New methodology for the synthesis of fluorinated aromatics

Rock, Michael Harold

NEW METHODOLOGY FOR THE SYNTHESIS OF FLUORINATED AROMATICS

by

Michael Harold Rock

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To mum and Dad

MEMORANDUM

The work described in this thesis was carried out at the University of Durham between October 1987 and September 1990. This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

ACKNOWLEDGEMENTS

I would like to express my thanks to Professor R.D. Chambers for his invaluable advice and encouragement throughout the course of this work.

My thanks also to Dr J.S. Moilliet (I.C.I.), for useful discussions and for his interest in this work.

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ABSTRACT

This thesis is concerned with new methodology for the introduction of fluorine atoms, and trifluoromethyl groups into aromatic systems and the following approaches have been adopted:

(*i*) The possibility of selective cleavage of the aryl-silicon bond of aryltrimethylsilanes by elemental fluorine to give the corresponding fluorinated aromatic compound was explored, and competing silicon and hydrogen substitution was observed. The affect of temperature and solvent upon this process was investigated.

(*ii*) Attempts to modify the reactivity of dilute elemental fluorine (10% fluorine/nitrogen) towards aromatic systems at low reaction temperatures were made by the addition of pyridine and substituted pyridines. The effectiveness of this methodology was limited by the reactivity of the pyridine systems towards elemental fluorine.

(*iii*) The potential electrophilic fluorinating agents N-fluoro-2,3-bis(2H hexafluoropropyl)pyrrolidine and N-fluorosuccinimide have been synthesised by the direct fluorination of the corresponding N-trimethylsilyl compounds.

(*iv*) The cycloaddition reactions of hexafluorobut-2-yne with furan and 2-substituted furans have been employed to synthesise a series of benzenoid and heteroaromatic compounds containing two trifluoromethyl groups in high yield.

(*v*) The synthesis of trifluoromethylpyridines by the cycloaddition of 3,3,3-trifluoropropene with oxazoles has also been investigated.

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SELECTIVE FLUORINATION OF AROMATIC COMPOUNDS

CHAPTER 1

SELECTIVE FLUORINATION OF AROMATIC COMPOUNDS

INTRODUCTION

The selective introduction of fluorine is not an easy synthetic task. Interest in this type of process remains high because many compounds containing a fluoroaromatic system show pronounced biological activity[1-4] and find a variety of applications, from agrochemicals to pharmaceuticals. Examples are shown in Table 1.

Incorporation of a fluorine atom into an organic molecule can impart biological activity for the following reasons:-

i fluorine can mimic hydrogen with respect to steric requirements at enzyme receptor sites (Van der Waals radii F, 1.35A; H, 1.2A);

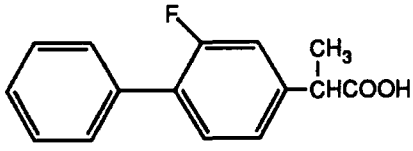
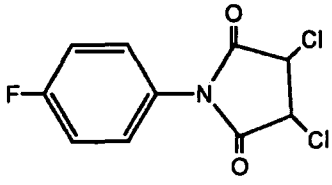
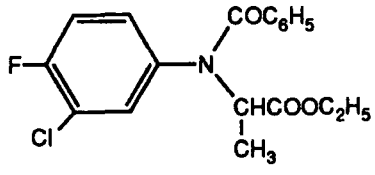
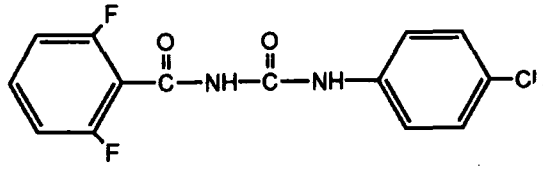
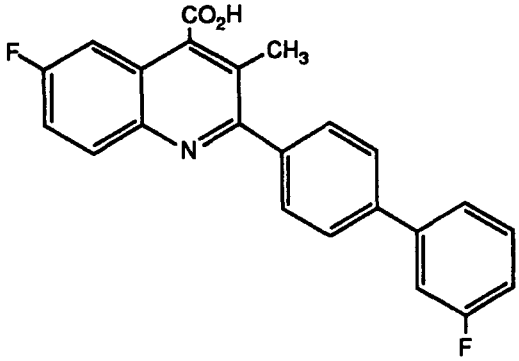
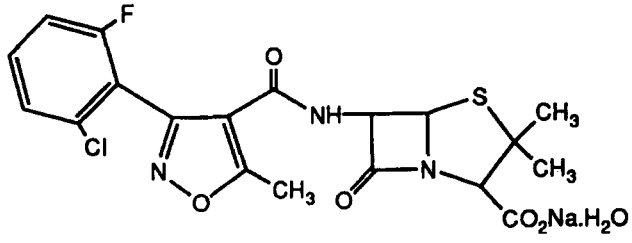
ii the electronegativity of fluorine can significantly influence reactivity and stability of functional groups, and reactivity of neighbouring reaction centres;

iii replacement of hydrogen by fluorine at, or near, reactive sites frequently causes inhibition of metabolism because of the high C-F bond energy;

iv lipid solubility of a compound is usually increased by the replacement of hydrogen by fluorine, thereby enhancing the rates of adsorption and transport in biological systems.

The methodology and the reagents used for the selective introduction of fluorine into an aromatic system will be reviewed here. The main industrial methods will only be mentioned briefly, whilst the recent advances will be reviewed in detail.

Table 1 Examples of biologicaly active compounds containing fluorinated aromatics

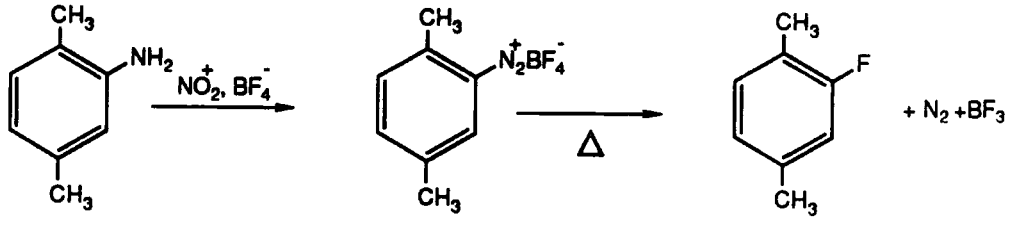
Compound	Biological Activity	Ref.
	Non-Steroidal anti-inflammatory drug: high analgesic and anti-inflamatory activity	2
	Fungicide: treatment of apple scab	2
	Herbicide: post emergent herbicide for protection of barley	3
	Insecticide	5
	Antitumor agent: undergoing clinical trials	2
	Antibiotic:- Penicillinase stable, narrow-spectrum antibiotic	6

INDUSTRIAL METHODOLOGY FOR THE SELECTIVE FLUORINATION OF AROMATIC COMPOUNDS

Balz-Schiemann Reaction

The Balz-Schiemann reaction, in which an aromatic amine moiety is selectively replaced by fluorine[7], is still the prominent industrial method of producing fluoroaromatic compounds. This method involves two steps: firstly, the preparation and isolation of a diazonium fluoroborate of an aromatic system, and secondly, the controlled decomposition of this salt by heating to yield the fluoroaromatic, nitrogen and boron trifluoride (Scheme 1)[8].

Scheme 1



There are two general procedures for the preparation of diazonium tetrafluoroborates:-[9,10]

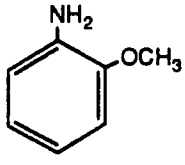
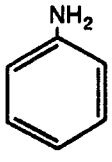
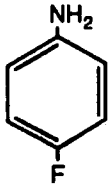
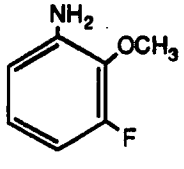
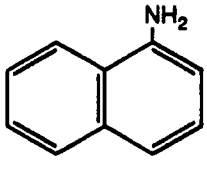
i diazotisation of the amine in hydrochloric acid followed by the addition of the tetrafluoroborate ion to precipitate the diazonium tetrafluoroborate salt;

ii. diazotisation in the presence of the fluoroborate ion, with continuous precipitation of the diazonium tetrafluoroborate during the reaction.

Decomposition of the diazonium fluoroborates usually proceeds smoothly and in high yield (Table 2), and methods of decomposition can be divided into two groups, dry decomposition and solvent decomposition. Dry decomposition, as its name implies, simply involves heating the dry

diazonium tetrafluoroborate with or without an inert solid such as sand[14], barium sulphate[16] or sodium fluoride[17], to its decomposition temperature.

Table 2 Examples of the Balz-Schiemann reaction

Aromatic Amine	Yield of diazonium Tetrafluoroborate %	Yield of fluoro-aromatic %	Ref.
	64	75	11
	91	67	12
	97	96	13
	29	55	14
	85	56	12
	91	98	15

Solvent decomposition involves heating the diazonium fluoroborate to its decomposition temperature in an inert solvent. Any inert liquid that can be heated to a temperature sufficiently high to start the decomposition can be used: hydrocarbons such as toluene [17], xylene[18], decalin[19], petroleum ether[20], whilst for higher temperatures chlorinated hydrocarbons[21], quinoline and nitrobenzene[23] have been used. Polar solvents such as acetone[23], water[24] and HF have been used in specific cases[25].

The Balz-Schiemann reaction can be used to replace up to four hydrogen atoms sequentially in benzene, but has the following limitations:-

i it requires a stable primary amine to form a diazonium fluoroborate;

ii the presence of electronegative substituents in the aromatic system impairs diazotisation;

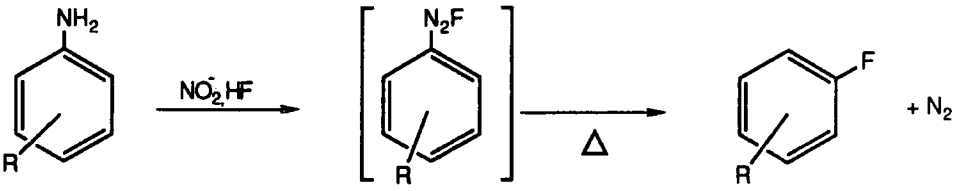
iii if more than one amine group is present, yields of the desired fluoroaromatic are low;

iv the presence of an active methylene or secondary amine group in the aromatic system promotes side reactions.

Diazotisation-Dediazotisation in HF

An alternative to the Balz-Schiemann reaction, which is finding increasing industrial application, is the diazotisation of aromatic amines in excess anhydrous hydrofluoric acid, followed by the thermal dediazotisation to give the desired fluoroaromatic (Scheme 2)[26,27].

Scheme 2



Not isolated

The yields obtained are often comparable, and in some cases superior, to those obtained by the Balz-Schiemann reaction (Table 3). The reaction is limited to simple aniline derivatives and cannot be used when the aromatic system has an *ortho* substituent with a lone pair of electrons. The availibilty of a pair of electrons in the *ortho* position stabilizes the diazonium intermediate, thus preventing decomposition in hydrofluoric acid.

Table 3

Amine	Product	Yield %	
		I	*II*
4-Chloroaniline	4-Chlorofluorobenzene	74	63
2-Aminobenzoic acid	2-Fluorobenzoic acid	57	7
3-Aminobenzoic acid	3-Fluorobenzoic acid	78	5
4-Aminobenzoic acid	4-Fluorobenzoic acid	78	32

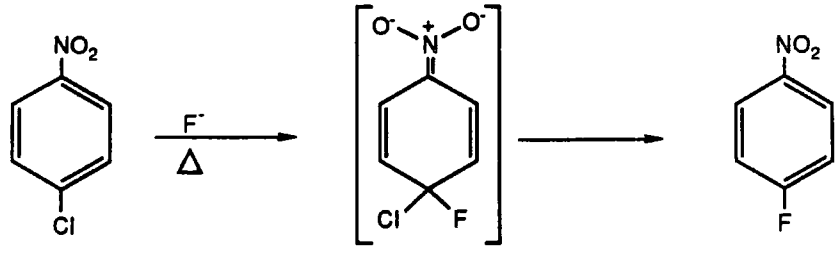
I Diazotisation-dediazotisation in HF; *II* Balz-Schiemann reaction

Halogen Exchange

Another industrial process for the production of fluoroaromatics is the halogen exchange reaction[28,29]. This reaction is used to a much lesser extent than the Balz-Schiemann reaction though its use as an industrial process is increasing. Halogen exchange involves the nucleophilic displacement of halogen atoms, which are suitably activated by electron withdrawing substituents, under vigorous

conditions by fluoride ions (Scheme 3). Crown ethers, solvents and other sources of fluoride ion enable the reaction conditions to be varied according to the starting materials and the required products[30,31].

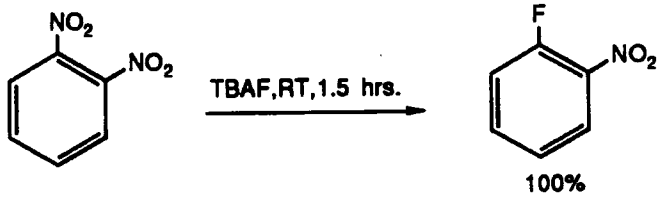
Scheme 3



The advantage of the halogen exchange reaction is that functional groups such as nitriles are unaffected[32]. However the positional requirement of the electron withdrawing substituents limits the synthetic utility of this reaction.

An alternative process to the nucleophilic displacement of halide ions is fluorodenitration, for example the reaction of 3-chloro-2-fluoro-nitrobenzene with potassium fluoride in the presence of phthaloyl chloride and tetraalkyl ammonium chloride, which yields 1-chloro-2,3-difluorobenzene[33]. The use of anhydrous tetrabutylammonium fluoride (T.B.A.F.) promotes fluorodenitration under mild conditions[34] (Scheme 4).

Scheme 4



The use of T.B.A.F. and other fluoride ion sources have been reviewed[35].

REAGENTS FOR SELECTIVE FLUORINATION OF AROMATIC SYSTEMS

ELEMENTAL FLUORINE

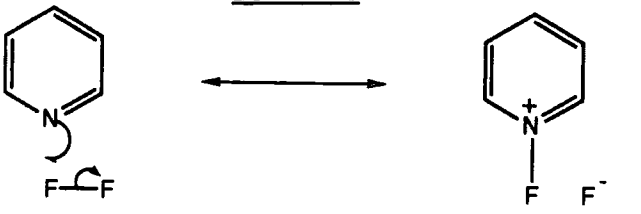
Elemental fluorine is such a strong oxidizing agent that it reacts with almost any organic compound, usually exothermically, and often with explosive results[36-39]. The poor solubility of fluorine results in reactions proceeding at the gas-liquid interface[38]. This behavior, coupled with the exothermic nature of the reaction, allows localized hot spots to form which can promote unwanted side reactions[38].

Early attempts to substitute aromatic rings[37] with elemental fluorine resulted in explosions and the fragmentation of the aromatic ring. In 1929 Bancroft and Jones[39] reported explosions during the attempted direct fluorination of benzene and toluene. Attempted moderation of these reactions by dilution of the elemental fluorine with nitrogen resulted in non-characterisable tars being produced[33]. During the 1930's Bockemüller[41] obtained tar-like products in the fluorination of several simple aromatic compounds and concluded that under direct liquid phase fluorination conditions aromatic systems undergo addition and polymerization rather than substitution.

The introduction of low concentration fluorine/nitrogen mixtures for the fluorination of aromatic systems at low temperature resulted in substitution by molecular fluorine[42,43]. In 1950 Simons claimed to have moderated the reactivity of dilute elemental fluorine in the fluorination of aromatic compounds at low temperature by using pyridine and related nitrogen heterocycles as the solvent[44]. It was claimed that fluorine formed a molecular complex with pyridine of type (1b),

(Scheme 5), in which the fluorine atoms are loosely held by pyridine molecules and that this complex (1b) acted as an electrophilic fluorinating agent. This pyridine fluorine complex (1b) has since been isolated by Meinert[45] at -80°C as a white crystalline solid which explodes on warming to room temperature.

SCHEME 5



(1a) (1b)

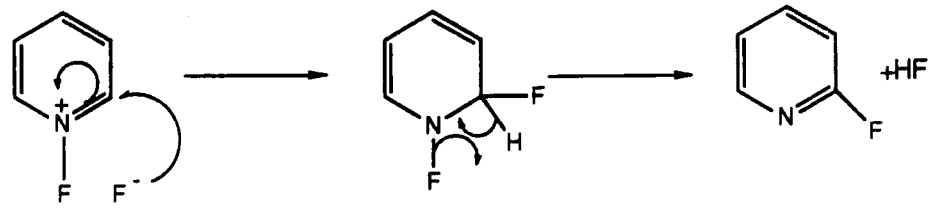
Van der Puy *et al*[46,47] have recently reported that pyridine fluorine complexes of type (1b) may be intermediates in the direct fluorination of substituted pyridines which give almost exclusively substituted 2-fluoropyridines as the products (see Table 4). The proposed mechanism involves the attack of F^- of the pyridine difluoride (1b) at C-2, followed by elimination of HF (Scheme 6).

TABLE 4 Direct fluorination of substituted pyridines without solvent[46,47]

Substituent	Temp(°C)	% Yield(a)	Product
4-methyl	-25	31	2-F-4-Me
4-ethyl	-25	32	2-F-4-Et
4-isopropyl	-25	47	2-F-4-*i*Pr
4-benzyl	-25	25	2-F-4-Bz
3-methyl	-25	43	2-F-3-Me (28%)
			2-F-5-Me (15%)
3,5-dimethyl	0	37	2-F-3,5-dimethyl
4-acetyl	0	26(b)	2-F-4-$COCH_3$
4-$COOCH_3$	0	61	2-F-4-$COOCH_3$

(a)isolated yield based on F_2 added, (b) yield after recrystallisation

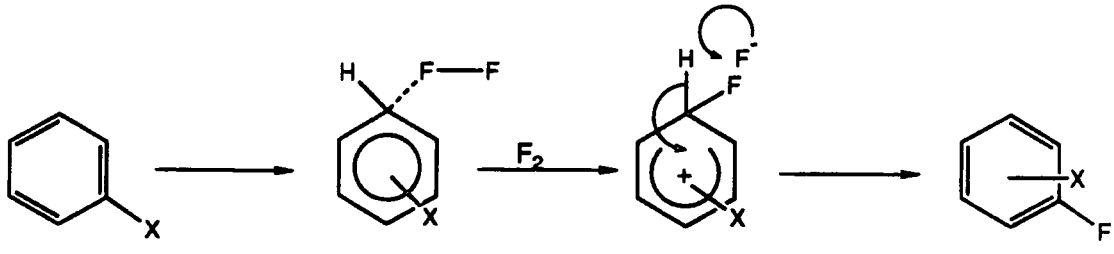
SCHEME 6 Proposed mechanism for the formation of 2 fluoropyridines.



(1b)

Cacace *et al*[48,49] performed aromatic substitution on a variety of aromatic systems with molecular fluorine (<0.76% F_2 in N_2), at low conversion (0.01%) near the lower limit of analytical sensitivity in order to investigate the mechanism involved. These reactions were carried out in $CFCl_3$ at -73°C and showed first order kinetics, dependent only on the amount of aromatic substrate present. Fluorination positions on substituted benzene rings mimicked the pattern generally observed for electrophilic substitution[50,51]. A plot of the partial rate factors *vs* σ constant for the polar aromatic substitution gave a $\rho+$ value of -2.45 (correlation coefficient of 0.993), which supports the mechanism in Scheme 7.

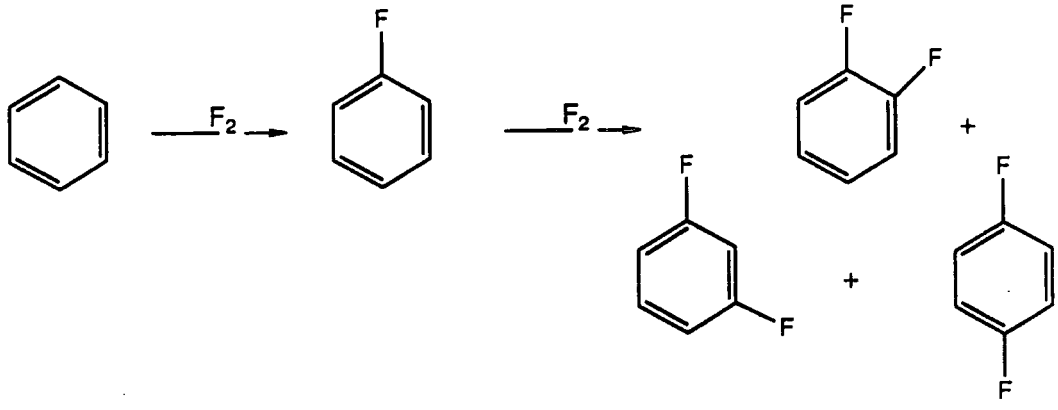
SCHEME 7



The direct liquid phase fluorination of benzene, toluene, nitrobenzene, methyl benzoate, naphthalene and several other aromatic compounds on a synthetically useful scale was carried out by Grakaukas[52,53].

The fluorination of a dilute solution of benzene in acetonitrile at -35°C with 0.7 moles of 1:8 elemental fluorine/nitrogen mixture yielded predominantly fluorobenzene and three isomers of difluorobenzene (Scheme 8).

SCHEME 8



The approximate relative ratio of the product mixture was 60:4:1:5 for fluorobenzene, *ortho*, *meta* and *para* difluorobenzene respectively. These results, along with the isomer distributions obtained by the direct fluorination of toluene at -70°C (*ortho*, *meta* and *para* fluorotoluene in 5:1:4 ratio) and nitrobenzene at -30°C (*ortho*, *meta* and *para* nitrobenzene in 1.5:9:1 ratio), are consistent with an electrophilic mechanism for direct fluorination of aromatic systems (Scheme 7).

Under exhaustive fluorination conditions the substitution products produced during the early stages of the reaction were consumed in addition and polymerization reactions, yielding highly fluorinated low molecular weight polycyclohexane derivatives. Sams *et al*[54] have utilized molecular sieves to minimize the possibility of secondary reactions with fluorine and as a result polymer formation was absent at high conversion of the starting material. After optimization of reaction conditions (-78°C, no solvent) Sams obtained 20% *ortho* and *para* difluorobenzenes from fluorobenzene.

The direct fluorination of phenol under a variety of conditions was investigated by Misaki[55]; the solvent used had a marked effect on the ratio of *ortho* to *para* fluorophenols formed, ranging from 1.80:1 in chloroform to 3.64:1 in acetonitrile. In water, large amounts of phenol were converted to products other than *ortho* and *para* fluorophenols (see Table 5).

TABLE 5 Fluorination of phenol in different solvents[55].

Reaction conditions		Conversion	Yield %		Isomer ratio
Temp. °C	Solvent	of phenol	*o*-fluoro phenol	*p*-fluoro phenol	*ortho/para*
-20	CH_3CN	56.1	38.9	10.7	3.64
-20	TG*	53.9	54.7	21.9	2.50
-20	CH_3OH	53.5	47.7	13.3	3.59
5	H_2O	52.9	7.0	2.6	2.69
5	CF_3COOH	52.0	56.1	17.0	3.30
-20	$CHCl_3$	51.4	54.5	30.2	1.80

* Tetraglyme

Although variations in temperature did not significantly affect *ortho/para* ratios of the fluorinated phenols produced, it drastically affected the conversion of the reaction (see Table 6). The highest conversion was obtained at the lowest temperature suggesting that reaction takes place with fluorine dissolved in the solvent.

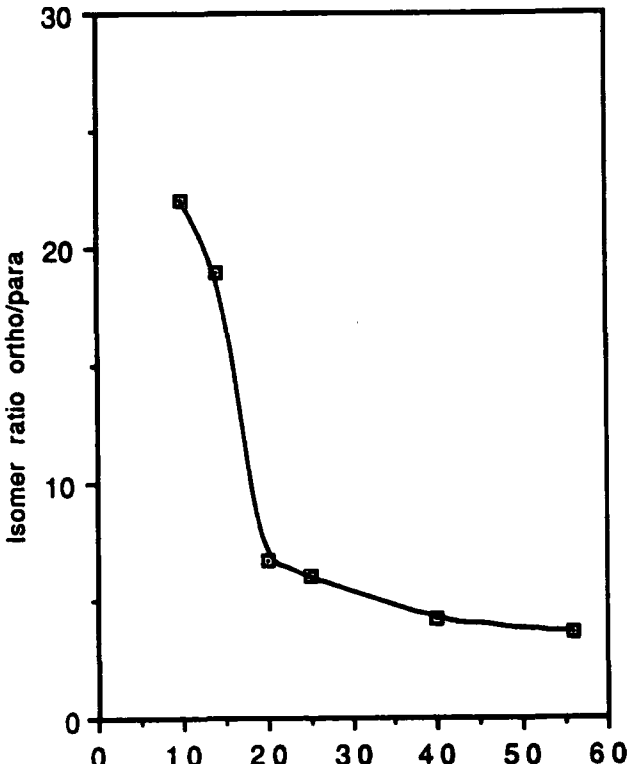
TABLE 6 Fluorination of phenol at different temperatures[55].

Reaction conditions		Conversion	Yield%		Isomer ratio
Temp. ^{0}C	Solvent	of phenol	*o*-fluoro phenol	*p*-fluoro phenol	*ortho/para*
-40	CH_3CN	63.5	42.4	11.0	3.85
-20	CH_3CN	56.1	38.9	10.7	3.64
0	CH_3CN	50.9	34.1	9.0	3.79
10	CH_3CN	44.7	53.9	16.6	3.25

Isomer ratios were found to change drastically with conversion of phenol (Figure 1). For example, at -20^{0}C in acetonitrile the *ortho/para* ratio was 22:1 at 10% conversion, and at 56% conversion under identical reaction conditions the *ortho* to *para* ratio was 3.6:1. It is assumed that the *ortho* isomer reacts further to give unidentified polymeric materials, which are observed bi-products at higher conversions.

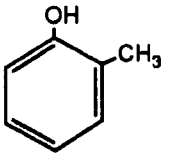
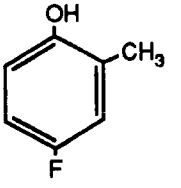
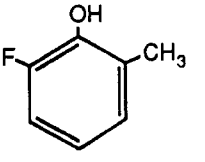
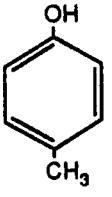
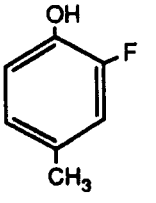
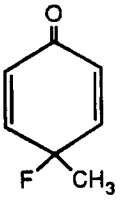
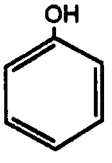
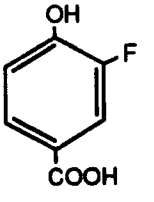
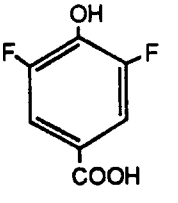
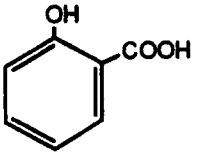
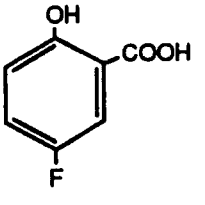
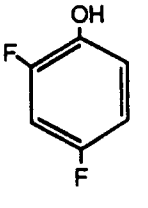
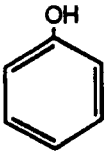
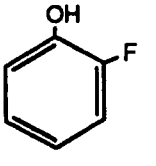
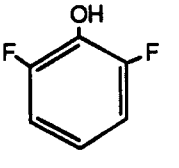
Figure 1

Fluorination of phenol in acetonitrile at -20^{0}C[55].



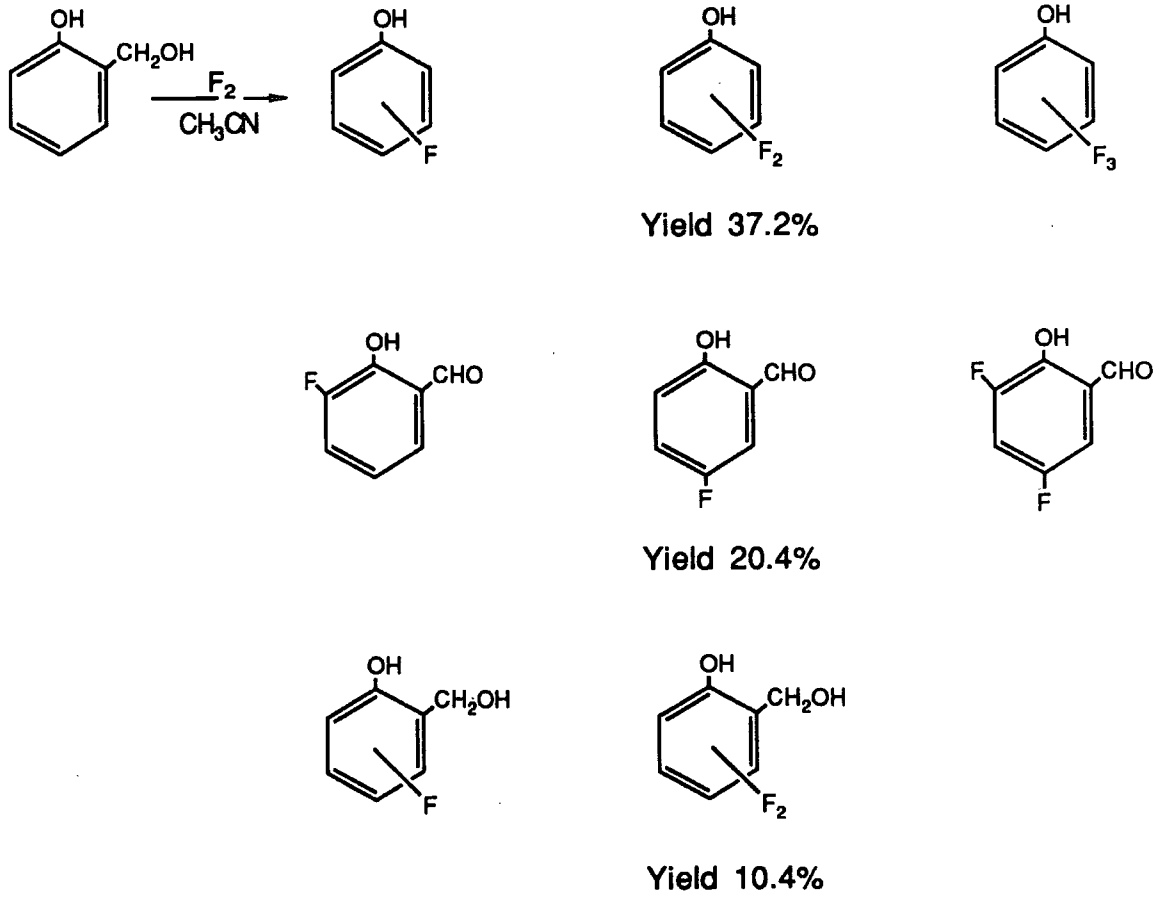
Misaki[55-57] also investigated the fluorination of various substituted phenols, sometimes with surprising results (Table 7). The direct fluorination of 4-methylphenol produced 4-fluoro-4-methyl-2,5-cyclohexadienone, in addition to the expected *ortho*-fluoro derivative.

Table 7 Direct Fluorination of Substituted Phenols[56,57].

Substrate	Temperature °C	Conversion %	Products %	
	-20	70.8	 27.5	 22.5
	-20	78.0	 38.4	 23.1
	-10	63.3	 59.4	 14.4
	-10	79.0	 55.6	 21.0
	-20	56.1	 38.9	 10.7

Interestingly, the fluorination of salicyl alcohol resulted in low yields of the expected fluorosalicyl alcohol but considerable amounts of the fluorophenols and fluorosalicylaldehydes (Scheme 9)[56]. When the fluorination of salicylaldehyde was attempted no oxidation was observed.

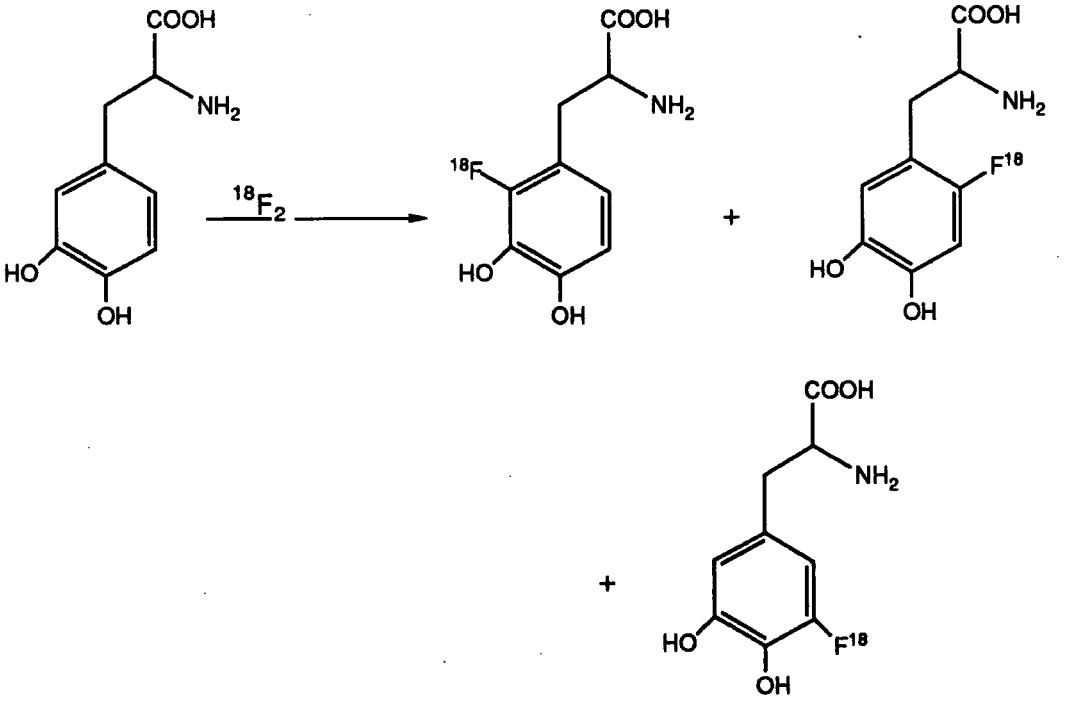
SCHEME 9



The preparation of radio labelled ^{18}F 6-fluorodopa requires a rapid method of synthesis due to the relatively short half life of the ^{18}F isotope and is therefore obtained by direct fluorination of a solution of l-dopa in anhydrous HF at -65^{0}C with dilute $^{18}F_2$. This reaction gives the desired 6-fluorodopa in a 5.8% chemical yield and a 3.0%

radiochemical yield with 2-and 5-fluorodopa in 12% and 1.7% yield respectively as the major biproducts[58] (Scheme 10). Anhydrous HF is used as the solvent to minimize the oxidation of l-dopa which is initiated by the deprotonation of the hydroxy groups. The synthesis of ^{18}F 6-fluorodopa is of interest because of its medical use in the non-invasive technique of Positron Emission Tomography to study the chemistry of dopamine in the brain of Parkinsonian patients[59].

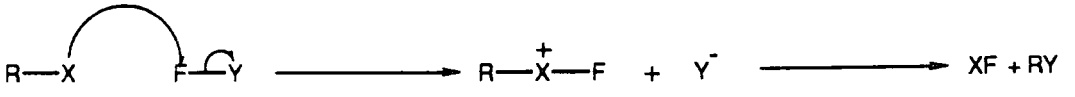
Scheme 10



ORGANIC HYPOFLUORITES AND INORGANIC FLUOROXY SALTS

These reagents all contain the O-F bond and, although the idea of electrophilic fluorination is still disputed[60-62], are broadly regarded as electrophilic fluorinating agents[63,64]. To achieve electrophilic fluorination it appears that the highly energetically unfavourable process of removal of a pair of electrons from fluorine is required. However, if electrophilic fluorination is regarded as nucleophilic attack on fluorine, concerted with ejection of a suitable leaving group from the fluorine, a deficiency of electrons on the fluorine need not arise[65] (Scheme 11).

Scheme 11



The prerequisites for an electrophilic fluorinating agent are: a fluorine atom must be bonded to a good leaving group, the leaving group must be highly electronegative, and the ligand attached to the fluorine must have no unoccupied d-orbitals which could facilitate either nucleophilic attack upon the ligand or electron transfer.

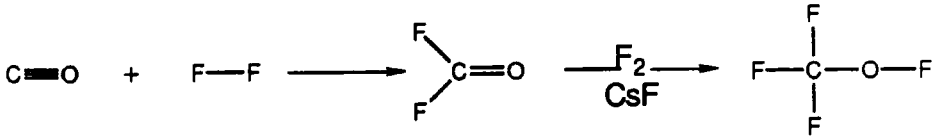
The synthesis of these reagents, their reactivity and limitations will be discussed here.

Trifluoromethyl Hypofluorite

Trifluoromethyl hypofluorite (3) is prepared by the reaction of elemental fluorine with carbon monoxide. The initial product is the carbonyl difluoride (2), formed by a spontaneous and highly exothermic

reaction. This product is passed though a bed of caesium fluoride which catalyzes the addition of the second mole of fluorine (Scheme 12)[65].

SCHEME 12



(2) (3)

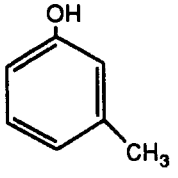
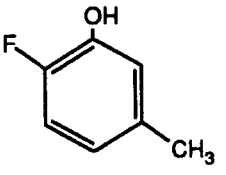
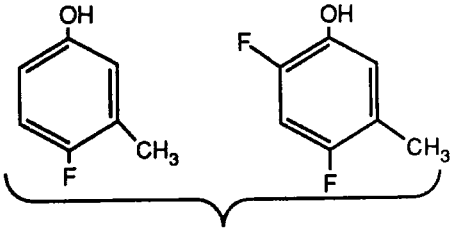
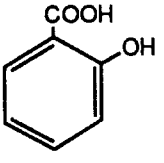
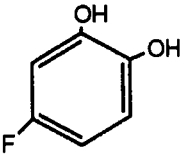
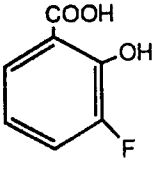
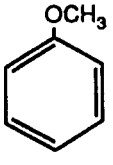
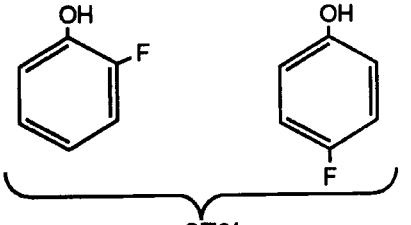
Trifluoromethyl hypofluorite (3) is a stable gas and can be stored under pressure without any appreciable decay. The ease of handling and its commercial availability has resulted in a large amount of research into its suitability as an electrophilic fluorinating agent[63,65-68]. It reacts with a variety of aromatic substrates in a manner characteristic of electrophilic species. The nature of any substituent already present on the aromatic ring plays a major role in determining the ease and extent of the fluorination[66].

When the aromatic system contains alkyl substituents, for example in toluene, a complex mixture of products and a poor mass balance are obtained. This complex mixture of products is obtained by competition between electrophilic substitution of the aromatic ring, side chain fluorinations and addition reactions[65].

The fluorination of oxygenated aromatic compounds, including anisole, substituted phenols and carboxylic acids, has been investigated [66,67]. The reactions were carried out with less than stoichiometic amounts of trifluoromethyl hypofluorite (3), and at low temperature, to facilitate the formation of monofluorinated aromatic compounds. Some examples are shown in Table 8. In these cases the aromatic ring is

sufficiently activated to favour electrophilic substitution over addition reactions.

Table 8 Fluorination of oxygenated aromatics with trifluoromethyl hypofluorite (3)

Substrate	Conversion %	Products %	
	82.0	 18.0	 58.0
	87.5	 70.0	 17.5
	82.0	 67%	

It reacts readily with benzene to give fluorobenzene in varying yields[67], depending on the reaction conditions and conversion rates. The maximum yield of fluorobenzene, 93%, was obtained at a conversion of about 40%, 5% (trifluoromethoxy)benzene was also produced at this conversion rate. The (trifluoromethoxy)benzene was produced by addition of CF_3OF to benzene with subsequent elimination of hydrogen fluoride [67,68]. These results demonstrate that CF_3OF is an excellent fluorinating agent for the synthesis of fluorobenzene at low conversion levels. However, since benzene and fluorobenzene have similar boiling points, the difficulty of separating and recycling benzene remains the

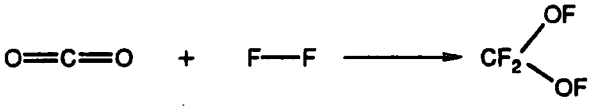
major problem in any large scale synthesis.

In contrast, trifluoromethyl hypofluorite (3) does not react readily with deactivated aromatic substrates. Nitrobenzene is unreactive towards electrophilic substitution by trifluoromethyl hypofluorite and the products obtained arose from addition of CF_3OF to the aromatic ring. Other deactivated aromatic systems show similar results[63,71,73,74].

Difluoromethyl bishypofluorite

Difluoromethyl bishypofluorite (4) is prepared by the reaction of elemental fluorine with carbon dioxide in the presence of a caesium fluoride catalyst. It is critical that the catalyst is prepared by fusion and subsequent grinding under anhydrous conditions for the reaction to occur (Scheme 13)[72].

SCHEME 13



(4)

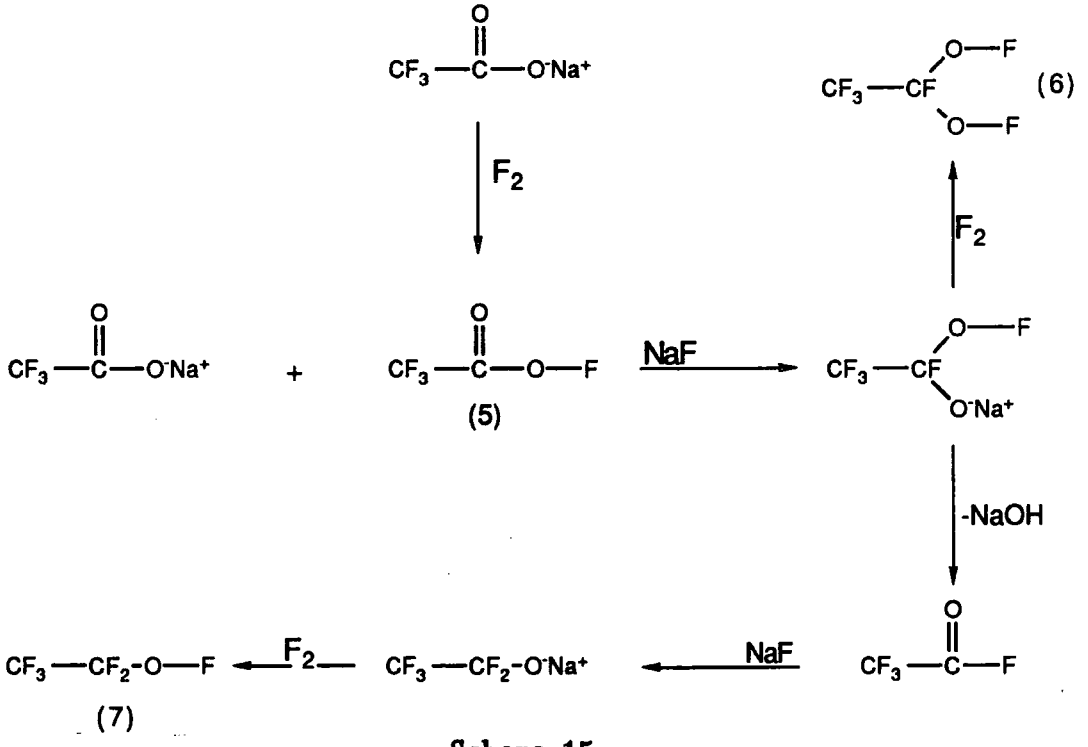
Difluoromethyl bishypofluorite (4) has similar chemical and physical properties to trifluoromethyl hypofluorite (3) and gives similar results with aromatic systems[65], but is not commercially available.

Trifluoroacetyl Hypofluorite and Perfluoroalkyl Hypofluorites

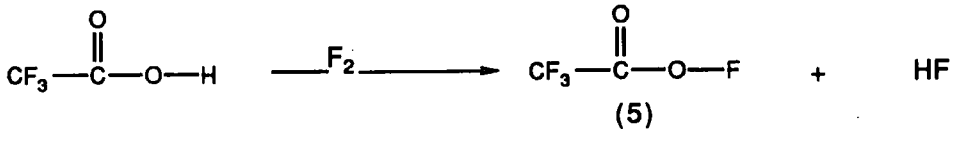
Trifluoroacetyl hypofluorite (5) was first prepared and character-ised in 1953 by Cady *et al*[74], but it was not until 1969, when Rozen

published a simple synthetic procedure for the synthesis of hypofluorites[75], that they became generally available to the organic chemist. The synthesis of trifluoroacetyl hypofluorite (5)[75-77], and of perfluoro- alkyl hypofluorites[78,79] (6) and (7), from sodium trifluoroacetate is outlined in Scheme 14. Compounds (6) and (7) are formed in the absence of moisture or acid and have similar synthetic utility to that of trifluoroacetyl hypofluorite (5). Reacting a solution of trifluoroacetic acid, rather than its sodium salt, yields predominantly trifluoroacetyl hypofluorite (5) from the replacement of hydrogen by fluorine (Scheme 15).

SCHEME 14



Scheme 15



Several perfluoro and chloroperfluoro fluoroxy compounds, for example $(CF_3)_3COF$ and $ClCF_2CF_2OF$, have been prepared in good yield by the

direct fluorination of the appropriate alcohol[80], but their chemistry has not been reported. Rozen and Barnette extended the solution preparation to the formation of stable long chain fluoroxy compounds, such as $CF_3(CF_2)_7OF$, $CF_3(CF_2)_6COOF$ and $CF_3(CF_2)_6C(OF)_2$, which were obtained as a mixture from $CF_3(CF_2)_6COOK$[81,82].

There have been relatively few investigations into the reactions of CF_3COOF and the other perfluoroalkyl hypofluorites[75,77]. The reaction products are subject to strong solvent and temperature effects which may indicate some involvement of radical processes similar to those observed for trifluoromethyl hypofluorite[83].

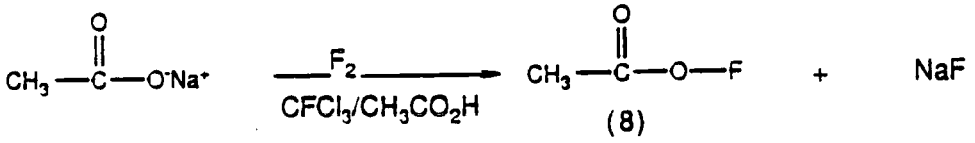
In the fluoroaromatic derivatives, produced by the reaction of these hypofluorites with aromatic systems, the fluorine atom was generally *ortho* to the substituent, although mixtures were routinely obtained. The best results for the selective introduction of fluorine into an aromatic system were obtained when activating substituents (OCH_3, OH, NHAc) were present. The *ortho*-substituted fluorine arose from an addition/elimination sequence at the electron-rich site in the substrate[83,84].

Acetyl Hypofluorite

Acetyl hypofluorite (8), CH_3COOF is prepared in situ by Rozen's general proceedure for the synthesis of hypofluorites[84-86]: fluorine gas, diluted to 5-10% concentration by nitrogen, is bubbled though a mixture of sodium acetate in glacial acetic acid and $CFCl_3$ at -78^oC (Scheme 16). The yield is generally between 50% and 80% when carried out on a 50 mmol scale. Acetyl hypofluorite (8) cannot be prepared by

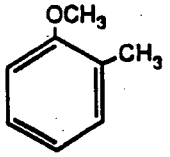
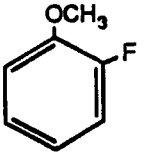
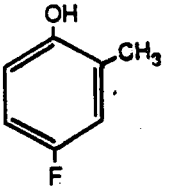
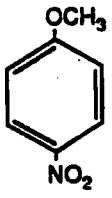
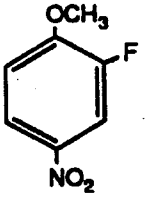
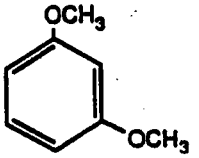
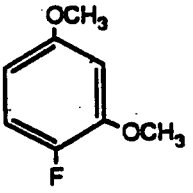
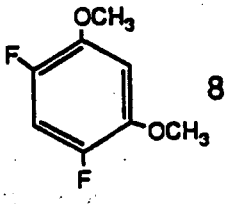
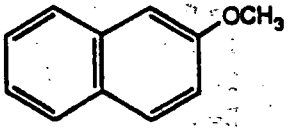
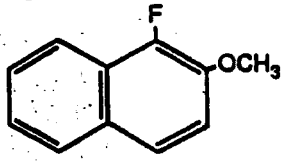
the direct fluorination of glacial acetic acid at low temperatures because of fluorines low solubility. It is noteworthy that this was the first acetyl hypofluorite prepared which is not perfluorinated.

Scheme 16



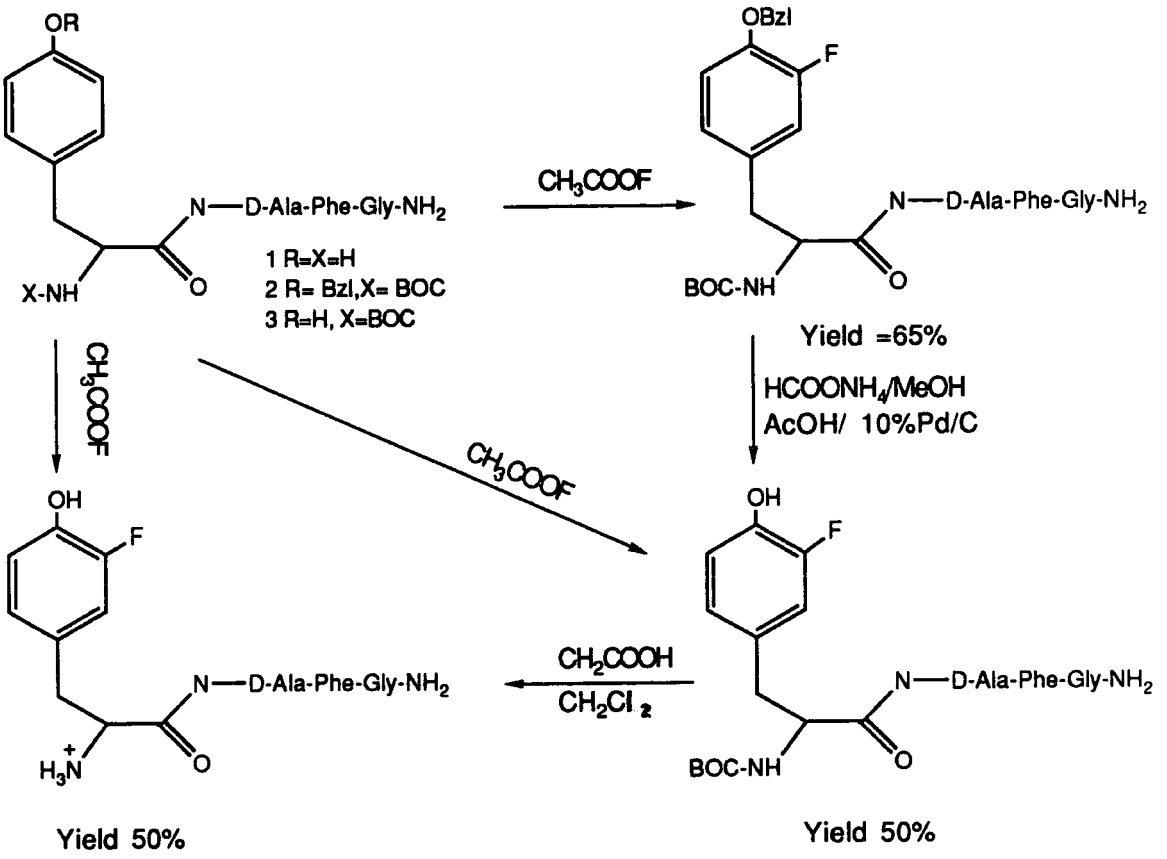
Acetyl hypofluorite (8) acts as a specific fluorinating agent for highly activated aromatic systems[84,85]. Whilst reaction usually takes place in seconds in highly activated aromatic systems, various alkyl benzenes[77], including toluene and t-butyl benzene, only react after relatively long periods. Nitrobenzene, and even phenyl acetate, are still less reactive. Some typical results of fluorinations of aromatic systems by acetyl hypofluorite are summarized in Table 9.

Table 9 Fluorinations by acetyl hypofluorite.

Substrate	Conversion %	Products %		Ref.
	95	 76.5	 8.5	85
	78	 43.0		85
	86	 32.5	 65.0	85
	100	 65		86

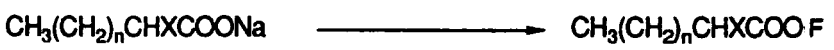
Acetyl hypofluorite has recently been used to fluorinate the aromatic rings of biologically interesting compounds and has resulted in the first selective fluorination of a peptide[87] (Scheme 17).

Scheme 17



Rozen *et al*[88] have recently reported the synthesis of a series of acyl hypofluorites in good yield from the corresponding carboxylic acid salts (Scheme 18). It was found that they are only stable if there is an electron withdrawing group in the *a* position, and the chain length smaller than six carbons. These two structural features prevent the elimination of HF. The reactivity of these systems with aromatic substrates has yet to be reported.

Scheme 18



n =1 x = Cl
n =1 x = NO_2
n =1 x = COOEt

Fluoroxysulphate salts

In 1926 Fichter[89] reported that the passage of elemental fluorine through an aqueous solution of sulphate or bisulphate led to the production of an "ephemeral oxidant", but it was not until 1979 that Appelmann *et al*[90] identified the oxidizing species as the fluoroxysulphate ion (9) by the isolation and characterization of its caesium and rubidium salts. These salts were prepared by the fluorination of saturated aqueous solutions of Rb_2SO_4 and Cs_2SO_4 with 20% elemental fluorine at temperatures between -4^0C and 0^0C, (Scheme 19). Caesuim fluoroxysulphate was isolated in a 50% yield, although this has since been increased to 70%[91]. The yield is limited by the instability of the fluoroxysulphate anion in aqueous media.

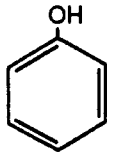
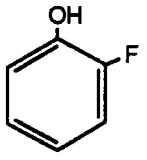
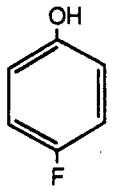
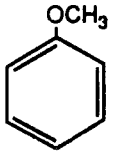
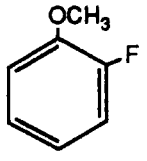
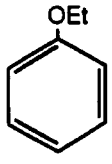
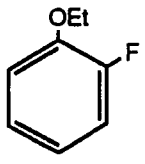
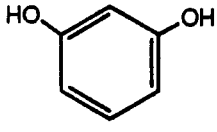
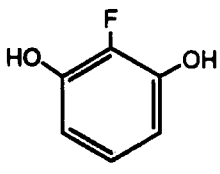
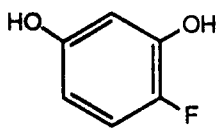
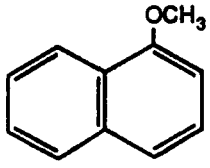
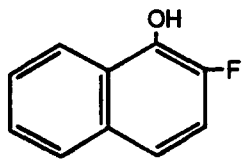
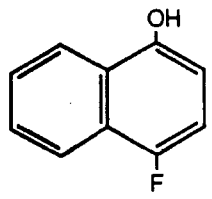
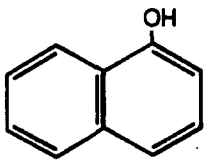
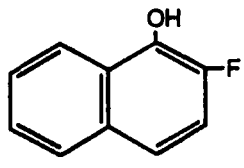
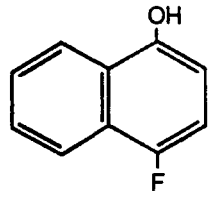
Scheme 19

$$M_2SO_4 + F_2 \longrightarrow \underset{(9)}{MSO_4F} + MF$$

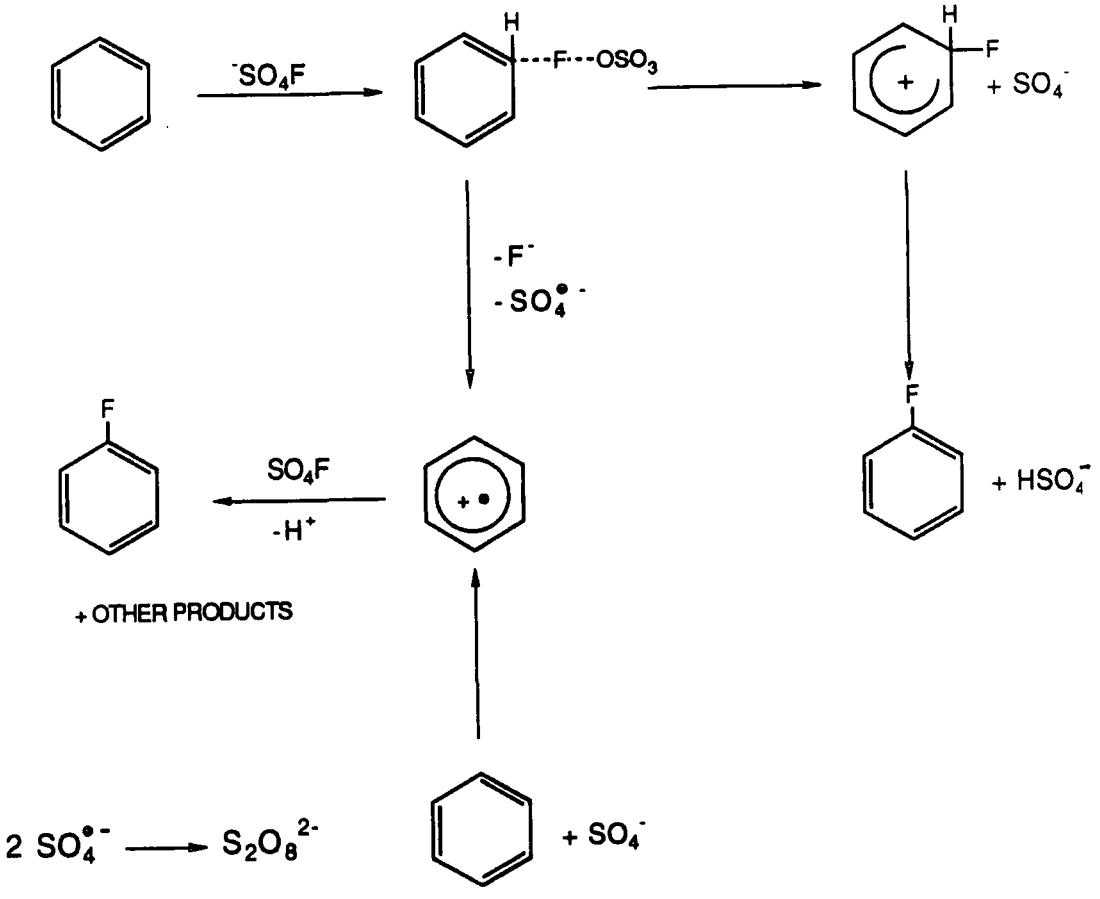
Caesium and rubidium fluoroxysulphate can be stored in polyethylene vessels at 0^0C without significant loss of activity, but have been reported to explode on contact with metal surfaces and under mechanical pressure[92].

The reaction of fluoroxysulphates with a variety of aromatic systems has been reported[90-98]. Fluorinations are normally carried out at room temperature in acetonitrile, occasionally with BF_3 as a catalyst. As with other hypofluorites, they give good yields of ring fluorinated products with activated aromatic systems, but low yields are obtained with unactivated and deactivated aromatics such as nitrobenzene Some typical results are summarised in Table 10.

Table 10 Fluorination of aromatic systems with caesium fluoroxysulphate.

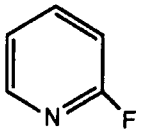
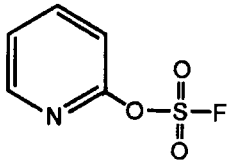
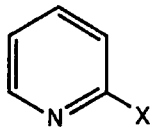
Substrate	Ratio $CsSO_4F$/ substrate	Conversion %	Products %	
	1:1	61	 58.1	 9.3
	1:1	73	 47.9	 17.1
	1:1	73	 40.1	 10.0
	1.3:1	100	 13.2	 39.7
	0.7:1	79.5	 48.0	 6.0
	0.7:1	77.5	 48.0	 6.0

The mechanism for the fluorination of aromatic compounds by $CsSO_4F$ and $RbSO_4F$ shows both electrophilic and radical character. Appleman has suggested the following mechanism[92].

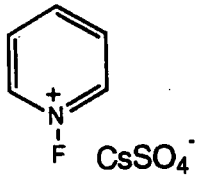


The reaction of caesium fluoroxysulphate with pyridine in a variety of solvents has been recently reported[98] to yield 2-fluoropyridine, 2-pyridyl fluorosulphonate and 2-substituted pyridines (Table 11).

Table 11 Fluorination of pyridine with $CsSO_4F$ in different solvents

Solvent	Products		
			
$n\text{-}C_5H_{12}$	56	44	–
$(CH_3CH_2)_2O$	61	39	–
CCl_4	70	30	–
$CHCl_3$	47	17	36,X=CL
CH_2Cl_2	26	12	62,X=CL
$C(CH_3)_2OH$	64	18	18,X=$OC(CH_3)_3$
CH_3OH	–	–	98,X=OCH_3

The mechanism of formation of these products has not been proposed but it is likely that they are formed by nucleophilic attack on the N-fluoropyridium cation (10)



(10)

$CsSO_4F$ has been used in the selective cleavage of aryl-metal bonds to give fluoroaromatic compounds. This will be discussed separately .

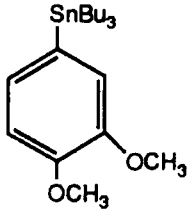
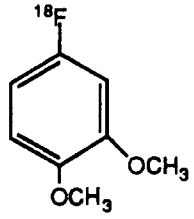
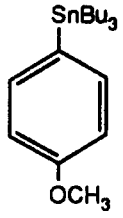
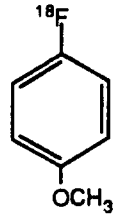
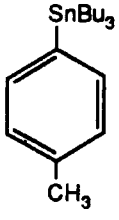
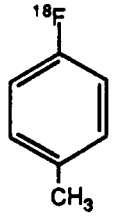
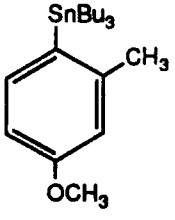
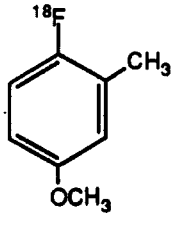
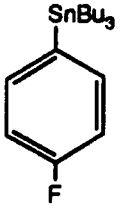
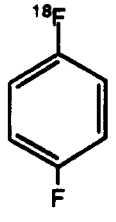
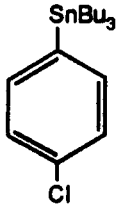
FLUORODEMETALLATION OF METALLOARENES

The Group IVb metals (Si, Ge, Sn, Pb), and also mercury and thallium, have all been employed successfully in halogenating aromatic compounds[99] with chlorine, bromine and iodine. These demetallation reactions enable the site specific substitution of a labile metal moiety by halogens in high yield. The major synthetic application for this process has been the introduction of radio-labelled bromine and iodine into aromatic systems. The success of the halodemetallation reaction for the introduction of short lived radio nuclei promoted investigation into the feasibility of the process for the introduction of ^{18}F ($T^1/_2$= 110 minutes)

In 1980 Adam *et al*[100] were the first group to demonstrate that elemental fluorine ($^{18}F_2$) could be used to form fluoroaromatic compounds from Group IVb metalloarenes by fluorodemetallation. The fluorodemetallation of tributylphenyltin with elemental fluorine ($^{18}F_2$) at -78^{o}C in $CFCl_3$ produced fluorobenzene in a 70% yield (38% radiochemical yield). Fluorodemetallation of other Group IVb metalloarenes gave disappointing yields of the desired fluorinated aromatic systems.

The high yield of fluorobenzene obtained in this reaction study initiated a considerable amount of research into the feasibility of fluorodemetallation of aryl-tin compounds, not only as a route to labelled aromatic compounds[100-104] (Table 13), but also as a general synthetic route to fluoroaromatics[105-108].

TABLE 13 Fluorodemetallation of Aryl-Tin compounds with $(^{18}F_2)$[102]

Substrate	Products	Radiochemical yield %
		56
		72
		82
		52
		>95
		>95

Chambers *et al*[106-108] have investigated the fluorodemetallation of a series of aryl-tin compounds with caesuim fluoroxysulphate, trifluoroacetyl hypofluorite and elemental fluorine. The highest yields were obtained when caesium fluoroxysulphate was used as the fluorinating agent; this can be attributed to its greater electrophilic character. They have also investigated fluorodemetallation of aryl-mercury compounds[106,107] with good results.

