14), 143(14), 128(20), 100(12). The remainder of the mixture comprised 4-nitroanisole.

f). 4-Nitrophenol (83) to give 2-Fluoro-4-nitrophenol (84) and 2,6-Difluoro-4-nitrophenol (85).

4-Nitrophenol (**83**) (2.54g, 18.2 mmol) and fluorine (30mmol) in 98% sulphuric acid (100ml) gave two products, mono- and difluorinated derivatives. Recovery of the materials was poor (1.3g). This resulting product mixture was dark and oily and was seen to include 2-fluoro-4-nitrophenol (**84**) (0.67g, 23.5 %); δ_F (235 MHz, $CDCl_3$) -133.9 (s); and 2,6-difluoro-4-nitrophenol (**85**) (0.25g, 7.9 %); δ_F (235 MHz, $CDCl_3$) -130.6 (2F, s).

6.3. Fluorinations of a Range of Aromatic Substrates in Formic Acid.

General Procedure.

A solution containing of a 1,4-disubstituted aromatic (15-20mmol) was prepared in formic acid (100ml), in a glass reaction vessel fitted with overhead stirrer. The solution was cooled to 0 °C. Elemental fluorine in 10 % dilution with nitrogen (30mmol) was then passed through the solution at a rate of 10 ml/min. over the course of 4-5 hours. The reaction mix was poured into water (200ml) then extracted with dichloromethane (3x100ml). This extract was washed with sodium bicarbonate solution (2x50ml) then dried ($MgSO_4$). Excess solvent was removed under reduced pressure. Crude yields were calculated from ^{19}F NMR integrated against a known quantity of a reference, benzotrifluoride (2.5-3mmol). All products were isolated by gravity column chromatography on silica gel using hexane/dichloromethane or hexane/diethyl ether solvent mixtures as the elutant.

a). 4-Nitrophenol (83) to give 2-Fluoro-4-nitrophenol (84) and 2,6-Difluoro-4-nitrophenol (85).

4-Nitrophenol (2.5g, 18.0 mmol) and fluorine (30mmol) in formic acid (100ml) gave two fluorinated products. 2-Fluoro-4-nitrophenol **(84)** (2.0g, 70 %) was isolated using hexane/dichloromethane (2:1) as elutant, obtained as white crystals (Found: C, 45.61; H, 2.5; N, 8.66. Calc. for $C_6H_4NO_3F$: C, 45.9; H, 2.5; N, 8.9 %); mp. 116.8-118.5 °C (lit.[161] 117-118 °C); R_f 0.22; υ_{max}/cm^{-1} 1335.5 (Symmetric NO_2), 1517 (Asymmetric NO_2), 3086 (Aromatic CH), 3328 (OH); m/z (EI^+) 157 (M^+, 100%), 127(46), 83(95), 57(94). NMR Spectrum No. 29; Mass Spectrum No. 29. Also gave 2,6-difluoro-4-nitrophenol **(85)** (0.25g, 7.9 %); δ_F (235 MHz, $CDCl_3$) -130.6 (2F, s).

b). 4-Nitroanisole (80) to give 2-Fluoro-4-nitroanisole (81) and 2,6-Difluoro-4-nitroanisole (82).

4-Nitroanisole **(80)** (2.5g, 16.3mmol) and fluorine (30mmol) in formic acid (100ml) gave two fluorinated products (conv. 79 %) isolated using hexane/dichloromethane (2:1) as elutant; 2-Fluoro-4-nitroanisole **(81)** (1.22g, 56 %) was obtained as white crystals (Found: C, 49.3; H, 3.65; N, 8.0. Calc. for $C_7H_6NO_3F$: C, 49.1; H, 3.5; N, 8.2 %); mp. 95.1-96.3 °C (from ethanol) (lit.[161] 103.6-104.6 °C); R_f 0.22; υ_{max}/cm^{-1} 1504 (NO_2), 3092.5 (CH); m/z (EI^+) 171 (M^+, 100%), 141(38), 125(9), 110(18). NMR Spectrum No. 27; Mass Spectrum No. 27; IR Spectrum No. 17. 2,6-Difluoro-4-nitroanisole **(82)** (0.35g, 15%) was also produced as pale yellow crystals (Found: C, 44.15; H, 2.6; N 7.1. Calc. for $C_7H_5NO_3F_2$. C, 44.4; H, 2.6; N, 7.4 %); R_f 0.35; υ_{max}/cm^{-1} 1508.3 (NO_2), 3102 (CH); m/z (EI^+) 189 (M^+, 100%), 159(45), 143(14), 128(20), 100(12). NMR Spectrum No. 28; Mass Spectrum No. 28; IR Spectrum No 18.

c). 4-Cyanophenol (89) to give 2-Fluoro-4-cyanophenol (90) and 2,6-Difluoro-4-cyanophenol (91).

4-Cyanophenol **(89)** (2.0g, 17.1 mmol) and fluorine (30mmol) in formic acid (100ml) gave two fluorinated products (conv. 89 %); 2-fluoro-4-cyanophenol **(90)** (1.7g, 66 %) obtained as white crystals using hexane/diethyl ether (2:1) as elutant; mp. 133.5-134.6 °C (lit.[162] 134-135 °C); R_f 0.44; m/z (EI^+) 137 (M^+, 100%), 117(14), 89(32). NMR Spectrum No. 33; Mass Spectrum No. 33; IR Spectrum No. 21; and 2,6-difluoro-4-cyanophenol **(91)** (0.43g, 15 %).

d) 1-Methoxy-4-benzonitrile (92) to give 2-Fluoro-1-methoxy-4-benzonitrile (93) and 2,6-Difluoro-1-methoxy-4-benzonitrile (94).

1-Methoxy-4-benzonitrile **(92)** (2.0g, 15.0 mmol) and fluorine (30mmol) in formic acid (100ml) gave two fluorinated products (conv. 88 %); 2-Fluoro-1-methoxy-4-benzonitrile **(93)** (1.1g, 55 %) isolated using hexane/diethyl ether (1:1) as elutant, obtained as white crystals (Found: C, 62.91; H, 3.93; N, 9.09%. Calc. for C_8H_6NFO: C, 63.5 H, 4.0; N, 9.3 %); mp.95.6-97.0 °C (lit.[162] 96-98 °C); Rf 0.51; m/z (EI^+) 151 (M^+, 100%), 136(50), 108(78). NMR spectrum No. 31; Mass spectrum No. 31; IR spectrum No. 19; and 2,6-Difluoro-1-methoxy-4-benzonitrile **(94)** (0.47g, 21 %), isolated using hexane/diethyl ether (2:1), obtained as white crystals (Found: C, 56.34; H, 3.02; N, 7.93%. Calc. for $C_8H_5NF_2O$: C, 56.8; H, 3.0; N, 8.2%); mp.83.9-85.4 °C ; Rf 0.77; m/z (EI^+) 169 (M^+, 100%), 154(45), 126(48), 75(26).NMR Spectrum No. 32; Mass spectrum No. 32; IR spectrum No. 20.

e). 1-Methyl-4-benzonitrile (95) to give 1-Methyl-2-fluoro-4-benzonitrile (96).

1-Methyl-4-benzonitrile (2.0g, 17.1 mmol) and fluorine (30mmol) in formic acid (100ml) gave 1-methyl-2-fluoro-4-nitrobenzene **(96)** (1.05g, conv. 79 %, yield 56 %) isolated using hexane/dichloromethane (2:1) as elutant and obtained as white crystals (Found: C, 70.6; H, 4.23; N, 10.17%. Calc. for C_8H_6NF: C, 71.0; H, 4.4; N, 10.1 %); Rf 0.44; m/z (EI^+) 135 (M^+, 100%), 134(86), 108(32), 107(23). NMR Spectrum No. 35; Mass Spectrum No. 35; IR Spectrum No. 23..

f). 1-Fluoro-4-benzonitrile (87) to give 1,2-Difluoro-4-benzonitrile (97).

1-Fluoro-4-benzonitrile **(87)** (2.0g, 16.5 mmol) and fluorine (30mmol) in formic acid (100ml) gave 1,2-difluoro-4-nitrobenzonitrile **(97)** (0.97g, conv. 69 %, yield 62%), isolated using hexane/dichloromethane (1:2) as elutant and obtained as white crystals; Rf 0.54; m/z (EI^+) 139 (M^+, 100%), 112(35), 88(34), 75(17). NMR Spectrum No. 34; Mass Spectrum No. 34; IR Spectrun No. 22.

g) Methyl-4-Methoxy-benzoate (77) to give 2-Fluoro-methyl-4-methoxybenzoate (78) and 2,6-Difluoro-methyl-4-methoxybenzoate (79).

Methyl-4-Methoxy-benzoate **(77)** (2.5g, 15.1mmol) and fluorine (30mmol) in formic acid (100ml) gave two fluorinated products (conv. 66 %); 2-fluoro-methyl-4-

methoxybenzoate (**78**) (0.97g, 54%) and 2,6-difluoro-methyl-4-methoxybenzoate (**79**) (0.27g, 16.5%) isolated using hexane/diethyl ether (2:1); data as above.

h) 4-Tolualdehyde (75) to give 2-fluoro-4-Tolualdehyde (76).

4-Tolualdehyde (**75**) (2.5g, 20.8mmol) and fluorine (40mmol) in formic acid (100ml) gave 2-fluoro-4-tolualdehyde (**76**) (0.31g, conv. 32%, yield 34%); δ_F (235 MHz, $CDCl_3$) -116.1 (s); m/z (EI^+) 138 (M^+, 58%), 137(100), 109(98), 83(58), 63(30). 57(39). Mass Spectrum No. 38.

6.4 Investigations into the Effect of Copper(II) Salts as Possible Catalysts for Fluorination.

General Procedure.

A solution containing of a 1,4-disubstituted aromatic (15-20mmol) with copper(II) nitrate (2% by weight) was prepared in formic acid (100ml), in a glass reaction vessel fitted with overhead stirrer. The solution was cooled to 0 °C. Elemental fluorine in 10 % dilution with nitrogen (30mmol) was then passed through the solution at a rate of 10 ml/min. over the course of 4-5 hours. The reaction mix was poured into water (200ml) then extracted with dichloromethane (3x100ml). This extract was washed with sodium bicarbonate solution (2x50ml) then dried ($MgSO_4$). Excess solvent was removed under reduced pressure. The resulting mixture of products was analysed by ^{19}F NMR and GC/MS. Crude yields are calculated from ^{19}F NMR integrated against a known quantity of a reference, benzotrifluoride (0.38g, 2.6mmol). All products were isolated by column chromatography on silica gel using hexane/dichloromethane or hexane/diethyl ether solvent mixtures as the elutant.

a). 4-Nitroanisole (80).

4-Nitroanisole (**80**) (3.0g, 19.6mmol), copper(II) nitrate (0.07g, 0.37mmol) and fluorine (30mmol) in formic acid (100ml) gave two fluorinated products (conv. 79%), 2-fluoro-4-nitroanisole (**81**) (1.68g, 63%) and 2,6-difluoro-4-nitroanisole (**82**) (0.81g, 27%); data as above.

b) Methyl-4-Methoxy-benzoate (77).

4-Methoxy-methylbenzoate (3.0g, 18.0mmol), copper(II) nitrate (0.0.7g, 0.37mmol)and fluorine (30mmol) in formic acid (100ml) gave two fluorinated products (conv. 65%), 2-fluoro-methyl-4-methoxybenzoate **(78)** (1.13g, 51%) and 2,6-difluoro-methyl-4-methoxybenzoate **(79)** (0.55g, 23%); data as above.

Chapter Seven Experimental to Chapter Four.

7.1 Fluorination of Mesitylene (98) in a Variety of Solvents.

General Procedure.

A solution containing mesitylene was prepared in a variety of different solvents (35ml) in PTFE Reactor B*. Elemental fluorine (25mmol) as a 10% mixture in nitrogen was passed at a rate of 20ml/min over the course of 4 to 5 hours. The reaction mixture was poured into water and extracted with dichloromethane. The extract was washed using 10% sodium hydrogen carbonate solution (2x50), dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The mixture of products recovered was analysed by ^{19}F NMR and GC/MS, and where possible products were isolated by preparative gas chromatography using a 3m *SE30* column of packed silicone elastomer.

a) Acetonitrile.

Mesitylene **(98)** (2.3g, 19.2mmol) and fluorine (25mmol) in acetonitrile (35ml) gave a mixture of compounds (2.4g), which, characterised by ^{19}F NMR and GC/MS, was shown to contain mesitylene (40 %), 2-fluoro-1,3,5-trimethylbenzene **(99)** (16 %); δ_F (235 MHz, $CDCl_3$, $CFCl_3$) -128.4 (s); m/z (EI^+) 138 (M^+, 67 %), 123 (100), 115 (9), 109 (12); and 1-fluoromethyl-3,5-dimethylbenzene **(100)** (24 %), with small traces of di- and trifluorinated analogues of each of these products (approx. 13 % in total). Some high molecular mass products were also observed, m/z 238 and 256 (7 %), possibly coupling products. The ratio of 2-fluoro-1,3,5-trimethylbenzene : 1-fluoromethyl-3,5-dimethylbenzene was measured by the relative intensities of ^{19}F NMR spectrum and shown to be approx. 1:2:

1-Fluoromethyl-3,5-dimethylbenzene was isolated by prep GC using an *SE30* column at 80-90 °C; δ_F (235 MHz, $CDCl_3$) -206.1(1F, t, $^2J_{HF}$ 52.9, CH_2F); m/z (EI^+) 138 (M^+, 53.71 %), 123(100), 105 (50), 91 (21), 77 (31). NMR Spectrum No. 38; Mass Spectrum No. 39.

b) 4:1 Acetonitrile/Formic Acid.

Mesitylene **(98)** (2.1g, 17.5mmol) and fluorine (25mmol) in 4:1

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* See Chapter Four, fig 4.2

acetonitrile/formic acid gave a mixture of compounds (2.3g) which, characterised by ^{19}F NMR and GC/MS, was shown to contain mesitylene (63 %), 2-fluoro-1,3,5-trimethylbenzene **(99)** (21 %) and 1-fluoromethyl-3,5-dimethylbenzene **(100)** (6 %), with small traces of di- and trifluorinated analogues of each of these products. The formate ester of 1-fluoromethyl-3,5-dimethylbenzene was also present, formic acid-3,5-dimethyl benyzl ester **(101)** (10 %). The ratio of 2-fluoro-1,3,5-trimethylbenzene:1-fluoromethyl-3,5-dimethylbenzene was measured by the relative intensities of ^{19}F NMR spectrum and shown to be 3:1, though this value was adjusted to include the amount of the ester from benzyl fluoride formed to give a final value of 3:2; data as above.

Formic acid-3,5-dimethyl benzyl ester was isolated by prep GC using an *SE30* column at 110-120 °C; m/z (EI$^+$) 164 (M$^+$, 100 %), 136(49), 119(84), 91 (37), 77 (20); NMR Spectrum No.39; Mass Spectrum No.40.

c) 3:2 Acetonitrile/Formic Acid.

Mesitylene **(98)** (2.1g, 17.5mmol) and fluorine (25mmol) in 3:2 acetonitrile/formic acid gave a mixture of compounds (2.2g), which, characterised by ^{19}F NMR and GC/MS, was shown to contain mesitylene (49 %), 2-fluoro-1,3,5-trimethylbenzene **(99)** (29 %) and 1-fluoromethyl-3,5-dimethylbenzene **(100)** (7 %), with small traces of di- and trifluorinated analogues of each of these products. Formic acid-3,5-dimethyl benzyl ester was also present **(101)** (14 %), as were traces of high molecular mass products. Again the ratio of 2-fluoro-1,3,5-trimethylbenzene:1-fluoromethyl-3,5-dimethylbenzene was measured by the relative intensities of ^{19}F NMR spectrum and shown to be 3:1, though this value was adjusted to include the amount of the ester from benzyl fluoride formed to give a final value of 3:2; data as above.

d) Trifluoroacetic Acid.

Mesitylene **(98)** (1.98g, 16.5mmol) and fluorine (25mmol) in trifluoroacetic acid (35ml) gave a mixture of starting material and product (1.3g). 2-Fluoro-1,3,5-trimethylbenzene **(99)** was the only product observed but conversion was low (5-6 %), the bulk of recovered material was mesitylene; data as above.

e) 1:1 Acetonitrile/Trifluoroacetic Acid.

Mesitylene **(98)** (1.82g, 15.0mmol) and fluorine (25mmol) in 1:1 acetonitrile/ trifluoroacetic acid (35ml) gave a mixture of compounds (1.8g), which, characterised by ^{19}F NMR and GC/MS, was shown to contain mesitylene (47 %), 2-fluoro-1,3,5-trimethylbenzene **(99)** (20 %) and 1-fluoromethyl-3,5-dimethylbenzene **(100)** (7 %), with small traces of di- and trifluorinated analogues of each of these products. The trifluoroacetate ester, trifluoroacetic acid-3,5-dimethyl benzyl ester **(105)** was also present (14 %); δ_F (235 MHz, $CDCl_3$, $CFCl_3$) -75.3 (s); m/z (EI^+) 232 (M^+, 71 %), 135 (30), 119 (100), 117 (49), 91 (28); Mass Spectrum No. 42; as was its ring fluorinated analogue (3%); m/z (EI^+) 250 (M^+, 45 %), 137 (100), 136 (46), 109 (15). Also observed was the amide derivative of 1-fluoromethyl-3,5-dimethylbenzene, N-(3,5-Dimethylbenzyl)-acetamide **(106)** (7 %); m/z (EI^+) 177 (M^+, 100 %), 134 (64), 120 (67), 118 (42),107 (20), 91 (16); as were some high molecular mass products, m/z 238 and 274 (8 %), possibly coupling products. In this analysis, the ratio of electrophilic:radical products was established as approx. 4:3; data as above.

f) 98 % Sulphuric Acid.

Mesitylene **(98)** (2g, 16.7mmol) and fluorine (25mmol) in 98 % sulphuric acid (30ml) gave a mixture of products. Recovery of the product mixture was poor (0.6g) with the recovered products obtained in a mixture of black tars. Analysis by ^{19}F NMR and GC/MS indicated that mesitylene had been completely sulphonated **(107)** then undergone fluorination to 2-fluoro-4-sulphonyl-1,3,5-trimethylbenzene **(108)** in 37 % conversion. Poor recovery may be due to sulphonated material being retained in the aqueous phase.

g) Lewis Acids.

N.B. Fluorinations of mesitylene in presence of Lewis Acids were carried out in a glass fluorination vessel at 0 °C, similar to that used in the fluorination of deactivated aromatics.‡

i) Boron Trifluoride Etherate.

Mesitylene **(98)** (10g, 83.3mmol), boron trifluoride etherate (15g, 105.6mmol) and fluorine (75.5mmol) in acetonitrile (200ml) gave a mixture of products (12.8g). Analysis by GC/MS and ^{19}F NMR showed a 15 % conversion of mesitylene to 2-fluoro-

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‡ See Chapter Three, fig 3.2

1,3,5-trimethylbenzene **(99)**, with the bulk of starting material unreacted; data as above.

ii) Boron Trifluoride Etherate with Excess Fluorine.

Mesitylene **(98)** (3.2g, 26.6mmol), boron trifluoride etherate (7g, 49.3mmol) and fluorine (60.4mmol) in acetonitrile (200ml) gave a complex mixture of black, viscous tars.

iii) Excess Boron Trifluoride Etherate.

Mesitylene **(98)** (2g, 16.7mmol), boron trifluoride etherate (9.5g, 66.9mmol) and fluorine (22.5mmol) in acetonitrile (200ml) gave a complex mixture of black, viscous tars.

iv) Boron Trifluoride Etherate and Triethylamine.

Mesitylene **(98)** (2.1g, 17.5mmol), boron trifluoride etherate (5.5g, 38.7mmol), triethylamine (2g, 19.8 mmol) and fluorine (30mmol) in acetonitrile (200ml) gave a mixture (1.8g) of mesitylene and 2-fluoro-1,3,5-trimethylbenzene (conv. approx. 3 %).

v) Boron Trifluoride Etherate and Potassium Carbonate.

Mesitylene **(98)** (5.0g, 41.6mmol), boron trifluoride etherate (15g, 105.6mmol), potassium carbonate (10.7g, 77.5 mmol) and fluorine (40mmol) in acetonitrile (200ml) gave a mixture (3.8g) of mesitylene and 2-fluoro-1,3,5-trimethylbenzene (conv. approx. 2 %).

h) Fluorination of Mesitylene (98) Using Selectfluor™ (31).

General Procedure.

A solution consisting of mesitylene (6mmol) was prepared in acetonitrile or trifluoroacetic acid (40ml) in a round bottom flask (250ml). Selectfluor™ (2.0 g, 5.6mmol) was added and the mixture was left overnight at room temperature with continuous stirring by a PTFE coated magnetic stirrer bar. After this time the reaction mixture was poured into water, extracted using dichloromethane (3 x 50ml), dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The product mixture was analysed by GC/MS and ^{19}F NMR and where possible products were isolated by preparative gas chromatography and further characterised.

i) Acetonitrile.

Mesitylene **(98)** (0.75 g, 6.25 mmol) and Selectfluor™ **(31)** (2.0 g, 5.6mmol) in acetonitrile (40ml) gave a single product, 1-fluoro-2,4,6-trimethylbenzene **(99)** (0.25g, conv. 50 % , yield 29%); δ_F (235 MHz, $CDCl_3$, $CFCl_3$) -128.4 (s); m/z (EI^+) 138 (M^+, 51 %) 123 (100)

ii) Trifluoroacetic acid.

Mesitylene **(98)** (0.75 g, 6.25 mmol) and Selectfluor™ **(31)** (2.0g, 5.6mmol) in trifluoroacetic acid (40ml) gave a single product, 1-fluoro-2,4,6-trimethylbenzene **(99)** (0.45g, conv. 75 %, yield 52%) which was isolated by prep GC using an *SE30* column at 140 °C and further characterised by ^1H and ^{13}C NMR; m/z (EI^+) 138.(M^+, 52.6 %) 123 (100); NMR Spectrum No.40; Mass Spectrum No. 41.

7.2 Fluorinations of 4-Nitrotoluene (67).

General Procedure.

A solution containing nitrotoluene (15-16mmol) was prepared in a variety of different solvents (30ml) in fluorination Reactor B. Elemental fluorine (25mmol) as a 10% mixture in nitrogen was passed at a rate of 20ml/min over the course of 4 to 5 hours. The reaction mixture was poured into water and extracted with dichloromethane. The extract was washed using dilute sodium hydrogen carbonate solution, dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The mixture of products recovered was analysed by ^{19}F NMR and GC/MS.

a) Trifluoroacetic Acid.

4-Nitrotoluene **(67)** (2.3g, 16.8mmol) and fluorine (25mmol) in trifluoroacetic acid (30ml) gave 2-fluoro-4-nitrotoluene **(68)** (0.47g, conv. 29 %, yield 71 %); See Chapter Six for data.

b) Acetonitrile.

4-Nitrotoluene **(67)** (2.2g, 16.1 mmol) and fluorine (25mmol) in acetonitrile (30ml) gave a mixture (2.3g) of start material and 2-fluoro-4-nitrotoluene **(68)** (conv. 17-18 %); See Chapter Six for data.

c) Selectfluor™ Fluorination in Trifluoroacetic acid.

A solution consisting of 4-nitrotoluene **(67)** (1.1g, 8mmol) and Selectfluor™ **(31)** (3g, 8.5mmol) was prepared in trifluoroacetic acid (30ml) in a round bottom flask (250ml). The mixture was left overnight at room temperature with continuous stirring by a PTFE coated magnetic stirrer bar. After this time the reaction mixture was poured into 10 % sodium bicarbonate solution, extracted using dichloromethane (3 x 50ml), dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. GC/MS and ^{19}F NMR indicated that no reaction had occurred.

7.3 Competition Reactions between Mesitylene and Nitro-derivatives.

General Procedure.

A solution containing mesitylene and a nitro-derivative, in varying amounts according to the experiment being carried out, was prepared in trifluoroacetic acid (30ml) in fluorination Reactor B. Elemental fluorine (9mmol) as a 10% mixture in nitrogen was passed at a rate of 10ml/min over the course of 4 to 5 hours. The reaction mixture was poured into water and extracted with dichloromethane. This extract was washed with 10% sodium bicarbonate solution (2x50ml), dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The resulting mixture of products and starting materials was analysed by GC/MS and ^{19}F NMR.

a) Competition Reactions between Mesitylene and Nitrotoluene.

i) 1:1 Mesitylene and Nitrotoluene.

Mesitylene **(98)** (1g, 8.3mmol), nitrotoluene **(67)** (1g, 7.3mmol) and fluorine (9mmol) in trifluoroacetic acid (30ml) gave a mixture of product and starting materials (1.7g), with analysis by GC/MS indicating a 20 % conversion of mesitylene to 2-fluoro-1,3,5-trimethylbenzene **(99)**, but no reaction of nitrotoluene; data as above.

ii) 5:1 Mesitylene and Nitrotoluene.

Mesitylene **(98)** (1.8g, 15mmol) and nitrotoluene **(67)** (0.4g, 3mmol) in trifluoroacetic acid (30ml) and elemental fluorine (9mmol) gave a mixture of product and starting materials (1.5g), with analysis by GC/MS indicating a 16-17 % conversion of mesitylene to 2-fluoro-1,3,5-trimethylbenzene **(99)**, but no reaction of nitrotoluene; data as above.

b) Competition between Mesitylene and Nitrobenzene (1:1).

Mesitylene **(98)** (1g, 8.3mmol) and nitrobenzene **(109)** (1g, 8.1mmol) in trifluoroacetic acid (30ml) and elemental fluorine (9mmol) gave a mixture of product and starting materials (1.8g), with analysis by GC/MS indicating a 21 % conversion of mesitylene to 2-fluoro-1,3,5-trimethylbenzene **(99)**, but no reaction of nitrobenzene; data as above.

c) Competition Reactions between Mesitylene and Nitromethane.

i) 1:2 Mesitylene and Nitromethane.

Mesitylene **(98)** (1g, 8.3mmol) and nitromethane **(110)** (1g, 16.3mmol) in trifluoroacetic acid (30ml) and elemental fluorine (9mmol) gave a mixture of product and starting materials (1.2g), with analysis by GC/MS indicating a 14 % conversion of mesitylene to 2-fluoro-1,3,5-trimethylbenzene **(99)**, but no reaction of nitromethane; data as above.

ii) 5:1 Mesitylene and Nitromethane.

Mesitylene **(98)** (1.8g, 15mmol) and nitromethane **(110)**(0.2g, 3.3mmol) in trifluoroacetic acid (30ml) and elemental fluorine (9mmol) gave a mixture of product and starting materials (1.7g), with analysis by GC/MS indicating a 17 % conversion of mesitylene to 2-fluoro-1,3,5-trimethylbenzene **(99)**, but no reaction of nitromethane; data as above.

iii) Nitromethane as a solvent.

Mesitylene **(98)** (2g, 16.7mmol) was prepared in nitromethane **(110)** (30ml) and elemental fluorine (25mmol) gave a complex series of products (2.2g), with analysis by GC/MS indicating approx. 75 % conversion of mesitylene, including products of fluorination on both the aromatic ring and methyl side chain.

d) Fluorinations of Mesitylene in Trifluoroacetic Acid with Added 2,4-Dinitrotoluene.

N.B. Fluorinations of mesitylene in presence of 2,4-dinitrotoluene were carried out in a glass fluorination vessel at 0 °C, similar to that used in the fluorination of deactivated aromatics.‡

i) 1:1 Mesitylene and 2,4-Dinitrotoluene.

Mesitylene **(98)** (2.1g, 17.5mmol), 2,4-dinitrotoluene **(111)** (2.5g, 13.7mmol) and fluorine (20mmol) in trifluoroacetic acid (100ml) gave a mixture of product and starting materials (3.7g), with analysis by GC/MS indicating a 31 % conversion of

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‡ See Chapter Three, fig 3.2

mesitylene to give 2-fluoro-1,3,5-trimethylbenzene **(99)** (21%) and 2,4-difluoro-1,3,5-trimethylbenzene **(112)** (10%), but no reaction of 2,4-dinitrotoluene; data as above.

ii) 5:1 Mesitylene and 2,4-Dinitrotoluene.

Mesitylene **(98)** (2.1g, 17.5mmol), 2,4-dinitrotoluene **(111)** (0.6g, 3.3mmol) and fluorine (20mmol) in trifluoroacetic acid (100ml) gave a mixture of product and starting materials (2.0g), with analysis by GC/MS indicating a 30 % conversion of mesitylene to give 2-fluoro-1,3,5-trimethylbenzene **(99)** (18%) and 2,4-difluoro-1,3,5-trimethylbenzene **(112)** (6%) with the remainder being a mixture of high mass products, m/z 238, 256 and 274 (6%), but no reaction of 2,4-dinitrotoluene; data as above.

iii) 1:2 Mesitylene and 2,4-Dinitrotoluene.

Mesitylene **(98)** (2.1g, 17.5mmol), 2,4-dinitrotoluene **(111)** (6.2g, 34.1mmol) and fluorine (25mmol) in trifluoroacetic acid (100ml) gave a mixture of product and starting materials (1.9g), with analysis by GC/MS indicating a 25 % conversion of mesitylene to give 2-fluoro-1,3,5-trimethylbenzene **(99)** (20%) and 2,4-difluoro-1,3,5-trimethylbenzene **(112)** (5%) but no reaction of 2,4-dinitrotoluene; data as above.

7.4 The Preparation of Electrophilic Fluorinating Agents *In Situ* by Direct Fluorination.

a) Caesium Fluoroxysulphate.

i) 1:1 Mesitylene/Caesium Fluoroxysulphate (Two Step Reaction).

A solution of caesium sulphate (13g, 35.9mmol) was prepared in deionised water (20ml) in PTFE Reactor A[§] and cooled to 0 °C. Elemental fluorine (30mmol), diluted to 10% with nitrogen, was passed at a rate of 20ml/min over the course of 5-6 hours, leading to the formation of a white precipitate, caesium fluoroxysulphate. A solution of mesitylene **(98)** (4.0g, 33mmol) prepared in acetonitrile (20ml) was then added to this suspension and allowed to stir overnight, over which time the precipitate redissolves. The reaction mixture was poured into water and extracted with dichloromethane. This extract was washed with dilute sodium bicarbonate solution, dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The resulting mixture of product and starting materials was characterised by GC/MS and ^{19}F NMR. This indicated a 12%

[§] See Chapter Two, fig 2.5

conversion of mesitylene to give its monofluorinated analogue (**99**).

ii) 1:2 Mesitylene/Caesium Fluoroxysulphate (Two Step Reaction).

A solution of caesium sulphate (6.5g, 17.9mmol) was prepared in deionised water (10ml) in PTFE Reactor A and cooled to 0 °C. Elemental fluorine (30mmol), diluted to 10% with nitrogen, was passed at a rate of 20ml/min over the course of 5-6 hours, leading to the formation of a white precipitate, caesium fluoroxysulphate. A solution of mesitylene (**98**) (1.01g, 8.4mmol) prepared in acetonitrile (10ml) was then added to this suspension and allowed to stir overnight, over which time the precipitate redissolves. The reaction mixture was poured into water and extracted with dichloromethane. This extract was washed with dilute sodium bicarbonate solution, dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The resulting mixture of product and starting materials was characterised by GC/MS and ^{19}F NMR. This indicated a 20% conversion of mesitylene to give its monofluorinated analogue (**99**).

iii) *In Situ* Reaction of Mesitylene and Caesium Fluoroxysulphate in Water.

A solution of caesium sulphate (30g, 82.9mmol) and mesitylene (2.0g, 16.7mmol) was prepared in deionised water (40ml) in PTFE Reactor A, with continuous stirring using a magnetic stirrer bar and cooled to 0 °C. Mesitylene (**98**) was poorly soluble in water, but vigorous stirring was employed to allow efficient mixing of reagents. Elemental fluorine (151mmol), diluted to 20% with nitrogen, was passed at a rate of 20ml/min overnight. The reaction mixture was poured into water and extracted with dichloromethane. This extract was washed with dilute sodium bicarbonate solution, dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The resulting mixture of product and starting materials was characterised by GC/MS and ^{19}F NMR. No mesitylene recovered, believed to been lost from the reaction vessel by evaporation.

iv) *In Situ* Reaction of Mesitylene and Caesium Fluoroxysulphate in 1:1 Acetonitrile/Water Mixture.

A solution of caesium sulphate (30g, 82.9mmol) and mesitylene (**98**) (2.0g, 16.7mmol) was prepared in a 1:1 mixture of acetonitrile and deionised water (60ml) in PTFE Reactor A, with continuous stirring using a magnetic stirrer bar and cooled to 0 °C. Elemental fluorine (151mmol), diluted to 20% with nitrogen, was passed at a rate of 20ml/min overnight. The reaction mixture was poured into water and extracted with dichloromethane. This extract was washed with dilute sodium bicarbonate solution, dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The resulting mixture of product and starting materials was characterised by GC/MS and ^{19}F NMR, which indicated that the conversion of mesitylene to the monofluoro. product (**99**) was less than 1% and the bulk of the recovered mixture was starting material.

b) The Attempted Regeneration of Selectfluor™ *In Situ* by Direct Fluorination.

A solution of mesitylene (**98**) (3.5g, 30mmol) with Selectfluor™ (**31**) (1.0g, 3mmol) was prepared in trifluoroacetic acid and allowed to stir overnight at room temperature. The mixture was then transferred to a glass fluorination reactor and cooled to 0 °C. Elemental fluorine (60mmol) was passed at a rate of 20ml/min overnight. The reaction mixture was poured into water and extracted with dichloromethane. This extract was washed with dilute sodium bicarbonate solution, dried ($MgSO_4$) and the excess solvent was removed under reduced pressure. The resulting mixture of product and starting materials was characterised by GC/MS and ^{19}F NMR. A mixture of products was obtained (3.0g), with analysis by GC/MS indicating a 69% conversion (30%) of mesitylene to give 2-fluoro1,3,5-trimethylbenzene (**99**) (28%) and 2,4-difluoromesitylene (10%) with a large portion of the recovered material composed of a mixture of high mass products (26% in total).

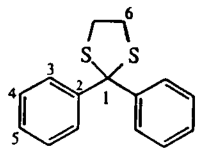
Appendices.

Appendix One Nuclear Magnetic Resonance Spectra.

No. 1 2,2 Diphenyl-1,3-dithiolane (**37**).
No. 2 2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane (**39**).
No. 3 2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane (**40**).
No. 4 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane (**41**).
No. 5 2,2-Bis(4-fluorophenyl)-1,3-dithiolane (**42**).
No. 6 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane (**38**).
No. 7 2-(4-Nitrophenyl)-2-phenyl-1,3-dithiolane (**48**).
No. 8 2-(3-Trifluoromethylphenyl)-2-phenyl-1,3-dithiolane (**47**).
No. 9 2-Butyl-2-phenyl-1,3-dithiolane (**43**).
No. 10 2-Butyl-2-methyl-1,3-dithiolane (**45**).
No. 11 2-Ethyl-2-pentyl-1,3-dithiolane (**46**).
No. 12 Cyclododecan-1,3-dithiolane (**44**).
No. 13 Benzophenone (**58**).
No. 14 Cyclododecanone (**59**).
No. 15 4-Chlorobenzophenone (**60**).
No. 16 Butyrophenone (**61**).
No. 17 2-Hexanone (**62**).
No. 18 3-Octanone (**63**).
No. 19 Diphenyldifluoromethane (**49**).
No. 20 1-Chlorophenyl-1-phenyl-difluoromethane (**50**).
No. 21 1-Bromophenyl-1-phenyl-difluoromethane (**52**).
No. 22 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane (**53**).
No. 23 2,2-Bis(4-fluorophenyl)-1,3-dithiolane (**54**).
No. 24 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane (**51**).
No. 25 2-Fluoro-4-nitrotoluene (**68**).
No. 26 1-Chloro-2-fluoro-4-nitrobenzene (**74**).
No. 27 2-Fluoro-4-nitroanisole (**81**).
No. 28 2,6-Difluoro-4-nitroanisole (**82**).
No. 29 2-Fluoro-4-nitrophenol (**84**).
No. 30 1,2-Difluoro-4-nitrobenzene (**71**).
No. 31 2-Fluoro-1 methoxy-4-benzonitrile (**93**).
No. 32 2,6-Difluoro-1-methoxy-4-benzonitrile (**94**).
No. 33 2-Fluoro-1-hydroxy-4-benzonitrile (**90**).
No. 34 1,2-Difluoro-4-benzonitrile (**97**).
No. 35 1-Methyl-2-fluoro-4-benzonitrile (**96**).
No. 36 2-Fluoro-4-methoxy-methylbenzoate (**78**).
No. 37 2,6-Difluoro-4-methoxy-methylbenzoate (**79**).