A number of aryl trimethylsilanes have been successfully substituted at the *ipso* position with both radioactive elemental fluorine and acetyl hypofluorite (CH_3COOF^{18})[104]. Reaction yields were generally low (under 30%) and gave various F for H substitutions.

In a recent publication by Coenen and Moerlien[105] the reactivity of a series of aryl-trimethylmetal systems (M= Sn, Ge, Si) with elemental fluorine and acetyl hypofluorite was compared (Table 14).

It was found that for a given substituent all fluorodemetallation yields decrease in the order Sn> Ge> Si. The fluorination yields decrease by a factor of approximately three when going from the stannylated to the silylated substrates, corresponding to the increase of carbon-metal bond energies (Sn-C 257 KJ/mol; Ge-C 308 KJ/mol; Si-C 352 KJ/mol) and the decrease in carbon metal bond lengths (Sn-C 1.54 Å; Ge-C 1.36 Å; Si-C 1.31 Å), factors which disfavour aromatic demetallation.

It was found that the fluorination yields for a given trimethyl metal substituent are dependent on the nature of the second substituent on the aromatic ring. The reactivity of the trimethyl metal compounds

TABLE 14 Effect of substituent and metal on fluorodemetallation[105]

R,X	Metal	% Chemical yield[a] Sn	Ge	Si
OCH_3		70.4^{+} 6.6	35.5^{+} 1.4	19.8^{+} 3.0
		(66.0^{+} 4.3)		
CH_3		78.4^{+} 6.4	40.6^{+} 5.8	22.4^{+} 4.0
		(16.4^{+} 1.8)	(9.1^{+} 1.1)	
F		73.8^{+} 6.8	55.8^{+} 3.6	30.4^{+} 3.2
H		64.4^{+} 7.0	40.4^{+} 4.0	23.0^{+} 4.0
		(68.2^{+} 5.7)	(8.5^{+} 0.5)	(3.5^{+} 0.3)
Br		34.2^{+} 3.4	24.8^{+} 0.8	10.2^{+} 0.6
CF_3		35.0^{+} 2.8	10.4^{+} 1.6	2.4^{+} 0.5
		(36.3^{+} 1.6)		

[a] Values are for fluorine, those in parentheses are for acetyl hypofluorite.

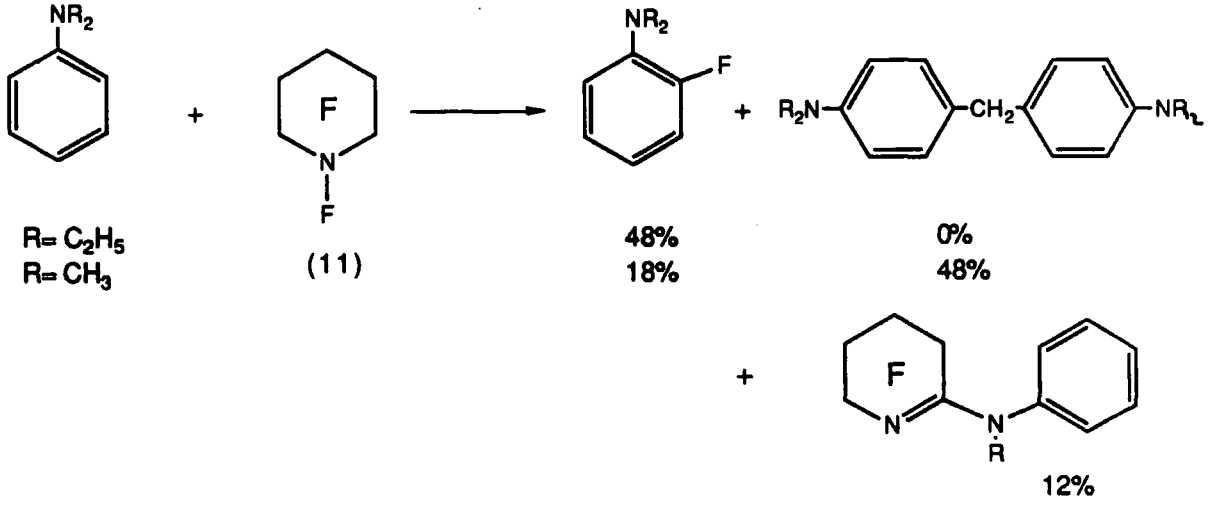
increases as electron withdrawing substituent (NO_2, CF_3, Br) are replaced by non-electron withdrawing groups (H, F). When electron donating groups (CH_3, OCH_3) are present, however, no further increase in yield is observed, but rather a decrease in fluorination yields with the less reactive organometallic compounds is obtained.

N-FLUORO COMPOUNDS

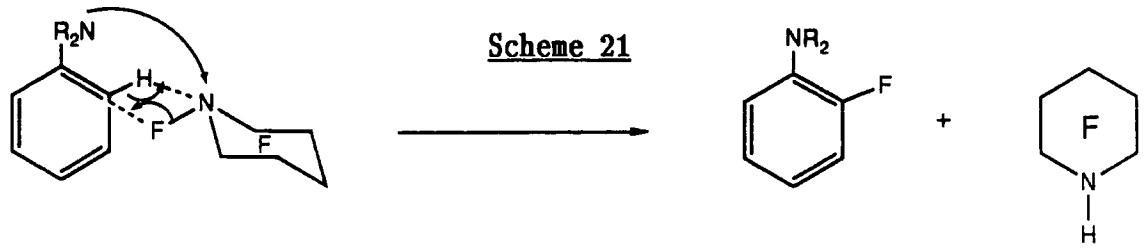
N-Fluoroperfluoro Piperidine

In 1964 Banks *et al*[109] reported that N-fluoroperfluoro piperidine, N.F.P., (11), reacts with sodium propane-2-nitronate in methanol under mild conditions to give 2-fluoro-2-nitropropane. This was the first indication that N-fluoro compounds possess useful reactivity for the fluorination of organic compounds. N-fluoroperfluoro piperidine is synthesized in low yield by the electrochemical fluorination of pyridine and has been shown to react with suitably activated aromatic compounds [110,111], for example the fluorination of tertiary aromatic amines which gave *ortho*-fluorinated products (Scheme 20)[111].

Scheme 20



E.S.R. studies have shown the mechanism of fluorination to involve a one electron transfer, followed by attack at the *ortho* position of the aniline derivative by fluorine in a concerted manner[111] (Scheme 21).



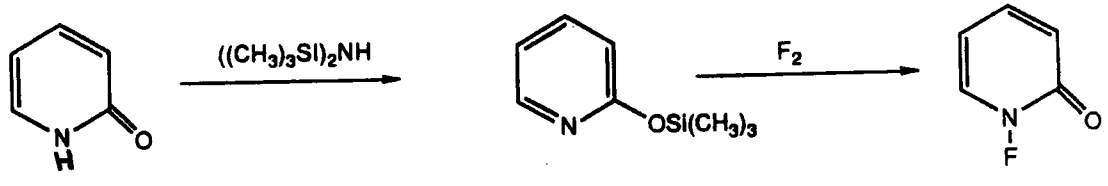
Scheme 21

Polymeric analogues of N.F.P. in which N-fluoropiperidine groups are attached to a perfluorinated backbone have been reported[112]. These reagents are no more reactive than the non-polymeric N.F.P. and therefore show little reactivity towards aromatic systems.

N-Fluoro-2-pyridone

N-Fluoro-2-pyridone (12) is a stable selective fluorinating reagent that requires no special handling techniques and is synthesised in good yield from pyridone in a simple two step process (Scheme 23)[114]. It has been used to fluorinate aryl-Grignards to give the corresponding fluoroaromatic in low yield[115].

Scheme 23



(12)

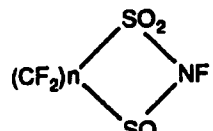
N-Fluoro perfluoroalkyl sulphonamides

The first selective fluorination of an aromatic system in good yield by an N-fluoro compound was reported by Desmarteau *et al*[116,117] in 1987 using N-fluoro perfluoroalkyl sulphonamides. This class of compound had previously been shown to selectively fluorinate carbanions in high yield[118,119], and were of the following types: (13), (14), and (15).

(13) $(RfSO_2)_2NF$

(14) $RfSO_2(NF)SO_2Rf$

(15)



(16)

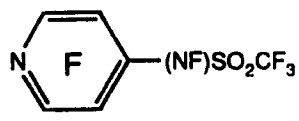


TABLE 15. Examples of Selective fluorinations with $(CF_3SO_2)_2NF$ at 22°C[116,117].

Compound[a]	Conditions[b] Solvent/time	Conversion	Products[c]
Nitrobenzene	Neat, 12	0%	no reaction
Acetophenone	$CDCl_3$, 12	0%	no reaction
Toluene	Neat, 10	80%	2-fluorotoluene(74) 3-fluorotoluene(4) 4-fluorotoluene(22)
Anisole	Neat, 2	100%	2-fluoroanisole(69) 4-fluoroanisole(24) Polyfluoroanisole(7)
Phenol	$CDCl_3$, 12	high	2-fluorophenol (60) 4-fluorophenol (40)
m-Cresol	$CDCl_3$, 12	high	2-fluoro-5-methyl-phenol (44) other (20)

[a] All aromatic compounds in 2:1 excess, or larger, with 1-2mmol of fluorinating agent.

[b] Time in hours.

[c] Figures in parentheses are NMR yields as a percentage of fluorinated products.

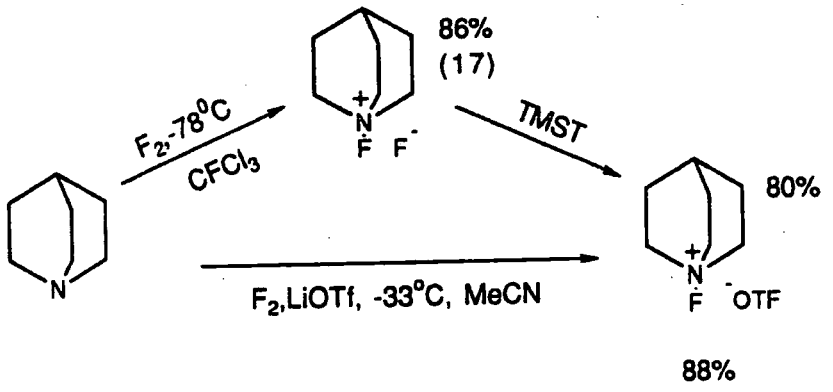
Benzene reacts slowly with N-fluoro perfluoroalkyl sulphonamides but as the ring is activated towards classical electrophilic halogenation the rate increases. Fluorination takes place preferentially in the *ortho* position under mild conditions, a selection of the results obtained are shown in Table 15. A new member of this class of compound, perfluoro-N-(pyridyl)methane sulphonamide (16), has recently been shown to selectively fluorinate benezene to give fluorobenzene (88%)[120].

They are prepared by the reaction of the parent perfluoroalkyl sulphonamide with elemental fluorine at low temperature, they are easily handled, and are stable in fluoropolymer plastic containers at room temperature for long periods of time. Their major drawback is the difficulty of synthesizing the parent perfluoroalkyl sulphonamides.

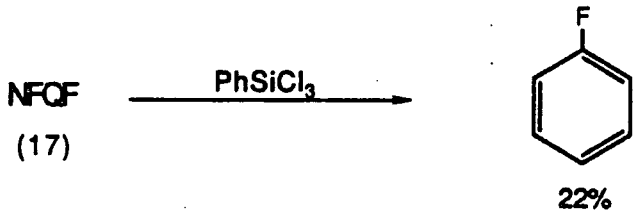
N-Fluoroquinuclidinium Fluoride and Triflate.

N-Fluoroquinuclidinium fluoride (NFQF) (17) is prepared in high yield by direct fluorination of quinuclidine at low temperature[121,122]. The corresponding triflate, (NFQT) (18)[123], can be prepared from NFQNF and trimethylsilyl triflate in acetonitrile at room temperature, or by the treatment of a cold solution of quinuclidine in acetonitrile containing lithium triflate with neat fluorine at low pressure (Scheme 23). NFQF (17) is an extremely hygroscopic solid but can be stored at room temperature under dry air in a poly(ethylene) bottle for considerable periods of time. It is capable of fluorinating aromatic systems in low yield (Scheme 24). NFQT (18) has similar chemical and physical properties, except it is not hygroscopic.

Scheme 23



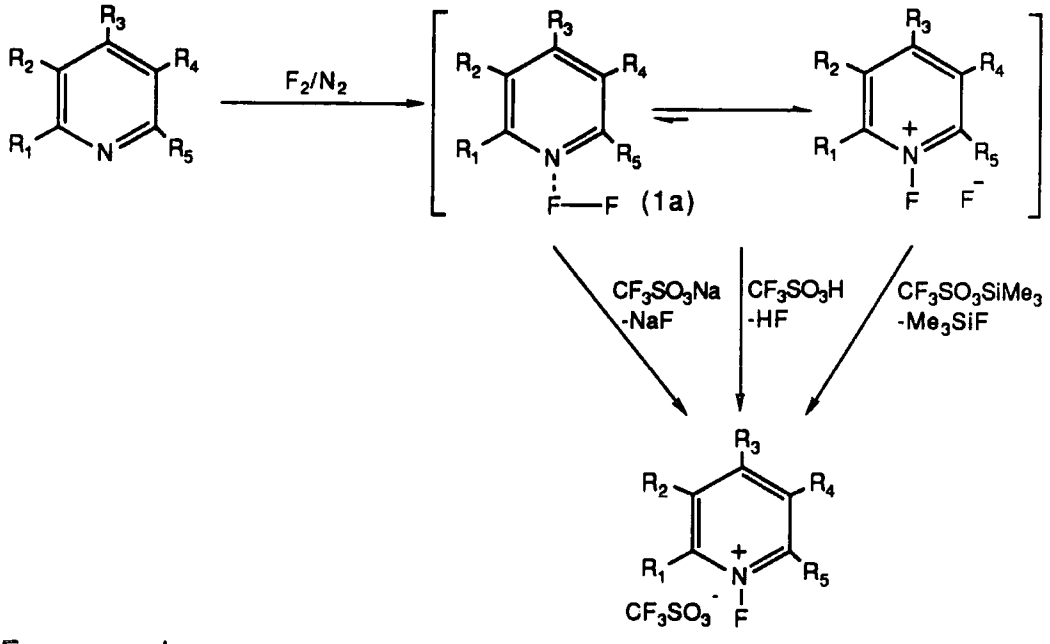
Scheme 24



N-Fluoropyridinium salts

The synthesis of a wide range of N-fluoropyridinium salts and their reactivity as selective fluorinating agents have been reported[124-133]. They can be prepared in high yield from substituted pyridines by direct fluorination to give a pyridine-F_2 complex of type (1a), followed by treatment with a strong Bronsted acid, Bronsted acid salts, the trimethylsilylester of Bronsted acids or Lewis acids (Scheme 25). An alternative method of preparation is by direct fluorination of N-trimethylsilyl pyridinium salts (Scheme 26)

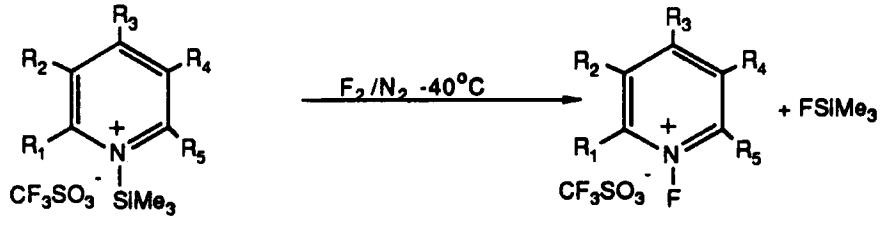
Scheme 25



For example

R_1, R_2, R_3, R_4, R_5, can = OCH_3,CH_3, Cl, OPh, etc

Scheme 26



They have been shown to selectively fluorinate aromatic compounds in good yield, some examples are shown in Table 16[128,129]. Recently polymeric analogues of this type of compound have been synthesised[131], and for example (19). These polymeric materials have been shown to selectively fluorinate aromatic compounds in good yield.

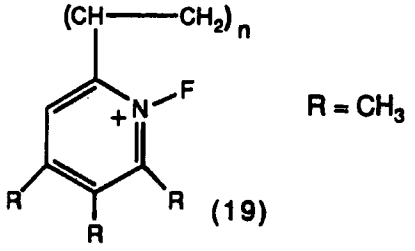
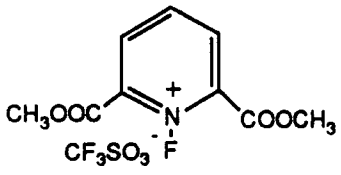
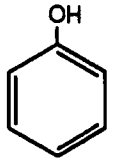
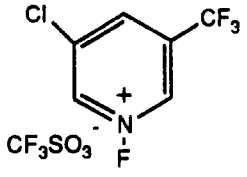
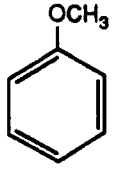
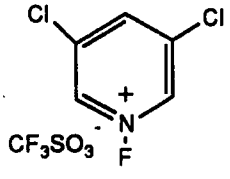
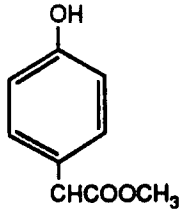
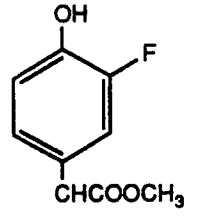
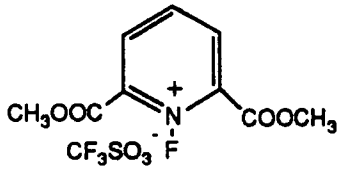
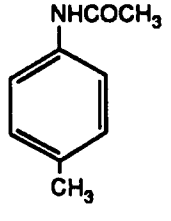
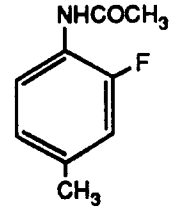
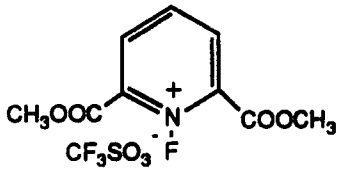
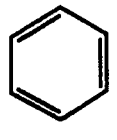
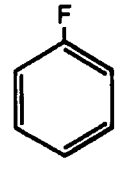
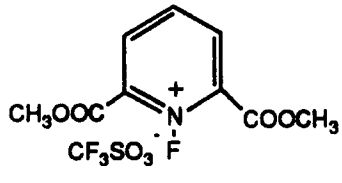
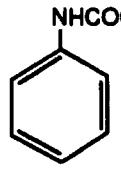
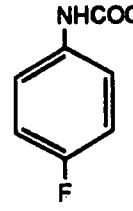


Table 16 Examples of selective fluorination of aromatic systems by N-fluoro pyridium salts

Fluorinating Agent	Substrate	Conversion	Products %
		78	2-Fluorophenol 30 4-Fluorophenol 24 2,4-Difluorophenol 30
		58	2-Fluoroanisole 40 4-Fluoroanisole 47
		57	 71
		50	 71
		-	 56
		54	 28
			 24

Xenon Difluoride

Xenon difluoride was first prepared by Weeks *et al*[134] in 1962 by a complicated low pressure ultraviolet (uv) initiated reaction between xenon and fluorine. Its availability to the organic chemist was restricted until a simple method for its synthesis by the uv initiated reaction of fluorine and xenon in glass apparatus at atmospheric pressure was published[135].

The reactivity of xenon difluoride with aromatic systems has been investigated[136-149]. Deactivated and unactivated aromatic compounds only react with XeF_2 in the presence of a Lewis acid as a catalyst for example anhydrous HF[136-138], to give selectively fluorinated aromatic compounds in high yield, along with some biphenyls and polymeric materials (Table 16).

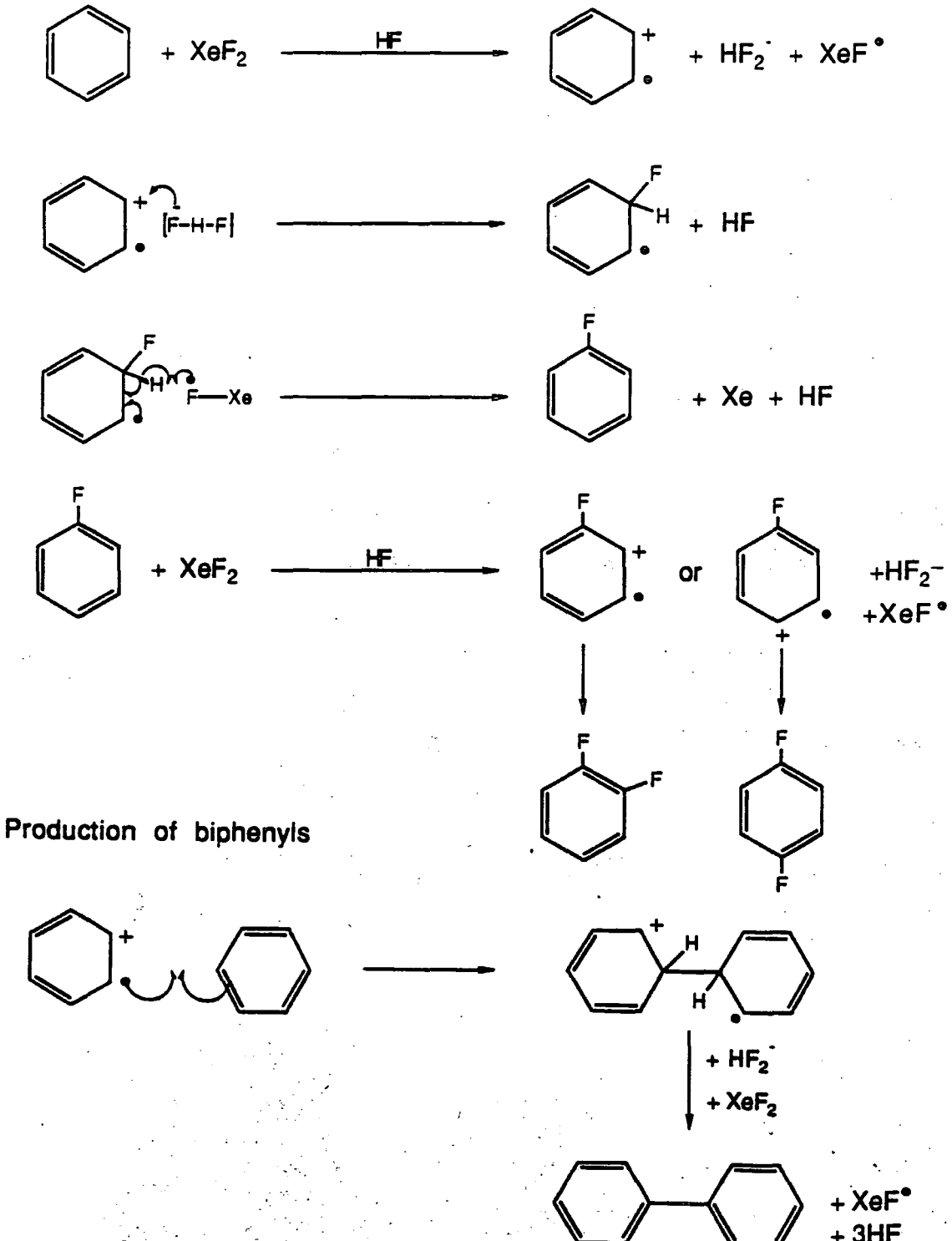
Table 16 Fluorination of aromatic systems with XeF_2 in the presence of HF

Aromatic	Monofluorinated products			Total Yield%
	ortho	*meta*	*para*	
Chlorobenzene	16	32.0	46.3	65.5
Fluorobenzene	11.8	2.8	32.3	46.9
Benzene				68.0
Benzotrifluoride	0	71.7	3.8	75.0
Nitrobenzene	18.9	50.9	11.4	81.2

Although the product distribution obtained is consistent with an electrophilic process, the requirement of HF as a catalyst and the

production of biphenyls indicate that it is not a simple one. Investigation of the mechanism by ESR has detected the presence of radical cations in the fluorination of benzene by xenon difluoride[142], and this has resulted in the proposal of a radical cation mechanism (Scheme 28), which explains both the requirement for a catalyst and the production of biphenyls.

Scheme 28 Mechanism for fluorination of deactivated aromatics

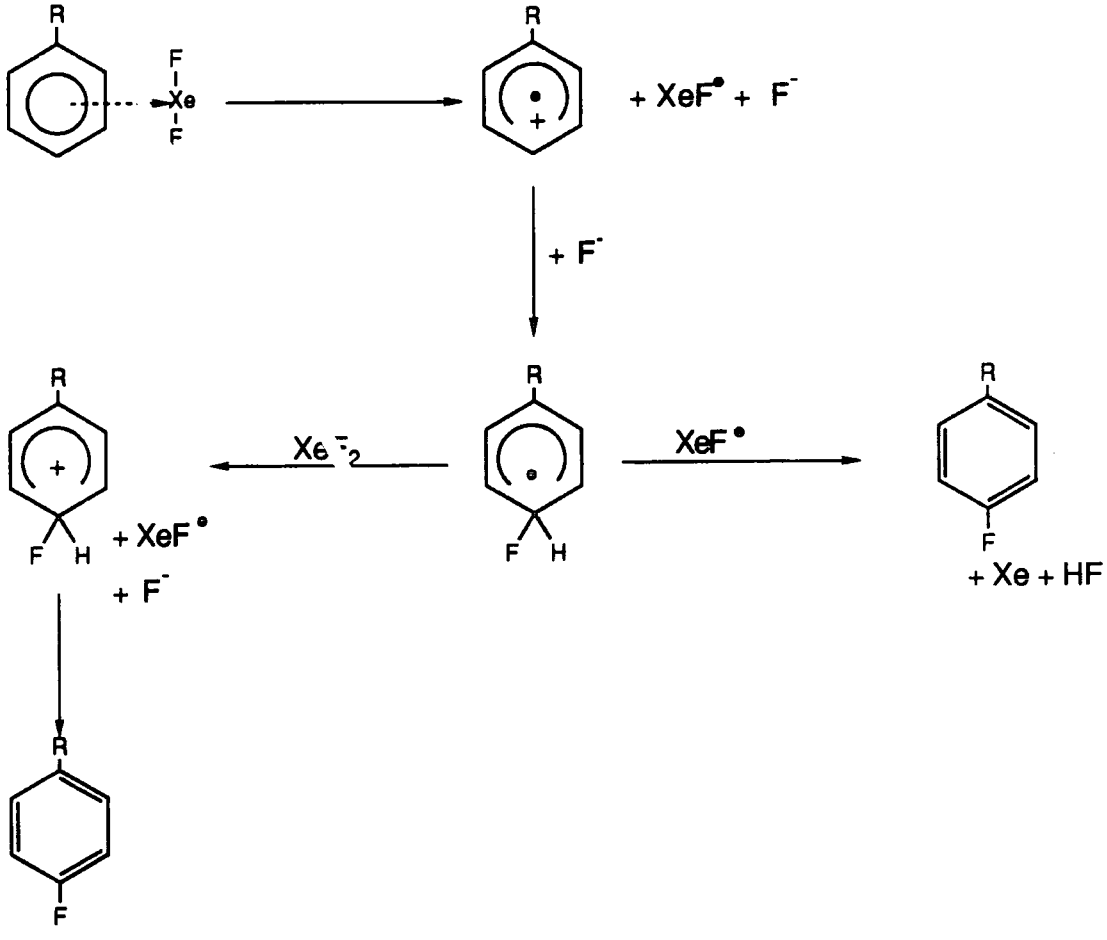


Highly activated aromatic systems for example anisole will also react with XeF_2 in the absence of a catalyst, to give fluorinated aromatic systems in good yield (Table 17). The mechanism proposed[141] for this reaction also involves radical cations, with the first step being the polarisation of XeF_2 by the aromatic substrate, whilst an electron is transfered to give the radical cation (Scheme 29).

Table 17 Fluorination of activated aromatics with XeF_2 in the absence of a catalyst.

Aromatic substrate	Products obtained	Yield%
Anisole	2-Fluoroanisole	37.6
	3-Fluoroanisole	3.7
	4-Fluoroanisole	30.1
Phenol	2-Fluorophenol	19.0
	3-Fluorophenol	18.9
	4-Fluorophenol	9.4
1,2-Dimethoxybenzene	4-Fluoro-1,2-dimethoxybenzene	37.0
1,2-Dihydroxybenzene	4-Fluoro-1,2-dihydroxybenzene	38.0
2-Naphthol	1-Fluoronaphthol	40.0

Scheme 29



Pyridine has also been shown to react wi h xenon difluoride with or without the addition of HF as a catalyst, to af ord a mixture of 2-fluoropyridine (35%), 3-fluoropyridine (20%) an 2,6-difluoropyridine (11%)[145]. The mechanism of this process is not yet clear.

CHAPTER TWO

FLUORODESILYLATION OF ARYLSILANES AS A POTENTIAL ROUTE TO FLUORINATED AROMATIC COMPOUNDS

CHAPTER 2

FLUORODESILYLATION OF ARYLSILANES AS A POTENTIAL ROUTE TO FLUORINATED AROMATIC COMPOUNDS

Introduction

The fluorodemetallation of aryltin compounds has been reported as a high yielding selective route to fluoroaromatic compounds[100-108] (see Chapter 1). Despite this, it has found little application other than in the synthesis of ^{18}F labelled compounds[100-103] due to the high cost of organotin reagents, their high toxcity[150] and the fact that the highly toxic alkyltin fluorides (20), produced as a bi-product, can not be regenerated due to the strength of the tin-fluorine bond.

$$Ar—SnR_3 \xrightarrow{F_2} Ar—F + F—SnR_3 \quad (20)$$

These limitations led to the consideration of fluorodemetallation of other group IV metalloarenes as a possible route to fluoroaromatic systems. The ease of synthesis of arylsilanes[151,152], their low toxicity and cost, coupled with reports of limited success of fluorodesilylation as a route to ^{18}F labelled aromatics[104-105], prompted our investigation into fluorodesilylation of arylsilanes as a general route to fluoroaromatic compounds.

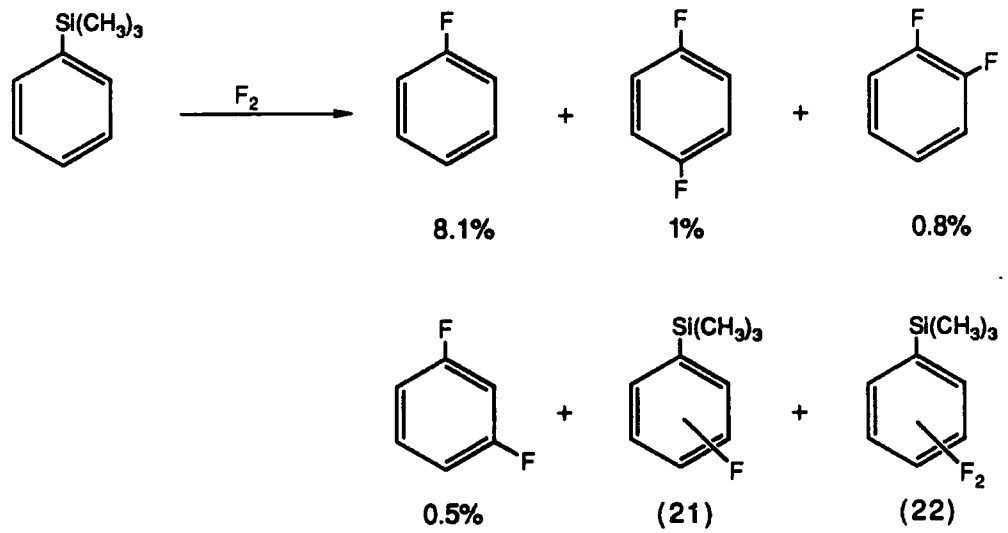
For the introduction of ^{18}F labelled fluorine into an aromatic system[104,105] the scale of the reaction has been small, typically on the micromole scale, and at high dilution using very low concentrations of fluorine in helium (<0.25%). We have attempted to effect fluorinations on a larger scale, with higher concentrations of fluorine in nitrogen (10%), under a variety of conditions.

Analysis of the reaction mixtures was carried out by g.c. mass spectrometry and ^{19}F n.m.r., products being identified by comparison with authentic samples and yields being calculated by comparison of ^{19}F n.m.r. integrals of the products with the integral of an added benzotrifluoride marker.

Direct fluorination of phenyltrimethylsilane

Investigation into the direct fluorination of phenyltrimethylsilane at -78^0C in $CFCl_3$ indicated that not only the desired *ipso* F for H substitution, but other F for H ring substitutions, had occurred (Scheme 30).

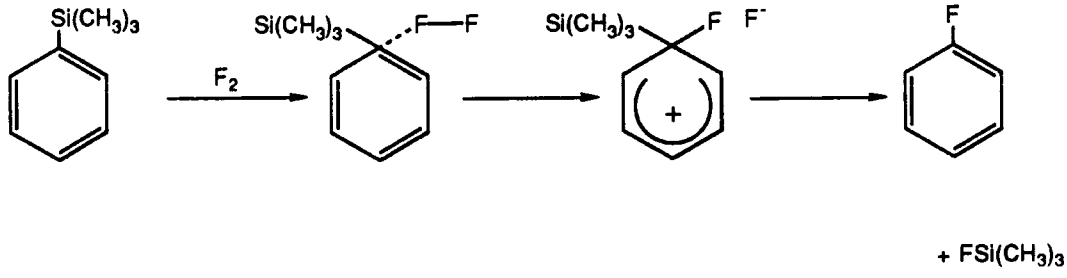
Scheme 30



As well as the undesired fluorotrimethylsilylbenzenes (21) and difluorotrimethylsilylbenzenes (22), difluorobenzenes were also produced in low yield. The formation of these difluorobenzenes will be discussed later in this chapter.

There is evidence that the direct fluorination of aromatic systems by elemental fluorine occurs *via* an electrophilic process (see Chapter 1). This, coupled with the selectivity of the reaction, and the fact that the cleavage of the aryl-silicon bond by other halogens is an electrophilic process[153], suggests that fluorodesilylation also proceeds *via* an electrophilic process (Scheme 31).

Scheme 31

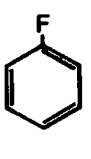
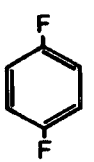
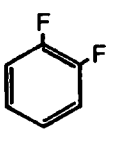
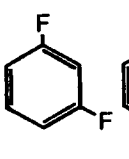
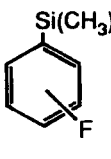
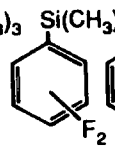
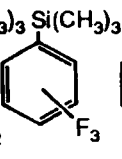
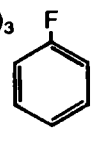
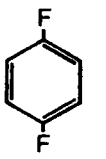
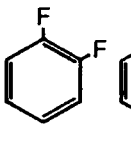
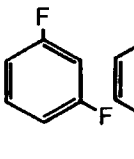
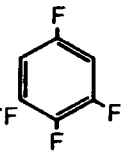


Effect of temperature on fluorodesilylation of phenyltrimethylsilane

The direct fluorination of phenyltrimethylsilane in acetonitrile with a 1 fold excess of 10% elemental fluorine in nitrogen was investigated at a range of temperatures from -30°C to +20°C. Yields of fluoroaromatics produced were calculated from ^{19}F n.m.r. integrals, and the presence of starting material was determined by g.c./mass spectrometry. Results are summarised in Table 18 and Figure 2.

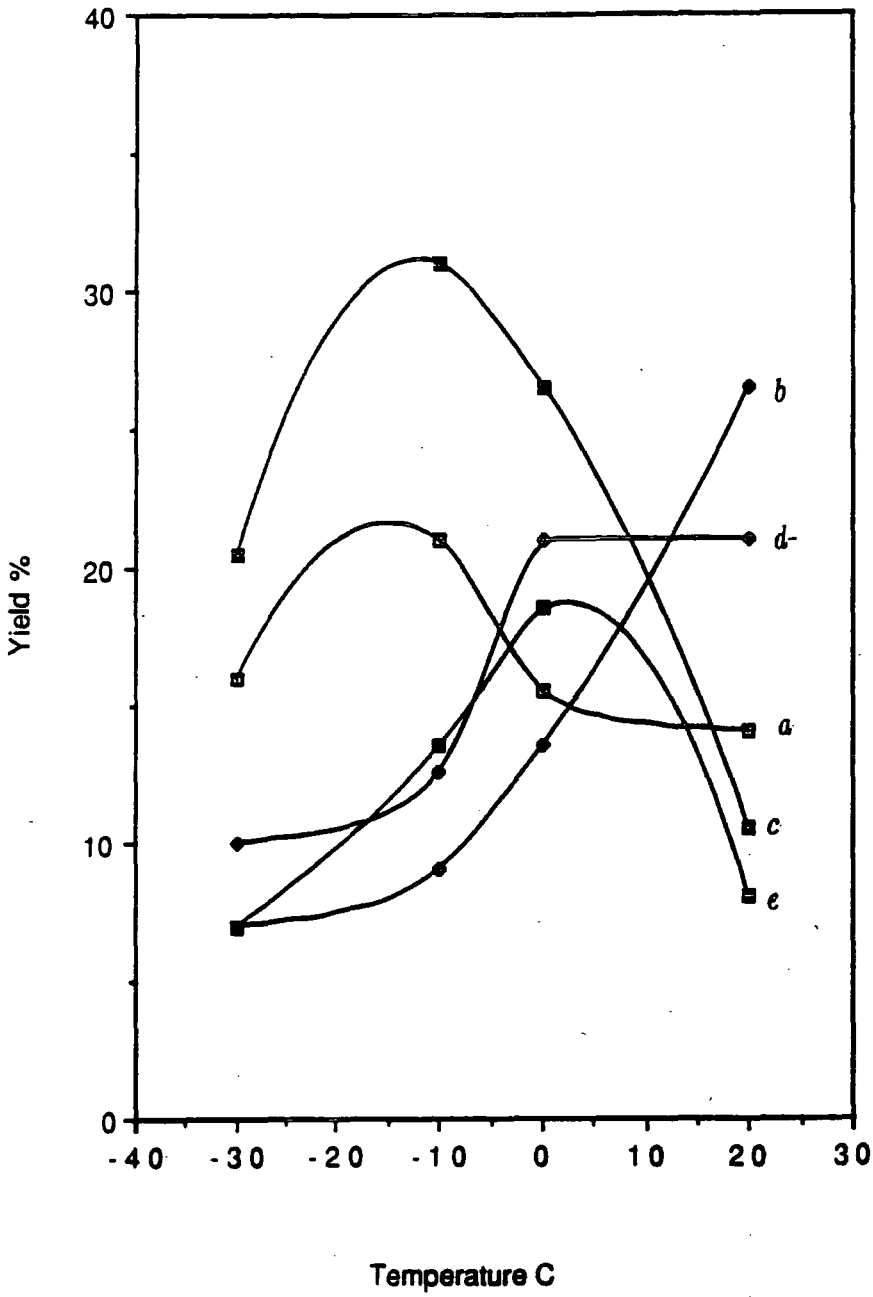
In order to elucidate the structure of the fluorinated trimethylsilylbenzenes produced by the competing F for H ring substitution reactions, the reaction mixture was hydrolysed by heating in a sealed system with acetic acid and sulphuric acid at 80°C for 2 hours. The simplified mixture of fluorobenzenes was analysed by the same method as that used prior to hydrolysis. Results are summarised in Table 18 and Figure 2.

Table 18 Direct fluorination of phenyltrimethylsilane in acetonitrile

Temperature °C	Comments	Products before hydrolysis %							Products after Hydrolysis				
													
-30	Very little decomposition, starting material present.	16.0 (32	3.5 :7	3.0 :6	0.5 :1)	4.5	3.0	—	20.5 (20.5	5.0 :5.0	4.0 :4.0	1.0 :1)	—
-10	Decomposition, starting material present.	21.0 (14	4.0 :2.6	3.5 :2.3	1.5 :1)	10.0	3.5	—	31.0 (20.6	7.0 :4.6	4.0 :2.6	1.5 :1)	—
0	Decomposition, starting material present.	15.5 (7.7	6.0 :3.0	5.5 :2.2	2.0 :1)	11.0	7.5	—	26.5 (10.6	11.0 :4.4	7.5 :3.0	2.5 :1)	—
20	Extensive decomposition, no starting material	14.0 (5.6	12.5 :5.0	11.5 :4.6	2.5 :1)	—	—	8.0	10.5 (5.2	9.5 :4.8	9.5 :4.8	2.0 :1	7.7 :4.0)

* Calculated from hydrolysis products. Ratios in parenthesis

Figure 2



a-Yield of fluorobenzene before hydrolysis.

b-Yield of difluorobenzenes before hydrolysis.

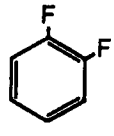
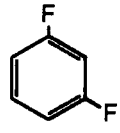
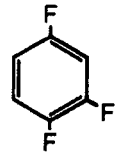
c-Yield of fluorobenzene after hydrolysis.

d-Yield of difluorobenzenes after hydrolysis.

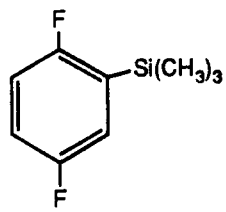
e-Yield of F for H substitution products.

At the lowest reaction temperature employed the predominant process was fluorodesilylation to give the desired fluorobenzene. As the reaction temperature was raised, F for H ring substitution to give fluorotrimethylsilylbenzenes, difluorotrimethylsilylbenzenes (and at the highest reaction temperature investigated trifluorotrimethylsilylbenzenes) increased. Hydrolysis of the difluorotrimethylsilylbenzenes, which were detected at all reaction temperatures employed except at +20°C, resulted in the formation of *para*-difluorobenzene as the predominant product. The other major product was *ortho*-difluorobenzene with the *meta*-difluorobenzenes formed in low yield (see Table 19).

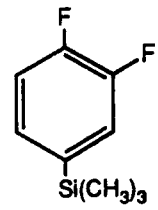
Table 19 Products obtained from the hydrolysis of difluoro- and trifluoro- trimethylsilylbenzenes produced by the direct fluorination of phenyltrimethylsilane

Reaction Temperature °C	Products %			
				
-30	1.5	1.0	0.5	—
-10	3.0	0.3	—	—
0	5.0	2.0	0.5	—
+20	—	—	—	8.0

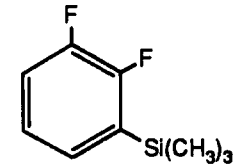
This indicates that the major F for H ring substitution products which gave rise to the difluorobenzenes were 1,4 difluoro-2-trimethylsilylbenzene (26), 1,2 difluoro-4-trimethylsilylbenzene (27), and 1,2 difluoro-3-trimethylsilylbenzene (28). The preferential formation of (26), (27), and (28) over other difluotrimethylsilylbenzenes in the F for H substitution process can be explained by considering the two substitution reactions involved in their formation.



(26)



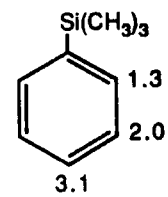
(27)



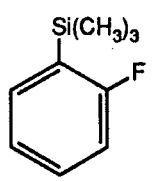
(28)

The first step is the direct fluorination of phenyltrimethylsilane and if this reaction is viewed as an electrophilic process then the products obtained will be dependent upon the directing effect exerted by the trimethylsilyl group as a substituent on the aromatic ring. As silicon is electropositive with respect to carbon[154], a trimethylsilyl group would be expected to supply electron density to an aromatic system by an inductive effect (+I), activating the *ortho* and *para* positions to electrophilic attack. In addition, the d orbitals of the silicon atom are available for conjugation with the π electrons of the aromatic ring, exerting a mesomeric (-M) effect which deactivates the *ortho* and *para* positions to electrophilic attack.

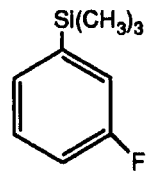
Figure 3



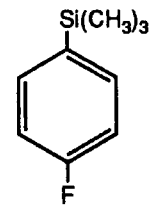
The combination of these two effects results in the trimethylsilyl group exerting a slightly activating *ortho/para* directing effect towards electrophiles[154,155]. This is demonstrated in the nitration of phenyltrimethylsilane by nitric acid in acetic anhydride at -10°C when the rate of nitration is 1.64 times faster than benzene with an isomer distribution of *ortho/meta/para* = 26.6/41.7/31.6[155]. The reactivities of the *ortho*, *meta*, and *para* positions relative to a single position in benzene are given in Figure 3. The direct fluorination of phenyltrimethylsilane will therefore yield all three isomers (23), (24) and (25).



(23)



(24)

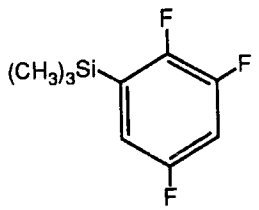


(25)

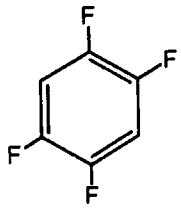
The second step is the direct fluorination of the three isomers of fluorotrimethylsilylbenzene (23), (24) and (25) to give (26), (27) and (28) as the major products. This can only be explained if the predominant directing effect towards the incoming fluorine is that exerted by the fluorine atom of (23), (24) and (25) in the *ortho* and *para* positions. This slightly deactivating effect towards electrophiles exerted by fluorine as a substituent on the aromatic ring can be explained as a combination of its inductive and mesomeric effects[156]. The high electronegativity of fluorine leads to the withdrawal of electron density by an inductive effect, exerting a deactivating *meta* directing effect towards electrophiles. Acting in the opposite direction, the fluorine atom donates electron density by interactions between its p-orbitals and the π system of the aromatic ring, activating the *ortho* and *para* positions towards electrophiles by a mesomeric effect. As the inductive effect decreases with distance but the mesomeric effect does not, the combined effect is that the *para* position is more activated than the *ortho* towards electrophiles (see Table 23).

Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane at $+20^0$C did not yield any additional difluorobenzenes but 1,2,4-trifluorobenzene. This indicated the presence of 1,2,4-trifluoro-6-trimethylsilylbenzene (29), 1,2,4-trifluoro-5-trimethylsilylbenzene (30), and 1,2,4-trifluoro-2-trimethylsilylbenzene (31), which would be produced by the fluorination of the

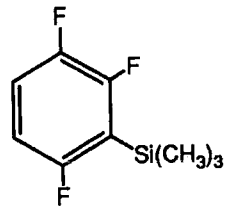
ring *ortho* or *para* to the fluorine atoms already present in the difluorotrimethylsilylbenzenes (26), (27), and (28).



(29)



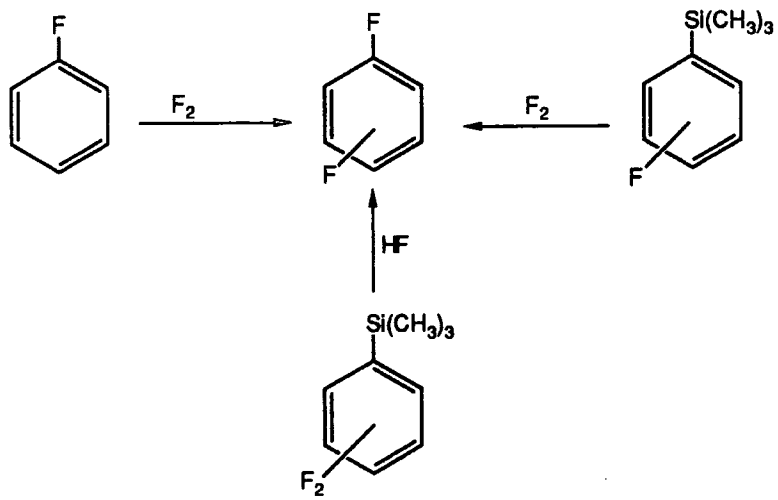
(30)



(31)

At the lowest reaction temperature employed difluorobenzenes were produced in low yield, but as the reaction temperature was increased they were produced in significant amounts. There are several possible routes by which these difluorobenzenes can be produced (Scheme 32).

Scheme 32



Direct fluorination of the desired fluorobenzene would give rise to the difluorobenzenes produced, the distribution of isomers obtained (Table 18) being consistent with electrophilic attack on fluorobenzene. The ratio of difluorobenzenes obtained from the direct fluorination of phenyltrimethylsilane at -30°C (*p*:*o*:*m* 7:6:1) is comparable to those obtained by Grakauskas[53] (5:4:1) as bi-products from the direct fluorination of benzene at -30°C (see Chapter 1), indicating that the direct fluorination of fluorobenzene is the predominant method of formation.

Fluorodesilylation of fluorotrimethylsilylbenzenes would also give rise to difluorobenzenes. This process would only occur for *ortho* and *para* fluorotrimethylsilylbenzenes (23) and (25) where the incoming fluorine would be directed towards the trimethylsilyl group by the fluorine atom already present.

Cleavage of the carbon-silicon bond of the difluorotrimethylsilyl benzenes (26), (27), and (28) by HF produced in their formation would give rise to the observed products. If this process was operating to any considerable extent then cleavage of the carbon-silicon bond in the starting material to give benzene would occur. However, no benzene was detected, making this an unlikely route to the fluorobenzenes.

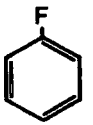
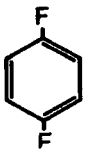
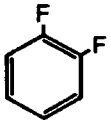
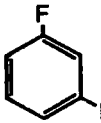
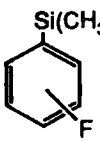
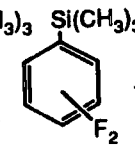
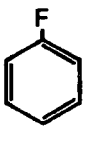
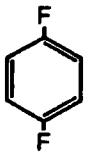
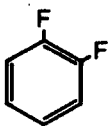
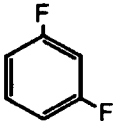
Effect of solvent on the direct fluorination of phenyltrimethylsilane

The direct fluorination of phenyltrimethylsilane at 0^0C with a 1 fold excess of 10% fluorine in nitrogen was investigated using a range of solvents. Yields of fluoroaromatics were calculated from ^{19}F n.m.r. integrals and the presence of starting material by g.c. mass spectrometry. The results are summarised in Table 20.

As with the investigation into the effect of temperature, the reaction mixture was hydrolysed to ascertain yields of fluorotrimethyl-silylbenzenes and difluotrimethylsilylbenzenes produced. The results are summarised in Table 20.

Nitromethane and water were the only solvents employed in which the direct fluorination of phenyltrimethylsilane was unsuccessful. The fluorination in nitromethane produced very low yields of fluoroaromatics

Table 20 Direct fluorination of phenyltrimethylsilane at 0°C in a variety of solvents

Solvent	Comments	Products before hydrolysis				*	*	Products after hydrolysis			
											
Acetonitrile		15.5	6.0	5.5	2.0	11.0	7.5	26.5	11.0	7.5	2.5
		(7.7	:3.0	:2.2	:1)			(10.6	: 4.4	:3.0	:1)
$CFCl_3$		7.0	2.5	2.0	1.0	16.0	8.0	23.0	7.0	4.5	1.5
		(7.0	:2.5	:2.0	:1)			(15.3	:4.6	:3	:1)
Chloroform		10.0	4.0	2.5	1.0	8.0	4.5	18.0	6.5	3.5	2.0
		(10.0	:4.0	:2.5	:1)			(9.0	:3.2	:1.7	:1)
Nitromethane	Extensive decomposition	2.0	0.5	0.5	0.1	—	—	—	—	—	—
		(20	:5.0	:5.0	:1)						
CF_2ClCF_2Cl		14.0	3.0	2.0	1.0	9.0	6.5	23.0	7.5	4.5	2.5
		(14.0	:3.0	:2.0	:1)			(9.2	:3	:1.8	:1)
Water	Extensive decomposition	Less than 5% aromatics detected.									

*Yields calculated from hydrolysis products

Ratios in parenthesis

and resulted in extensive decomposition. The reason for failure of this reaction is believed to be the reactivity of nitromethane towards fluorine at 0^0C, as it has been successfully employed as a solvent for the fluorination of organic compounds at low temperature[157]. The reaction in water resulted in extensive decomposition and a low yield of fluoroaromatic compounds. The decomposition results from oxidation and polymerisation of the starting material and products.

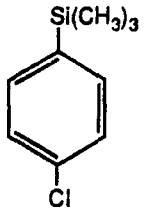
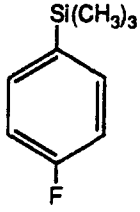
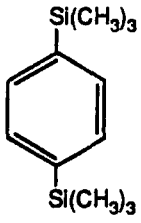
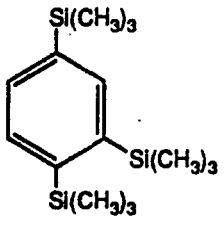
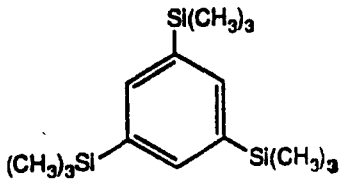
All other solvents used gave similar ratios of products before and after hydrolysis to those obtained in acetonitrile. The highest yields of fluoroaromatic compounds were obtained when acetonitrile was the solvent.

Direct fluorination of substituted phenyltrimethylsilanes

A series of substituted phenyltrimethylsilanes were synthesised from the corresponding aryl chlorides or bromides *via* Grignard reagents or litho derivatives. The compounds prepared were all identified by comparison of observed spectral data with literature values.

The direct fluorination of these arylsilanes was investigated in order to ascertain the effect of the substituents on fluorodesilylation and its competing ring fluorination reactions. All fluorinations were carried out with 1.5 equivalents of 10% fluorine in nitrogen in acetonitrile, where solubility allows. Results are summarised in Table 21.

Table 21

Substrate	Reaction conditions	Products
	-30°C, CH_3CN	4-Fluorochlorobenzene 16%, 3,4-difluoro-chlorobenzene 5%, fluoro-4-chlorophenyltrimethylsilane 4%, starting material.
	-30°C, CH_3CN	*p*-Difluorobenzene 21%, *o*-difluoro-benzene 5%, 3,4-difluorophenyl-trimethylsilane 4%, starting material.
	0°C, $CFCl_3$	*p*-Difluorobenzene 7.0%,4-fluorophenyl-silane 8%, 2-fluoro-1,4-bis(trimethyl silyl)benzene 4%, starting material.
	10°C, CH_3CN	Complex mixture of products containing bis(trimethylsilyl)benzene, fluoro-bis(trimethylsilyl)benzene difluoro-(trimethylsilyl)benzene, trifluoro-bis(trimethylsilyl)benzene.
	-30°C CH_3CN	Complex mixture of products.

The predominant process in both the direct fluorination of *p*-chloro-phenyltrimethylsilane and *p*-fluorophenyltrimethylsilane was the desired fluorodesilylation. In both cases the selectivity of the fluorodesilylation (ratio F for Si: F for H) was higher than that obtained for the direct fluorination of phenyltrimethylsilane under similar conditions (see Table 22)

Table 22

Substrate	Fluorodesilylation products (F for Si) %	Ring fluorination Products (F for H) %	Ratio of products
p-Fluorophenyltrimethylsilane	26.0	4.5	5.8:1
p-Chlorophenyltrimethylsilane	16.0	5.0	3.2:1
Phenyltrimethylsilane	28.7*	28.7	1.4:1

*Includes difluorobenzenes produced before hydrolysis

Fluorodesilylation was higher for the *p*-fluorophenyltrimethylsilane than for the *p*-chlorophenyltrimethylsilane, which can be explained by consideration of the directing effects exerted by the fluorine and chlorine substituents on the benzene ring. They both exert a strong *ortho/para* directing effect towards electrophiles, with the *para* position being the more favoured in both cases. This difference (between the *ortho* and *para* directing effect) is more pronounced for fluorine (see table 23) and thus a higher proportion of electrophiles will be directed *para* to the halogen in the fluoro compound, which in turn gives rise to a higher proportion of the desired fluorodesilylation product.

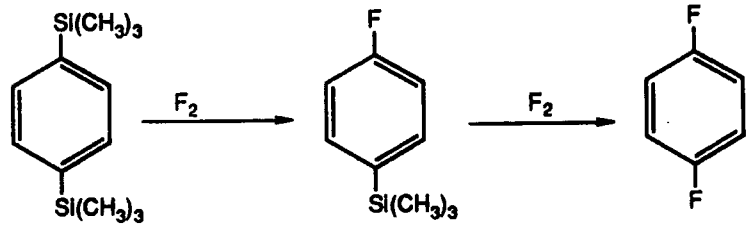
Table 23 Directive effects in substitution reactions on halobenzenes[158]

Reaction	Products %					
	Fluorobenzene			Chlorobenzene		
	ortho	*meta*	*para*	*ortho*	*meta*	*para*
Chlorination	10.9	—	89.1	32.4	—	67.6
Nitration	8.5	—	91.5	22.1	0.7	76.6
Benzylation	14.7	0.2	85.1	33.0	0.6	66.4

Far greater yields of the desired fluoroaromatic compound were obtained in the direct fluorination of *p*-fluorophenyltrimethylsilane than for the corresponding chloro compound, supporting the proposed electrophilic mechanism (Scheme 31), as fluorine would stabilise the proposed carbocation to a greater extent than chlorine.

Direct fluorination of bis(trimethylsilyl)benzene (32) gave 4-fluorophenyltrimethylsilane (33) and *p*-difluorobenzene as the major products. The *p*-difluorobenzene was produced by elemental fluorine reacting with the initial product (33) (Scheme 31).

Scheme 31

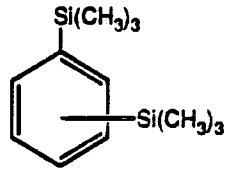


(32) (33)

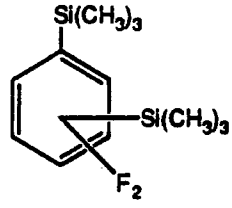
p-Difluorobenzene was produced in surprisingly high yield. This may be explained by the poor solubility of the starting material (32) in the solvent system employed, which would give rise to similar concentrations of the initial product (33) and starting material, resulting in competing reactions. The slightly activating *ortho* directing effect of

the trimethylsilyl group resulted in the F for H ring substitution products.

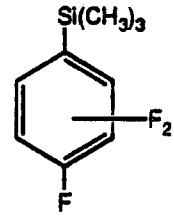
The direct fluorination of tris(trimethylsilyl)benzenes resulted in the formation of complex mixtures of products *via* a variety of competing processes. Analysis by mass spectrometry of the reaction products from the fluorination of 1,3,5-tris(trimethylsilyl)benzene indicated the presence of 1,3-bis(trimethylsilyl)benzene (34), difluoro(trimethylsilyl)benzenes (35), difluoro-bis(trimethylsilyl)benzenes (36) and many other products (see table 21).



(34)



(35)



(36)

The production of (34), (35) and (36) indicates that not only the desired fluorodesilylation (F for Si), but ring fluorination (F for H) and cleavage of the carbon-silicon bond in the arylsilanes by HF produced in the reaction, are also taking place. A complex mixture of products was also obtained in the fluorination of 1,2,3,4-tetrakis (trimethylsilyl)benzene.

Direct fluorination of trimethylsilyl thiophenes

2,5-Bis(trimethylsilyl)thiophene was synthesised from the corresponding arylchloride in high yield *via* its Grignard reagent. Direct fluorination, even at -30°C, resulted in extensive decomposition to give polymeric products, with no fluoroaromatic compounds being detected by ^{19}F n.m.r. or mass spectrometry.

3,4-Dichloro-2,5-bis(trimethylsilyl)thiophene, which was synthesised from the corresponding arylchloride *via* its lithio derivative, also gave extensive decomposition upon fluorination. The failure of this reaction indicates that ring fluorination at positions 3 and 4 does not play a role in the decomposition observed for the 2,5,-bis(trimethylsilyl)thiophene. The decomposition observed for both thiophenes upon fluorination may be due to instability of the desired compounds or oxidation of the ring sulphur by fluorine.

Conclusions

i Direct fluorination of arylsilanes proceeds *via* an electrophilic process.

ii As the reaction temperature is raised fluorodesilylation becomes less selective and F for H ring substitution increases.

iii Solvent has little effect upon the product distribution and acetonitrile is the best solvent for fluorination of aryltrimethylsilane.

iv Fluorodesilylation is not a selective route to fluoroaromatics.

CHAPTER THREE

INVESTIGATION INTO SELECTIVE FLUORINE FOR HYDROGEN SUBSTITUTION IN AROMATIC SYSTEMS AS A POTENTIAL ROUTE TO FLUORINATED AROMATIC COMPOUNDS

CHAPTER 3

INVESTIGATION INTO SELECTIVE FLUORINE FOR HYDROGEN SUBSTITUTION IN AROMATIC SYSTEMS AS A POTENTIAL ROUTE TO FLUORINATED AROMATIC COMPOUNDS

Introduction

The direct fluorination of aromatic systems by elemental fluorine has been reviewed in Chapter One. In this study into direct fluorination of aromatic compounds, the following separate approaches have been investigated:

I) The use of pyridines as a solvent to modify the reactivity of elemental fluorine towards aromatic systems;

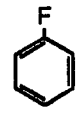
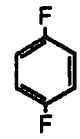
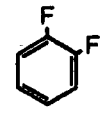
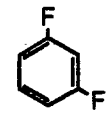
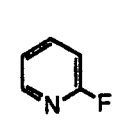
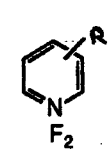
II) The use of specific substituents on an aromatic system to modify the reactivity of the aromatic system towards elemental fluorine.

Investigation into the effect of pyridines on the direct fluorination of aromatic systems.

It has been reported that the use of pyridine as a solvent for the direct fluorination of aromatic systems results in modification of the reactivity of elemental fluorine[37] due to the formation of a pyridine/fluorine complex[38] (see Chapter One). This reported effect of pyridine, coupled with a report that nitrogen-containing heterocycles have been used as templates to direct selective chlorination of steroids[159], prompted our investigation into the use of pyridine as a solvent for direct fluorination of aromatic systems.

The direct fluorination of benzene in the presence of a series of substituted pyridines under identical conditions was investigated. Fluorinations were carried out in acetonitrile at -30°C with the pyridine and the benzene present at identical concentrations and using 10% elemental fluorine in nitrogen. Analysis of the reaction mixtures was carried out by ^{19}F n.m.r., with products being identified by comparison with authentic samples and yields being calculated by comparison of ^{19}F n.m.r. integrals of the products with the integral of an added benzotrifluoride marker (results Table 24).

Table 24

Substrate	Products %[#]					
						
Benzene	11.0	7.5	5.5	4.0	—	—
Benzene/4-Ethylpyridine	13.5	1.0	0.5	—	5.0	10
Benzene/4-Methylpyridine	15.0	1.5	1.0	0.5	5.0	6.0
Benzene/pyridine	20.0	1.0	0.5	—	3.0	7.0
Benzene/2,6-Dimethylpyridine*	2	0.5				

[#]Actual yield based on aromatic.

*Unidentified product present δ_F -131.

The presence of pyridine and 4-alkylpyridines during the direct fluorination of benzene had a pronounced effect on the product distribution obtained. It resulted in a far higher ratio of fluorobenzene to difluorobenzenes, i.e. selectivity, and in the formation of 2-fluoropyridines. It has been reported that the direct fluorination of pyridine forms exclusively 2-fluoropyridine from the decomposition of the initial pyridine/fluorine complex (see Chapter One)[46,47].

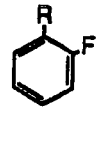
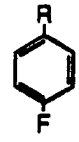
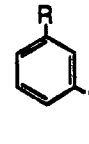
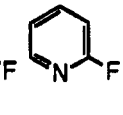
This increase in selectivity when pyridines are present can only be explained if the pyridine is involved in the fluorination step, which suggests that the major fluorinating species is a fluorine/pyridine complex. The presence of a such a complex in the reaction mixture was indicated by a singlet δ_F +40 in the ^{19}F n.m.r., and by the fact that the addition of potassium iodide resulted in the formation of iodine and the disappearance of this singlet. These complexes are structurally similar to the electrophilic fluorinating agents N-fluoropyridium salts[117-125] (see Chapter One). This coupled with the increase in selectivity indicates that they may operate as electrophilic fluorinating agents.

2,6-Dimethylpyridine was used, in an attempt to prevent the decomposition of the desired pyridine/fluorine complex to 2-fluoropyridines, but instead of encouraging the formation of the desired fluorobenzene, it resulted in extensive decomposition and formation of an unidentified fluoroaromatic, most likely a fluorinated pyridine.

The direct fluorination of anisole and toluene in the presence of pyridine under identical conditions employed for the fluorination of

benzene has also been investigated (see Table 25).