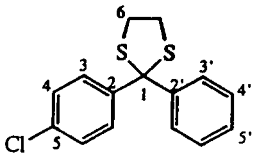
No. 38	1-Fluoromethyl-3,5-dimethylbenzene (**100**).
No. 39	Formic Acid-3,5-dimethylbenzyl ester (**101**).
No. 40	2-Fluoro-1,3,5-trimethylbenzene (**99**).

No. 1 **2,2 Diphenyl-1,3-dithiolane.**



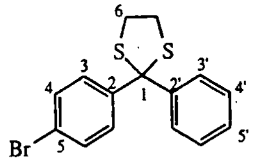
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H :-			
3.9	s	4 H	SCH_2
7.3-7.5	m	10 H	Ar-H
^{13}C:-			
40.1	s		6
76.8	s		1
127.2	s		5
127.9	s		3
128.1	s		4
144.5	s		2

No. 2 **2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane.**



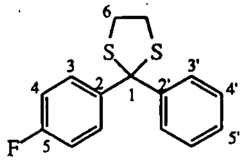
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
3.4	s	4 H	SCH_2
7.2-7.6	m	9 H	Ar-H
^{13}C:-			
40.3	s		6
76.2	s		1
127.4	s		5'
128.0	s		3'
128.05	s		3
128.1	s		4'
129.7	s		4
133.0	s		5
143.4	s		2
143.9	s		2'

No. 3 2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane.



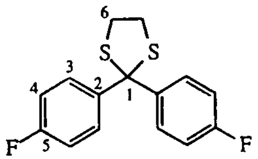
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H :-			
3.37	s	4 H	SCH_2
7.2-7.6	m	9 H	Ar-H
^{13}C:-			
40.3	s		6
76.2	s		1
121.2	s		5
127.4	s		5'
128.05	s		3'
128.1	s		4'
130.0	s		4
130.9	s		3
143.8	s		2
144.0	s		2'

No. 4 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane.



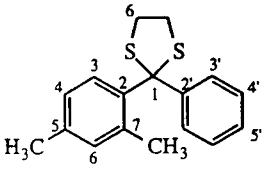
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H :-			
3.5	s	4 H	SCH_2
7.0-8.0	m	9 H	Ar-H
^{13}C:-			
40.3	s		6
76.1	s		1
114.4	d, ^{2}J 21.7		4
128.0	s		5'
128.05	s		3'
128.1	s		4'
129.8	d, ^{3}J 8.04		3
140.2	d, ^{4}J 3.03		2
144.1	s		2'
161.6	d, ^{1}J 247		5
^{19}F:-			
-115.58	s	1 F	

No. 5 2,2-Bis(4-fluorophenyl)-1,3-dithiolane.



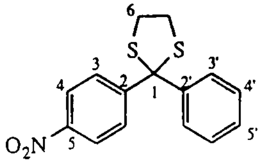
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
3.4	s	4 H	SCH_2
6.99	m	4 H	Ar-H
7.62	m	4 H	Ar-H
^{13}C:-			
40.3	s		6
76.3	s		1
114.7	d, ^2J 21.5		4
130.1	d, ^3J 8.0		3
140.1	d, ^4J 3.1		2
162.4	d, ^1J 246		5
^{19}F:-			
-115.7	s	2 F	

No. 6 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane.



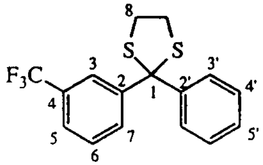
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H :-			
1.93	s	3 H	CH_3
2.35	s	3 H	CH_3
3.45	m	4 H	SCH_2
6.9-8.1	m	8 H	Ar-H
^{13}C:-			
20.7	s		CH_3
21.8	s		CH_3
40.4	s		8
76.0	s		1
125.8	s		4
126.9	s		3
127.0	s		3'
128.0	s		4'
133.4	s		6
136.3	s		5
137.2	s		7
139.6	s		2
144.1	s		2'

No. 7 2-(4-Nitrophenyl)-2-phenyl-1,3-dithiolane.



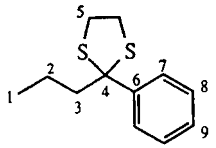
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
3.5	s	4 H	SCH_2
7.0-8.5	m	9 H	Ar-H
^{13}C:-			
41.2	s		6
76.8	s		1
123.7	s		
124.0	s		
128.3	s		
128.5	s		
128.8	s		
129.2	s		
130.6	s		
131.2	s		
134.0	s		

No. 8 2-(3-Trifluoromethylphenyl)-2-phenyl-1,3-dithiolane.



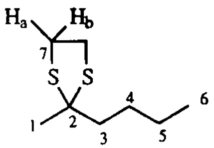
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H :-			
3.4	s	4 H	SCH_2
7.2-8.1	m	9 H	Ar-H
^{13}C:-			
41.0	s		8
76.9	s		1
124.0	q, ^1J 264.5		CF_3
124.05	q, ^3J 3.82		3
124.7	q, ^3J 3.82		5
127.5	s		5'
128.1	s		4'
127.5	s		3'
128.4	s		8
130.2	q, ^2J 33.5		4
131.8	s		7
143.6	s		2'
146.2	s		2
^{19}F:-			
-62.7	s	3 F	CF_3

No. 9 2-Butyl-2-phenyl-1,3-dithiolane.



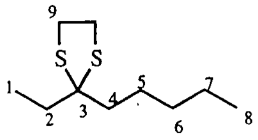
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
0.8	m	3H	$^1CH_3$
1.4	m	2H	$^2CH_2$-
2.3	m	2H	$^3CH_2$-
3.4	s	4 H	SCH_2
7.2	m	3 H	Ar-$H_{ortho\ \&\ para}$
7.7	m	2 H	Ar-H_{meta}
^{13}C:-			
14.7	s		1
21.7	s		2
39.6	s		3
48.8	s		5
74.8	s		4
127.4	s		9
127.6	s		7 or 8
128.4	s		8 or 7
145.7	s		6

No. 10 2-Butyl-2-methyl-1,3-dithiolane.



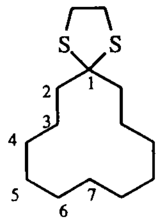
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
1.7	m	6 H	CH_3
1.9	m	6 H	CH_2
3.2	s	2 H	SCH_a
3.2	s	2 H	SCH_b
^{13}C:-			
14.5	s		6
23.4	s		1
30.0	s		5
32.8	s		4
40.2	s		3
46.1	s		7
67.3	s		2

No. 11 2-Ethyl-2-pentyl-1,3-dithiolane.



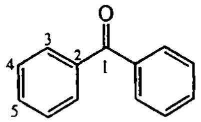
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
0.8	t, ^{2}J 7.0	3 H	$^{1}CH_3$
1.0	t, ^{2}J 7.19	3 H	$^{8}CH_3$
1.2	m	2 H	$^{7}CH_2$
1.4	m	2 H	$^{5}CH_2$
1.8	m	2 H	$^{4}CH_2$
1.9	q, J 7.33	2 H	$^{3}CH_2$
3.2	s	4 H	SCH_2
^{13}C:-			
11.0	s		1
13.9	s		8
22.4	s		7
26.4	s		5
31.8	s		6
36.0	s		9
39.3	s		2
42.8	s		4
72.2	s		3

No. 12 Cyclododecan-1,3-dithiolane.



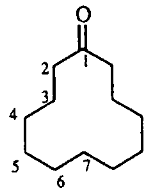
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
1.3	br m	14 H	$-CH_2-$
2.0	m	4 H	$^{2}CH_2$
3.2	s	4 H	SCH_2
^{13}C:-			
22.4	s		
22.6	s		
22.7	s		
25.9	s		
26.4	s		
38.6	s		
38.9	s		
71.1	s		1

No. 13 Benzophenone.



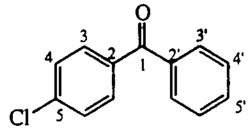
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H :-			
7.4-7.9	m	10 H	Ar-H
^{13}C:-			
128.3	s		4
130.1	s		3
132.4	s		5
137.6	s		2
196.8	s		1

No. 14 Cyclododecanone.



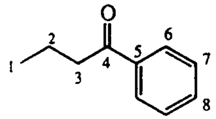
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
1.3	br m	14 H	$-CH_2-$
1.7	m	4 H	$^2CH_2$
2.4	s	4 H	$^1CH_2$
^{13}C:-			
22.3	s		
22.6	s		
24.2	s		
24.6	s		
24.8	s		
40.4	s		
213.0	s		1

No. 15 4-Chlorobenzophenone.



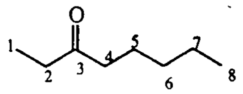
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H :-			
7.4-7.9	m	9 H	Ar-H
^{13}C:-			
128.4	s		4'
128.6	s		4
129.9	s		3'
131.2	s		3
132.6	s		3
135.8	s		2'
137.2	s		2
138.9	s		5
195.9	s		1

No. 16 Butyrophenone.



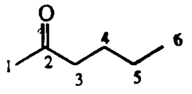
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
1.0	t, J 7.32	3H	$^1CH_3$
1.8	sex, J 7.32	2H	$^2CH_2$-
2.9	t, J 7.32	2H	$^3CH_2$-
7.4	m	3 H	Ar-$H_{ortho\ \&\ para}$
7.9	m	2 H	Ar-H_{meta}
^{13}C:-			
13.9	s		1
17.8	s		2
40.5	s		3
128.0	s		6
128.5	s		7
132.9	s		8
137.1	s		5
200.4	s		4

No. 18 3-Octanone.



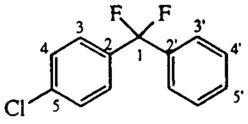
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
0.6	t, J 6.73	3 H	$^1CH_3$
0.7	t, J 7.33	3 H	$^8CH_3$
0.9	br m	2 H	$^6CH_2$
1.2	p, J 7.30	2 H	$^7CH_2$
2.08	t, J 7.5	2 H	$^4CH_2$
2.085	q, J 7.5	2 H	$^2CH_2$
^{13}C:-			
6.6	s		8
12.7	s		1
21.2	s		
21.4	s		
30.6	s		
34.7	s		
41.2	s		
210.9	s		3

No. 17 2-Hexanone.



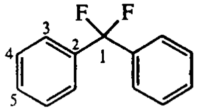
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
0.9	t	3 H	$-^6CH_3$
1.3-2.4	m	9 H	$-CH_2-$
^{13}C:-			
13.4	s		6
22.0	s		1
25.7	s		5
29.6	s		4
43.2	s		3
209.3	s		2

No. 20 1-Chlorophenyl-1-phenyl-difluoromethane.



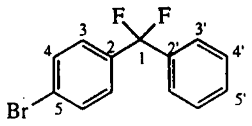
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
7.4-7.6	m	9 H	Ar-H
^{13}C:-			
120.3	t, ^{1}J 241		1
125.7	t, ^{3}J 5.04		4'
127.3	t, ^{3}J 5.04		4
128.5	s		5'
128.6	s		5
130.0	t, ^{4}J 2.01		3'
136.0	t, ^{4}J 2.01		3
136.2	t, ^{2}J 30.2		2
137.1	t, ^{2}J 30.2		2'
^{19}F:-			
-89.3	s	2 F	

No. 19 Diphenyldifluoromethane.



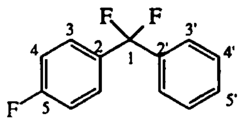
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H :-			
7.4	m	10 H	Ar-H
^{13}C:-			
120.7	t, ^{1}J 239		1
125.8	t, ^{3}J 5.67		3
128.7	s		5
129.8	t, ^{4}J 1.74		4
137.7	t, ^{2}J 28.40		2
^{19}F:-			
-89.3	s	2 F	

No. 21 1-Bromophenyl-1-phenyl-difluoromethane.



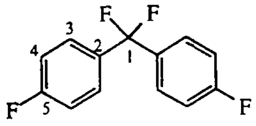
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H :-			
7.2-7.5	m	9 H	Ar-H
^{13}C:-			
120.3	t, ^1J 242		1
124.3	t, ^4J 1.91		3'
125.6	t, ^3J 5.53		4'
127.5	t, ^3J 5.53		4
128.5	s		5'
130.0	t, ^4J 1.91		3
131.6	s		5
136.7	t, ^2J 28.67		2
137.0	t, ^2J 28.67		2'
^{19}F:-			
-89.6	s		

No. 22 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane.



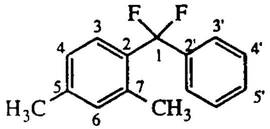
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H :-			
7.0-7.7	m	9 H	Ar-H
^{13}C:-			
115.4	d, ^2J 21.7		4
120.4	t, ^1J 241.6		1
125.8	t, ^3J 5.3,		3'
128.1	td, ^3J 5.53, ^3J 8.75		3
128.5	s		4'
130.0	s		5'
133.7	td, ^2J 27.2, ^4J 3.4		2
137.4	t, ^2J 28.3,		2'
163.5	d, ^1J 249.4		5
^{19}F:-			
-88.0	s	2 F	$-CF_2$
-111.4	s	1 F	Ar-F

No. 23 2,2-Bis(4-fluorophenyl)-1,3-dithiolane.



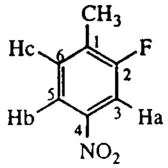
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H :-			
7.2-7.6	m	8 H	Ar-H
^{13}C:-			
115.5	d, ^{2}J 22.1		4
120.1	t, ^{1}J 241		1
128.0	m		3
133.4	td, ^{2}J 28.9, ^{4}J 3.32		2
163.6	d, ^{1}J 250,		5
^{19}F:-			
-89.6	s	2 F	-CF$_2$
-111.1	s	2 F	Ar-F

No. 24 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane.



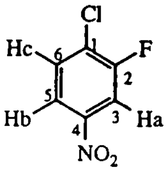
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
2.1	s	3 H	CH$_3$
2.2	s	3 H	CH$_3$
7.2-7.5	m	8 H	Ar-H
^{13}C:-			
20.0	s		CH$_3$
20.1	s		CH$_3$
121.5	t, ^{1}J 236		1
125.7	s		
126.0	m		
126.4	t, ^{3}J 8.05		
128.2	d, ^{3}J 6.5		
129.7	t, ^{4}J 1.91		
130.0	s		
132.5	s		
136.3	t, ^{3}J 2.87		
139.9	s		
^{19}F:-			
-89.3	s	2 F	-CF$_2$

No. 25 2-Fluoro-4-nitrotoluene.



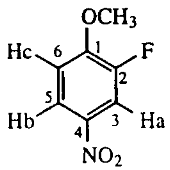
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
2.17	s	3H	CH_3
7.2	m	1 H	Ar-H_c
7.47	m	1 H	Ar-H_b
7.65	m	1 H	Ar-H_a
^{13}C:-			
15.9	s		CH_3
112.0	d, $^2J_{CF}$ 27.4,		Ar-C_3
120.7	s		Ar-C_5
133.7	d, $^3J_{CF}$ 5.28 ,		Ar-C_6
135.1	d, $^2J_{CF}$ 17.3		Ar-C_1
148.6	d, $^3J_{CF}$ 8.4		Ar-C_4
162.2	d, $^1J_{CF}$ 248.7		Ar-C_2
^{19}F:-			
-113.4	s	1F	Ar-F

No. 26 1-Chloro-2-fluoro-4-nitrobenzene.



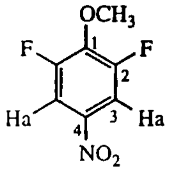
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
7.6	m	1 H	Ar-H_c
8.0	m	2 H	Ar-H_{b+a}
^{13}C:-			
112.3	d, $^2J_{CF}$ 25.9,		Ar-C_3
119.9	d, $^4J_{CF}$ 4.2		Ar-C_5
128.7	d, $^2J_{CF}$ 17.6		Ar-C_1
131.2	s		Ar-C_6
147.0	s		Ar-C_4
162.2	d, $^1J_{CF}$ 254		Ar-C_2
^{19}F:-			
-110.4	s	1F	Ar-F

No. 27 2-Fluoro-4-nitroanisole.



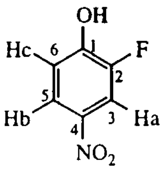
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
4.0	s	3H	OCH$_3$
7.0	t, $^3J_{HcHb}$ 8.4, $^4J_{HcF}$ 8.4	1H	Ar-H$_c$
7.95	dd, $^3J_{HbHc}$ 10.6, $^4J_{HbHa}$ 2.6	1H	Ar-H$_b$
8.06	ddd, $^3J_{HaF}$ 9.2, $^4J_{HaHb}$ 2.3, $^5J_{HaHb}$ 1.5	1H	Ar-H$_a$
^{13}C:-			
56.6	s		OCH$_3$
112.0	d, $^3J_{CF}$ 2.3		Ar-C$_6$
112.1	d, $^2J_{CF}$ 27.4,		Ar-C$_3$
120.9	d, $^4J_{CF}$ 3.1		Ar-C$_5$
141.5	s		Ar-C$_4$
151.1	d, $^1J_{CF}$ 251.4		Ar-C$_2$
153.3	d, $^2J_{CF}$ 10.7		Ar-C$_1$
^{19}F:-			
-131.4	s	1F	Ar-F

No. 28 2,6-Difluoro-4-nitroanisole.



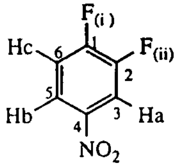
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
4.17	t, $^4J_{HF}$ 1.99	3H	OCH$_3$
7.8	m	2H	Ar-H$_a$
^{13}C:-			
61.8	t, $^3J_{CF}$ 4.22		OCH$_3$
109.0	X portion of ABX, coupling constants undetermined		Ar-C$_3$
140.9	s		Ar-C$_4$
142.5	d, $^2J_{CF}$ 12.97		Ar-C$_1$
153.9	dd, $^1J_{CF}$ 252.2, $^3J_{CF}$ 6.43		Ar-C$_2$
^{19}F:-			
-125.1	s	1F	Ar-F

No. 29 2-Fluoro-4-nitrophenol.



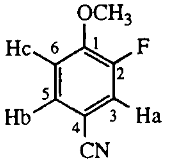
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
7.2	m	1 H	Ar-H_c
8.0	m	2 H	Ar-H_{b+a}
10.15	br s	1 H	OH
^{13}C:-			
112.2	d, $^2J_{CF}$ 22.9		Ar-C_3
117.2	d, $^3J_{CF}$ 1.9		Ar-C_6
121.5	d, $^4J_{CF}$ 3.1		Ar-C_5
140.8	s		Ar-C_4
149.7	d, $^1J_{CF}$ 242.6		Ar-C_2
149.9	d, $^2J_{CF}$ 14.0		Ar-C_1
^{19}F:-			
-133.9	s	1F	Ar-F

No. 30 1,2-Difluoro-4-nitrobenzene.



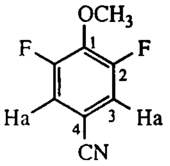
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
7.3	m	1 H	Ar-H_c
8.1	m	2 H	Ar-H_{b+a}
^{13}C:-			
113.9	d, $^2J_{CF}$ 21.3,		Ar-C_3
117.8	d, $^2J_{CF}$ 19.4		Ar-C_6
120.7	dd, $^3J_{CF}$ 7.99, $^4J_{CF}$ 3.77		Ar-C_5
144.0	br s		Ar-C_4
149.8	dd, $^1J_{CF}$ 254.5, $^2J_{CF}$ 14.1		Ar-C_2
154.6	d, $^1J_{CF}$ 260.3, $^2J_{CF}$ 12.8		Ar-C_1
^{19}F:-			
-126.6	s	1F	Ar-$F_{(i)}$
-133.0	s	1F	Ar-$F_{(ii)}$

No. 31 2-Fluoro-1 methoxy-4-benzonitrile.



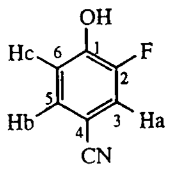
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
4.0	s	3H	OCH_3
7.0	t, $^{3}J_{HcHb}$ 8.4, $^{4}J_{HcF}$ 8.4	1H	Ar-H_c
7.95	dd, $^{3}J_{HbHc}$ 10.6, $^{4}J_{HbHa}$ 2.6	1H	Ar-H_b
8.06	ddd, $^{3}J_{HaF}$ 9.2, $^{4}J_{HaHb}$ 2.3, $^{5}J_{HaHb}$ 1.5	1H	Ar-H_a
^{13}C:-			
56.3	s		OCH_3
103.9	d, $^{3}J_{CF}$ 8.4		Ar-C_6
113.5	d, $^{3}J_{CF}$ 2.3		Ar-C_4
118.0	s		CN
119.5	d, $^{2}J_{CF}$ 20.9		Ar-C_3
	d, $^{4}J_{CF}$ 3.8		Ar-C_5
151.7	d, $^{1}J_{CF}$ 250		Ar-C_2
151.8	d, $^{2}J_{CF}$ 10.7		Ar-C_1
^{19}F:-			
-132.9	s	1F	Ar-F

No. 32 2,6-Difluoro-1-methoxy-4-benzonitrile.



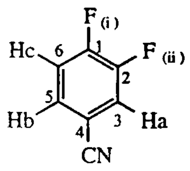
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^{1}H:-			
4.1	s	3H	OCH_3
7.2	m	2H	Ar-H_a
^{13}C:-			
61.7	t, $^{4}J_{CF}$ 4.02		OCH_3
105.1	t, $^{3}J_{CF}$ 11.1		Ar-C_4
116.7	s		CN
116.8	dd, $^{2}J_{CF}$ 17.95, $^{4}J_{CF}$ 8.3		Ar-C_3
141.15	t, $^{2}J_{CF}$ 12.6		Ar-C_1
154.8	dd, $^{1}J_{CF}$ 252, $^{3}J_{CF}$ 6.49		Ar-C_2
^{19}F:-			
-125.8	s	1F	Ar-F

No. 33 2-Fluoro-1-hydroxy-4-benzonitrile.



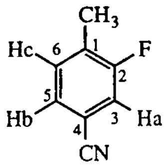
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
7.2	m	1 H	Ar-H_c
8.0	m	2 H	Ar-H_{b+a}
10.15	br s	1 H	OH
^{13}C:-			
104.0	d, $^3J_{CF}$ 8.35		Ar-C_4
117.8	d, $^4J_{CF}$ 2.72		Ar-C_6
118.4	d, $^4J_{CF}$ 2.62		CN
119.6	d, $^2J_{CF}$ 20.9		Ar-C_3
130.0	d, $^4J_{CF}$ 3.42		Ar-C_5
148.1	d, $^2J_{CF}$ 14.1		Ar-C_1
150.3	d, $^1J_{CF}$ 242		Ar-C_2
^{19}F:-			
-137.9	s	1F	Ar-F

No. 34 1,2-Difluoro-4-benzonitrile



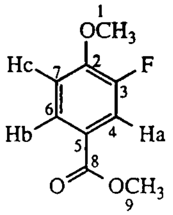
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
7.3	m	1 H	Ar-H_c
8.1	m	2 H	Ar-H_{b+a}
^{13}C:-			
113.9	d, $^2J_{CF}$ 21.3		Ar-C_3
117.8	dd, $^2J_{CF}$ 19.4,		Ar-C_6
120.7	dd, $^3J_{CF}$ 7.99, $^4J_{CF}$ 3.77		Ar-C_5
144.0	s		Ar-C_4
149.8	dd, $^1J_{CF}$ 254.5, $^2J_{CF}$ 14.1		Ar-C_2
154.6	dd, $^1J_{CF}$ 260.3, $^2J_{CF}$ 12.8		Ar-C_1
^{19}F:-			
-126.6	s	1F	Ar-F (i)
-133.0	s	1F	Ar-F (ii)

No. 35 1-Methyl-2-fluoro-4-benzonitrile



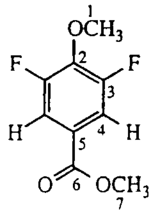
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
2.3	s	3 H	CH_3
7.3	br m	3 H	Ar-H_{b+a+c}
^{13}C:-			
14.7	d, $^3J_{CF}$ 3.42		CH_3
110.7	d, $^3J_{CF}$ 9.15		Ar-C_4
117.7	d, $^4J_{CF}$ 2.72		CN
118.4	d, $^2J_{CF}$ 25.5		Ar-C_3
127.7	d, $^4J_{CF}$ 3.82		Ar-C_5
131.2	d, $^2J_{CF}$ 17.1		Ar-C_1
132.3	d, $^3J_{CF}$ 5.73		Ar-C_6
160.5	d, $^1J_{CF}$ 248		Ar-C_2
^{19}F:-			
-114.5	s	1F	Ar-F

No. 36 2-Fluoro-4-methoxy-methylbenzoate



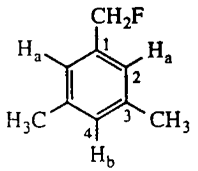
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
3.8	s	3 H	OCH_3
3.9	s	3 H	OCH_3
6.9	t, $^3J_{HbHc}$, $^4J_{HF}$ 8.4	1 H	Ar-H_c
7.7	dd, $^2J_{HF}$ 11.8, $^4J_{HbHa}$ 2.2	1 H	Ar-H_a
7.8	ddd, $^3J_{HbHc}$ 8.7, $^4J_{HbHa}$ 1.9, $^5J_{HF}$ 1.3	1 H	Ar-H_b
^{13}C:-			
52.0	s		$^9OCH_3$
56.1	s		$^1OCH_3$
112.15	d, $^3J_{CF}$ 1.5		Ar-C_7
117.05	d, $^2J_{CF}$ 19.8		Ar-C_4
122.7	d, $^3J_{CF}$ 6.4		Ar-C_5
126.5	d, $^4J_{CF}$ 3.4		Ar-C_6
151.5	d, $^2J_{CF}$ 19.8		Ar-C_2
151.5	d, $^1J_{CF}$ 247		Ar-C_3
165.8	s		Ar-C_8
^{19}F:-			
-135.2	s	1F	Ar-F

No. 37 2,6-Difluoro-4-methoxy-methylbenzoate



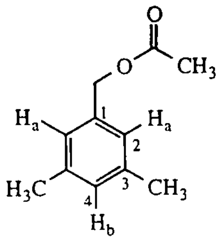
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
3.8	s	3 H	OCH_3
4.0	br m	3 H	OCH_3
7.5	d, $^3J_{HF}$ 8.4	2 H	Ar-H
^{13}C:-			
52.5	s		$^7OCH_3$
61.6	t, $^3J_{CF}$ 4.3		$^1OCH_3$
113.8	dd, $^2J_{CF}$ 17.3, $^4J_{CF}$ 7.2		Ar-C_4
124.1	t, $^3J_{CF}$ 8.45		Ar-C_5
140.5	t, $^2J_{CF}$ 13.2		Ar-C_2
154.6	dd, $^1J_{CF}$ 249, $^3J_{CF}$ 6.1		Ar-C_3
164.9	t, $^2J_{CF}$ 17.6		Ar-C_6
^{19}F:-			
-127.7	s	2 F	Ar-F

No. 38 1-Fluoromethyl-3,5-Dimethylbenzene.



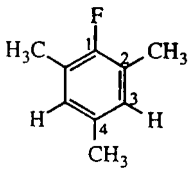
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
2.3	m	6 H	CH_3
5.3	d, $^2J_{HF}$ 47.6	2 H	CH_2F
7.0	br s	3 H	Ar-H_{a+b}
^{13}C:-			
21.2	s		CH_3
81.8	d, $^1J_{CF}$ 165.0		CH_2F
125.4	d, $^3J_{CF}$ 5.73		Ar-C_2
130.3	d, $^4J_{CF}$ 3.12		Ar-C_3
136.0	d, $^2J_{CF}$ 20.1		Ar-C_1
138.2	s		Ar-C_4
^{19}F:-			
-206.1	t, $^2J_{HF}$ 52.9	1 F	CH_2F

No. 39 Formic Acid-3,5-Dimethylbenzyl Ester.



Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
2.3	m	6 H	CH_3
5.2	s	2H	OCH_2
7.0	s	3 H	Ar-H_{b+a}
8.2	s	1 H	CHO
^{13}C:-			
21.2	s		CH_3
65.9	s		CH_2
126.2	s		Ar-C_2
130.1	s		Ar-C_3
135.0	s		Ar-C_4
138.3	s		Ar-C_1
161.0	s		CHO

No. 40 2-Fluoro-1,3,5-trimethylbenzene.



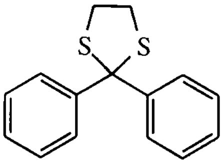
Chemical Shifts (ppm)	Multiplicity / Coupling Constants (Hz)	Relative Intensity	Assignment
^1H:-			
2.25	m	9 H	CH_3
6.8	m	2 H	Ar-H
^{13}C:-			
14.5	d, ^3J 4.22		ortho-CH_3
20.5	s		para-CH_3
123.8	d, ^2J 17.9		Ar-C_2
129.2	d, ^3J 4.53		Ar-C_3
132.4	s		Ar-C_4
158.0	d, ^1J 240		Ar-C_1
^{19}F:-			
-128.4	s	1 F	Ar-F

Appendix Two Mass Spectra.

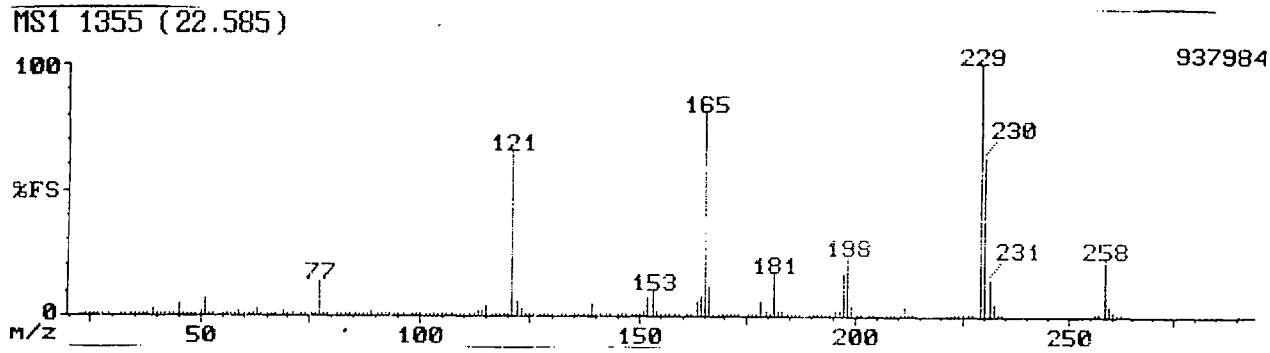
No. 1	2,2 Diphenyl-1,3-dithiolane (**37**).
No. 2	2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane (**39**).
No. 3	2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane (**40**).
No. 4	2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane (**41**).
No. 5	2,2-Bis(4-fluorophenyl)-1,3-dithiolane (**42**).
No. 6	2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane (**38**).
No. 7	2-(4-Nitrophenyl)-2-phenyl-1,3-dithiolane (**48**).
No. 8	2-(3-Trifluoromethylphenyl)-2-phenyl-1,3-dithiolane (**47**).
No. 9	2-Butyl-2-phenyl-1,3-dithiolane (**43**).
No. 10	2-Butyl-2-methyl-1,3-dithiolane (**45**).
No. 11	2-Ethyl-2-pentyl-1,3-dithiolane (**46**).
No. 12	Cyclododecan-1,3-dithiolane (**44**).
No. 13	Benzophenone (**58**).
No. 14	Cyclododecanone (**59**).
No. 15	4-Chlorobenzophenone (**60**).
No. 16	Butyrophenone (**61**).
No. 17	2-Hexanone (**62**).
No. 18	3-Octanone (**63**).
No. 19	Diphenyldifluoromethane (**49**).
No. 20	1-Chlorophenyl-1-phenyl-difluoromethane (**50**).
No. 21	1-Bromophenyl-1-phenyl-difluoromethane (**52**).
No. 22	2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane (**53**).
No. 23	2,2-Bis(4-fluorophenyl)-1,3-dithiolane (**54**).
No. 24	2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane (**51**).
No. 25	2-Fluoro-4-nitrotoluene (**68**).
No. 26	1-Chloro-2-fluoro-4-nitrobenzene (**74**).
No. 27	2-Fluoro-4-nitroanisole (**81**).
No. 28	2,6-Difluoro-4-nitroanisole (**82**).
No. 29	2-Fluoro-4-nitrophenol (**84**).
No. 30	1,2-Difluoro-4-nitrobenzene (**71**).
No. 31	2-Fluoro-1 methoxy-4-benzonitrile (**93**).
No. 32	2,6-Difluoro-1-methoxy-4-benzonitrile (**94**).
No. 33	2-Fluoro-1-hydroxy-4-benzonitrile (**90**).
No. 34	1,2-Difluoro-4-benzonitrile (**97**).
No. 35	1-Methyl-2-fluoro-4-benzonitrile (**96**).
No. 36	2-Fluoro-4-methoxy-methylbenzoate (**78**).
No. 37	2,6-Difluoro-4-methoxy-methylbenzoate (**79**).

No. 38 2-Fluoro-4-tolualdehyde (**76**).
No. 39 1-Fluoromethyl-3,5-dimethylbenzene (**100**).
No. 40 Formic Acid-3,5-dimethylbenzyl ester (**101**).
No. 41 2-Fluoro-1,3,5-trimethylbenzene (**99**).
No. 42 Trifluoroacetic Acid-3,5-dimethylbenzyl ester (**105**).

No. 1 2,2 Diphenyl-1,3-dithiolane. EI⁺/CI⁺

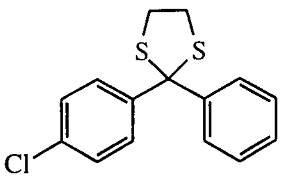


M.Wt 258

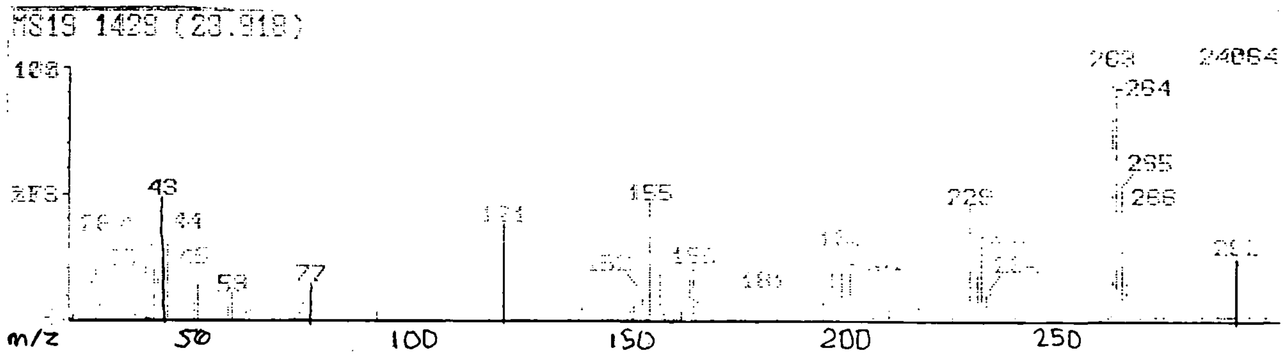


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
24	0.02	48	0.08	73	0.10	96	0.10	119	0.31	142	0.03	166	12.12	190	0.19	221	0.12
25	0.05	49	0.07	74	0.99	98	1.26	120	0.46	143	0.03	167	1.37	191	1.06	222	0.06
26	0.42	50	1.68	75	1.07	99	0.72	121	65.07	145	0.48	168	0.21	192	0.80	223	0.31
27	1.45	51	6.41	76	1.16	100	0.23	122	5.51	146	0.11	169	0.30	193	0.27	224	0.10
28	0.93	52	0.69	77	13.86	101	0.42	123	3.30	147	0.72	170	0.26	194	0.09	225	0.40
29	0.06	53	0.15	78	1.21	102	0.78	124	0.29	148	0.11	171	0.88	195	1.66	226	0.09
32	0.26	55	0.06	79	0.16	103	0.61	125	0.24	149	0.14	172	0.15	196	1.58	227	0.35
33	0.11	56	0.06	81	0.29	104	0.22	126	1.34	150	1.04	173	0.08	197	16.92	229	100.00
34	0.26	57	0.35	82	1.23	105	0.57	127	0.89	151	2.16	175	0.03	198	22.82	230	63.32
35	0.13	58	1.20	83	0.44	106	0.15	128	0.42	152	7.42	176	0.33	199	3.90	231	14.30
36	0.03	59	2.02	84	0.10	107	0.12	129	0.18	153	9.39	177	0.27	200	1.23	232	5.13
37	0.08	60	1.39	85	0.22	108	0.41	130	0.05	154	1.69	178	5.57	201	0.18	233	0.81
38	0.33	61	0.80	86	0.77	109	0.32	132	0.08	155	0.80	179	1.51	203	0.15	234	0.17
39	2.78	62	1.10	87	1.08	110	0.41	133	0.10	156	0.10	180	0.17	204	0.03	256	0.04
40	0.18	63	2.95	88	0.66	111	0.57	134	0.83	157	0.05	181	16.48	207	0.07	257	0.12
41	0.14	64	0.97	89	1.70	112	0.35	135	0.99	158	0.22	182	1.99	208	0.24	258	22.71
42	0.02	65	0.80	90	0.31	113	1.94	136	0.16	159	0.06	183	1.55	209	0.24	259	3.90
43	0.06	66	0.15	91	0.99	114	1.58	137	0.74	161	0.20	184	0.96	210	0.48	260	2.32
44	0.30	67	0.03	92	0.65	115	3.02	138	0.63	162	0.64	185	0.41	211	3.63	261	0.35
45	4.67	69	2.18	93	0.83	116	0.47	139	5.24	163	6.30	186	0.10	212	0.59	262	0.09
46	1.11	70	0.42	94	0.44	117	0.21	140	0.66	164	7.75	187	0.04	213	0.23	290	0.08
47	0.42	71	0.37	95	0.50	118	0.05	141	0.17	165	80.79	189	0.23	214	0.06		

No. 2 2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane. EI+

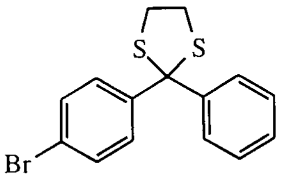


M.Wt 292

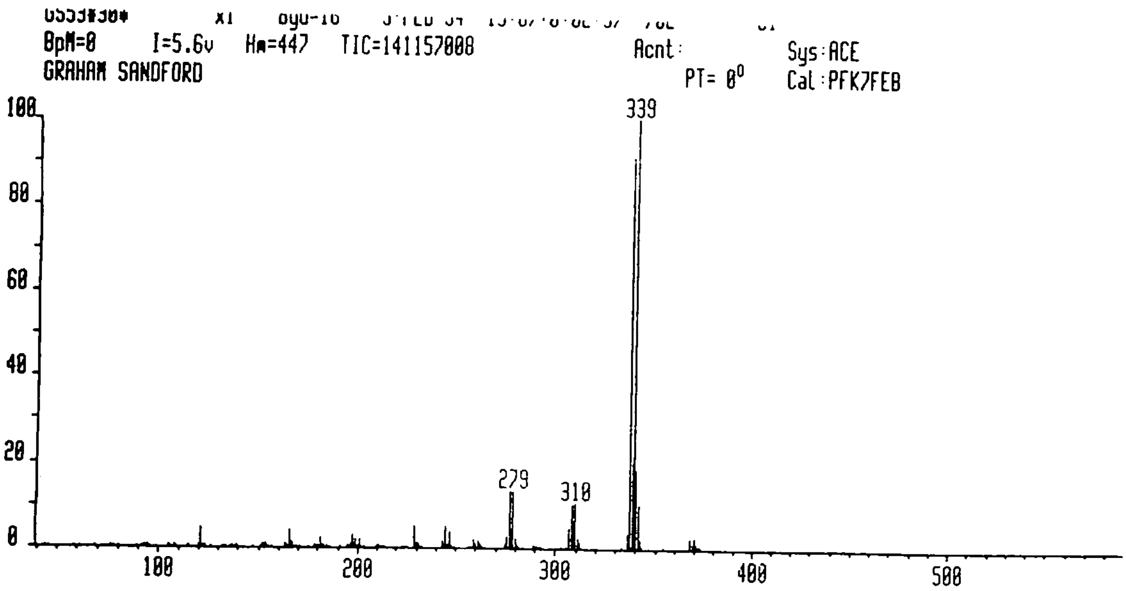


	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
43	48.94	62	2.64	67	[illegible]	120	1.54	[illegible]	5.24	[illegible]	[illegible]	[illegible]	1.40	234	10.04
44	[illegible]	63	[illegible]	[illegible]	[illegible]	121	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	235	1.51
45	[illegible]	64	4.14	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	245	2.69
46	[illegible]	65	1.21	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	262	0.66
47	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	263	100.00
50	[illegible]	71	1.06	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	1.76	264	88.38
51	[illegible]	73	1.70	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	265	50.80
52	[illegible]	74	3.13	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	266	36.44
55	[illegible]	75	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	267	3.97
57	[illegible]	76	1.89	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	44.55	268	2.59
58	[illegible]	77	14.36	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	292	24.20
59	[illegible]	78	1.20	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	293	2.59
60	[illegible]	[illegible]	2.34	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		[illegible]	[illegible]	[illegible]	[illegible]	294	10.17
61	4.59	[illegible]	1.58	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	295	1.70

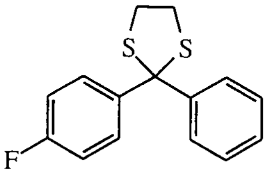
No. 3 2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane. CI+



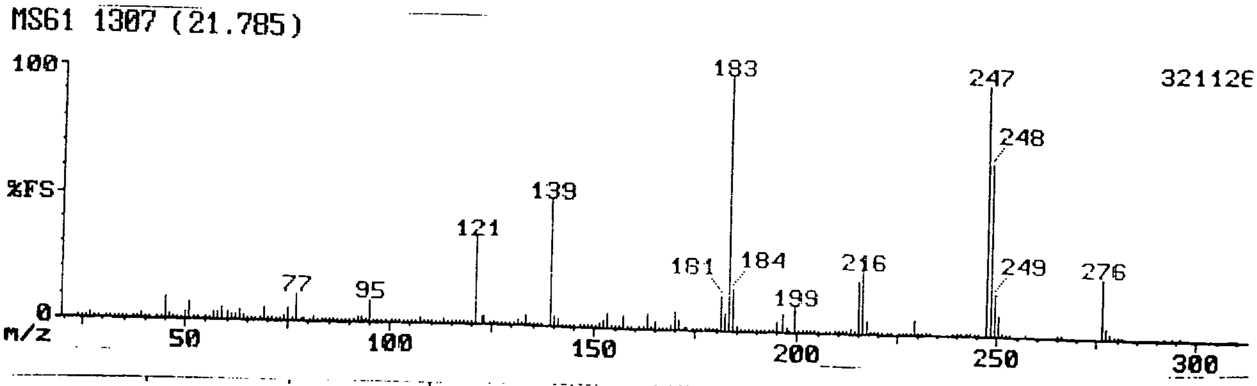
M.Wt 336/338



No. 4 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane. EI+

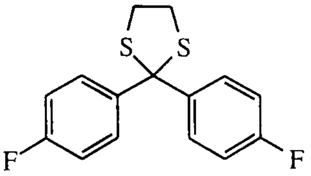


M.Wt 276

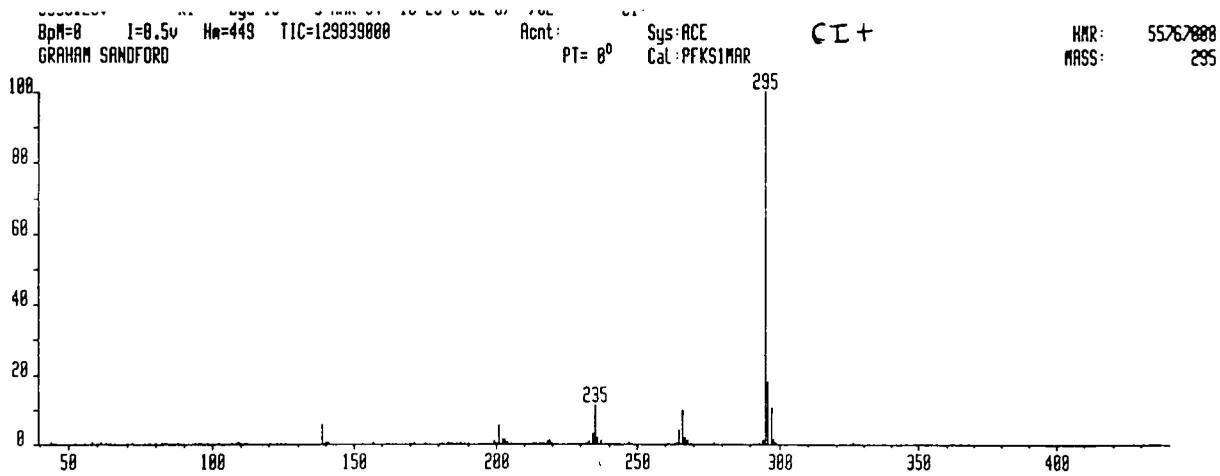


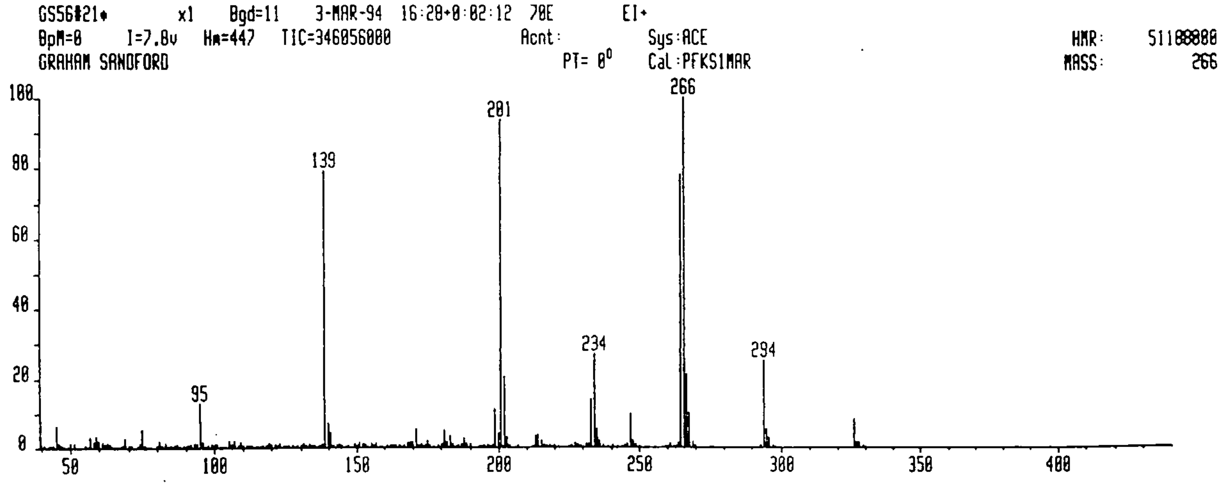
Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel In
24	0.01	52	0.63	79	0.24	105	1.12	131	1.48	158	0.69	185	1.75	212	0.08	244	0.10
25	0.04	53	0.13	80	0.18	106	0.95	132	0.81	159	0.16	186	0.19	213	1.64	245	0.33
26	0.49	55	0.05	81	1.72	107	2.10	133	3.48	161	0.44	187	0.28	214	1.29	247	99.49
27	1.55	56	0.16	82	1.03	108	0.79	134	0.98	162	0.97	188	0.25	215	20.66	248	68.37
28	0.80	57	2.81	83	1.12	109	1.10	135	0.60	163	5.52	189	0.91	216	24.62	249	16.64
29	0.05	58	2.65	84	0.17	110	0.59	136	0.13	164	1.36	190	0.16	217	4.46	250	7.43
31	0.12	59	4.43	85	0.49	111	0.77	137	0.82	165	2.87	191	0.08	218	1.40	251	1.19
32	0.20	60	2.74	86	0.96	112	0.31	139	49.49	166	0.40	192	0.03	219	0.21	252	0.28
33	0.17	61	1.70	87	1.44	113	1.48	140	4.27	167	0.14	193	0.14	220	0.03	253	0.05
34	0.28	62	1.64	88	0.51	114	0.57	141	2.58	168	0.90	194	0.31	221	0.17	257	0.03
35	0.17	63	3.83	89	0.81	115	0.53	142	0.24	169	1.92	195	3.99	222	0.04	265	0.05
36	0.03	64	1.97	90	0.28	116	0.18	143	0.21	170	6.95	196	6.86	223	0.03	266	0.04
37	0.09	65	0.60	91	1.10	117	0.47	144	1.30	171	3.89	197	2.26	225	0.02	276	23.34
38	0.30	66	0.25	92	1.71	118	0.29	145	0.68	172	1.37	198	0.22	226	0.21	277	4.05
39	2.14	67	0.02	93	1.57	119	0.83	146	0.46	173	0.32	199	9.95	227	0.40	278	2.38
40	0.11	68	0.36	94	1.40	120	1.00	147	0.40	174	0.07	200	1.30	228	0.69	279	0.37
41	0.03	69	4.56	95	9.06	121	33.67	148	0.09	175	0.16	201	1.04	229	6.06	280	0.10
43	0.02	70	0.81	96	0.99	122	3.25	149	0.34	176	0.42	202	0.79	230	0.97	281	0.03
44	0.23	71	0.51	97	0.28	123	2.49	150	1.07	177	0.26	203	0.29	231	0.43	292	0.02
45	0.42	72	0.09	98	1.04	124	0.43	151	1.67	178	0.25	204	0.07	232	0.08	294	0.05
46	2.33	73	0.16	99	0.79	125	0.73	152	2.55	179	0.44	205	0.03	233	0.02	296	0.02
47	0.80	74	1.89	100	0.32	126	0.82	153	5.48	180	0.73	207	0.21	239	0.11	308	0.12
48	0.14	75	4.85	101	0.54	127	0.72	154	0.65	181	13.65	208	0.39	240	0.05	309	0.03
49	0.12	76	1.20	102	0.35	128	0.21	155	1.33	182	6.70	209	1.30	241	0.28	310	0.02
50	2.55	77	10.59	103	0.32	129	0.28	156	0.82	183	100.00	210	1.04	242	0.08		
51	6.82	78	1.00	104	0.32	130	0.17	157	5.29	184	16.96	211	0.41	243	0.51		

No. 5 2,2-Bis(4-fluorophenyl)-1,3-dithiolane. EI+/CI+

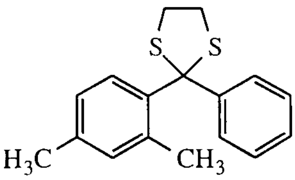


M.Wt 294

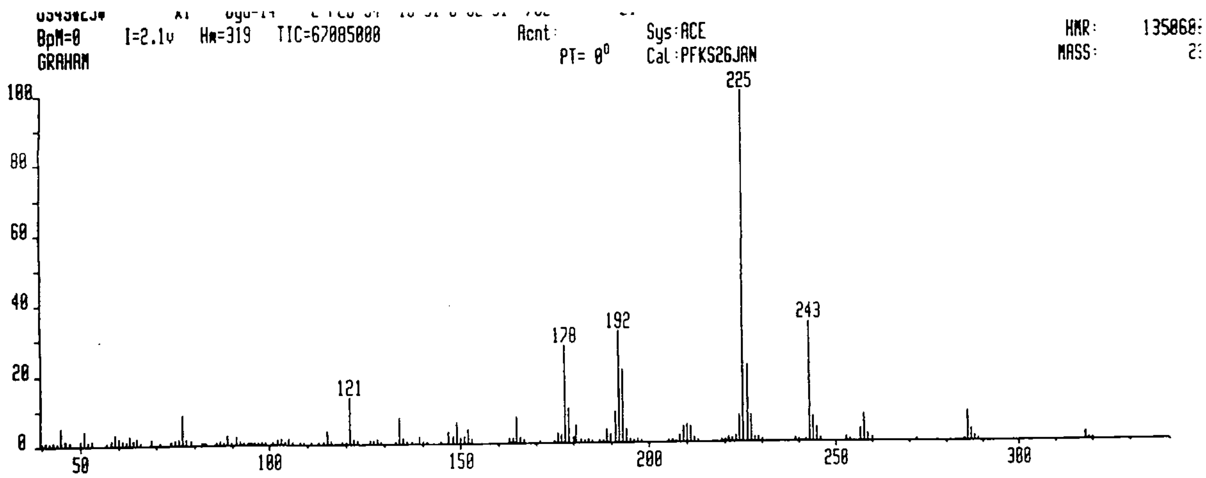


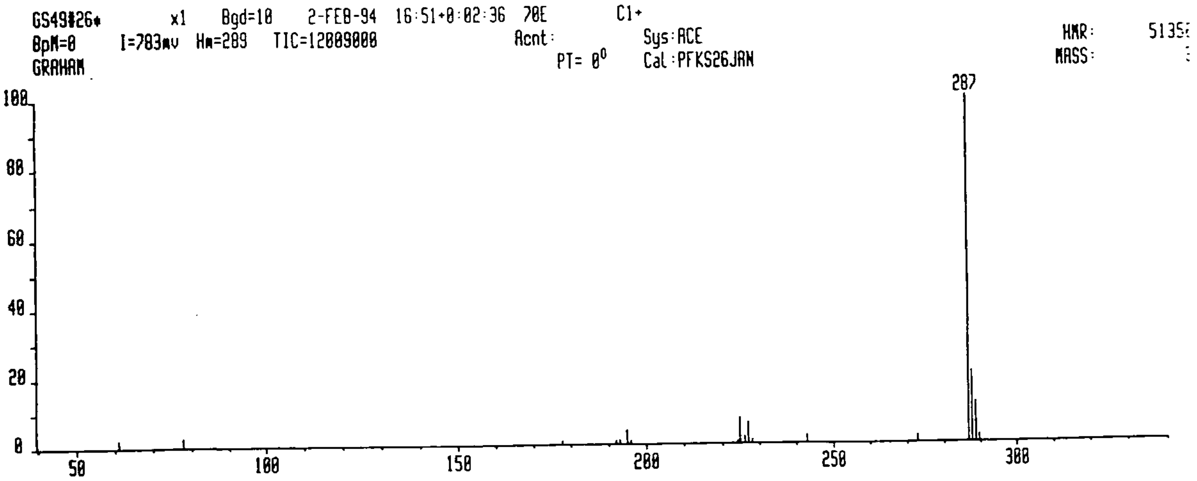


No. 6 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane. CI+

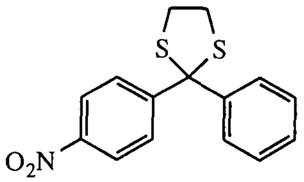


M.Wt 286

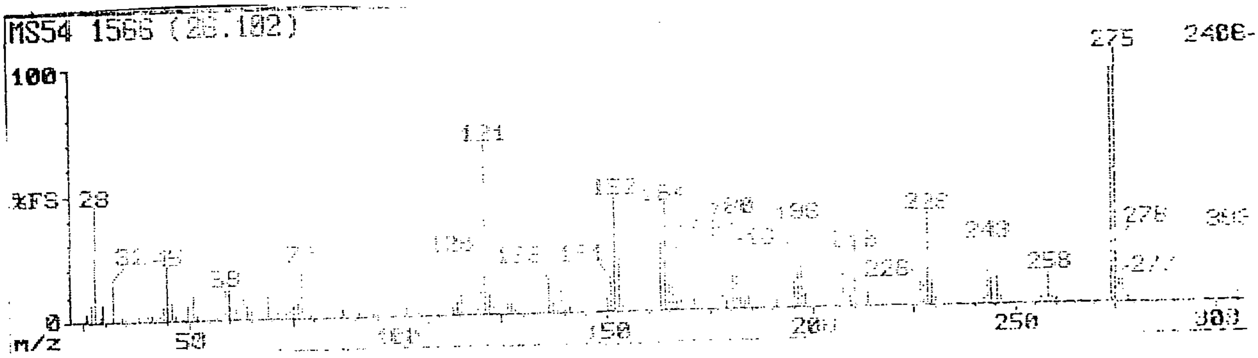




No. 7 **2-(4-Nitrophenyl)-2-phenyl-1,3-dithiolane.** **EI+**

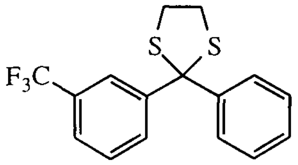


M.Wt 303

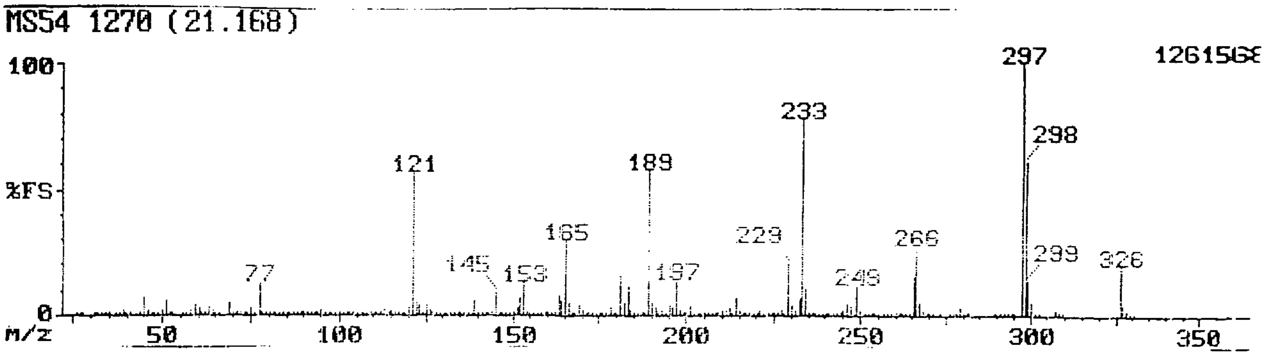


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
26	2.76	46	7.18	70	2.13	92	2.89	126	4.26	152	46.01	178	5.72	209	3.41	256	1.7
27	6.52	47	2.23	71	1.45	93	2.42	127	4.26	153	22.87	179	2.73	210	22.34	258	12.5
28	45.21	50	5.33	73	1.68	94	1.33	128	1.53	154	2.15	180	36.97	211	4.39	259	2.3
29	1.83	51	10.17	74	3.11	95	1.53	133	1.25	155	0.66	181	24.73	212	3.17	260	1.7
30	7.18	52	1.91	75	4.72	101	1.55	134	2.06	162	2.88	182	4.12	213	5.25	273	3.5
32	14.76	55	1.30	76	5.33	102	2.51	135	1.91	163	26.60	183	2.56	216	1.86	274	33.5
34	2.09	57	2.24	77	21.81	105	1.88	136	11.84	164	42.82	184	4.39	226	10.51	275	100.0
35	1.01	58	5.78	78	2.55	108	5.65	137	3.69	165	38.56	185	1.58	227	7.71	276	23.1
38	1.56	59	12.77	79	1.33	113	2.56	138	1.94	166	20.48	191	2.51	228	36.70	277	11.0
39	7.71	60	11.50	82	1.99	114	4.45	139	8.84	167	2.98	193	2.24	229	9.31	278	1.6
40	1.78	61	3.55	86	2.04	115	7.45	140	2.21	168	3.86	195	11.90	230	3.66	281	1.5
41	1.53	62	3.42	87	3.34	119	2.73	141	1.98	169	3.03	196	22.07	242	1.88	303	23.-
42	1.01	63	8.38	88	1.85	120	16.62	145	1.60	170	1.70	197	21.81	243	25.00	304	3.5
43	1.55	64	4.65	89	2.34	121	67.82	147	1.41	171	3.56	198	5.05	244	11.84	305	2.5
44	6.16	65	3.52	90	1.28	122	7.58	150	4.72	176	0.89	207	13.03	245	11.97		
45	21.81	69	8.51	91	1.38	123	4.11	151	12.10	177	2.14	208	4.53	246	2.63		

No. 8 2-(3-Trifluoromethylphenyl)-2-phenyl-1,3-dithiolane. EI$^+$

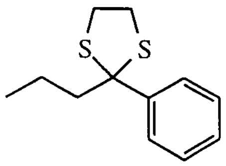


M.Wt 326

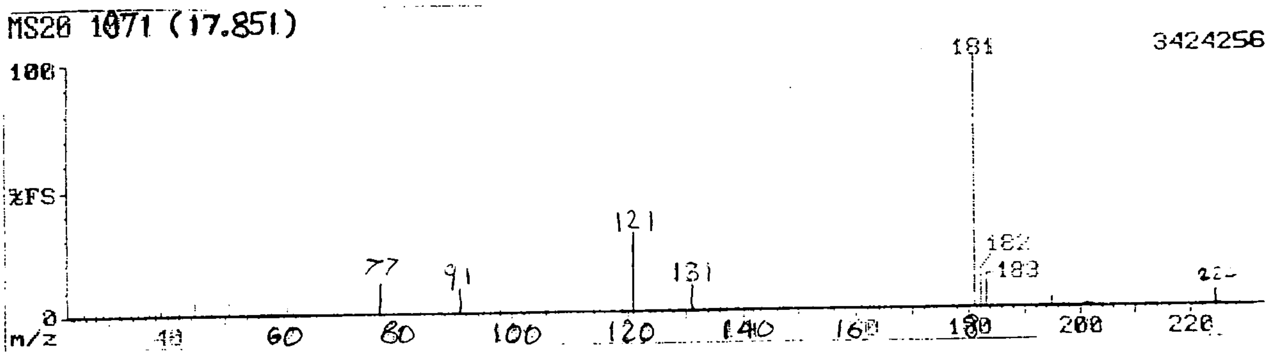


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel In
26	0.26	63	3.21	95	2.15	125	4.16	155	1.28	185	0.40	215	2.33	245	2.25	279	3.2
27	0.85	64	1.46	96	0.31	126	2.19	156	0.58	186	0.64	216	0.30	246	4.71	280	0.5
28	0.51	65	0.64	97	0.27	127	0.72	157	1.42	187	0.65	217	0.16	247	4.22	281	0.2
31	0.03	66	0.20	98	0.72	128	0.51	158	0.33	188	0.99	218	0.11	248	0.55	282	0.0
32	0.14	69	4.61	99	0.95	129	0.56	159	0.77	189	57.47	219	1.08	249	11.61	289	0.0
33	0.09	70	0.55	100	0.41	130	0.10	160	0.10	190	5.19	220	1.42	250	1.52	291	0.3
34	0.19	71	0.50	101	0.58	131	0.41	161	0.57	191	3.25	221	2.23	251	1.18	292	0.1
35	0.12	72	0.08	102	0.53	132	0.66	162	1.34	192	0.67	222	1.26	252	0.37	293	0.3
37	0.05	73	0.06	103	0.34	133	1.16	163	7.63	193	2.05	223	0.51	253	0.16	294	0.0
38	0.21	74	1.24	104	0.21	134	1.20	164	6.17	194	1.30	224	0.20	254	0.04	295	0.1
39	1.64	75	2.44	105	0.83	135	1.22	165	29.55	195	3.53	225	0.49	255	0.09	297	100.0
40	0.10	76	1.38	106	0.45	136	0.40	166	4.59	196	3.06	226	0.97	257	0.46	298	61.0
41	0.05	77	12.58	107	1.03	137	1.17	167	0.70	197	13.64	227	1.89	258	0.23	299	13.3
44	0.17	78	1.03	108	0.62	138	1.22	168	0.47	198	2.15	228	0.53	259	1.27	300	4.7
45	6.82	79	0.08	109	0.50	139	5.60	169	4.34	199	1.29	229	20.78	260	0.78	301	0.7
46	1.70	80	0.04	110	0.53	140	0.71	170	2.07	200	0.49	230	3.47	261	0.28	302	0.1
47	0.64	81	0.65	111	0.70	141	0.24	171	1.16	201	4.00	231	2.31	262	0.15	307	1.70
48	0.11	82	0.63	112	0.36	142	0.08	172	0.23	202	0.87	232	6.33	263	0.42	308	0.3
49	0.07	83	0.25	113	1.46	143	0.58	173	0.34	203	0.39	233	77.27	264	0.65	309	0.1
50	1.81	84	0.12	114	1.24	144	0.80	174	0.22	204	0.15	234	11.12	265	15.18	326	19.0
51	5.36	85	0.25	115	1.66	145	9.17	175	1.21	205	0.19	235	1.10	266	26.95	327	3.4
52	0.50	86	0.82	116	0.34	146	1.09	176	0.67	206	0.93	236	0.14	267	4.75	328	1.6
53	0.12	87	1.38	117	0.47	147	0.52	177	0.41	207	0.80	237	0.07	268	1.48	329	0.3
56	0.07	88	0.73	118	0.22	148	0.14	178	3.10	208	0.61	238	0.22	269	0.21	330	0.0
57	1.00	89	1.22	119	1.34	149	0.42	179	0.78	209	0.59	239	1.12	270	0.05	358	0.2
58	2.13	90	0.27	120	2.64	150	1.29	180	0.32	210	1.64	240	0.24	271	0.12	359	0.0
59	4.16	91	0.87	121	56.17	151	2.76	181	15.83	211	1.89	241	0.12	273	0.06	360	0.04
60	2.82	92	1.03	122	5.19	152	6.41	182	4.59	212	2.86	242	0.06	276	0.23		
61	1.23	93	1.36	123	3.51	153	12.50	183	11.44	213	1.44	243	0.06	277	0.22		
62	1.24	94	1.12	124	0.45	154	1.36	184	2.17	214	7.22	244	1.14	278	0.55		

No. 9 2-Butyl-2-phenyl-1,3-dithiolane. EI+

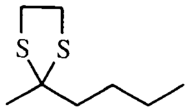


M.Wt 224

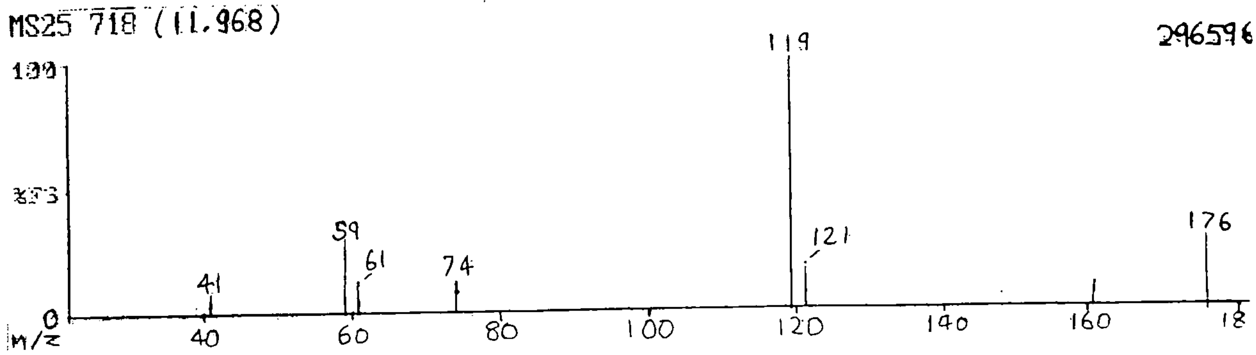


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
26	0.17	46	0.07	[illegible]	[illegible]	[illegible]	0.50	106	0.13	126	0.17	145	0.02	163	0.32	195	[illegible]
27	1.37	47	0.53	[illegible]	[illegible]	[illegible]	0.22	107	0.11	127	0.55	146	0.09	164	0.36	196	0.17
28	0.38	48	0.04	[illegible]	[illegible]	[illegible]	0.35	108	0.46	128	1.75	147	1.05	165	0.33	197	0.15
29	0.63	50	1.72	[illegible]	[illegible]	[illegible]	[illegible]	109	0.68	129	5.22	148	0.15	166	0.43	198	0.02
30	0.02	51	7.22	[illegible]	[illegible]	[illegible]	11.64	110	0.13	130	1.38	149	0.55	167	0.25	199	0.02
32	0.08	52	1.03	[illegible]	[illegible]	[illegible]	[illegible]	111	0.06	131	11.60	150	0.11	168	0.10	222	[illegible]
33	0.05	53	1.77	73	[illegible]	[illegible]	0.47	112	0.23	132	1.65	151	0.21	169	0.26	223	0.02
34	0.11	54	0.22	[illegible]	[illegible]	[illegible]	0.22	113	0.10	133	0.23	152	0.03	175	0.02	224	[illegible]
35	0.25	55	0.12	75	[illegible]	[illegible]	[illegible]	115	0.37	134	2.18	153	1.00	177	0.40	225	[illegible]
36	0.02	57	0.17	[illegible]	[illegible]	[illegible]	0.35	[illegible]	1.38	135	0.66	154	0.23	179	0.29	226	[illegible]
37	0.04	58	1.57	77	[illegible]	[illegible]	[illegible]	117	4.48	136	3.32	155	0.14	181	100.00	227	[illegible]
38	0.15	59	0.82	[illegible]	[illegible]	[illegible]	[illegible]	118	0.46	137	0.03	156	0.02	182	13.16	228	[illegible]
39	2.36	60	0.64	[illegible]	[illegible]	[illegible]	[illegible]	119	0.25	138	0.13	157	0.04	183	11.12		
40	0.21	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	22.5	[illegible]	[illegible]	[illegible]	0.02	184	1.08		
41	1.53	62	0.57	[illegible]	[illegible]	[illegible]	[illegible]	122	1.76	141	0.65	159	0.02	185	0.35		
42	0.28	63	2.00	[illegible]	[illegible]	[illegible]	6.54	123	1.75	142	0.06	160	0.04	186	0.04		
43	0.34	64	0.92	[illegible]	[illegible]	[illegible]	0.07	124	0.14	143	0.13	161	0.22	189	0.03		
45	5.26	65	1.13	[illegible]	[illegible]	[illegible]	1.27	125	0.24	144	0.03	162	0.13	191	0.07		

No. 10 **2-Butyl-2-methyl-1,3-dithiolane.** EI+

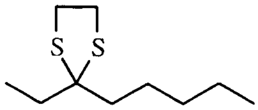


M.Wt 176

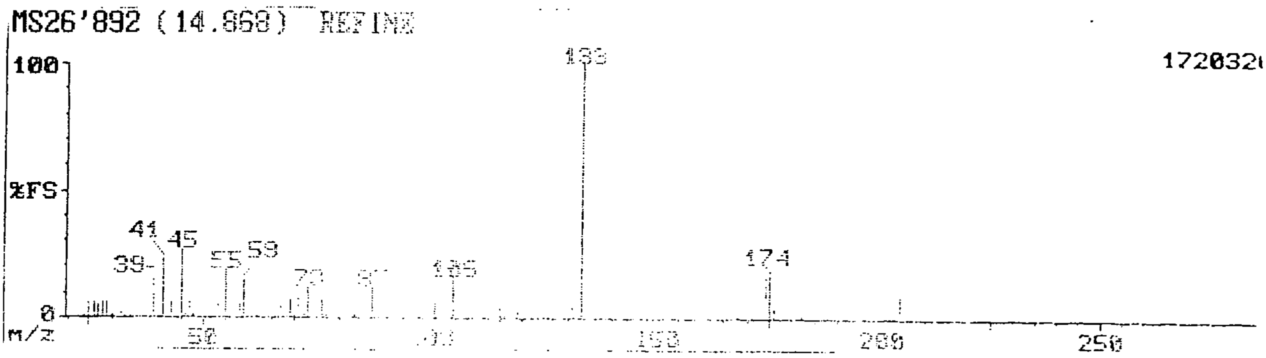


No. 11 2-Ethyl-2-pentyl-1,3-dithiolane.