Table 25

Substrate	Comments	Products			
					
Toluene	Difluorotoluenes formed	20.0	13.0	5.5	—
Toluene/pyridine	No difluorotoluenes present but products δ_F -65 to -81	9.5	5.0	1.5	21
Anisole	Side chain fluorination, 2,4-difluoroanisole,2% extensive decomposition	13.0	9.5	—	
Anisole/ pyridine	Side chain fluorination, 2,4-difluoroanisole,1% extensive decomposition	12.5	7.0	—	10.5

The addition of pyridine has reduced the yields of fluoroaromatics and has resulted in little change in the product distribution. The production of 2-fluoropyridine as a major bi-product in all cases limits the use of pyridine as solvent for the fluorination of aromatic systems unless the intramolecular decomposition of the pyridine/fluorine complex can be prevented.

Direct fluorination of benzenesulphonyl chlorides

The direct fluorination of benzenesulphonyl chlorides was investigated for the following reasons:

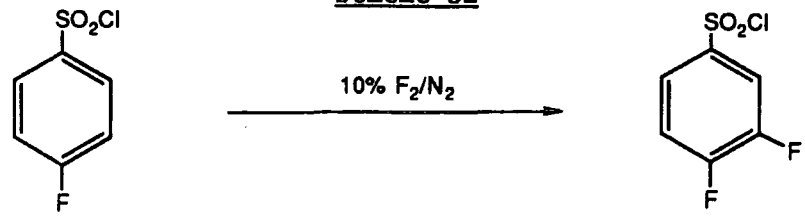
I) The sulphonyl chloride substituent exerts an *ortho/para* deactivating effect towards electrophiles, thus deactivating the aromatic ring towards elemental fluorine and making the fluorination more controllable;

II) Hydrolysis of the sulphonyl chloride substituent to sulphonic acid followed by steam distillation, would enable the removal of the sulphonyl chloride group if not required in the final fluoroaromatic.

A series of benzenesulphonyl chlorides have been fluorinated at -30°C in acetonitrile with 10% elemental fluorine in nitrogen. Analysis of the reaction mixture was carried out by mass spectrometry and ^{19}F n.m.r., with products being identified by comparison with literature values. Yields were calculated by comparison of ^{19}F n.m.r. integrals of products with the integral of an added benzotrifluoride marker, or starting material in the case of 4-fluorobenzylsulphonyl chloride (Results in Table 25). **Table 25**

Substrate	**Conditions**	**Products %**
4-Fluorobenzene-sulphonyl chloride	1 equivalent of F_2 at -30°C	3,4-difluorobenzenesulphonyl chloride 50%, starting material 50%
4-Fluorobenzene-sulphonyl chloride	2 equivalent of F_2 at -30°C	3,4-difluorobenzenesulphonyl chloride 90%, starting material 5%
Benzenesulphonyl chloride	1 equivalent of F_2, -30°C	3-fluorobenzenesulphonyl chloride 18%, 2-fluorobenzene-sulphonylchloride 1%.
Chlorobenzene-sulphonylchloride	1 equivalent of F_2 at -30°C	3-fluoro-4-chlorobenzenesulphonyl chloride 14.5% and unidentified product 7.4%.

Scheme 32



(34) (38) 90%

The direct fluorination of 4-fluorobenzenesulphonyl chloride gave exclusively the expected 3,4-difluorobenzenesulphonyl chloride (38), (Scheme 32). This can be explained by consideration of the combined directing effect of the sulphonyl chloride[50] (deactivating and *meta* directing towards electrophiles) and fluorine[158] (deactivating and *ortho/para* directing towards electrophiles) substituents, which would direct incoming fluorine *meta* to the sulphonyl chloride group. The success of this reaction not only offers a route to 3,4-difluorobenzenesulphonyl chloride but also a possible route to *ortho*-difluorobenzene by hydrolysis of the sulphonyl chloride to the acid, followed by steam distillation to the difluorobenzene.

Direct fluorination of benzenesulphonyl chloride gave 3-fluorobenzenesulphonyl chloride as the major product together with a small amount of the 2-fluoro isomer. Attempts to fluorinate 4-chlorobenzenesulphonyl chloride resulted in the formation of the desired 4-chloro-3-fluorobenzenesulphonyl chloride and an unidentified product, which may be the 4-chloro-2-fluorobenzenesulphonyl chloride. In both of these reactions, but not for the direct fluorination of 4-fluorobenzenesulphonyl chloride, there was a signal at δ_F -230 which is as yet unidentified.

The success of this preliminary study indicates that the direct fluorination of benzenesulphonyl chloride merits further investigation. Direct fluorination of the related benzenesulphonic acids would also be of interest.

CHAPTER FOUR

SYNTHESIS OF POTENTIAL ELECTROPHILIC FLUORINATING AGENTS OF THE N-F CLASS

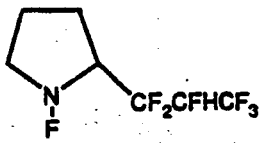
CHAPTER FOUR

SYNTHESIS OF POTENTIAL ELECTROPHILIC FLUORINATING AGENTS OF THE N-F CLASS

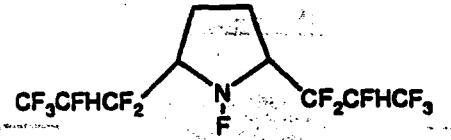
Introduction

There is considerable interest in compounds which contain a nitrogen-fluorine bond as they have been shown to be sources of electrophilic fluorine[109-133], and in certain cases they are able to selectively fluorinate aromatic systems in good yield[116,117,128-130] (see Chapter 1 for a review of their chemistry).

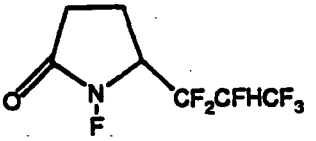
Although there are many different structural types of N-fluoro reagents, they all contain at least one electron withdrawing substituent adjacent to the nitrogen atom of the N-F bond[109-119], or are salts[120-133]. The presence of these electron withdrawing groups reduces the possibility of elimination of hydrogen fluoride, which can be a major decomposition route for these reagents[160], by strengthening the nitrogen-fluorine bond and reducing the accessibility of hydrogen atoms. This structural requirement of an N-fluoro compound, coupled with the research groups expertise in free radical addition of fluoroalkenes to amines and amides[161-164], prompted investigation into the synthesis of N-fluoro(2H hexafluoropropyl)pyrrolidines (39) and (40), pyrrolid-2-one (40) and N-fluorosuccinimide (41) as possible fluorinating agents for aromatic systems.



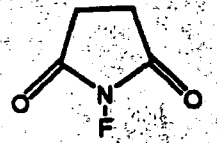
(39)



(40)



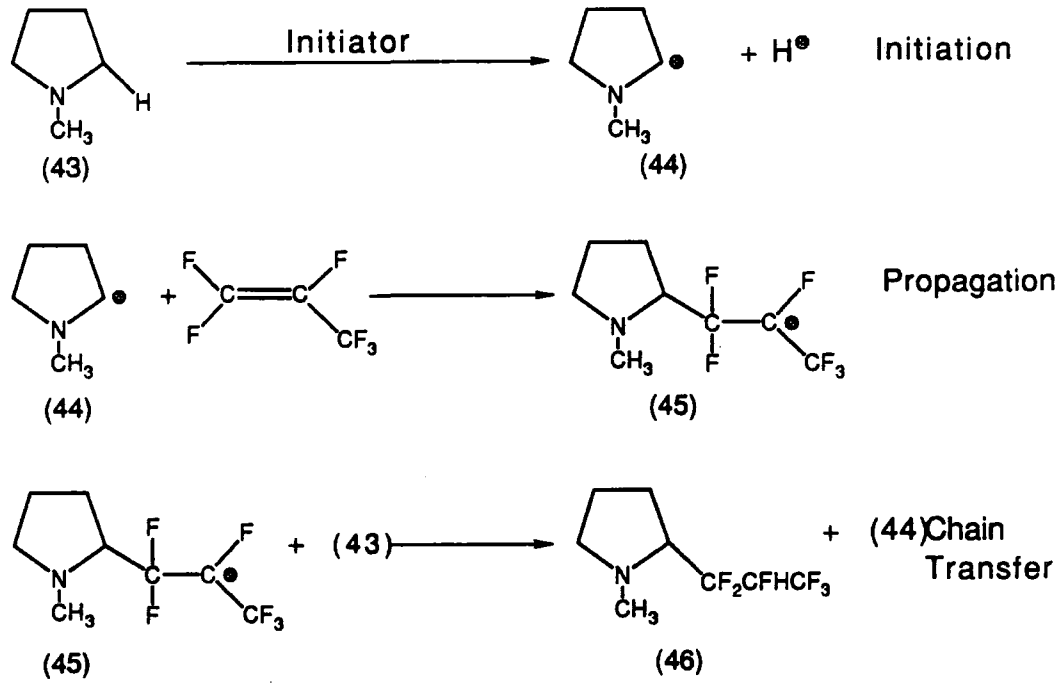
(41)



Free radical additions of fluoroalkenes to cyclic amines and amides

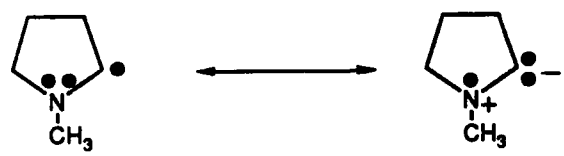
Free radical addition occurs via three important steps[165], though in some cases competing reactions such as telomerisation may also occur simultaneously. These important steps are illustrated in the free radical addition of hexafluoropropene to the tertiary cyclic amine N-methylpiperidine (43)[163] (Scheme 33).

Scheme 33

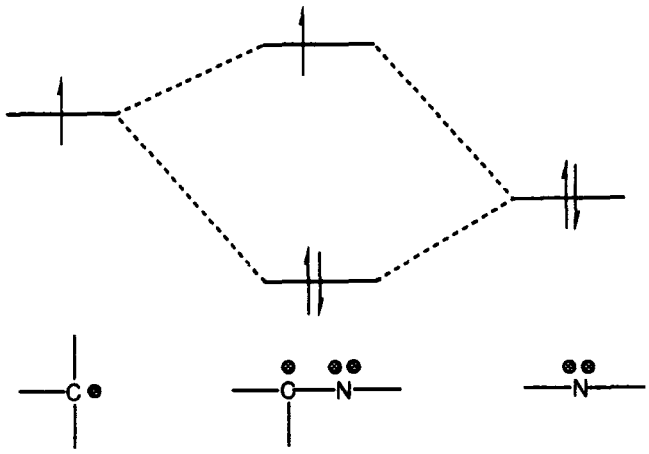


The initiation step involves abstraction of a hydrogen atom from the amine to give the stabilised α amino radical (44). This radical (44) is stabilised by interaction with the coplanar nitrogen lone pair and can be explained by simple valence bond theory (Scheme 34) or frontier orbital theory[165](Scheme 35).

Scheme 34



Scheme 35

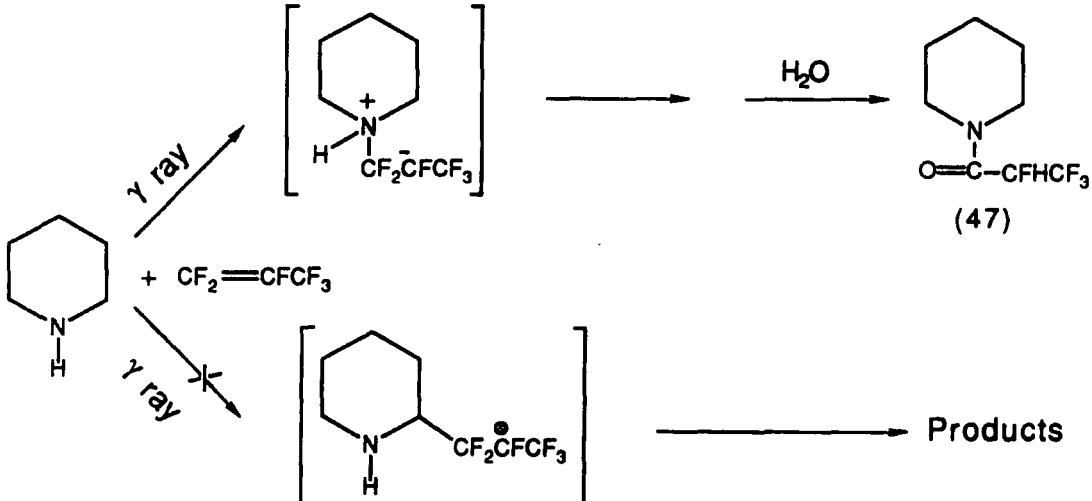


Propagation involves the addition of the radical (44) to a hexafluoropropene molecule, forming a new single bond and generating a new adduct radical (45).

Chain transfer involves abstraction of a hydrogen atom from the amine substrate (43) by the adduct radical (45), leading to a mono adduct of the amine and the perfluoroalkene (46). This step also regenerates the initial stabilised α-amino radical (44).

The high basicity of secondary amines[167] results in nucleophilic addition to fluoroalkenes[168,169], rather than the desired free radical process. This is illustrated by the γ-ray initiated reaction of piperidine and hexafluoropropene, which yields only products of nucleophilic attack (47)[163] (Scheme 36)

Scheme 36



Many tertiary amines undergo smooth free radical additions to fluoroalkenes[163] due to the increased steric crowding around the nitrogen atom, compared with secondary amines, which hinders nucleophilic processes thus allowing the free radical process to compete. Protection of secondary amines such as pyrrolidine by a trimethylsilyl group produces a compound more structurally akin to tertiary amines, enabling free radical process to predominate[164].

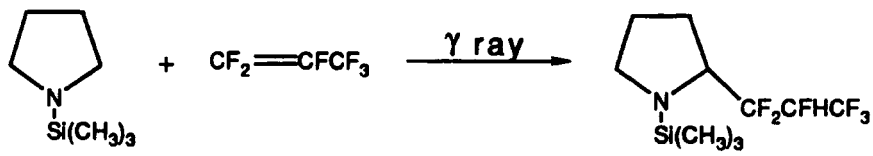
Amides are far less basic than amines[167], thus the possibility of competing nucleophilic reactions is reduced and free radical reaction proceed smoothly[162,163,170,171]

Synthetic approaches to N-fluoro compounds

N-fluoro-perfluoroalkyl pyrrolidines

The γ-ray initiated free radical addition of N-trimethylsilyl pyrrolidine to a deficiency of hexafluoropropene resulted in 2(2H hexa -fluoropropyl)-N-trimethylsilylpyrrolidine (48) being formed in good yield[164] (Scheme 37)

Scheme 37

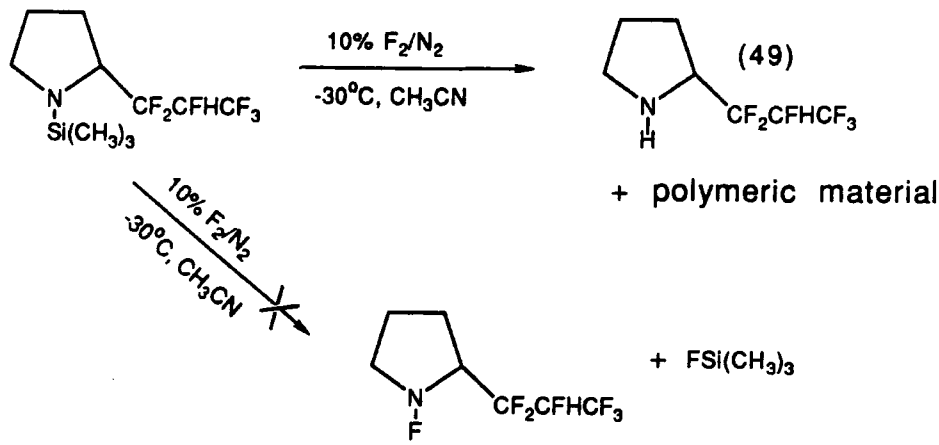


(48) 62%

The direct fluorination of the mono adduct (48) in acetonitrile or $CFCl_3$ at $-30^{o}C$ with a 10% mixture of fluorine and nitrogen did not yield the desired N-fluoro-2(2H hexafluoropropyl)pyrrolidine (37) but the corresponding free amine (49) and unidentified polymeric material

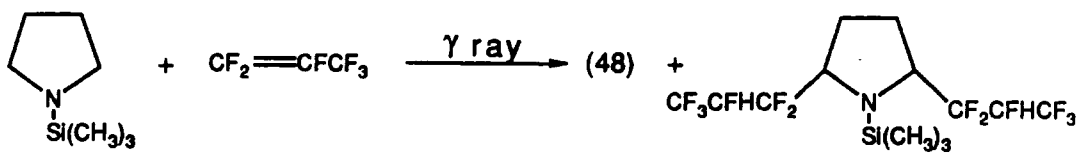
(Scheme 38). The free amine (49) was produced by the cleavage of the nitrogen-silicon bond by hydrogen fluoride. As extensive measures were taken to remove hydrogen fluoride from the fluorine it must have been produced by the attack of fluorine on the mono adduct (48). Addition of calcium carbonate to the fluorination resulted in a slight decrease in the amount of free amine produced, but did not promote the formation of the desired N-fluoro compound (39).

Scheme 38



Free radical addition of N-trimethylsilylpyrrolidine to an excess of hexafluoropropene gave a mixture of mono- (48) and di adducts (50) (scheme 39).

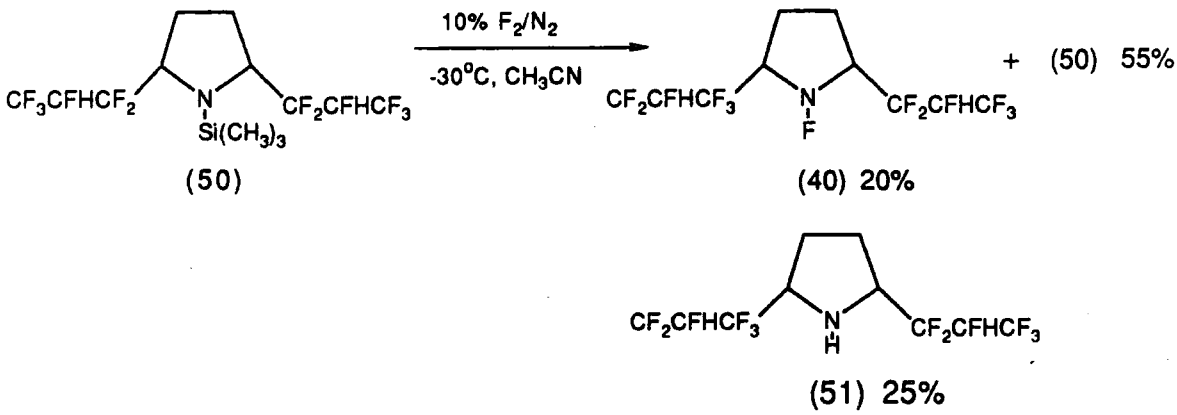
Scheme 39



Fluorination of the di adduct (50) in acetonitrile at -30°C with a 10% mixture of fluorine and nitrogen resulted in the formation of the desired N-fluoro 2,5-bis(2H hexafluoropropyl)pyrrolidine (40) and the free amine (51) (Scheme 40). The presence of the desired N-fluoro compound (40) was indicated by mass spectrometry [Chemical ionisation, *m/z* 390.1 (*M*+1, 0.37%), 370.9 (*M*-F, 1.85%)] and the presence of a

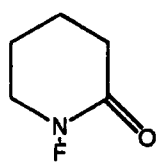
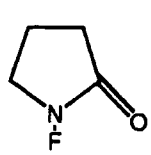
singlet at -33.77ppm in the ^{19}F n.m.r., which is consistent with published data for N-Fluoro compounds (see Table 27). Addition of potassium iodide resulted in the formation of iodine and the disappearance of the ^{19}F n.m.r. resonance for the N-F bond, the combination of these two results is indicative of an N-fluoro compound.

Scheme 40



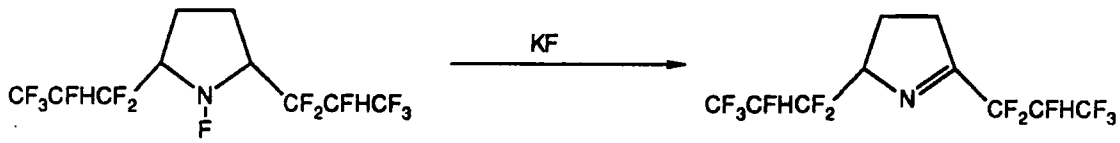
The free amine was produced, as with the mono adduct by cleavage of the nitrogen-silicon bond by hydrogen fluoride formed in the reaction of the fluorine with the solvent and/or the substrate.

Table 27

Compound	δ_F N-F	Reference
$(CF_3SO_2)_2NF$	-33.7	109
$CF_3SO_2N(F)SO_2C_6F_{13}$	-32.4	109
$C_4F_6SO_2N(F)SO_2C_6F_{13}$	-31.1	109
	-13.9	109
$CF_3SO_2N(F)CH_3$	-40.5	109
$CF_3C_6H_4SO_2N(F)CH_3$	-37.62	111
$CH_3N(F)CHO$	-67.1	173
	-69.98	174
	-50.66	174

Addition of anhydrous potassium fluoride to a mixture of the N-fluoro compound (40) and the free amine (51) resulted in an immediate reaction, which was followed by g.c.. The results from this gas chromatography study indicated that only the N-fluoro compound (40) reacted, and that only one product was formed, which was not the free amine. Investigation by mass spectrometry indicated that the reaction was the elimination of hydrogen fluoride (Scheme 41), to give compound (52) [Electron impact, m/z 368.88 (M^+, 2.81%), 299.9 (M-CF_3, 19.33%), 267 (M-$CFHCF_3$, 2.69%), 217.93 (M-CF_2CFHCF_3, 100%), 67.01 (M -2x CF_2CFHCF_3, 6.72%)]. Further characterisation of compound (52) was not attempted due to insufficient material.

Scheme 41

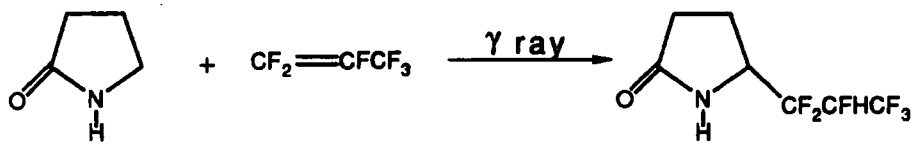


(40) (52)

Attempts to fluorinate activated aromatic systems such as anisole with this N-fluoro compound (40) on a n.m.r. scale failed.

N-fluoro amides

Scheme 42

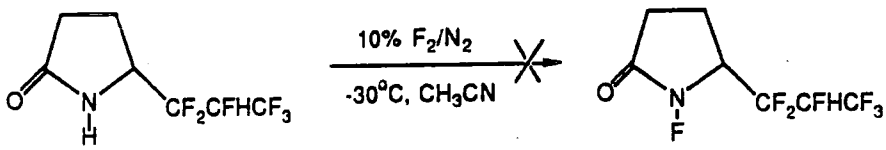


(53) 78%

The synthesis of 2(2H hexafluoropropyl)pyrrolid-2-one (53)[163] by the γ-ray initiated free radical addition of pyrrolid-2-one to an excess of hexafluoropropene went in good yield (Scheme 42). The direct fluorination under identical conditions to those used for the successful

synthesis of N-fluoro compound (41) resulted in the formation of unidentified decomposition products (Scheme 43).

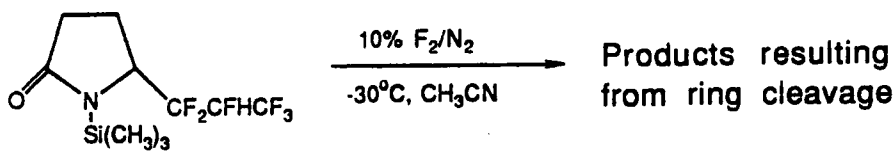
Scheme 43



(41)

The trimethylsilyl derivative of the adduct (53) was synthesised in good yield by the free radical addition of hexafluoropropene to N-trimethylsilylpyrrolid-2-one. The presence of the trimethylsilyl moiety did not facilitate the formation of the desired N-fluoro compound (41) upon fluorination at -30°C in acetonitrile, but resulted in ring cleavage to give a mixture of acyl fluorides (Scheme 44).

Scheme 44



N-trimethylsilyl succinimide (54)[172] was synthesised in good yield by the silylation of N-bromo succinimide by bis(trimethylsilyl)-acetamide . Fluorination at -30°C in acetonitrile with 10% fluorine resulted in the formation of the desired N-fluoro compound (42), indicated by the presence of a singlet at -59ppm in the ^{19}F n.m.r., which is consistent with published data for N-fluoro lactams (see Table 27). Addition of potassium iodide to the reaction mixture resulted in the formation of iodine and the disappearance of the ^{19}F n.m.r. resonance assigned to the N-F bond. Attempts to fluorinate aromatic systems with N-fluoro succinimide failed.

CHAPTER FIVE

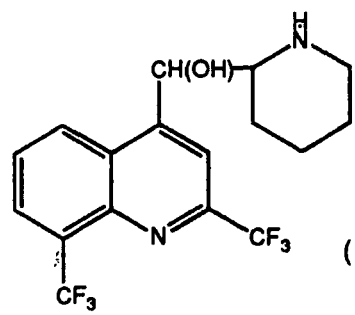
SYNTHESIS OF BIS(TRIFLUOROMETHYL) AND TRIFLUOROMETHYL AROMATIC COMPOUNDS BY CYCLOADDITION REACTIONS OF FLUORINATED ALKYNES AND ALKENES

CHAPTER FIVE

SYNTHESIS OF BIS(TRIFLUOROMETHYL) AND TRIFLUOROMETHYL AROMATIC COMPOUNDS BY CYCLOADDITION REACTIONS OF FLUORINATED ALKYNES AND ALKENES

Introduction

Due to the nature of fluorine, the trifluoromethyl group is amongst the most lipophilic of all substituents and its introduction into a biologically active compounds often brings about unique enhancement of physiological activities[1-4]. There are numerous examples of commercially important biologically active compounds which contain this group[1,3], one such is Mefloquine[175](54), which is used throughout South East Asia to treat chloroquine resistant strains of malaria. For these reasons new methodology for the introduction of the trifluoromethyl group is of interest.



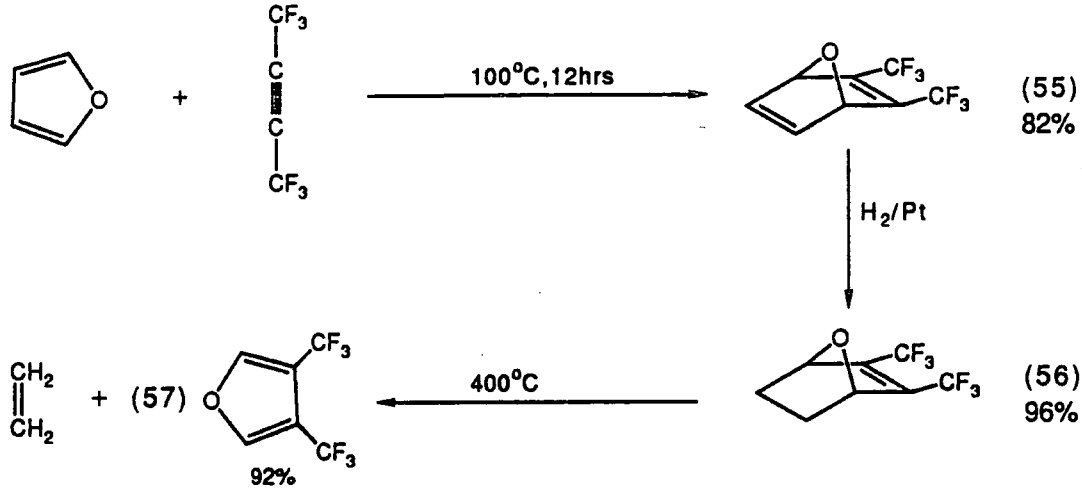
(54)

Introduction of the trifluoromethyl group into an aromatic system can be carried out by several methods, including trifluoromethylation [176], fluorination of carbonyl substituents by sulphur tetrafluoride[177] and, most importantly, halogen exchange[178]. Many of these methods have disadvantages, such as the requirement of a carbonyl group in the aromatic system, low yields, low selectivity or the use of highly toxic organometallic reagents. An alternative approach is to use an

appropriate building block with the trifluoromethyl group or groups already present, to synthesise the aromatic system[179-184].

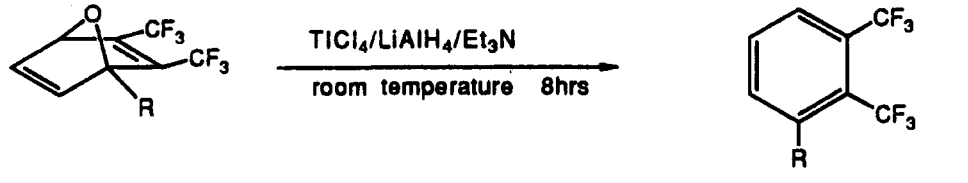
Benzenoid and heteroaromatic compounds containing two trifluoromethyl groups have been synthesised in high yield from the cycloaddition products of hexafluorobut-2-yne with furan and 2-methylfuran. 3,4-Bis(trifluoromethyl)furan (57) was synthesised from the Diels-Alder adduct (55) by selective reduction to the endoxide (56), followed by pyrolysis (Scheme 45)[184].

Scheme 45



The corresponding benzenoid systems were synthesised by the selective removal of the bridging oxygen from the endoxides, (55) and (58), by a low valent titanium complex (Scheme 46)[185].

Scheme 46



(55) R=H
(58) R=CH_3

(59) R=H 60%
(60) R=CH_3 73%

The success of this Diels-Alder chemistry of furan and 2-methylfuran as a route to aromatic systems, coupled with the possibility of

selective ring opening of the endoxides of type (55) to give phenols[186], prompted our investigation into the chemistry of substituted furans with fluorinated alkynes and alkenes, to see how tolerant these reactions are of substituents.

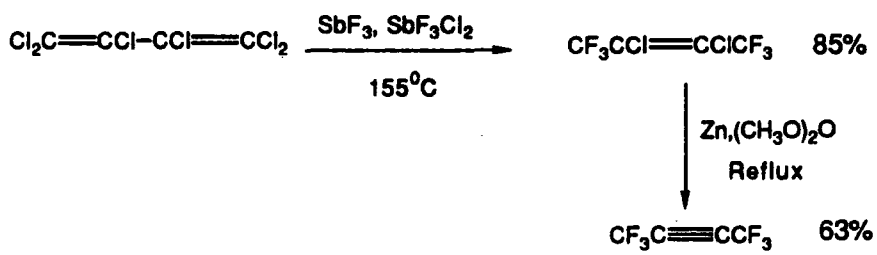
Although the cycloaddition reactions of oxazoles with alkenes to give substituted pyridines are well documented[187,188], there are no examples of their reaction with fluorinated alkenes. This was investigated as a possible route to trifluoromethylpyridines.

Diels-Alder Chemistry of Furan and Substituted Furans as a Route to Fluorinated Aromatics

Hexafluorobut-2-yne

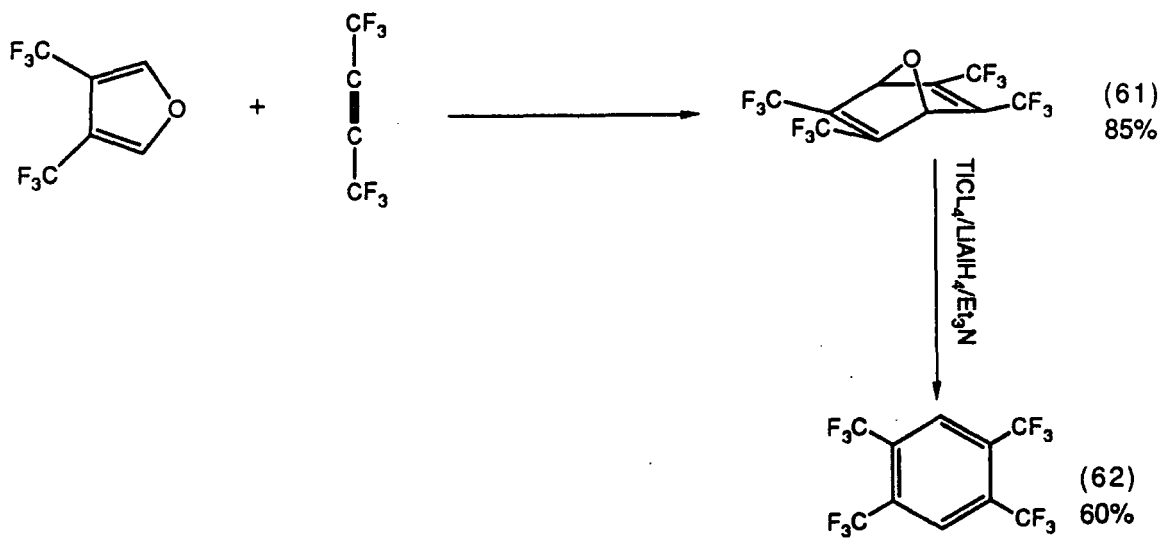
Hexafluorobut-2-yne was the major fluoroalkyne used in this investigation into the scope and limitations of Diels-Alder chemistry of furans as a route to fluoroaromatics. This alkyne was chosen because of its reactivity towards furan[184], its symmetry (which will give rise to simple mixtures of products) and ability to introduce two trifluoromethyl groups. It is commercially available and is easily prepared in a two step process from hexachloro-1,3-butadiene (Scheme 47)[189].

Scheme 47



The initial Diels-Alder reaction attempted was the addition of hexafluorobut-2-yne to furan to give the endoxide (55), followed by its conversion in good yield to 3,4-bis(trifluoromethyl)furan (57) by the literature procedure (Scheme 45)[184]. The furan (57) was then added to hexafluorobut-2-yne to give 2,3,5,6-tetrakis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (61)[184] and the bridging oxygen was removed by a low valent titanium reagent to give 1,2,4,5-tetrakis(trifluoromethyl)benzene in good yield (Scheme 48). Compound (62) has also been prepared by the reaction of pyromellitic acid with sulphur tetrafluoride, but isolation from the partially fluorinated materials is difficult[190].

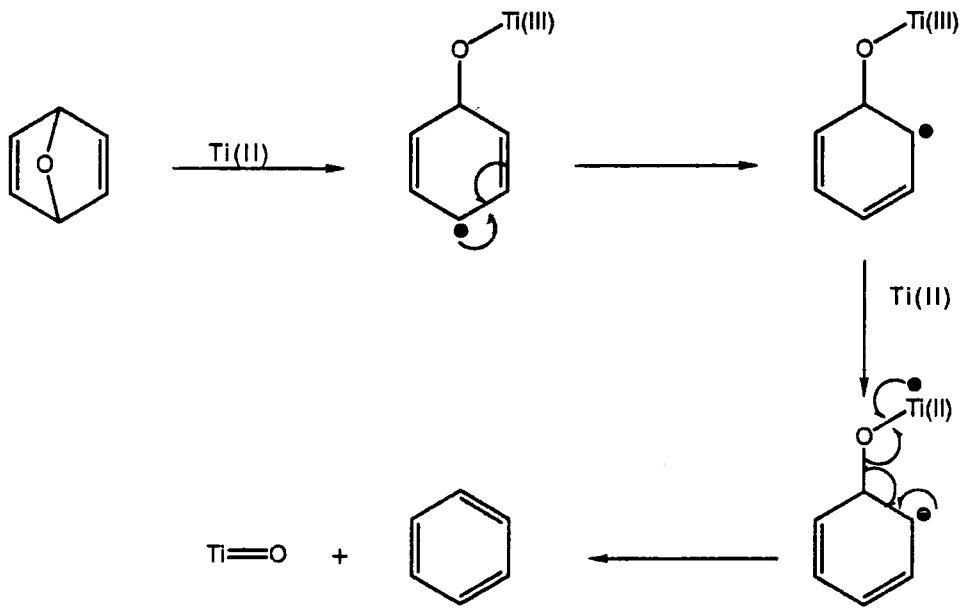
Scheme 48



The low valent titanium reagent was prepared from titanium tetrachloride, lithium aluminum hydride and triethylamine in a molar ratio of 6.1:1.3:1 respectively. The mechanism proposed[191] for the deoxygenation of 1,4 endoxides is analogous to that proposed for the reduction of epoxides[192]. The first step involves a Ti(II) species which cleaves the carbon-oxygen bond of the endoxide to form a Ti(III) radical complex (63). Then double bond migration and reduction of the

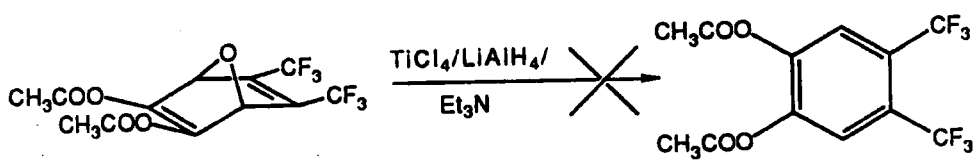
Ti(III) radical to Ti(II) followed by the loss of titanium (II) oxide yields the aromatic system (Scheme 49).

Scheme 49



Cycloaddition of 3,4-bis(trifluoromethyl)furan and dimethyl-acetylenedicarboxylate (DMAD) to give the corresponding endoxide (64) went in good yield. However, attempts to deoxygenate the endoxide (64) under identical conditions to those employed for the deoxygenation of (61) resulted in decomposition, and not the formation of the desired aromatic (65) (Scheme 50).

Scheme 50

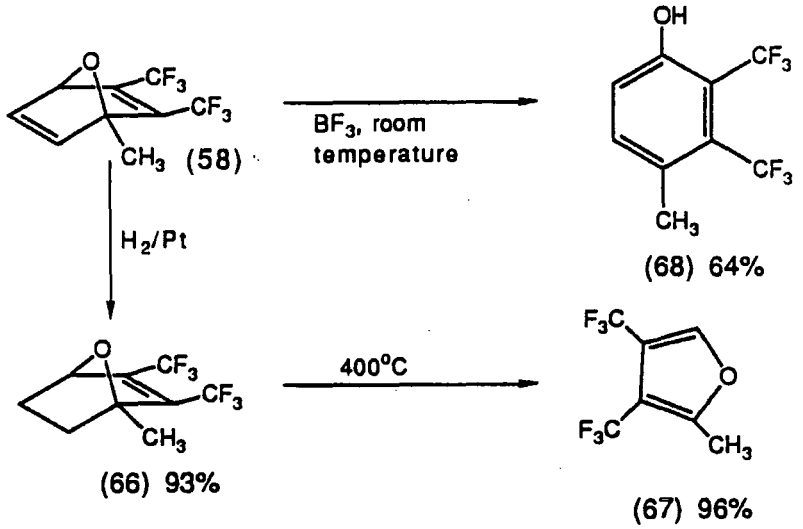


(64) (65)

Endoxide (58) was synthesised in good yield by the cycloaddition of hexafluorobut-2-yne and 2-methylfuran[185]. Its selective reduction and pyrolysis to give the desired 2-methyl-3,4-bis(trifluoromethyl)furan

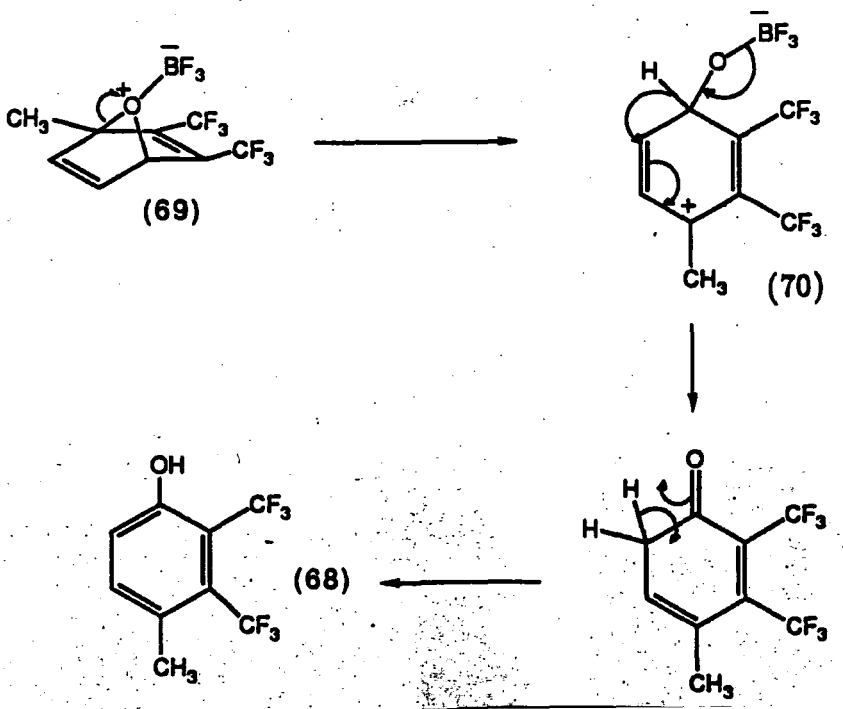
(67) was successful. The endoxide (58) was also successfully ring opened to give 2,3-bis(trifluoromethyl)-4-methylphenol (68) as the only product by treatment with boron trifluoride etherate at room temperature (Scheme 51).

Scheme 51



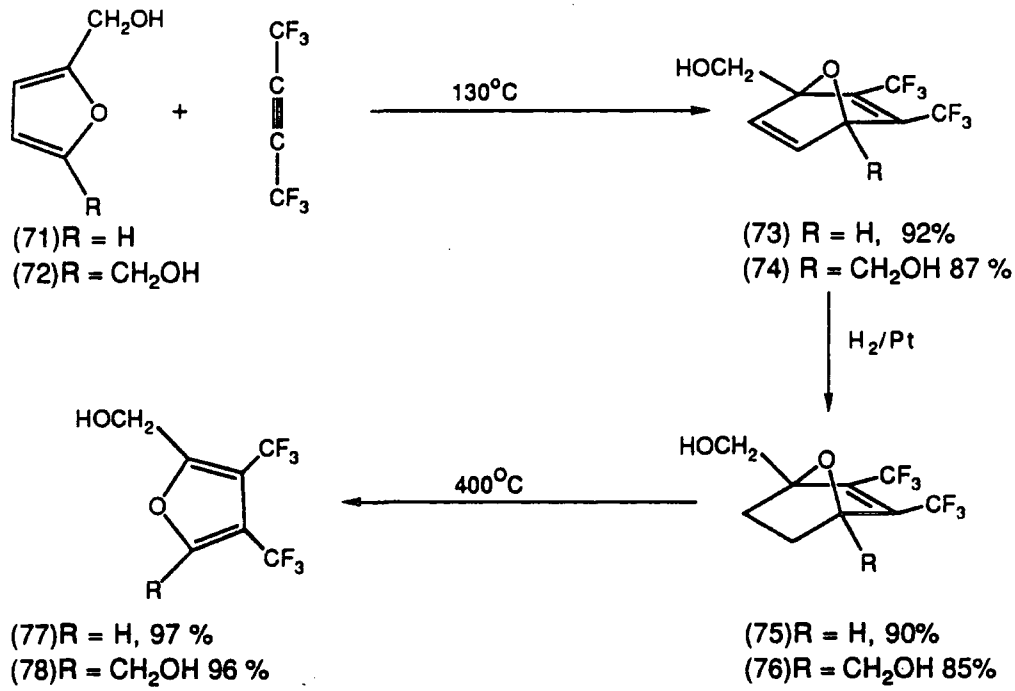
The first step in the production of the phenol (68) is probably the formation of a complex between boron trifluoride and the endoxide of type (69). This is followed by the fission of the oxygen bridge to give the carbonium ion (70), which is facilitated by the stabilising effect of the methyl group. Rearrangement gives the aromatic (68) (Scheme 52). The failure to ring open endoxides (55), (61) and (73) is attributed to the lack of electron releasing substituents to stablise carbonium ion intermediates.

Scheme 52



Addition of hexafluorobut-2-yne to 2-(hydroxymethyl)- and 2,5-di(hydroxymethyl)furan to the corresponding adducts (73) and (74) went in high yield. Selective reduction and pyrolysis of the resulting endoxides (73) and (74) resulted in the formation of the desired 2-(hydroxymethyl)-3,4-bis(trifluoromethyl)furan (77) and 2,5-di(hydroxymethyl)-3,4-bis(trifluoromethyl)furan (78) (Scheme 53).

Scheme 53



(71)R = H
(72)R = CH_2OH

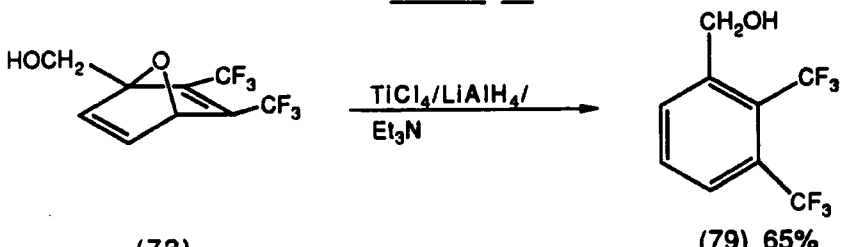
(73) R = H, 92%
(74) R = CH_2OH 87 %

(77)R = H, 97 %
(78)R = CH_2OH 96 %

(75)R = H, 90%
(76)R = CH_2OH 85%

Selective removal of the bridging oxygen from the endoxide (73) with a low valent titanium reagent resulted in the formation of 2,3-bis(trifluoromethyl)benzyl alcohol (79) as the only product (Scheme 54).

Scheme 54



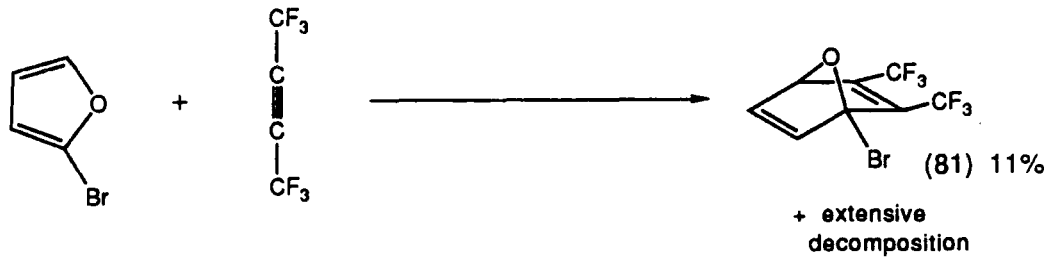
(73)

(79) 65%

Attempts to synthesise 1-formyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1.]hepta-2,5-diene (80) from furalaldehyde and hexafluorobut-

2-yne resulted in a mixture of products; isolation of (80) by distillation and by preparative g.c. failed. Further investigation was not attempted.

Scheme 55



At 140°C the Diels-Alder addition of hexafluorobut-2-yne to 2-bromofuran gave the endoxide (81) in low yield with extensive decomposition (Scheme 55). At lower temperatures no reaction occurred.

Finally hexafluorobut-2-yne was reacted with 2-trimethylstannylfuran to give the desired endoxide (82) in a high yield (Scheme 56). This reaction was investigated because a trimethyltin group can be selectively replaced by halogens[99-108], thus offering a route to halogenated bistrifluoromethylfurans and benzenes.

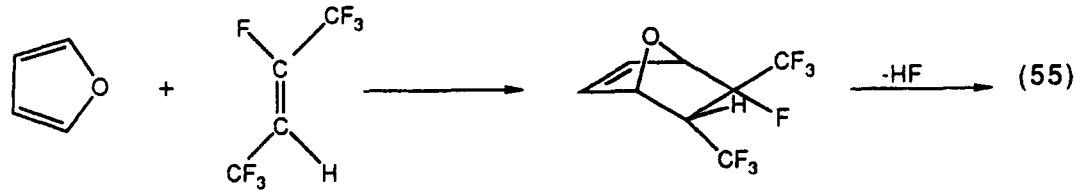
Scheme 56

Trans-2H-heptafluorobut-2-ene

Although hexafluorobut-2-yne is easily prepared (Scheme 47)[189], it is only produced on a small scale commercially due to limited industrial demand and is therefore relatively expensive at present. This coupled with the availability of *trans*-2H-heptafluorobut-2-ene (83) prompted

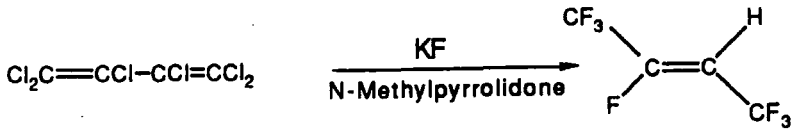
our investigation into the use of this alkene (83) as a synthetic equivalent for hexafluorobut-2-yne (Scheme 57).

Scheme 57



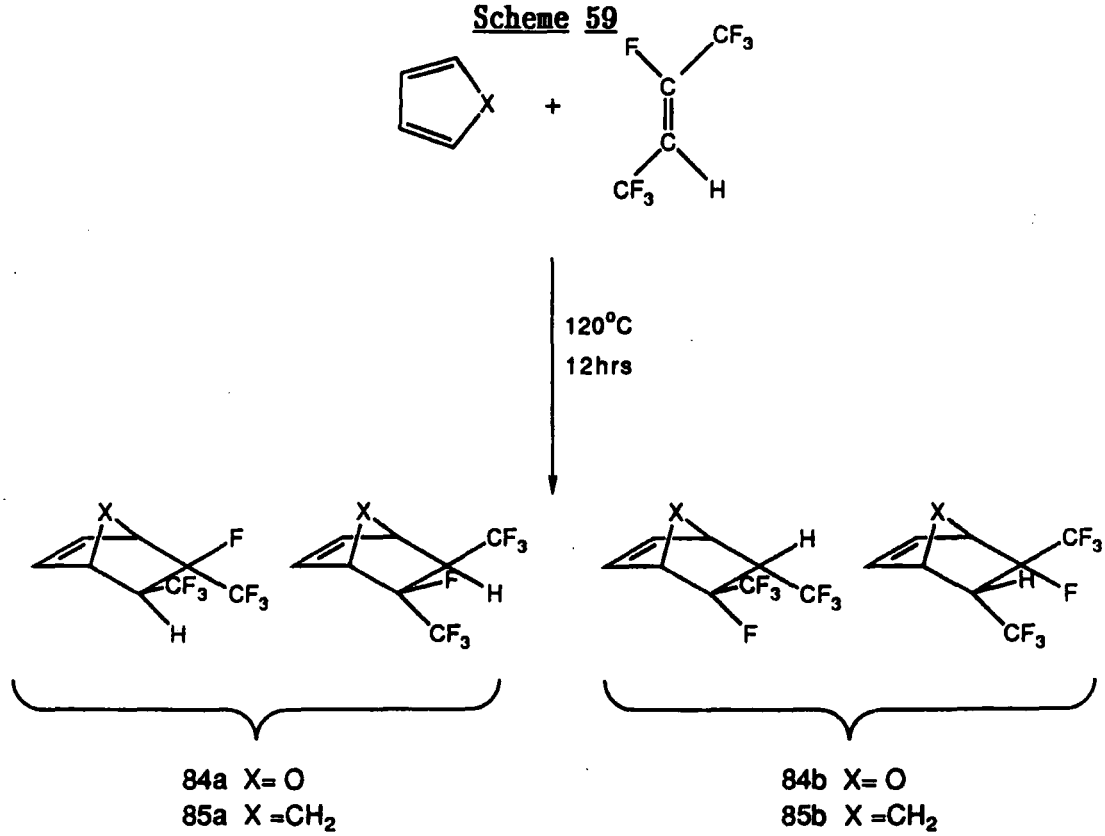
Trans-2H-heptafluorobut-2-ene was synthesised from hexachlorobutadiene in one step in high yield (Scheme 58)[193]. It underwent cycloaddition reactions with furan and cyclopentadiene to give the two pairs of enantiomers (84a), (84b) and (85a), (85b) in good yield (Scheme 59). Isolation of the two pairs of isomers of the adducts derived from furan was carried out by preparative g.c. but exact conformational analysis by ^{19}F n.m.r. was not possible.

Scheme 58



(83) 85%

Scheme 59

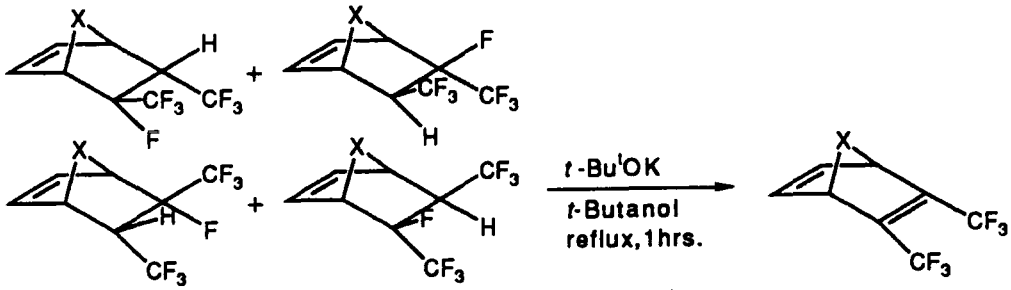


84a X= O
85a X =CH_2

84b X= O
85b X =CH_2

The elimination of hydrogen fluoride from the adducts (85a) and (85b), which are derived from cyclopentadiene and hexafluorobut-2-yne, using potassium tert-butoxide/tert-butanol[194], to give 2,3-bis(trifluoromethyl)-7-bicyclo[2.2.1]hepta-2,5-diene (86), went in good yield. In contrast, attempts to remove HF from the endoxides (84a) and (84b) resulted in extensive decomposition with very little of the desired compound (55) being formed (Scheme 60).

Scheme 60



(84a)X= O
(85a)X= CH_2

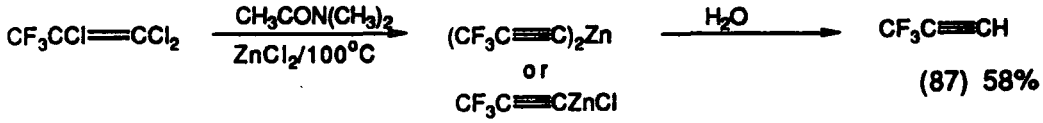
(84b)X= O
(85b)X= CH_2

(55) X= O, <5%
(86) X= CH_2, 55%

The only structural difference between the two sets of adducts (84a), (84b) and (85a), (85b) is the oxygen bridge; it is therefore likely that the extensive decomposition observed during the attempted dehydrofluorination of the adducts derived from furan resulted from cleavage of this oxygen bridge. The failure of this dehydrofluorination step prevented the synthesis of the desired aromatic systems by this route.

3,3,3-Trifluoropropyne

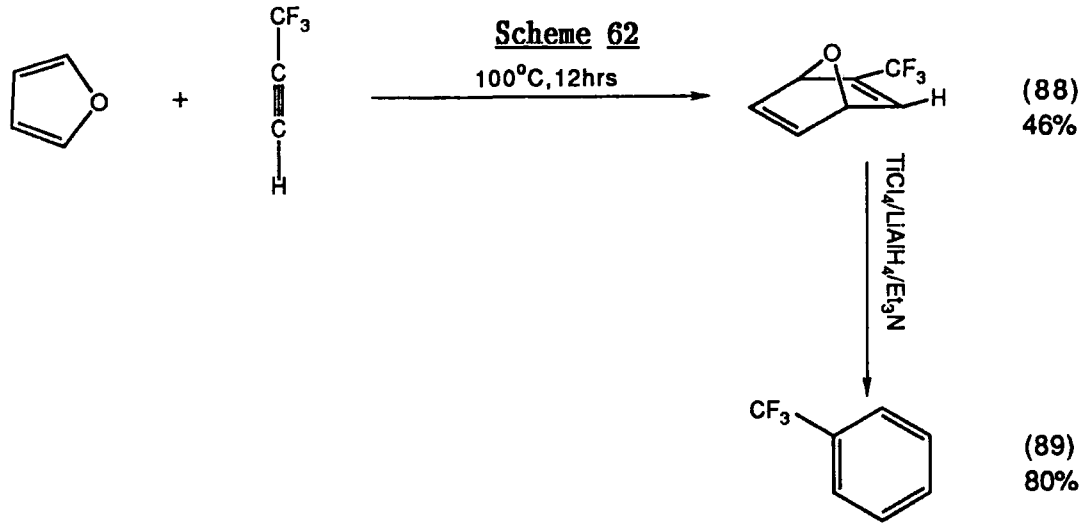
Scheme 61



(87) 58%

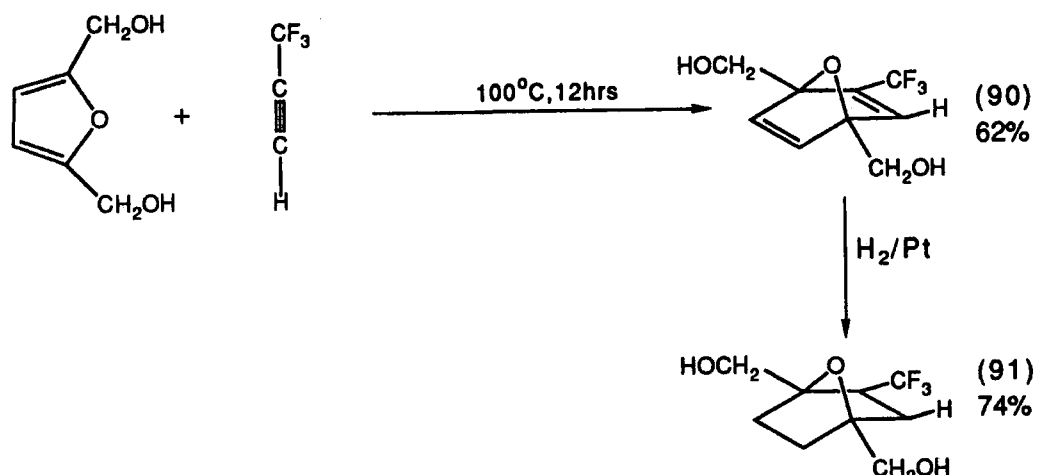
The chemistry carried out with hexafluorobut-2-yne was attempted with 3,3,3-trifluoropropyne (87). This alkyne is easily prepared in good yield[195] by zinc dechlorination of 1,1,2-trichloro-3,3,3-trifluoropropene (Scheme 61). It readily underwent cycloaddition reactions with furan to give the adduct (88), and the bridging oxygen was removed with a low valent titanium complex to give benzotrifluoride in good yield (Scheme 62).

Scheme 62



More significantly the addition of the fluoroalkyne (87) to 1,4-di(hydroxymethyl)furan was successful, but all attempts to selectively reduce the adduct (90) resulted in complete reduction (Scheme 63). The failure of this reduction prevented the synthesis of the desired 2,5-di(hydroxymethyl)-3-trifluoromethylfuran (91) and therefore the chemistry of 3,3,3-trifluoropropyne was not investigated further.

Scheme 63



Conclusion

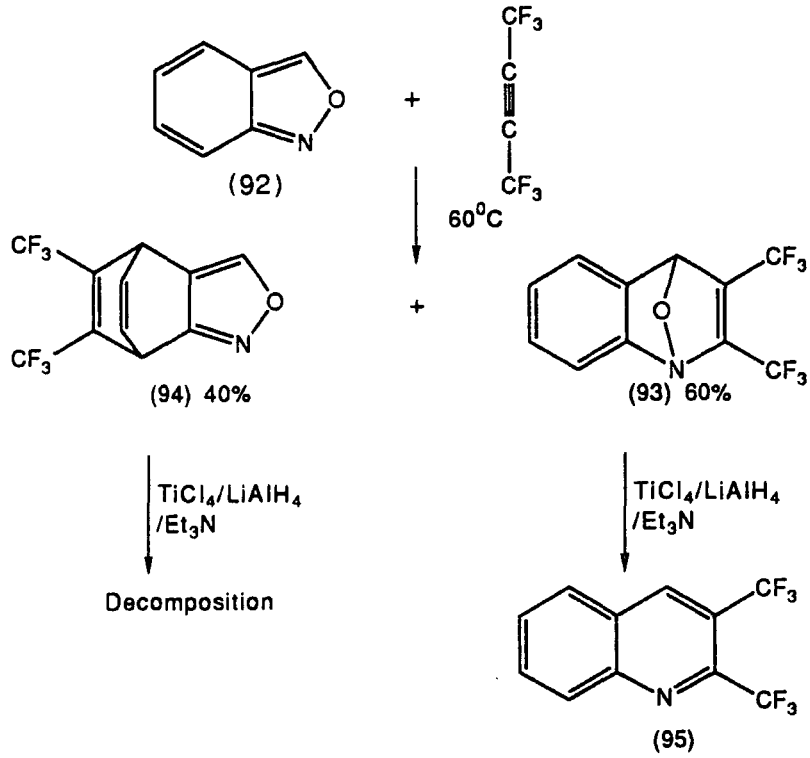
The cycloaddition reaction of substituted furans with hexafluorobut-2-yne is a versatile method of synthesising bis(trifluoromethyl)-aromatic systems. However, the potentially important Diels-Alder reactions of *trans*-2H-heptafluorobut-2-ene are currently frustrated as a route to the desired bis(trifluoromethyl) aromatic compounds until an alternative method for the dehydrofluorination step can be found. Initial results from the reaction of 3,3,3-trifluoropropyne indicate that its cycloaddition reactions are successful, but another method for the selective reduction of the adducts is required.

Addition of hexafluorobut-2-yne to 2,1-benzisoxazole as a route to 2,3-bis(trifluoromethyl)quinoline

It has been reported that the cycloaddition reaction of 2,1-benzisoxazole (92) with acetylenic compounds in the presence of sulphuric acid provides a low yielding synthetic route to quinolines[196]. This route involves two distinct steps; the first is cycloaddition and the second is the removal of the bridging oxygen to give the aromatic compound. The low yield of this synthetic route may be due to the aromatisation step; it was therefore decided to investigate the cycloaddition of hexafluorobut-2-yne with 2,1-benzisoxazole and its subsequent reaction as separate reactions.

The addition of hexafluorobut-2-yne and 2,1-benzisoxazole went readily, even at reaction temperatures as low as 60°C, to give the desired 2,3-bis(trifluoromethyl)-1,4-oxoquinoline (93) and its isomer (94) (Scheme 64). Separation was possible by preparative g.c..

Scheme 64

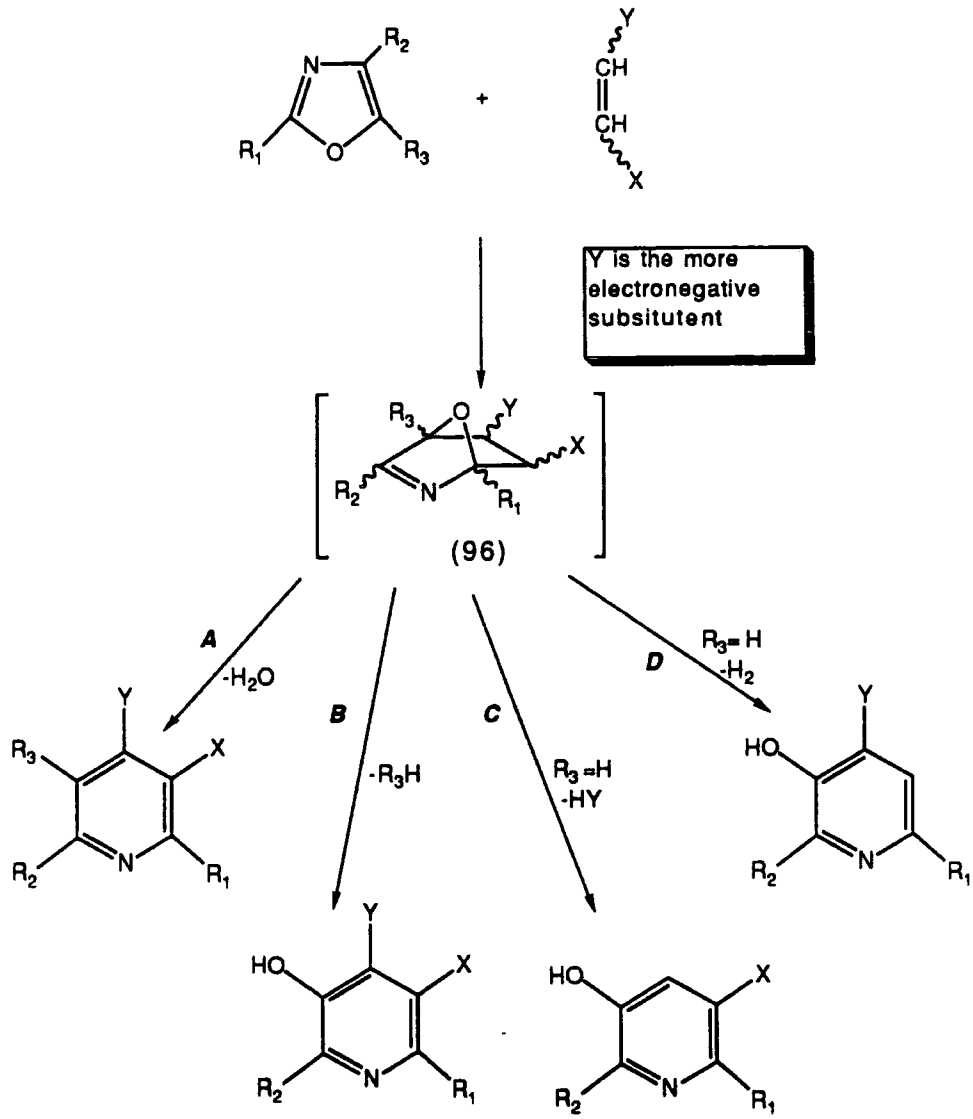


Treatment of the adducts (93) and (94) with a low valent titanium reagent[185] resulted in the aromatisation of (93) to the desired bis(tri-fluoromethyl)quinoline (95) and in destruction of (94) (Scheme 64).