EI+

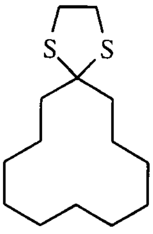


M.Wt 204

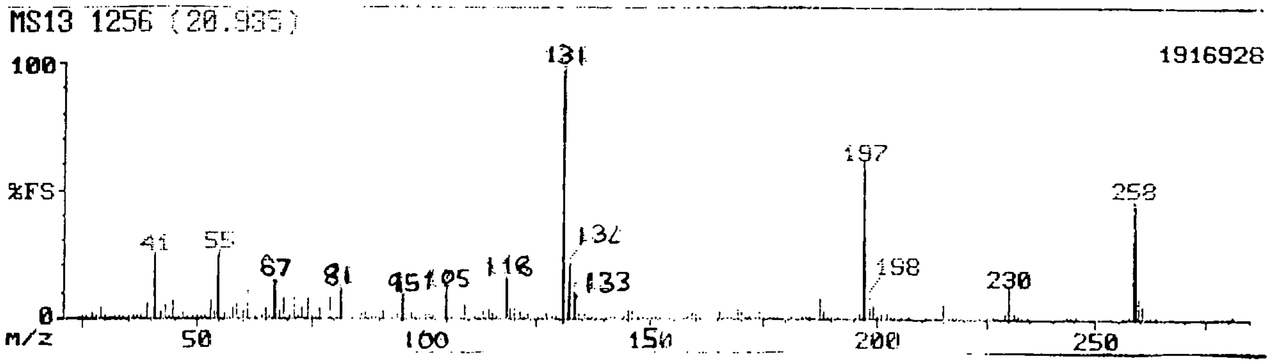


Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
0.21	42	1.00	58	5.30	73	11.55	93	0.63	119	1.98	140	0.03	170	0.15	203	4.55
5.36	43	6.25	59	14.11	74	0.73	95	0.70	120	0.33	141	0.19	171	0.31	204	8.63
5.83	45	26.67	60	4.11	75	0.91	97	0.20	121	0.40	143	2.41	174	20.46	205	1.73
5.06	46	1.10	61	3.87	76	6.90	99	1.38	122	0.08	144	1.16	175	18.33	206	1.06
5.77	47	6.25	62	1.19	77	1.77	101	5.71	123	0.05	145	0.72	176	3.68	207	0.15
5.71	48	2.71	63	0.60	78	0.74	102	0.20	125	0.15	146	0.95	177	1.29	208	0.24
0.50	49	2.51	64	0.82	79	1.15	105	15.48	127	0.35	147	0.34	178	0.33	221	0.03
1.67	50	0.92	65	1.25	83	0.40	106	0.66	129	0.52	152	0.02	179	0.13		
0.41	51	1.41	66	0.43	85	2.10	107	1.00	131	5.24	153	0.03	182	0.02		
0.64	52	0.35	67	4.25	87	11.67	109	0.77	133	100.00	155	0.02	187	0.04		
0.80	53	4.40	68	0.34	88	7.02	111	2.51	134	2.80	159	0.44	188	0.02		
0.15	54	1.21	69	6.49	89	1.07	113	1.38	135	2.12	[illegible]	0.11	195	0.01		
0.83	55	10.23	70	0.70	90	0.52	115	4.29	136	0.41	[illegible]	0.26	200	0.05		
11.90	56	1.14	71	5.23	91	0.13	[illegible]	2.19	138	2.27	[illegible]	0.04	201	0.42		
21.90	57	3.33	72	1.74	92	0.35	[illegible]	4.42	139	0.21	[illegible]	0.02	202	0.55		

No. 12 Cyclododecan-1,3-dithiolane. EI⁺

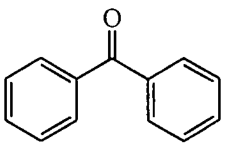


M.Wt 258

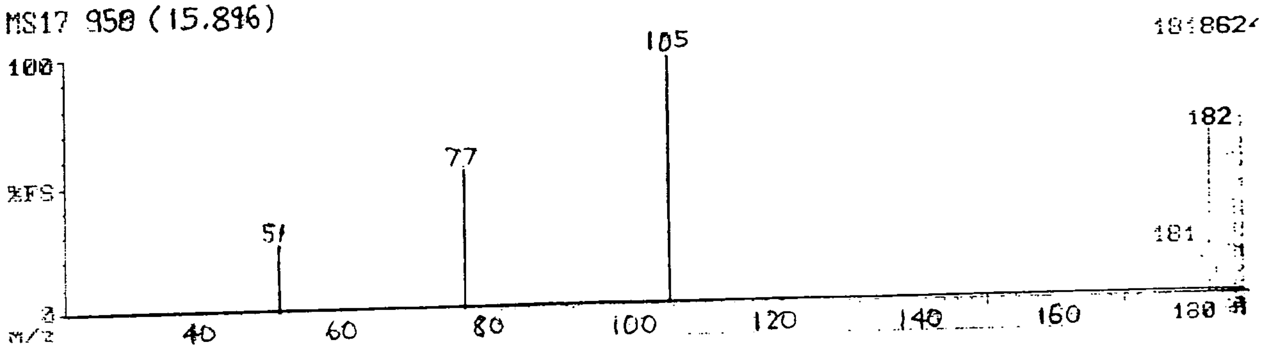


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
25	0.02	49	0.17	72	1.18	95	9.72	118	16.88	142	0.87	165	2.44	195	0.11	229	2.16
26	0.17	50	0.15	73	3.74	96	1.94	119	3.63	143	1.67	166	0.34	196	1.78	230	11.91
27	2.14	51	0.72	74	7.56	97	4.65	120	3.47	144	0.22	167	0.24	197	60.66	231	[illegible]
28	0.91	52	0.46	75	1.94	98	0.80	121	2.64	145	2.39	168	0.24	198	9.03	232	1.20
29	4.01	53	7.02	76	1.07	99	3.56	122	0.78	146	3.13	169	3.65	199	5.40	233	0.13
30	0.11	54	3.25	77	2.85	100	5.82	123	1.64	147	0.99	170	1.32	200	0.69	234	0.25
31	0.12	55	26.59	78	0.65	101	3.52	124	0.33	148	0.36	171	0.23	201	1.22	243	0.12
32	2.06	56	2.13	79	7.25	102	0.60	125	0.44	149	0.12	172	0.13	202	1.56	244	0.03
34	0.15	57	1.46	80	2.26	103	1.31	126	0.30	150	0.05	173	3.95	203	0.35	245	0.02
35	0.57	58	3.35	81	11.45	104	1.42	127	1.90	151	2.05	174	3.13	204	0.22	255	0.34
36	0.64	59	7.33	82	[illegible]	105	11.32	128	0.11	152	[illegible]	175	0.74	205	0.64	257	1.11
37	2.26	60	1.46	83	11.22	106	1.30	129	1.26	153	0.30	176	0.37	207	0.21	258	41.37
38	0.29	61	11.11	84	1.52	107	2.96	131	100.00	154	0.20	177	0.07	211	0.05	259	7.73
39	2.48	62	0.32	85	4.32	108	0.52	132	13.15	155	0.32	178	0.20	212	0.30	260	4.53
40	1.62	63	0.33	86	2.12	109	6.78	133	11.11	156	0.40	181	0.27	215	[illegible]	261	1.27
41	25.21	64	1.07	87	5.07	110	1.54	134	3.38	157	0.37	182	0.42	216	0.71	262	0.15
42	2.73	65	3.74	88	0.91	111	0.55	135	1.79	158	0.02	184	0.05	217	0.56	263	0.03
43	5.16	66	1.24	89	0.55	112	0.41	136	0.55	159	1.88	185	0.06	218	0.07	264	0.02
44	0.42	67	15.50	90	1.55	113	2.86	137	0.35	160	1.70	187	7.32	219	0.02		
45	5.73	68	2.36	91	2.95	114	3.42	138	0.71	161	0.46	188	2.55	222	0.24		
46	0.95	69	7.75	92	2.02	115	2.11	139	0.42	162	0.32	189	0.92	225	0.49		
47	2.66	70	0.65	93	4.36	116	0.76	140	0.17	163	1.74	190	0.15	226	0.06		
48	0.10	71	0.17	94	2.06	117	0.64	141	1.23	164	1.32	191	0.20	227	0.05		

No. 13 Benzophenone. EI+

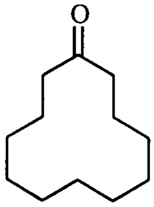


M.Wt 182

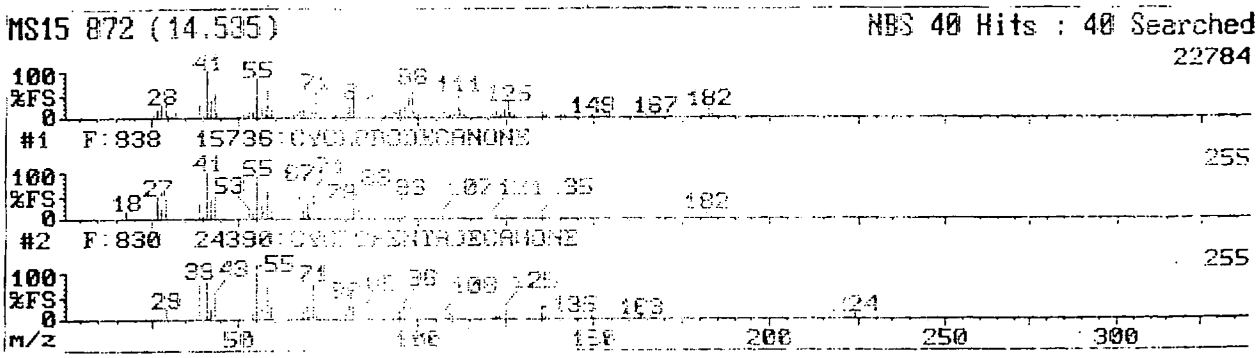


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
[illegible]	0.01	43	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	44	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	45	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	50	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		

No. 14 Cyclododecanone. EI+



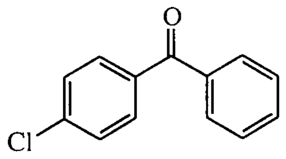
M.Wt 182



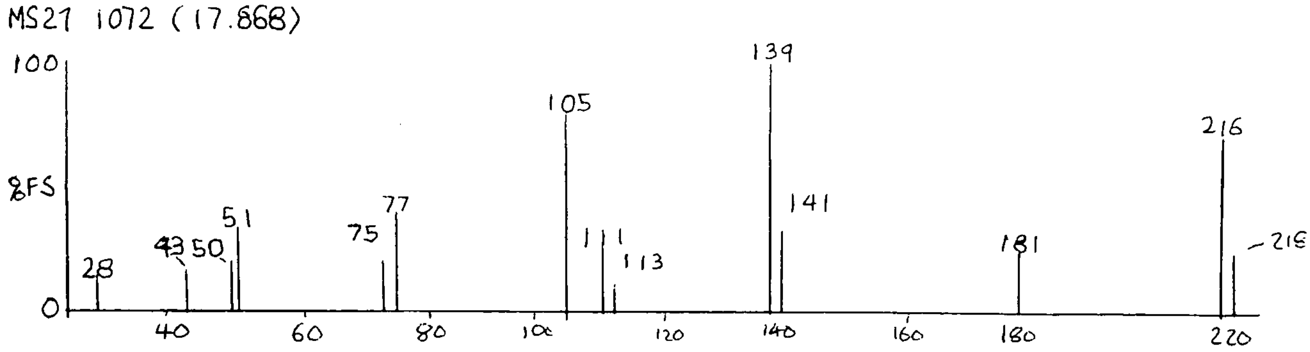
Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
26	1.18	41	100.00	55	82.02	69	28.37	82	34.27	96	18.82	111	51.12	126	9.55	154	2.25
27	15.80	42	37.06	56	24.44	70	16.82	83	35.39	97	40.45	112	17.56	127	3.90	164	1.00
28	28.93	43	52.53	57	14.12	71	59.27	84	25.84	98	66.85	113	4.39	135	10.39	167	2.55
29	[illegible]	44	12.01	58	[illegible]	72	6.25	85	10.32	99	10.35	114	4.65	136	1.39	182	21.07
30	1.03	45	1.45	59	17.98	77	2.04	86	3.53	100	5.69	121	8.09	139	18.54	183	3.14
31	1.16	51	1.74	65	2.12	78	1.84	91	1.79	107	9.41	122	11.52	140	2.97		
32	5.12	52	2.54	66	2.41	79	10.04	93	10.88	108	7.72	123	3.25	141	1.40		
39	27.52	53	[illegible]	67	17.78	80	2.32	94	6.01	109	6.11	124	17.02	149	4.16		
40	7.51	54	11.71	68	14.82	81	19.94	95	15.15	110	3.44	125	32.58	153	3.46		

No. 15 4-Chlorobenzophenone.

EI$^+$

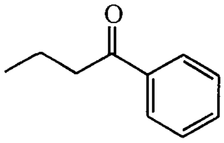


M.Wt 216/218

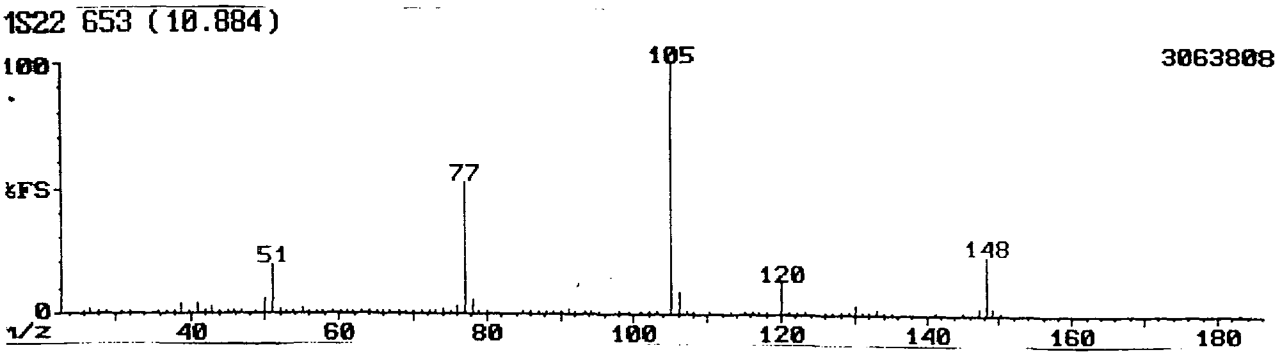


No. 16 Butyrophenone.

EI+

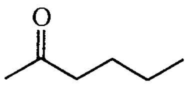


M.Wt 148

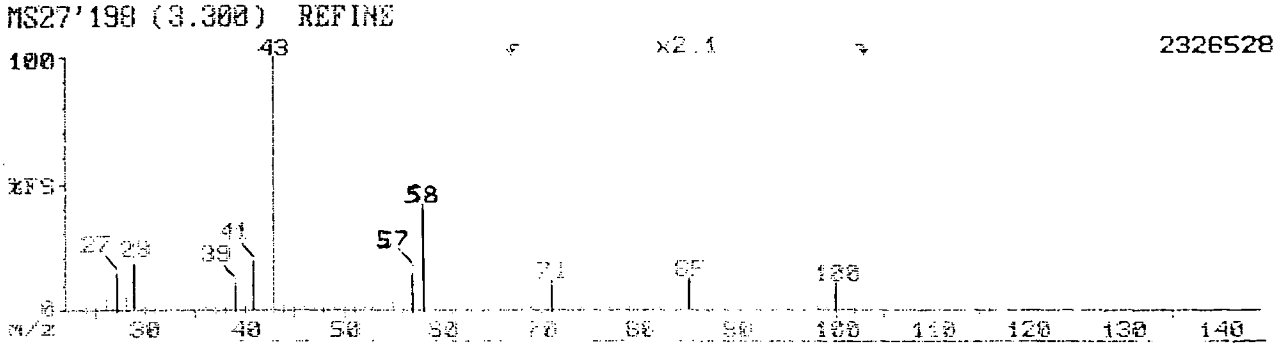


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
26	0.17	41	3.44	53	0.50	64	0.50	75	1.25	90	0.12	105	100.00	121	1.05	134	0.20
27	1.83	42	0.79	54	0.03	65	1.45	76	2.91	91	1.83	106	8.82	122	0.08	135	0.02
28	0.40	43	3.04	55	2.10	66	0.69	77	52.41	92	0.29	107	0.67	123	0.02	141	0.02
29	0.28	44	0.16	56	0.09	67	0.13	78	5.65	93	0.02	108	0.05	126	0.03	145	0.05
31	0.02	45	0.07	57	0.11	68	0.04	79	0.55	94	0.01	110	0.02	127	0.13	147	2.54
32	0.05	46	0.02	58	0.09	69	0.28	80	0.03	95	0.01	113	0.03	128	0.20	148	23.26
36	0.01	47	0.01	59	0.03	70	0.09	85	0.05	98	0.05	115	0.58	129	0.35	149	2.61
37	0.17	49	0.20	60	0.03	71	0.35	86	0.11	99	0.01	116	0.11	130	3.54	150	0.19
38	0.59	50	6.05	61	0.15	72	0.09	87	0.11	101	0.06	117	0.11	131	0.52	183	0.02
39	3.61	51	19.52	62	0.48	73	0.31	88	0.04	102	0.25	118	0.09	132	0.05		
40	0.40	52	1.74	63	1.08	74	1.66	89	0.45	103	0.39	120	12.43	133	2.14		

No. 17 2-Hexanone. EI+

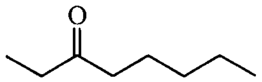


M.Wt 100

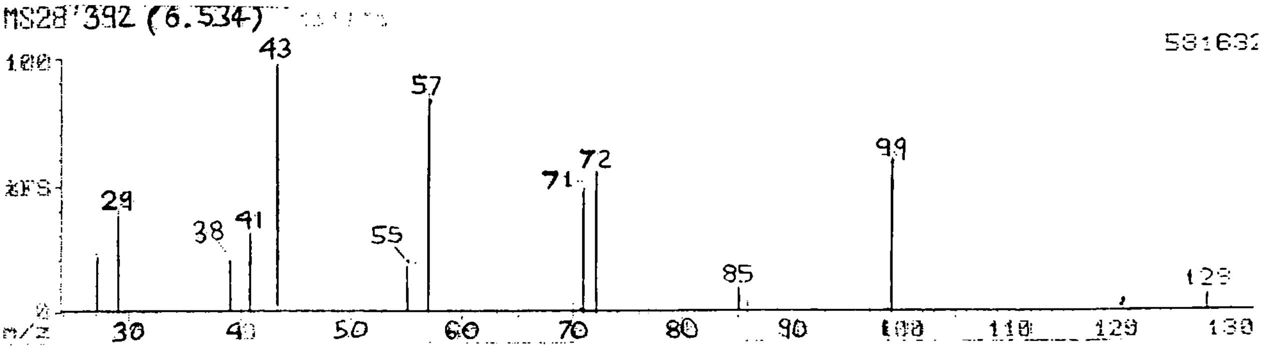


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
24	0.12	31	0.22	40	1.86	48	0.03	57	15.85	65	0.13	79	0.05	98	0.01	142	0.02
25	0.43	33	0.03	41	19.72	49	0.13	58	42.06	67	0.25	81	0.04	99	1.10		
26	3.48	34	0.03	43	100.00	50	0.62	59	2.34	69	0.14	82	0.04	100	5.24		
27	14.79	35	0.05	44	2.11	51	0.66	60	0.10	71	5.41	83	0.14	101	1.05		
28	7.75	37	0.61	45	3.74	52	0.24	61	0.04	72	0.86	85	5.85	102	0.07		
29	20.60	38	1.28	46	0.03	53	1.22	62	0.07	74	0.03	86	0.24	116	0.03		
30	0.38	39	11.09	47	0.07	55	3.04	63	0.05	77	0.04	87	0.02	127	0.21		

No. 18 3-Octanone. EI+



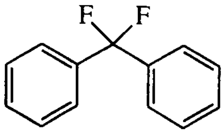
M.Wt 128



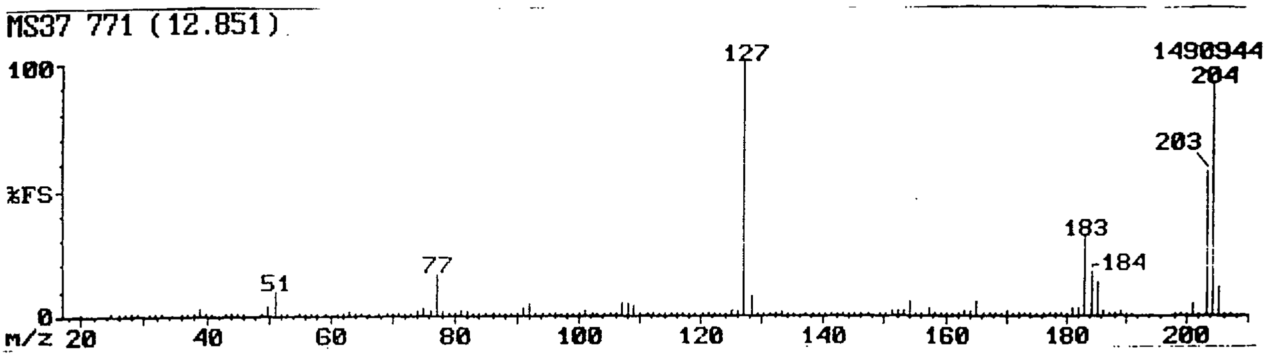
Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
40	3.54	50	1.04	60	0.03	69	1.17	79	0.35	91	0.12	105	0.08	130	[illegible]
41	32.22	51	1.72	61	0.08	70	3.27	80	0.22	92	0.05	109	0.07		
42	20.10	52	0.57	62	0.13	71	48.25	81	1.55	94	2.03	110	0.17		
43	100.00	53	4.28	63	0.33	72	55.34	82	0.13	95	0.14	111	0.04		
44	2.41	55	18.01	64	0.11	73	7.21	83	0.42	97	0.22	113	0.25		
45	0.57	56	6.04	65	0.51	74	0.40	84	0.45	98	2.55	126	0.12		
46	0.25	57	85.31	66	0.22	75	0.28	85	18.55	99	58.44	127	0.21		
47	2.07	58	2.64	67	0.75	77	0.34	86	3.41	100	4.20	128	3.02		
48	0.85	59	0.58	68	0.42	78	0.86	87	0.22	101	0.28	129	3.89		

No. 19 Diphenyldifluoromethane.

EI^+

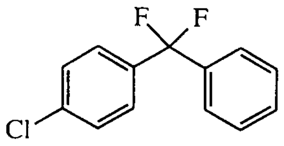


M.Wt 204



Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.05	49	0.15	71	0.03	90	0.58	109	3.73	128	8.17	149	0.17	168	0.24	187	0.22
25	0.04	50	3.00	72	0.06	91	2.63	110	0.50	129	0.42	150	0.56	169	0.39	188	0.97
26	0.33	51	9.82	73	0.14	92	4.95	111	0.26	130	0.07	151	1.73	170	1.70	189	2.30
27	1.10	52	0.00	74	1.82	93	0.39	112	0.11	131	0.59	152	2.13	171	0.89	190	0.29
28	1.44	53	0.08	75	2.70	94	0.30	113	0.36	132	0.24	153	1.85	172	0.10	191	0.01
29	0.03	55	0.07	76	1.91	95	0.10	114	0.17	133	1.92	154	5.49	173	0.02	198	0.03
31	0.35	56	0.15	77	16.41	96	0.23	115	0.58	134	0.25	155	1.04	174	0.03	199	0.37
32	0.41	57	1.05	78	1.73	97	0.04	116	0.09	135	0.07	156	0.31	175	0.53	200	0.34
33	0.09	58	0.07	79	0.54	98	0.45	117	0.06	137	0.29	157	2.44	176	0.09	201	4.40
36	0.02	59	0.12	80	0.35	99	0.88	118	0.09	138	0.28	158	0.33	177	0.71	202	0.85
37	0.18	61	0.23	81	1.94	100	0.87	119	0.07	139	0.70	159	0.25	178	0.10	203	56.87
38	0.62	62	1.00	82	1.79	101	2.03	120	0.27	140	0.11	160	0.04	179	0.14	204	91.21
39	2.68	63	1.92	83	1.09	102	0.89	121	0.03	141	0.03	161	0.21	180	0.36	205	11.88
40	0.16	64	0.34	84	0.09	103	0.10	122	0.11	142	0.02	162	0.48	181	3.33	206	0.82
41	0.05	65	0.16	85	0.35	104	0.09	123	0.16	143	0.12	163	1.99	182	3.35	207	0.07
43	0.02	66	0.14	86	0.63	105	1.37	124	0.08	144	0.48	164	1.49	183	31.32		
44	0.17	68	0.18	87	0.92	106	0.34	125	2.09	145	0.20	165	5.91	184	17.86		
45	0.04	69	0.42	88	0.64	107	4.95	126	2.27	146	0.61	166	0.86	185	13.67		
46	0.02	70	0.26	89	0.73	108	4.74	127	100.00	147	0.09	167	0.13	186	1.84		

No. 20 1-Chlorophenyl-1-phenyl-difluoromethane. EI$^+$



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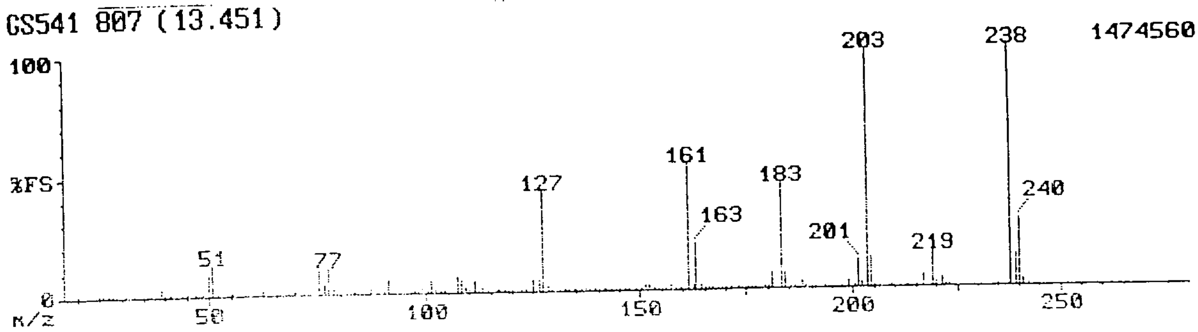
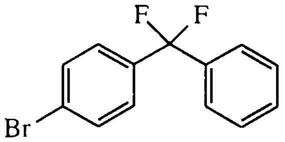


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.06	77	11.11	123	0.40	171	0.09
25	0.04	78	1.81	125	4.51	173	0.15
26	0.37	79	0.08	126	5.21	175	0.84
27	1.16	80	0.57	127	41.39	176	0.14
28	0.29	81	2.97	128	3.02	177	0.22
29	0.01	82	1.13	129	0.25	179	0.12
31	0.48	83	0.64	130	0.18	180	1.07
32	0.10	84	0.34	131	0.78	181	7.22
33	0.11	85	1.06	132	0.66	183	43.89
35	0.12	86	1.11	133	1.20	184	6.60
36	0.13	87	1.46	134	0.10	185	0.73
37	0.36	88	0.45	135	0.31	186	0.20
38	0.98	89	0.52	136	0.08	188	3.18
39	2.59	90	1.13	137	0.43	189	0.28
40	0.12	91	5.83	138	0.37	190	0.76
41	0.03	92	1.94	139	0.58	191	0.31
44	0.04	93	0.38	140	0.05	193	0.12
45	0.05	94	0.39	141	0.22	197	0.07
47	0.08	95	0.28	142	1.10	199	3.11
49	0.34	96	0.26	143	1.25	200	1.42
50	8.75	97	0.28	144	0.82	201	11.53
51	12.29	98	0.81	145	0.54	202	2.05
52	0.82	99	1.67	146	0.20	203	98.89
53	0.07	100	2.10	147	0.04	204	12.36
55	0.18	101	4.51	149	0.39	205	0.85
56	0.16	102	0.46	150	0.94	206	0.08
57	1.82	103	0.04	151	1.74	209	0.05
58	0.09	104	0.13	152	2.07	211	0.09
59	0.06	105	1.08	153	0.55	213	0.03
61	0.95	106	0.65	154	0.12	215	0.04
62	1.86	107	6.39	155	0.63	217	4.93
63	2.88	108	4.58	156	0.63	219	14.31
64	0.27	109	2.12	157	1.82	220	1.94
65	0.20	110	0.88	158	0.25	221	3.65
66	0.06	111	4.51	159	0.04	222	0.49
67	0.23	112	0.49	161	52.50	223	0.07
68	0.64	113	1.72	162	2.31	235	0.29
69	0.47	114	0.34	163	19.72	238	100.00
70	0.11	115	0.22	164	2.33	239	13.75
71	0.03	116	0.04	165	0.62	240	28.61
72	0.18	117	0.20	166	0.11	241	3.23
73	1.15	118	0.08	167	0.44	242	0.23
74	4.24	119	0.47	168	0.11		
75	9.51	120	0.21	169	0.39		
76	4.10	122	0.26	170	0.58		

No. 21 1-Bromophenyl-1-phenyl-difluoromethane. EI+



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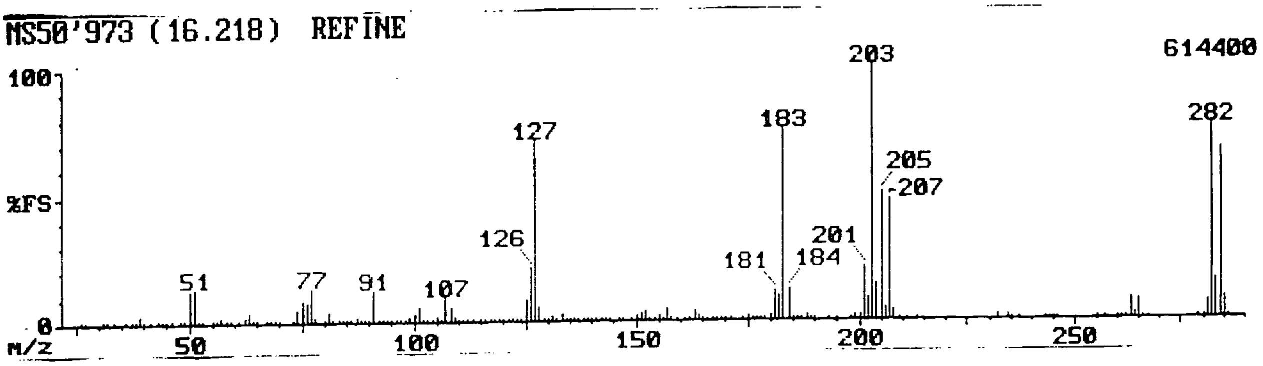
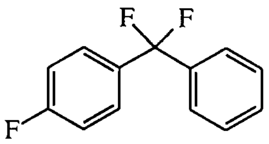


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
26	0.21	55	0.23	81	3.67	102	1.23	124	0.34	146	0.34	169	0.36	195	0.04	245	0.24
27	0.62	56	0.42	82	1.41	103	0.14	125	8.96	147	0.08	170	1.14	198	0.14	246	0.06
31	0.37	57	2.20	83	0.74	104	0.37	126	21.17	149	0.43	171	0.17	199	1.57	255	0.05
32	0.45	58	0.12	84	0.11	105	1.46	127	70.67	150	1.50	174	0.13	200	1.69	257	0.04
33	0.10	59	0.15	85	0.54	106	1.08	128	5.54	151	3.13	175	1.69	201	21.33	260	0.19
36	0.07	61	0.59	86	1.31	107	9.29	129	0.65	152	4.08	176	0.33	202	9.04	261	0.72
37	0.35	62	2.20	87	1.76	108	6.13	130	0.30	153	0.89	177	0.51	203	100.00	262	0.72
38	1.24	63	3.42	88	1.11	109	1.91	131	1.88	154	0.16	178	0.09	204	14.50	263	8.96
39	2.96	64	0.36	89	0.71	110	0.75	132	1.11	155	2.10	179	0.58	205	50.00	264	1.50
40	0.20	65	0.24	90	1.26	111	0.73	133	2.54	156	1.01	180	1.47	206	4.58	265	8.17
41	0.07	67	0.12	91	12.50	112	0.27	134	0.43	157	4.71	181	11.50	207	47.33	266	1.16
43	0.06	68	0.70	92	1.04	113	0.66	135	0.22	158	0.62	182	9.38	208	3.67	267	0.11
44	0.14	69	0.56	93	0.41	115	0.39	136	0.10	159	0.09	183	74.67	209	0.19	279	0.05
45	0.07	70	0.30	94	0.45	116	0.32	137	0.57	161	0.71	184	13.00	211	0.09	280	0.10
46	0.05	73	0.56	95	0.31	117	0.47	138	0.48	162	1.09	185	1.42	213	0.08	281	6.38
48	0.04	74	5.13	96	0.26	118	0.25	139	0.38	163	3.92	186	0.85	232	1.64	282	75.33
49	0.46	75	8.75	97	0.12	119	0.32	140	0.10	164	2.14	187	1.28	234	1.54	283	15.50
50	12.17	76	7.71	98	1.05	120	0.30	141	0.57	165	0.95	188	2.20	235	0.24	284	66.67
51	14.00	77	13.17	99	2.14	121	0.11	142	0.51	166	0.15	189	1.25	237	0.05	285	9.00
52	1.11	78	1.95	100	3.04	122	0.39	143	0.36	167	0.12	190	0.12	243	0.22	286	0.67
53	0.11	80	0.67	101	5.54	123	0.57	144	0.66	168	0.33	193	0.05	244	0.04		

No. 22 2-(4-Fluorophenyl)-2-phenyl-1,3-dithiolane. EI+



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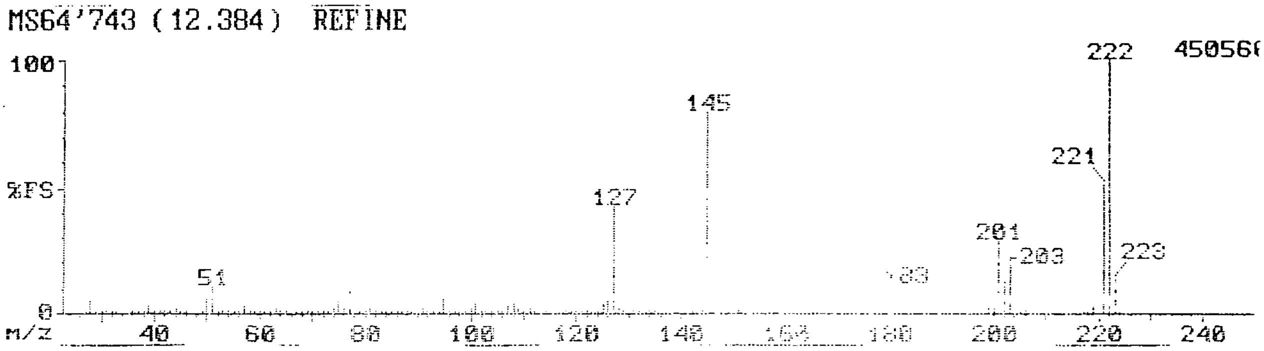
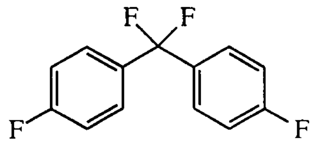
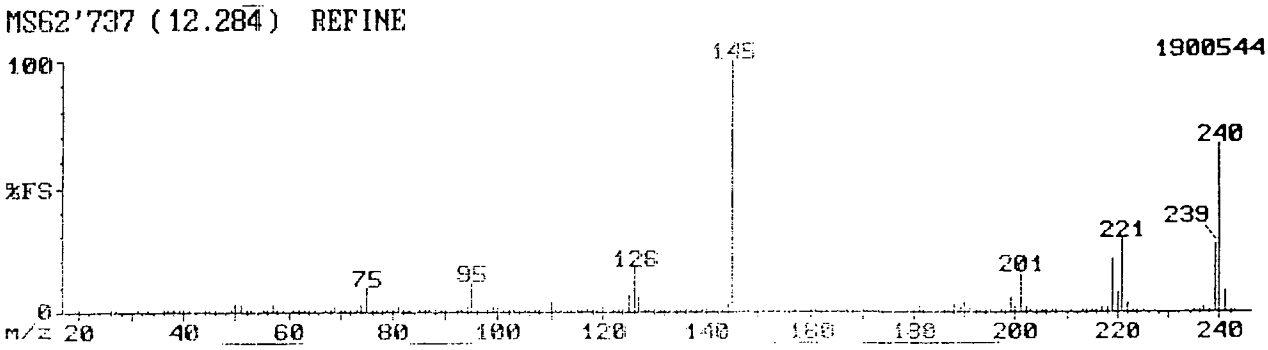


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
50	5.91	71	0.27	91	1.89	111	1.53	132	0.28	156	0.38	180	0.76	205	0.26
51	11.08	72	0.15	92	0.72	112	0.15	133	1.02	157	1.22	181	4.09	206	0.43
52	0.86	73	0.49	93	0.60	113	0.22	134	0.21	158	0.20	182	1.78	207	0.79
53	0.12	74	2.56	94	1.16	114	0.26	135	0.14	161	0.31	183	11.19	208	0.13
54	0.10	75	6.48	95	6.48	115	0.18	137	0.19	162	0.54	184	1.51	217	0.15
55	0.44	76	1.63	96	0.88	116	0.12	138	0.30	163	0.83	185	0.17	218	0.16
56	0.51	77	8.47	97	0.29	117	0.26	139	0.17	164	0.75	186	0.19	219	3.14
57	2.70	78	0.94	98	0.72	118	0.26	141	0.09	165	0.16	187	0.15	220	0.58
58	0.23	79	0.06	99	1.42	119	0.43	142	0.12	167	0.19	188	1.31	221	51.36
59	0.18	80	0.44	100	1.78	120	0.44	143	0.94	168	0.66	189	0.66	222	100.00
60	0.19	81	1.80	101	3.98	121	0.12	144	1.35	169	1.25	193	0.19	223	14.03
61	0.27	82	0.36	102	0.20	122	0.19	145	80.00	170	1.43	195	0.45	224	0.97
62	1.19	83	0.52	103	0.12	123	0.67	146	6.48	171	1.80	197	0.14		
63	1.76	84	0.07	104	0.23	124	0.24	147	0.20	172	4.38	198	0.19		
64	0.22	85	0.82	105	0.92	125	4.60	149	0.67	173	0.88	199	2.95		
65	0.12	86	0.79	106	0.45	126	5.45	150	0.72	174	0.25	200	2.02		
67	0.14	87	1.04	107	3.32	127	42.50	151	2.36	175	2.13	201	29.09		
68	0.79	88	0.37	108	4.72	128	3.42	152	0.69	176	0.30	202	12.95		
69	1.26	89	0.27	109	2.06	129	0.36	153	0.22	177	0.35	203	19.77		
70	0.47	90	0.68	110	0.61	131	0.78	155	0.39	179	0.47	204	2.71		

No. 23 2,2-Bis(4-fluorophenyl)-1,3-dithiolane. EI+

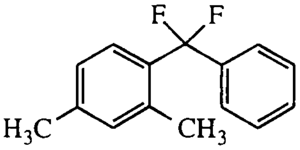


M.Wt 240

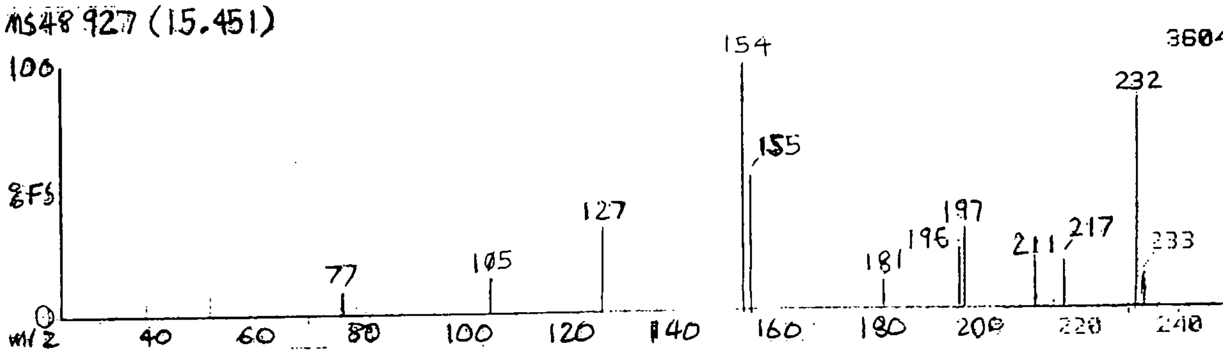


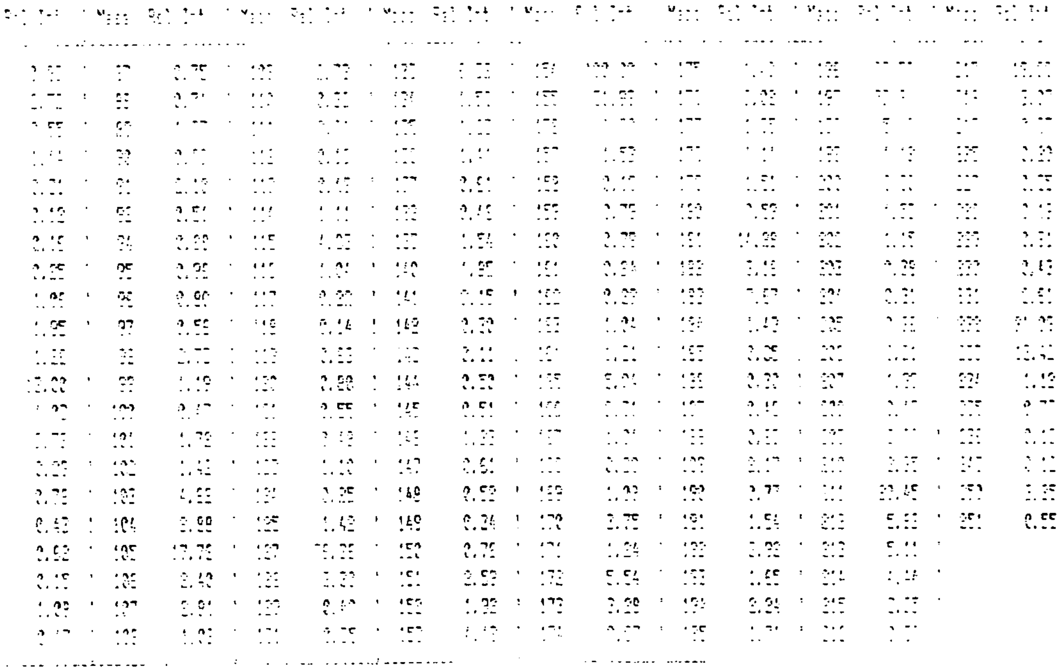
Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
57	2.77	80	0.49	104	0.25	127	5.71	148	0.07	170	1.16	192	0.10	217	2.03
58	0.12	81	1.72	105	0.93	128	0.47	149	0.66	171	0.42	193	0.89	218	1.71
59	0.04	82	0.35	106	0.42	129	0.28	150	0.35	172	0.05	194	0.13	219	21.77
61	0.42	83	0.25	107	1.41	130	0.08	151	1.17	173	0.52	195	0.26	220	7.38
62	0.96	85	1.00	108	0.38	131	0.53	152	0.15	174	0.29	197	0.43	221	28.88
63	1.10	86	0.63	110	4.09	132	0.17	153	0.09	175	1.40	198	0.79	222	3.93
64	0.11	87	0.81	111	0.48	133	0.26	154	0.05	176	0.18	199	5.93	223	0.28
65	0.04	88	0.47	112	0.21	134	0.10	155	0.43	177	0.05	200	1.94	224	0.10
67	0.09	89	0.09	113	0.09	135	0.08	156	0.22	179	0.71	201	15.09	225	0.12
68	1.20	90	0.77	114	0.36	136	0.07	157	0.31	180	0.57	202	2.13	235	0.08
69	2.09	92	0.44	115	0.03	137	0.09	158	0.06	181	1.89	203	0.17	236	0.06
70	0.54	93	0.90	116	0.14	138	0.29	160	0.03	182	0.64	204	0.09	237	1.99
71	0.06	94	2.11	117	0.35	139	0.06	161	0.19	183	0.14	205	0.09	238	0.52
72	0.13	95	12.12	118	0.40	140	0.04	162	0.63	184	0.02	206	0.76	239	27.37
73	0.30	96	1.13	119	0.75	141	0.11	163	0.31	185	0.07	207	0.31	240	67.24
74	2.56	98	0.72	120	2.03	142	0.15	164	0.46	186	0.59	208	0.05	241	8.94
75	9.97	99	1.76	122	0.27	143	1.50	165	0.06	187	0.75	211	0.07	242	0.58
76	1.01	100	2.41	123	1.10	144	2.71	166	0.03	188	3.00	213	0.16	243	0.04
77	0.33	101	1.33	124	0.31	145	100.00	167	0.36	189	1.56	214	0.03		
78	0.07	102	0.06	125	7.06	146	7.70	168	1.14	190	3.50	215	0.05		
79	0.11	103	0.12	126	17.46	147	0.40	169	1.59	191	0.51	216	0.11		

No. 24 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane. EI+

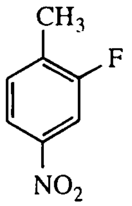


M.Wt 232

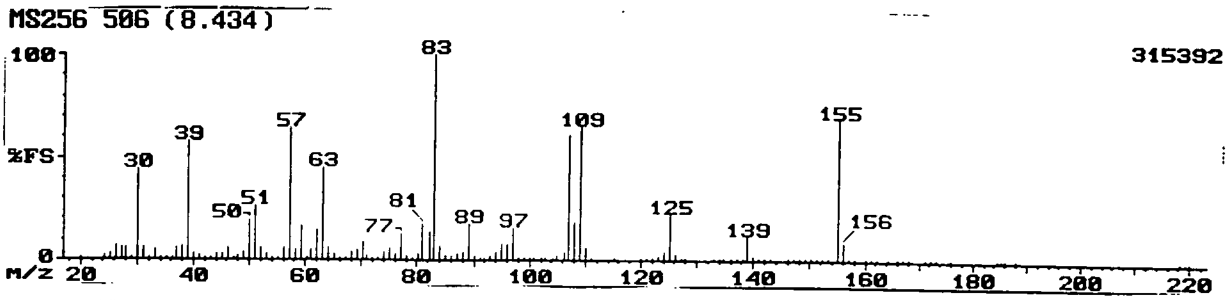




No. 25 2-Fluoro-4-nitrotoluene. EI+

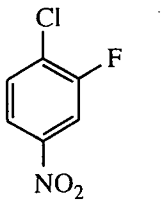


M.Wt 155

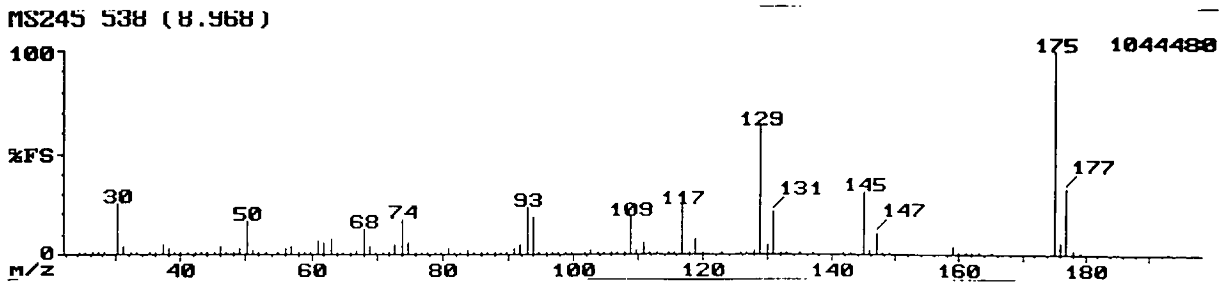


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.21	58	4.40	93	1.48	139	11.85
24	1.93	59	16.64	94	4.14	140	1.50
25	2.60	60	1.11	95	7.47	141	0.19
26	6.74	61	4.73	96	7.63	142	0.09
27	5.60	62	14.61	97	15.99	143	0.07
28	6.01	63	44.48	98	1.28	146	0.12
29	0.85	64	5.52	99	0.20	147	0.15
30	43.51	65	2.74	100	0.13	148	0.30
31	5.93	66	0.32	101	0.14	149	0.27
32	0.64	67	0.40	102	0.36	150	0.09
33	4.93	68	3.65	103	0.19	151	0.08
34	0.10	69	4.71	104	0.55	152	0.05
35	0.21	70	8.93	105	1.68	153	0.15
36	0.69	71	2.37	106	4.14	155	68.83
37	5.52	72	0.52	107	61.04	156	9.01
38	6.49	73	1.23	108	18.67	157	0.87
39	57.14	74	4.14	109	64.94	158	0.12
40	3.35	75	5.93	110	6.17	160	0.15
41	1.81	76	3.39	111	0.40	161	0.13
42	0.34	77	12.74	115	0.09	162	0.09
43	0.73	78	1.95	120	0.11	164	0.08
44	2.54	79	0.52	121	0.32	166	0.08
45	2.74	80	2.66	122	1.44	167	0.17
46	6.09	81	17.69	123	2.01	168	0.07
47	0.50	82	13.64	124	3.61	171	0.12
48	1.70	83	100.00	125	22.73	172	0.12
49	3.90	84	6.41	126	2.46	173	0.23
50	19.72	85	1.50	127	0.30	176	0.07
51	26.62	86	2.09	128	0.08	184	0.03
52	6.17	87	3.13	133	0.17	185	0.11
53	2.44	88	3.79	134	0.10	186	0.10
54	0.42	89	17.86	135	0.07	188	0.12
55	0.50	90	2.01	136	0.34	218	0.22
56	6.25	91	0.26	137	0.15	219	0.07
57	63.64	92	0.39	138	1.11	220	0.17

No. 26 1-Chloro-2-fluoro-4-nitrobenzene. EI+

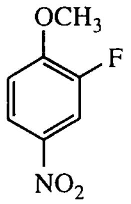


M.Wt 175/177

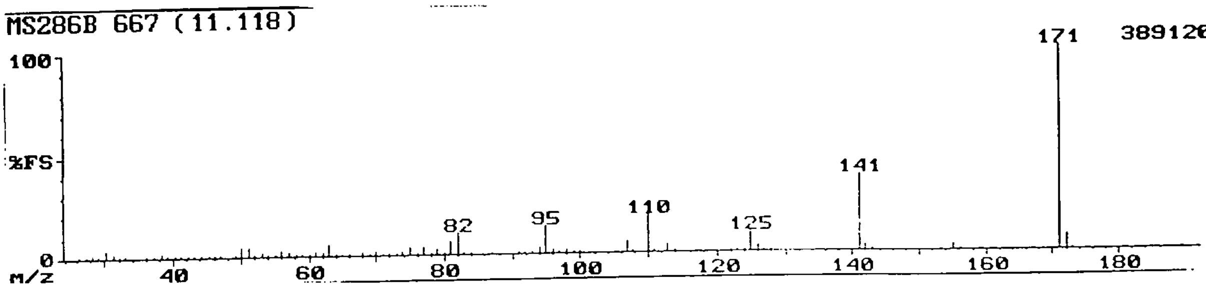


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
24	0.04	58	0.18	89	0.14	126	0.10
25	0.17	59	0.06	90	0.20	127	0.22
26	0.35	60	1.28	91	3.24	128	1.99
27	0.12	61	6.37	92	4.44	129	63.14
28	0.55	62	5.54	93	23.73	130	4.85
30	25.10	63	8.24	94	18.92	131	20.98
31	3.55	64	0.72	95	1.35	132	1.41
32	0.31	65	0.07	96	0.30	133	0.04
33	0.15	66	0.20	97	0.60	135	0.10
35	0.74	67	1.99	98	0.17	137	0.04
36	0.85	68	12.16	99	0.20	142	0.03
37	4.44	69	3.41	100	0.04	143	0.17
38	2.99	70	0.26	102	0.39	145	30.59
39	1.11	71	0.35	103	1.84	146	2.08
40	0.08	72	1.18	104	0.23	147	10.49
41	0.04	73	5.12	105	0.63	148	0.73
42	0.03	74	17.55	106	0.19	149	0.09
43	0.08	75	6.23	107	0.15	159	3.43
44	0.70	76	0.61	108	1.40	160	0.25
45	0.40	77	0.07	109	18.73	161	1.23
46	3.95	78	0.22	110	1.81	162	0.10
47	0.93	79	0.40	111	6.15	163	0.15
48	0.59	80	0.67	112	0.51	165	0.04
49	3.26	81	3.19	113	0.03	175	100.00
50	16.67	82	1.32	115	0.12	176	6.27
51	2.25	83	0.21	116	0.15	177	32.55
52	0.42	84	2.03	117	24.51	178	2.18
53	0.23	85	1.24	118	1.45	179	0.16
55	0.73	86	0.90	119	8.24	193	0.22
56	2.67	87	0.64	120	0.48	195	0.05
57	3.65	88	0.24	123	0.03		

No. 27 2-Fluoro-4-nitroanisole. EI+

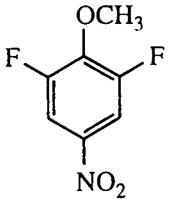


M.Wt 171

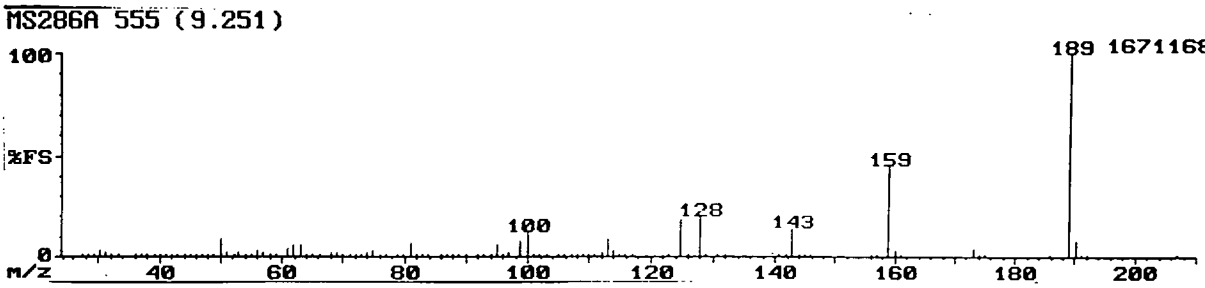


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
26	0.17	51	4.87	74	1.91	107	5.66
27	0.25	52	0.87	75	3.75	108	0.46
28	1.71	53	2.11	76	0.83	110	18.16
29	0.53	54	0.35	77	4.28	111	1.30
30	3.68	55	0.44	78	0.40	113	3.77
31	2.25	56	2.88	79	2.73	114	0.30
32	0.72	57	1.88	80	0.81	122	0.08
33	0.12	58	0.13	81	6.32	123	0.22
36	0.11	59	0.84	82	10.53	124	1.23
37	1.07	60	0.09	83	0.95	125	9.41
38	1.91	61	2.04	84	0.22	126	2.50
39	1.43	62	2.27	87	0.10	127	0.22
40	0.19	63	5.79	91	0.08	128	0.08
41	0.61	64	0.49	92	0.83	141	37.89
42	0.14	65	0.66	93	1.18	142	2.99
43	0.31	66	0.12	94	2.66	143	0.29
44	1.09	68	1.78	95	13.68	155	3.36
45	0.14	69	1.05	96	2.15	156	0.28
46	0.93	70	1.68	97	1.15	171	100.00
47	0.14	71	0.59	98	1.55	172	7.76
49	0.61	72	0.36	99	0.14	173	0.97
50	5.26	73	0.47	100	0.07	189	0.09

No. 28 2,6-Difluoro-4-nitroanisole. EI+



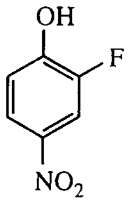
M.Wt 189



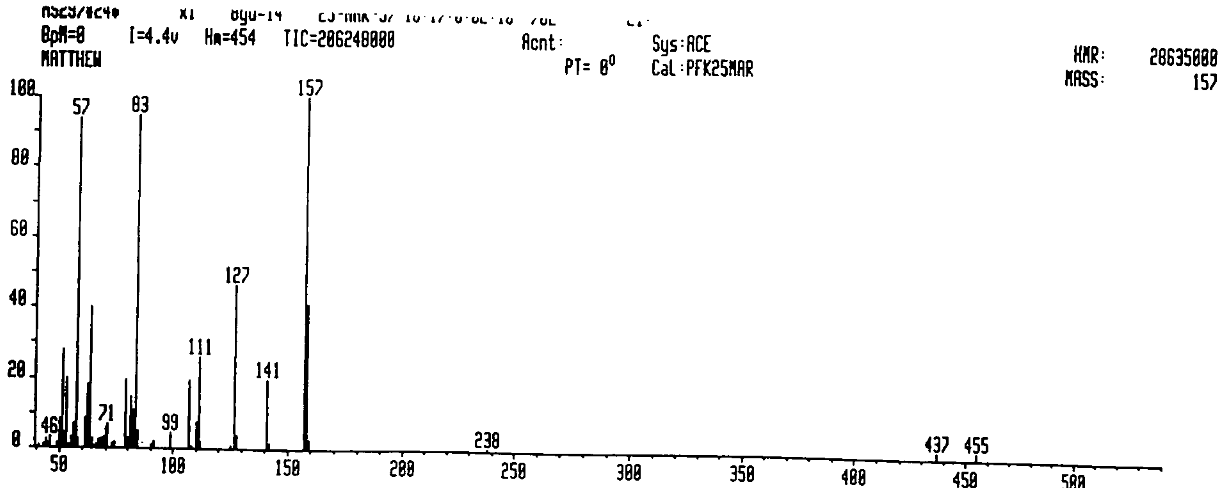
Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
27	0.04	57	1.59	89	0.58	126	1.24
28	0.33	58	0.09	90	0.04	128	19.85
29	0.59	59	0.16	92	0.83	129	1.24
30	3.22	61	3.69	93	0.94	131	1.41
31	2.19	62	5.51	94	1.27	132	0.09
32	0.16	63	5.45	95	5.58	141	0.33
33	0.10	64	0.72	96	0.70	142	1.35
36	0.07	65	0.64	97	2.36	143	13.97
37	0.69	66	0.04	99	7.72	144	1.24
38	0.70	68	1.55	100	11.95	145	0.17
39	0.90	69	2.41	101	0.93	146	0.10
40	0.07	70	0.80	102	0.07	156	0.14
41	0.09	71	0.40	103	0.04	157	0.13
42	0.05	72	0.30	105	0.61	159	44.61
43	0.31	73	0.56	106	0.07	160	3.09
44	1.42	74	1.47	107	0.02	161	0.29
45	0.31	75	2.44	108	0.06	173	3.74
46	0.76	76	0.26	109	0.20	174	0.29
47	0.10	77	0.39	110	0.42	175	0.08
48	0.05	79	0.87	111	0.70	186	0.33
49	0.58	80	1.38	112	2.24	189	100.00
50	8.39	81	7.11	113	8.82	190	7.35
51	1.93	82	0.49	114	2.54	191	0.89
52	0.12	83	0.29	115	0.47	192	0.06
53	2.22	84	0.08	116	0.85	207	0.03
54	0.08	86	0.32	117	0.07		
55	0.49	87	0.58	123	0.21		
56	3.17	88	1.16	125	18.14		

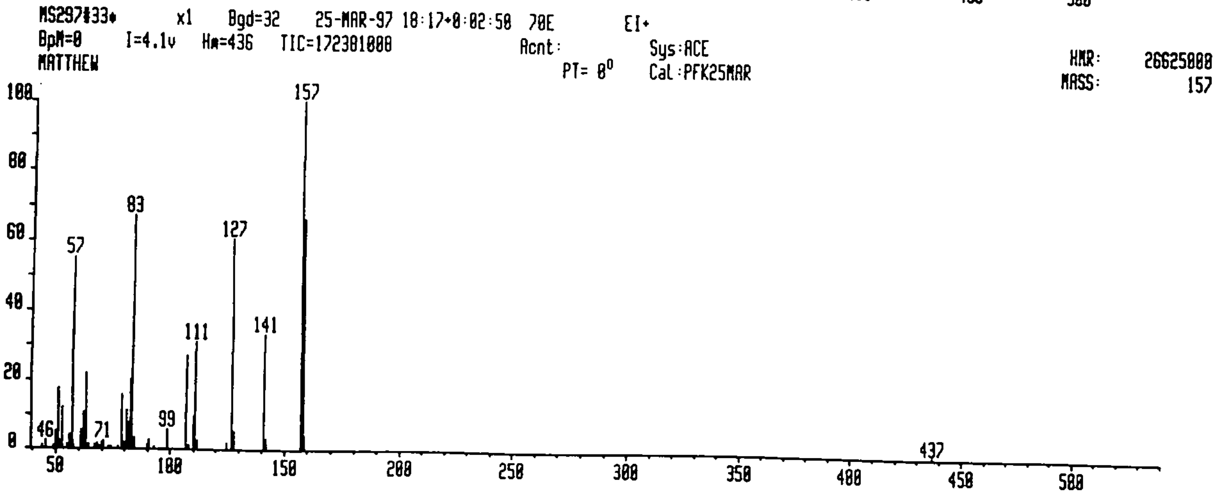
No. 29 2-Fluoro-4-nitrophenol.

EI+

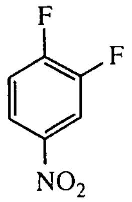


M.Wt 157

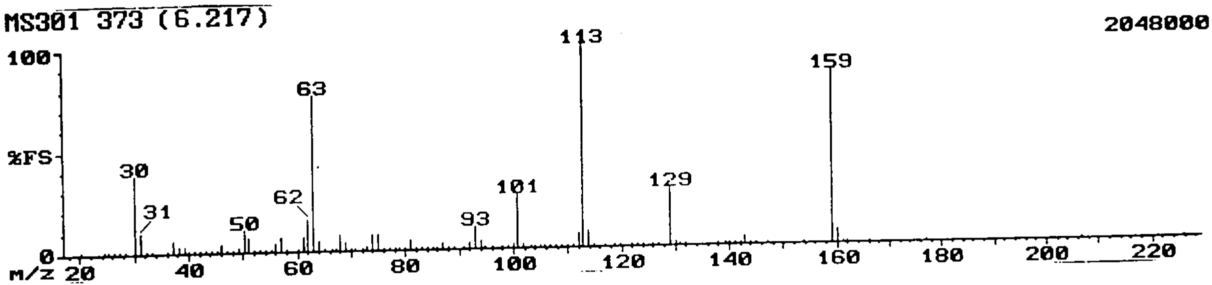




No. 30 1,2-Difluoro-4-nitrobenzene. EI$^+$

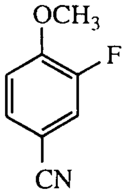


M.Wt 159

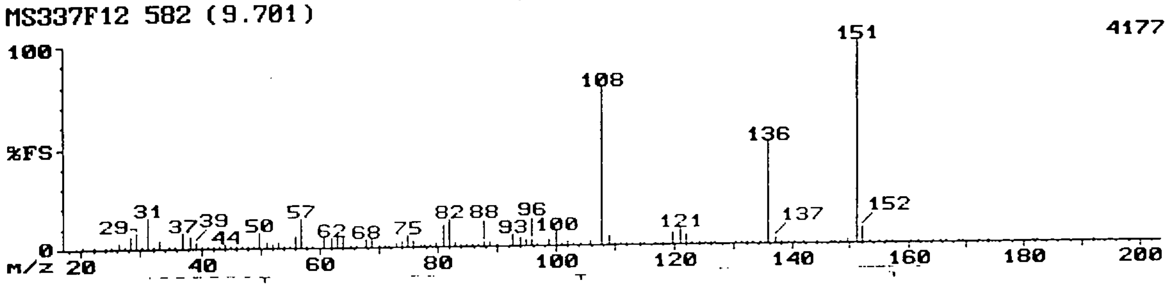


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.04	56	4.05	87	3.11	122	0.03
24	0.06	57	6.50	88	0.37	123	0.07
25	0.21	58	0.30	89	0.03	124	0.04
26	0.57	60	0.88	91	0.44	126	0.38
27	0.22	61	7.05	92	3.18	127	0.47
28	1.45	62	15.20	93	10.85	129	28.40
30	37.60	63	76.80	94	3.60	130	1.96
31	9.35	64	4.80	95	0.33	131	0.19
32	0.67	65	0.20	96	0.02	132	0.02
33	0.21	66	0.01	98	0.03	138	0.02
36	0.69	67	0.29	99	1.19	139	0.01
37	5.90	68	8.15	100	1.78	140	0.20
38	3.35	69	4.20	101	26.00	141	0.02
39	2.91	70	0.47	102	1.59	142	0.11
40	0.19	71	0.08	103	0.04	143	4.25
41	0.08	72	0.22	104	0.02	144	0.32
42	0.05	73	2.11	105	0.06	145	0.04
43	0.20	74	7.30	106	0.20	147	0.03
44	1.30	75	8.20	107	0.25	154	0.03
45	1.03	76	0.95	108	0.10	159	85.60
46	3.40	77	0.33	109	0.14	160	6.40
47	0.10	78	0.02	110	0.42	161	0.63
48	0.43	79	0.60	111	0.98	162	0.03
49	2.38	80	1.45	112	7.00	166	0.02
50	10.65	81	4.85	113	100.00	177	0.08
51	6.55	82	0.84	114	7.35	207	0.02
52	0.59	83	0.04	115	0.27	226	0.02
53	0.18	84	0.02	117	0.03		
54	0.05	85	0.02	119	0.07		
55	0.95	86	0.70	120	0.03		

No. 31 2-Fluoro-1 methoxy-4-benzonitrile. EI+

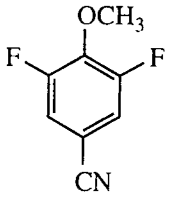


M.Wt 151

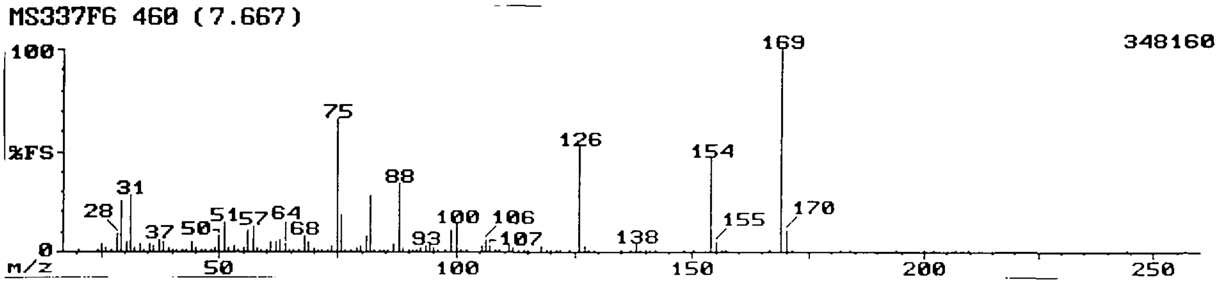


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.07	56	5.76	93	5.37	133	0.02
22	0.01	57	14.61	94	4.17	134	0.22
24	0.09	58	0.92	95	2.48	136	50.59
25	0.47	59	0.06	96	2.50	137	3.01
26	2.65	61	4.61	97	0.67	138	0.11
27	1.29	62	4.68	99	2.55	139	0.03
28	5.96	63	4.49	100	6.76	140	0.01
29	7.55	64	4.44	101	0.72	142	0.02
30	1.05	65	0.30	102	1.69	144	0.01
31	15.10	66	0.07	103	1.19	147	0.25
32	1.20	68	3.97	104	0.24	147	0.28
33	3.77	69	3.46	106	1.96	148	0.18
35	0.04	70	1.16	108	78.04	150	1.57
36	0.38	71	0.30	109	4.95	151	100.00
37	7.55	72	0.10	110	0.39	152	8.24
38	5.56	73	1.47	111	0.02	153	0.35
39	3.04	74	2.89	112	0.03	155	0.02
40	0.23	75	5.71	113	0.01	156	0.01
41	0.59	76	3.06	114	0.02	157	0.01
42	0.25	77	0.40	115	0.01	160	0.01
43	0.53	78	0.16	117	1.24	162	0.02
44	2.35	79	0.72	118	0.31	164	0.01
45	1.08	80	2.23	120	6.20	166	0.01
46	0.52	81	10.88	121	7.75	166	0.01
47	0.08	82	13.73	122	4.90	169	0.01
48	0.20	83	2.11	123	1.42	169	0.02
49	1.42	84	0.28	124	0.11	172	0.00
50	8.14	85	0.23	125	0.03	174	0.04
51	3.01	86	0.66	126	0.05	182	0.01
52	1.59	87	1.41	127	0.01	182	0.00
53	2.45	88	2.35	130	0.13	192	0.02
54	0.32	89	1.91	131	0.06	207	0.02
55	0.59	90	0.27	132	0.02		

No. 32 2,6-Difluoro-1-methoxy-4-benzonitrile. EI+

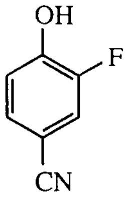


M.Wt 169

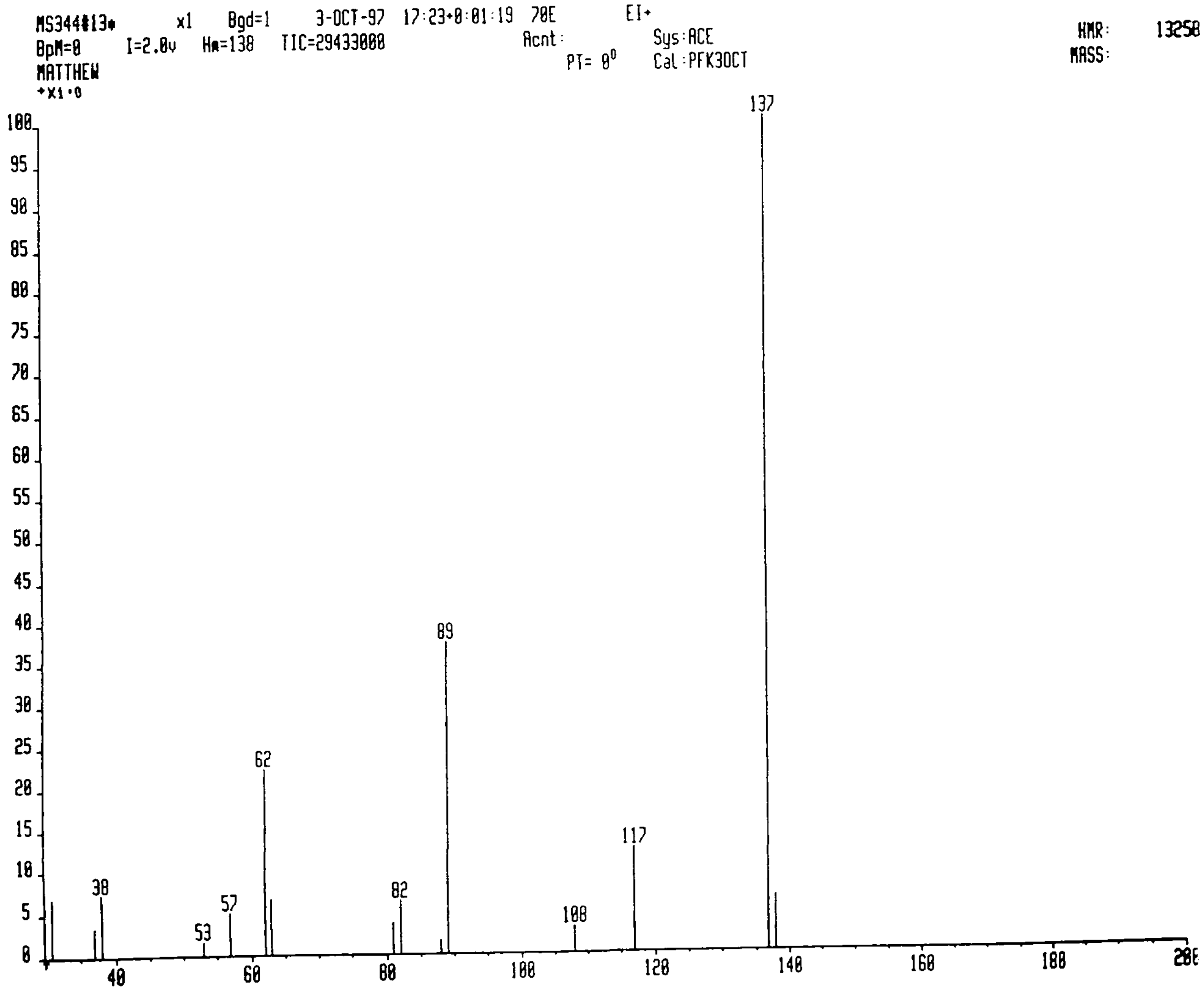


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.10	55	1.56	87	3.73	126	52.35
24	1.12	56	10.96	88	33.53	127	2.83
25	3.66	57	12.94	89	2.19	128	0.50
26	1.62	58	1.60	90	0.19	129	0.05
27	1.34	59	0.09	91	0.86	135	1.18
28	8.46	60	0.44	92	0.40	137	0.79
29	25.59	61	5.00	92	2.26	138	3.95
30	5.00	62	4.78	93	2.94	139	1.29
31	28.24	63	5.51	94	3.09	140	1.27
32	1.54	64	3.90	95	1.58	141	0.86
33	3.49	65	0.41	96	0.24	142	0.10
34	0.06	66	0.11	97	0.33	148	0.12
35	3.81	67	0.21	99	10.96	150	0.05
36	2.70	68	7.50	100	13.46	154	46.76
37	6.03	69	5.07	101	1.12	155	5.15
38	5.07	70	1.93	102	0.18	156	0.60
39	1.71	71	0.74	105	2.65	157	0.07
40	0.19	72	0.46	106	5.66	166	0.33
41	0.16	73	0.60	107	3.05	169	100.00
42	0.23	74	3.01	108	0.46	170	10.96
43	1.09	75	65.88	109	0.08	171	0.85
44	4.38	76	18.09	111	2.52	182	0.09
45	1.84	77	0.66	112	2.02	184	0.21
46	0.78	78	0.12	113	0.80	194	0.15
47	0.53	79	1.73	114	0.73	200	1.21
48	1.09	80	3.13	115	0.22	202	0.14
49	2.26	81	8.09	118	3.03	207	0.07
50	8.01	82	28.53	119	1.29	210	0.10
51	14.12	83	0.99	120	1.27	244	0.05
52	1.73	84	0.35	121	0.65	257	0.03
53	2.94	85	0.08	122	0.36		
54	0.18	86	0.82	124	1.21		