Diels-Alder chemistry of oxazoles as a route to trifluoromethyl pyridines

Diels-Alder addition of alkenes to substituted oxazoles gives substituted pyridines as the products[187,188]. The pyridines obtained are dependent on the substituted oxazole and the processes which occur are shown in Scheme 65.

Scheme 65



R_3 is not a good leaving group, (eg alkyl), then path A is followed

R_3 is a good leaving group, (eg. OEt), then path B is followed

R_3 =H, and Y is a good leaving group, then path C is followed

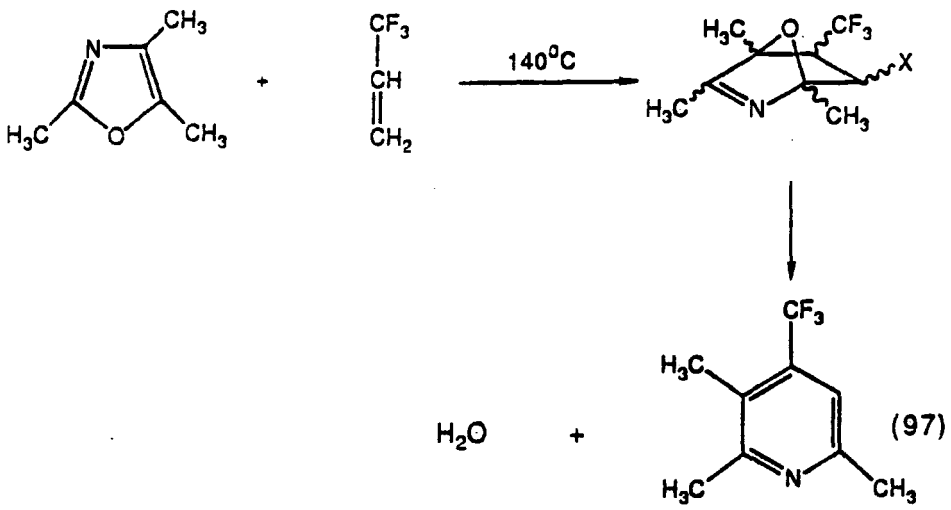
R_3 =H, and Y is not a good leaving group, then path D is followed

The initial adducts (96) are not stable and are not isolated. Aromatisation of the adducts (96) depends on the nature of the groups at the 4 and 5 positions (R_3 and Y) and in general the above rules apply.

It is found that the more electronegative substituent of the dienophile (Y) occupies position 4 of the adduct.

Initial investigations into the Diels-Alder chemistry of oxazoles with fluorinated alkenes was carried out with trifluoropropene. This was chosen because it is commercially available and has been shown to undergo addition reactions with dienes[197,198]. The addition of trifluoropropene to 2,4,5-trimethyloxazole gave the expected 2,3,6-trimethyl-3-trifluoromethylpyridine (97) in low yield, with extensive decomposition and low conversion (Scheme 66). The pyridine (97) was isolated as its hydrogen fluoride salt, the hydrogen fluoride being a decomposition product.

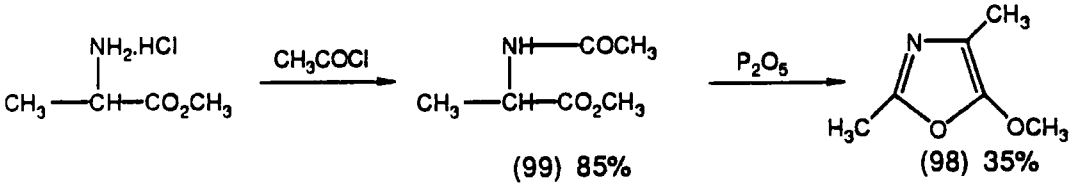
Scheme 66



The low conversion of this reaction indicated that a more reactive oxazole was required. It has been reported that 5-alkoxyoxazoles are the most active dienes amongst oxazoles, with a reactivity comparable to carbocyclic dienes[187]. For this reason, and the fact that the products of the cycloaddition reactions of 5-alkoxyoxazoles yield hydroxypyridines, 2,4-dimethyl-5-methoxyoxazole (98)[199] was synthesised and its Diels-Alder chemistry investigated. 2,4-Dimethyl-5-methoxyoxazole was

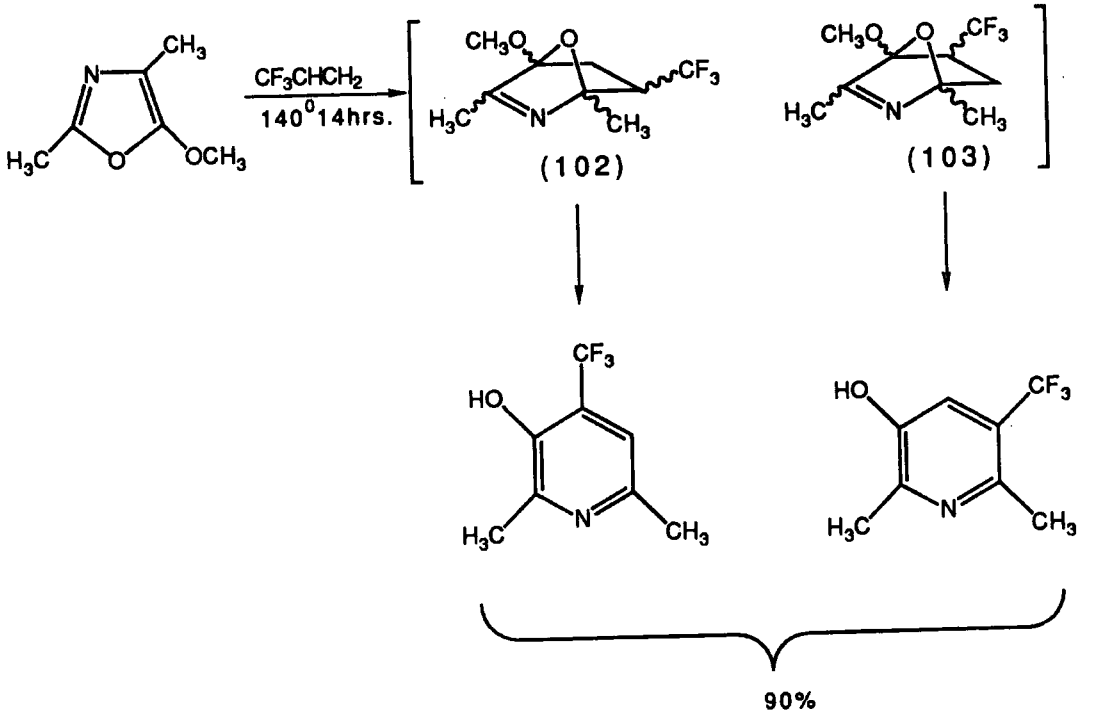
prepared from methylalanate hydrogen chloride in a two step process. The first step was synthesis of methylacetylalanate (99) by treatment with acetylchloride, then cyclisation of methylacetylalanate with P_2O_5 (Scheme 67).

Scheme 67



Cycloaddition of 2,4-dimethyl-5-methoxyoxazole and trifluoropropene went in high conversion to yield a mixture of 2,6-dimethyl-3-trifluoromethyl-5-hydroxypyridine (100) and 2,6-dimethyl-4-trifluoromethyl-5-hydroxypyridine (101) as the only products (Scheme 68). Separation of the two compounds (100) and (101) was achieved by flash chromatography. The intermediate adducts (102) and (103) were identified by mass spectrometry as the major reaction products when the reaction time was shortened from 14 hrs to 8 hrs.

Scheme 68



No reaction of 2,4-dimethyl-5-methoxyoxazole with the following fluoroalkenes; hexafluoropropene, 2-H-hexafluoropropene, perfluorocyclobutadiene, tetrafluoroethylene and vinylfluoride was observed.

Conclusion

The Diels-Alder reactions of 5-alkoxy oxazoles offer a potential route to perfluoroalkyl hydroxypyridines and deserve further investigation. Initial results suggest that this cycloaddition reaction requires the perfluoroalkyl group to be attached to a $CH=CH_2$ moiety.

INSTRUMENTATION AND REAGENTS

INSTRUMENTATION

Gas liquid chromatographic (g.c.) analyses were carried out on a Varian Aerograph Model 920 gas chromatograph (flame ionisation detector) using columns packed with 10% silicone elastomer 30 on chromosorb P (column 10% SE30). A Hewlett-Packard 5890A gas chromatograph fitted with a 25m cross-linked methyl silicone capillary column was also used. Preparative g.c. was carried out using a Varian Aerograph Model 920 (catharometer detector) gas chromatograph.

Fractional distillation of product mixtures was carried out using Fischer-Spaltrohor MMS 255 and HMS 500, small and large concentric tube systems.

Boiling points were determined at atmospheric pressure unless otherwise stated and are uncorrected. Boiling points were recorded during distillation.

Carbon, hydrogen and nitrogen analyses were obtained using a Perkin-Elmer 240 Elemental Analyser or a Carlo Erba 1106 Elemental Analyser. Analysis for halogens was performed as described in the literature[200].

Infrared (i.r.) spectra were recorded on either a Perkin-Elmer 457 or 577 Grating Spectrophotometer using conventional techniques.

Proton (^{1}H) n.m.r. spectra were recorded on a Hitachi Perkin-Elmer R-24B spectrometer operating at 60MHz or a Bruker AC250 spectrometer operating at 250MHz.

Fluorine (^{19}F) n.m.r. spectra were recored on a Varian EM360L spectrometer operating at 56.45 MHz or a Brucker AC250 Spectrometer operating at 235.3 MHz.

Mass spectra of solid or one component liquid samples were recorded on a VG 7070E spectrometer. G.c./mass spectra were recored on the VG 7070E spectrometer linked to a Hewlett-Packard 5790A gas chromatograph fitted with a 25m cross-linked methyl silicone capillary column.

REAGENTS

In general all chemicals were used as received from suppliers and solvents were dried by literature procedures[201].

CHAPTER SIX

EXPERIMENTAL TO CHAPTER TWO

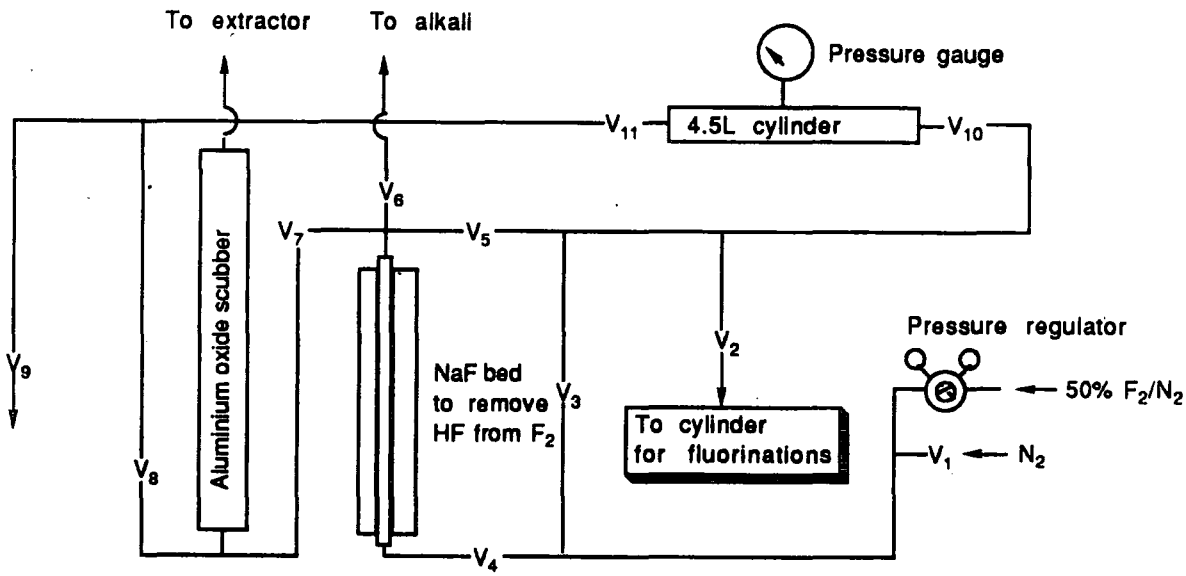
CHAPTER SIX

EXPERIMENTAL TO CHAPTER TWO

GENERAL PROCEDURE

Reactions With Elemental Fluorine

Due to the reactive nature of elemental fluorine all fluorinations were carried out in a specialised laboratory. Manipulations and dilutions of elemental fluorine, which is supplied as a 50% mixture with oxygen-free nitrogen (see reagents), was carried out using the following system:



V = Valve

All tubes and valves are made of stainless steel and have been made passive with elemental fluorine

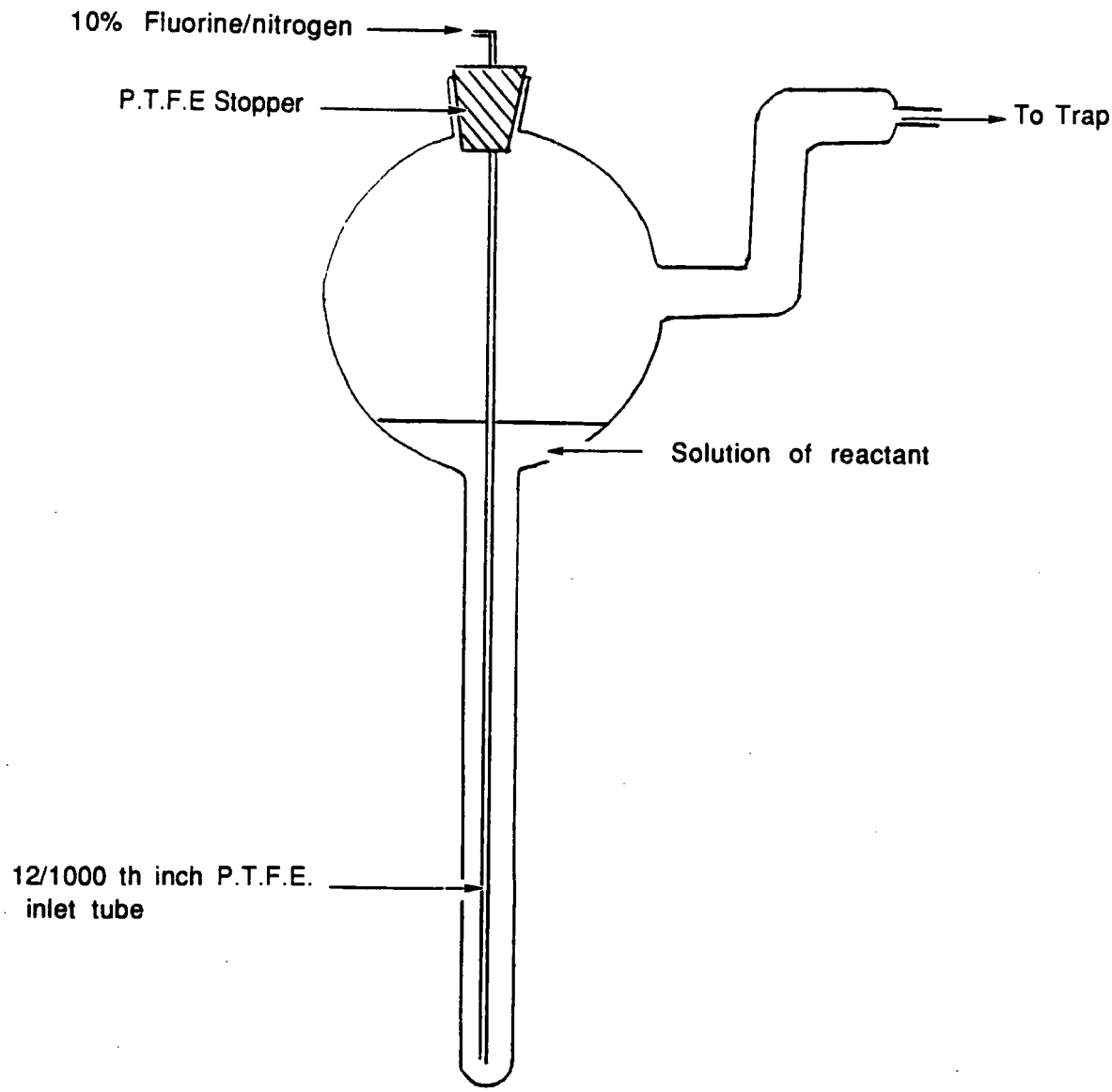
The specific concentrations of elemental fluorine/nitrogen mixtures were prepared by filling an evacuated, purged steel cylinder with elemental fluorine at 1 atmosphere, followed by pressurisation of the cylinder with nitrogen until the required dilution of fluorine was obtained. The weight of available fluorine was calculated from the volume of the cylinder and the pressure of fluorine in the cylinder.

All fluorinations were carried out in glass fluorination chambers (diagram 1) with the fluorine/nitrogen mixtures introduced through a 12/100th inch internal diameter P.T.F.E. capillary inlet tube. Any unreacted fluorine passing through the reaction mixture was destroyed by an Al_2O_3 scrubber.

Standard procedure for direct fluorination of arylsilanes

A solution of arylsilane (0.01mol) in an inert solvent was cooled to the desired temperature under a flow of nitrogen, then elemental fluorine, as a 10% mixture in nitrogen (0.015-0.030mol), was bubbled through the solution at *ca* 1.5cm^3 per minute. Once the addition was complete the solution was warmed to room temperature with nitrogen bubbling through the reaction mixture. Once at room temperature the reaction mixture was transferred under high vacuum, and benzotrifluoride (0.18g, 1.23mmol) was added as a n.m.r. marker. Reaction mixtures were analysed by ^{19}F n.m.r. and mass spectrometry using authentic samples as standards, ^{19}F n.m.r. data for standards are shown in table 30 of appendix 1. Yields were calculated from ^{19}F n.m.r. integrations by comparison with the integral of the added benzoltrifluoride marker.

Diagram 1



Standard procedure for the hydrolysis of products from direct fluorination reactions

Volatiles from the direct fluorination of phenyltrimethylsilane were added to a stirred mixture of acetic acid ($4cm^3$) and concentrated sulphuric acid ($1cm^3$) in a rotaflo flask. After heating at 80^oC for 4 hours the reaction mixture was cooled to room temperature and analysed by ^{19}F n.m.r..

6:1 Direct fluorination of phenyltrimethylsilane in $CFCl_3$ at $-78^{o}C$

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethylsilane in $CFCl_3$ ($10cm^3$) with elemental fluorine (1.1g, 0.03mol) resulted in the isolation of decomposition products (0.4g). Analysis of the volatiles by ^{19}F n.m.r., g.c. and mass spectrometry showed the reaction mixture to contain: fluorobenzene, 8.0%, δ_F -114, *m/z* 96.02 (M^+100%); *p*-difluorobenzene, 1%, δ_F -120.3, *m/z* 114.01 (M^+100%); *m*-difluorobenzene, 0.5%, δ_F -110.9, *m/z* 113.9 (M^+100%); *o*-difluorobenzene, 1.0%, δ_F -139.9, *m/z* 113.9 (M^+100%); phenyltrimethylsilane, *m/z* 150.1 (M^+9.64%); fluorophenyltrimethylsilane, *m/z* 167.22 (M^+4.07%), and difluorophenyltrimethylsilane, *m/z* 186.28 (M^+19.48%).

6:2 Direct fluorination of phenyltrimethylsilane in acetonitrile at $-30^{o}C$

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethylsilane in acetonitrile ($10cm^3$) with elemental fluorine (1.1g, 0.03mol) resulted in the isolation of decomposition products (0.5g). Analysis of the volatiles by ^{19}F n.m.r., g.c. and mass spectrometry showed the reaction mixture to contain: fluorobenzene, 16%, δ_F -114, *m/z* 96.06 (M^+100%); *p*-difluorobenzene, 3.5%, δ_F -120.3, *m/z* 114 (M^+100%); *m*-difluorobenzene, 0.5%, δ_F -110.9, *m/z* 114.0 (M^+100%); *o*-difluorobenzene, 3%, δ_F -139.9, *m/z* 113.99 (M^+100%); phenyltrimethylsilane, *m/z* 150.1 (M^+11%); fluorophenyltrimethylsilane, *m/z* 167.22 (M^+6.01%), and difluorophenyltrimethylsilane, *m/z* 186.28 (M^+22.39%).

6:3 Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane at -30°C

Analysis of the hydrolysis products from the direct fluorination of phenyltrimethylsilane by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 20.5%, δ_F -114.3; *p*-difluorobenzene, 5.0%, δ_F -120.5; *m*-difluorobenzene, 1%, δ_F -111.2, and *o*-difluorobenzene, 4.5%, δ_F -140.16.

6:4 Direct fluorination of phenyltrimethylsilane in acetonitrile at -10°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethylsilane in acetonitrile ($10cm^3$) with elemental fluorine (1.12g, 0.03mol) resulted in the isolation of polymeric material (0.7g). Analysis of the volatiles by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 21.0%, δ_F -113.4; *p*-difluorobenzene, 4.0%, δ_F -119.7; *m*-difluorobenzene, 1.5%, δ_F -110.4, and *o*-difluorobenzene, 3.5%, δ_F -139.3, *m/z* 114 (M^+100%).

6:5 Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane at -10°C

Analysis of the hydrolysis products from the direct fluorination of phenyltrimethylsilane by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 31.0%, δ_F -113.4; *p*-difluorobenzene, 7.0%, δ_F -119.8; *m*-difluorobenzene, 1.5%, δ_F -110.1, and *o*-difluorobenzene, 4.0%, δ_F -138.8.

6:6 Direct fluorination of phenyltrimethylsilane in acetonitrile at 0°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethylsilane in acetonitrile ($10cm^3$) with elemental fluorine (1.12g, 0.03mol) resulted in the isolation of polymeric material (0.7g). Analysis of the volatiles by ^{19}F n.m.r., g.c. and mass spectrometry showed the reaction mixture to contain: fluorobenzene, 15.5%, δ_F -114.3, *m/z* 96.01 (M^+100%); *p*-difluorobenzene, 6.0%, δ_F -120.4, *m/z* 114.05 (M^+100%); *m*-difluorobenzene, 2.0%, δ_F -111.0, *m/z* 114.0 (M^+100%); *o*-difluorobenzene, 5.5%, δ_F -140.2, *m/z* 114.0 (M^+100%); phenyltrimethylsilane, *m/z* 150.14 (M^+ 8.9%); fluorophenyltrimethylsilane, *m/z* 167.22 (M^+5.7%), and difluorophenyltrimethylsilane, *m/z* 186.28 (M^+19.24%).

6:7 Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane at 0°C

Analysis of the hydrolysis products from the direct fluorination of phenyltrimethylsilane by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 26.5%, δ_F -114; *p*-difluorobenzene, 11%, δ_F -120.1; *m*-difluorobenzene, 3.0%, δ_F -110.8, and *o*-difluorobenzene, 7.5%, δ_F -139.9.

6:8 Direct fluorination of phenyltrimethylsilane in acetonitrile at 20°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethylsilane in acetonitrile ($10cm^3$) with

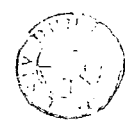
elemental fluorine (1.12g, 0.03mol) resulted in the isolation of polymeric material (0.9g). Analysis of the volatiles by ^{19}F n.m.r., g.c. and mass spectrometry showed the reaction mixture to contain: fluorobenzene, 14.0%, δ_F -114.4, *m/z* 96.0 (M^+100%); *p*-difluorobenzene, 12.5%, δ_F -120.6, *m/z* 114.17 (M^+100%); *m*-difluorobenzene, 2.5%, δ_F -111.2, *m/z* 114 (M^+100%); *o*-difluorobenzene, 11.5%, δ_F -140.3, *m/z* 114 (M^+100%); fluorophenyltrimethylsilane, *m/z* 167.22 (M^+5.7%); difluorophenyltrimethylsilane, *m/z* 186.28 (M^+19.24%), and trifluorophenyltrimethylsilane, *m/z* 205.18 (M^+28.77%).

6:9 Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane at 20°C

Analysis of the hydrolysis products from the direct fluorination of phenyltrimethylsilane by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 10.5%, δ_F -114; *p*-difluorobenzene, 9.5%, δ_F -120.1; *m*-difluorobenzene, 2%, δ_F -110.8; *o*-difluorobenzene, 9.5%, δ_F -140.0, and 1,2,4-trifluorobenzene, 7.5% δ_F -115.7, 127.7, 144.

6:10 Direct fluorination of phenyltrimethylsilane in $CFCl_3$ at 0°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethyl silane in $CFCl_3$ (10cm^3) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (0.5g). Analysis of the volatiles by ^{19}F n.m.r., g.c. and mass spectrometry showed the reaction mixture to contain: fluorobenzene, 7.0%, δ_F -113.9, *m/z* 96.24 (M^+100%); *p*-difluorobenzene, 2.5%, δ_F -120.3, *m/z* 114.0 (M^+100%); *m*-difluorobenzene, 1.0%, δ_F -110.9, *m/z* 114 (M^+100%); *o*-difluorobenzene, 2%, δ_F -140.0, *m/z* 114 (M^+100%);



phenyltrimethylsilane, m/z 150.0 (M^+9.2%), and ring fluorinated phenyltrimethylsilanes.

6:11 Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane in $CFCl_3$ at 0^oC

Analysis of the hydrolysis products from the direct fluorination of phenyltrimethylsilane by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 23.0%, δ_F -133.9; *p*-difluorobenzene, 7.0%, δ_F -120.2; *m*-difluorobenzene, 1.5% δ_F -110.9, and *o*-difluorobenzene, 4.5% δ_F -140.0

6:12 Direct fluorination of phenyltrimethylsilane in $CHCl_3$ at 0^oC

Vacuum transfer of the reaction mixture obtained from the dir- ect fluorination of phenyltrimethyl silane in chloroform ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (0.6g). Analysis of the volatiles by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 10.0%, δ_F -113.8; *p*-difluorobenzene, 4.0%, δ_F -120.2; *m*-difluorobenzene, 1.0%, δ_F -110.8; *o*-difluorobenzene, 2.5%, δ_F -139.8, and ring fluorinated phenyltrimethylsilanes δ_F -100 to -145.

6:13 Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane in $CHCl_3$ at 0^oC

Analysis of the hydrolysis products from the direct fluorination of phenyltrimethylsilane by ^{19}F n.m.r. showed the reaction mixture to

contain: fluorobenzene, 18.0%, δ_F -113.4; *p*-difluorobenzene, 6.5%, δ_F -119.8; *m*-difluorobenzene, 2%, δ_F -110.6 and *o*-difluorobenzene, 3.5%, δ_F -138.8.

6:14 Direct fluorination of phenyltrimethylsilane in nitromethane at 0°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethyl silane in nitromethane ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of decomposition products (1.1g). Analysis of the volatiles by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 2.0%, δ_F -114.0; *p*-difluorobenzene, 0.5%, δ_F -120.3; *m*-difluorobenzene, 0.1%, δ_F -110.9, and *o*-difluorobenzene, 0.5%, δ_F -139.9.

6:15 Direct fluorination of phenyltrimethylsilane in $CF_2ClCFCl_2$ at 0°C

The vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethyl silane in $CF_2ClCFCl_2$ ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (0.6g). Analysis of the volatiles by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 14.0%, δ_F -114.1; *p*-difluorobenzene, 3.0%, δ_F -120.4; *m*-difluorobenzene, 1.0%, δ_F -111.0, and *o*-difluorobenzene, 2.0%, δ_F -140.1.

6:16 Hydrolysis of the reaction products obtained from the direct fluorination of phenyltrimethylsilane in $CF_2ClCFCl_2$ at 0°C

Analysis of the hydrolysis products from the direct fluorination of

phenyltrimethylsilane by ^{19}F n.m.r. showed the reaction mixture to contain: fluorobenzene, 23%, δ_F -113.9; *p*-difluorobenzene, 7.5%, δ_F -120.1; *m*-difluorobenzene, 2.5%, δ_F -110.8, and *o*-difluorobenzene, 4.5%, δ_F -139.7.

6:17 Direct fluorination of phenyltrimethylsilane in water at 0°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of phenyltrimethyl silane in water ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of white solid (1.2g). Analysis of the volatiles by ^{19}F n.m.r. and g.c. mass spectrometry indicate extensive decomposition with less than 5% of fluoroaromatics produced.

6:18 Synthesis of substituted aryltrimethylsilanes

Method 1[152]

A solution of the appropriate arylchloride in hexamethylphosphoramide (H.M.P.A.) was added dropwise to a stirred suspension of magnesium powder, trimethylsilylchloride and iodine (0.1g) in H.M.P.A. under an atmosphere of dry nitrogen. Once the addition was complete the reaction was heated at 70°C for 48 hours, poured on to ice and extracted with ether. After drying the ether extract over magnesium sulphate the solvent was evaporated and the resulting oil was distilled under reduced pressure to give the require aryltrimethylsilane. Results are shown in Table 28.

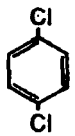
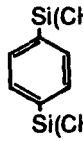
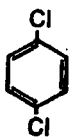
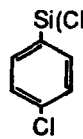
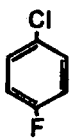
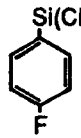
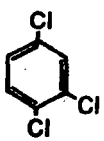
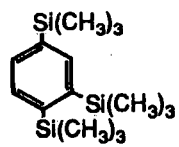
Method 2[151]

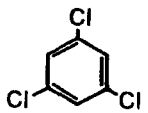
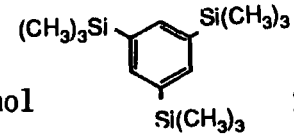
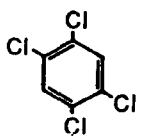
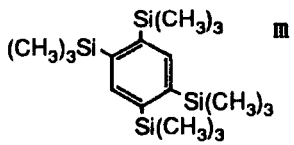
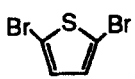
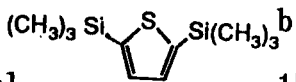
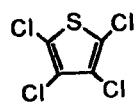
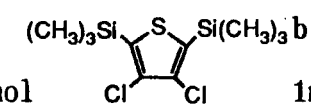
A solution of trimethylsilylchloride in dry diethylether was added to an ethereal solution of a Grignard reagent prepared from the appropriate arylchloride. The reaction mixture was stirred at room temperature for 18 hours then poured onto ice. The ether layer was separated and combined with ether extracts of the aqueous layer. After drying over magnesium sulphate the solvent was removed under reduced pressure and the resulting oil distilled under reduced pressure to give the desired aryltrimethylsilane. Results are given in Table 28.

Method 3[151,153]

To a stirred solution of the appropriate arylbromide or arylchloride at -78°C a solution of butyl lithium was added dropwise over an hour. After two hours at -78°C trimethylsilyl chloride was added dropwise and the reaction mixture was allowed to warm to room temperature. After one hour at room temperature the reaction mixture was filtered, evaporated to dryness and distilled under reduced pressure to give the desired aryltrimethylsilanes. Results are given in table 28.

Table 28 Synthesis of substituted aryltrimethylsilanes

Starting material (g/mol)	Method	Mg/Butyl-lithium	Trimethyl-silyl chloride	Product yield %	B.p. mmHg /m.p.	^{1}H n.m.r.	Mass spec. m/z	Infra red	reference
	1	Mg 8g	42.6g		m.p.92^{o}C	δ_H 0.2(s, 4.5H),	*m/z* 222.2	1	152,153
		0.33mol	0.40mol			6.8(s, 1H)	(3.4%)		
20g/ 0.15mol				67%					
	2	Mg 4g	42.6g		b.p.123^{o}C	δ_H 0.25(s, 2.25H)	*m/z* 184.9	2	152
		0.16mol	0.4mol		43mmHg	6.6(ab, 1H)	(0.3%)		
28.5g 0.15mol				52%					
	3	BuLi	21.3g		b.p.91.5^{o}C	δ_H 0.25(s, 2.25H)	*m/z* 168	3	151
		0.015mol	0.20mol		62mmHg	6.9(ab, 1H)	(5.1%)		
26.2g 0.15mol				67%		δ_F -112.1			
	1	Mg 16.8g	97g		b.p.125^{o}C	δ_H 0.3(s, 9H)	*m/z* 369.2	4	152
		0.67mol	0.87mol		2mmHg	7.6(m, 1H)	(3.2%)		
36.2g 0.2mol				40%					

Starting material (g/mol)	Method	Mg/Butyl-lithium	Trimethyl-silyl chloride	Product yield %	B.p. mmHg /m.p.	^{1}H n.m.r.	Mass spec. m/z	Infra red	reference
	1	Mg 16.8g	97g		b.p.137^{o}C	δ_H 0.3(s, 9H)	*m/z* 369.0	5	152
		0.67mol	0.87mol		2mmHg	7.7(s, 1H)	(2.05%)		
36.2g 0.2mol				33%					
	1	Mg 12g	65g		m.p.172^{o}C	δ_H 0.4(s, 18H)	*m/z* 366.7	6	152
		0.48mol	0.6mol			7.9(s, 1H)	(4.5%)		
21.6g 0.1mol				44%					
	1	Mg 3.8g	20g		b.p.78.6^{o}C	δ_H 0.4(s, 9H)	*m/z* 227	7	152
		0.15mol	0.18mol		15mmHg	7.5(s,1H)	(1.4%)		
0.07mol				76%					
	3	BuLi	13g		b.p.72^{o}C	δ_H 0.3(s)	*m/z* 299.72	8	151
		0.1mol	0.12mol		1mmHg		(0.09%)		
11g, 0.05mol				70%					

6:19 Direct fluorination of *p*-chlorophenyltrimethylsilane in acetonitrile at -30°C

The solvent was removed under reduced pressure from the reaction mixture produced by direct fluorination of *p*-chlorophenyltrimethylsilane in acetonitrile ($10cm^3$) with elemental fluorine (0.56g, 0.015mol), to give a yellow liquid (2.1g), which was analysed by ^{19}F n.m.r., g.c. and mass spectrometry to contain: *p*-fluorochlorobenzene, 16%, δ_F -116.9 , *m/z* 131.99 (M^+100%); 3,4-difluorochlorobenzene, 5%, δ_F -136.2, -141.2, *m/z* 147.98 (M^+100%); fluoro-4-chlorophenyltrimethylsilane, 4%, δ_F -112.2, *m/z* 204.99 (M^+100%), and 4-chlorophenyltrimethylsilane, 70%, *m/z* 184.6 (M^+100%).

6:20 Direct fluorination of *p*-fluorophenyltrimethylsilane in acetonitrile at -30°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of *p*-fluorophenyltrimethylsilane in acetonitrile ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (0.3g). Analysed by ^{19}F n.m.r., g.c. and mass spectrometry showed the reaction mixture to contain: *p*-difluorobenzene, 21%, δ_F -120.1, *m/z* 114.1 (M^+100%); 3,4-difluorophenyltrimethylsilane, 4%, δ_F -112, *m/z* 186.3 (M^+100%), and 4-fluorophenyltrimethylsilane, 75%, *m/z* 169.0 (M^+100%).

6:21 Direct fluorination of 1,4-bis(trimethylsilyl)benzene in $CFCl_3$ at 0^oC

Vacuum transfer of the reaction mixture obtained from the direct fluorination of 1,4-bis(trimethylsilyl)benzene in $CFCl_3$ ($20cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of starting material (2.2g). Analysis of the reaction mixture by ^{19}F n.m.r., g.c. and mass spectrometry indicated the presence of: *p*-difluorobenzene, 7.0%, δ_F -120, *m/z* 114.1 (M^+100%); *p*-fluorophenyltrimethylsilane, 8%, δ_F -112.2, *m/z* 168.2 (M^+98%); 2-fluoro-1,4-bistrimethylsilylbenzene, 4%, δ_F -107, *m/z* 240.7 (M^+100%), and unreacted 1,4-bis(trimethylsilyl)benzene, *m/z* 222.1 (M^+100%).

6:22 Direct fluorination of 1,3,5 tris(trimethylsilyl)benzene in acetonitrile at 10^oC

Vacuum transfer of the reaction mixture obtained from the direct fluorination of 1,3,5 tris(trimethylsilyl)benzene in acetonitrile ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (0.5g). Analysis of the volatiles by ^{19}F n.m.r., g.c. and mass spectrometry indicated the presence of: bis(trimethylsilyl)benzene, *m/z* 222.2 (M^+2.6%); fluorobis(trimethylsilyl)benzene, *m/z* 222.2 (M^+2.6%); difluoro(trimethylsilyl)benzene, 2 isomers, *m/z* 185.87 (M^+7.7%), *m/z* 186.0 (M^+4.4%); trifluoro(trimethylsilyl)benzene, 2 isomers, *m/z* 203.8 (M^+32.17), *m/z* 203.9 (M^+27.0%); difluoro bis(trimethylsilyl)benzene, 2 isomers, *m/z* 258.0 (M^+1.1%) *m/z* 258.1 (M^+2.5%), and other unidentified products, δ_F -80 to -150.

6:23 Direct fluorination of 1,2,4 tris(trimethylsilyl)benzene in acetonitrile at -30°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of 1,2,4 tris(trimethylsilyl)benzene in acetonitrile ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (0.5g). Analysis of the volatiles by ^{19}F n.m.r. and g.c. indicated a complex mixture of products, δ_F -90 to -160, which was not investigated further.

6:24 Direct fluorination of 1,2,4,5 tetrakis(trimethylsilyl)benzene in acetonitrile at 20°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of 1,2,4,5 tetrakis(trimethylsilyl)benzene in acetonitrile ($10cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of starting material (1.2g). Analysis of the volatiles by ^{19}F n.m.r., g.c. and mass spectrometry showed the reaction mixture to be a complex mixture of products, δ_F -64 to -160, which was not investigated further.

6:25 Direct fluorination of 2,5 bis(trimethylsilyl)thiophene in acetonitrile at -30°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of 2,5 bis(trimethylsilyl)thiophene in acetonitrile ($15cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (1.75g). Analysis of the volatiles by ^{19}F n.m.r. and

g.c. mass spectrometry did not indicate the presence of any fluorinated aromatic compounds.

6:26 Direct fluorination of 3,4-dichloro-2,5-bis(trimethylsilyl) thiophene in $CF_2ClCFCl_2$ at -30°C

Vacuum transfer of the reaction mixture obtained from the direct fluorination of 2,5 bis(trimethylsilyl)thiophene in acetonitrile ($15cm^3$) with elemental fluorine (0.56g, 0.015mol) resulted in the isolation of polymeric material (2.2g). Analysis of the volatiles by ^{19}F n.m.r. and g.c. mass spectrometry did not indicate the presence of the desired fluoroaromatic.

CHAPTER SEVEN

EXPERIMENTAL TO CHAPTER THREE

CHAPTER SEVEN

EXPERIMENTAL TO CHAPTER THREE

GENERAL PROCEDURE

See Chapter Six.

Investigation into the effect of pyridines on the direct fluorination of benzene and derivatives.

General procedure for direct fluorination of aromatic systems

A solution of the aromatic (0.01mol) and pyridine (0.01mol) in acetonitrile ($10cm^3$) was cooled to -30^0C under a flow of nitrogen, then elemental fluorine, as a 10% mixture in nitrogen (0.030mol), was bubbled through the solution at *ca* $1.5cm^3$ per minute. Once the addition was complete the solution was warmed to room temperature with nitrogen bubbling through the reaction mixture. Once at room temperature benzoltrifluoride (0.18g, 1.23mmol) was added as a n.m.r. marker. Reaction mixtures were analysed by ^{19}F n.m.r. using authentic samples as standards; ^{19}F n.m.r. data for standards are shown in Table 30 of Appendix 1. Yields* were calculated from ^{19}F n.m.r. integrations by comparison with the integral of the added benzoltrifluoride marker.

* Yields were calculated to the nearest 0.5%

7:1 Direct fluorination of benzene in acetonitrile at -30^0C

Investigation by ^{19}F n.m.r. of the reaction mixture obtained from

the direct fluorination of benzene (1.55g, 0.02mol) in acetonitrile ($10cm^3$) indicated the presence of fluorobenzene, 11.0%, δ_F -114.52, *para*-difluorobenzene, 7.5%, δ_F -120.8, *ortho*-difluorobenzene, 5.5%, δ_F -140.6, and *meta*-difluorobenzene, 4.0%, δ_F -111.4.

7:2 Direct fluorination of benzene and 4-ethylpyridine in acetonitrile at -30°C

Investigation by ^{19}F n.m.r.of the reaction mixture obtained from the direct fluorination of benzene (1.55g, 0.02mol) and 4-ethylpyridine (2.15g, 0.02mol) in acetonitrile ($10cm^3$) indicated the presence of fluorobenzene, 13.5%, δ_F -114.37, *para*-difluorobenzene, 1.0%, δ_F -120.6, *ortho*-difluorobenzene, 0.5%, δ_F 140.3, 2-fluoro-4-ethylpyridine, 5%, δ_F 70.0 (lit[47] δ_F -69.9), and a 4-ethylpyridine:fluorine complex, 10%, δ_F +40. Addition of potassium iodide resulted in the disapperance of the singlet at δ_F +40 and in the formation of iodine.

7:3 Direct fluorination of benzene and 4-methylpyridine in acetonitrile at -30°C

Investigation by ^{19}F n.m.r. of the reaction mixture obtained from the direct fluorination of benzene (1.55g, 0.02mol) and 4-methylpyridine (1.85g, 0.02mol) in acetonitrile ($10cm^3$) indicated the presence of fluorobenzene, 15.0%, δ_F -114.42, *para*-difluorobenzene, 1.5%, δ_F -120.5, *ortho*-difluorobenzene, 1.0%, δ_F 140.4, *meta*-difluorobenzene, 0.5%, 111.2, 2-fluoro-4-methylpyridine, 5%, δ_F 70.2 (lit[47] δ_F -70.3), and a 4-methyl-pyridine:fluorine complex, 6%, δ_F-39.7. Addition of potassium iodide resulted in the disappearance of the singlet at δ_F +39.7 and in the formation of iodine.

7:4 Direct fluorination of benzene and pyridine in acetonitrile at -30°C

Investigation by ^{19}F n.m.r. of the reaction mixture obtained from the direct fluorination of benzene (1.55g, 0.02mol) and pyridine (1.6g, 0.02mol) in acetonitrile (10cm^3), indicated the presence of fluorobenzene, 20.0%, δ_F -114.0, *para*-difluorobenzene, 1.0%, δ_F -120.6, *ortho*-difluorobenzene, 0.5%, δ_F -140.4, 2-fluoropyridine, 3%, δ_F -70.38 and a pyridine:fluorine complex, 7%, δ_F -38.0.

7:5 Direct fluorination of benzene and 2,6-dimethylpyridine in acetonitrile at -30°C

The direct fluorination of benzene (1.55g, 0.02mol) and 2,6-dimethylpyridine (2.15g, 0.02mol) in acetonitrile (10cm^3) resulted in extensive decomposition. Investigation by ^{19}F n.m.r. indicated the presence of fluorobezene, 2%, δ_F -114.37 *para*-difluorobenzene, 0.5%, δ_F -120.65, and an unidentified compound, δ_F -131.0, as the major product.

7:6 Direct fluorination of toluene in acetonitrile at -30°C

Investigation by ^{19}F n.m.r. of the reaction mixture obtained from the direct fluorination of toluene (1.85g, 0.02mol) in acetonitrile (10cm^3) by ^{19}F n.m.r. indicated the presence of *ortho*-fluorotoluene, 20.0%, δ_F -116.9, *para*-fluorotoluene, 13.0%, δ_F -119.6, and *meta*-fluorotoluene, 5.5%, δ_F -115.57.

7:7 Direct fluorination of toluene and pyridine in acetonitrile at -30°C

Investigation by ^{19}F n.m.r. of the reaction mixture obtained from the direct fluorination of toluene (1.85g, 0.02mol) and pyridine (1.6g, 0.02mol) in acetonitrile (10cm^3) indicated the presence of *ortho*-fluorotoluene, 9.5%, δ_F -116.7, *para*-fluorotoluene, 5.0%, δ_F -119.6, *meta*-fluorotoluene, 1.5%, δ_F -115.4, and 2-fluoropyridine, 21%, δ_F -70.2,

7:8 Direct fluorination of anisole in acetonitrile at -30°C

Investigation by ^{19}F n.m.r. of the reaction mixture obtained from the direct fluorination of anisole (2.2g, 0.02mol) in acetonitrile (10cm^3) indicated the presence of *ortho*-fluoroanisole, 17.0%, δ_F -136.0, *para*-fluoroanisole, 13.0%, δ_F -124.6, *meta*-fluoroanisole, 2.0%, δ_F -115.4, and 2,4-difluoroanisole, 3%, δ_F -129.3, -131.2.

7:9 Direct fluorination of anisole and pyridine in acetonitrile at -30°C

Investigation by ^{19}F n.m.r. of the reaction mixture, obtained from the direct fluorination of toluene (2.2g, 0.02mol) and pyridine (1.6g, 0.02mol) in acetonitrile (10cm^3) indicated the presence of *ortho*-fluoroanisole, 12.5%, δ_F -136.5, *para*-fluoroanisole, 7.0%, δ_F -124.5, 2,4-difluoroanisole, 1%, δ_F -129.1, -131.0 and 2-fluoropyridine, 8.5%, δ_F -70.8.

Direct fluorination of benzenesulphonyl chlorides

7:10 Direct fluorination of 4-fluorobenzenesulphonyl chloride

A solution of 4-fluorobenzenesulphonyl chloride (1.95g, 0.01mol) in acetonitrile (10cm^3) was cooled to -30^{0}C under a flow of nitrogen, then elemental fluorine, as a 10% mixture in nitrogen (0.56g, 0.015mol) was bubbled through the solution at *ca* 1.5 cm^3 per minute. Once the addition was complete the solution was warmed to room temperature with nitrogen bubbling through the reaction mixture. Analysis of the reaction mixture by ^{19}F n.m.r. and g.c./mass spectrometry showed the reaction to contain: 4-fluorobenzenesulphonyl chloride, 50%, δ_F -101.1, *m/z* 195.99 (*m*+ 100%); 3,4-difluorobenzenesulphonyl chloride, 50%, δ_F -123.87 and 131.6, mass spectrum 1.

7:11 Direct fluorination of 4-fluorobenzenesulphonyl chloride

This experiment was carried out under identical conditions as used above (experiment 7:1) except with twice the mass of fluorine (1.12g, 0.03mol). Once the fluorination was complete the solvent was removed under reduced pressure to leave a red oil (2.5g), which was shown by ^{19}F n.m.r. and g.c./mass spectrometry to be 4-Fluorobenzenesulphonyl chloride, <5%, and 3,4-difluorobenzenesulphonyl chloride as the only other aromatic product. The mixture was separated by preparative g.c. (column 10% SE 30) to give the desired 3,4-difluorobenzenesulphonyl chloride. (Found: C, 33.9; H, 2.0. $C_6H_4ClF_2O_2S$ requires C 33.7; H 1.85.%) ; n.m.r. spectrum 15 and mass spectrum 1.

7:12 Direct fluorination of benzenesulphonyl chloride

A solution of benzenesulphonyl chloride (2.1g, 0.01mol) in acetonitrile ($10cm^3$) was cooled to -30^0C under a flow of nitrogen, then elemental fluorine, as a 10% mixture in nitrogen (0.56g, 0.015mol) was bubbled through the solution at *ca* 1.5 cm^3 per minute. Once the addition was complete the solution was warmed to room temperature with nitrogen bubbling through the reaction mixture. Analysis of the reaction mixture by ^{19}F n.m.r. and g.c./mass spectrometry showed the reaction to contain: 3-fluorobenzenesulphonyl chloride, 18%, δ_F -107.1, (lit$^{202}\delta_F$ -107.3), electron impact, *m/z* 195.99 (*m*+1, 6.81%), 159.04 (-Cl, 100%), 92.5 ($-SO_2Cl$, 94.5); 2-fluorobenzenesulphonyl chloride, 1%, δ_F -127.1 (lit$^{202}\delta_F$ -127.3); electron impact, *m/z* 195.95 (*m*+1, 10.1%), 159.02 (-Cl, 100%), 92.55 ($-SO_2Cl$, 92.3) and starting material.

7:13 Direct fluorination of 4-chlorobenzenesulphonyl chloride

A solution of 4-chlorobenzenesulphonyl chloride (1.75g, 0.01mol) in acetonitrile ($10cm^3$) was cooled to -30^0C under a flow of nitrogen, then elemental fluorine, as a 10% mixture in nitrogen (0.56g, 0.015mol) was bubbled through the solution at *ca* 1.5 cm^3 per minute. Once the addition was complete the solution was warmed to room temperature with nitrogen bubbling through the reaction mixture. Analysis of the reaction mixture by ^{19}F n.m.r. showed the reaction to contain: 4-chloro-3-fluorobenzenesulphonyl chloride, 14.5%, δ_F -129.9d and unidentified products 7.4%, δ_F -150.74, and unidentified singlet δ_F -230

CHAPTER EIGHT

EXPERIMENTAL TO CHAPTER FOUR

CHAPTER EIGHT

EXPERIMENTAL TO CHAPTER FIVE

A GENERAL PROCEDURE

1 γ-Ray Initiated Reactions

Liquid reagents were introduced into a pyrex Carius tube (ca. 100 cm^3) and degassed. Any gaseous reagents were then transferred into the tube using normal vacuum line techniques. The tube was sealed with the reagents frozen (liquid air) and under vacuum. The tube was placed in a metal sleeve and, unless otherwise stated, was then irradiated with γ-rays to a total dose of ca. 10 Mrad at a temperature of 18^oC. The tube was opened while the contents were frozen (liquid air) and any gaseous species were transferred under vacuum.

2 Direct fluorination

See chapter 6 for general procedure.

Standard procedure for direct fluorination of amines and amides

A solution of the amine or amide (0.01mol) in an inert solvent was cooled to the desired temperature under a flow of nitrogen, then elemental fluorine, as a 10% mixture in nitrogen (0.015mol), was bubbled through the solution at *ca* 1.5cm^3 per minute. Once the addition was complete the solution was warmed to room temperature with nitrogen bubbling through the reaction mixture. Once at room temperature the solvent was removed under reduced pressure. Reaction mixtures were analysed by ^{19}F n.m.r. and mass spectrometry

B SYNTHESIS OF POTENTIAL ELECTROPHILIC FLUORINATING AGENTS OF THE N-F CLASS

8:1 Synthesis of 1-trimethylsilyl-2-(2H hexafluoropropyl)pyrrolidine (48)

A mixture of N-trimethylsilylpyrrolidine (9.6g, 0.067mol) and hexafluoropropene (4.0g, 0.026mol) was irradiated with γ-rays. Excess alkene (0.1g) was removed by transfer under vacuum (100mmHg) to leave a liquid (12.2g). The liquid was distilled under vacuum to give the desired 2-(2H-hexafluoropropyl)-N-(trimethylsilyl)pyrrolidine (48)[164], (4.8g, 63%); b.p. 86^{o}C at 24mmHg; (Found C, 50.0; H, 5.7; N, 4.96; F, 39.3. calc. for $C_{10}H_{17}F_6NSi$ C, 40.95; H, 5.8; N, 4.8; F, 38.9%); n.m.r. spectrum 16, i.r. spectrum 9, mass spectrum 2.

8:2 Direct fluorination of 1-trimethylsilyl-2-(2H hexafluoropropyl) -pyrrolidine in acetonitrile at -30^{o}C

The solvent was removed under reduced pressure to leave an orange oil (3.0g) which was analysed by ^{19}F n.m.r., ^{1}H n.m.r. and mass spectrometry to be a mixture of 2-(2H hexafluoropropyl)pyrrolidine[164], mass spectrum 3, 2-(2H hexafluoropropyl)-N-trimethylsilylpyrrolidine [164], mass spectrum 2, n.m.r. spectrum 16, and polymeric material.

8:3 Direct fluorination of 1-trimethylsilyl-2-(2H hexafluoropropyl) -pyrrolidine in acetonitrile at -30°C in the presence of calcium carbonate

The fluorination was carried out by the standard procedure with calcium carbonate (1.0g) present. The reaction mixture was filtered and then the solvent was removed under reduced pressure to leave an yellow oil (3.4g), which was analysed by ^{19}F n.m.r., ^{1}H n.m.r. and mass spectrometry to be a mixture of 2-(2H hexafluoropropyl)pyrrolidine[164], mass spectrum 3, 2-(2H hexafluoropropyl)-N-trimethylsilylpyrrolidine [164], mass spectrum 2, n.m.r. spectrum 16, and polymeric material.

8:4 Direct fluorination of 1-trimethylsilyl-2-(2H hexafluoropropyl) -pyrrolidine in $CFCl_3$ at -30°C

Solvent was removed under reduced pressure to leave a brown oil (2.9g), which was analysed by ^{19}F n.m.r., ^{1}H n.m.r. and mass spectrometry to be a mixture of 2-(2H hexafluoropropyl)pyrrolidine[164], mass spectrum 3, 2-(2H hexafluoropropyl)-N-trimethylsilylpyrrolidine[164], mass spectrum 2, n.m.r. spectrum 16, and polymeric material.

8:5 Synthesis of 2,5-bis(2H hexafluoropropyl)-N-(trimethylsilyl) pyrrolidine (50)

A mixture of N-trimethylsilylpyrrolidine (9.6g, 0.067mol) and hexafluoropropene (31.0g, 0.207mol) was irradiated with γ-rays. Excess alkene (15.6g) was removed by transfer under vacuum (100mmHg) to leave a liquid (21.0g) and a solid (1.2g). The liquid was distilled under

vacuum to give the desired 2,5-bis-(2H-hexafluoropropyl)-N-(trimethyl -silyl)pyrrolidine (50), (10.6g, 36%); b.p.76°C at 2mmHg; (Found C, 35.0; H, 3.6; N, 3.5; F, 51.4. $C_{13}H_{17}F_{12}NSi$ requires C, 35.25; H, 3.8; N, 3.2; F, 51.5%); n.m.r. spectrum 17, i.r. spectrum 10, mass spectrum 4. The solid was identified as (50) (1.2g, 4%) by comparison with spectra of the distilled material.

8:6 Direct fluorination of 2,5-bis(2H hexafluoropropyl)-N-(trimethyl -silyl)pyrrolidine in acetonitrile at -30°C

The solvent was removed under reduced pressure to leave a yellow oil (3.9g) which was shown to be a mixture of the desired N-fluoro 2,5-bis(2H hexafluoropropyl)pyrrolidine (40), 20%, and 2,5 bis(2H hexafluoropropyl)pyrrolidine (51), 25%, and 2,5-bis(2H hexafluoropropyl)-N-(trimethylsilyl)pyrrolidine (50), 55%, by ^{19}F n.m.r.. The desired (40) and the free amine (51) were isolated by preparative g.c. (10% SE30, 80°C); N-fluoro 2,5-bis(2H hexafluoropropyl)pyrrolidine (40), n.m.r. spectrum 18, mass spectrum 5, and 2,5-bis(2H hexafluoropropyl)pyrrolidine, (51), n.m.r. spectrum 19, mass spectrum 6. The addition of potassium iodide to N-fluoro-2,5-bis(2H hexafluoropropyl) pyrrolidine, (40), resulted in the disappearance of the singlet δ_F-33.77 assigned to the N-F bond and the oxidation of the potassium iodide to iodine, which is a chemical test for N-fluoro compounds.

8:7 Reaction of N-fluoro 2,5-bis(2H hexafluoropropyl)pyrrolidine with anhydrous potassium fluoride

Anhydrous potassium fluoride (0.5g) was added to a mixture of N-fluoro 2,5-bis(2H hexafluoropropyl)pyrrolidine (40) and 2,5 bis(2H

hexafluoropropyl) pyrrolidine (51), and the resulting reaction followed by g.c.. After 1.5hrs. all of the N-fluoro 2,5-bis(2H hexafluoropropyl) pyrrolidine (40) reacted to give a new compound (57), which using g.c. mass spectrometry was indicated to be formed by elimination of HF, mass spectrum 7, Electron impact, m/z 368.88 (M^+, 2.81%), 299.9 (M-CF_3, 19.33%), 267 (M-$CFHCF_3$, 2.69%), 217.93 (M-CF_2CFHCF_3, 100%), 67.01 (M-2x CF_2CFHCF_3, 6.72%). Further characterisation of compound was not attempted due to insufficient material.

8:8 Synthesis of 5-(2H hexafluoropropyl)pyrrolid-2-one (53)

A mixture of pyrrolid-2-one (8.5g, 0.1mol), acetone (10 cm^3) and hexafluoropropene (15.0g, 0.1mol) was irradiated with γ-rays. Excess alkene (2.1g) was removed by transfer under vacuum (100mmHg) to leave a colourless liquid (31.5g). The liquid was distilled under vacuum to give the desired 5-(2H-hexafluoropropyl)pyrrolid-2-one (53)[163], (18.3g, 78%); b.p.99°C at 0.5mmHg (lit[163] b.p. 96°C at 0.01mmHg); n.m.r. spectrum 20, i.r. spectrum 11.

11:9 Direct fluorination of 5-(2H hexafluoropropyl)pyrrolid-2-one in acetonitrile at -30°C

The solvent was removed under reduced pressure to leave an orange oil (2.5g) which was analysed by ^{19}F n.m.r., and ^{1}H n.m.r. to be a mixture of 5-(2H hexafluoropropyl)pyrrolid-2-one, n.m.r. spectrum 20, and polymeric material.

8:10 Synthesis of 1-trimethylsilyl pyrrolid-2-one

To a stirred solution of pyrrolid-2-one (17g, 0.2mol) and triethylamine (20g, 0.2mol) in dry diethyl ether (100cm^3), trimethylsilylchloride (38g, 0.35mol) was added dropwise under an atmosphere of nitrogen. Once the addition was completed the reaction mixture was heated under reflux for 12hrs, filtered under nitrogen and distilled under reduced pressure to yield the desired 1-trimethylsilyl-2-pyrrolid-2-one (22.2g, 72%); b.p.80-82^{o}C at 12mmHg.

8:11 Synthesis of 5-(2H hexafluoropropyl)-1-trimethylsilyl-pyrrolid-2-one

A mixture of 1-trimethylsilylpyrrolid-2-one (15.7g, 0.1mol) and hexafluoropropene (15.0g, 0.1mol) was irradiated with γ-rays. Excess alkene (3.1g) was removed by transfer under vacuum (100mmHg) to leave a colourless liquid (27.4g). The liquid was distilled under vacuum to give the desired 5-(2H-hexafluoropropyl)-1-trimethylsilylpyrrolid-2-one, (19.1g, 62%); b.p.97^{o}C at 10mmHg ; n.m.r. spectrum 21, i.r. spectrum 12, mass spectrum 8.

8:12 Direct fluorination of 5-(2H hexafluoropropyl)-1trimethylsilyl pyrrolid-2-one in acetonitrile at -30^{o}C

The solvent was removed under reduced pressure to leave a yellow oil (2.5g), which was analysed by ^{19}F n.m.r. to be a mixture of acyl fluorides derived from ring cleavage, δ_F +31 to +45 and polymeric material.

11:13 Synthesis of N-trimethylsilyl succinimide

Bis(trimethylsilyl)acetamide (25.0g, 0.123mol) was added dropwise to N-bromosuccinimide, with stirring, under an atmosphere of nitrogen. After stirring at room temperature for 6 hours the reaction mixture was distilled under reduced pressure to give the desired N-trimethylsilyl succinamide (15g, 80%); b.p.110^{o}C at 11mmHg (lit[172] b.p. 114^{o}C at 12mmHg).

8:14 Direct fluorination of N-trimethylsilyl succinimide in acetonitrile at -30^{o}C

The solvent was removed under reduced pressure to leave an colourless oil (2.0g) which oxidised potassium iodide to iodine, indicative of an N-F compound. ^{19}F n.m.r. showed one singlet at δ_F -59 which disappeared upon addition of potassium iodide.

CHAPTER NINE

EXPERIMENTAL TO CHAPTER FIVE

CHAPTER NINE

EXPERIMENTAL FOR CHAPTER FIVE

GENERAL PROCEDURES

Diels-Alder Reactions

Unless otherwise stated, liquid and gaseous reagents were introduced into a stainless steel tube (*ca.* 150cm^3) which was then sealed with the reagents frozen (liquid air) and under vacuum. The tube was heated at the required temperature in a thermostatically controlled rocking furnace. The tube was opened while the contents were frozen (liquid air) and any gaseous species were transferred under vacuum.

N.B. all stainless steel tubes used were fitted with a 2000 psi bursting disc.

9:1 Synthesis of 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene (55)

A mixture of furan (6.9g, 0.1mol), hexafluorobut-2-yne (16g, 0.1mol) and tetrahydrofuran (14g, 0.2mol) was heated at 100^{o}C in a rocking furnace for 12hrs. Excess alkyne (0.7g) was removed under vacuum (100mmHg) to leave a liquid (36.1g). This liquid was distilled to give the desired product 2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1] hepta-2,5-diene (55) (18.4g, 82%), b.p.118-122^{o}C at 760mmHg (lit.[184] 100-126^{o}C at 760mmHg). (Found: C, 41.8; H, 1.7; F, 50.1. Calc. for $C_8H_4F_6O$,

C, 41.75; H, 1.75; F, 50.1%); n.m.r. spectrum 22, i.r. spectrum 14, mass spectrum 9.

9:2 Synthesis of 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hept-2-ene (56)

2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (55) (18.2g, 0.08mol) was dissolved in tetrahydrofuran (100cm^3) and hydrogen -ated in the presence of a platinum catalyst on activated carbon (0.1g) in a Parr apparatus. The hydrogen uptake ceased sharply after the consumption of one equivalent of hydrogen. The reaction mixture was filtered through a bed of celite, then distilled to yield the desired product 2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (56) (18.1, 96%), b.p.124-126^{0}C at 760mmHg (lit.[184] 125-128^{0}C at 760mmHg). (Found: C, 41.4; H, 2.5; F, 48.9. Calc. for $C_8H_6F_6O$, C, 41.4; H, 2.5; F, 49.1%); n.m.r. spectrum 23,i.r. spectrum 15, mass spectrum 10.

9:3 Synthesis of 3,4-bis(trifluoromethyl)furan (57)

2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (56) (18.1g) was passed dropwise through a glass tube packed with glass wool at 400^{0}C in a slow current of nitrogen. The desired product 2,3-bis(trifluoro -methyl)furan (57) was collected in a dry ice trap (15.0g, 92%), b.p. 88^{0}C at 760mmHg (lit[184] 88-89^{0}C at 760mmHg). (Found: C, 35.8; H, 1.2; F, 56.3. Calc. for $C_6H_2F_6O$, C, 35.5; H, 1.0; F, 55.9%); n.m.r. spectrum 24, i.r. spectrum 16, mass spectrum 11.

9:4 Synthesis of 2,3,5,6-Tetrakis(trifluoromethyl)oxabicyclo[2.2.1]-hepta-2,5-diene (61)

A mixture of 3,4-bis(trifluoromethyl)furan (57) (3.0g, 0.017mol) and hexafluorobut-2-yne (3.35g, 0.02mol) was heated at 100°C in a rocking furnace for 6hrs to give a white solid. This was sublimed (at 50°C oil bath temperature) to give the desired product 2,3,5,6-tetrakis-(trifluoromethyl)oxabicyclo[2.2.1]hepta-2,5-diene (61) as white needles (5.12g, 85%).(Found: C, 32.5; F, 62.5. Calc. for $C_{10}H_2F_{12}O$, C, 32.75; H, 0.0054; F, 62.3%); n.m.r. spectrum 25,i.r. spectrum 17, mass spectrum 12.

9:5 Synthesis of 1,2,4,5-Tetrakis(trifluoromethyl)benzene (62)

Tetrahydrofuran (100cm^3) was added to titanium (IV) chloride (10cm^3, 0.60mol) at 0°C, with stirring ,under an atmosphere of nitrogen. To this stirred suspension lithium aluminium hydride (0.27g) and triethylamine (1.6g, 0.19mol) were added separately. After refluxing for 15 minutes the reaction mixture was allowed to cool to room temper-ature before 2,3,5,6-tetrakis(trifluoromethyl)oxabicyclo[2.2.1]-hepta-2,5-diene (61) (2g, 0.006mol) was added. Once the addition was completed the reaction was stirred at room temperature for 48hrs, then poured into water (40 cm^3) and extracted with dichloromethane. The dichloromethane solution was dried with magnesium sulphate and evaporated. The desired 1,2,4,5-tetrakis(trifluoromethyl)benzene[190] (62), (1.3g, 60%) was isolated by sublimation (oil bath temperature 60°C). (Found: C, 33.5; F, 64.8. calc. for $C_{10}H_2F_{12}$ C, 34.3; H, 0.005; F, 65.1%); n.m.r. spectrum 26, i.r. spectrum 18, mass spectrum 13.