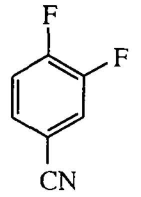
No. 33 2-Fluoro-1-hydroxy-4-benzonitrile. EI$^+$



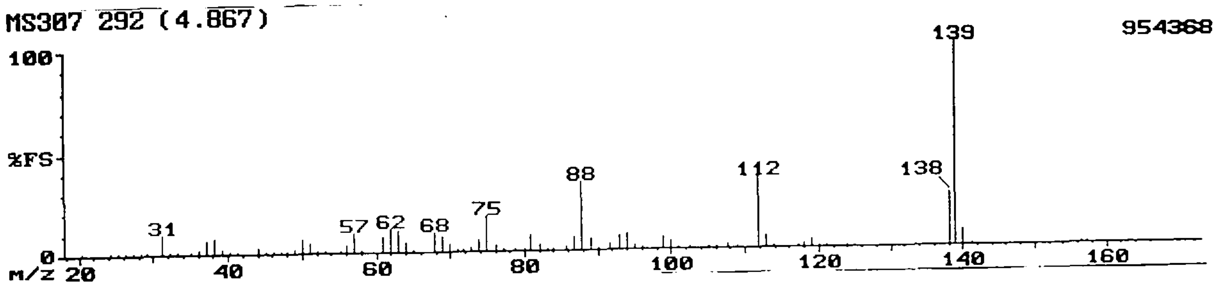
M.Wt 137



No. 34 1,2-Difluoro-4-benzonitrile EI+

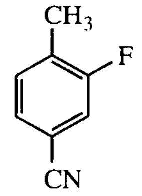


M.Wt 139

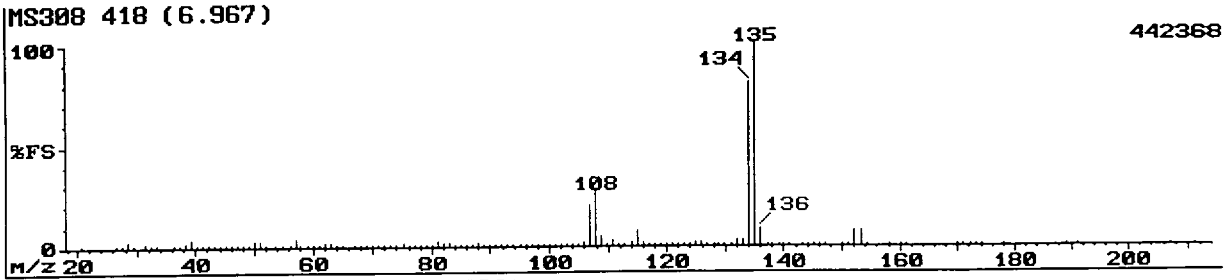


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.10	49	2.23	76	2.49	105	1.11
24	0.18	50	7.19	77	0.20	106	1.38
25	0.42	51	5.34	79	0.79	108	2.12
26	1.03	52	1.07	80	0.74	109	0.14
27	0.86	53	0.06	81	7.51	112	34.76
28	1.37	55	0.43	82	3.08	113	5.74
29	0.03	56	3.70	83	0.19	114	0.31
31	9.98	57	9.76	84	0.14	117	0.62
32	0.46	58	0.46	86	1.98	118	1.72
33	0.50	61	7.40	87	7.19	119	3.97
35	0.26	62	11.48	88	34.33	120	1.39
36	2.09	63	10.62	89	5.50	121	0.15
37	6.97	64	5.02	90	0.37	124	0.21
38	7.94	65	0.16	92	3.00	125	0.16
39	1.88	68	10.09	93	6.87	138	26.50
40	0.15	69	7.62	94	8.15	139	100.00
41	0.04	70	3.94	95	2.31	140	8.15
44	2.74	71	0.17	96	0.10	141	0.24
45	1.31	72	0.44	99	5.79	156	0.01
46	0.47	73	1.80	100	3.73	157	0.07
47	0.11	74	5.42	101	0.30	169	0.01
48	0.66	75	17.38	103	0.02	170	0.07

No. 35 1-Methyl-2-fluoro-4-benzonitrile. EI+

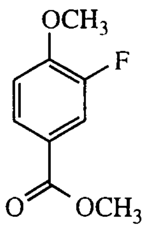


M.Wt 135

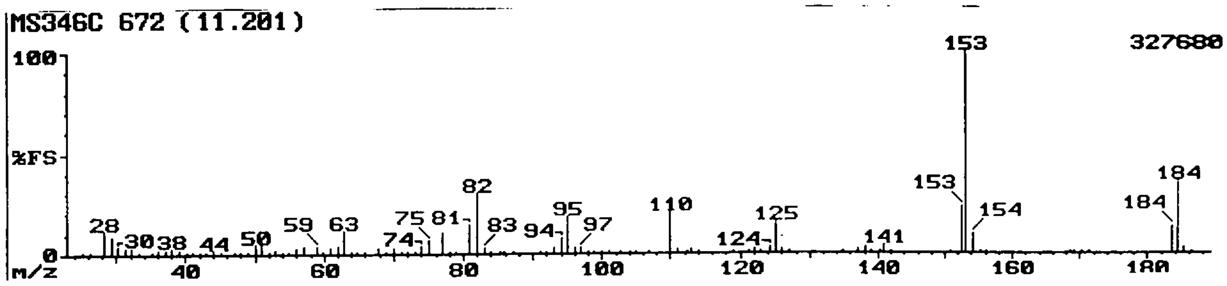


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.05	63	2.37	98	0.26	132	2.69
26	0.37	64	1.22	99	0.67	133	3.18
27	0.77	65	0.47	100	0.89	134	80.56
28	2.99	67	0.71	101	0.45	135	100.00
29	0.10	68	1.14	102	0.44	136	9.20
31	2.05	69	0.68	103	0.30	137	0.44
32	0.94	70	0.46	104	0.27	138	0.15
33	0.88	71	0.10	105	1.06	139	0.12
36	0.10	72	0.08	106	2.00	140	0.30
37	1.36	73	0.26	107	20.83	141	0.06
38	1.79	74	0.85	108	27.31	143	0.16
39	3.44	75	1.74	109	4.69	144	0.11
40	0.35	76	1.27	110	0.42	145	0.18
41	0.19	77	0.54	111	2.68	146	0.08
42	0.06	78	0.41	112	0.37	147	0.07
43	0.42	79	0.76	113	0.19	150	0.33
44	0.90	80	0.62	114	2.01	151	0.50
45	0.55	81	2.91	115	7.87	152	7.87
46	0.25	82	1.94	116	1.87	153	7.52
47	0.18	83	2.10	117	0.15	154	0.67
48	0.13	84	0.54	118	0.09	158	0.12
49	0.66	85	0.59	119	0.10	160	0.07
50	2.88	86	0.69	120	0.29	161	0.09
51	2.86	87	1.36	121	0.38	170	0.83
52	0.92	88	1.91	122	0.40	171	0.43
54	0.17	89	1.16	123	0.14	172	0.10
55	0.36	90	0.28	124	0.20	173	0.04
56	1.10	91	0.24	125	1.59	174	0.10
57	4.34	92	0.26	126	1.82	178	0.06
58	0.55	93	0.59	127	0.71	189	0.09
59	0.18	94	0.74	128	0.13	191	0.09
60	0.22	95	0.60	129	0.10	207	0.13
61	1.24	96	0.37	130	0.04	211	0.09
62	1.77	97	0.12	131	0.04		

No. 36 2-Fluoro-4-methoxy-methylbenzoate. EI+

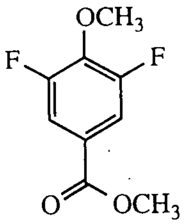


M.Wt 189

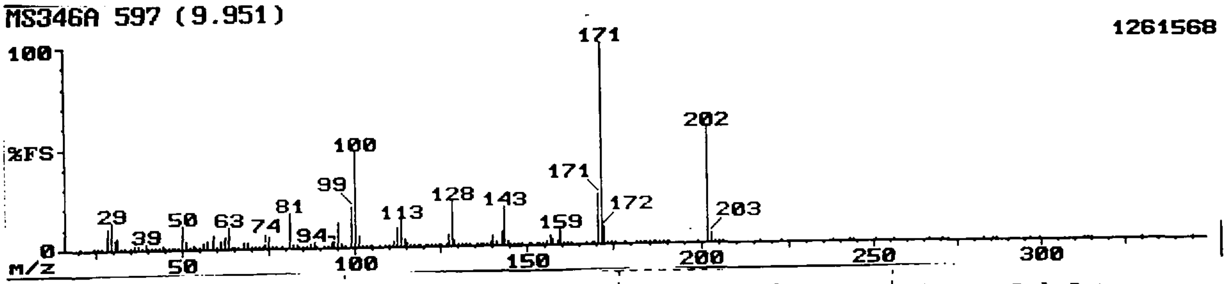


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
25	0.12	55	0.39	86	0.06	125	15.08
26	0.35	56	3.32	87	0.09	126	1.54
28	11.64	57	3.54	91	0.59	127	0.26
29	8.91	59	4.32	92	1.41	135	0.13
30	3.42	60	0.23	93	2.73	137	1.97
31	3.28	61	2.70	94	8.20	138	2.58
32	2.44	62	3.52	95	18.20	139	1.14
33	0.20	63	11.56	96	2.95	140	1.20
35	1.23	64	0.29	97	2.99	141	4.06
36	2.21	65	0.86	98	0.67	142	0.37
37	1.60	66	0.30	99	0.21	151	0.30
38	2.44	68	2.89	100	0.07	153	23.75
39	1.89	69	1.19	101	0.05	153	100.00
40	0.40	70	2.44	103	0.12	154	9.30
41	0.38	71	0.48	104	0.27	155	0.90
42	0.16	72	0.30	105	0.24	156	0.10
43	0.37	73	0.49	107	0.20	169	0.15
44	2.11	74	3.63	110	20.00	169	0.41
45	0.70	75	6.95	111	1.74	170	0.18
47	0.25	77	10.39	112	0.38	171	0.13
48	0.16	78	0.96	113	1.56	184	13.75
49	0.57	79	0.77	114	0.08	184	35.94
50	5.00	81	14.30	119	0.59	185	3.36
51	4.69	82	29.69	121	0.41	186	0.45
52	0.47	83	3.22	122	2.27		
53	1.88	84	0.53	123	0.85		
54	0.17	85	0.15	124	3.34		

No. 37 2,6-Difluoro-4-methoxy-methylbenzoate. EI+



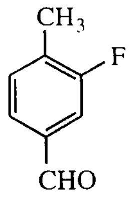
M.Wt 202



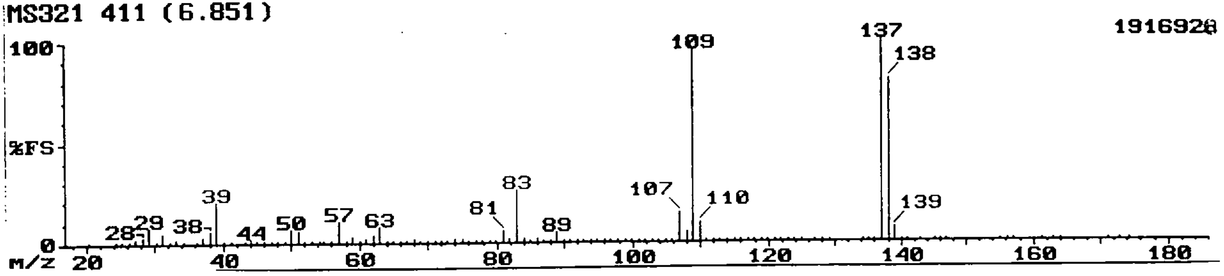
Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.06	71	0.93	121	0.65	171	100.00
24	0.09	72	0.38	122	1.06	172	9.17
25	0.20	73	0.87	123	0.63	173	0.86
26	0.27	74	2.25	124	0.22	174	0.10
28	10.55	75	5.84	125	0.51	175	0.04
29	13.15	76	0.57	126	0.45	178	0.01
30	4.38	77	1.29	127	6.09	181	0.04
31	5.84	79	1.19	128	22.08	183	0.02
32	1.28	81	17.37	129	3.13	183	0.05
33	0.44	82	1.54	130	0.78	184	0.22
35	1.23	83	2.15	131	1.13	185	0.15
36	1.50	84	0.34	132	0.10	187	0.43
37	1.75	85	0.25	133	0.02	187	1.30
38	1.36	86	0.45	135	0.03	188	0.65
39	2.58	87	2.11	136	0.40	189	0.18
40	0.24	88	2.88	137	1.40	190	0.08
41	0.08	89	1.18	138	0.69	191	0.02
42	0.10	91	0.47	139	2.15	199	0.26
43	0.63	92	1.29	140	5.28	202	57.47
44	2.31	93	3.02	141	1.62	203	5.01
45	1.06	94	3.29	142	6.57	204	0.60
46	0.07	95	12.74	143	19.81	205	0.18
47	0.25	96	1.52	144	2.17	206	0.05
48	0.31	97	1.16	145	0.48	217	0.14
49	0.80	99	20.62	146	0.08	223	0.03
50	11.77	100	47.73	147	0.06	238	0.05
51	4.36	101	5.68	148	0.02	243	0.25
52	0.33	102	0.47	151	0.03	244	0.02
53	1.89	103	0.27	151	0.12	251	0.02
54	0.08	104	0.05	153	0.06	256	0.04
55	0.57	105	0.10	153	0.18	267	0.02
56	2.82	107	0.14	154	0.28	271	0.13
57	3.61	109	1.17	155	2.01	272	0.02
59	6.33	110	1.15	156	4.81	283	0.07
60	0.16	111	2.72	157	2.88	286	0.10
61	3.59	112	9.90	158	2.39	287	0.08
62	5.52	113	13.72	159	7.95	297	0.03
63	11.12	114	3.75	160	0.67	300	0.02
64	0.60	115	1.77	161	0.09	313	0.02
65	1.00	116	0.44	162	0.03	314	0.03
66	0.08	117	0.25	167	0.03	315	0.06
68	2.66	118	0.05	168	0.11	330	0.10
69	3.19	119	0.23	169	0.43	345	0.05
70	0.70	120	0.12	171	25.32		

No. 38 2-Fluoro-4-tolualdehyde.

EI+



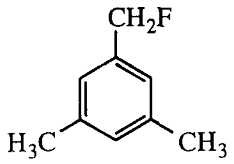
M.Wt 138



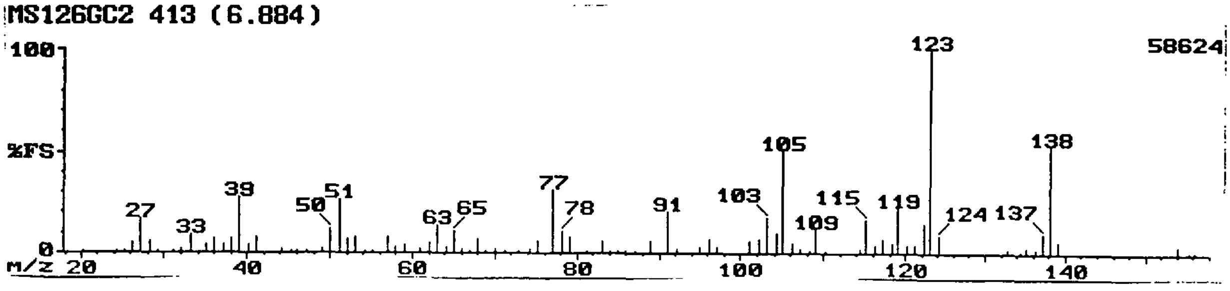
Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
26	1.30	55	1.20	79	1.62	103	0.66
27	1.96	56	5.96	80	5.30	104	1.05
28	15.30	57	30.10	81	20.23	105	4.81
29	21.88	58	1.89	82	1.84	106	1.67
31	8.51	59	1.30	83	5.35	107	31.41
32	4.98	60	0.69	84	1.31	108	4.36
33	1.50	61	7.52	85	3.99	109	3.33
37	2.75	62	11.18	86	4.19	112	0.82
38	3.33	63	14.97	87	3.45	113	0.64
39	7.69	64	3.13	88	1.93	119	0.67
40	1.08	65	0.39	89	1.73	123	0.38
41	1.07	67	0.63	90	0.45	125	19.08
43	2.23	68	5.43	92	1.77	126	7.52
44	4.73	69	3.04	93	2.01	127	88.82
45	1.43	70	2.96	94	2.20	128	9.25
46	0.49	71	1.10	95	0.75	129	0.65
49	2.10	73	2.50	96	1.57	141	0.80
50	10.86	74	8.72	98	0.73	154	0.56
51	19.57	75	21.05	99	5.35	155	100.00
52	1.46	76	3.82	100	2.41	156	69.74
53	1.95	77	15.63	101	35.36	157	6.21
54	0.50	78	1.52	102	2.29		

No. 39 1-Fluoromethyl-3,5-dimethylbenzene.

EI+

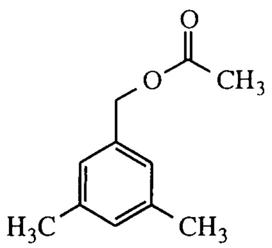


M.Wt 138

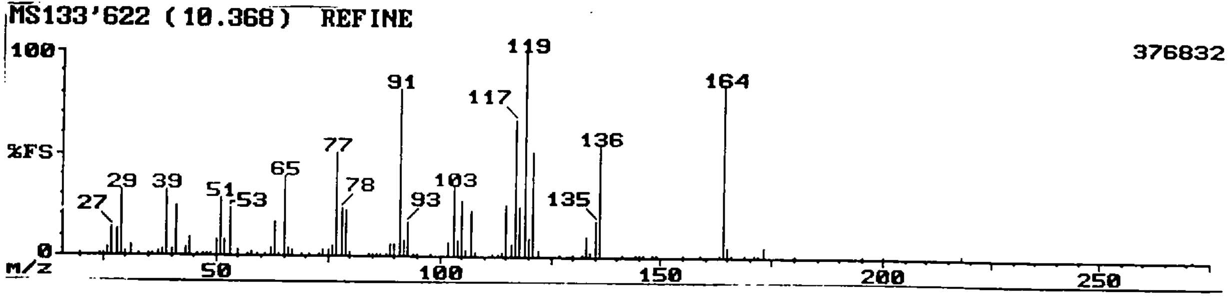


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.93	51	26.42	78	10.81	110	1.45
24	0.29	52	6.88	79	7.75	114	1.73
25	1.02	53	7.97	81	1.15	115	16.05
26	4.99	54	0.81	83	5.62	116	4.12
27	16.16	55	0.31	84	0.77	117	6.52
28	5.54	57	7.97	85	0.91	118	4.83
29	1.13	58	2.62	86	0.74	119	21.94
31	1.10	59	3.90	87	1.22	120	3.85
32	1.59	61	1.56	89	5.46	121	3.93
33	9.06	62	4.80	91	20.52	122	14.52
35	4.07	63	13.65	92	2.16	123	100.00
36	6.58	64	2.54	95	3.14	124	9.06
37	3.68	65	11.14	96	6.50	133	1.55
38	7.10	66	1.91	97	2.97	134	0.43
39	27.18	67	0.76	101	5.65	135	2.48
40	3.47	68	7.21	102	6.52	136	1.75
41	7.86	69	1.02	103	17.58	137	9.50
44	1.88	70	1.97	104	9.28	138	53.71
45	0.57	71	1.01	105	50.22	139	6.11
46	0.68	73	0.61	106	5.02	154	4.12
47	0.68	74	2.10	107	1.55	155	0.36
49	1.51	75	5.79	108	1.11	156	1.41
50	11.24	77	31.00	109	11.35		

No. 40 Formic Acid-3,5-Dimethylbenzyl Ester. EI+

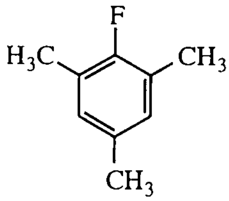


M.Wt 164

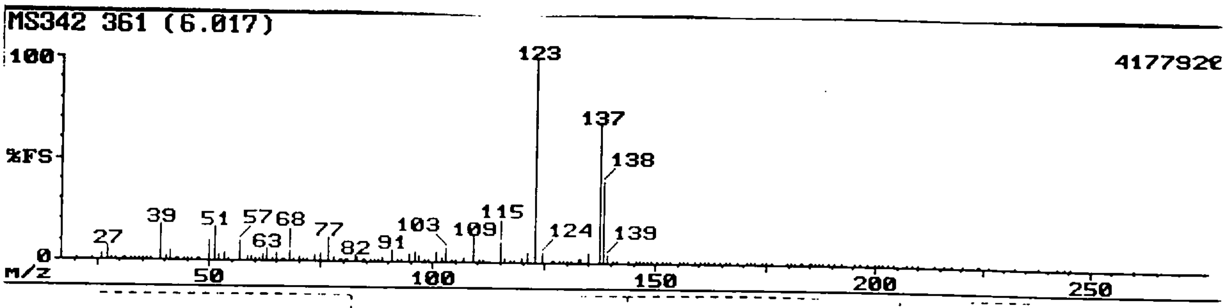


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
25	0.17	55	0.32	87	0.99	119	3.24
26	1.95	56	0.14	89	5.77	120	2.00
27	6.43	57	7.35	91	19.85	121	4.07
28	0.69	59	4.62	94	0.15	122	12.41
29	0.67	61	2.21	95	1.07	123	100.00
31	0.45	62	3.38	96	8.64	124	7.08
32	0.25	63	12.87	97	2.90	125	0.45
33	3.19	64	2.16	101	4.07	126	0.07
35	0.12	65	13.60	102	2.44	127	0.07
37	1.34	66	1.63	103	16.91	132	0.31
39	23.53	67	1.72	104	3.22	133	3.24
40	2.37	70	3.15	105	56.99	134	0.78
41	6.25	71	2.09	106	3.91	135	2.80
42	0.44	73	0.80	108	1.22	136	2.32
45	0.65	74	4.16	109	10.48	137	17.65
46	0.68	75	8.00	110	1.02	138	61.03
47	0.55	77	47.06	113	0.17	139	4.73
49	0.35	78	3.79	114	1.28	140	0.31
50	7.08	79	10.94	115	14.80	141	0.61
51	19.39	81	2.32	116	3.03	156	0.24
52	4.53	83	7.17	117	5.35		
53	6.62	86	0.83	118	3.26		

No. 41 2-Fluoro-1,3,5-trimethylbenzene. EI+

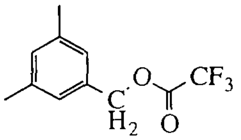


M.Wt 138

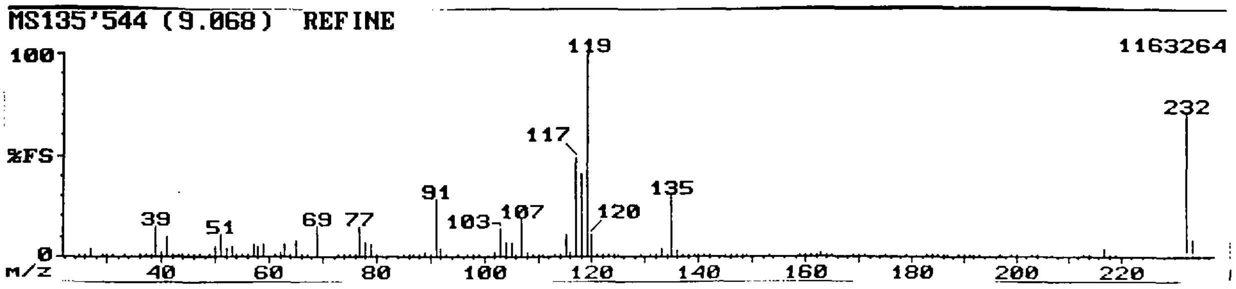


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
20	0.07	70	1.74	123	100.00	175	0.02
24	0.21	71	1.07	124	4.71	176	0.02
26	3.16	72	0.20	127	0.16	180	0.03
27	7.16	74	2.60	127	0.14	180	0.03
28	1.31	75	4.09	128	0.07	181	0.01
29	0.37	77	11.27	129	0.03	183	0.05
31	0.57	78	1.89	130	0.04	183	0.03
31	0.59	79	0.60	131	0.08	185	0.02
33	0.73	80	0.09	133	1.91	185	0.03
33	0.53	80	0.91	133	1.99	186	0.01
34	0.02	81	0.84	135	4.41	187	0.01
35	0.12	82	2.89	137	67.84	188	0.01
36	0.36	83	2.21	138	39.61	189	0.02
37	1.42	84	0.29	139	3.65	191	0.02
39	17.45	85	0.38	141	1.13	192	0.03
40	2.03	86	0.42	141	0.97	195	0.01
41	4.68	87	0.63	144	0.02	197	0.01
42	0.10	88	0.15	146	0.06	198	0.04
43	0.17	89	1.84	146	0.07	200	0.04
44	0.39	91	5.91	147	0.04	201	0.02
45	0.83	92	0.47	148	0.02	202	0.01
46	0.72	93	0.31	149	0.02	203	0.01
47	0.69	95	3.50	150	0.08	204	0.01
48	0.13	96	4.68	152	0.10	207	0.01
50	9.41	97	2.72	153	0.09	209	0.03
51	16.08	98	0.38	153	0.04	210	0.01
52	3.38	99	0.31	156	0.95	214	0.02
53	3.90	101	5.29	156	0.49	216	0.01
54	0.23	102	2.35	157	0.06	218	0.01
57	9.41	103	6.96	159	0.07	220	0.02
59	2.03	104	0.56	160	0.06	224	0.03
59	1.99	105	0.99	161	0.02	224	0.02
60	0.31	107	1.76	162	0.07	226	0.01
61	1.45	109	12.35	163	0.01	233	0.01
62	2.65	110	0.87	165	0.04	238	0.01
63	6.27	111	0.23	166	0.01	243	0.01
64	1.39	115	9.51	167	0.03	244	0.01
65	4.31	116	1.64	169	0.01	245	0.01
66	0.79	117	1.24	171	0.03	260	0.01
67	0.59	118	0.29	172	0.03	272	0.00
68	4.46	120	2.28	172	0.01		
69	1.35	121	4.73	174	0.11		

No. 42 Trifluoroacetic Acid-3,5-Dimethylbenzyl Ester. EI+



M.Wt

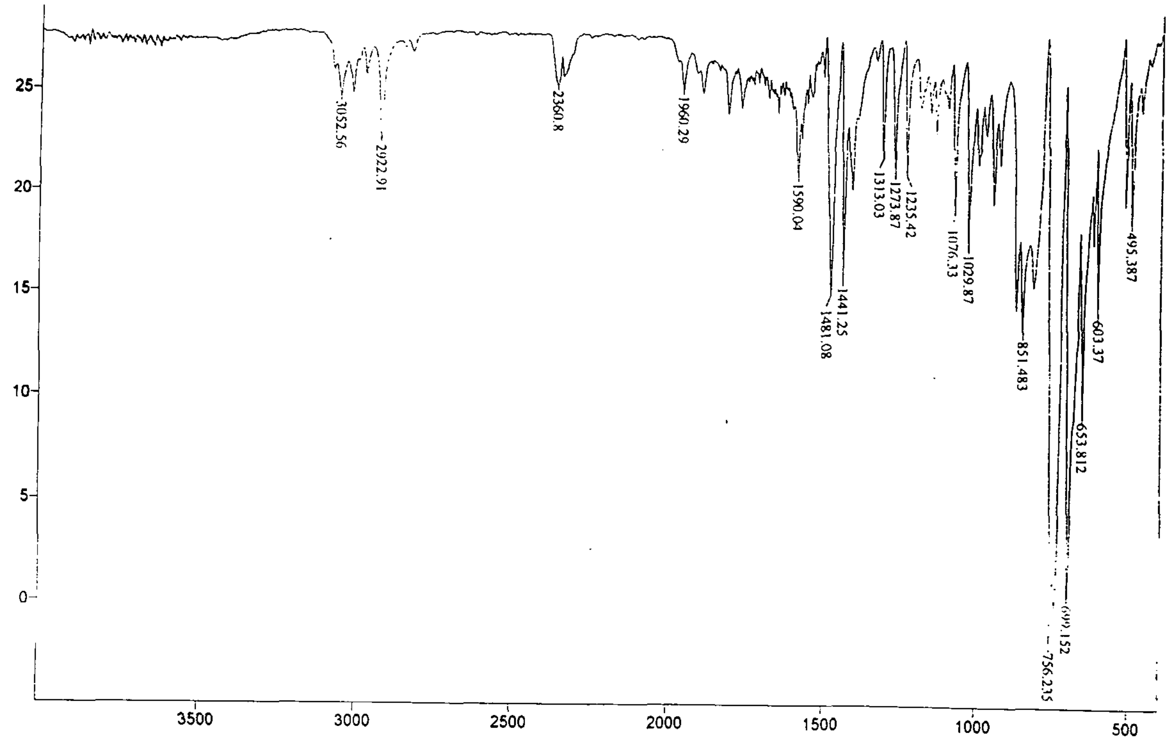


Mass	Rel Int	Mass	Rel Int	Mass	Rel Int	Mass	Rel Int
25	0.02	66	0.98	114	0.07	163	1.50
26	0.28	67	0.51	115	11.09	164	0.22
27	3.72	69	14.35	116	2.24	165	0.05
29	1.09	73	0.09	117	48.94	169	0.19
30	0.08	74	0.94	118	40.49	170	0.04
31	0.27	75	1.01	119	100.00	171	0.02
33	0.03	76	1.03	120	10.39	175	0.03
36	0.03	77	14.70	121	0.61	179	0.01
37	0.28	78	6.78	122	0.10	183	0.08
38	1.39	79	5.63	123	0.24	184	0.02
39	14.79	80	0.45	124	0.04	185	0.02
40	1.78	85	0.09	125	0.03	186	0.04
41	10.04	86	0.25	129	0.04	187	0.03
42	0.40	87	0.35	131	0.06	189	0.75
43	0.67	88	0.14	132	0.05	190	0.09
44	0.95	89	1.91	133	4.01	191	0.03
45	0.40	90	0.72	134	0.77	192	0.07
46	0.08	91	27.82	135	30.28	193	0.04
47	0.10	92	3.43	136	3.04	197	0.03
49	0.12	93	1.18	137	0.48	199	0.03
50	5.04	95	0.06	138	0.05	200	0.03
51	10.74	97	0.85	139	0.02	203	0.37
52	4.07	98	0.14	140	0.05	204	0.05
53	5.22	99	0.12	141	0.25	207	0.01
54	0.38	102	2.24	142	0.06	213	0.07
55	0.51	103	13.64	145	0.06	214	0.03
56	0.08	104	7.13	146	0.03	217	3.72
57	5.59	105	7.13	147	0.09	218	0.41
58	4.82	106	1.17	148	0.04	219	0.04
59	5.81	107	18.75	149	0.03	230	0.22
61	0.32	108	1.76	153	0.01	231	2.31
62	1.56	109	0.22	159	0.08	232	71.13
63	5.50	110	0.03	160	0.02	233	8.36
64	1.34	111	0.03	161	0.23	234	0.80
65	8.10	113	0.09	162	0.09		

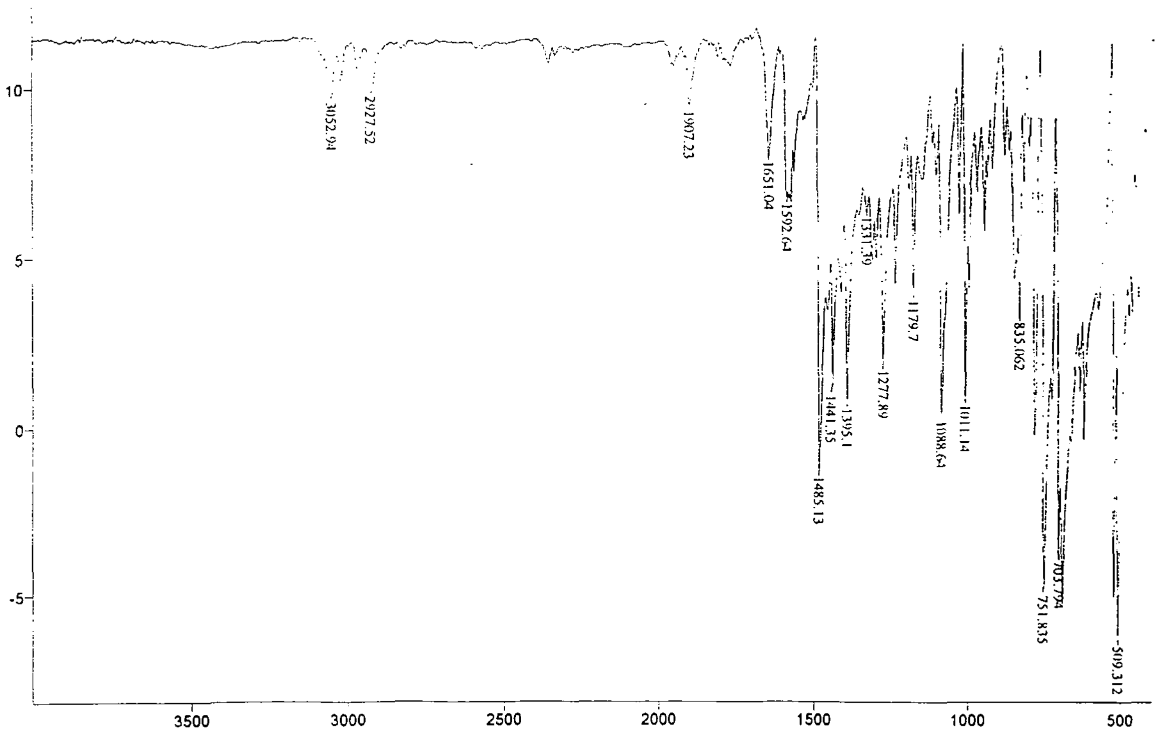
Appendix Three IR Spectra.

No. 1	2,2 Diphenyl-1,3-dithiolane (**37**).
No. 2	2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane (**39**).
No. 3	2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane (**40**).
No. 4	2,2-Bis(4-fluorophenyl)-1,3-dithiolane (**42**).
No. 5	2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane (**38**).
No. 6	2-Butyl-2-phenyl-1,3-dithiolane (**43**).
No. 7	2-Butyl-2-methyl-1,3-dithiolane (**45**).
No. 8	2-Ethyl-2-pentyl-1,3-dithiolane (**46**).
No. 9	Cyclododecan-1,3-dithiolane (**44**).
No. 10	Benzophenone (**58**).
No. 11	Cyclododecanone (**59**).
No. 12	4-Chlorobenzophenone (**60**).
No. 13	2-Hexanone (**62**).
No. 14	3-Octanone (**63**).
No. 15	2-Fluoro-4-nitrotoluene (**68**).
No. 16	1-Chloro-2-fluoro-4-nitrobenzene (**74**).
No. 17	2-Fluoro-4-nitroanisole (**81**).
No. 18	2,6-Difluoro-4-nitroanisole (**82**).
No. 19	2-Fluoro-1-methoxy-4-benzonitrile (**93**).
No. 20	2,6-Difluoro-1-methoxy-4-benzonitrile (**94**).
No. 21	2-Fluoro-1-hydroxy-4-benzonitrile (**90**).
No. 22	1,2-Difluoro-4-benzonitrile (**97**).
No. 23	1-Methyl-2-fluoro-4-benzonitrile (**96**).
No. 24	2,6-Difluoro-4-methoxy-methylbenzoate (**79**).

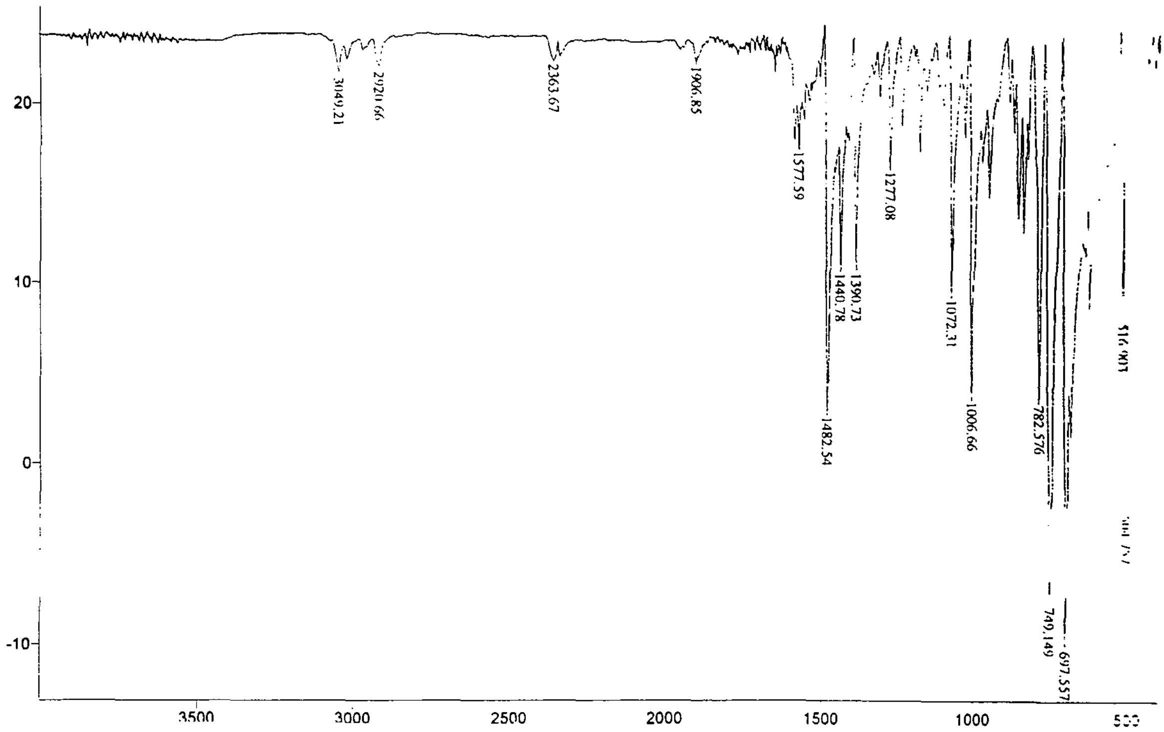
No. 1 **2,2 Diphenyl-1,3-dithiolane.**



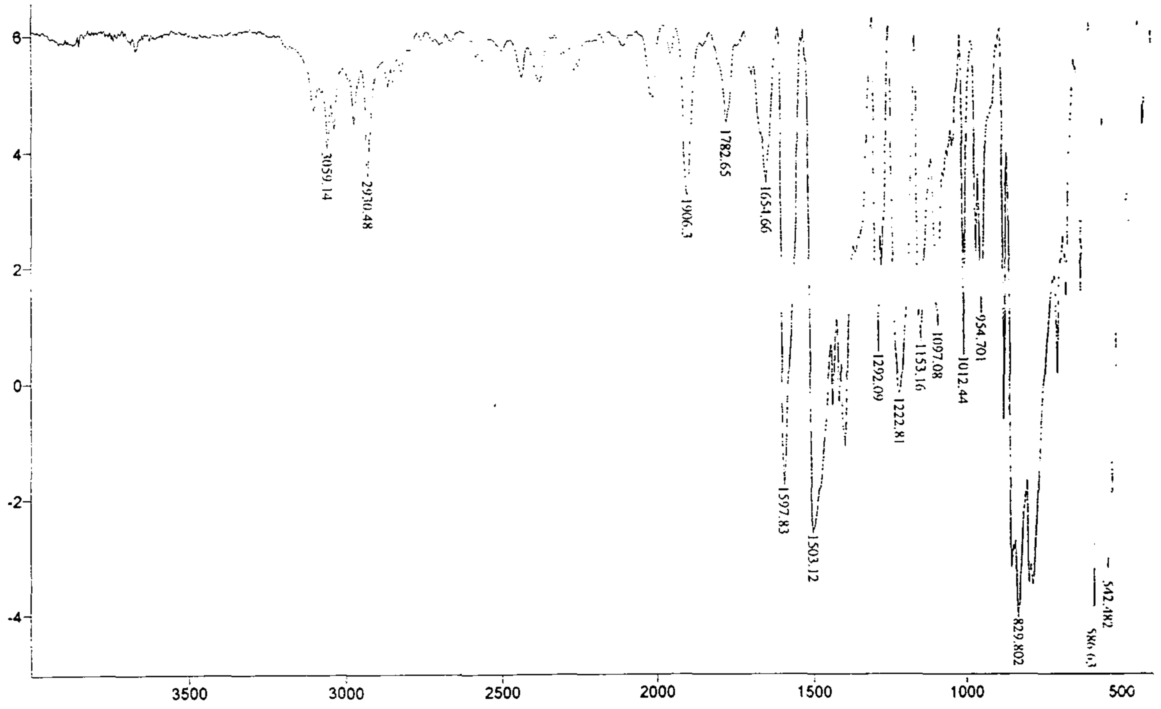
No. 2 **2-(4-Chlorophenyl)-2-phenyl-1,3-dithiolane.**



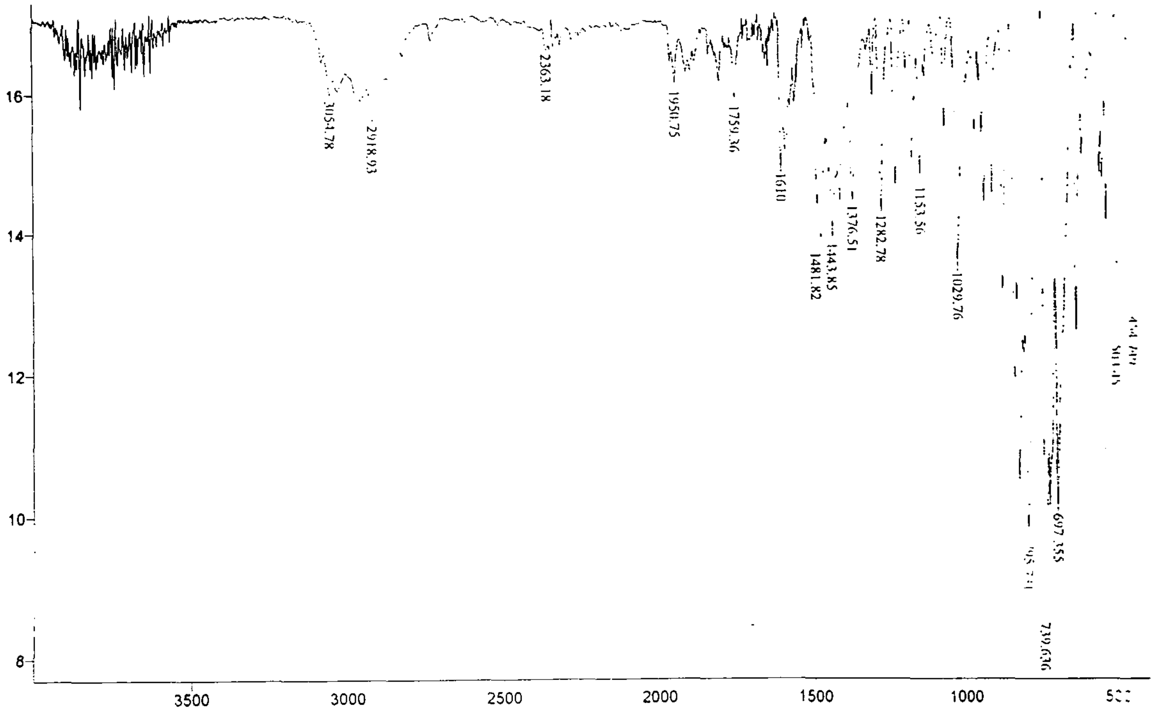
No. 3 2-(4-Bromophenyl)-2-phenyl-1,3-dithiolane.



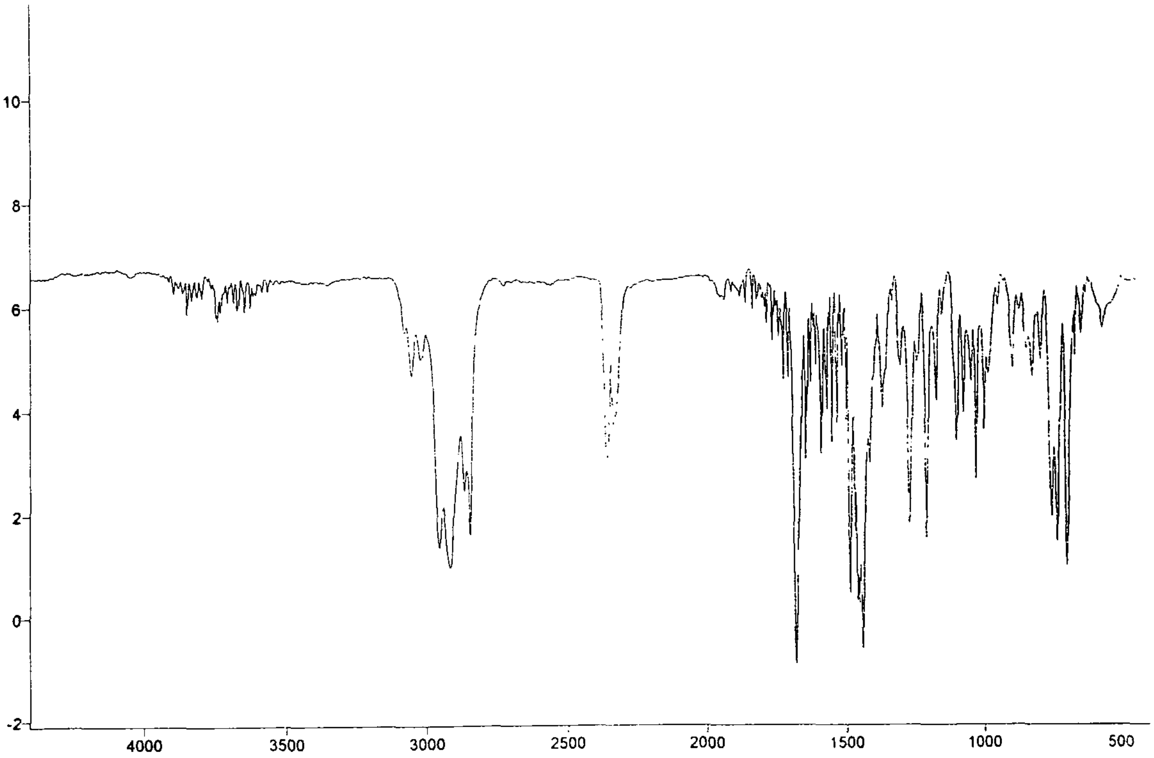
No. 4 2,2-Bis(4-fluorophenyl)-1,3-dithiolane.



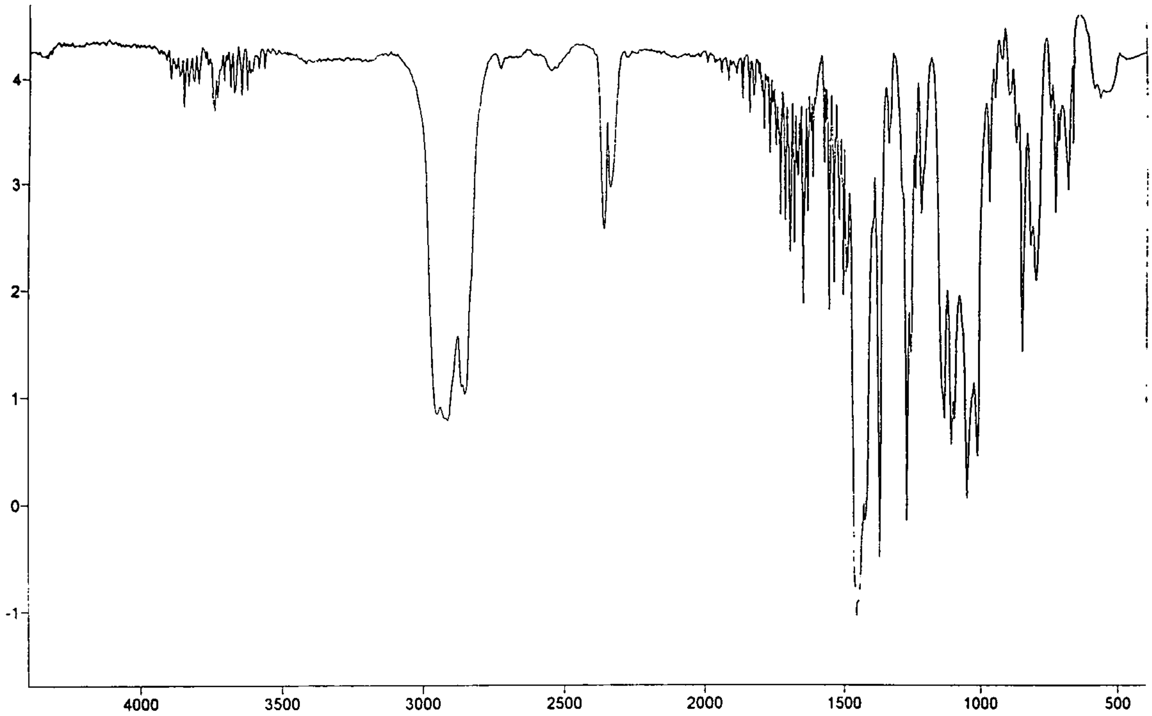
No. 5 2-(2,4-Dimethylphenyl)-2-phenyl-1,3-dithiolane.



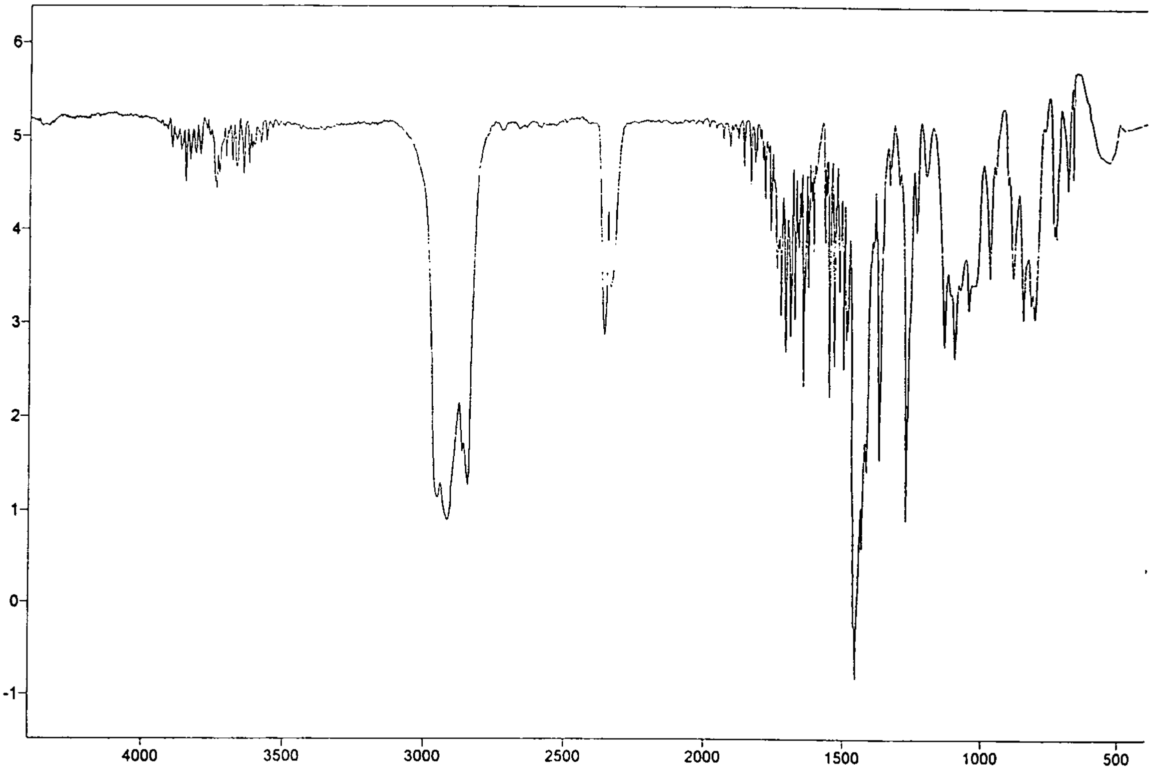
No. 6 2-Butyl-2-phenyl-1,3-dithiolane.



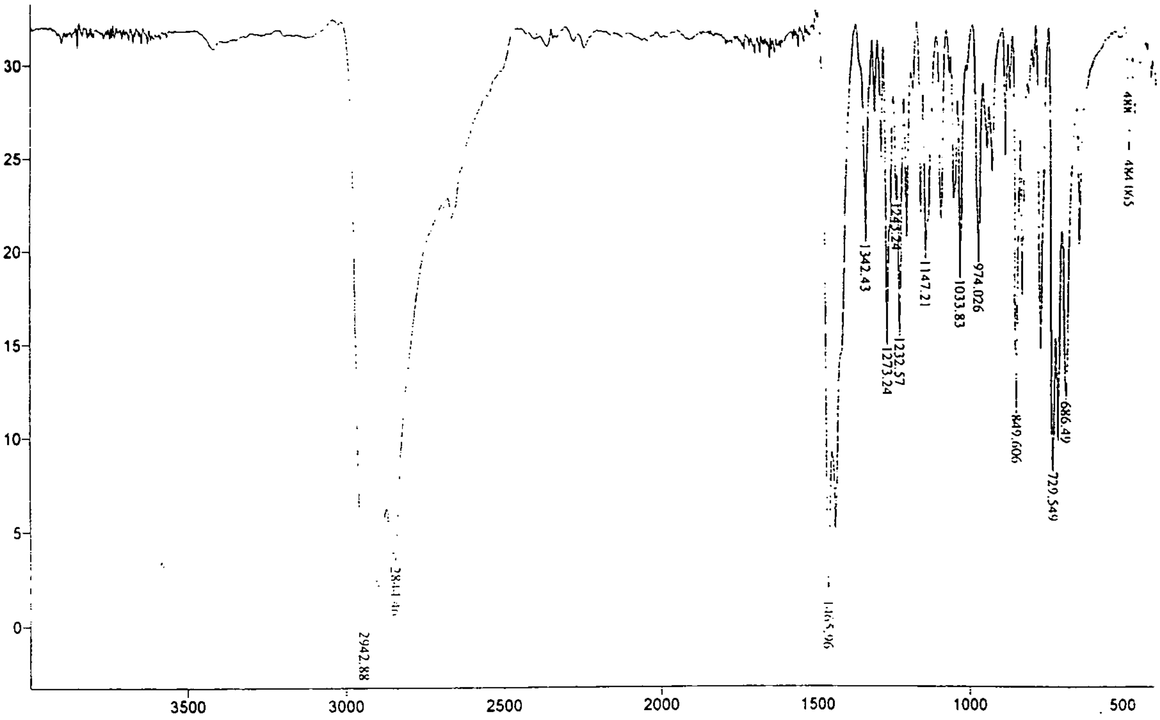
No. 7 **2-Butyl-2-methyl-1,3-dithiolane.**



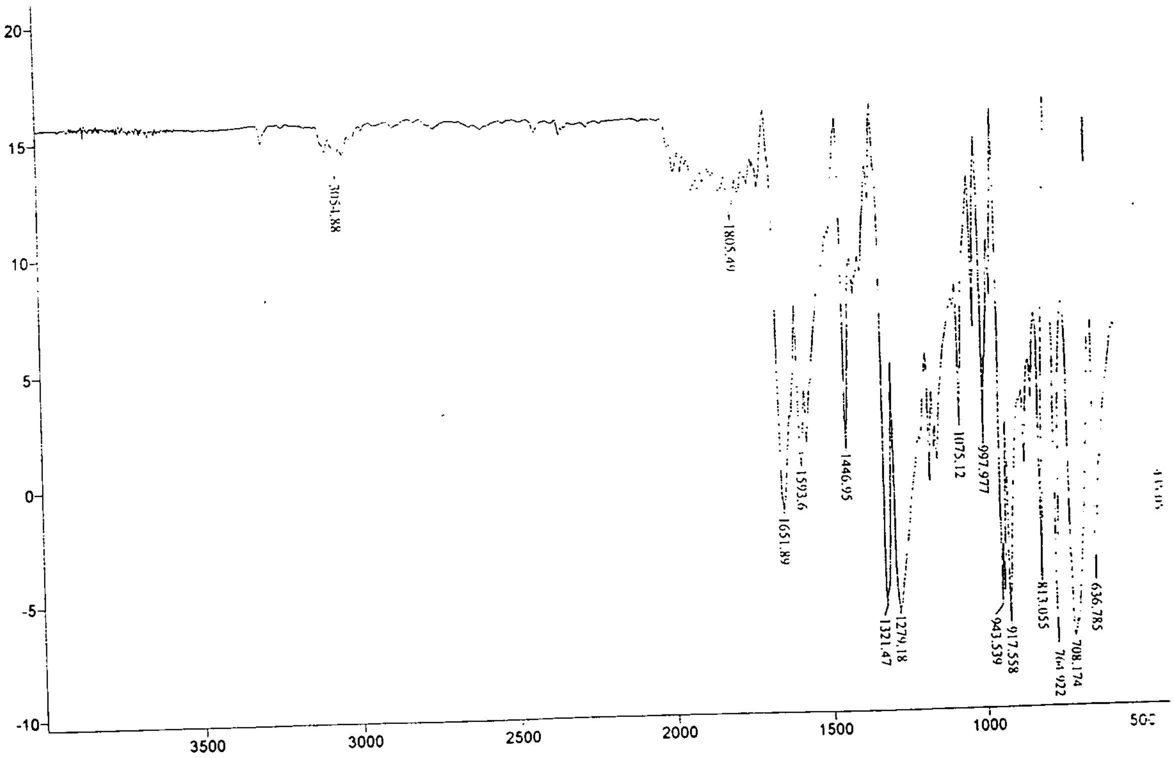
No. 8 **2-Ethyl-2-pentyl-1,3-dithiolane.**



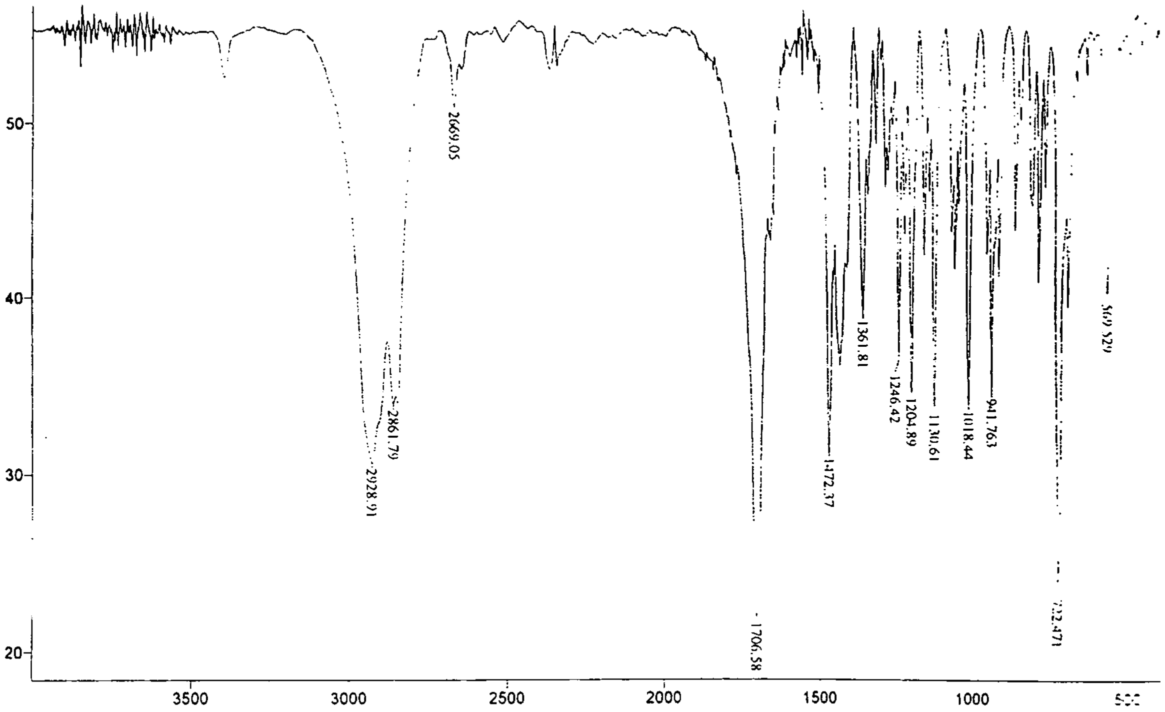
No. 9 Cyclododecan-1,3-dithiolane.



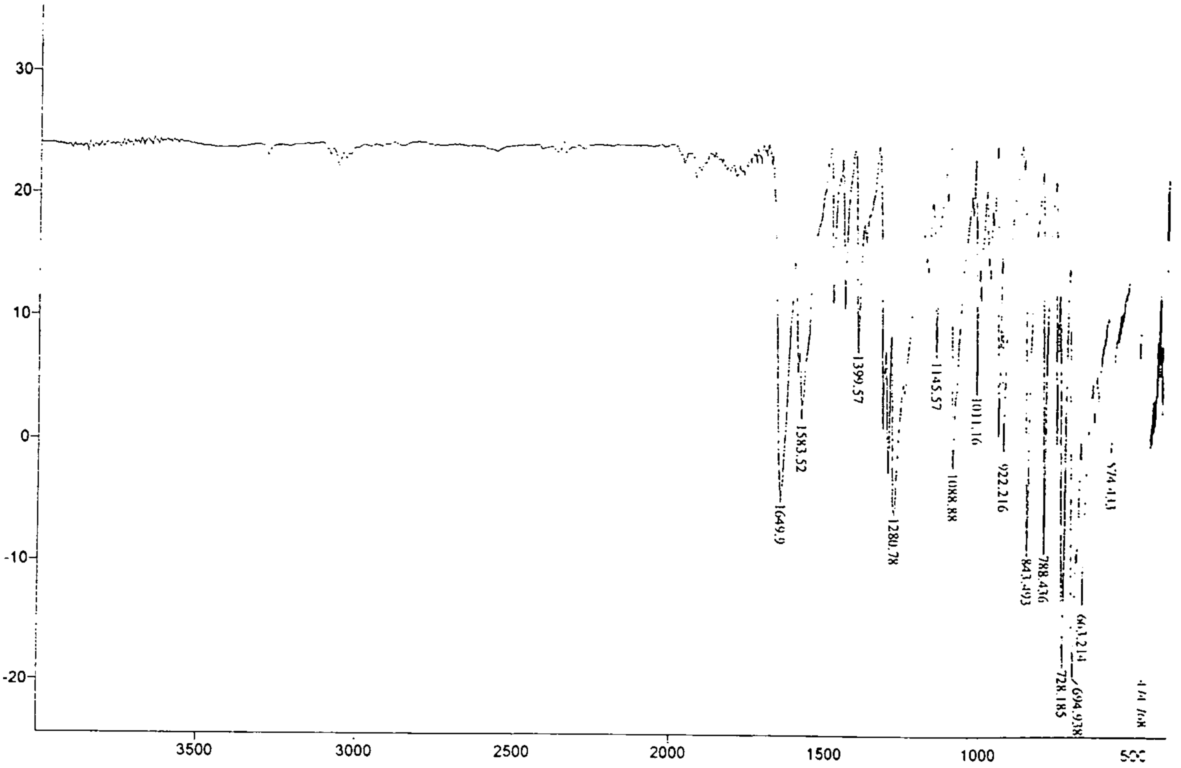
No. 10 Benzophenone.



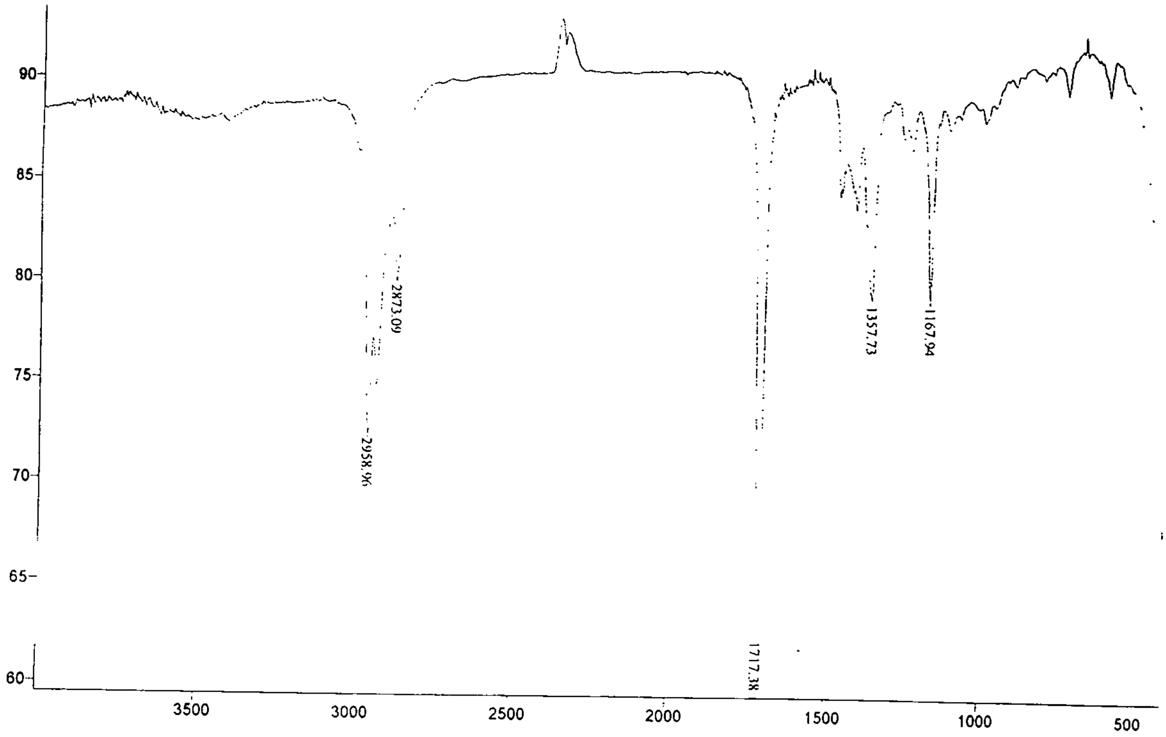
No. 11 **Cyclododecanone.**



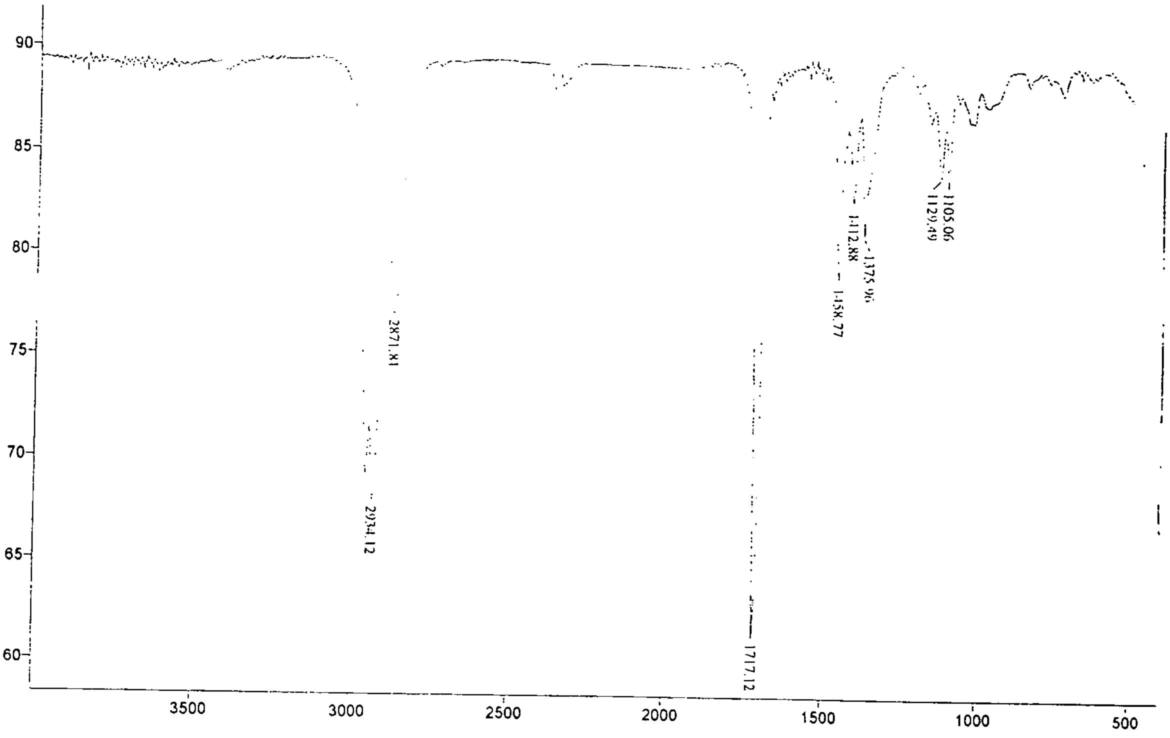
No. 12 **4-Chlorobenzophenone.**



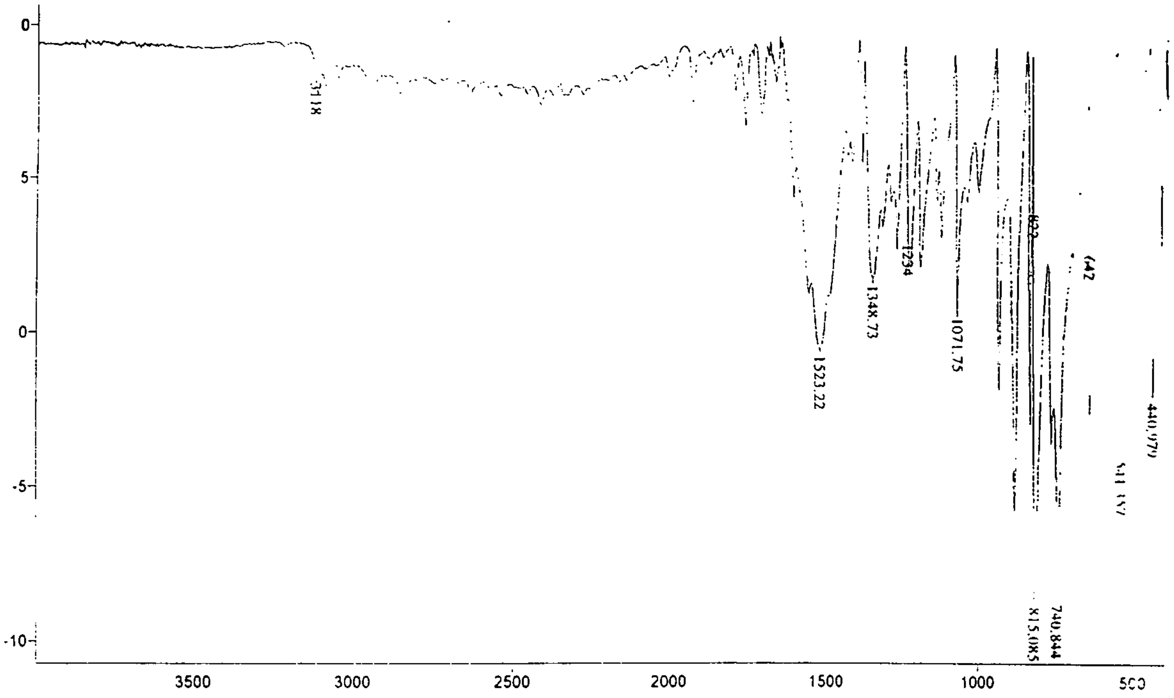
No. 13 2-Hexanone.