9:6 Synthesis of 2,3-Bis(trifluoromethyl)-5,6-bis(methylcarboxy)-7-oxabicyclo[2.2.1]hepta-2,5-diene (64)

A mixture of 3,4-bis(trifluoromethyl)furan (57) (3.0g, 0.017mol) and dimethyl acetylene dicarboxalate (2.9g, 0.02mol) was heated at 100°C in a rocking furnace for 24hrs to give a brown solid. This was sublimed (at 50°C bath temperature) to give the desired product 2,3-bis(trifluoro-methyl)-5,6-bis(methylcarboxy)-7-oxabicyclo[2.2.1]hepta-2,5-diene (64) as white needles (5.1g, 91%) (m.p.68°C). (Found: C, 41.4; H, 2.2, F, 33.6. $C_{12}H_8F_6O_5$ requires C, 41.7; H, 2.3; F, 33.7%); n.m.r. spectrum 27, i.r. spectrum 19, mass spectrum 14.

9:7 Synthesis of 1-Methyl-2,3-bis(trifluoromethyl)-7-oxa-bicyclo[2.2.1]hepta-2,5-diene (58)

A mixture of 2-methylfuran (8.4g, 0.1mol), hexafluorobut-2-yne (16g, 0.1mol) and tetrahydrofuran (14g) was heated at 130°C in a rocking furnace for 24hrs. Excess alkyne (0.3g) was removed under vacuum (100mmHg) to leave a liquid (38.1g). This liquid was distilled to give the desired product 1-methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]-2,5-heptadiene (58) at 118°C at 760mm Hg (21.1g, 86%).(Found: C, 44.5; H, 2.45; F, 47.1. Calc. for $C_9H_7F_6O$, C, 44.2; H, 2.45; F, 46.7%); n.m.r. spectrum 28, i.r. spectrum 20, mass spectrum 15.

9:8 Synthesis of 1-Methyl-2,3-bis(trifluoromethyl)-7-oxa-bicyclo-[2.2.1]hept-2-ene (66)

1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (58) (21.0g, 0.086mol) was dissolved in tetrahydrofuran (100cm^3)

and hydrogenated in the presence of a platinum catalyst on activated carbon (0.1g) in a Parr apparatus. The hydrogen uptake ceased sharply after the consumption of one equivalent of hydrogen. The reaction mixture was filtered through a bed of celite and distilled at atmospheric pressure to yield the desired product 1-methyl-2,3-bis-(trifluoromethyl)-7-oxabicyclo[2.2.1]hep-2-tene (66) (19.8g, 93%) b.p.104°C at 50mmHg.(Found: C, 43.9; H, 3.2; F, 47.1. $C_9H_8F_6O$ requires C, 43.9; H, 3.25; F, 46.7%) n.m.r.spectrum 29, i.r. spectrum 21, mass spectrum 16.

9.9 Synthesis of 2-Methyl-3,4-bis(trifluoromethyl)furan (67)

1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (66) (20.0g, 0.05mol) was passed dropwise through a glass tube packed with glass wool at 400°C in a slow current of nitrogen. The desired product 2-methyl-3,4-bis(trifluoromethyl)furan (67) was collected in a dry ice trap as a colourless liquid (10.5g, 96%) b.p.88°C at 760mmHg. (Found: C, 38.8; H, 2.0; F, 52.7. $C_7H_4F_6O$ requires C, 38.6; H, 1.8; F, 52.3%); n.m.r. spectrum 30, i.r. spectrum 22, mass spectrum 17.

9:10 Synthesis of 2,3-Bis(trifluoromethyl)-4-methylphenol (68)

A mixture of 1-methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene (58) (1g, 0.04mol) and boron trifluoride etherate (0.05mol) was stirred at room temperature for 3hrs, then neutralized with aqueous potassium carbonate and extracted with ether . The ether solution was dried over magnesium sulphate and evaporated under reduced pressure to leave an orange solid (0.71g). This was sublimed (at 100°C

oil bath temperature) to give the desired product 2,3-bis(trifluoromethyl)-4-methylphenol (68) as white needles (0.58g, 64%). (Found: C, 44.4; H, 2.1; F, 46.7 $C_9H_4F_6O$ requires C, 44.25; H, 2.4; F, 46.7%); n.m.r. spectrum 31, i.r. spectrum 23, mass spectrum 18.

9:11 Synthesis of 1-(Hydroxymethyl)2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (73)

A mixture of 2-(hydroxylmethyl)furan (10.g, 0.1mol), hexafluorobut-2-yne (16g, 0.1mol) and tetrahydrofuran (14g, 0.2mol) was heated at 130°C in a rocking furnace for 24hrs. Excess alkyne (0.5g) was removed under vacuum (100mmHg) to leave a liquid (40.0g). This liquid was distilled to give the desired product 1-(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (73) (23.9g, 92%), b.p.142°C at 760mmHg. (Found: C, 41.2; H, 2.1; F, 44.4. $C_9H_6F_6O_2$ requires C, 41.5; H, 2.3; F, 43.9%) ; n.m.r. spectrum 32, i.r. spectrum 24, mass spectrum 19.

9:13 Synthesis of 1-(Hydroxymethyl)2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (75)

1-(Hydroxymethyl)2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (73) (18.2g, 0.07mol) was dissolved in tetrahydrofuran (100 cm^3) and hydrogenated in the presence of a platinum catalyst on activated carbon (0.1g) in a Parr apparatus. The hydrogen uptake ceased sharply after the consumption of one equivalent of hydrogen. The reaction mixture was filtered through a bed of celite the distilled at

reduced pressure to yield the desired product 1-(hydroxymethyl)2,3-bis (trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (75) at 105°C at 50mmHg (17.5g, 90%).(Found: C, 41.0; H, 2.9, F, 43.4 $C_9H_8F_6O_2$ requires C, 41.2 ; H, 3.0; F, 43.5%) n.m.r. spectrum 33, i.r. spectrum 25, mass spectrum 20.

9:14 Synthesis of 2-(Hydroxymethyl)3,4-bis(trifluoromethyl)furan (77)

1-(Hydroxymethyl)2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hept-2-ene (75) (16.0g, 0.061mol) was passed through a glass tube packed with glass wool at 400°C dropwise in a slow current of nitrogen. The desired product 1-(hydroxymethyl)2,3-bis(trifluoromethyl)furan (77) was collected in a dry ice trap (13.8g, 97%) B.p.108°C at 760mmHg. (Found: C, 35.7; H, 1.8; F, 49.2 $C_7H_4F_6O_2$ requires C, 35.9; H, 1.7; F, 48.7%) n.m.r. spectrum 34, i.r. spectrum 26, mass spectrum 21.

9:15 Synthesis of 2,3-Bis(trifluoromethyl)benzyl alcohol (79)

Tetrahydrofuran (100cm^3) was added to titanium (IV) chloride (10cm^3, 0.60mol) at 0°C, with stirring, under an atmosphere of nitrogen. To this stirred suspension lithium aluminium hydride (0.27g) and triethylamine (1.6g, 0.19mol) were added separately. After refluxing for 15 minutes the reaction mixture was allowed to cool to room temperature before 1-(hydroxymethyl)2,3-bis(trifluoromethyl)-7-oxa-bicyclo[2.2.1]hepta-2,5-diene (73) (2g, 0.7mmol) was added. Once the addition was completed the reaction was stirred at room temperature for 48hrs, then poured into water (40cm^3) and extracted with dichloro-methane. The dichloromethane solution was dried with magnesium sulphate

and evaporated. The desired product was isolated by preparative g.c. (10% SE30 100°C) (12g, 65%). (Found: C, 4.5; H, 2.4; $C_9H_6F_6O$ requires C, 44.2; H, 2.45; F, 46.72%); n.m.r. spectrum 35, i.r. spectrum 27, mass spectrum 22.

9:16 Synthesis of 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxa-bicyclo[2.2.1]hepta-2,5-diene (74)

A mixture of 2,5-Di(hydroxymethyl)furan (12.8g, 0.1mol), hexafluoro-but-2-yne (16g, 0.1mol) and tetrahydrofuran (20g) was heated at 100°C in a rocking furnace for 24hrs. Excess alkyne (0.3g) as removed under vacuum (100 mmHg) to leave a colourless liquid (48.4g). Solvent was removed under reduced pressure to give an off white solid, which was recrystalised from methanol to give the desired product 1,4-di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (74) (25.1g, 87%), m.p. 130°C (Found: C, 41.3; H, 2.75; F, 39.2. $C_{10}H_8F_6O_3$ requires C, 41.3; H, 2.75; F, 39.3%) ; n.m.r. spectrum 36, i.r. spectrum 28, mass spectrum 23.

9:17 Synthesis of 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxa-bicyclo[2.2.1]hept-2-ene (76)

1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene (74) (20.2g, 0.07mol) was dissolved in tetrahydrofuran (100cm^3) and hydrogenated in the presence of a platinum catalyst on activated carbon (0.1g) in a Parr apparatus. The hydrogen uptake ceased sharply after the consumption of one equivalent of hydrogen. The

reaction mixture was filtered through a bed of celite and the solvent removed under reduced pressure to give an off-white solid which was recrystallised from methanol to give the desired product 1,4-di(hydroxy-methyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (76) (17.3g, 85%), m.p.152°C. (Found: C, 41.1; H, 3.4, F, 39.5 $C_{10}H_{10}F_6O_3$ requires C, 41.0 ; H, 3.4; F, 39.0%) n.m.r. spectrum 37, i.r. spectrum 29, mass spectrum 24.

9:18 Synthesis of 2,5-Di(hydroxymethyl)-3,4-bis(trifluoromethyl)furan (78)

1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1] hept-2-ene (76) (8.0g, 0.027mol) was passed dropwise through a glass tube packed with glass wool at 400°C in a slow current of nitrogen. The desired product 1,5-di(hydroxymethyl)-2,3-bis(trifluoromethyl)furan (78) was collected in a dry ice trap (6.85g, 96%) m.p.64°C. (Found: C, 36.3; H, 2.3; F, 43.2 $C_8H_6F_6O_3$ requires C, 36.35; H, 2.3; F, 43.1%) n.m.r. spectrum 37, i.r. spectrum 30, Mass spectrum 25.

12:19 Synthesis of 2-bromofuran

A mixture of 2-bromofuroic acid (5g, 0.026mol), quinoline (10g) and copper bronze (4g) were place in a distillation apparatus and lowered into a Woods metal bath at 200°C. The desired 2-bromofuran distilled into the receiving flask. Once the decarboxylation was completed a second portion of the 2-bromofuroic acid (5g) was added to the reaction mixture and the process repeated. The decarboxylation of the 2-bromo furoic acid (20g, 0.15mol) went smoothly to the desired 2 bromofuran (6.1g, 41%).

9:20 Synthesis of 1-Bromo-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1] hepta-2,5-diene (81)

A mixture of 2-bromofuran (6.4g, 0.045mol), hexafluorobut-2-yne (8g, 0.05mol) and tetrahydrofuran (14g, 0.2mol) was heated at 140°C in a rocking furnace for 24hrs. Excess alkyne (0.4g) was removed under vac -uum (100mmHg) to leave a dark brown liquid (28.4g). The desired product 1-bromo-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (81) (1.5g, 11%), was isolated by preparative g.c. (10% Se 30, 110°C) (Found: C, 33.0; H, 1.4; F, 39.4 $C_8H_3BrF_6O$ requires C, 32.9; H, 1.0; F, 39.05%) n.m.r. spectrum 39, i.r. spectrum 31, mass spectrum 26.

9:21 Synthesis of 1-Formyl-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hepta-2,5-diene

A mixture of furalaldehyde (4.45g, 0.05mol), hexafluorobutyne (8g, 0.05mol) and tetrahydrofuran (14g) was heated at 140°C in a rocking furnace for 24hrs. Excess alkyne (2.2g) was removed under vacuum (100 mmHg) to leave a dark brown liquid (18.1g). This liquid was shown to be a mixture of products by g.c./mass spectrometry and attempted isolation of the desired 1-formyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene by distillation and preparative gc failed. Mass spectrum 27.

12:22 2-Trimethylstanylfuran

To a stirred solution of furan (4g, 0.06mol) in hexane (50cm^3) at room temperature a solution of butyl lithium (0.06mol) was added dropwise. After heating at reflux for 2 hours the reaction mixture was

cooled to room temperature and a solution of trimethyltin chloride (12.5g,0.06mol) in ether added. Once the addition was complete the reaction was stirred for a further 2 hours, then poured onto ice and extracted with ether. The extract was dried over magnesium sulphate and distilled at reduced pressure to give 1-trimethyltinfuran (6.2g, 44.5%), b.p.74^{0}C at 20mmHg.

9:23 Synthesis of 1-Trimethylstanyl-2,3-bis(trifluoromethyl)-7-oxa-bicyclo[2.2.1]hepta-2,5-diene (82)

A mixture of trimethyltinfuran (5.8g, 0.025mol), hexafluorobut-2-yne (4g, 0.025mol) and tetrahydrofuran (20g) was heated at 100^{0}C in a rocking furnace for 24hrs. Excess alkyne (0.3g) as removed under vacuum (100 mmHg) to leave a brown liquid (29.7g). Solvent was removed under reduced pressure to give a brown solid, 1-trimethylstanyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (82); n.m.r. spectrum 40, i.r. spectrum 32, mass spectrum 28.

9:24 *Trans*-2H-Heptafluorobut-2-ene[193]

Hexachloro-1,3-butadiene (133g, 0.51mol) was added over a period of 3 hrs, to a mixture of N-methyl-2-pyrrolidone (750cm^{3}), and potassium fluoride (270g, 4.6mol) contained in a flask at 200^{0}C which was fitted with a stirrer and reflux condenser connected to a trap at -183^{0}C. The temperature was maintained for a further 4 hr while the product (54.3g) collected in the trap. Fractional distillation of the product gave *trans*-2H-heptafluorobut-2-ene (52.7g, 58%) containing a trace of the *cis* isomer: i.r.spectrum 33.

9:25 Synthesis of 5-Fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hept-2-ene (84)

A mixture of furan (4.5g, 0.66mol), *trans*-2H-heptafluorobut-2-ene (12g, 0.066mol) and tetrahydrofuran (14g) was heated at 120°C in a rock-ing furnace for 24hrs. Excess alkene (0.2g) was removed under vacuum (100mmHg) to leave a liquid (30.3g). The solvent was then removed by distillation to give two pairs of enantiomers of the desired 5-fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84) (13.7g, 78%). The two sets of isomers were isolated by preparative g.c. (10% SE30, 50°C).

Trans-5-fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84) (46.8%) (Found: C, 38.8; H, 2.11; F, 52.9. $C_8H_5F_7O$ requires C, 38.5; H, 2.0; F, 53.2%) n.m.r. spectrum 41, i.r. spectrum 34, mass spectrum 29.

Trans-5-fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84) (31.2%) (Found: C, 38.7; H, 2.22: $C_8H_5F_7O$ requires C, 38.5; H, 2.0%) n.m.r. spectrum 42, i.r. spectrum 35, mass spectrum 30.

9:26 Dehydrofluorination of 5-fluoro-5,6-bis trifluoromethyl)-7-oxa-bicylo[2.2.1]hept-2-ene (84)

5-Fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (3.75g, 0.015mol) was added dropwise to a stirred solution of potassium tertiary butoxide (3.4g, 0.031mol) in tertiary butanol. After refluxing for 15 minutes the reaction mixture was poured into water (15cm^3), extracted with ether, dried over magnesium sulphate and evaporated to give a black liquid (4.1g). The presence of the desired

compound 2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-2,5-heptadiene (55) (<5%) was shown to be present by gc/mass spectrometry, mass spectrum 9.

12:27 *Trans*-5-Fluoro-5,6-bis(trifluoromethyl)-7-bicylo[2.2.1]hept-7-ene (85)

A mixture of cyclopentadiene (4.35g, 0.066mol), *trans*-2H-heptafluorobut-2-ene (12g, 0.066mol) and tetrahydrofuran (14g) was heated at 120°C in a rocking furnace for 24hrs. Excess alkene (0.1g) was removed under vacuum (100mmHg) to leave a liquid (30.1g). The reaction mixture was distilled at reduced pressure to give a mixture of the two entantiomers of the desired *Trans*-5-fluoro-5,6-bis(trifluoromethyl)-7-bicylo-[2.2.1]hept-2-ene (85) (13.9g, 89%), bp. 85.6°C at 105mmHg. (Found: C, 44.0; H, 2.96; F, 53.2 $C_9H_7F_7$ requires C, 43.6; H, 2.8; F, 53.6%); n.m.r. spectrum 41, i.r. spectrum 36, mass spectrum 31.

9:28 Dehydrofluorination of 5-fluoro-5,6-bis(trifluoromethyl)-7-bicylo [2.2.1]-2-heptene (85)

Trans-5-Fluoro-5,6-bis(trifluoromethyl)-7-bicyclo[2.2.1]-2-heptene (85) (3.7g, 0.015mol) was added dropwise to a stirred solution of potassium tertiary butoxide (3.35g, 0.035mol) in tertiary butanol (25 cm^3). After refluxing for 1 hour the reaction mixture was poured into water (15cm^3), extracted with ether, dried over magnesium sulphate and evaporated to give a yellow liquid (3.8g). The desired compound 2,3-Bis(trifluoro- methyl)-7-bicyclo[2.2.1]-2,5-heptadiene (86) (55%) was isolated by preparative g.l.c (10% SE30 100°C) (Found: C, 47.7; H, 2.6; F, 50.5 calc. for $C_9H_6F_6$ C, 47.4; H, 2.6;F, 50.0 %); n.m.r. spectrum 44, i.r. spectrum 37, mass spectrum 32.

9:29 Synthesis of 3,3,3,Trifluoropropyne[195]

Zinc dust (36.0g, 0.5mol), fused zinc chloride (3.4g, 0.025mol) and N,N dimethylacetamide (200cm^3) were placed in a 500cm^3 three neck flask fitted with a thermometer, pressure equalizing dropping funnel and a water cooled condenser leading to a dry ice acetone cold trap. The reaction mixture was the heated to 100^{o}C with stirring and the slow addition of 1,1,2-trichloro-3,3,3 trifluoropropene (28g, 0.24mol) was started. An exothermic reaction occurred, raising the temperature above 100^{o}C. Heating was discontinued and the temperature was maintained above 95^{o}C by adjusting the olefin addition rate. Once the addition was completed the reaction mixture was cooled to 50^{o}C and water (100cm^3) was added slowly. The temperature was maintained between 50-60^{o}C by the use of a heating mantle and the gaseous product (13.2g, 58%), was collected in the dry ice acetone cold traps, i.r. spectrum 38.

9:30 2-(Trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (88)

A mixture of furan (6.9g,0.1mol), 3,3,3,trifluopropyne (8.2g, 0.1mol) and tetrahydrofuran (24g) was heated at 100^{o}C in a rocking furnace for 24hrs. Excess alkyne (0.2g) was removed under vacuum (100mmHg) to leave a liquid (31.1g). This liquid was distilled under reduced pressure to give the desired product 2-(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (88) at 117^{o}C at 760mm Hg (7.51g, 46%). (Found: C, 54.1; H, 3.8; F, 36.7 $C_7H_5F_3O$ requires C, 51.8; H, 3.1; F,35.1%); n.m.r. spectrum 45, i.r. spectrum 39, mass spectrum 34.

9:31 Synthesis of Benzotrifluoride

Tetrahydrofuran ($100cm^3$) was added to titanium (IV) chloride ($10cm^3$, 0.60mol) at 0^oC with stirring under an atmosphere of nitrogen. To this stirred suspension, lithium aluminum hydride (0.27g) and tri-ethylamine (1.6g, 0.015mol) were added separately. After refluxing for 15 minutes the reaction mixture was allowed to cool to room temperature before 2-(trifluoromethyl)-7-oxabicyclo [2.2.1]-2,5-heptadiene (88) (2g, 0.012mol) was added. Once the addition was completed the reaction was stirred at room temperature for 48hrs, then poured into water ($40cm^3$) and extracted with dichloromethane. The dichloromethane solution was dried with magnesium sulphate and evaporated. The desired product was isolated by preparative g.c. (10% SE30, 90^oC) (80%); δ_F -62.2, i.r. spectrum 38, mass spectrum 35.

9:32 Synthesis of 1,4-Di(hydroxymethyl)-2-trifluoromethyl-7-oxabicyclo [2.2.1]hept-2-ene (90)

A mixture of 2,5-Di(hydroxymethyl)furan (4.2g, 0.033mol), 3,3,3,tri-fluoropropyne (3.1g, 0.033mol) and tetrahydrofuran (20g) was heated at 120^oC in a rocking furnace for 24hrs. Excess alkyne (0.5g) was removed under vacuum (100mmHg) to leave a liquid. Solvent was then removed under reduced pressure to give an orange gum (8.1g) which was purified by column chromatography (eluent chloroform 80%, methanol 20%) to give the desired 1,4-di(hydroxymethyl)-2-trifluoromethyl-7-oxabicyclo[2.2.1]-hept-2,5-ene (90) (4.5g, 62%); n.m.r. spectrum 46, i.r. spectrum 41, mass spectrum 36.

9:33 Attempted synthesis of 1,4-Di(hydroxymethyl)-2-trifluoromethyl-7-oxabicyclo[2.2.1]hept-2,5-ene

1,4-Di(hydroxymethyl)-2-trifluoromethyl-7-oxabicyclo[2.2.1]-2,5-heptene (90) (3g, 0.015mol) was dissolved in tetrahydrofuran ($75cm^3$) and hydrogenated in the presence of a platinum catalyst on activated carbon (0.1g) in a Parr apparatus. The hydrogen uptake did not cease after the consumption of one equivalent of hydrogen, however after the consumption of 1.5 equivalents of hydrogen the reaction was stopped. The reaction mixture was filtered through a bed of celite and the solvent removed under reduced pressure to give a brown gum (3.1g) which was indicated to be 1,4 di(hydroxymethyl)-2-trifluoromethyl-7-oxabicyclo [2.2.1]heptane by infra red spectroscopy. No further investigation was attempted.

9:34 Synthesis of 2,3-bis(trifluoromethyl)-1,4-oxoquinoline (93)

A mixture of 2,1-benzisoxazole (2.5g, 0.021mol), hexafluoro-but-2-yne (4g, 0.025mol) and tetrahydrofuran was heated at $60^{o}C$ in a rocking furnance for 18hrs. Excess alkyne (0.4g) was removed under vacuum (100mmHg) to leave a dark brown liquid (12.1g). Solvent was removed under reduced pressure to give a brown oil (2.2g), which was shown to be a mixture of the desired 2,3-bis(trifluoromethyl)-1,4-oxoquinoline (93) and its isomer 8,9-bis(trifluoromethyl)-3-aza-4-oxatricyclo[5.2.2.0.$^{2.6}$] undeca-2,5,8,10-tetraene (94) by g.c./mass spectrometry, i.r. spectrum 42. The two isomers were isolated by preparative g.c. (10% SE30, $100^{o}C$); (93) (60%); n.m.r. spectrum 47, mass spectrum 37; (94) (20%); n.m.r. spectrum 48, mass spectrum 38.

9:35 Synthesis of 2,3-bis(trifluoromethyl)quinoline (95)

Tetrahydrofuran ($100cm^3$) was added to titanium (IV) chloride ($10cm^3$, 0.60mol) at 0^oC, with stirring under an atmosphere of nitrogen. To this stirred suspension lithium aluminium hydride (0.27g) and triethylamine (1.6g, 0.19mol) were added separately. After refluxing for 15 minutes the reaction mixture was allowed to cool to room temperature before a mixture of 2,3-bis(trifluoromethyl)-1,4-oxo-quinoline (93) and its isomer (94) (1g) was added. Once the addition was completed the reaction was stirred at room temperature for 48hrs, then poured into water ($40cm^3$) and extracted with dichloromethane. The dichloromethane solution was dried with magnesium sulphate and evaporated under reduced pressure. The desired 2,3-bis(trifluoro-methyl)quinoline (95) was isolated by preparative g.c. (10% SE30 100^oC), n.m.r. spectrum 49, mass spectrum 39.

9:36 Synthesis of 2,3,6-trimethyl-3-trifluoromethylpyridine

A mixture of 2,4,5-trimethyloxazole (4g, 0.036mol) and trfluoro-propene (6g, 0.06mol) was heated at 140^oC in a rocking furnance for 24hrs. Excess alkene (4.8g) was removed under vacuum (100mmHg) to leave a brown oil (5.2g), which was shown to contain the desired product and HF by ^{19}F n.m.r.. The desired 1,2,5-trimethyl,3-trifluoromethylpyridine was isolated as its HF salt upon cooling (1.1g, 13%); n.m.r. spectrum 50, i.r. spectrum 43, mass spectrum 40.

9:36 Synthesis of Methylacetylalaninate (99)

A mixture of methylalanate hydrogen chloride (30g, 0.18mol) and acetylchloride (50g, 0.53mol) was refluxed with stirring for 8hrs. Distillation under vacuum gave the desired methylacetylalaninate (99) (22.1g, 85%), b.p. 121-123°C at 9mmHg (Lit[199] 126-127°C at 10mmHg). (Found: C, 49.3; H, 7.75; N, 9.2. calc. for $C_6H_{11}NO_3$ C, 49.65; H, 7.6; N,9.65%)

12:37 Synthesis of 2,4-dimethyl-5-methoxyoxazole (98)

A mixture of methylacetylalanate (99) (20g, 0.14mol) and phosphorous pentoxide (65g, 0.46mol) in chloroform (150cm^3) was refluxed for 12hrs. After cooling to room temperature the reaction mixture was neutralised with sodium hydroxide solution and continously extracted with chloroform. The extract was dried over magnesium sulphate and distilled under vacuum to give the desired 2,4 dimethyl-5-methoxy oxazole (11.5g, 59%), b.p.74-76°C at 48mmHg (lit[199] 78-80°C at 50mmHg). (Found: C, 56.3; H, 7.3; N, 11.2. calc. for $C_6H_9NO_2$ C, 56.75; H, 7.1; N,11.2%), i.r. spectrum 45.

9:38 Attempted synthesis of 2,6-Dimethyl-3-trifluoromethyl-5-hydroxy-pyridine

A thick walled, small diameter Carius tube was charged with 2,4-dimethyl-5-methoxy oxazole (0.65g, 0.005mol) and trifluoropropene (0.5g, 0.005mol) and heated to 130°C for 6hrs. Excess alkene (0.27g) was removed under vacuum (100mmHg) to leave a pale yellow liquid (0.87g). Analysis by g.c./mass spectrometry indicated a mixture of

starting oxazole and cycloaddition adducts (102) and (103) mass spectra 41 and 42.

9:39 Synthesis of 2,6-Dimethyl,3-trifluoromethyl,5-hydroxypyridine

A thick walled, small diameter Carius tube was charged with 2,4-dimethyl-5-methoxyoxazole (0.65g, 0.005mol) and trifluoropropene (0.5g, 0.005mol) was heated to 130^{o}C for 14hrs. Excess alkene (0.1g) was removed under vacuum (100mmHg) to leave an orange solid (0.87g). This solid was shown to be a mixture of 2,6-dimethyl-3-trifluoromethyl-5-hydroxypyridine 101, and 2,6-dimethyl-4-trifluoromethyl-5-hydroxy-pyridine 100 by g.c./mass spectrometry. Recrystalisation from chlorofrom gave a white solid, which was a mixture of the two isomers (Found: C, 50.0; H, 4.0; F, 29.2; N, 7.0. $C_8H_8F_3NO$ requires C, 50.25; H, 4.2; F,29.8 ;N,7.3%) n.m.r. spectrum 51, i.r. spectrum 45, mass spectrum 42, 43.

APPENDIX 1

N.M.R. SPECTRA

APPENDIX 1

N.M.R. SPECTRA

1. Benzotrifluoride.
2. Fluorobenzene.
3. *otho*-Difluorobenzene.
4. *meta*-Difluorobenzene.
5. *para*-Difluorobenzene.
6. *ortho*-Fluorotoluene.
7. *meta*-Fluorotoluene.
8. *para*-Fluorotoluene.
9. *ortho*-Fluoroanisole.
10. *meta*-Fluoroanisole.
11. *para*-Fluoroanisole.
12. *ortho*-Fluoronitrobenzene.
13. *meta*-Fluoronitrobenzene.
14. *para*-Fluoronitrobenzene.
15. 3,4-Difluorobenzenesulphonyl chloride (38).
16. 2-(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (48).
17. 2,5-bis(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (50).
18. N-Fluoro-2,5-bis(2H hexafluoropropyl)pyrrolidine (40).
19 2,5-bis(2H hexafluoropropyl)pyrrolidine.
20. 2-(2H hexafluoropropyl)pyrrolid-2-one (53).
21. 2-(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolid-2-one.
22. 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (55).
23. 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (56).
24. 3,4-Bis(trifluoromethyl)furan (57).

25. 2,3,5,6-Tetrakis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (61).
26. 2,3,5,6-Tetrakis(trifluoromethyl)benzene (62).
27. 2,3-Bis(trifluoromethyl)-5,6-di(methylcarboxy)-7-oxabicyclo[2.2.1]hepta-2,5-diene (64).
28. 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (58).
29. 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (66).
30. 2-Methyl-3,4-bis(trifluoromethyl)furan (67).
31. 2,3-Bis(trifluoromethyl)-4-methylphenol (68).
32. 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (73).
33. 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (75).
34. 2-(Hydroxymethyl)-3,4-bis(trifluoromethyl)furan (77).
35. 2,3-Bis(trifluoromethyl)benzyl alcohol (79).
36. 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (74).
37. 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (76).
38. 2,5-Di(hydroxymethyl)-3,4-bis(trifluoromethyl)furan (78)
39. 1-Bromo-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (81)
40. 1-(Trimethylstanyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (82).
41 *Trans*-5-fluoro,5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84)

42. *Trans*-5-fluoro,5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84)
43. *Trans*-5-Fluoro,5,6-bis(trifluoromethyl)-7-bicyclo[2.2.1]hept-2-ene (85).
44. 2,3-Bis(trifluoromethyl)-7-bicyclo[2.2.1]hepta-2,5-diene (86).
45. 2-(Trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (88).
46. 1,4-Di(hydroxymethyl)-2-(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (90).
47. 2,3-Bis(trifluoromethyl)-1,4-oxo-quinoline (93).
48. 8,9-bis(trifluoromethyl)-3-aza-4-oxatricyclo[5.2.2.$0^{2.6}$]undeca-2,5,8,10-tetraene (94).
49. 2,3-Bis(trifluoromethyl)quinoline (95).
50. 2,3,6-Trimethyl-4-trifluoromethylpyridine (97).
51 2,6-Dimethyl-3-trifluoromethyl-5-hydroxypridine (100) and 2,6-dimethyl-4-trifluoromethyl-5-hydroxypyridine (101).

Unless otherwise stated, spectra were recorded of samples in solution in deuterochloroform ($CDCl_3$).

For proton spectra, chemical shifts are quoted in ppm relative to external tetramethylsilane with downfield shifts positive. For fluorine spectra, chemical shifts are quoted in ppm relative to external trichlorofluoromethane with upfield shifts negative.

For the splitting patterns of the n.m.r. resonances the following abbreviations are used:

S = singlet

D = doublet

T = triplet

Q = quartet

M = multiplet

For an AB system, chemical shifts are quoted as the 'centre of gravity' or $\pm$ $V/2$ from the mid-piont of the pattern, calculated from:

$$(\delta_1 - \delta_3) = (\delta_2 - \delta_4) = \sqrt{(\Delta\nu)^2 + J^2}$$

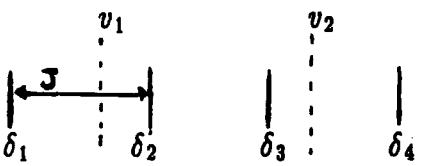
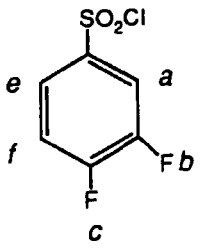


Table 30 ^{19}F n.m.r. of authentic samples

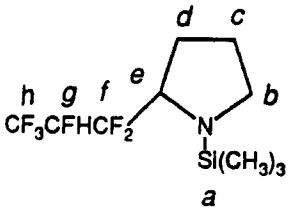
n.m.r. number	Compound	δ_F
1	Benzotrifluoride	-62.1
2	Fluorobenzene	-114.0
3	*ortho*-Difluorobenzene	-140.2
4	*meta*-Difluorobenzene	-111.1
5	*para*-Difluorobenzene	-120.1
6	*ortho*-Fluorotoluene	-116.8
7	*meta*-Fluorotoluene	-119.1
8	*para*-Fluorotoluene	-115.6
9	*ortho*-Fluoroanisole	-136.1
10	*meta*-Fluoroanisole	-105.1
11	*para*-Fluoroanisole	-121.4
12	*ortho*-Fluoronitrobenzene	-120.8
13	*meta*-Fluoronitrobenzene	-111.5
14	*para*-Fluoronitrobenzene	-105.1

No.15 3,4-Fluorobenzenesulphonyl chloride (38)



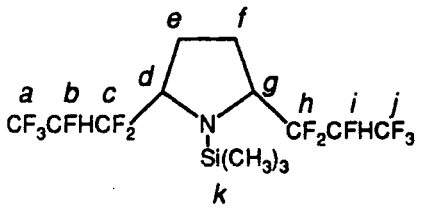
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
7.7	S(Board)	1	*a*
8.17	D(board)	2	*d*,*e*
^{19}F			
-123.9	S	1	*b*,*c*
-131.4	S	1	

No.16 2-(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (48)



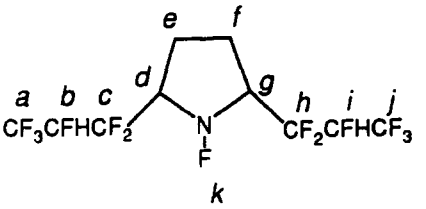
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
0.17	S	9	*a*
2.00	M(board)	4	*c*, *d*
3.02	M	2	*b*
3.23	M		
3.86	M	1	*e*
4.93	D of M, J_{HF}= 45	1	g
^{19}F			
-74.7	S	3	*h*
-116.6	S	2	*f*
-121.8	AB, J_{AB} =271		
-124.6			
-210.6	D, J_{HF} =42	1	*g*
-211.7	D, J_{HF} =38		

No.17 2,5-bis(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (50)



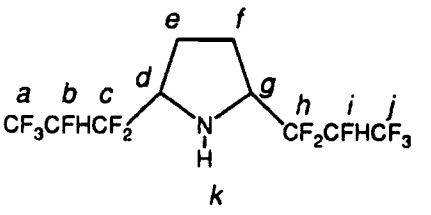
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
0.21	S	9	*k*
2.11	M(board)	4	*e,f*
3.59 to 3.90	M	2	*d,g*
4.03	M(major isomer)		
4.66 to 5.31	M	2	*b,i*
4.94	D of M, J_{HF}= 44 (major isomer)		
^{19}F			
-74.8	S(major isomer)	3	*a,j*
-75.0	S		
-113.4		2	*c,h*
-119.4	AB, J_{AB} = 274 (major isomer)		
-104 to-125.9	Unassigned		
-211.0	D, J_{HF}=40 (major isomer)	1	*b,i*
-211.6	D,		
-212.4			

No.18 2,5-bis(2H hexafluoropropyl)-1-fluoropyrrolidine (40)



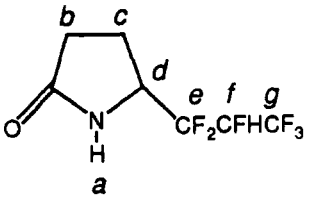
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.18	S(board)	4	*e*,*f*
4.20	M	2	*d*,*g*
4.98	M	2	*b*,*i*
^{19}F			
-33.7	S	1	*k*
-71.78	S	3	*a*,*j*
-117.7	M	1	*c*,*h*
-210.3	D	1	*b*,*i*

No.17 2,5-bis(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (50)



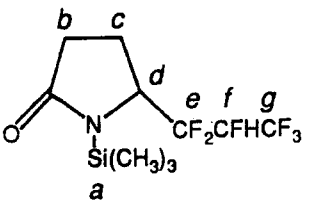
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.1	M	5	*e,f,k*
3.8	M	2	*d,g*
5.1	M	2	*b,i*
^{19}F			
-74.6	S	3	*a,j*
-117.2			
-121.8	AB, J_{AB} = 269	2	*c,h*
-215.2	D, J_{HF}=40	1	*b,i*

No.20 2-(2H hexafluoropropyl)pyrrolid-2-one (53)



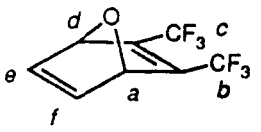
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.40	M(board)	4	*b*,*c*
4.17	S	1	*d*
5.25	D	1	*f*
8.5	S	1	*a*
^{19}F			
-75.1	S	3	*g*
-122.2 -121.8	M	2	*e*
-213.4 to -215.9	M	1	*f*

No.21 2-(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolid-2-one



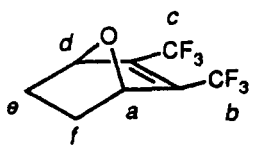
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
0.2	S	4.5	*a*
2.45	M(board)	4	*b,c*
4.23	S	1	*d*
5.29	D	1	*f*
^{19}F			
-74.8	S	3	*g*
-122.1	M	2	*e*
-215.4	M	1	*f*

No.22 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (55)



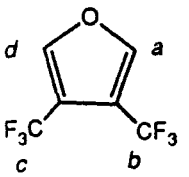
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
5.82	S	1	*a,d*
7.38	S	1	*e,f*
^{19}F			
-64.18	S	-	*b,c*

No.23 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (56)



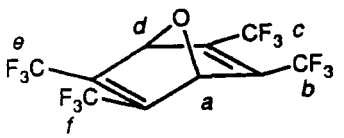
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.0	D	1	*e,f*
1.48	D	1	
5.23	S	1	*a,d*
^{19}F			
-61.4	S	-	*b,c*

No.24 3,4-Bis(trifluoromethyl)furan (57)



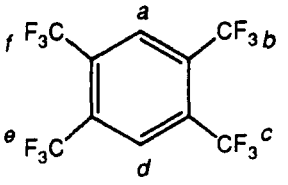
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
7.33	S	-	*a,d*
^{19}F			
-59.38	S	-	*b,c*

No.25 2,3,5,6-Tetrakis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (61)



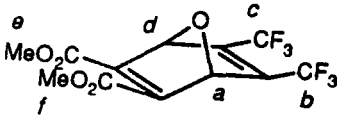
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
5.65	S	-	*a,d*
^{19}F			
-63.4	S	-	*c,d,e,f*

No.26 2,3,5,6-Tetrakis(trifluoromethyl)benzene (62)



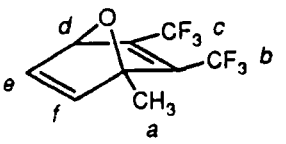
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
8.5	S	-	*a,d*
^{19}F			
-59.5	S	-	*c,d,e,f*

No.27 2,3-Bis(trifluoromethyl)-5,6-di(methylcarboxy)-7-oxabicyclo [2.2.1]hepta-2,5-diene (64)



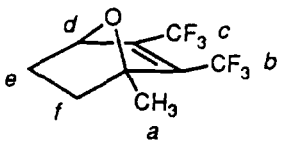
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
3.8	S	3	*e,f*
5.92	S	1	*a,d*
^{19}F			
-61.3	S	-	*b,c*

No.28 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (58)



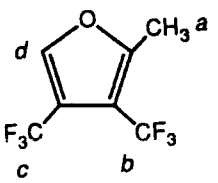
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.0	S	3	*a*
5.66	S	1	*d*
7,2	S	1	*e*
7.3	S	1	*f*
^{19}F			
-62.23	S	1	*b*
-63.37	S	1	*c*

No.29 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (66)



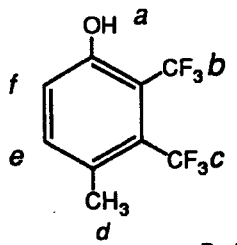
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
1.7	S	3	*a*
1.90	S(board)	2	*e*
2.10	S(board)	2	f
5.7	S	1	*d*
^{19}F			
-59.83	S	1	*b*
-60.7	S	1	*c*

No.30 2-Methyl-3,4-bis(trifluoromethyl)furan (67)



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.41	S	3	*d*
7.6	S	1	*d*
^{19}F			
-57.57	S	1	*c*
-60.0	S	1	*b*

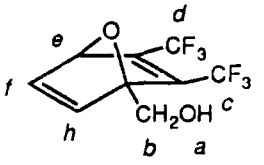
No.31 2,3-Bis(trifluoromethyl)-4-methylphenol (68)



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.48	Q	3	*a*
7.33	AB doublet	2	*e,f*
9.8	S (board)	1	*a*
^{19}F			
-53.7	S (board)	1	*b,c*
-55.0	S (board)	1	

No.32 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene (73)

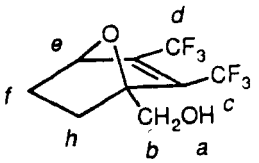
(d_6-Acetone nmr solvent)



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^1H			
3.0	S	1	*a*
4.23	S	2	*b*
5.61	S	1	*e*
7.08	S	1	*g*
7.21	S	1	*f*
^{19}F			
-62.54	S	-	c,d

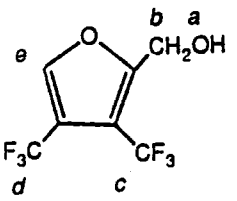
No.33 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hept-2-ene

(d_6-Acetone nmr solvent)



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^1H			
1.88	S (broad)	2	*f*
2.13	S (broad)	2	*g*
2.54	S (broad)	1	*a*
4.18	D (broad)	2	*b*
5.17	S (broad)	1	*e*
^{19}F			
-59.97	S	1	*c,d*
-60.13	S	1	

No.34 2-(Hydroxymethyl)-3,4-bis(trifluoromethyl)furan (77)



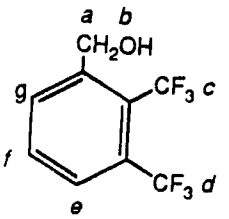
^{1}H

3.26	S	1	*a*
4.26	S	2	*b*
7.4	S	1	*e*

^{19}F

-55.78	S	1	*c*
-58.29	S	1	*d*

No.35 2,3-bis(trifluoromethyl)benzyl alcohol (79)

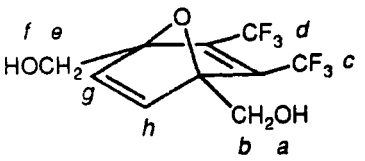


(d_6-Acetone nmr solvent)

Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^1H			
3.69	S(Board)	1	*a*
5.71	S(Board)	2	*b*
8.71	M	2	e,*f*,*g*
9.06	M	1	
^{19}F			
-54.8	S	1	*c*
-57.78	S	1	*d*

No.36 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hepta-2,5-diene (74)

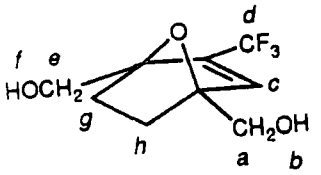
(d_6-Acetone nmr solvent)



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^1H			
4.1	S	2	*b,e*
4.42	S	1	*a,f*
7.21	S	2	*g,h*
^{19}F			
-60.9	S	–	*c,d*

No.37 1,4-Di(hydroxymethyl) 2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hept-2-ene (76)

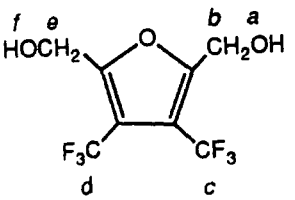
(d_6-Acetone nmr solvent)



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^1H			
1.52	D	1	
1.50	D		
1.99	S	1	*g,h*
2.04	D		
3.99	M	1	*e,a*
4.17	M	1	*e,a*
4.20	M	1	*b,f*
^{19}F			
-59.85	S	-	*d*

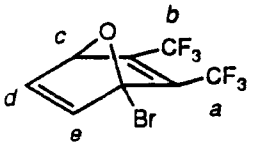
No.38 2,5-Di(hydroxymethyl)-3,4-bis(trifluoromethyl)furan (78)

(d_6-Acetone nmr solvent)



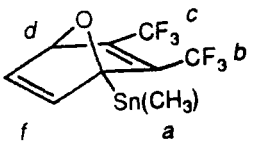
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^1H			
4.66	S	2	*b*,*e*
5.00	S(board)	1	*a*,*f*
^{19}F			
-56.46	S	-	*c*,*d*

No.39 1-Bromo-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (81)



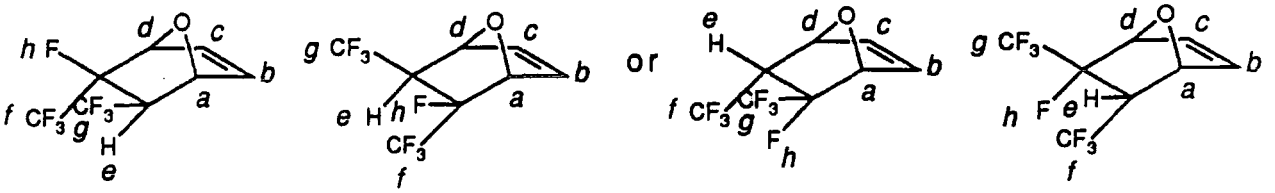
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
5.53	S(board)	1	*c*
7.10	D(board)	2	*d*,*e*
7.16	D(board)	2	
^{19}F			
-61.9	S	1	*b*
-62.99	S	1	*a*

No.40 1-(Trimethylstanyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hepta-2,5-diene (82)



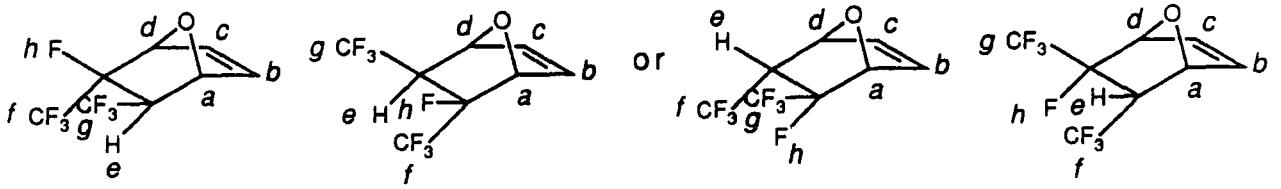
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
0.36	S	9	*a*
5.67	S	1	*d*
7.26	S(board)	2	*e*,*f*
^{19}F			
-62.5	S	-	*b*,c

No.41 *Trans*-5-Fluoro,5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1] hept-2-ene (84)



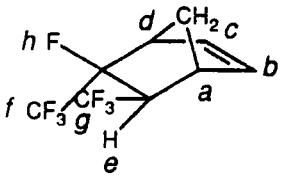
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
5.62	S	1	*c,b*
5.42	S	1	*c,b*
4.0	S	2	*a,d*
2.09	S(board)	1	*e*
^{19}F			
-65.1	S	3	*f*
-77.16	S	3	*g*
-177.2	S	1	*h*

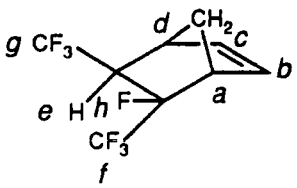
No.42 *Trans*-5-Fluoro,5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hept-2-ene (84)

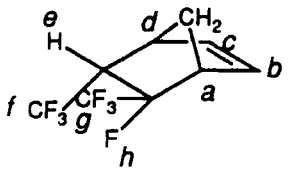


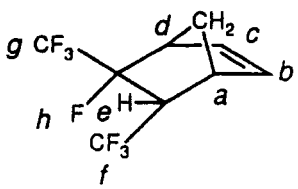
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
5.5	S	1	*c*
5.31	S	1	*b*
4.10	M	1	*a*
3.91	M	1	*d*
1.51	M	1	*e*
^{19}F			
-63.84	S	3	*f*
-78.59	S	3	*g*
-180.6	S(board)	1	*h*

No43 Trans-5-Fluoro,5,6-bis(trifluoromethyl)-7-bicyclo[2.2.1]hept-2-ene (85)



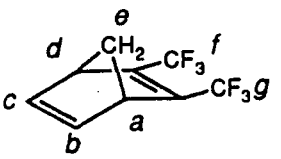






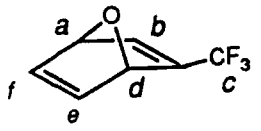
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
1.67	M(Board)	1.5	*e,g*
3.5	M(Board)	1	*a,d*
5.03 to 6.5	M	1	*c.d*
^{19}F			
-63.9	S	3	
-65.7	S(minor isomer)		*f,h*
-77.0	S(minor isomer)	3	
-80.32	S		
-184.16	S(minor isomer)	1	*i*
-184.63	S		

No.44 5,6-Bis(trifluoromethyl)-7-bicyclo[2.2.1]hepta-2,5-diene (86)



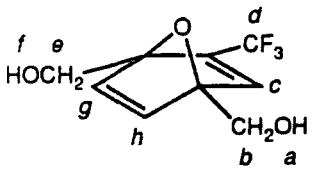
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.23	M	1	*e*
4.12	M(Board)	1	*d*,*e*
7.01	S	1	*c*,*d*
^{19}F			
62.4	S		*f*, *g*

No.45 2-(Trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (88)



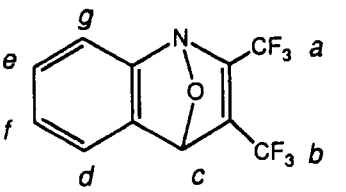
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
7.4	M	1	*b*
7.2	M	1	*e,f*
7.1	M	1	*e,f*
5.6	S	1	*d*
5.5	S	1	*a*
^{19}F			
68.1	S	1	*c*

No.46 1,4-Di(hydroxymethyl)-2-(trifluoromethyl)-7-oxabicyclo[2.2.1] hepta-2,5-diene (90)



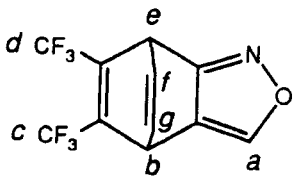
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
3.4	S	2	*b*
3.7	M	2	*e*
4.16	D	2	*a,f*
6.95	D	1	*h*
7.1	D	1	*g*
7.4	S	1	*c*
^{19}F			
65.44	S	–	*d*

No.47. 2,3-Bis(trifluoromethyl)-1,4-oxo-quinoline (93).



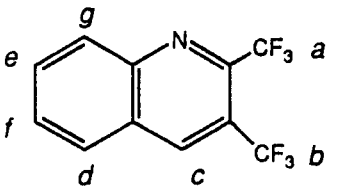
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
6.87	M	1	*c*
7.07 to 7.24	M	4	*d,e,f,g*
^{19}F			
-60.01	Q	1	*a*
-70.03	Q	1	b

No.48. 8,9-bis(trifluoromethyl)-3-aza-4-oxatricyclo[5.2.2.$0^{2,6}$]undeca-2,5,8,10-tetraene (94).



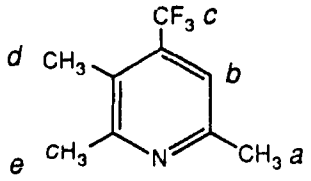
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
3.13	S	2	*b*,*e*
6.86	S(board)	1	*a*
7.29 to 7.59	M	2	*f*,*g*
^{19}F			
-68.49	S	1	*c*
-73.72	S	1	*d*

No.49. 2,3-Bis(trifluoromethyl)quinoline (95).



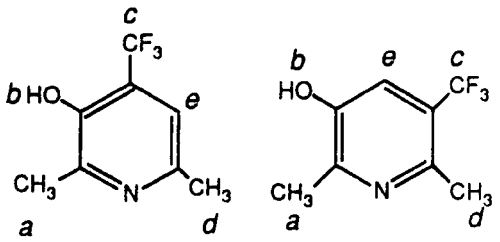
Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
8.5	S	1	*c*
7.5	M	2	*g,e,f,d*
7.27	M	2	
^{19}F			
-62.1	S	1	*a,b*
-69.17	S	1	

No.50. 2,3,6-Trimethyl-4-trifluoromethylpyridine (97).



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^{1}H			
2.65	S(board)	3	*d*
2.95	S	6	*a*,*e*
7.69	S	1	*b*
^{19}F			
-62.7	S	1	*c*

No.51 2,6-Dimethyl-3-trifluoromethyl-5-hydroxypridine (100) and 2,6-dimethyl-4-trifluoromethyl-5-hydroxypyridine (101).



Shift(ppm)	Fine structure Coupling Constants	Relative Intensity	Assignment
^1H			
2.40	S(board)	3	*a*, *e*
2.46	S		
2.6	D	3	
2.7	D		
7.35	S	1	*d*
7.6	S		
^{19}F			
-66.34	S		*c*
-57.46	S		

APPENDIX 2

INFRARED SPECTRA

APPENDIX 2

I.R. SPECTRA

1. 1,4-Bis(trimethylsilyl)benzene.
2. 1-Chloro,4-(trimethylsilyl)benzene.
3. 1-Fluoro,4-(trimethylsilyl)benzene.
4. 1,2,4-Tris(trimethylsilyl)benzene.
5. 1,3,5-Tris(trimethylsilyl)benzene.
6. 1,2,4,5-Tetrakis(trimethylsilyl)benzene.
7. 2,5-Bis(trimethylsilyl)thiophene.
8. 2,5-Bis(trimethylsilyl)-3,4-dichlorothiophene.
9. 2-(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (48).
10. 2,5-Bis(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (50).
11. 5-(2H hexafluoropropyl)pyrrolid-2-one (53).
12. 5-(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolid-2-one.
13. N-Trimethylsilylsuccinamide.
14. 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (55).
15. 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (56).
16. 3,4-Bis(trifluoromethyl)furan (57).
17. 2,3,5,6-Tetrakis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (61).
18. 2,3,5,6-Tetrakis(trifluoromethyl)benzene (62).
19. 2,3-Bis(trifluoromethyl)-5,6-di(methylcarboxy)-7-oxabicyclo[2.2.1]hepta-2,5-diene (64).
20. 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (58).
21. 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (66).
22. 2-Methyl-3,4-bis(trifluoromethyl)furan (67).

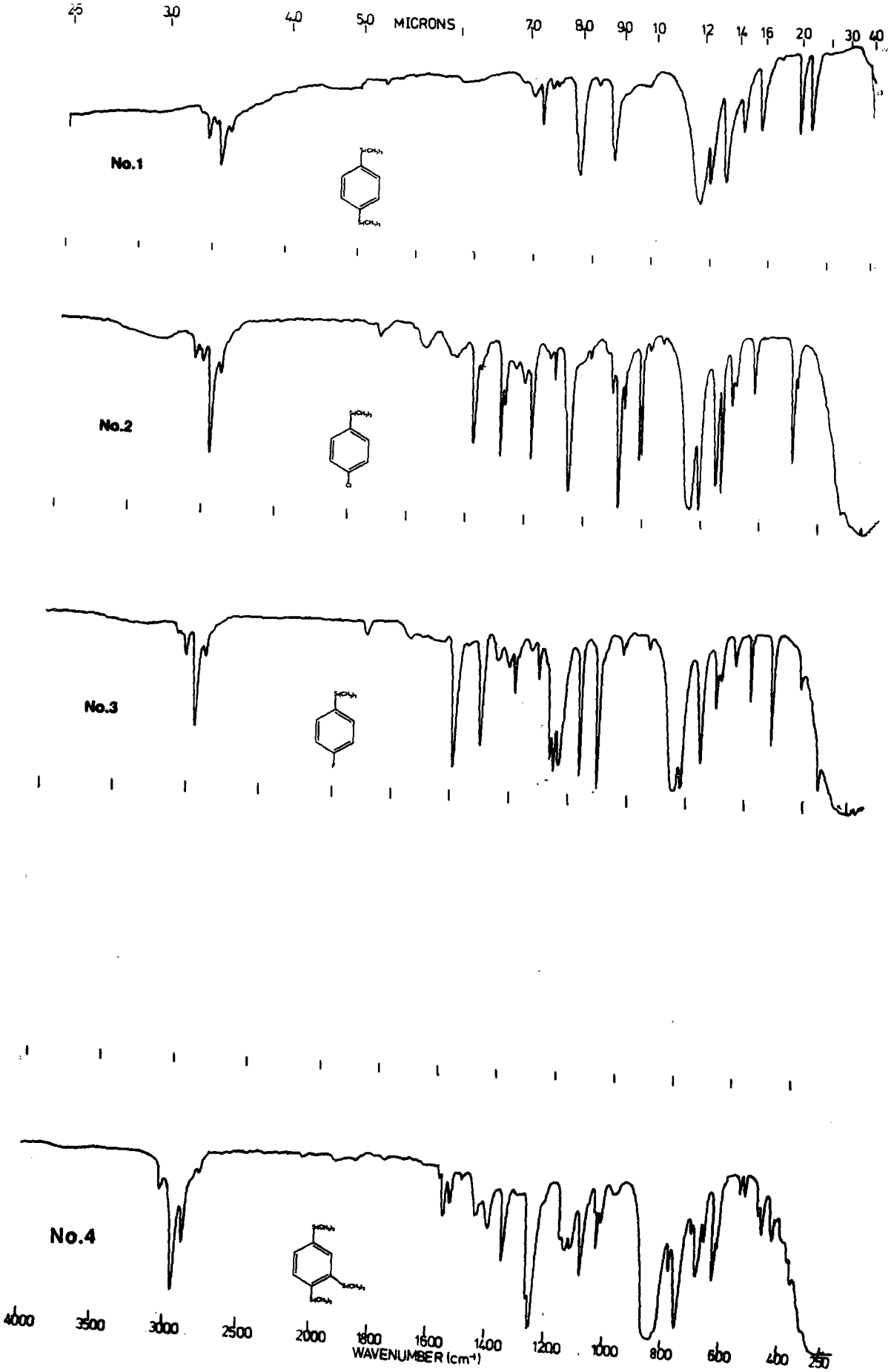
23. 2,3-Bis(trifluoromethyl)-4-methylphenol (68).
24. 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1] hepta-2,5-diene (73).
25. 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-2-heptene (75).
26. 2-(Hydroxymethyl)-3,4-bis(trifluoromethyl)furan (77).
27. 2,3-Bis(trifluoromethyl)benzyl alcohol (79).
28. 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hepta-2,5-diene (74).
29. 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hept-2-ene (76).
30. 2,5-Di(hydroxymethyl)-3,4-bis(trifluoromethyl)furan (78).
31. 1-Bromo-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (81).
32. 1-(Trimethylstanyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene (82).
33. *Trans*-2H-heptafluoro-2-butene (83).
34. *Trans*-5-fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84).
35. *Trans*-5-fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84).
36. *Trans*-5-Fluoro-5,6-bis(trifluoromethyl)-7-bicyclo[2.2.1]hept-2-ene (85).
37. 2,3-Bis(trifluoromethyl)-7-bicyclo[2.2.1]hepta-2,5-diene (86).
38. 3,3,3-Trifluoropropyne (87).
39. 2-(trifluoromethyl)-7-oxabicyclo [2.2.1]hepta-2-diene (88).
40. Benzoltrifluoride (89).
41. 1,4-Di(hydroxymethyl)-2-(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene (90).

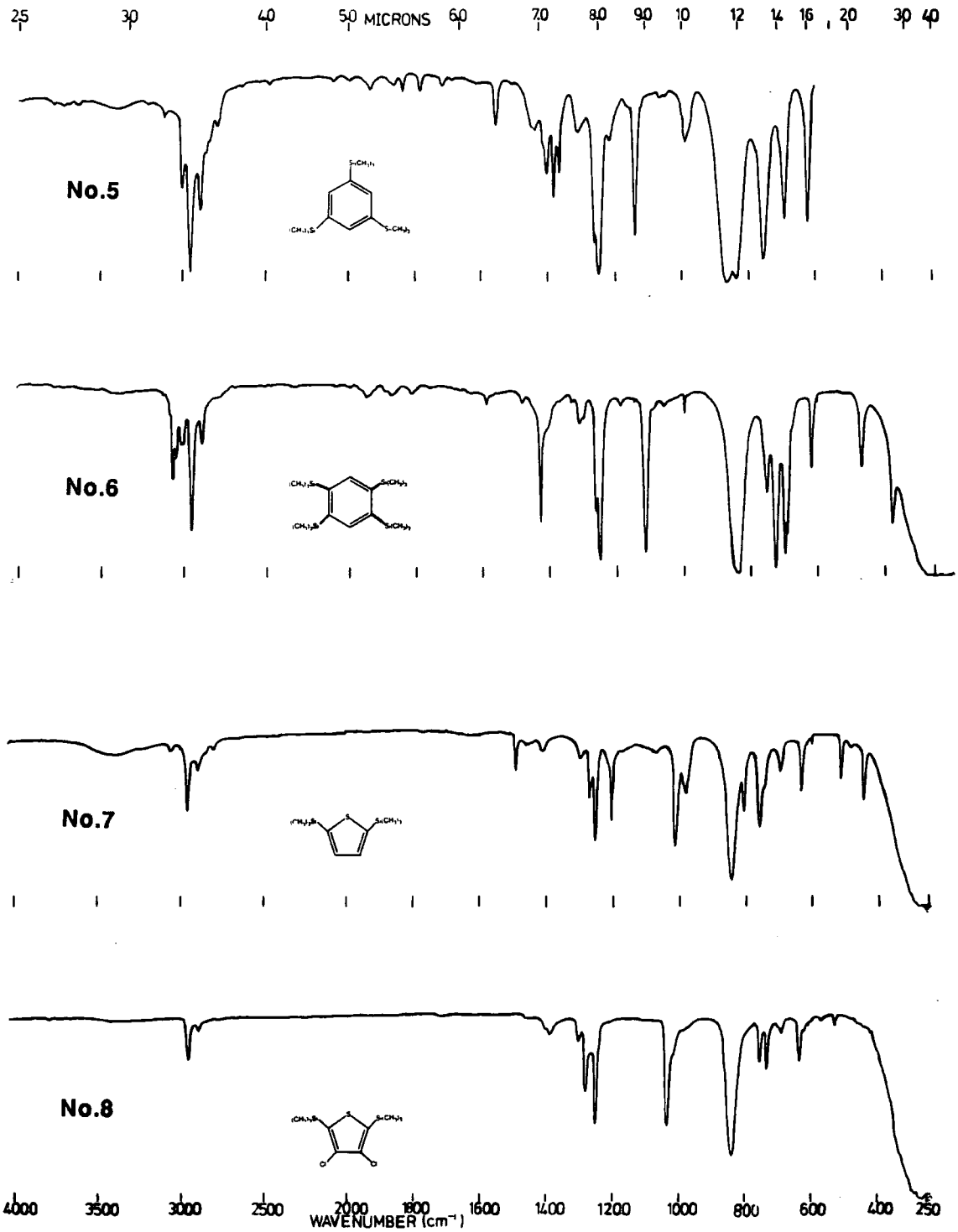
42. Mixture of 2,3-bis(trifluoromethyl)-1,4-oxoquinoline (93) and 8,9-bis(trifluoromethyl)-3-aza-4-oxatricyclo[5.2.2.$0^{2,6}$]undeca-2,5,8,10-tetraene (94).