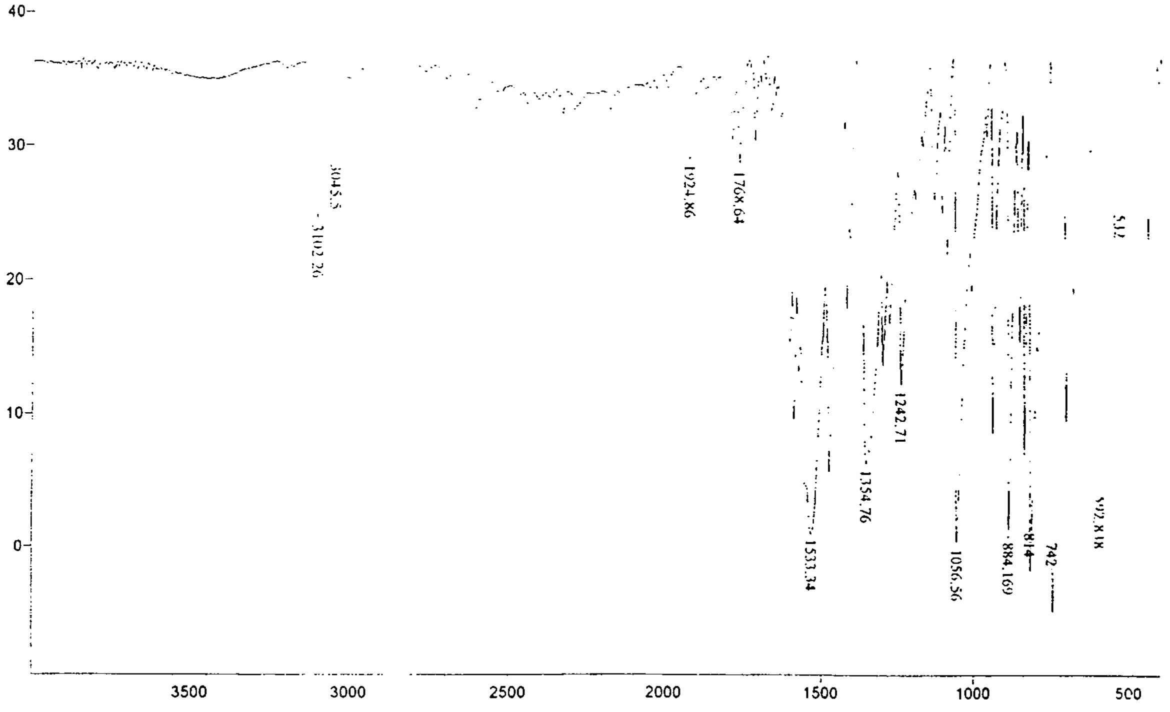
No. 14 3-Octanone.



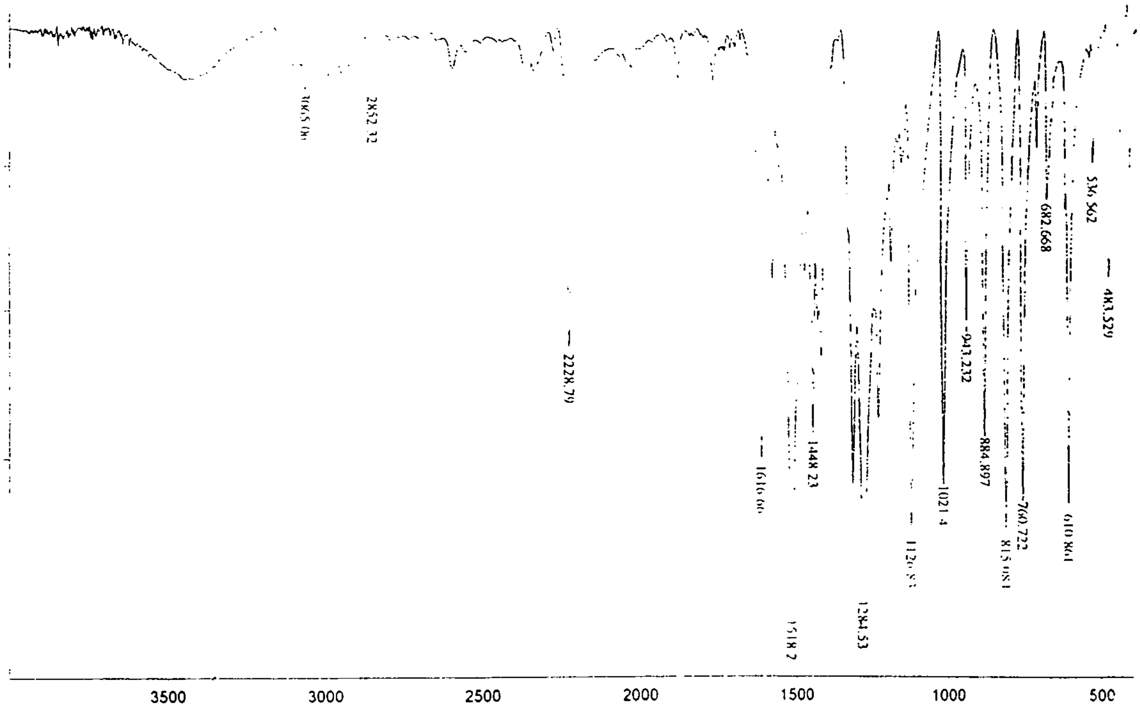
No. 15 2-Fluoro-4-nitrotoluene.



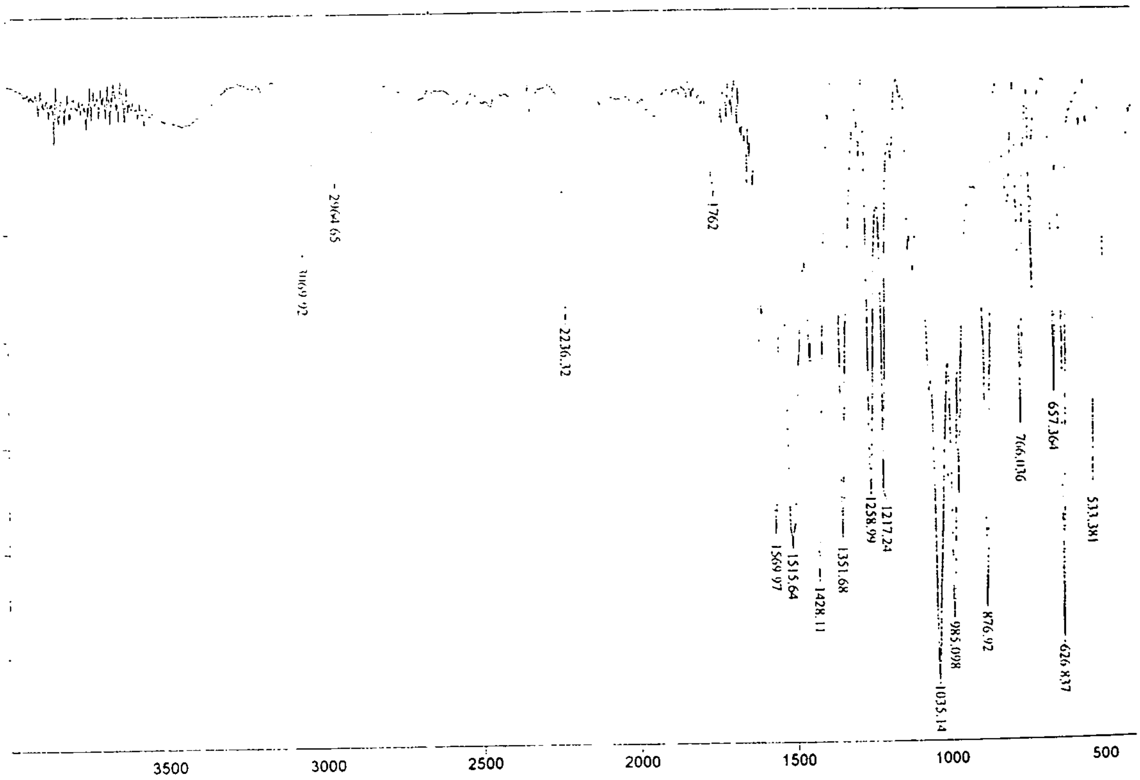
No. 16 1-Chloro-2-fluoro-4-nitrobenzene.



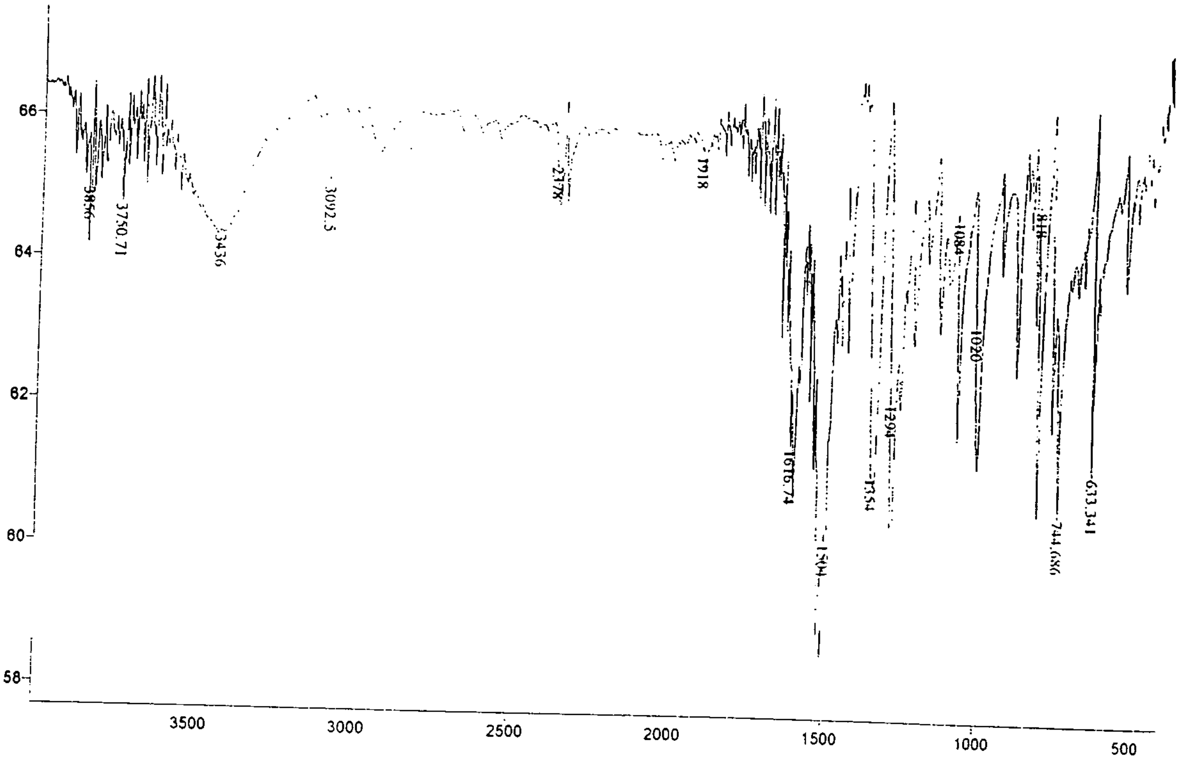
No. 19 2-Fluoro-1-methoxy-4-benzonitrile.



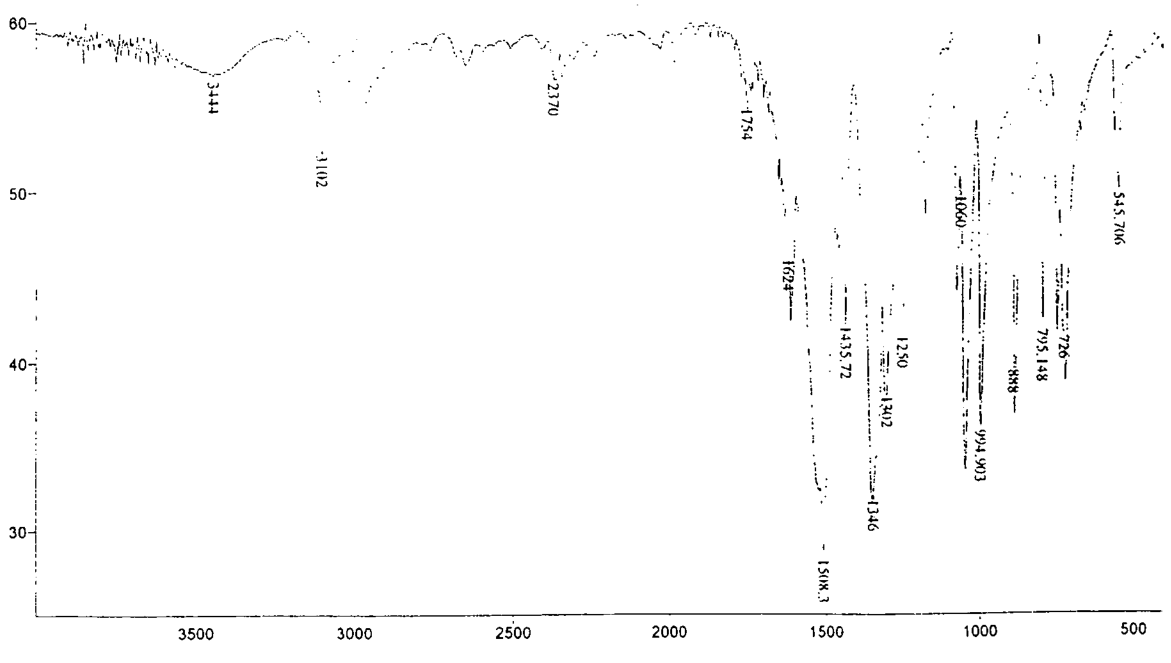
No. 20 2,6-Difluoro-1-methoxy-4-benzonitrile.



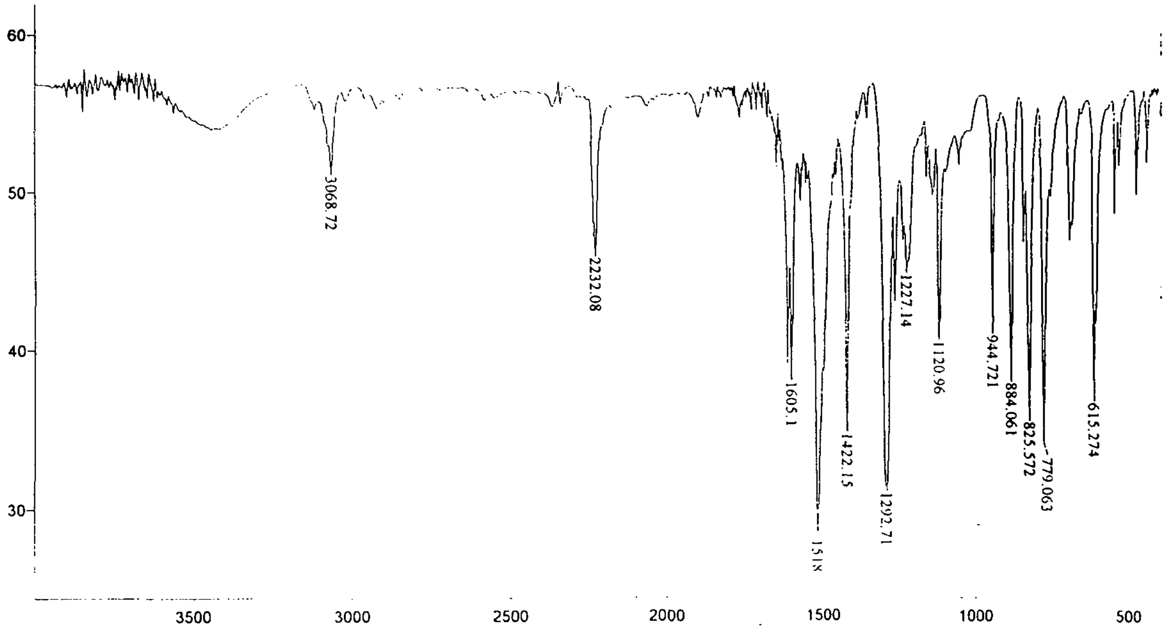
No. 17 2-Fluoro-4-nitroanisole.



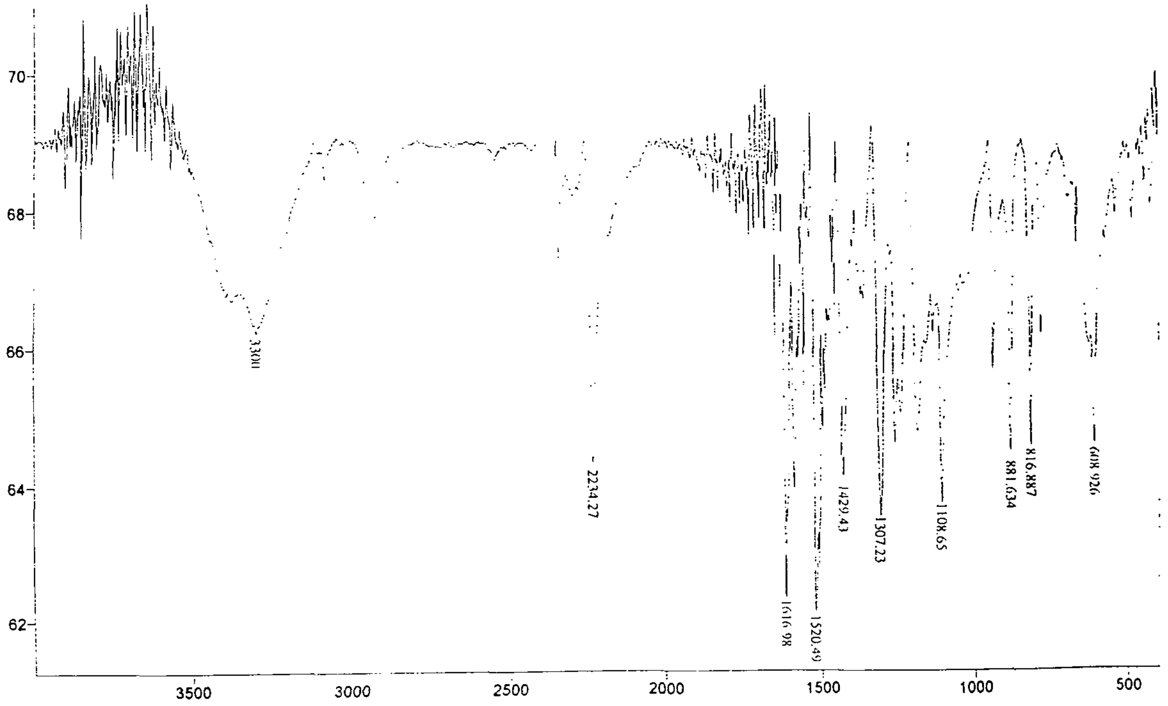
No. 18 2,6-Difluoro-4-nitroanisole.



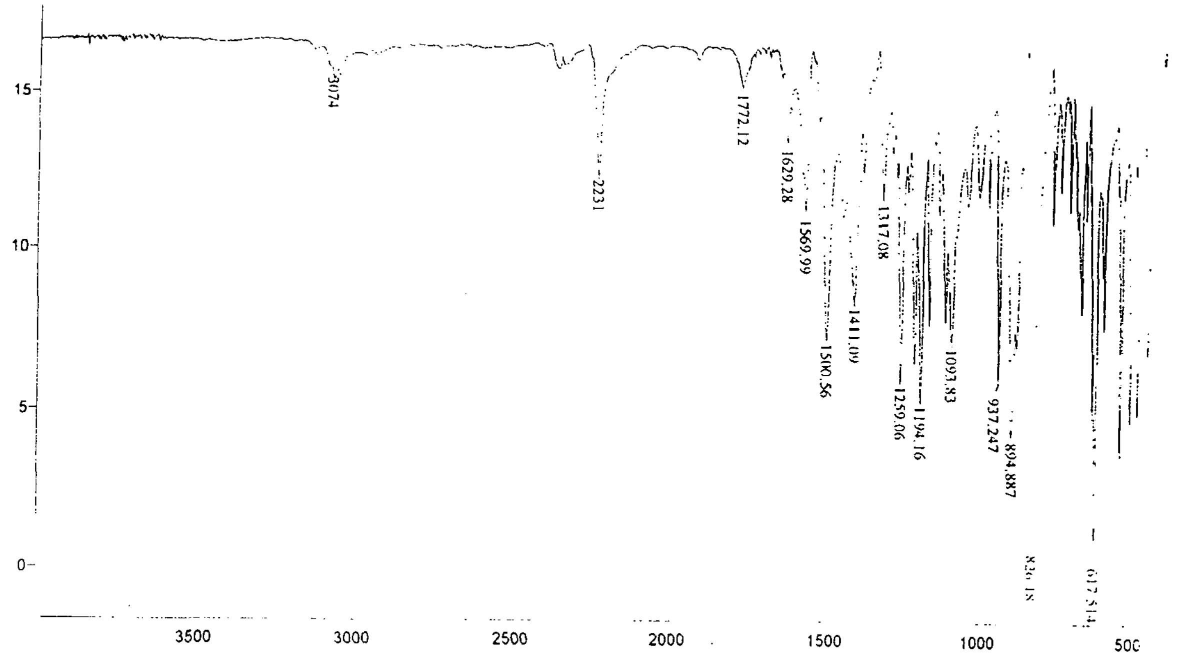
No. 21 2-Fluoro-1-hydroxy-4-benzonitrile.



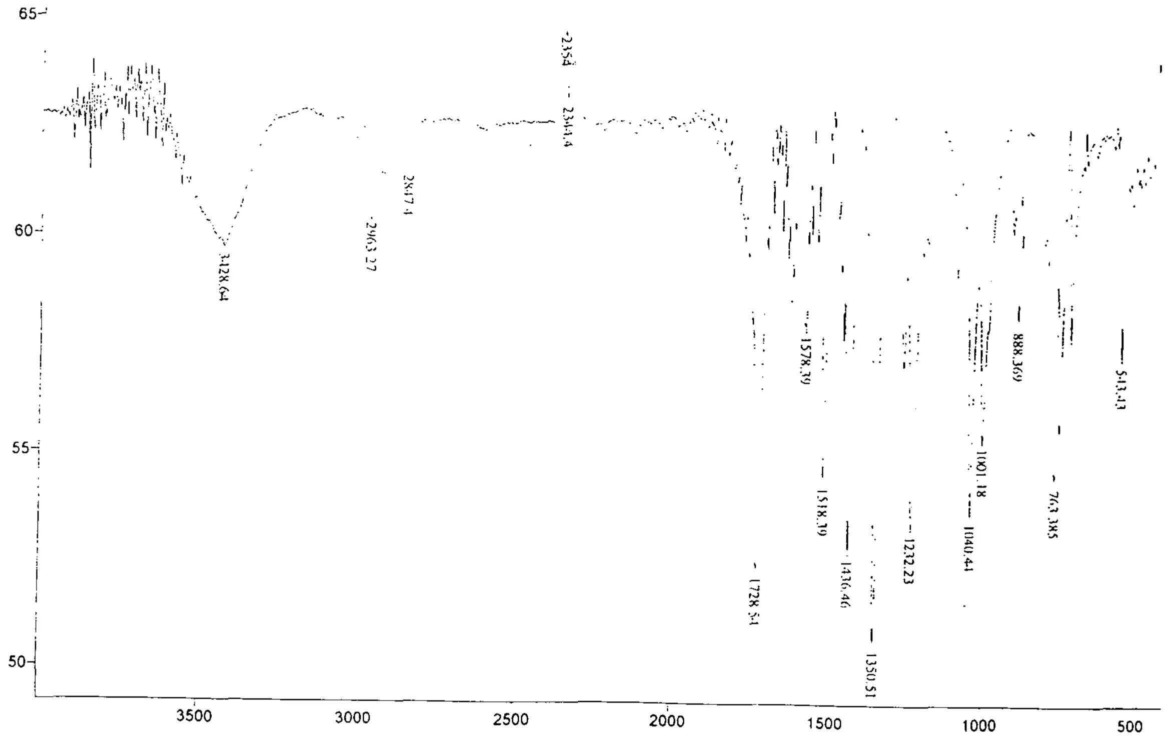
No. 22 1,2-Difluoro-4-benzonitrile.



No. 23 1-Methyl-2-fluoro-4-benzonitrile.



No. 24 2,6-Difluoro-4-methoxy-methylbenzoate.



Appendix Four. Requirements of the Board of Studies.

The Board of Studies in Chemistry requires that each postgraduate research thesis contains an appendix listing:-

(A) all research colloquia, seminars and lectures arranged by the Department of Chemistry during the period of the author's residence as a postgraduate student;

(B) lectures organised by Durham University Chemical Society;

(C) details of postgraduate induction courses;

(D) all research conferences attended and papers presented by the author during the period when research for the thesis was carried out.

Colloquia, Lectures and Seminars From Invited Speakers 1994-1997

1994

October 5	Prof. N. L. Owen, Brigham Young University, Utah, USA* *Determining Molecular Structure - the INADEQUATE NMR way*
October 19	Prof. N. Bartlett, University of California* *Some Aspects of Ag(II) and Ag(III) Chemistry*
November 2	Dr P. G. Edwards, University of Wales, Cardiff *The Manipulation of Electronic and Structural Diversity in Metal Complexes - New Ligands*
November 3	Prof. B. F. G. Johnson, Edinburgh University* *Arene-metal Clusters*
November 9	Dr G. Hogarth, University College, London *New Vistas in Metal-imido Chemistry*
November 10	Dr M. Block, Zeneca Pharmaceuticals, Macclesfield* *Large-scale Manufacture of ZD 1542, a Thromboxane Antagonist Synthase Inhibitor*
November 16	Prof. M. Page, University of Huddersfield* *Four-membered Rings and b-Lactamase*
November 23	Dr J. M. J. Williams, University of Loughborough* *New Approaches to Asymmetric Catalysis*
December 7	Prof. D. Briggs, ICI and University of Durham* *Surface Mass Spectrometry*

1995

January 11	Prof. P. Parsons, University of Reading* *Applications of Tandem Reactions in Organic Synthesis*
January 18	Dr G. Rumbles, Imperial College, London *Real or Imaginary Third Order Non-linear Optical Materials*

January 25	Dr D. A. Roberts, Zeneca Pharmaceuticals* *The Design and Synthesis of Inhibitors of the Renin-angiotensin System*
February 1	Dr T. Cosgrove, Bristol University* *Polymers do it at Interfaces*
February 8	Dr D. O'Hare, Oxford University* *Synthesis and Solid-state Properties of Poly-, Oligo- and Multidecker Metallocenes*
February 22	Prof. E. Schaumann, University of Clausthal* *Silicon- and Sulphur-mediated Ring-opening Reactions of Epoxide*
March 1	Dr M. Rosseinsky, Oxford University *Fullerene Intercalation Chemistry*
March 22	Dr M. Taylor, University of Auckland, New Zealand *Structural Methods in Main-group Chemistry*
April 26	Dr M. Schroder, University of Edinburgh *Redox-active Macrocyclic Complexes : Rings, Stacks and Liquid Crystals*
May 4	Prof. A. J. Kresge, University of Toronto *The Ingold Lecture Reactive Intermediates : Carboxylic-acid Enols and Other Unstable Species*
October 11	Prof. P. Lugar, Frei Univ Berlin, FRG *Low Temperature Crystallography*
October 13	Prof. R. Schmutzler, Univ Braunschweig, FRG. *Calixarene-Phosphorus Chemistry: A New Dimension in Phosphorus Chemistry*
October 18	Prof. A. Alexakis, Univ. Pierre et Marie Curie, Paris* *Synthetic and Analytical Uses of Chiral Diamines*
October 25	Dr.D.Martin Davies, University of Northumbria *Chemical reactions in organised systems.*

November 1	Prof. W. Motherwell, UCL London* *New Reactions for Organic Synthesis*
November 3	Dr B. Langlois, University Claude Bernard-Lyon* *Radical Anionic and Psuedo Cationic Trifluoromethylation*
November 8	Dr. D. Craig, Imperial College, London* *New Stategies for the Assembly of Heterocyclic Systems*
November 15	Dr Andrea Sella, UCL, London *Chemistry of Lanthanides with Polypyrazoylborate Ligands*
November 17	Prof. David Bergbreiter, Texas A&M, USA* *Design of Smart Catalysts, Substrates and Surfaces from Simple Polymers*
November 22	Prof. I Soutar, Lancaster University *A Water of Glass? Luminescence Studies of Water-Soluble Polymers.*
November 29	Prof. Dennis Tuck, University of Windsor, Ontario, Canada *New Indium Coordination Chemistry*
December 8	Professor M.T. Reetz, Max Planck Institut, Mulheim *Perkin Regional Meeting*

<u>1996</u>

January 10	Dr Bill Henderson, Waikato University, NZ *Electrospray Mass Spectrometry - a new sporting technique*
January 17	Prof. J. W. Emsley , Southampton University* *Liquid Crystals: More than Meets the Eye*
January 24	Dr Alan Armstrong, Nottingham Univesity* *Alkene Oxidation and Natural Product Synthesis*
January 31	Dr J. Penfold, Rutherford Appleton Laboratory, *Soft Soap and Surfaces*

February 7	Dr R.B. Moody, Exeter University *Nitrosations, Nitrations and Oxidations with Nitrous Acid*
February 12	Dr Paul Pringle, University of Bristol *Catalytic Self-Replication of Phosphines on Platinum(O)*
February 14	Dr J. Rohr, Univ Gottingen, FRG *Goals and Aspects of Biosynthetic Studies on Low Molecular Weight Natural Products*
February 21	Dr C R Pulham , Univ. Edinburgh *Heavy Metal Hydrides - an exploration of the chemistry of stannanes and plumbanes*
February 28	Prof. E. W. Randall, Queen Mary & Westfield College *New Perspectives in NMR Imaging*
March 6	Dr Richard Whitby, Univ of Southampton* *New approaches to chiral catalysts: Induction of planar and metal centred asymmetry*
March 7	Dr D.S. Wright, University of Cambridge *Synthetic Applications of* Me_2N*-p-Block Metal Reagents*
March 12	RSC Endowed Lecture - Prof. V. Balzani, Univ of Bologna *Supramolecular Photochemistry*
March 13	Prof. Dave Garner, Manchester University* *Mushrooming in Chemistry*
April 30	Dr L.D.Pettit, Chairman, IUPAC Commission of Equilibrium Data *pH-metric studies using very small quantities of uncertain purity*
October 9	Professor G. Bowmaker, University Aukland, NZ *Coordination and Materials Chemistry of the Group 11 and Group 12 Metals : Some Recent Vibrational and Solid State NMR Studies*
October 14	Professor A. R. Katritzky, University of Gainesville,University of Florida, USA* *Recent Advances in Benzotriazole Mediated Synthetic Methodology*

October 16	Professor Ojima, Guggenheim Fellow, State University of New York at Stony Brook* *Silylformylation and Silylcarbocyclisations in Organic Synthesis*
October 22	Professor Lutz Gade, Univ. Wurzburg, Germany* *Organic transformations with Early-Late Heterobimetallics: Synergism and Selectivity*
October 22	Professor B. J. Tighe, Department of Molecular Sciences and Chemistry, University of Aston *Making Polymers for Biomedical Application - can we meet Nature's Challenge?* Joint lecture with the Institute of Materials
October 23	Professor H. Ringsdorf (Perkin Centenary Lecture), Johannes Gutenberg-Universitat, Mainz, Germany *Function Based on Organisation*
October 29	Professor D. M. Knight, Department of Philosophy, University of Durham. *The Purpose of Experiment - A Look at Davy and Faraday*
October 30	Dr Phillip Mountford, Nottingham University *Recent Developments in Group IV Imido Chemistry*
November 6	Dr Melinda Duer, Chemistry Department, Cambridge *Solid-state NMR Studies of Organic Solid to Liquid-crystalline Phase Transitions*
November 12	Professor R. J. Young, Manchester Materials Centre, UMIST* *New Materials - Fact or Fantasy?* Joint Lecture with Zeneca & RSC
November 13	Dr G. Resnati, Milan* *Perfluorinated Oxaziridines: Mild Yet Powerful Oxidising Agents*
November 18	Professor G. A. Olah, University of Southern California, USA* *Crossing Conventional Lines in my Chemistry of the Elements*

November 19 Professor R. E. Grigg, University of Leeds*
Assembly of Complex Molecules by Palladium-Catalysed Queueing Processes

November 20 Professor J. Earnshaw, Deptartment of Physics, Belfast
Surface Light Scattering: Ripples and Relaxation

November 27 Dr Richard Templer, Imperial College, London
Molecular Tubes and Sponges

December 3 Professor D. Phillips, Imperial College, London
"A Little Light Relief"

December 4 Professor K. Muller-Dethlefs, York University
Chemical Applications of Very High Resolution ZEKE Photoelectron Spectroscopy

December 11 Dr Chris Richards, Cardiff University*
Stereochemical Games with Metallocenes

1997

January 15 Dr V. K. Aggarwal, University of Sheffield*
Sulfur Mediated Asymmetric Synthesis

January 16 Dr Sally Brooker, University of Otago, NZ
Macrocycles: Exciting yet Controlled Thiolate Coordination Chemistry

January 21 Mr D. Rudge, Zeneca Pharmaceuticals*
High Speed Automation of Chemical Reactions

January 22 Dr Neil Cooley, BP Chemicals, Sunbury
Synthesis and Properties of Alternating Polyketones

January 29 Dr Julian Clarke, UMIST
What can we learn about polymers and biopolymers from computer-generated nanosecond movie-clips?

February 4 Dr A. J. Banister, University of Durham

	From Runways to Non-metallic Metals - A New Chemistry Based on Sulphur
February 5	Dr A. Haynes, University of Sheffield *Mechanism in Homogeneous Catalytic Carbonylation*
February 12	Dr Geert-Jan Boons, University of Birmingham* *New Developments in Carbohydrate Chemistry*
February 18	Professor Sir James Black, Foundation/King's College London* *My Dialogues with Medicinal Chemists*
February 19	Professor Brian Hayden, University of Southampton *The Dynamics of Dissociation at Surfaces and Fuel Cell Catalysts*
February 25	Professor A. G. Sykes, University of Newcastle *The Synthesis, Structures and Properties of Blue Copper Proteins*
February 26	Dr Tony Ryan, UMIST* *Making Hairpins from Rings and Chains*
March 4	Professor C. W. Rees, Imperial College* *Some Very Heterocyclic Chemistry*
March 5	Dr J. Staunton FRS, Cambridge University* *Tinkering with biosynthesis: towards a new generation of antibiotics*
March 11	Dr A. D. Taylor, ISIS Facility, Rutherford Appleton Laboratory *Expanding the Frontiers of Neutron Scattering*
March 19	Dr Katharine Reid, University of Nottingham *Probing Dynamical Processes with Photoelectrons*

* lectures attended

First Year Induction Courses

This course consists of a series of one hour lectures on the services available in the department.

Departmental Organisations -	Dr. E. J. F. Ross
Safety Matters -	Dr. G. M. Brooke
Electrical Appliances -	Mr. B. T. Barker
Chromatography and Microanalysis -	Mr. T. F. Holmes
Atomic Absorptiometry and Inorganic Analysis -	Mr. R. Coult
Library Facilities -	Mrs. M. Hird
Mass Spectroscopy -	Dr. M. Jones
NMR Spectroscopy -	Dr. A. Kenwright
Glass-blowing Techniques -	Mr. R. Hart Mr. G. Haswell

Research Conferences Attended

April 1995	North Eastern Graduate Symposium, University of Durham.
June 1997	11th Postgraduate Heterocyclic Symposium, University of Keele.
August 1997	15th International Symposium on Fluorine Chemistry, University of British Columbia, Vancouver, CANADA.

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