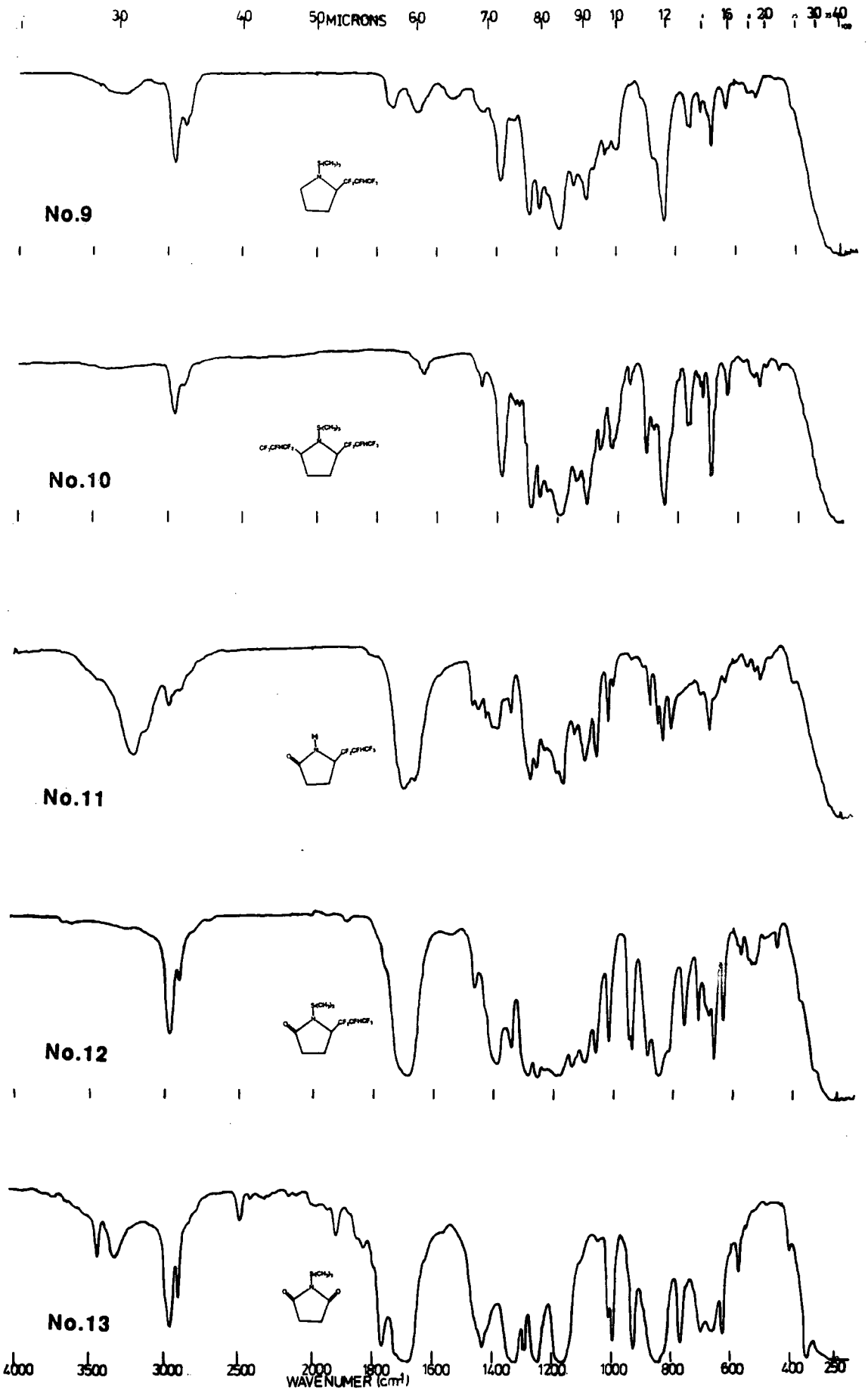
44. 2,3,6-trimethyl-4-trifluoromethylpyridine hydrogen fluoride (97).

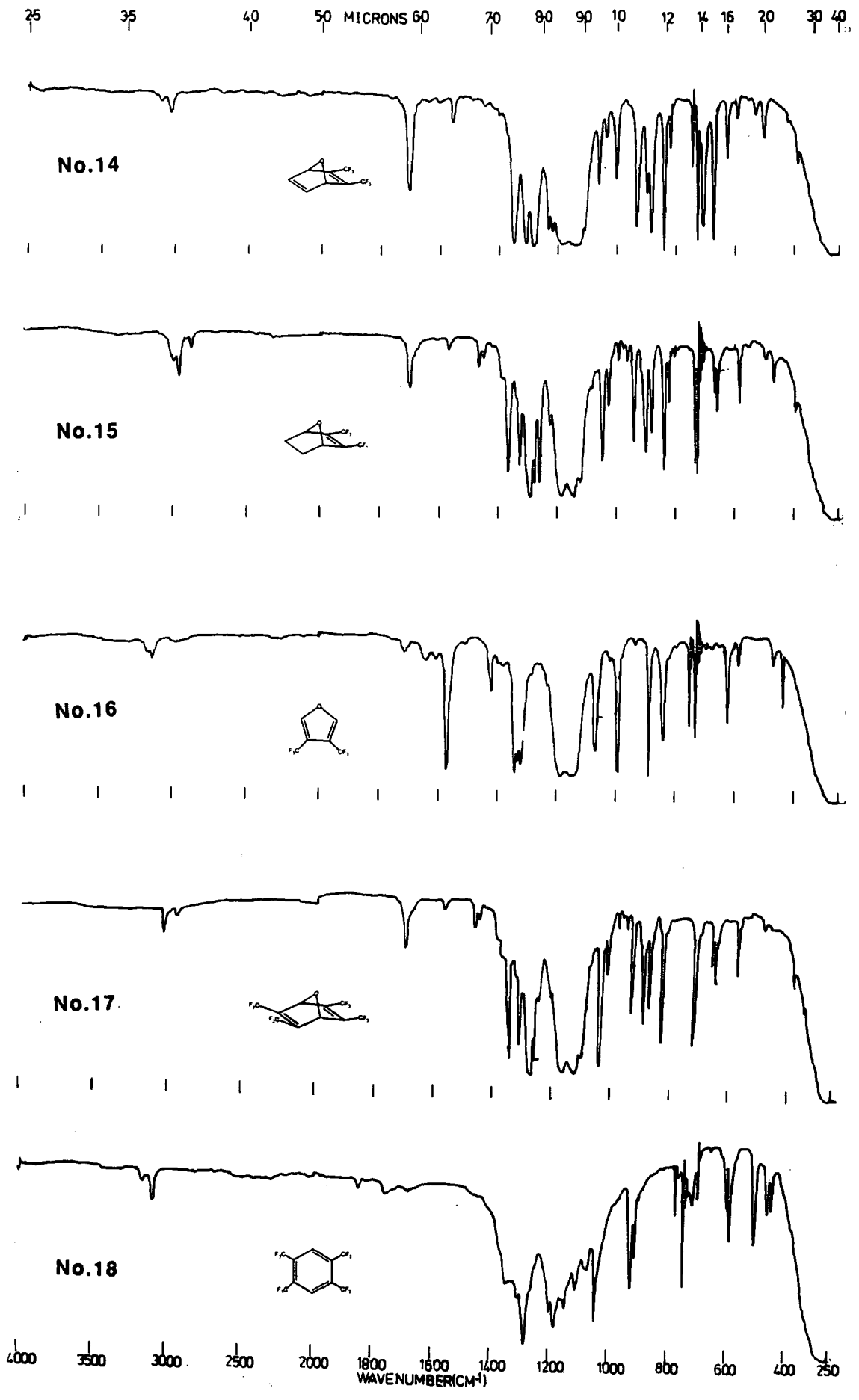
45. 2,4-Dimethyl-5-methoxyoxazole (98).

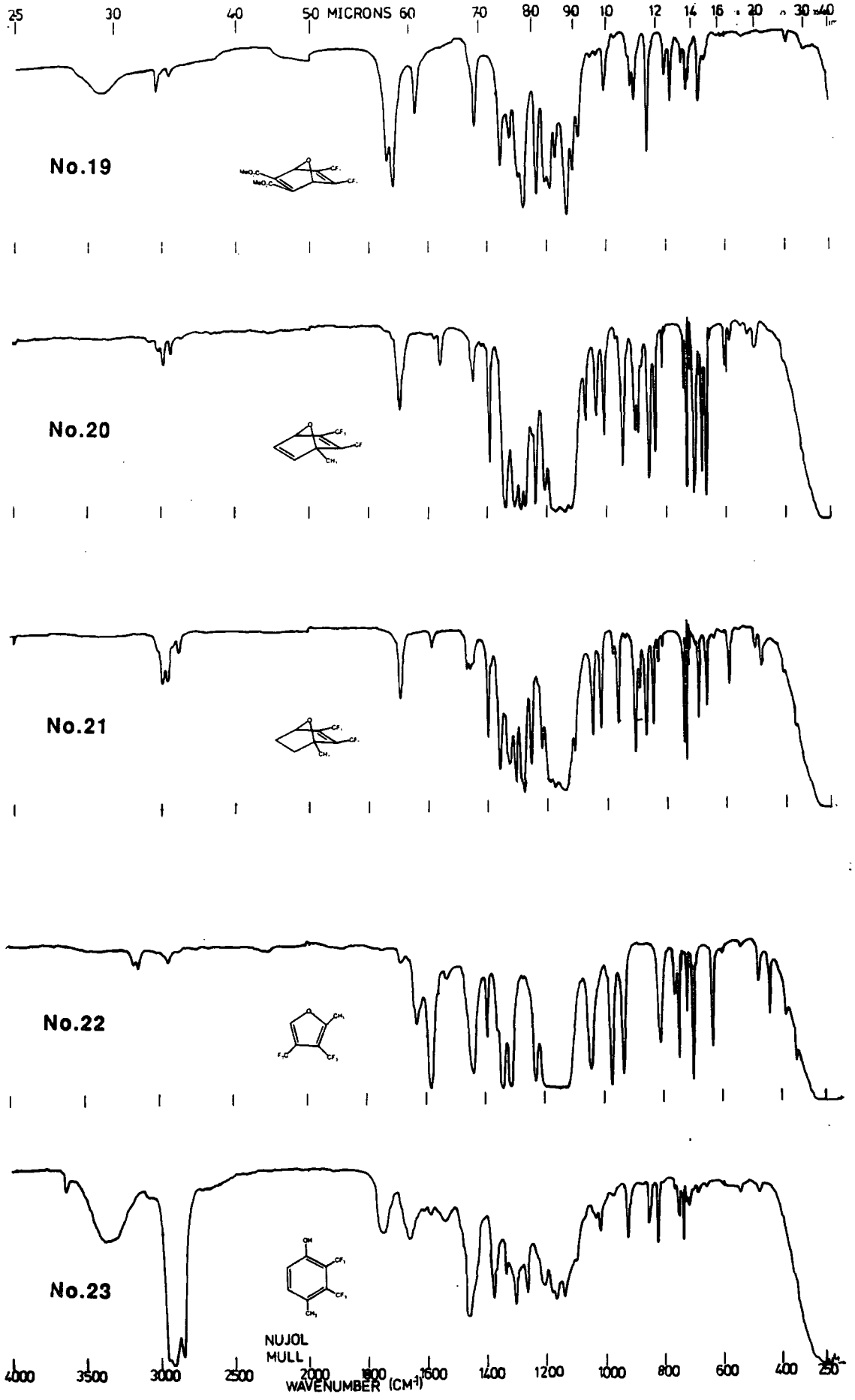
46. 2,6-dimethyl-3-trifluoromethyl-5-hydroxypyridine (100) and 2,6-dimethyl-4-trifluoromethyl-5-hydroxypyridine (101)

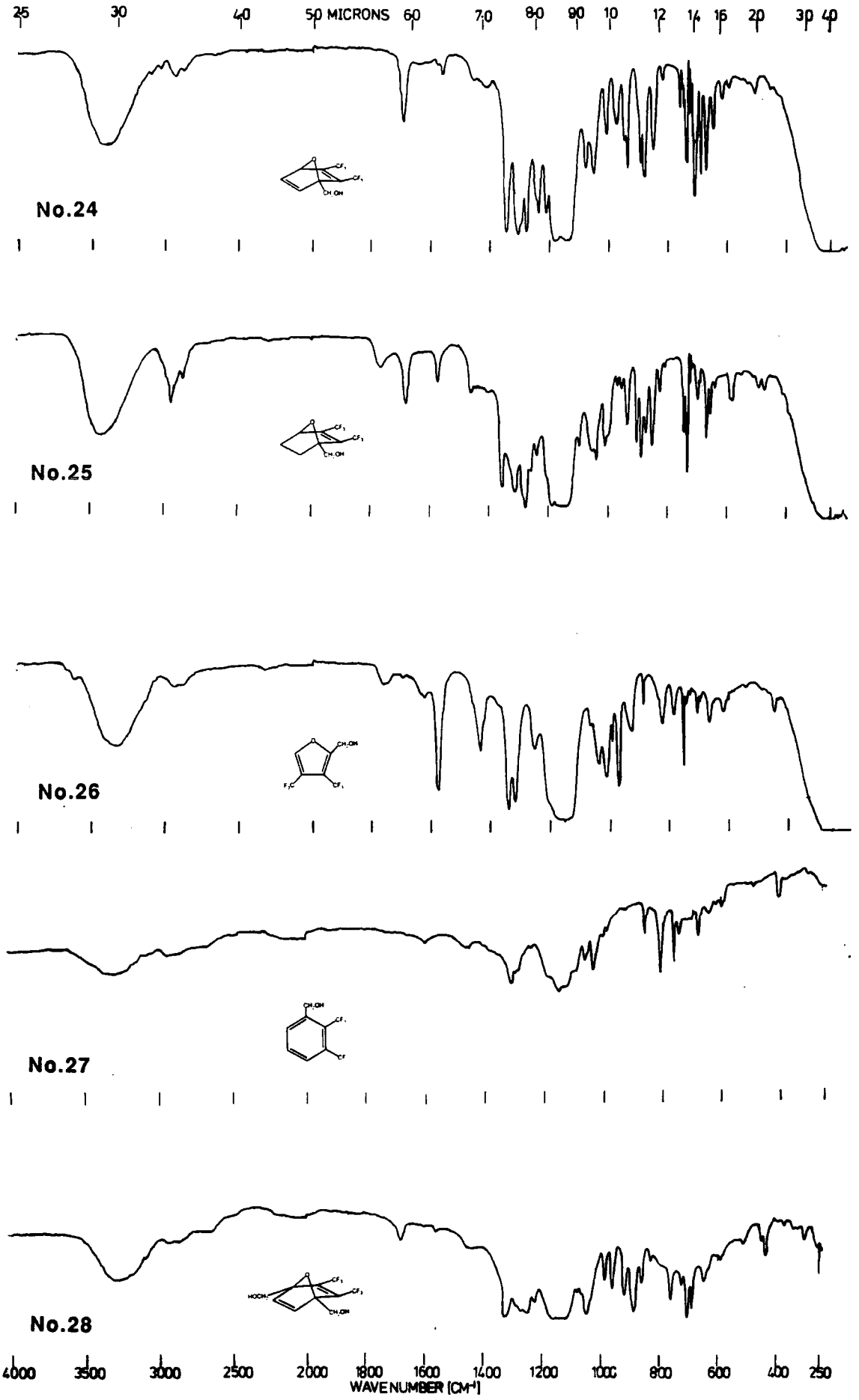

MICRONS
No.1
No.2
No.3
No.4
WAVENUMBER (cm⁻¹)

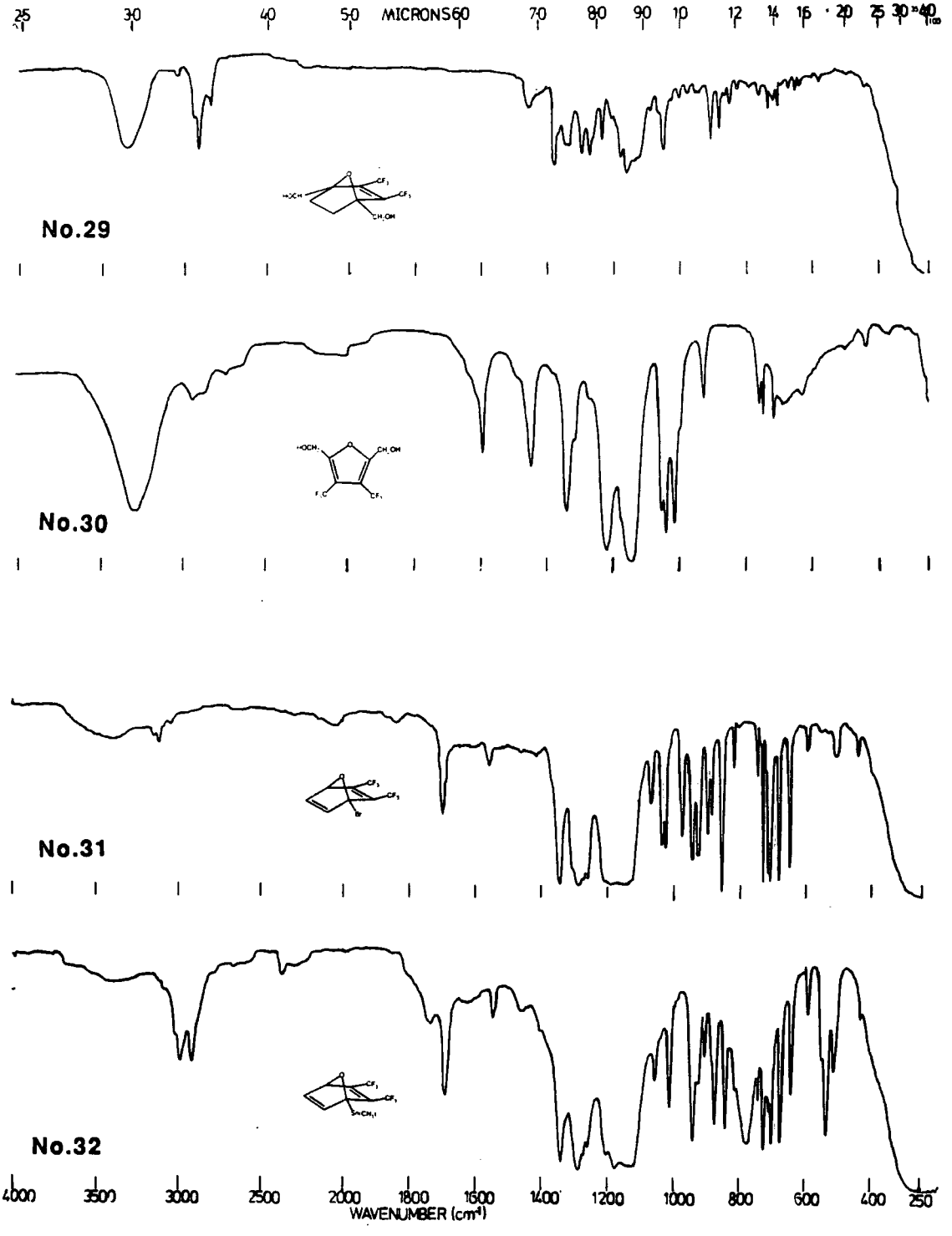

25
30
40
50 MICRONS
60
70
80
90
10
12
14
16
20
30
40
No.5
No.6
No.7
No.8
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVENUMBER (cm⁻¹)

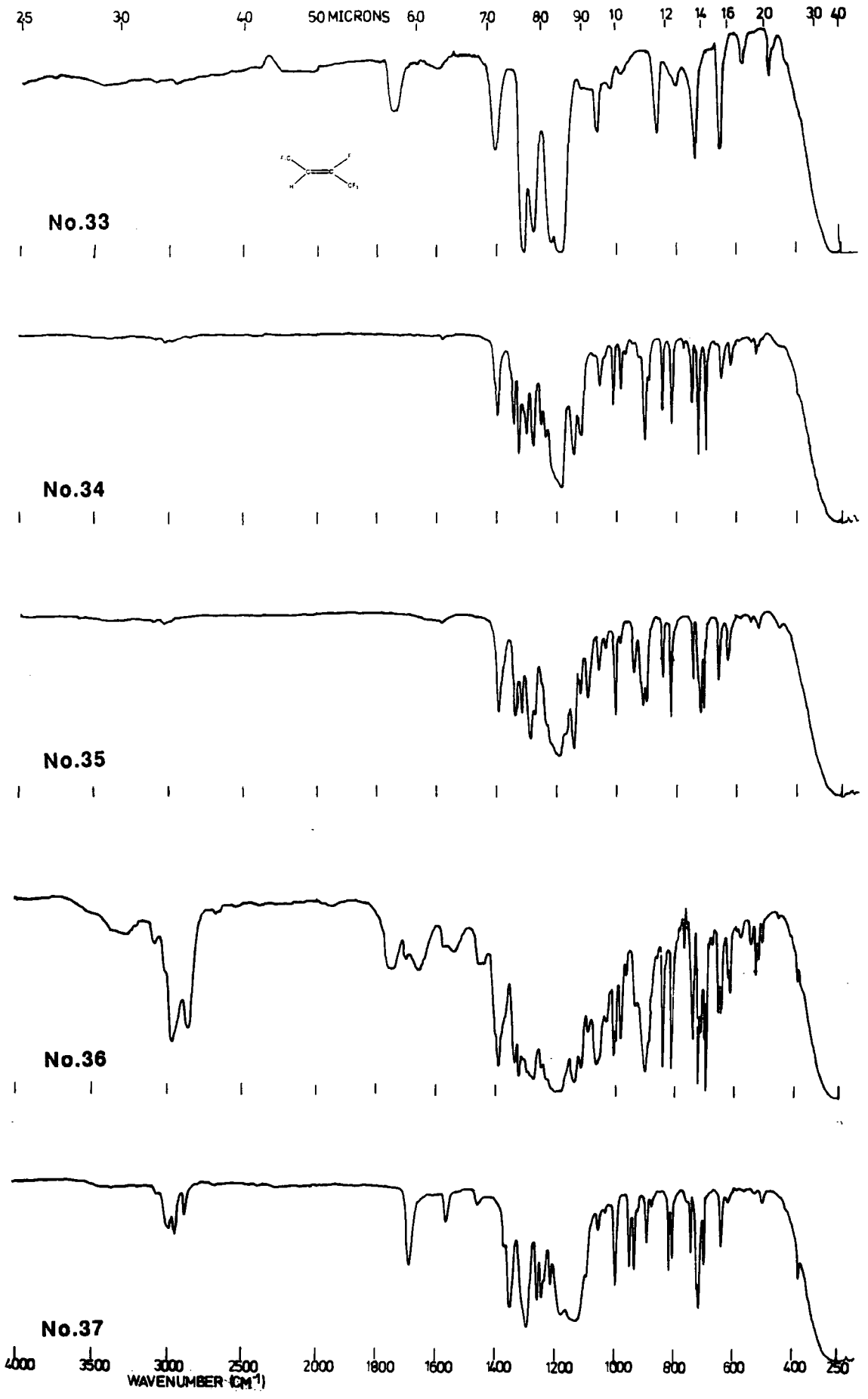

30
40
50 MICRONS
60
70
80
90
10
12
16
20
30
40
No.9
No.10
No.11
No.12
No.13
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVENUMER (cm-1)

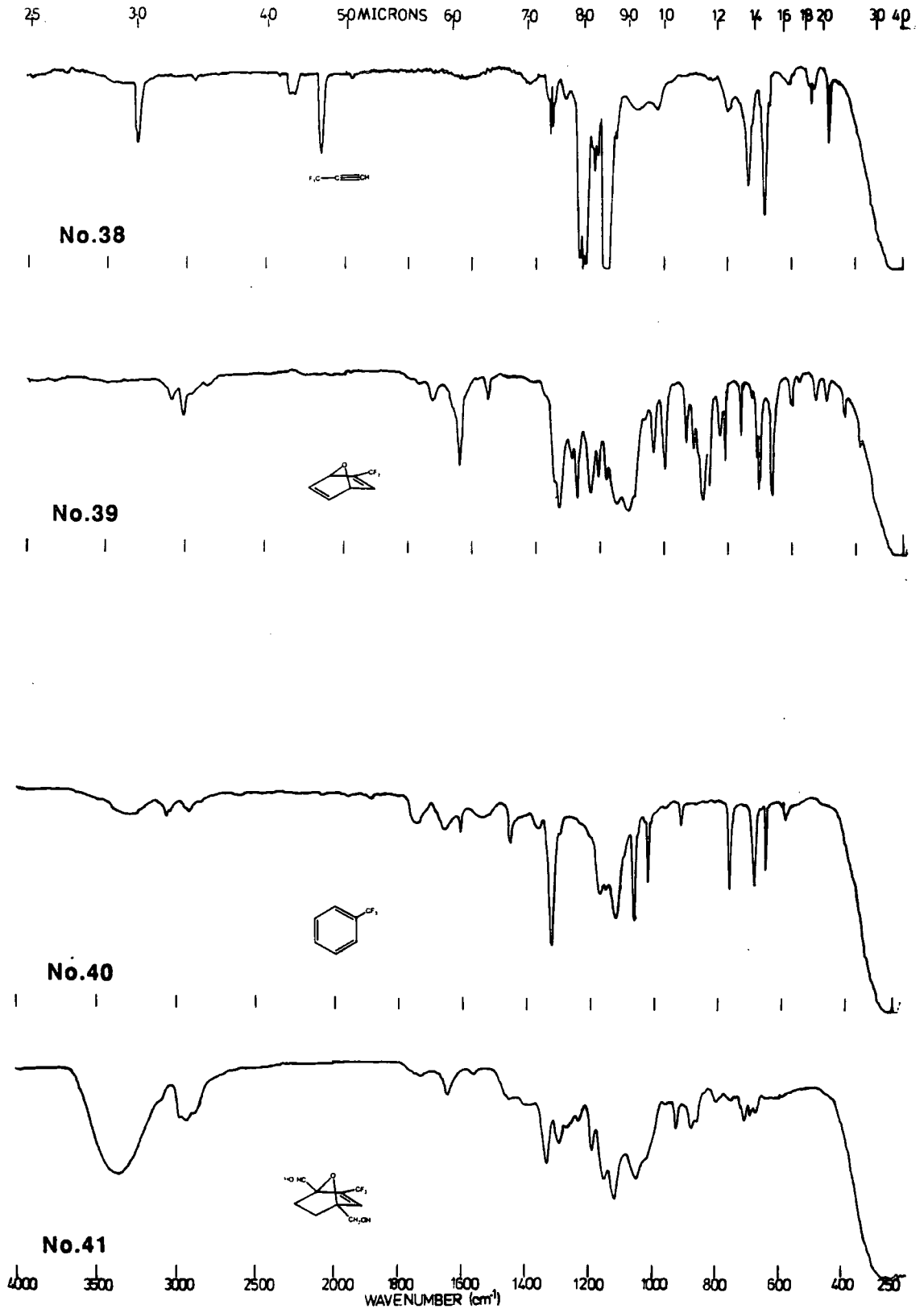

25
35
40
50 MICRONS 60
70
80
90
10
12
14
16
20
30 40
No.14
No.15
No.16
No.17
No.18
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVENUMBER(CM-1)

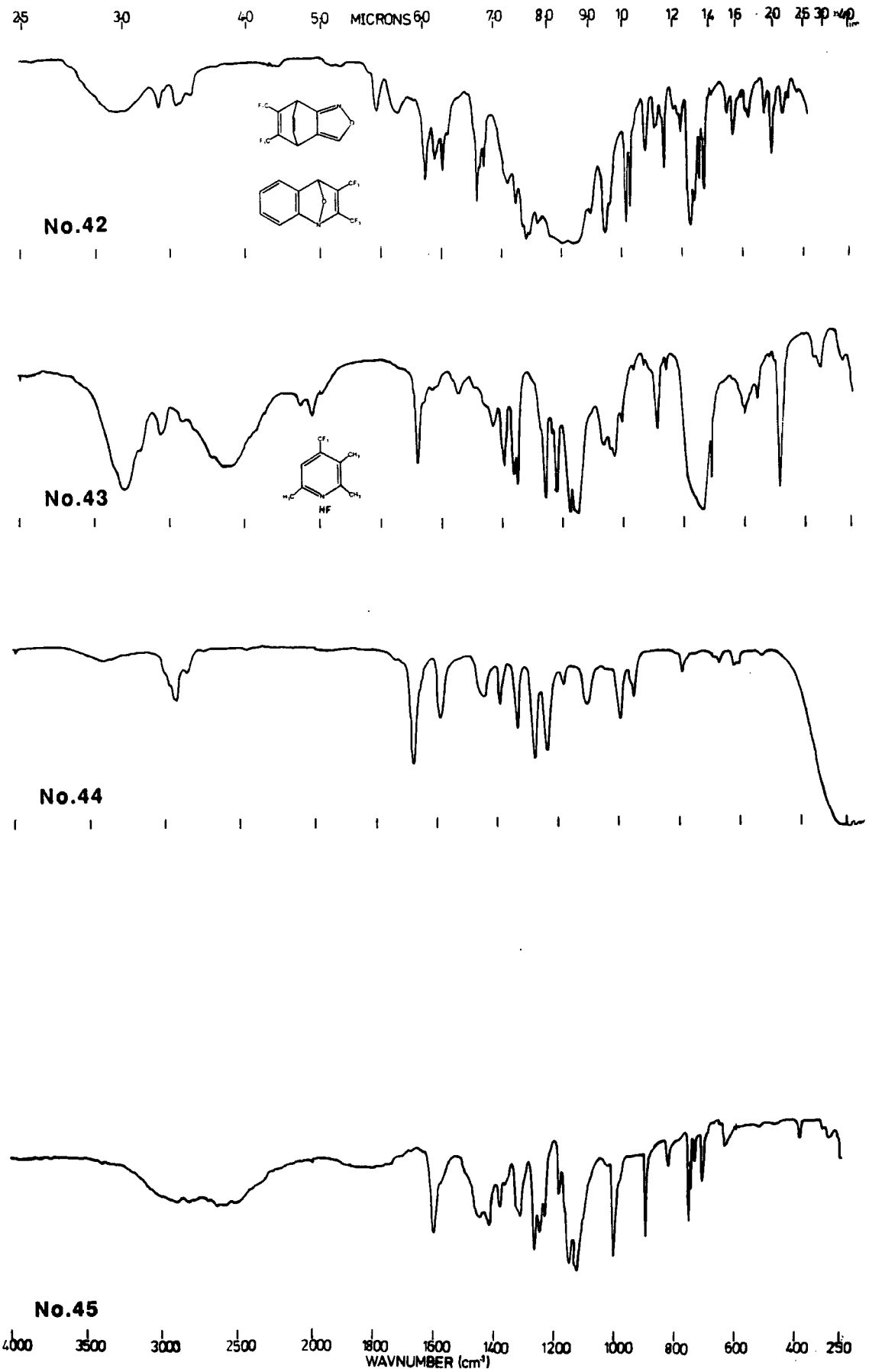

25
30
40
50 MICRONS
60
70
80
90
10
12
14
16
20
30
40
No.19
No.20
No.21
No.22
No.23
NUJOL
MULL
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVENUMBER (CM-1)


25
30
40
50 MICRONS
60
70
80
90
10
12
14
16
20
30
40
No.24
No.25
No.26
No.27
No.28
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVE NUMBER [CM⁻¹]


25
30
40
50
MICRONS60
70
80
90
10
12
14
16
20
25
30
40
No.29
No.30
No.31
No.32
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVENUMBER (cm-1)


2.5
3.0
4.0
50 MICRONS
6.0
7.0
8.0
9.0
10
12
14
16
20
30
40
No.33
No.34
No.35
No.36
No.37
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVENUMBER (CM⁻¹)


25 30 40 50 MICRONS 60 70 80 90 10 12 14 16 18 20 30 40
No.38
No.39
No.40
No.41
4000 3500 3000 2500 2000 1800 1600 1400 1200 1000 800 600 400 250
WAVENUMBER (cm⁻¹)


2.5
3.0
4.0
5.0
MICRONS
6.0
7.0
8.0
9.0
10
12
14
16
20
25
30
40
No.42
No.43
HF
No.44
No.45
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
250
WAVNUMBER (cm⁻¹)

APPENDIX 3

MASS SPECTRA

APPENDIX 3

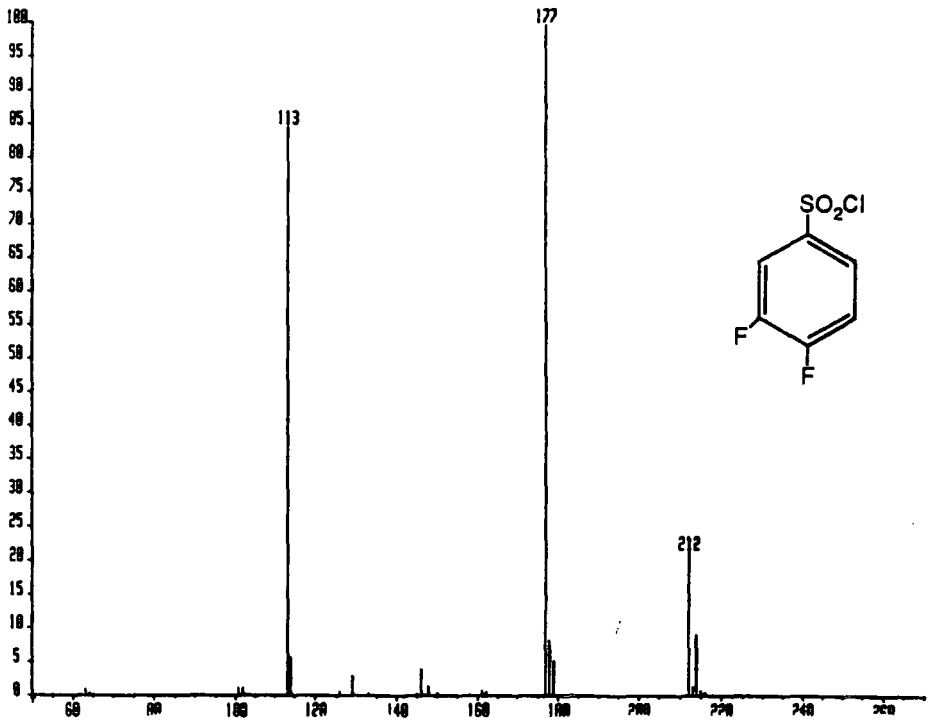
MASS SPECTRA

1. 3,4-Difluorobenzenesulphonyl chloride (38).
2. 2-(2H Hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (48).
3. 2-(2H Hexafluoropropyl)pyrrolidine.
4 2,5-Bis(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolidine (50).
5. N-fluoro-2,5-bis(2H hexafluoropropyl)pyrrolidine (40).
6. 2,5-Bis(2H hexafluoropropyl)pyrrolidine.
7. Product from dehydrofluorination of N-fluoro-2,5-bis(2H hexafluoropropyl)pyrrolidine (40)
8. 5-(2H hexafluoropropyl)-1-(trimethylsilyl)pyrrolid-2-one.
9. 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (55).
10. 2,3-Bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (56).
11. 3,4-Bis(trifluoromethyl)furan (57).
12. 2,3,5,6-Tetrakis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (61).
13. 2,3,5,6-Tetrakis(trifluoromethyl)benzene (62).
14. 2,3-Bis(trifluoromethyl)-5,6-di(methylcarboxy)-7-oxabicyclo [2.2.1]hepta-2,5-diene (64).
15. 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5 -diene (58).
16. 1-Methyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (66).
17. 2-Methyl-3,4-bis(trifluoromethyl)furan (67).
18. 2,3-Bis(trifluoromethyl)-4-methylphenol (68).
19. 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-hepta-2,5-diene (73).

20. 1-(Hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]-2-heptene (75).
21. 2-(Hydroxymethyl)-3,4-bis(trifluoromethyl)furan (77).
22. 2,3-Bis(trifluoromethyl)benzyl alcohol (79).
23. 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hepta-2,5-diene (74).
24. 1,4-Di(hydroxymethyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo [2.2.1]hept-2-ene (76).
25. 2,5-Di(Hydroxymethyl)-3,4-bis(trifluoromethyl)furan (78).
26. 1-Bromo-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene (81).
27. 1-Formyl-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2,5-diene.
28. 1-(Trimethylstanyl)-2,3-bis(trifluoromethyl)-7-oxabicyclo[2.2.1] hepta-2,5-diene (82).
29. *Trans*-5-fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84).
30. *Trans*-5-fluoro-5,6-bis(trifluoromethyl)-7-oxabicyclo[2.2.1]hept-2-ene (84).
31 *Trans*-5-fluoro-5,6-bis(trifluoromethyl)-7-bicyclo[2.2.1]hept-2-ene (85)
32. *Trans*-5-fluoro-5,6-bis(trifluoromethyl)-7-bicyclo[2.2.1]hept-2-ene (85)
33. 2,3-Bis(trifluoromethyl)-7-bicyclo[2.2.1]hepta-2,5-diene (86).
34. 2-(Trifluoromethyl)-7-oxabicyclo[2.2.1]hepta-2-diene (88).
35. Benzoltrifluoride.
36. 1,4-Di(hydroxymethyl)-2-(trifluoromethyl)-7-oxabicyclo[2.2.1] hepta-2,5-diene (90).
37. 2,3-Bis(trifluoromethyl)-1,4-oxoquinoline (93).

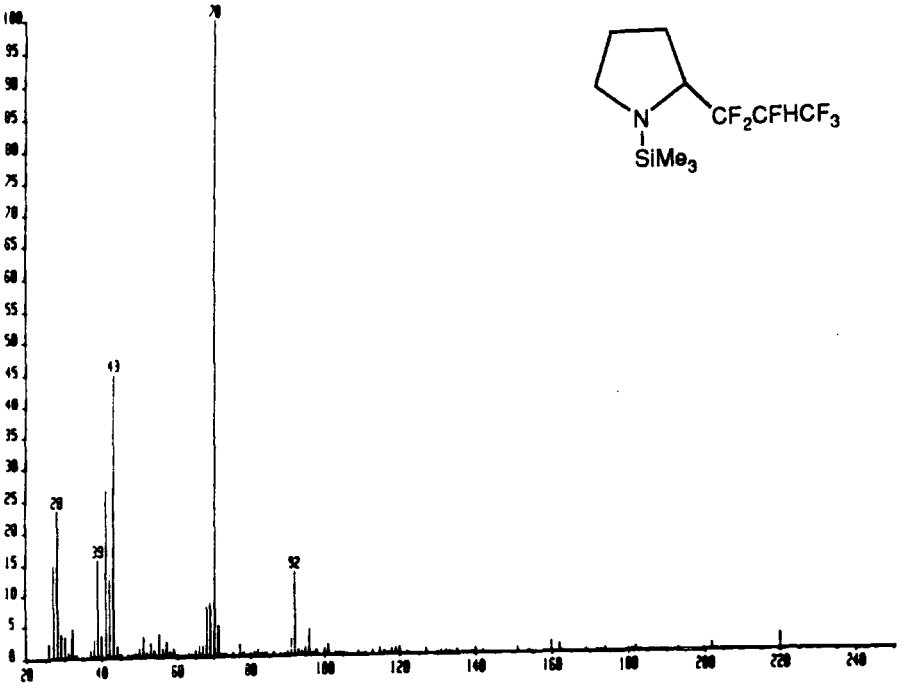
38. 8,9-Bis(trifluoromethyl)-3-aza-4-oxatricyclo[5.2.2.$0^{2,6}$]undeca-2,5,8,10-tetraene (94).
39. 2,3-Bis(trifluoromethyl)Quinoline
40. 2,3,6-Trimethyl-4-trifluoromethylpyridine (97)
41. Adduct from 3,3,3-trifluoropropene and 2,4-Dimethoxyoxazole (102)
42. Adduct from 3,3,3-trifluoropropene and 2,4-Dimethoxyoxazole (103)
43. 2,6-Dimethyl-3-trifluoromethyl-5-hydroxypyridine (100).
44. 2,6-Dimethyl-4-trifluoromethyl-5-hydroxypyridine (101).

EI+ M.Wt. 212.5 No. 1.



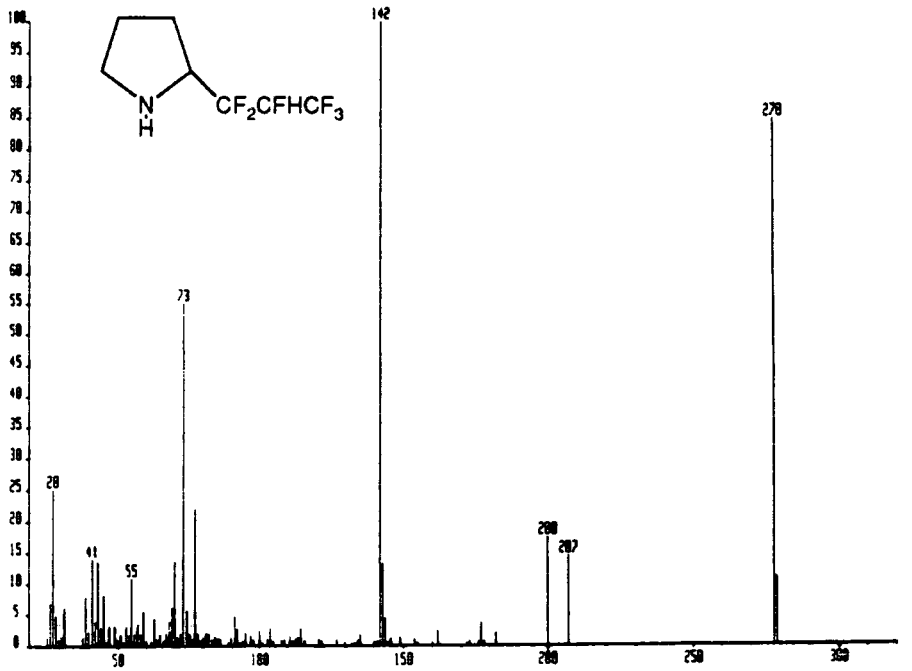
Mass	% Base
83.13	0.75
100.72	1.07
101.75	0.95
112.97	84.73
113.99	5.49
126.03	0.51
129.04	2.81
146.01	3.73
148.01	1.27
161.04	0.63
162.06	0.31
177.01	100.00
178.03	8.03
179.02	5.06
211.99	21.18
213.00	1.23
213.99	8.97
215.01	0.58
216.00	0.36

EI$^+$ M.Wt. 293 No. 2



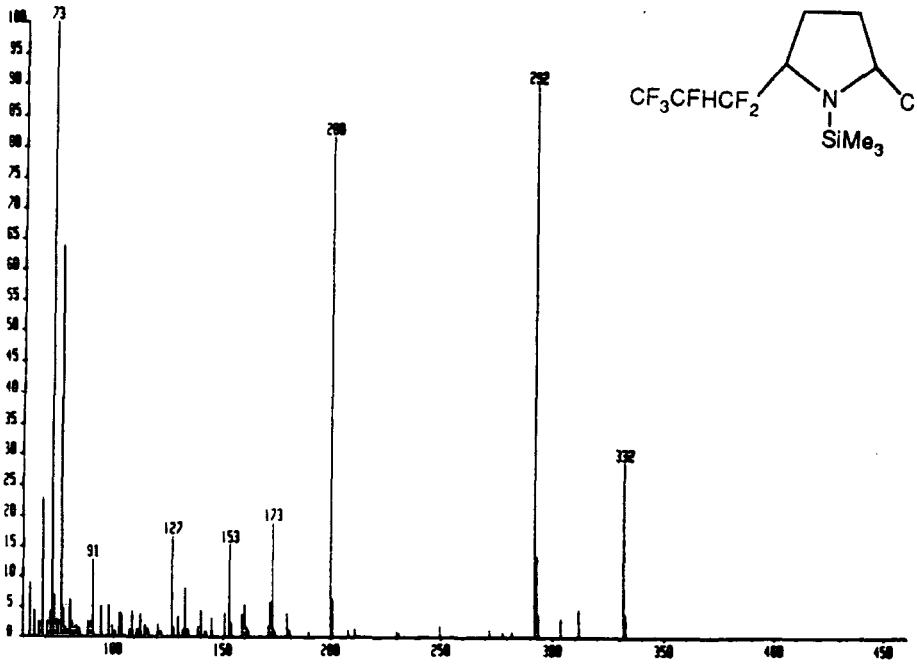
Mass	% Base
26.00	2.27
27.01	14.81
27.99	20.14
29.00	23.50
29.01	2.22
29.98	0.96
29.01	1.13
29.02	3.56
30.02	3.14
30.98	0.75
31.00	0.31
31.97	4.58
33.00	0.44
36.99	1.09
38.00	2.66
39.00	15.66
39.94	1.70
40.01	3.27
41.02	26.55
41.99	0.57
42.02	12.43
43.03	48.10
43.96	0.86
44.03	1.62
49.98	1.30
50.97	3.07
50.99	1.64
51.99	0.61
53.00	2.16
54.00	0.87
55.02	3.39
56.02	1.08
56.98	0.92
57.03	2.12
57.98	0.10
58.04	0.67
58.99	1.09
65.00	1.02
66.00	1.61
67.00	1.74
67.98	4.34
68.01	7.88
68.95	8.70
69.02	2.91
70.02	100.00
70.98	0.23
71.02	4.78
71.98	0.32
73.00	0.32
74.96	0.50
76.97	1.73
90.99	2.53
91.96	13.56
92.00	1.59
92.93	0.14
92.97	0.83
93.01	0.19
93.98	0.54
94.95	1.16
96.02	0.33
96.96	3.91
96.96	0.25
97.04	0.24
97.97	0.70
99.93	0.31
99.99	0.94
100.94	0.30
101.00	1.64
119.96	1.01
121.95	0.26
128.93	0.69
129.96	0.23
130.91	0.49
131.97	0.37
132.94	0.23
134.02	0.12
134.95	0.66
138.93	0.15
139.92	0.82
141.95	0.32
150.89	0.75
153.92	0.29
159.91	1.62
161.94	1.03
168.88	0.26
171.90	0.36
172.92	0.19
173.91	0.50
179.91	0.33
180.88	0.34
181.93	0.77
192.89	0.45
199.90	0.33
201.92	1.07
219.90	2.33

EI$^+$ M.Wt. 221 No. 3.



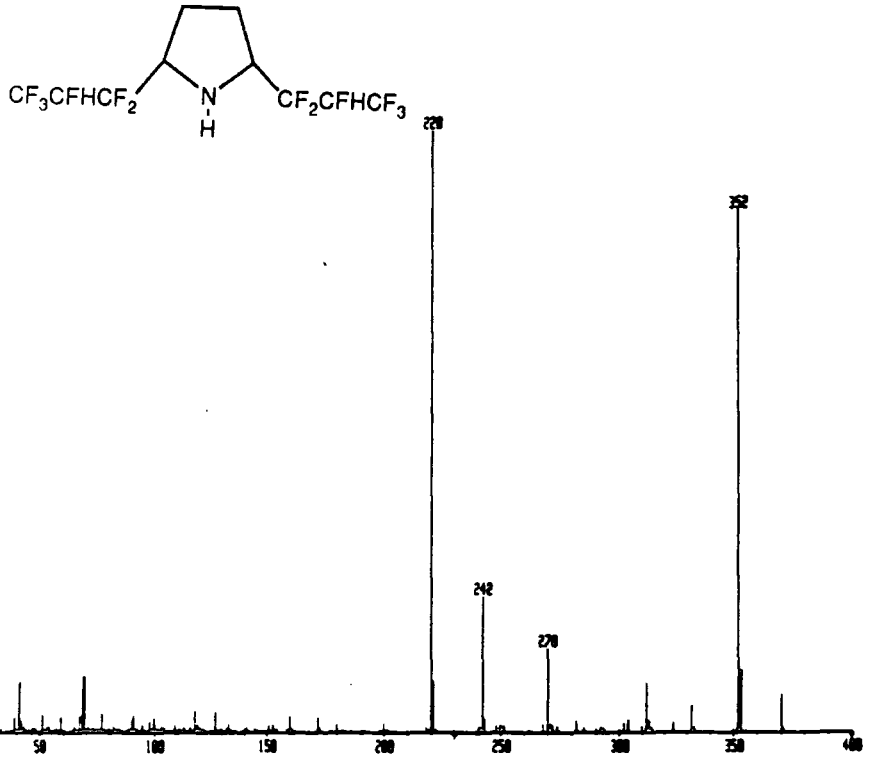
Mass	% Base						
26.00	1.34	58.06	0.47	101.04	0.26
27.01	6.97	59.01	5.39	103.02	1.07
27.96	0.40	62.99	4.29	104.01	2.85
27.99	24.96 F	63.52	0.74	111.03	1.38
28.00	6.36 F	63.99	0.83	112.04	0.61
28.97	1.93	65.01	1.56	112.98	0.97
29.99	0.58	66.02	0.71	113.05	0.99
29.02	4.70	67.03	1.84	114.05	1.27
30.02	0.89	68.03	3.80	115.02	2.44
30.98	1.34	68.97	6.23	116.02	0.64
31.00	0.74	69.05	1.75	121.01	0.93
31.97	6.01	70.00	0.58	122.01	0.56
38.00	1.11	70.05	13.69	127.00	1.08
39.01	7.94	71.01	1.25	130.03	0.42
39.94	2.13	71.05	1.24	132.04	0.34
40.01	1.01	72.02	1.88	133.01	0.47
41.02	14.01	73.03	54.94	134.01	0.66
41.98	0.73	74.03	5.53	135.03	1.59
42.02	3.77	75.02	1.73	140.00	0.43
42.98	5.95	75.99	1.07	140.97	0.48
43.03	13.58	77.00	22.03	141.98	0.70
43.98	2.73	78.00	1.76	142.99	100.00
44.96	0.50	79.00	0.69	143.99	13.28
44.99	8.06	80.03	1.18	144.99	4.25
46.00	0.65	80.98	1.98	145.99	0.48
46.96	2.88	81.04	1.04	146.96	1.03
47.01	1.18	82.01	1.80	149.01	1.11
48.97	2.90	83.01	0.76	154.01	0.90
50.99	1.66	83.97	0.91	155.04	0.32
52.01	0.49	84.01	1.25	160.02	0.43
53.02	2.90	84.97	0.95	162.04	2.16
54.02	1.67	85.02	1.00	172.02	0.38
54.98	0.83	90.00	1.16	173.02	0.75
55.04	10.85	91.03	4.71	176.06	0.99
55.98	0.89	92.03	2.54	177.07	3.49
56.04	1.77	94.99	1.93	178.07	0.62
57.00	2.23	95.06	0.86	182.05	1.98
57.05	3.31	96.99	1.27	200.05	0.87
58.01	1.58	100.04	2.21	207.04	0.72
				278.10	4.23
				279.09	0.54

EI+ M.Wt. 443 No. 4.



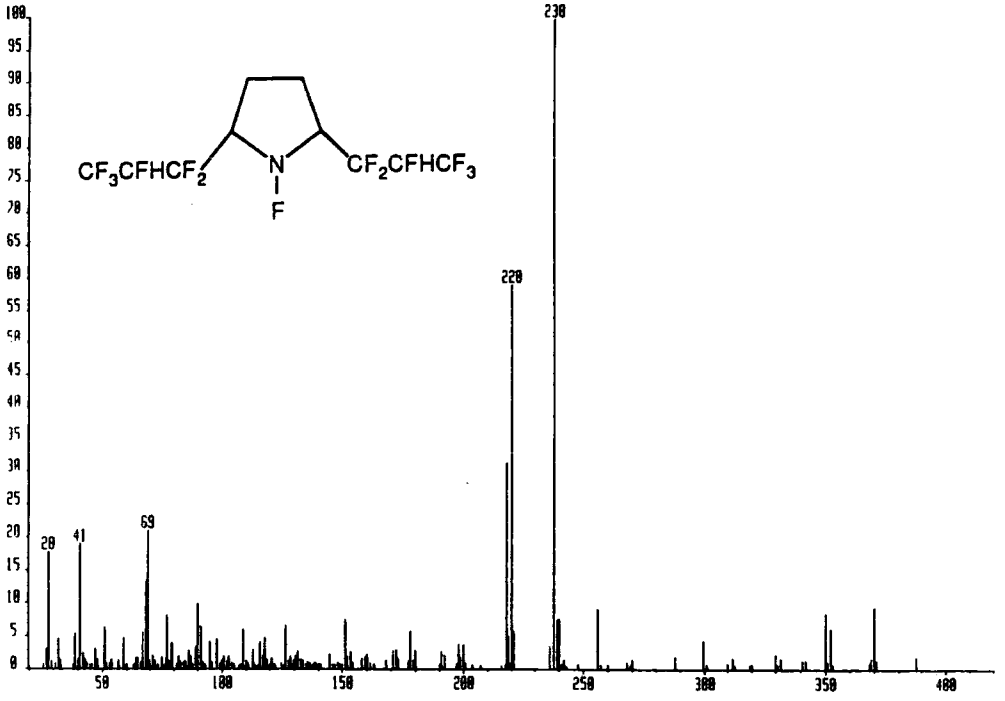
Mass	% Base		
62.97	8.89	127.91	1.46
64.98	4.34	129.94	3.29
67.00	2.52	131.91	1.06
68.01	2.11	132.92	8.04
68.95	22.82	133.93	1.18
70.99	2.72	138.92	1.94
71.99	4.34	139.97	4.30
73.00	100.00	141.95	0.81
74.00	7.02	144.92	3.13
74.96	1.14	150.91	4.02
75.00	2.76	152.93	15.23
75.97	2.72	153.93	2.15
76.97	63.91	158.92	3.65
77.97	4.99	159.92	5.32
78.97	1.46	160.94	1.50
80.01	1.02	161.95	1.10
80.95	6.29	170.90	1.83
81.95	2.44	171.89	5.81
82.98	1.46	172.91	18.88
83.98	1.79	173.93	1.10
84.99	1.30	179.91	3.86
88.96	2.52	180.92	0.97
89.96	2.48	189.97	0.81
90.97	12.71	199.93	81.93
94.95	5.08	200.93	6.17
97.98	5.20	207.96	1.04
99.99	1.71	210.92	1.26
100.95	0.73	229.91	0.89
102.97	3.90	230.91	0.57
103.97	3.65	249.91	1.83
107.94	1.14	271.86	1.18
108.95	4.30	277.84	0.89
110.98	1.22	281.91	0.73
111.98	1.22	291.92	90.01
112.93	3.69	292.91	13.28
114.95	1.87	293.92	3.65
115.94	1.18	303.85	2.92
120.92	2.07	311.87	4.38
121.92	0.93	331.86	28.70
126.91	16.61	332.87	3.65

EI+ M.Wt. 371 No. 5.



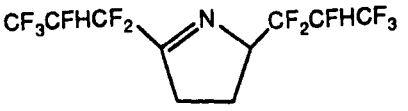
Mass	% Base
28.00	9.22
39.01	2.31
41.02	8.35
42.02	1.68
50.99	2.74
59.01	2.40
67.02	2.76
68.03	9.22
68.97	7.50 F
69.03	9.20 F
76.99	2.83
89.98	1.88
90.99	2.73
94.97	1.04
98.00	1.66
100.02	2.13
118.01	3.51
126.97	3.25
132.98	1.36
150.96	1.03
152.98	1.13
159.98	2.64
171.98	2.32
179.99	1.16
199.98	1.42
220.01	100.00
220.36	0.04
220.43	0.08
220.63	0.05
221.01	8.30
222.00	0.36
222.97	0.06
227.99	0.05
229.01	0.05
229.99	0.09
239.97	0.08
240.98	0.08
241.97	2.28
242.98	0.20
247.98	0.09
248.99	0.05
250.00	0.11
251.00	0.09
262.01	0.04
268.00	0.12
270.00	1.40
271.01	0.12
271.98	0.09
274.00	0.08
282.01	0.16
284.96	0.05
285.00	0.06
289.99	0.05
291.98	0.08
292.80	0.05
293.86	0.05
299.98	0.04
302.00	0.14
303.98	0.18
309.97	0.08
311.99	0.80
312.62	0.04
312.74	0.07
313.15	0.16
313.79	0.06
313.90	0.03
314.32	0.04
323.98	0.14
332.00	0.43
333.01	0.07
349.98	0.05
351.58	0.06
352.00	8.67
352.51	0.04
353.01	1.02
369.99	0.61
371.01	0.07

EI^+ M.Wt. 389 No. 6.



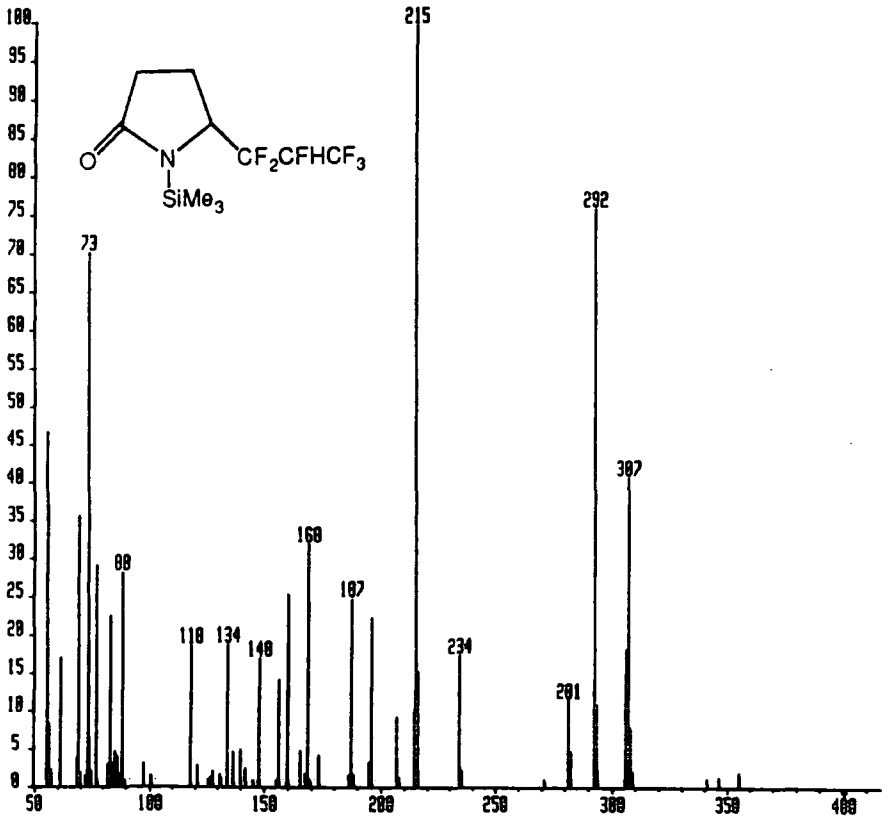
Mass	% Base		Mass	% Base		Mass	% Base		Mass	% Base
27.03	2.97		102.00	1.08		207.04	0.47		341.93	1.18
28.01	17.58		103.01	1.76		215.98	0.40		349.98	8.41
29.04	1.05		109.00	5.89		217.73	0.53		350.96	1.05
31.98	4.37		110.01	1.02		218.00	31.40		351.99	6.09
33.00	1.23		112.98	2.82		219.00	4.96		353.02	0.66
39.01	5.31		116.01	4.00		219.69	0.31		367.98	1.03
40.02	1.37		117.02	1.94		219.82	0.69		368.96	1.57
41.03	18.77		118.02	4.54		220.01	59.14		369.98	9.38
42.03	2.24		119.01	1.28		221.01	5.57		370.98	1.24
43.05	1.28		121.00	1.42		235.98	3.34		387.94	1.79
47.02	2.89		127.00	6.47		237.71	0.73			
48.02	1.34		128.00	1.24		237.77	1.11			
51.00	6.15		128.88	1.76		238.00	100.00			
54.03	1.28		129.02	1.61		239.00	7.38			
57.01	1.11		130.01	1.18		239.96	7.51			
59.02	4.54		130.92	1.86		240.91	0.66			
64.00	1.42		131.88	2.58		240.96	0.79			
65.02	1.69		133.00	1.28		241.95	1.28			
67.04	5.47		133.88	1.18		242.97	0.31			
68.04	13.16		144.98	2.24		247.96	0.60			
68.98	20.84	F	150.97	7.34		255.98	9.02			
69.05	5.21	F	151.98	1.79		256.99	0.53			
70.00	1.15		153.00	2.45		259.93	0.53			
71.02	1.89		157.98	1.47		267.98	0.82			
72.02	1.18		158.98	1.76		269.08	0.40			
74.99	1.57		159.99	2.13		269.99	1.28			
77.01	7.96		168.00	1.16		287.98	1.73			
78.01	1.24		170.98	2.73		299.98	4.34			
78.99	3.89		171.98	2.82		301.00	0.66			
81.99	1.79		172.99	1.47		309.99	0.69			
85.02	1.03		176.97	1.03		311.98	1.69			
86.03	2.60		177.96	5.70		312.94	0.52			
87.03	1.79		178.99	1.18		318.95	0.40			
89.01	3.24		179.99	2.60		319.00	0.47			
90.01	9.83		190.97	2.58		319.98	0.53			
91.02	6.44		191.97	1.35		329.98	2.02			
95.00	4.05		197.99	3.76		330.94	0.53			
98.03	4.41		199.00	1.69		331.97	1.55			
100.03	1.18		200.01	3.50		340.93	1.24			
101.00	1.76		200.99	0.69						
			203.98	0.40						

EI^+ M.Wt. 369 No. 7.



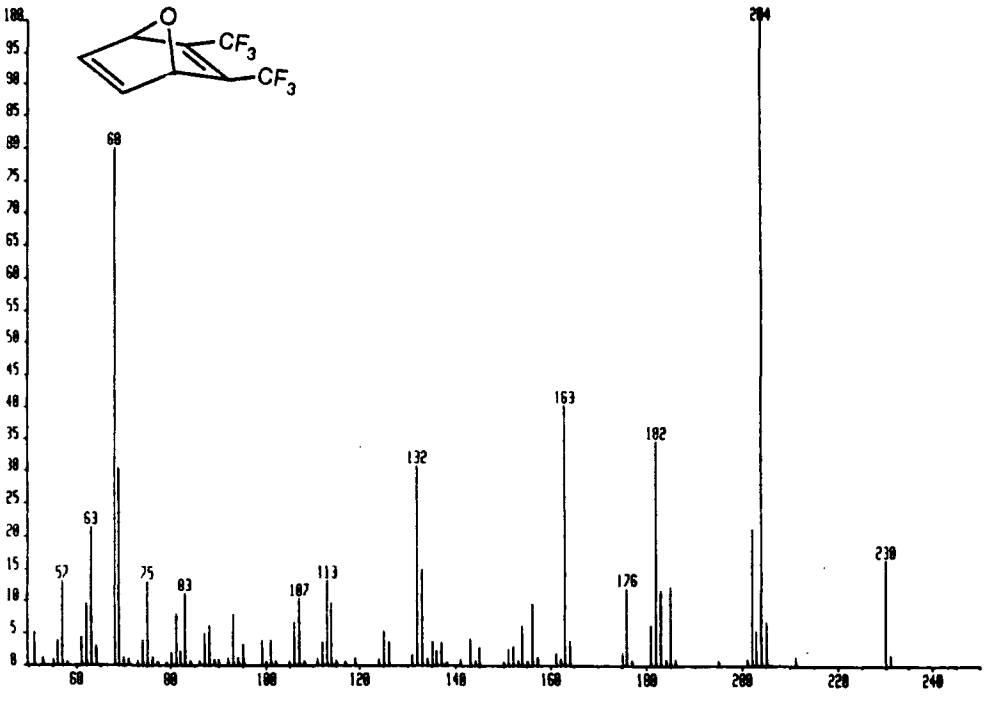
Mass	% Base		Mass	% Base		Mass	% Base	
27.02	1.74		140.95	5.88		217.59	5.88	
29.01	6.47		144.93	2.07		217.93	100.00	
39.00	5.78		145.93	0.32		218.33	0.10	
40.00	1.47		146.85	0.07		218.39	0.08	
41.01	23.06	F	146.93	5.88		218.49	0.06	
41.03	10.08	F	147.85	0.06		218.71	0.18	
42.02	1.15		147.87	0.10		218.89	19.33	F
50.99	5.52		147.95	0.76		218.96	19.33	F
56.99	5.88		148.89	0.13		219.93	0.85	
59.01	2.96		148.96	0.19		220.86	5.88	
60.01	5.88		149.93	5.88		221.90	0.15	
63.98	1.49		150.92	6.32	F	225.87	0.18	
64.99	1.11		150.99	5.88	F	227.94	5.88	
67.01	6.72		151.93	1.21		228.92	0.19	
68.02	5.88		152.94	5.88		229.90	0.13	
68.96	19.33		153.95	0.38		234.87	5.88	
71.00	2.18		156.92	0.26		238.85	0.11	
74.96	1.58		157.92	0.35		238.95	0.08	
76.98	5.09		158.93	0.63		239.48	0.10	
81.96	1.78		159.94	0.46		239.62	0.22	
82.98	5.88		160.88	0.13		239.88	23.45	
87.97	5.88		160.92	0.11		240.88	1.79	
88.98	5.88		160.94	5.88		245.88	0.15	
89.97	19.33		162.92	0.29		247.91	0.45	
90.99	6.72		163.94	5.88		258.85	5.88	
92.00	5.88		164.92	0.27		259.90	0.14	
94.96	5.88		165.93	0.35		260.88	0.10	
100.96	1.78		166.95	0.49		265.89	0.11	
101.97	1.49		167.26	0.07		265.93	0.11	
102.98	0.98		167.95	5.88		267.91	2.69	
103.99	0.21		168.95	5.88		268.93	0.25	
105.95	0.13		169.93	0.14		269.90	0.14	
106.95	0.27		170.93	6.14		271.89	0.32	
107.96	0.71		171.93	1.94		279.90	0.18	
108.86	0.11		172.95	0.98		283.87	0.11	
108.97	10.88		176.91	5.88		285.88	0.10	
109.97	0.56		177.92	1.06		289.91	5.88	
110.99	0.10		178.94	0.67		299.61	5.88	
112.94	2.02		179.50	0.08		299.90	19.33	
113.95	0.33		179.53	0.09		300.90	1.40	
114.97	0.29		179.68	0.15		301.84	0.11	
115.97	4.68		179.70	0.11		301.89	0.11	
116.06	0.08		179.73	0.11		302.85	5.88	
116.98	1.74		179.76	0.08		303.84	5.88	
117.99	4.37		179.94	0.55		309.84	5.88	
118.97	0.35		180.17	0.08		310.35	0.11	
119.94	0.19		180.92	0.13		310.44	5.88	
120.86	0.11		181.08	0.11		311.15	5.88	
120.96	1.39		183.91	0.13		311.78	0.13	
121.96	1.03		185.91	0.10		311.96	0.08	
122.97	5.88		188.90	0.19		312.20	0.10	
124.94	0.21		189.90	0.36		312.24	0.11	
125.94	0.13		190.91	2.11		312.29	0.11	
126.95	4.21		191.91	0.32		318.91	5.88	
127.96	0.58		194.91	5.88		319.86	0.16	
128.65	0.09		195.90	0.06		320.87	0.07	
128.72	0.11		196.90	0.15		321.86	5.88	
128.79	5.88		197.91	5.88		329.88	5.88	
128.84	0.24		198.92	1.00		330.92	5.88	
128.97	1.14		199.93	0.23		340.86	2.32	
129.07	0.11		200.92	0.08		341.80	5.88	
129.83	0.10		201.88	0.11		349.20	0.09	
129.85	0.11		202.92	0.11		349.24	0.10	
129.98	0.95		203.92	0.51		349.33	0.14	
130.91	0.84		204.91	0.08		349.46	5.88	
131.83	0.19		206.89	0.08		349.84	19.44	F
131.94	0.32		207.88	5.88		349.98	10.33	F
132.95	0.72		208.91	0.21		350.88	2.24	
133.85	0.11		209.91	0.16		351.82	0.11	
133.95	0.27		215.39	0.09		353.86	0.32	
134.85	0.09		215.90	0.13		367.92	0.15	
135.97	0.50		216.34	0.08		368.47	0.06	
136.92	0.14		216.53	0.11		368.88	2.81	
137.93	0.16		216.61	0.11		369.88	0.50	
138.93	0.54		216.88	5.88		370.18	0.08	
139.94	0.43		217.09	0.08				

EI+ M.Wt. 307 No. 8.



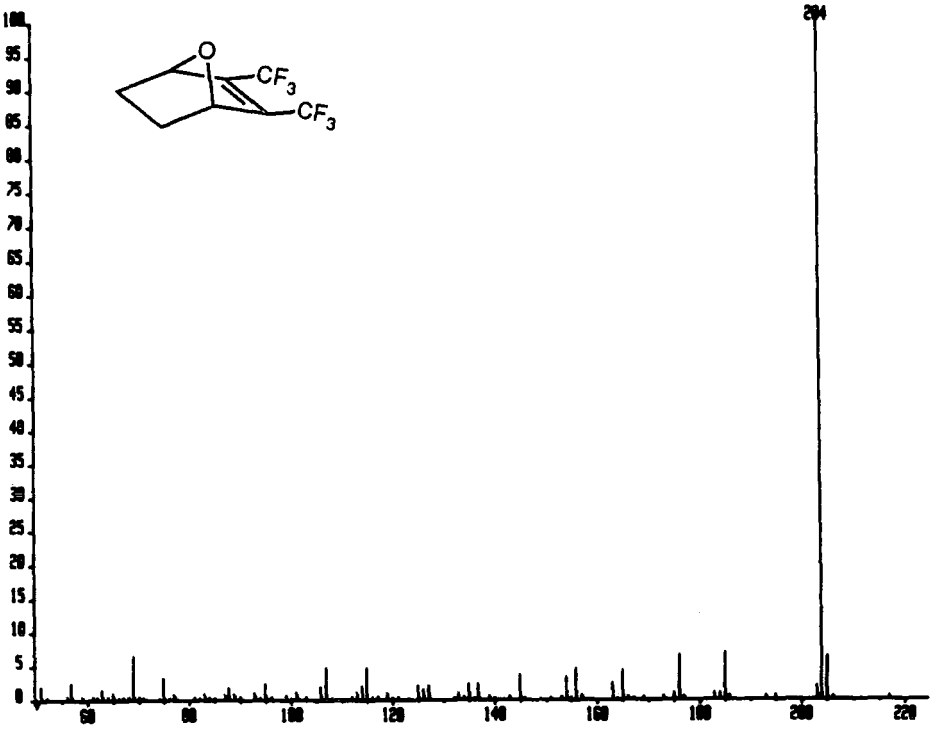
Mass	% Base
55.26	46.45
56.26	8.12
57.26	2.05
61.21	16.76
68.09	3.58
69.08	35.39
70.01	1.77
71.88	1.33
72.81	70.03
73.73	6.42
74.65	1.95
76.49	28.98
77.41	0.65
82.17	2.94
83.20	22.35
84.25	3.04
85.28	4.51
86.32	3.89
87.35	1.60
88.39	27.99
89.16	0.68
97.71	3.00
100.77	1.30
118.11	18.43
121.09	2.73
126.12	0.96
127.10	1.23
128.01	0.72
128.10	1.95
131.08	1.50
131.59	1.09
134.12	18.70
137.12	4.51
140.09	4.88
142.14	2.29
145.12	0.82
147.14	0.68
148.11	16.79
155.14	0.78
156.20	14.03
159.17	0.61
160.14	25.26
165.16	4.71
167.15	1.67
168.16	31.81
169.20	0.75
173.14	4.06
186.17	1.50
187.14	24.64
188.18	1.47
195.16	3.14
196.14	22.22
207.16	9.15
208.16	1.26
214.15	10.20
215.16	100.00
216.17	15.15
234.17	17.27
235.17	2.08
271.16	0.89
281.20	11.43
282.20	4.51
292.21	76.04
293.21	10.75
294.23	2.15
305.40	0.96
306.23	18.12
307.23	40.78
308.23	7.78
309.22	1.84
341.20	1.06
346.20	1.23
355.26	1.81
429.31	4.85
431.29	1.16

EI^+ M.Wt. 230 No. 9.



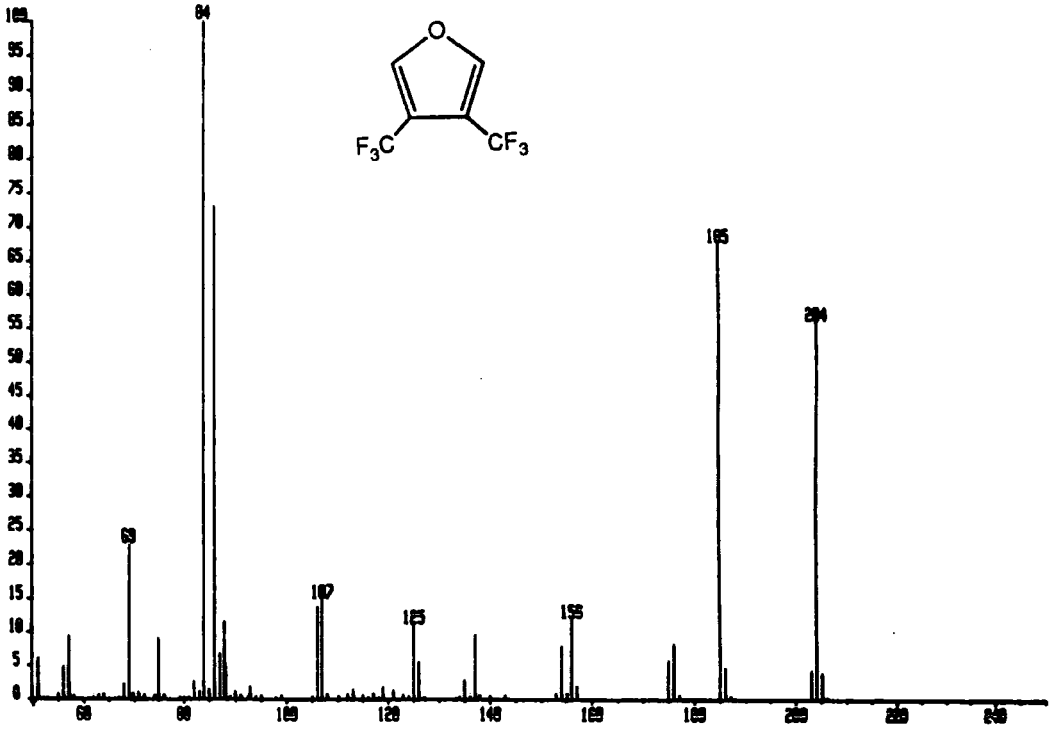
51.17	5.16
57.16	13.05
62.15	9.41
63.16	21.27
69.15	80.03
69.11	30.20
75.12	13.08
81.11	7.82
83.13	11.18
88.12	6.22
93.11	7.84
106.13	6.67
107.14	10.40
113.14	13.15
114.15	9.67
125.12	5.46
132.14	30.85
133.15	15.04
154.16	6.22
156.15	9.43
163.17	40.31
176.17	11.84
181.18	6.19
182.19	34.61
183.19	11 63
185.17	12 13
202.17	21.23
203.16	5.36
204.16	100.00
205.15	6.59
229.61	0.03
229.66	0.04
230.20	16.41
231.04	0.04
231.21	1.57
232.22	0.14
232.29	0.04

EI^+ M.Wt. 232 No. 10.



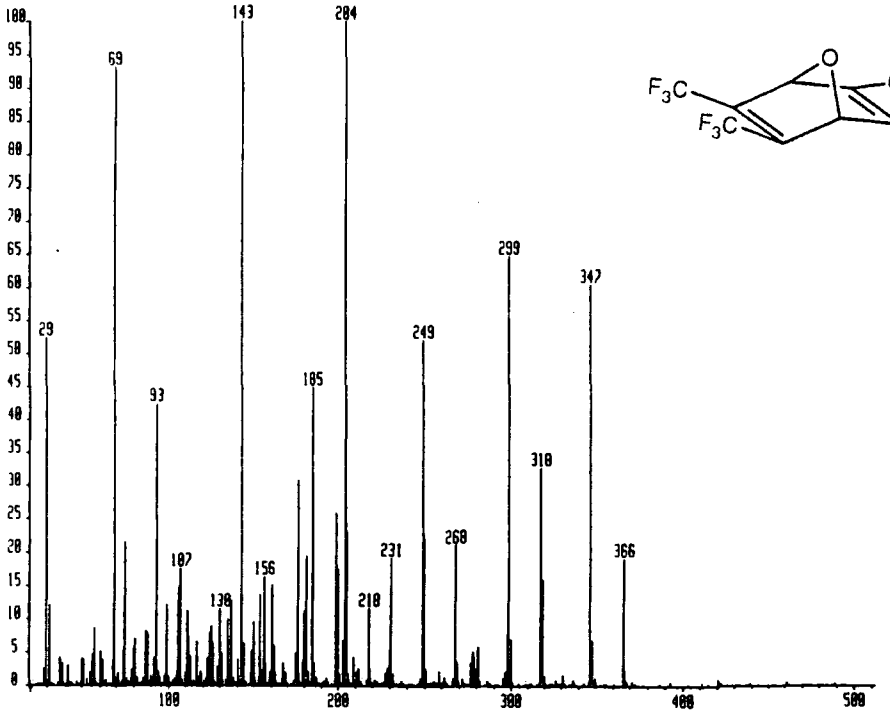
Mass	% Base
51.00	1.83
52.02	0.15
55.99	0.43
57.00	2.42
59.02	0.33
61.00	0.25
62.00	0.36
63.01	1.31
64.01	0.32
65.02	0.85
66.99	0.28
68.00	0.36
68.98	6.38
70.01	0.36
71.00	0.12
73.99	0.13
74.99	3.24
76.00	0.14
77.01	0.73
81.00	0.33
81.99	0.12
83.01	0.85
84.02	0.33
85.03	0.14
86.99	0.81
88.00	1.70
89.00	0.74
89.98	0.25
92.98	0.88
94.00	0.13
95.00	2.33
96.02	0.28
98.99	0.60
100.00	0.12
101.00	1.01
103.01	0.31
105.98	1.81
106.99	4.74
108.00	0.18
111.98	0.27
112.99	1.03
114.01	1.90
115.01	4.68
116.02	0.31
117.00	0.33
118.99	0.93
119.99	0.12
121.00	0.30
123.00	0.14
124.98	1.92
125.99	1.39
127.02	1.91
132.00	0.35
133.01	0.85
134.02	0.28
134.99	2.30
136.00	0.15
136.98	2.25
139.00	0.39
139.98	0.16
142.99	0.43
145.00	3.66
146.01	0.17
151.00	0.12
152.97	0.24
153.99	3.37
154.99	0.20
155.98	4.55
156.99	0.63
163.00	2.43
164.02	0.22
165.01	4.17
166.02	0.25
166.99	0.14
169.00	0.28
173.00	0.52
174.98	0.94
175.98	6.57
176.99	0.33
183.01	0.85
184.01	0.91
184.99	6.93
186.00	0.47
193.02	0.49
195.03	0.56
203.00	1.93
204.00	100.00
205.00	6.41
206.02	0.26
216.99	0.49

EI^+ M.Wt. 204 No. 11.



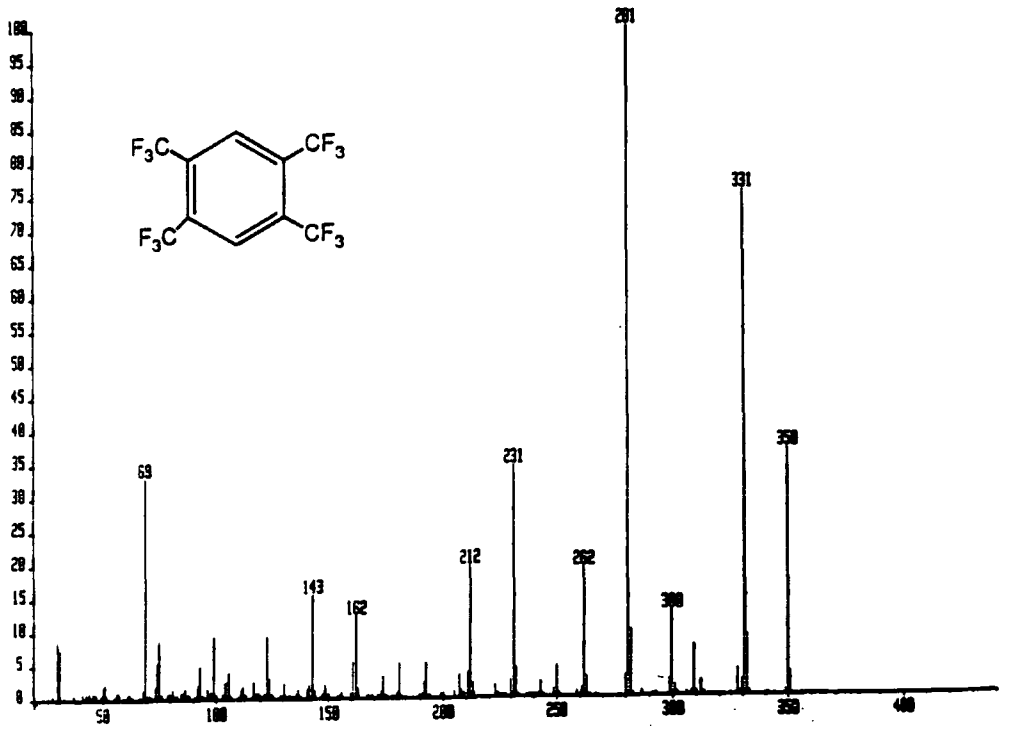
Mass	% Base	
50.99	5.93	
56.02	4.70	
57.03	9.25	
68.02	2.09	
69.01	22.72	
75.02	8.94	
81.96	2.63	F
82.03	1.05	F
83.02	1.12	
83.98	100.00	0
84.97	1.41	
85.96	73.21	
87.01	6.65	
87.96	11.44	F
88.04	5.13	F
90.01	1.14	
93.01	1.86	
106.02	13.76	
107.03	14.75	
113.02	1.30	
118.95	1.66	
120.95	1.25	
125.03	10.97	
126.04	5.49	
135.03	2.76	
137.03	9.59	
154.04	7.94	
156.04	11.84	
157.05	1.83	
175.04	5.69	
176.05	9.15	
185.05	67.86	
186.06	4.58	
203.07	4.17	F
204.08	56.28	F
205.09	3.74	

EI^+ M.Wt. 366 No. 12.



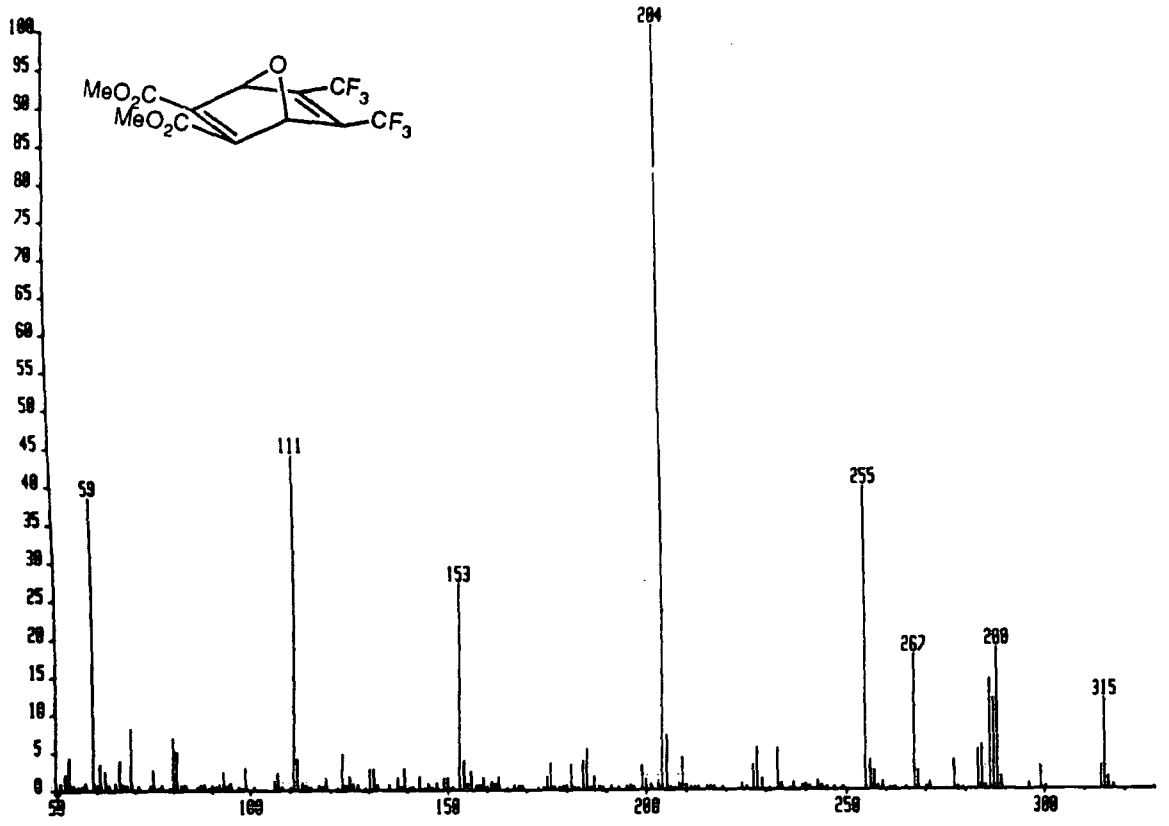
Mass	% Base	
27.93	2.46	
28.94	52.22	
30.93	11.99	
36.94	4.05	
37.95	3.16	
41.94	2.92	
49.91	3.98	F
50.92	3.83	
55.91	4.61	
56.92	8.46	
60.91	4.95	
61.91	3.81	
67.89	3.49	
68.88	92.99	
73.89	5.13	
74.89	21.58	
78.89	2.27	
79.90	5.54	
80.90	6.85	
86.89	8.00	
87.90	7.71	
91.89	4.00	
92.88	42.31	
98.89	12.02	
104.88	2.03	
105.88	14.64	
106.89	17.38	
110.88	10.99	
111.88	7.17	
112.88	4.23	
116.86	6.49	
118.87	2.03	
122.87	3.98	
123.86	7.72	
124.86	8.85	
125.87	6.22	
128.86	2.67	
129.86	11.43	
130.87	4.71	
134.87	9.88	
135.86	2.90	
136.86	12.58	
140.86	3.75	
142.85	100.00	
143.86	6.17	
148.86	5.21	
149.87	9.38	
153.86	13.68	
154.86	2.11	
155.86	16.17	
156.87	3.21	
160.86	15.06	
161.86	5.92	
167.86	3.13	
174.86	4.88	
175.86	30.76	
178.85	3.58	
179.86	11.04	
180.87	19.47	
181.87	2.04	
184.86	44.84	
185.86	3.18	
198.86	25.68	
199.86	17.44	
202.84	6.62	
203.88	100.00	
204.86	23.05	
208.86	4.12	
211.87	2.39	
217.85	11.48	
218.86	2.32	
228.85	2.65	
229.86	5.19	
230.87	19.07	
248.86	52.15	
249.87	22.53	
250.87	2.38	
258.86	2.16	
267.85	21.08	
268.85	3.37	
276.86	3.31	
277.87	4.99	
278.87	4.44	
279.86	2.40	
280.87	5.80	
297.88	7.52	
298.86	64.86	
299.87	6.89	
317.88	32.67	
318.89	15.85	
346.88	60.53	
347.89	6.64	
365.90	19.10	
366.90	2.10	

EI+ M.Wt. 350 No. 13.



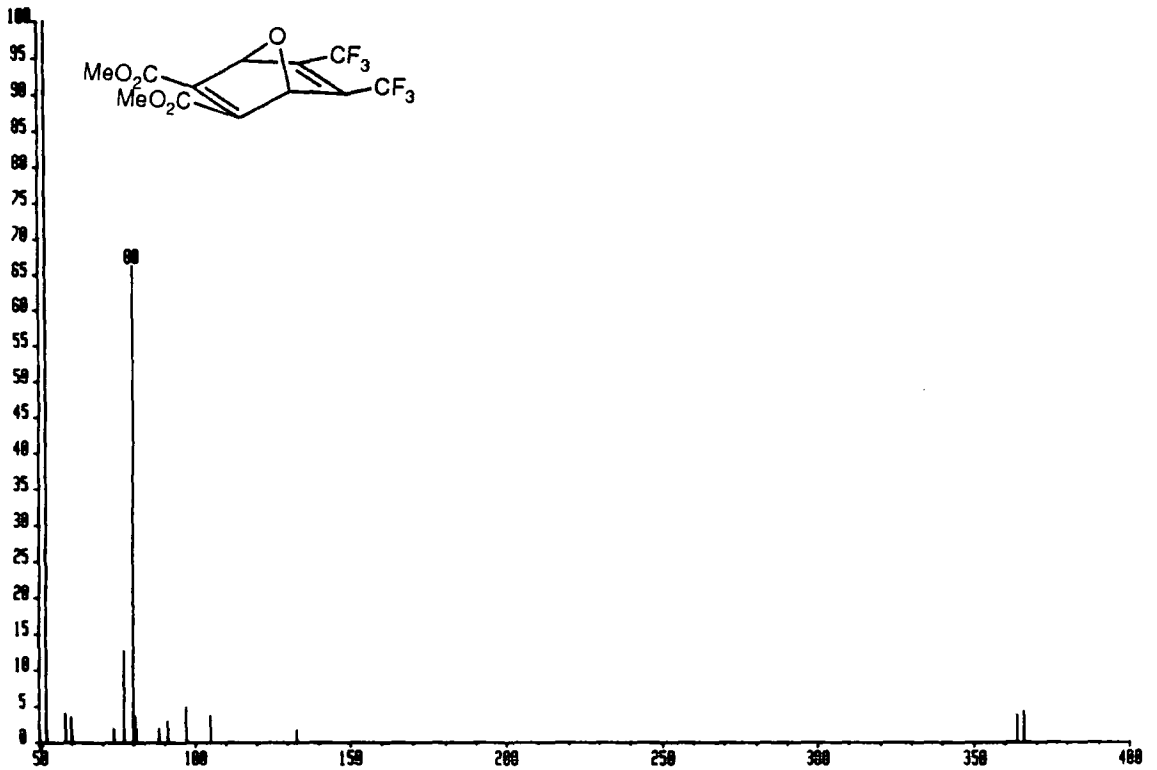
49.99	1.86	230.92	34.56
50.99	2.06	231.92	4.31
67.97	1.39	242.89	2.20
68.96	32.97	248.91	1.11
73.00	1.64	249.91	4.53
73.99	5.31	260.90	1.19
74.98	3.49	261.90	19.25
80.99	1.27	262.90	2.91
86.98	1.41	279.91	2.96
91.99	2.00	280.91	100.00
92.97	4.66	281.92	9.87
96.47	1.32	298.88	2.28
98.97	9.24	299.88	12.63
103.97	2.21	300.89	1.42
104.98	2.50	308.88	7.35
105.97	3.78	311.88	2.13
110.97	1.14	327.87	3.83
111.98	1.68	329.86	2.05
116.96	2.41	330.87	75.51
122.96	9.28	331.87	8.94
123.96	2.82	349.87	36.81
130.96	2.05	350.87	3.30
136.95	1.17		
140.95	1.29		
141.95	1.93		
142.96	15.49		
143.97	1.02		
148.96	1.80		
160.94	5.27		
161.95	12.31		
162.95	1.37		
173.95	3.21		
180.94	5.13		
191.93	2.22		
192.94	5.23		
206.96	3.36		
207.95	1.06		
210.92	3.82		
211.93	19.77		
212.93	2.19		
222.91	1.69		
229.90	2.41		

EI$^+$ M.Wt. 346 No. 14a.



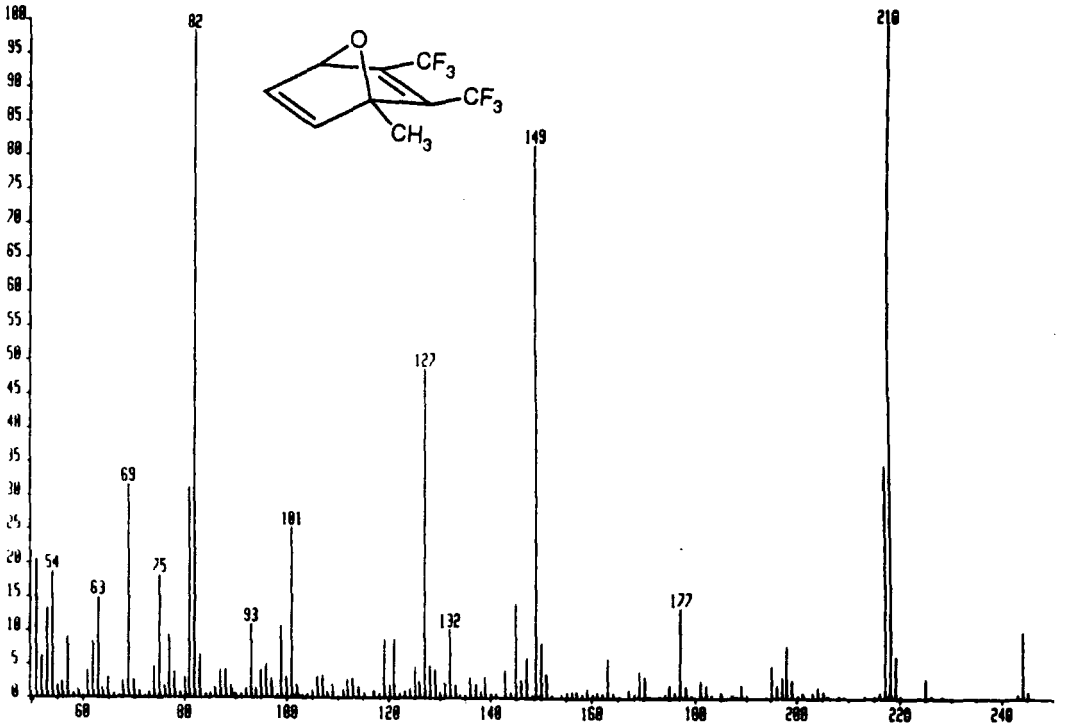
Mass	% Base
52.00	1.93
53.01	4.24
59.03	38.32
61.02	3.36
62.03	2.45
66.03	3.84
69.01	8.09
75.05	2.65
80.02	6.81
81.03	4.96
93.02	2.28
99.03	2.84
106.03	1.15
107.04	2.27
111.04	43.81
112.04	4.14
119.05	1.44
123.05	4.68
125.04	1.73
130.05	2.71
131.05	2.68
137.05	1.58
139.05	2.74
143.05	1.60
149.05	1.56
150.05	1.53
153.07	26.96
154.07	3.71
156.06	2.49
159.06	1.58
161.06	1.02
163.06	1.62
175.07	1.61
176.07	3.45
181.07	3.33
184.11	3.86
185.08	5.27
187.08	1.74
199.09	3.14
200.10	1.33
203.10	1.15
204.10	100.00
205.10	7.05
209.10	4.17
227.08	3.12
228.09	5.46
229.10	1.40
233.08	5.32
243.09	1.02
255.07	39.37
256.09	3.80
257.09	2.45
259.11	1.04
267.11	17.62
268.11	2.45
277.14	3.76
283.13	5.11
284.10	5.80
286.10	14.32
287.11	11.78
288.12	18.51
289.14	1.65
299.11	2.89
300.12	0.30
314.12	3.06
315.12	11.60
316.13	1.50
317.14	0.40
327.20	0.21

$Cl^+ NH_3$ M.Wt. 346 No. 14b.



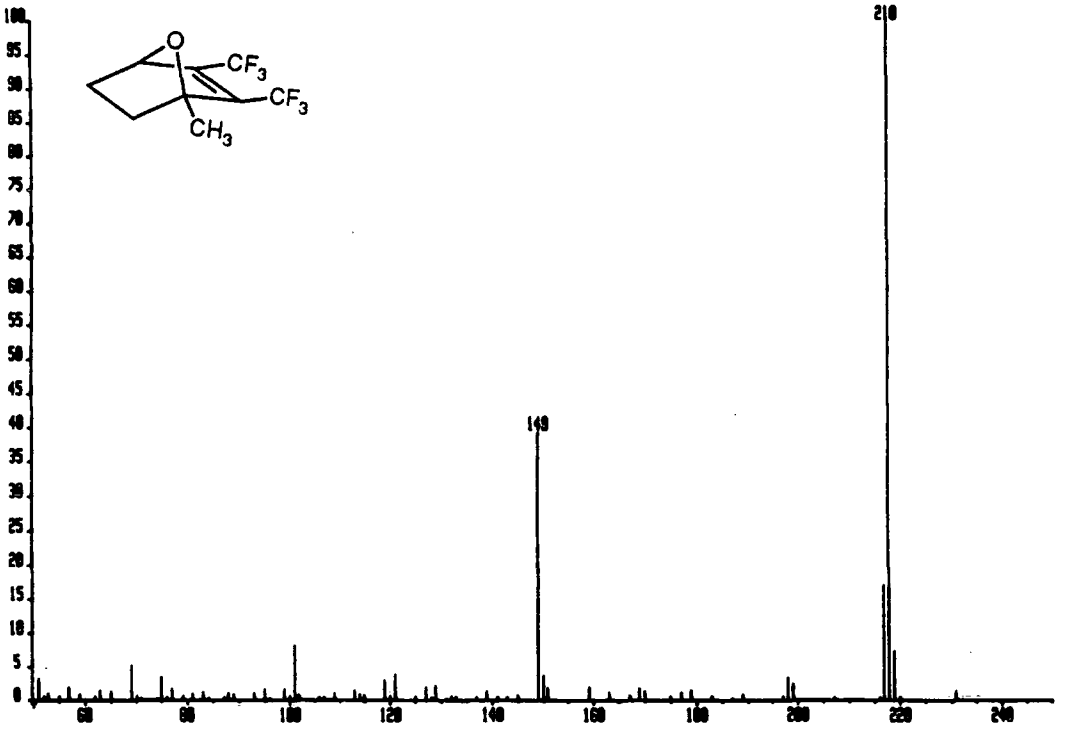
Mass	% Base
52.01	100.00
57.99	3.96
59.97	3.49
73.98	1.79
76.98	12.54
79.95	66.16
80.95	3.49
87.98	1.79
90.99	2.83
96.96	4.81
104.98	3.58
132.99	1.60
363.87	3.68
365.89	4.24

EI$^+$ M.Wt. 244 No. 15.



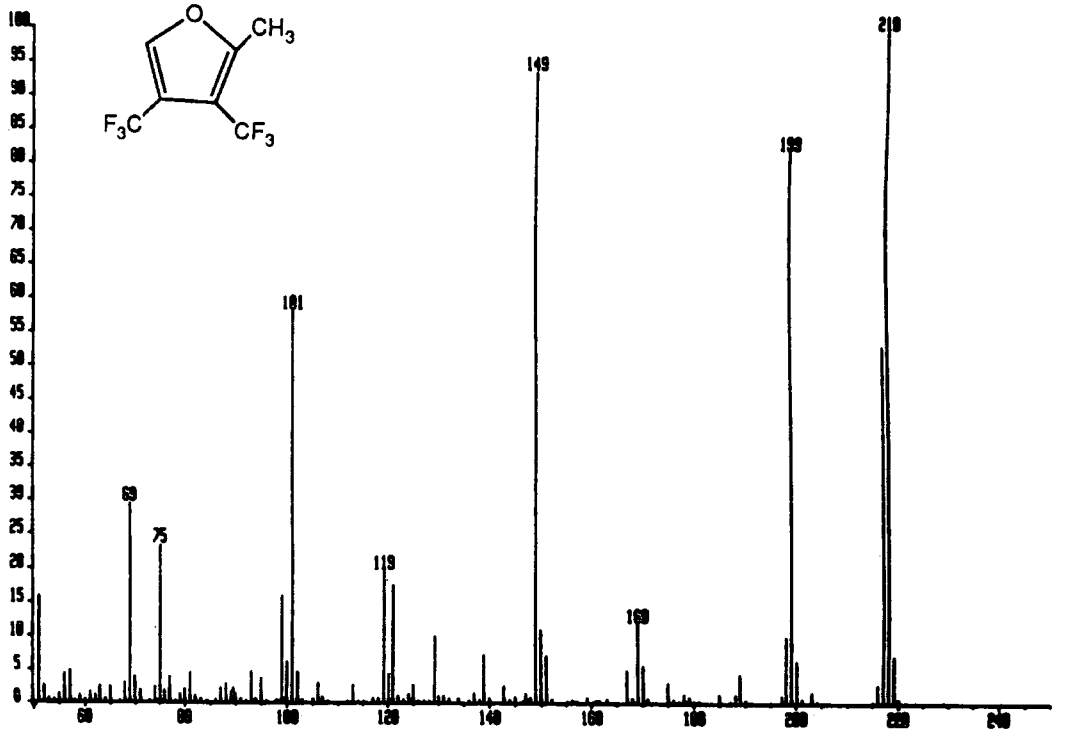
51	15	20	39	217.69	0.20
52	16	6	03	217.89	0.93
53	16	13	30	218.11	100.00
54	17	18	57	219.39	0.26
57	13	8	94	218.51	0.08
62	12	8	30	219.11	6.43
63	12	14	87	220.11	0.29
69	08	31	54	225.12	2.85
75	08	18	18	226.14	0.29
77	10	9	25	228.14	0.16
81	09	31	26	243.12	0.55
82	11	98	41	244.13	9.78
83	11	6	47	245.13	0.94
93	07	10	98		
99	08	10	55		
101	09	25	14		
119	07	8	80		
121	09	8	68		
127	11	48	83		
132	09	10	15		
145	12	14	13		
147	13	6	02		
149	12	81	81		
150	12	8	08		
163	12	5	84		
177	14	13	33		
198	11	7	73		
200	12	0	24		
201	12	0	70		
203	09	0	73		
204	09	1	57		
205	12	0	90		
206	10	0	16		
208	14	0	35		
209	13	0	13		
213	11	0	35		
215	09	0	18		
215	91	0	16		
216	14	0	77		
217	09	54	63		

EI$^+$ M.Wt. 246 No. 16.



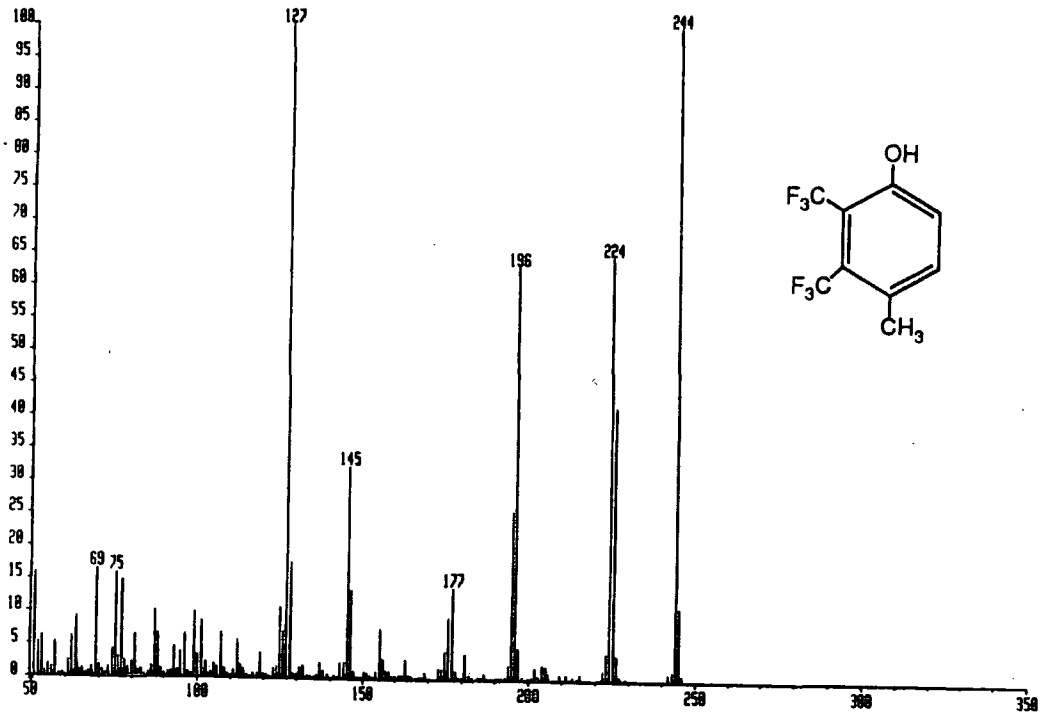
Mass	% Base
51.00	3.05
52.02	0.48
53.03	0.86
55.02	0.52
57.01	1.76
59.02	0.71
62.01	0.44
63.01	1.29
65.01	1.15
68.98	5.19
70.01	0.44
71.02	0.21
74.00	0.22
75.00	3.36
76.00	0.23
77.02	1.50
79.05	0.48
81.01	0.70
83.02	1.08
84.04	0.16
87.00	0.24
88.00	0.85
89.02	0.69
92.98	0.86
95.00	1.49
96.02	0.19
99.00	1.44
100.01	0.47
101.01	8.22
102.02	0.74
106.00	0.24
107.01	0.38
109.03	0.93
113.00	1.33
114.01	0.78
115.02	0.63
119.00	2.82
120.01	0.44
121.01	3.76
125.00	0.44
127.03	1.80
128.03	0.28
129.01	2.18
131.02	0.22
132.01	0.47
133.02	0.50
137.01	0.28
139.01	1.20
141.05	0.30
142.99	0.33
145.01	0.64
149.01	39.31
150.01	3.50
151.01	1.59
159.04	1.76
163.02	1.09
167.02	0.55
169.01	1.60
170.01	1.24
175.00	0.42
177.04	1.08
179.05	1.43
183.04	0.47
187.04	0.19
189.03	0.79
197.06	0.52
198.03	3.32
199.05	2.31
207.07	0.30
216.07	0.23
217.01	17.11
218.01	100.00
219.02	7.25
220.03	0.26
231.04	0.62

EI+ M.Wt. 218 No. 17.



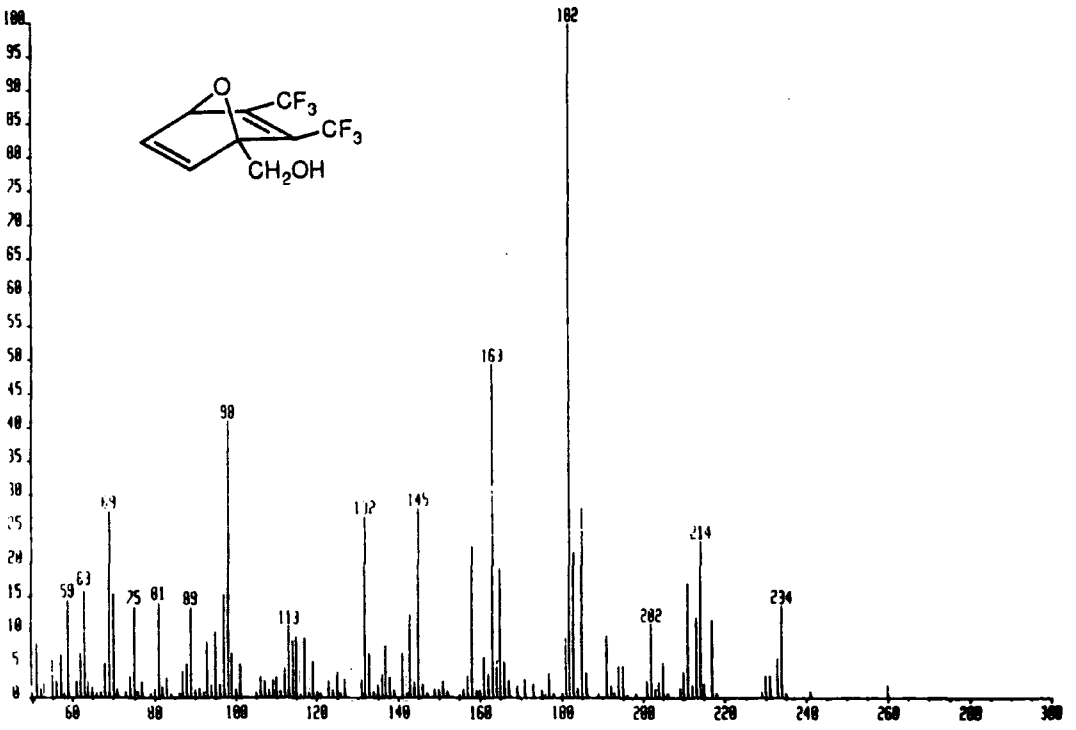
Mass	% Base
51.04	15.73
52.05	2.50
55.03	1.28
56.03	4.27
57.04	4.72
61.04	1.52
62.04	1.12
63.05	2.47
65.05	2.27
68.04	2.94
69.03	29.25
70.06	3.83
71.05	1.78
74.04	2.31
75.04	23.17
76.05	1.73
77.06	3.84
79.04	1.26
80.05	1.95
81.05	4.33
87.05	2.10
88.06	2.70
89.06	1.58
89.55	2.17
90.05	1.22
93.04	4.71
95.06	3.71
99.05	15.91
100.06	5.99
101.07	57.96
102.08	4.60
106.05	3.10
113.06	2.57
119.07	19.32
120.08	4.20
121.09	17.37
124.06	1.23
125.07	2.52
129.08	9.88
137.08	1.31
139.09	7.15
143.07	2.44
147.09	1.33
149.10	93.70
150.10	10.72
151.10	7.00
167.11	4.80
169.11	11.70
170.12	5.42
175.10	2.91
178.11	1.15
185.12	1.17
188.13	1.22
189.14	4.28
197.14	1.06
198.14	9.82
199.15	82.01
200.16	6.23
201.17	0.41
203.14	1.48
204.16	0.14
215.12	0.14
216.14	2.73 F
217.13	53.23 F
218.14	100.00 F
219.15	6.96
220.16	0.40

EI+ M.Wt. 244 No. 18.



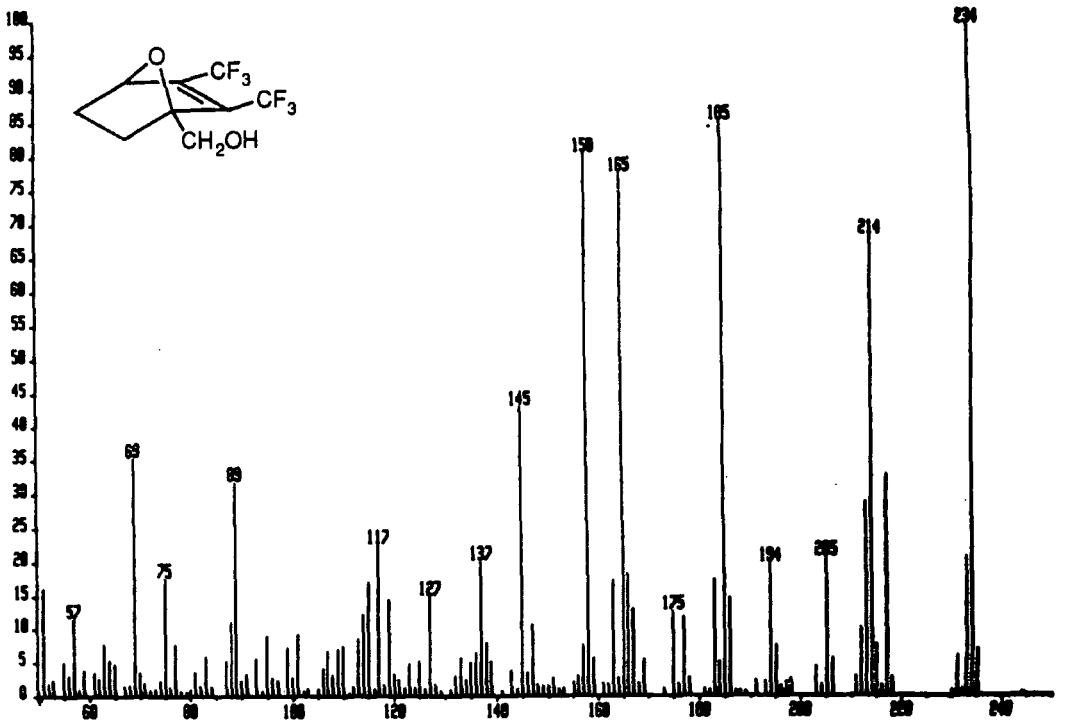
Mass	% Base	
51.04	15.71	
52.06	5.11	
53.03	6.13	F
53.07	2.89	F
57.04	5.18	
61.04	2.43	
62.04	6.01	
63.05	9.12	
69.03	16.31	
74.04	4.25	
75.04	15.83	
76.06	3.02	
77.07	14.64	
78.07	2.48	
80.04	2.18	
81.05	6.32	
87.06	9.94	
88.06	6.51	
93.05	4.52	
95.07	3.85	
96.08	6.51	
99.06	9.78	
100.07	3.39	
101.07	8.41	
102.57	2.33	
105.07	2.01	
107.08	6.59	
112.07	5.67	
119.08	3.69	
125.09	10.61	F
126.07	6.93	F
127.10	100.00	FO
128.11	17.62	
137.09	2.32	
143.08	2.30	
144.11	2.48	
145.09	32.21	
146.11	13.39	
155.11	7.39	
156.10	2.92	
163.10	2.92	
175.12	4.03	
176.12	9.20	
177.12	13.82	
181.11	3.82	
194.09	2.17	F
195.11	25.52	F
196.12	63.14	F
197.12	4.68	F
204.13	2.11	
205.12	2.04	F
223.10	3.96	F
224.13	64.91	F
225.14	41.68	F
226.15	3.69	F
244.14	100.00	FO
245.15	10.89	

EI^+ M.Wt. 260 No. 19.



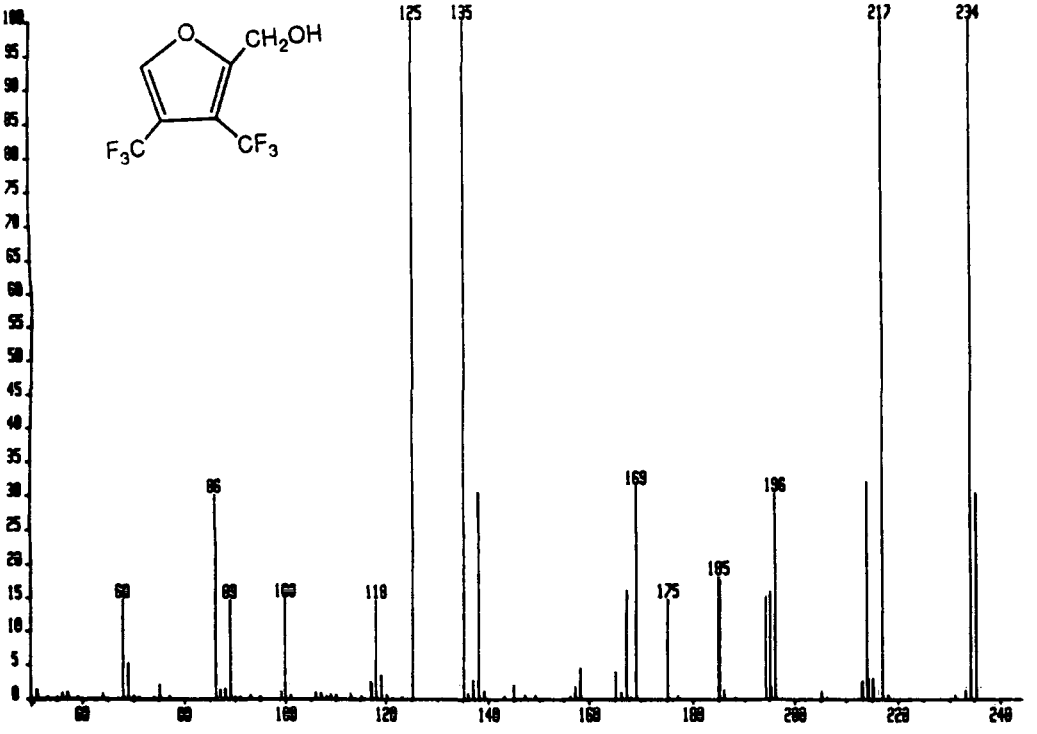
Mass	% Base
50.94	8.01
54.97	6.38
56.97	6.35
58.98	14.43
61.99	6.72
63.00	16.16
64.00	3.20
68.01	5.29
69.00	27.43
70.03	15.36
74.01	3.11
75.01	13.50
81.03	14.05
87.02	3.99
88.02	4.95
89.03	13.30
93.02	8.51
95.04	9.67
97.05	15.20
98.06	40.91
99.04	6.49
101.05	4.92
106.02	3.09
112.03	4.36
113.03	10.46
114.05	8.37
115.05	8.99
117.03	8.76
119.03	5.26
125.04	3.77
132.04	26.59
133.05	6.65
136.03	3.29
137.03	7.60
141.04	6.72
143.04	12.34
145.04	27.89
157.04	3.22
158.04	22.49
161.05	6.06
162.03	3.88
163.04	49.35
164.05	5.40
165.04	19.08
166.03	5.29
177.05	3.56
181.04	8.83
182.04	100.00
183.05	21.51
185.03	28.02
186.04	3.97
191.05	9.12
194.03	4.65
195.05	4.77
202.05	10.94
205.04	5.11
210.05	3.83
211.05	17.00
213.03	11.89
214.04	23.24
217.04	11.53
230.05	3.13
231.05	3.20
233.04	5.74
234.04	13.64
241.05	0.93
260.07	1.77

EI$^+$ M.Wt. 262 No. 20.



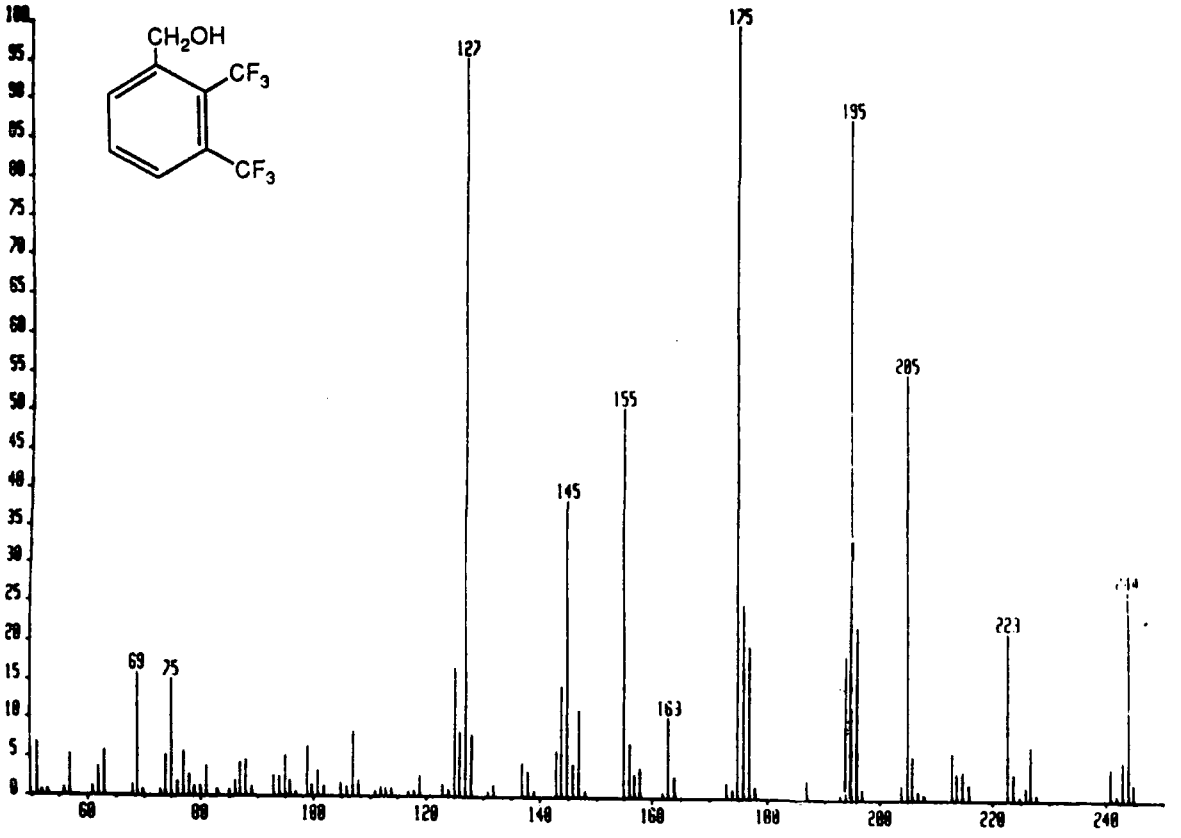
Mass	% Base
51.03	16.12
52.04	1.61
53.03	2.24
55.04	4.84
56.03	2.63
57.04	11.43
59.05	3.70
61.03	3.28
62.04	2.48
63.05	7.53
64.04	5.22
65.06	4.62
67.03	1.39
68.04	1.59
69.02	35.12
70.05	3.28
71.04	1.76
74.04	2.19
75.04	17.49
76.04	1.24
77.05	7.53
81.05	3.40
82.05	1.29
83.06	5.71
84.07	1.14
87.04	5.04
88.04	10.98
89.05	31.72
90.05	2.06
91.04	2.96
93.03	5.49
95.06	8.84
96.06	2.61
97.07	2.09
99.04	7.18
100.05	2.56
101.06	9.17
106.04	3.85
107.05	6.53
108.06	2.81
109.07	6.88
110.04	7.28
112.06	1.24
113.05	8.40
114.07	12.02
115.07	17.01
117.06	22.38
118.06	1.54
119.06	14.38
120.06	2.98
121.07	2.33
122.06	1.02
123.06	4.60
124.05	1.12
125.06	5.07
127.09	14.78
128.09	1.54
132.08	2.91
133.08	5.61
134.10	2.29
135.07	4.79
136.07	6.36
137.07	20.07
138.06	7.70
139.07	4.97
143.07	3.58
145.07	43.02
146.08	3.40
147.10	10.43
148.09	1.59
149.08	1.39
150.07	1.29
151.08	2.58
153.10	1.02
155.10	1.91
156.07	2.81
157.08	7.38
158.09	80.75
159.09	5.46
161.09	1.69
162.10	1.69
163.09	17.29
164.10	2.56
165.09	77.92
166.08	18.26
167.09	12.89
168.09	1.66
169.08	5.29
175.11	12.62
176.11	1.61
177.10	11.72
178.10	2.58
183.11	17.44
184.12	4.97
185.09	85.59
186.10	14.68
191.11	2.11
193.12	1.94
194.10	19.62
195.12	7.43
196.07	1.42
197.14	2.04
198.13	2.36
203.14	4.25
204.13	1.44
205.13	20.54
206.14	5.41
211.12	2.73
212.13	10.03
213.10	28.81
214.10	68.48
215.11	7.55
216.11	1.39
217.10	32.89
218.12	2.61
231.11	5.76
233.11	20.74
234.12	100.00
235.13	6.78

EI^+ M.Wt. 234 No. 21.



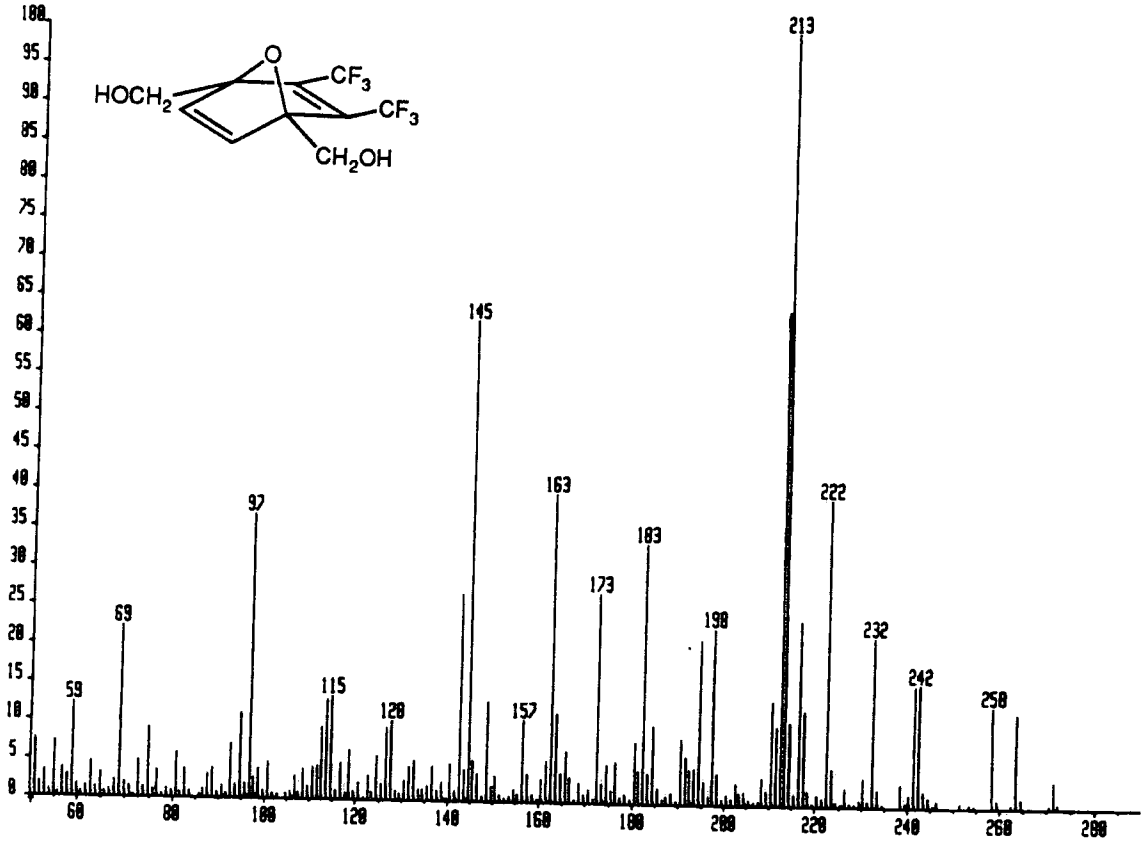
Mass	% Base
51.06	1.26
51.08	0.88
53.06	0.13
55.08	0.17
56.08	0.79
57.08	0.88
59.10	0.20
64.09	0.55
68.08	14.59
69.07	5.04
70.10	0.26
71.08	0.14
74.09	0.14
75.09	2.01
77.11	0.30
86.13	30.05
87.10	1.17
88.10	1.34
88.13	1.32
89.12	14.54
90.10	0.18
91.10	0.20
93.10	0.50
95.11	0.36
99.11	1.10
100.11	14.66
100.13	0.47
101.10	0.26
101.14	0.45
106.11	0.94
107.12	0.82
108.14	0.29
109.14	0.58
110.12	0.45
113.10	0.42
113.13	0.79
115.12	0.31
117.11	2.42
117.16	2.13
118.12	14.60
119.13	3.32
120.15	0.48
123.14	0.18
125.12	99.84
125.15	0.44
135.14	100.00
136.16	0.73
137.15	2.63
138.12	0.77
138.17	30.52
139.16	1.09
143.14	0.33
145.16	1.92
147.13	0.32
147.18	0.40
149.17	0.46
156.17	0.37
157.17	1.73
158.18	4.38
165.10	0.39
165.17	3.73
165.24	2.89
166.16	0.95
166.21	0.95
167.19	16.05
168.19	0.16
169.17	31.15
169.22	2.32
175.22	14.63
177.22	0.38
185.17	18.10
185.24	17.63
186.14	0.30
186.21	1.15
188.22	0.15
194.22	15.15
195.22	15.91
195.29	1.49
196.23	30.11
205.21	0.83
205.28	1.00
206.27	0.11
213.19	2.41
213.28	2.51
214.23	32.00
214.29	2.89
215.21	2.85
215.30	1.79
217.15	99.84
217.21	6.86
218.25	0.41
231.24	0.45
233.16	0.36
233.25	1.16
234.25	99.84
234.32	5.64
235.24	30.29
235.29	0.51

EI$^+$ M.Wt. 244 No. 22.



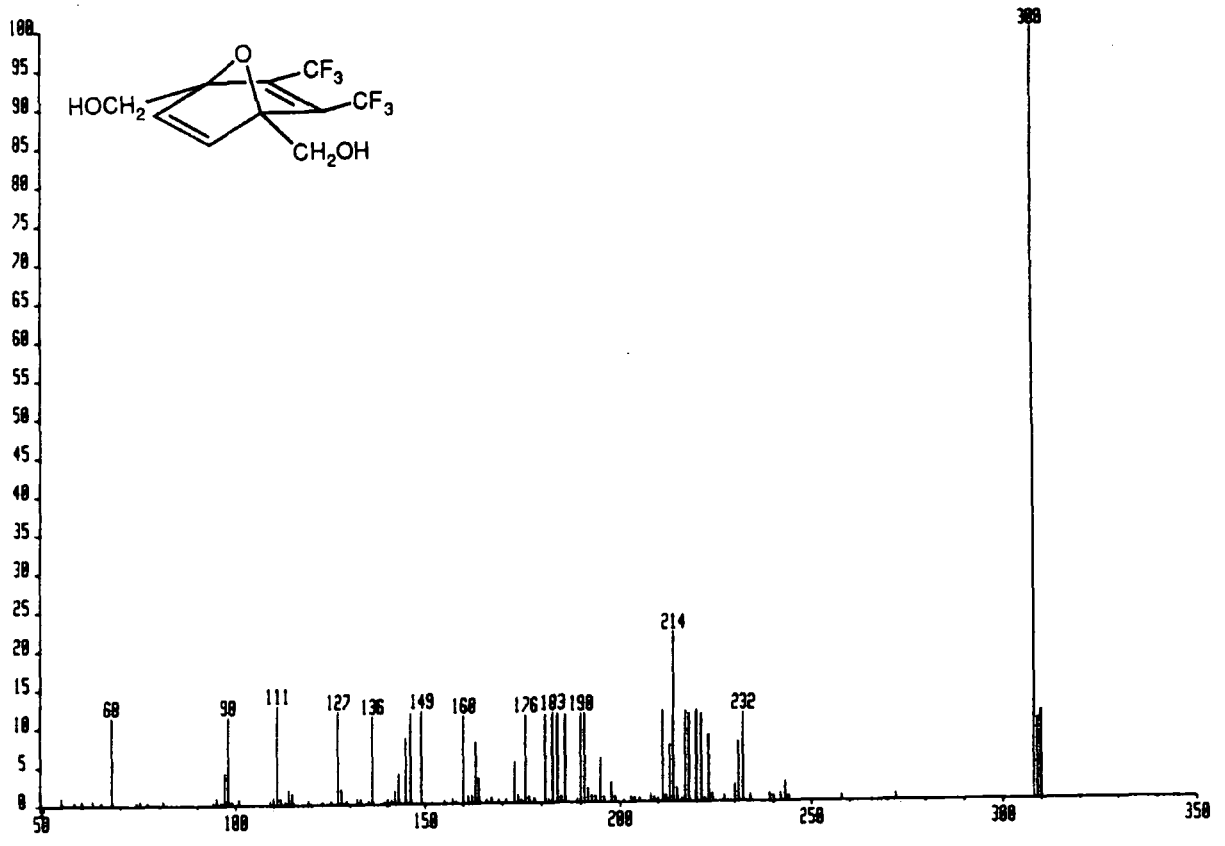
Mass	% Base
50.96	6.62
56.96	5.22
61.96	3.61
62.96	5.68
68.93	15.82
73.95	5.13
74.94	14.89
76.96	5.66
77.96	2.72
80.94	3.64
86.94	4.17
87.94	4.57
92.92	2.45
93.94	2.39
94.94	4.97
98.92	6.18
100.93	3.10
106.93	8.12
118.91	2.46
124.91	16.47
125.91	8.13
126.93	95.62
127.93	7.82
136.91	4.28
137.91	3.22
142.89	5.72
143.89	14.26
144.90	38.48
145.91	4.22
146.92	11.08
154.90	50.52
155.90	6.82
156.90	2.96
157.91	3.77
162.89	10.19
163.90	2.67
174.90	100.00
175.89	24.74
176.90	19.54
186.88	2.46
193.88	19.66
194.89	97.78
195.90	12.23
204.89	85.14
205.90	9.49
212.86	5.95
213.87	3.37
214.88	3.57
222.85	21.54
223.85	3.31
226.86	6.88
240.83	4.19
242.84	8.06
243.84	16.99
244.85	2.13

EI+ M.Wt. 290 No. 23a.



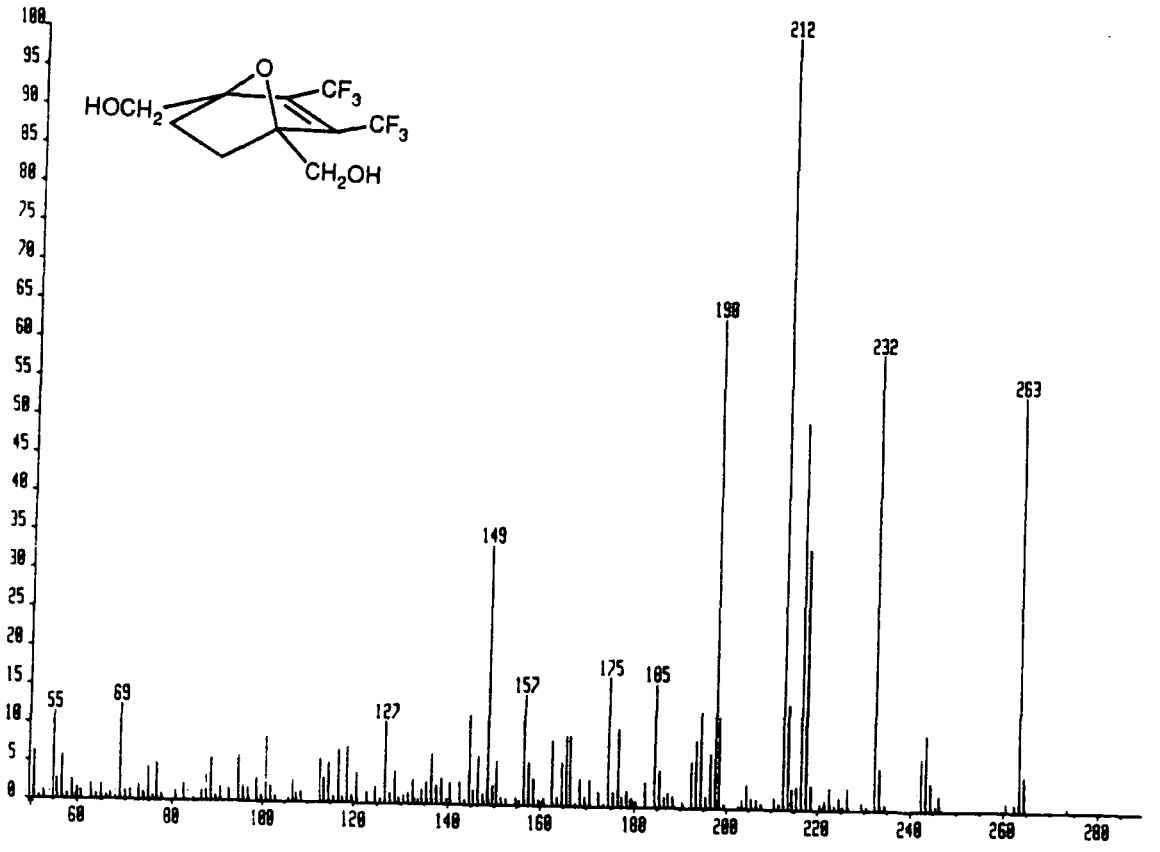
Mass	% Base	
50.85	7.47	
54.85	7.07	
58.83	12.14	
68.80	22.14	
74.79	8.95	
80.78	5.74	
92.73	6.98	
94.75	10.86	
96.75	36.60	
112.69	9.20	
113.70	12.82	
114.71	13.28	
118.68	6.36	
124.67	5.65	
126.68	9.28	
127.70	10.17	
142.64	26.73	
144.63	62.16	
145.64	5.14	
148.61	12.95	
156.59	10.47	
161.60	5.28	
162.59	39.85	
163.60	11.40	
165.59	6.52	
172.58	26.95	
176.56	5.31	
180.53	7.85	
182.54	33.42	
184.52	10.01	
190.52	8.34	
191.53	6.00	
194.50	21.27	
197.50	22.78	
210.48	13.42	
211.48	9.98	F
212.44	63.92	F
213.47	100.00	F
214.47	10.55	
216.46	23.76	
217.46	12.18	
222.45	39.58	
232.42	21.81	
241.41	15.54	
242.42	15.77	
258.39	13.04	
262.40	0.37	
263.38	12.16	
264.39	1.04	
270.36	0.31	
271.38	3.40	
272.37	0.47	

Cl^+NH_3 M.Wt. 290 No. 23b.



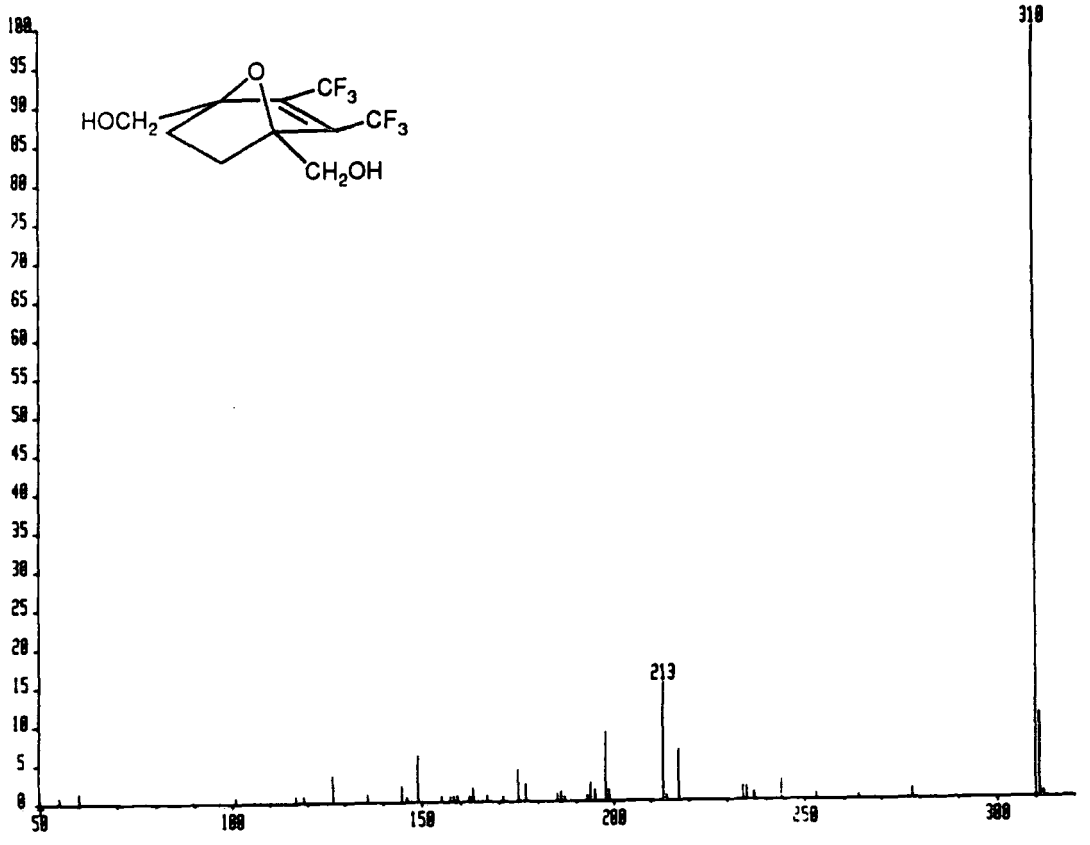
Mass	% Base
55.01	0.85
58.06	0.35
60.04	0.52
63.02	0.52
65.04	0.24
68.02	11.27
74.06	0.27
75.01	0.50
81.02	0.46
94.05	0.34
95.04	1.08
96.04	0.35
97.02	4.13
98.04	11.27
99.01	0.30
101.02	0.58
109.04	0.51
110.04	0.83
111.05	12.69
112.04	0.73
113.01	0.35
114.03	1.82
115.04	1.39
119.03	0.47
123.03	0.22
125.02	0.29
127.03	11.86
128.05	1.83
129.07	0.31
132.02	0.60
133.04	0.41
135.04	0.30
136.00	11.15
139.10	0.22
140.05	0.57
141.03	0.25
142.04	1.54
143.02	3.78
145.02	8.40
146.04	11.47
149.02	11.88
155.03	0.26
157.01	0.52
160.01	11.19
161.05	0.90
162.05	0.90
163.01	7.68
164.02	2.96
166.02	0.24
167.03	0.62
169.02	0.30
171.03	0.26
173.03	5.13
174.04	0.83
175.05	0.24
176.01	11.26
177.03	0.72
178.04	0.40
181.02	11.19
182.03	0.36
183.01	11.49
184.05	11.32
185.01	0.75
186.05	11.29
189.04	0.24
190.05	11.40
191.02	11.39
192.03	1.66
193.02	0.77
194.02	0.75
195.02	5.54
196.03	0.62
198.02	2.43
199.02	0.60
201.04	0.22
203.05	0.67
204.05	0.47
205.04	0.32
208.05	0.85
209.02	0.49
210.04	0.35
211.03	11.68
212.05	0.75
213.01	7.29
214.02	21.83
215.03	1.69
216.04	0.30
217.02	11.73
218.05	11.26
220.04	11.66
221.07	11.27
222.04	0.37
223.02	8.47
224.02	0.92
227.03	0.54
230.04	2.13
231.05	7.53
232.09	11.41
234.06	0.71
239.04	0.88
240.05	0.63
242.04	0.92
243.04	2.40
244.06	0.57
258.06	0.60
272.05	0.68
308.08	100.00
309.09	10.32
310.14	11.39

EI+ M.Wt. 292 No. 24a.



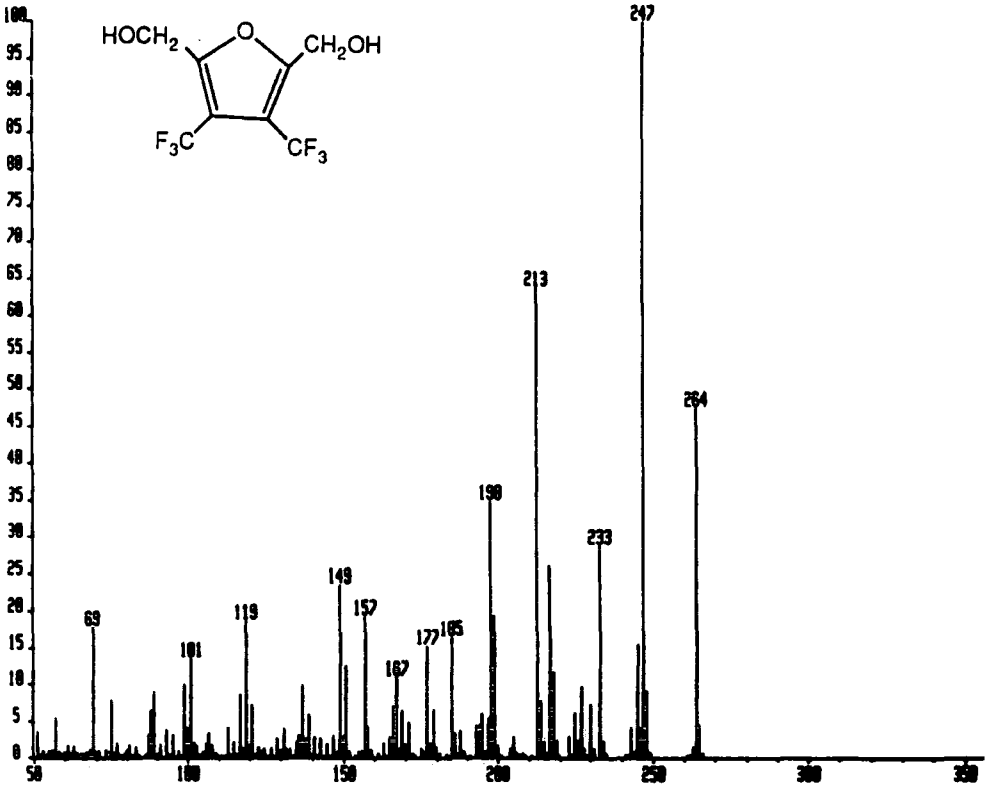
Mass	% Base
50.85	6.04
52.88	1.13
54.85	11.15
55.86	2.55
56.86	5.65
58.85	2.41
59.86	1.46
60.83	1.13
62.85	1.97
64.84	1.88
68.80	12.28
69.82	1.05
70.84	1.23
72.82	1.98
74.80	4.25
76.81	4.75
80.77	1.21
82.80	2.05
86.78	1.21
87.76	3.43
88.77	5.40
90.77	1.63
92.76	1.51
94.76	5.69
95.78	1.90
96.78	1.69
98.74	2.84
100.75	8.30
101.76	1.90
106.73	2.66
107.72	1.11
108.74	1.40
112.71	5.67
113.73	3.03
114.72	5.06
116.71	6.61
118.69	7.07
120.70	3.95
122.68	1.40
124.68	2.20
126.70	10.50
127.72	1.23
128.71	4.06
130.71	1.05
131.69	1.34
132.69	3.10
134.67	1.86
135.66	2.76
136.66	6.38
137.65	2.32
138.66	3.18
140.65	2.76
142.66	2.72
144.65	11.44
145.67	1.84
146.66	6.27
147.69	1.40
148.64	33.44
149.64	2.41
150.63	5.56
156.61	14.18
157.63	5.52
158.66	3.26
162.61	8.37
163.67	1.11
164.61	5.44
165.61	8.93
166.61	9.08
168.59	3.45
169.63	1.17
170.62	3.33
172.63	1.76
174.60	16.69
175.58	1.80
176.58	10.00
177.60	1.28
178.58	1.99
179.55	1.07
182.57	3.14
184.54	15.83
185.54	4.71
186.58	1.23
187.55	1.78
188.57	1.34
192.53	5.84
193.54	8.68
194.48	12.22
195.52	1.42
196.55	6.90
197.52	63.40
198.53	11.71
203.48	1.05
204.53	2.99
205.50	1.28
206.52	1.13
210.52	1.42
212.48	100.00
213.48	13.53
214.50	2.53
215.53	2.87
216.48	49.97
217.48	33.47
218.51	3.07
221.53	1.11
222.45	2.70
224.51	1.53
226.49	2.74
232.45	58.84
233.46	5.23
242.43	6.61
243.45	9.64
244.44	3.47
246.44	1.76
260.49	0.84
262.43	0.98
263.40	53.59
264.42	4.35
273.44	0.44

Cl^+NH_3 M.Wt. 292 No. 24b.



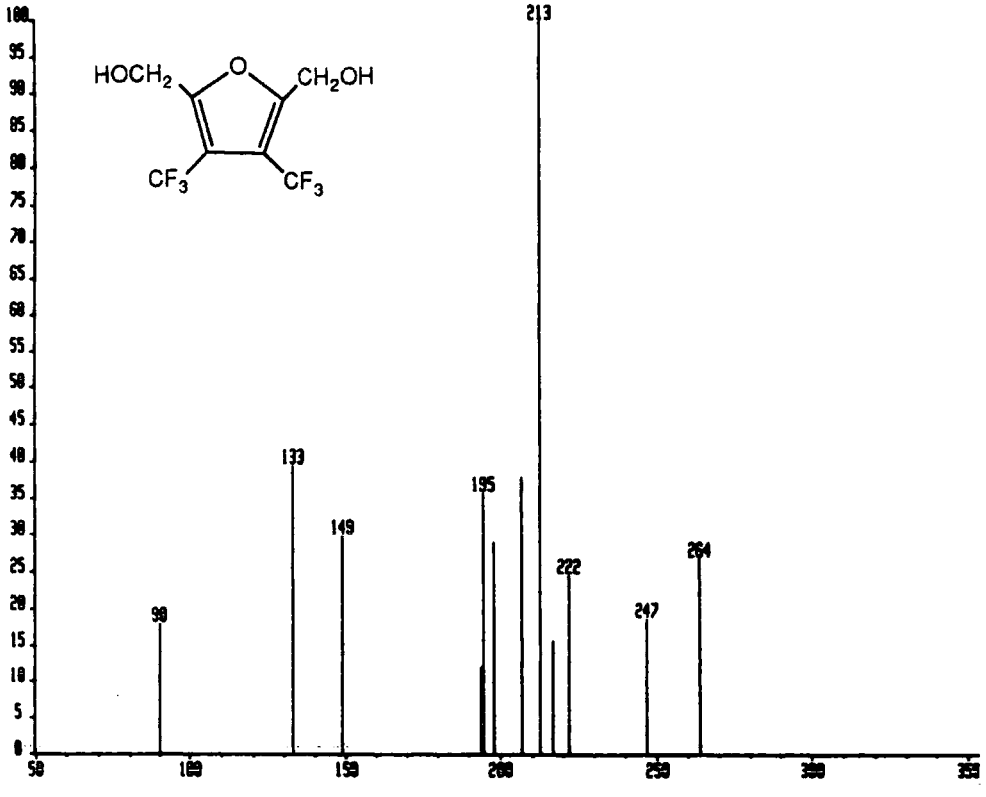
Mass	% Base
55.01	0.68
60.04	1.22
101.01	0.53
117.02	0.83
119.02	0.71
127.03	3.39
136.02	0.95
145.02	1.96
146.02	0.42
149.00	5.88
155.02	0.80
157.01	0.65
158.03	0.65
159.04	0.77
162.04	0.62
163.02	1.63
167.01	0.80
171.06	0.65
175.03	4.16
177.01	2.05
185.00	0.86
186.01	1.28
187.05	0.42
193.00	0.62
194.01	2.35
195.01	1.40
197.99	8.86
199.00	1.40
212.99	15.10
214.00	0.59
217.00	6.51
234.03	1.60
235.04	1.66
237.03	0.89
243.00	0.48
244.04	2.73
253.04	0.71
264.03	0.51
278.06	1.19
310.08	100.00
311.08	10.70
312.11	0.59

EI$^+$ M.Wt. 264 No. 25a.



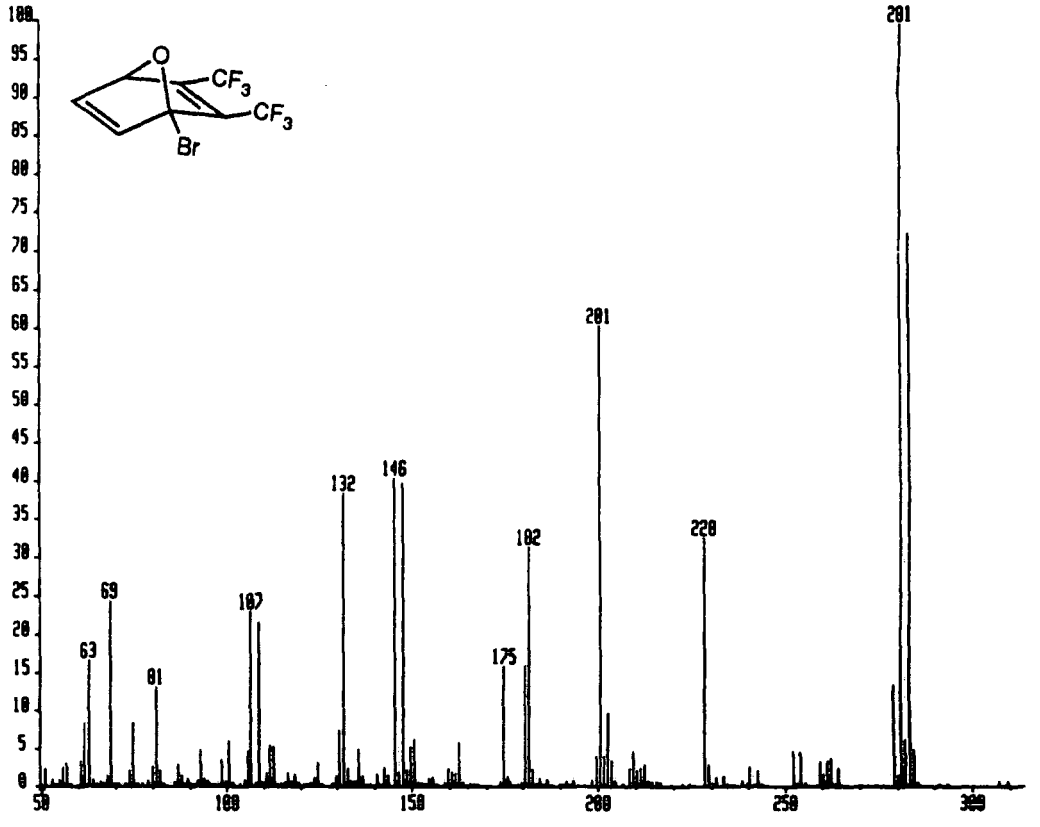
Mass	% Base
28.96	24.00
30.97	41.03
38.97	9.57
56.94	5.30
68.91	17.67
74.91	7.85
87.92	6.39
88.93	8.93
98.91	9.87
100.92	13.33
116.90	8.55
118.89	18.52
120.90	7.05
136.88	9.78
138.89	5.74
148.89	23.46
150.89	12.38
156.87	19.15
165.87	6.94
166.87	10.80
168.87	6.40
176.87	15.06
178.87	6.49
184.86	16.24
194.86	5.88
196.86	5.38
197.86	34.67
198.87	19.20
212.84	63.89
213.84	7.76
216.85	26.12
217.86	11.53
224.86	6.09
226.85	9.70
229.86	7.30
232.84	28.78
244.86	15.41
246.86	100.00
247.86	9.03
260.84	0.20
261.85	0.27
262.85	1.32
263.86	47.45
264.86	4.43
265.86	0.39

$Cl^+ NH_3$ M.Wt. 264 No. 25b.



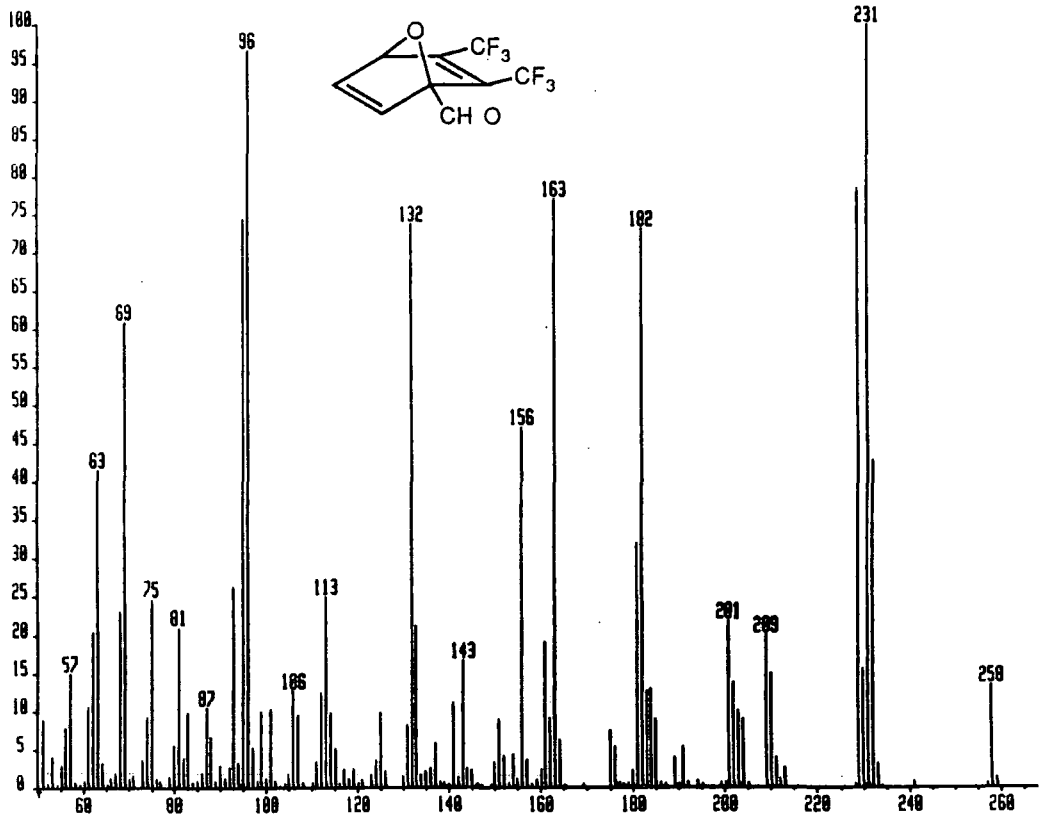
Mass	% Base
32.00	0.58
33.00	0.26
35.02	100.00
36.01	0.56
44.00	0.23
133.00	0.39
148.92	0.29
194.91	0.35
197.89	0.29
206.91	0.37
212.86	0.99
221.90	0.24
263.91	0.26

EI+ M.Wt. 309 No. 26.



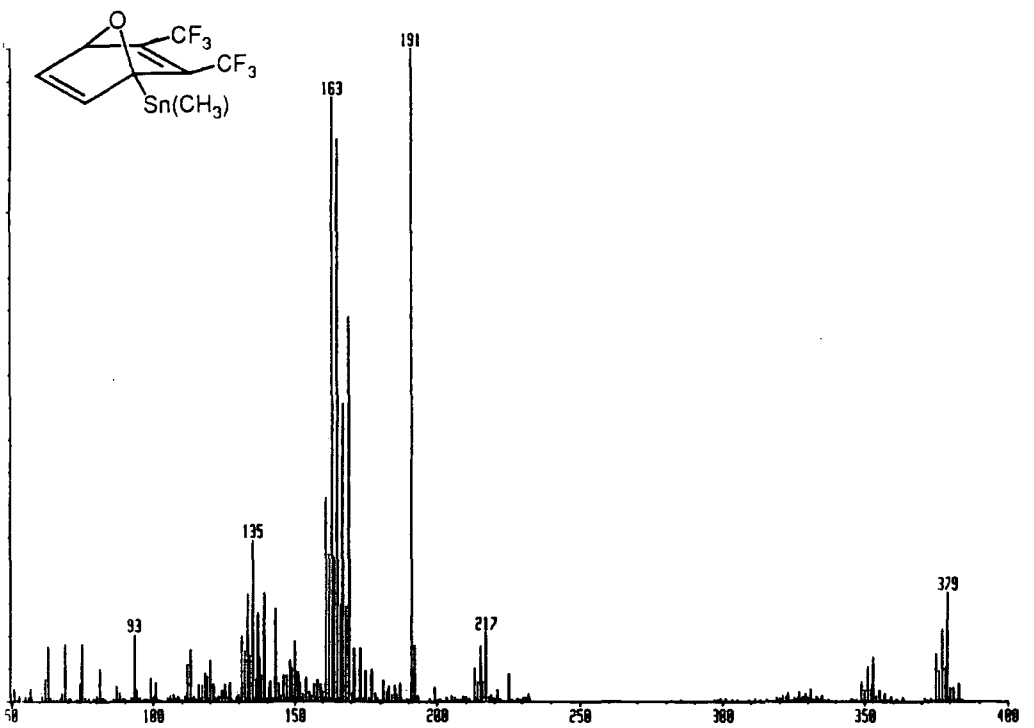
Mass	% Base
50.85	2.34
52.84	0.80
54.85	0.83
55.84	2.49
56.84	3.04
60.83	3.31
61.83	8.36
62.84	16.55
63.84	0.75
65.82	0.41
66.82	0.32
67.81	1.43
68.80	24.22
69.81	0.34
73.80	2.18
74.79	8.34
78.72	0.60
79.77	2.60
80.78	13.09
81.77	1.98
85.77	0.52
86.76	2.83
87.76	1.36
89.26	0.87
89.75	0.36
91.75	0.66
92.74	4.70
93.75	0.98
94.72	0.63
98.73	3.46
99.74	0.50
100.75	5.96
101.75	0.33
104.70	0.74
105.71	4.54
106.62	22.88
107.67	0.32
108.61	21.56
110.70	1.61
111.70	5.32
112.70	5.22
115.64	0.33
116.65	1.62
117.65	0.64
118.64	1.56
119.62	0.37
122.67	0.35
123.67	1.01
124.68	2.98
129.66	1.29
130.66	7.31
131.67	38.30
132.68	2.20
133.65	0.62
134.59	0.53
135.66	4.81
136.62	1.20
140.64	1.47
142.65	2.45 F
145.57	40.36 F
146.48	1.75 F
147.55	39.69 F
148.57	2.17
149.62	5.10 F
150.61	6.07 F
151.63	0.35
152.54	0.32
154.57	0.84
155.61	1.11
159.61	2.31
160.59	1.74
161.60	1.61
162.61	5.75
163.61	0.39
173.57	0.54
174.57	15.71
175.56	1.15 F
176.22	0.53 F
179.60	0.50 F
180.54	15.92 F
181.55	31.28 F
182.56	2.13
198.50	0.78 F
199.50	4.01 F
200.51	60.40 F
201.50	3.93 F
202.49	9.49 F
203.50	3.27
204.44	0.57
208.49	2.24
209.46	4.49
210.43	2.00
211.41	2.32
212.43	2.70
213.41	0.83
214.40	0.40
215.41	0.40
228.48	32.42
229.46	2.77
231.36	1.14
233.36	1.19
238.36	0.89
240.37	2.50
242.35	1.96
252.32	4.47
253.35	0.30
254.31	4.34
259.33	3.25
260.33	1.61
261.32	3.17
262.32	3.69
264.30	2.29
279.30	13.36 F
280.26	1.40 F
281.26	100.00 F
282.25	8.10 F
283.26	72.36 F
284.26	4.75 F
307.24	0.57
309.26	0.56

EI+ M.Wt. 258 No. 27.



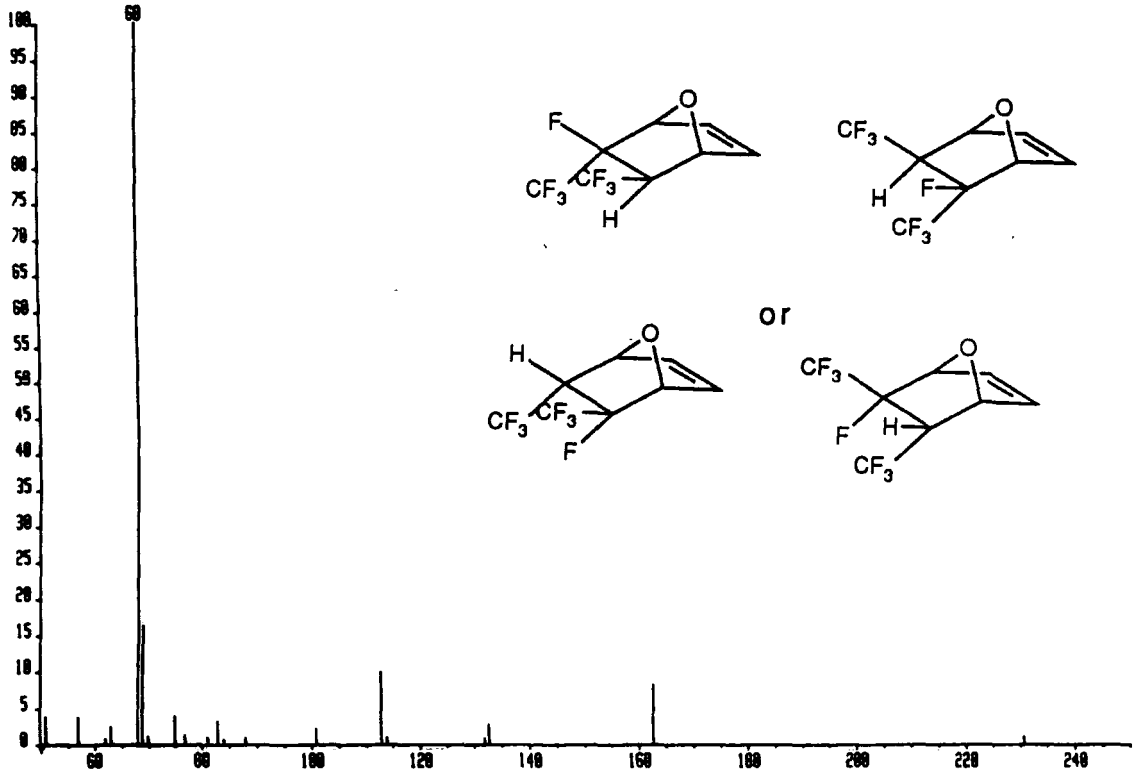
51.13	3.73	175.12	7.22	258.14	13.40
56.11	7.74	176.13	5.14	259.15	1.19
57.12	14.83	181.13	31.79		
61.10	10.43	182.14	72.99		
62.11	20.26	183.14	12.36		
63.11	41.32	184.12	12.69		
68.09	23.10	185.13	9.81		
69.06	60.75	191.14	5.08		
74.07	3.12	200.13	0.65		
75.07	24.55	201.14	21.70		
80.06	5.44	202.15	13.60		
81.07	20.94	203.11	3.89		
83.08	3.67	203.29	0.21		
87.06	10.33	203.32	0.24		
88.07	6.48	203.48	0.24		
93.06	26.25	203.52	0.24		
95.08	74.39	203.61	0.24		
96.08	96.53	203.64	0.30		
97.09	5.10	204.12	3.79		
99.07	9.80	205.14	0.51		
101.09	10.12	209.13	19.86		
106.08	12.62	210.14	14.86		
107.08	9.39	211.15	3.80		
112.08	12.30	212.12	1.07		
113.09	24.81	213.14	2.43		
114.10	9.73	228.15	0.52		
125.07	9.67	228.76	0.17		
131.08	8.02	229.15	78.51		
132.09	73.67	230.16	15.60		
133.10	21.06	230.43	0.25		
137.09	5.59	230.48	0.30		
141.10	11.13	230.59	0.36		
143.09	16.52	231.13	100.00		
151.12	8.85	231.34	0.25		
156.09	46.95	232.14	42.68		
161.12	18.99	233.14	2.96		
162.11	8.97	234.15	0.21		
163.13	76.90	241.14	0.71		
164.13	6.07	257.14	0.52		

EI+ M.Wt. 379 No. 28.



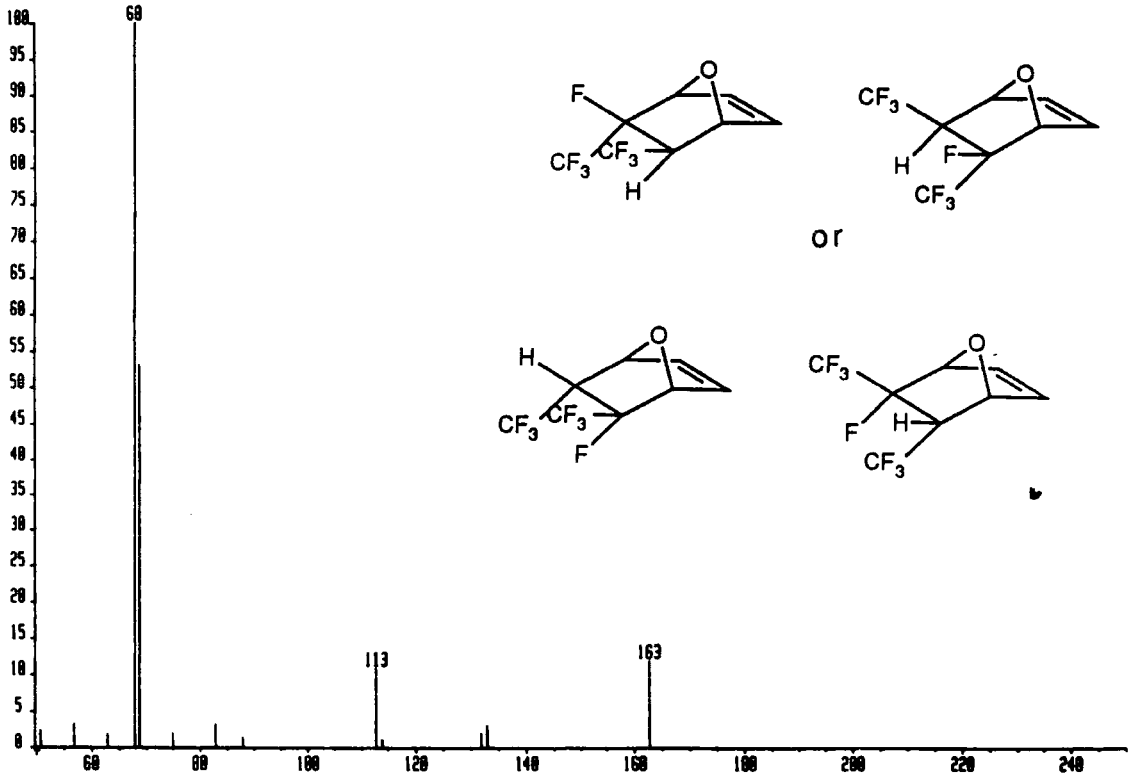
Mass	% Base		Mass	% Base		Mass	% Base
62.07	3.31		150.06	9.07		378.21	4.96
63.07	8.29		151.07	4.42		379.21	16.56
69.05	8.71		152.05	2.76		380.22	2.04
74.06	2.64		154.05	3.46		383.21	2.50
75.06	8.61		157.08	2.59			
81.08	4.80		158.12	3.25			
87.08	2.30		159.08	2.51			
93.07	10.13		161.09	31.10			
99.09	3.53		162.10	22.50			
101.10	2.75		163.11	92.55			
112.09	5.61		164.10	21.96			
113.10	7.88		165.09	86.28			
115.99	2.61		166.07	14.63			
117.00	2.43	F	167.08	45.63			
118.01	4.21		168.07	14.44			
119.02	3.83		169.08	58.94			
120.00	6.27		171.08	7.98			
121.01	2.54		173.08	8.11			
125.11	2.53		175.15	4.48			
127.12	2.85		177.16	4.86			
131.04	9.98		181.14	3.13			
132.03	7.78	F	183.07	2.27			
132.13	5.93	F	185.09	2.36			
133.04	16.30		187.07	2.75			
134.03	7.04		191.15	100.00			
135.03	24.50		192.16	8.42			
136.02	3.38		199.15	2.10			
137.01	13.49	F	213.13	5.00			
137.12	6.63	F	214.13	2.89			
138.03	3.87		215.13	8.26			
139.01	16.48		216.13	2.95			
141.01	2.24	F	217.12	10.48			
141.13	2.96	F	225.19	4.02			
143.09	14.17		349.18	2.83			
144.11	2.50		351.18	5.10			
146.06	3.89		353.18	6.69			
147.06	3.91		375.20	7.16			
148.06	6.16		376.20	4.53			
149.06	5.01		377.20	10.88			

EI+ M.Wt. 250 No. 29.



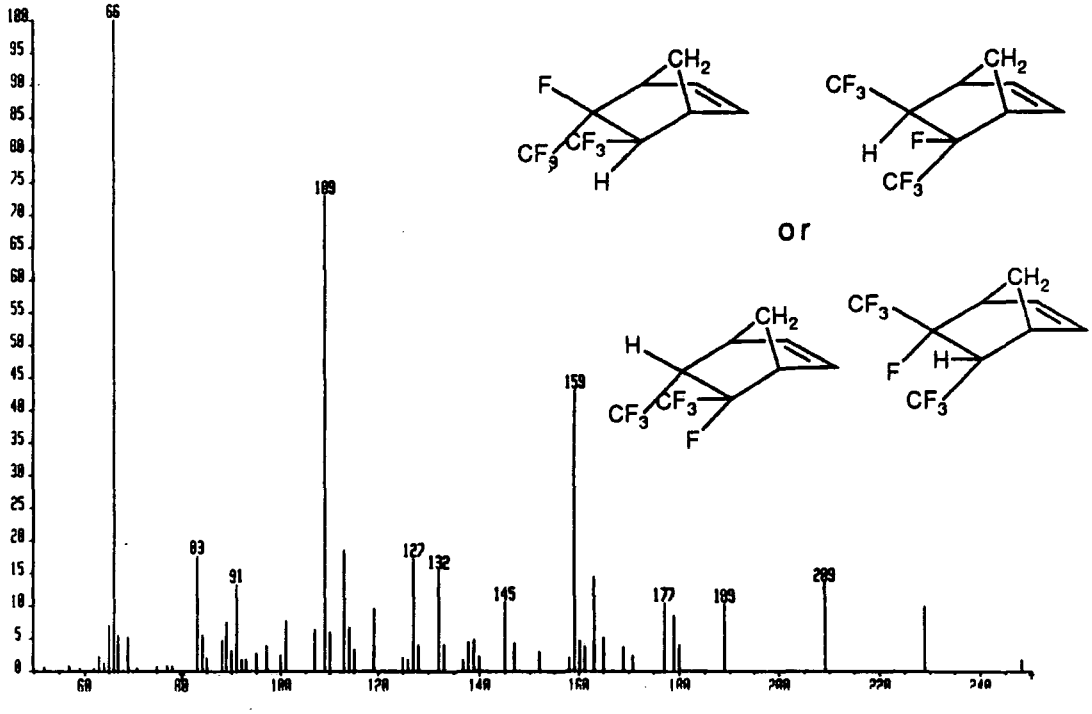
Mass	% Base
50.94	3.79
56.93	3.73
61.93	0.76
62.94	2.47
67.92	100.00
68.90	16.37
69.92	1.04
74.90	3.89
76.91	1.26
80.89	0.95
82.91	3.19
83.91	0.54
87.88	0.95
100.87	2.05
112.84	9.89
113.86	0.92
131.80	0.70
131.86	0.63
132.83	2.72
162.77	8.22
230.75	1.07

EI$^+$ M.Wt. 250 No. 30.



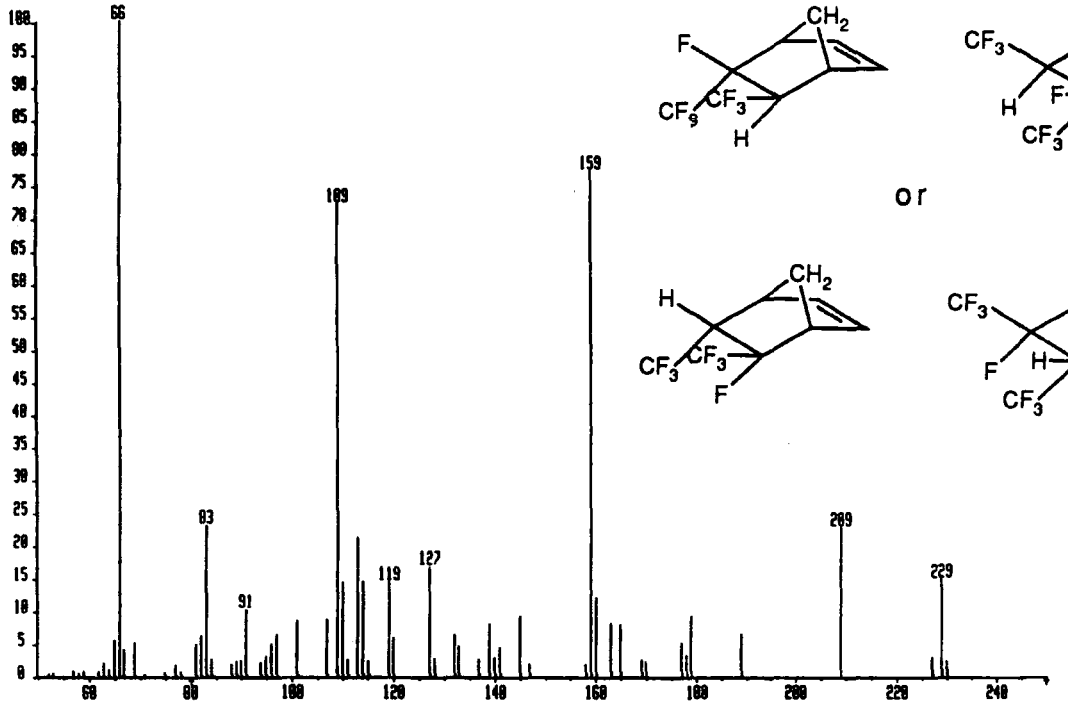
Mass	% Base
50.93	2.34
56.93	3.16
62.93	1.83
67.92	100.00
68.90	53.00
74.90	1.99
82.92	3.21
87.89	1.37
112.84	10.74
113.85	1.07
131.82	1.93
132.83	3.11
162.77	11.86

EI$^+$ M.Wt. 248 No. 31.



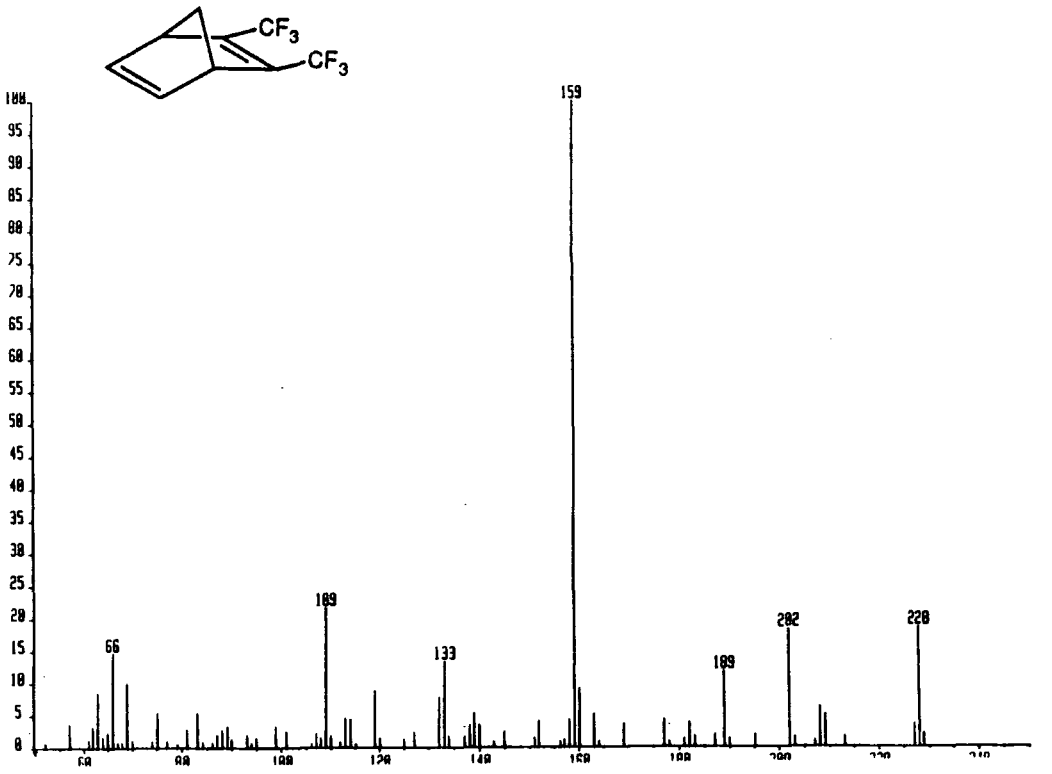
Mass	% Base
52.01	0.42
57.00	0.80
59.01	0.34
62.01	0.30
63.02	2.14
64.02	1.15
64.09	0.21
65.03	6.95
65.88	0.19
66.04	100.00
67.05	5.47
68.01	0.17
69.00	5.21
71.03	0.31
75.01	0.62
77.03	0.78
78.04	0.65
83.04	1.75
84.05	0.54
84.99	0.19
85.07	0.19
88.03	0.48
89.04	0.74
89.94	0.32
91.06	1.32
92.07	0.17
93.03	0.17
95.03	0.26
97.06	0.38
100.02	0.25
101.03	0.76
107.04	0.63
109.06	7.31
110.07	0.59
113.02	1.85
114.03	0.67
115.06	0.32
119.03	0.94
125.01	0.19
126.05	0.16
127.04	1.71
128.03	0.39
132.01	1.54
133.05	0.40
137.01	0.17
138.05	0.43
139.05	0.48
140.05	0.22
145.03	1.04
147.04	0.42
152.05	0.28
158.04	0.19
159.05	4.30
160.07	0.45
161.11	0.37
163.02	1.44
165.05	0.51
169.04	0.37
170.83	0.23
177.03	1.03
179.05	0.84
180.06	0.40
189.04	1.02
209.07	1.34
229.07	0.98
248.09	0.16

EI$^+$ M.Wt. 248 No. 32.



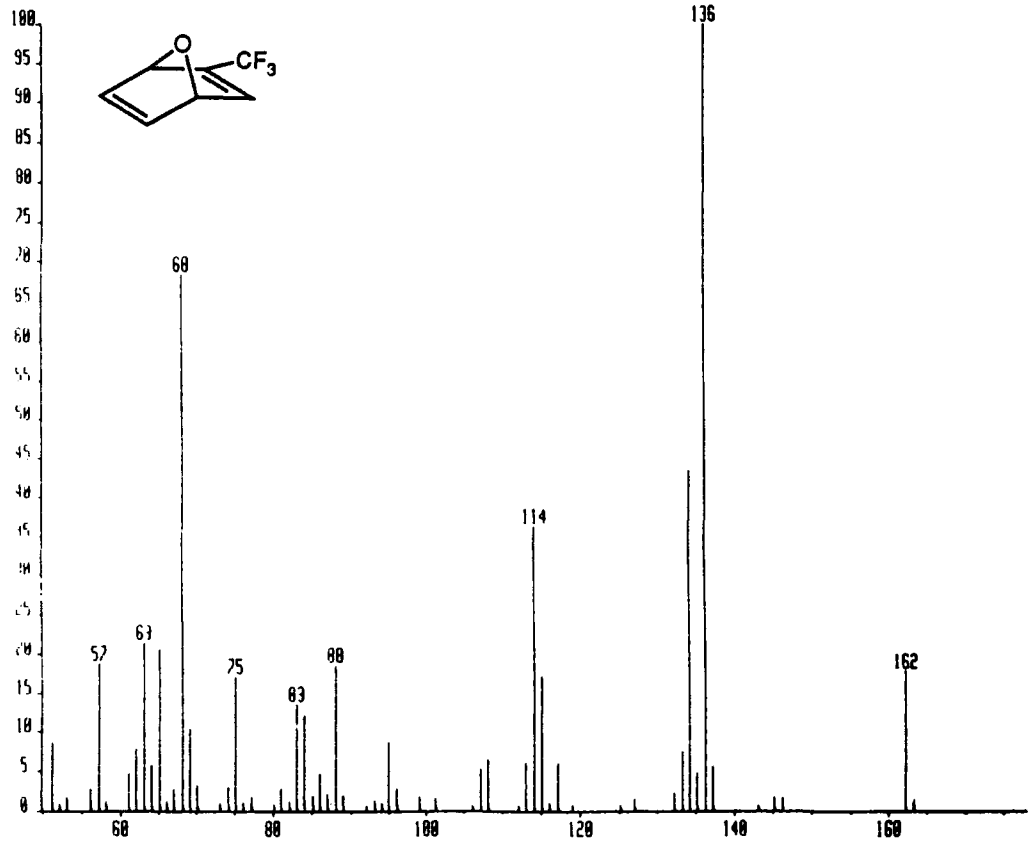
Mass	% Base
52.02	0.29
53.02	0.41
57.00	0.70
58.00	0.39
59.01	0.83
62.01	0.83
63.02	2.06
64.03	1.00
64.07	0.22
65.03	5.63
66.04	100.00
67.05	4.10
69.00	5.09
71.03	0.26
75.02	0.65
77.03	1.72
78.06	0.76
81.03	0.50
82.02	0.62
83.04	2.30
84.07	0.26
88.03	0.19
89.09	0.23
90.03	0.25
91.07	1.02
94.03	0.21
95.02	0.26
95.06	0.30
96.05	0.50
97.05	0.63
101.05	0.84
107.04	0.86
109.06	7.22
110.08	1.44
111.11	0.26
113.03	2.13
114.04	1.46
115.03	0.23
119.03	1.44
120.02	0.60
127.03	1.68
128.03	0.27
132.00	0.63
133.03	0.47
137.01	0.26
139.04	0.81
140.05	0.29
141.06	0.44
145.04	0.92
147.05	0.19
158.03	0.18
159.06	7.71
160.07	1.19
163.03	0.81
165.04	0.78
169.06	0.26
170.03	0.22
177.04	0.51
178.07	0.33
179.06	0.92
189.05	0.65
209.05	2.28
227.11	0.30
229.05	1.48
230.14	0.25

EI$^+$ M.Wt. 228 No. 33.



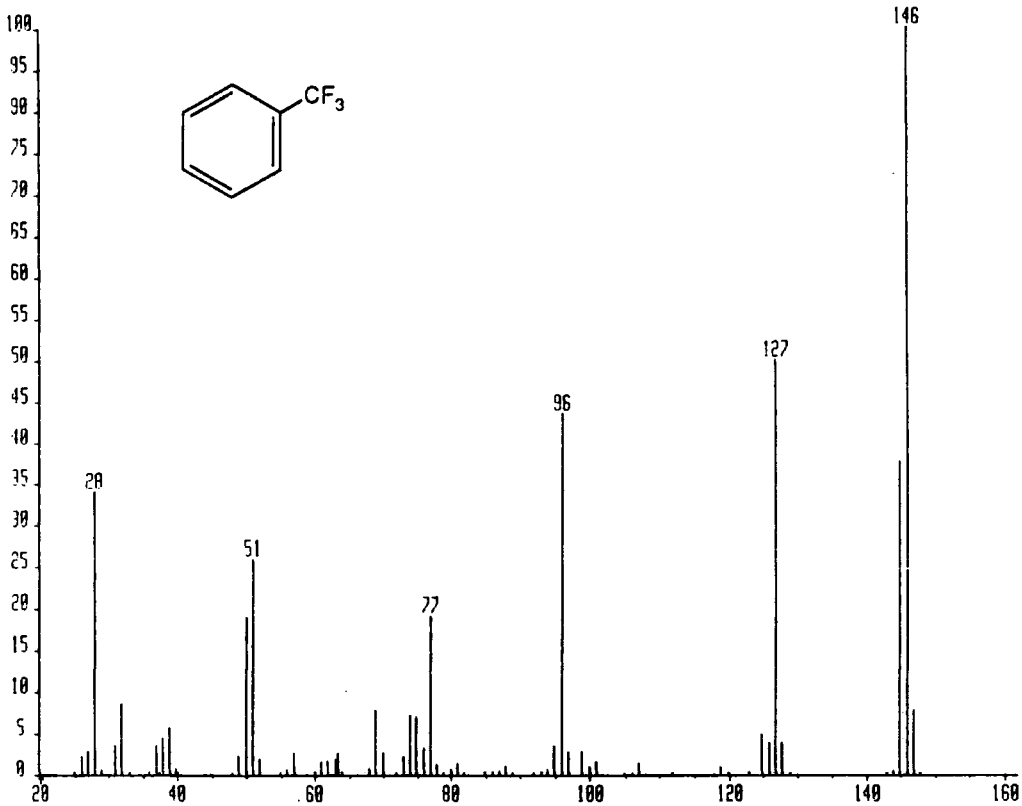
Mass	% Base				
52.04	0.56	106.07	0.60	163.10	5.07
53.04	0.22	107.09	2.15	164.11	0.69
56.02	0.49	108.10	1.43	167.10	0.11
57.03	3.49	109.10	21.45	169.11	3.51
59.05	0.49	110.11	1.60	170.14	0.40
61.03	1.00	110.89	0.13	171.42	0.11
62.04	3.22	111.07	0.34	176.11	0.42
63.04	8.36	111.49	0.12	177.11	4.14
64.05	1.51	112.08	0.80	178.12	0.71
65.06	2.26	113.08	4.35	181.09	1.28
66.07	14.48	114.09	4.26	182.09	3.58
67.08	0.77	115.09	0.51	183.10	1.46
68.03	0.81	118.06	0.25	187.10	1.78
69.03	9.97	119.07	8.61	188.11	0.33
69.55	0.13	120.08	1.44	189.11	11.52
70.05	1.03	121.08	0.42	190.12	1.22
73.05	0.11	125.06	1.19	194.08	0.11
74.06	0.94	126.08	0.31	195.11	1.78
75.05	5.29	127.09	2.23	196.09	0.13
76.06	0.24	130.05	0.14	201.12	0.44
77.07	0.98	131.06	0.35	202.11	17.97
78.07	0.13	132.07	7.79	203.11	1.39
79.06	0.53	133.08	13.12	207.12	0.93
80.06	0.44	134.08	1.70	208.12	6.03
81.06	2.68	137.07	1.53	209.13	4.80
82.06	0.43	138.09	3.31	210.14	0.48
83.08	5.32	139.10	5.08	213.12	1.80
84.08	0.74	140.11	3.28	227.13	3.38
85.06	0.42	141.11	0.18	228.13	18.26
86.07	0.80	143.08	0.68	229.14	1.91
87.07	1.82	144.09	0.45		
88.07	2.64	145.09	2.31		
89.09	3.25	146.10	0.24		
90.10	1.24	150.07	0.36		
92.06	0.32	151.09	1.38		
93.06	1.80	152.09	3.91		
94.07	0.63	153.11	0.14		
95.08	1.36	156.10	0.72		
96.10	0.28	157.10	1.12		
99.07	3.25	158.10	4.06		
100.07	0.49	159.11	100.00		
101.08	2.38	160.12	8.92		
102.09	0.41	161.11	0.45		
105.07	0.37	162.12	0.39		

EI$^+$ M.Wt. 162 No. 34.



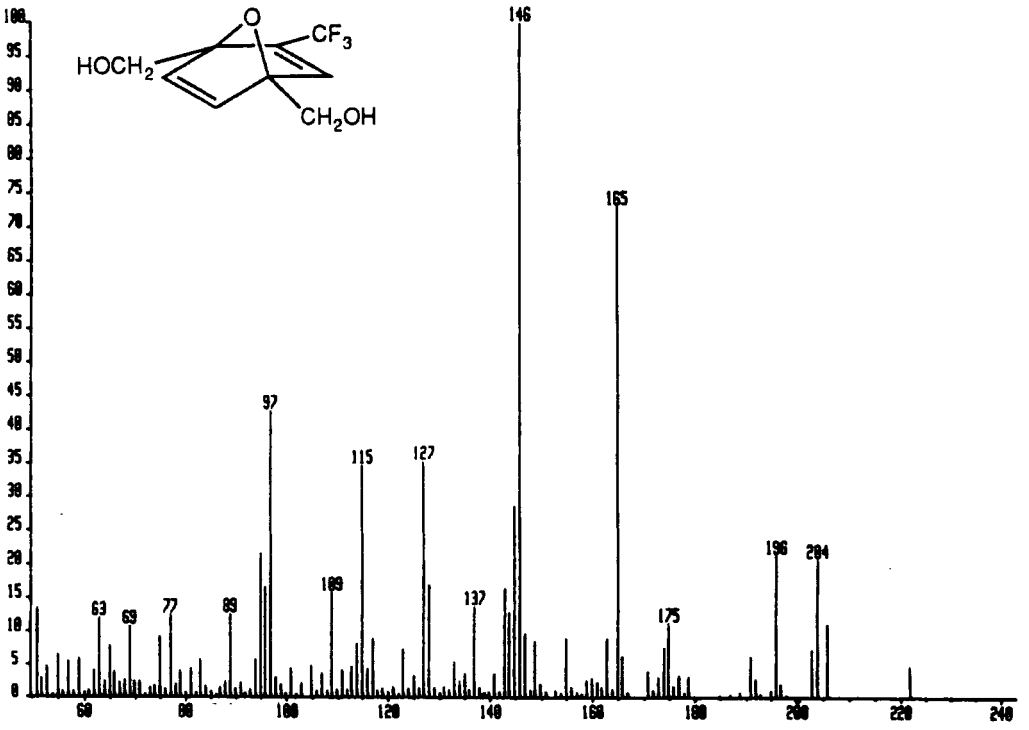
Mass	% Base
51.18	8.61
57.17	18.71
62.16	7.88
63.16	21.30
64.16	5.62
65.17	20.66
68.15	68.30
69.12	10.29
75.12	17.10
83.14	13.45
84.15	12.01
88.13	18.49
95.16	8.56
107.15	5.12
108.16	6.43
113.16	6.11
114.17	36.26
115.17	17.20
117.15	5.94
133.17	7.47
134.18	43.37
136.17	100.00
137.17	5.42
161.22	0.24
162.21	17.76
162.45	0.10
163.22	1.39

EI$^+$ M.Wt. 146 No. 35.



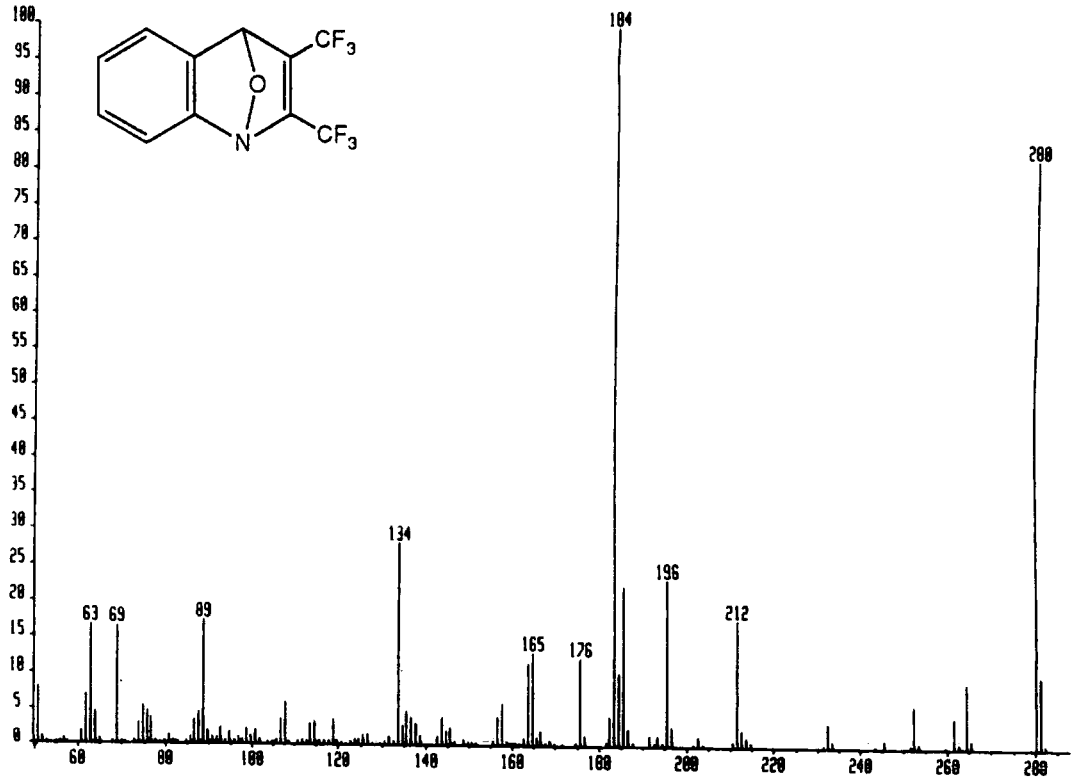
Mass	Base
24.94	0.29
25.95	2.08
26.95	2.66
27.94	33.92
28.93	0.51
30.92	3.48
30.94	0.51
31.92	8.42
31.95	0.29
35.92	0.34
36.93	3.46
37.93	4.38
38.94	5.61
39.88	0.53
48.91	2.24
49.92	18.95
50.92	25.98
51.93	1.85
55.90	0.60
56.91	2.56
59.89	0.30
60.89	1.49
61.90	1.66
62.90	1.85
63.40	2.55
63.90	0.26
67.88	0.82
68.87	7.79
69.89	2.61
72.88	2.15
73.89	7.06
74.89	6.97
75.90	3.14
76.91	19.13
77.91	1.26
79.88	0.57
80.88	1.39
84.87	0.29
85.89	0.24
86.88	0.46
87.88	1.12
92.87	0.24
93.88	0.66
94.89	3.53
95.90	43.67
96.90	2.69
98.86	2.74
99.87	0.95
100.88	1.57
106.88	1.40
118.85	0.92
122.84	0.31
124.85	4.78
125.86	3.73
126.87	50.17
127.87	3.83
143.88	0.48
144.86	37.66
145.86	100.00
146.87	7.69

EI+ M.Wt. 222 No. 36.



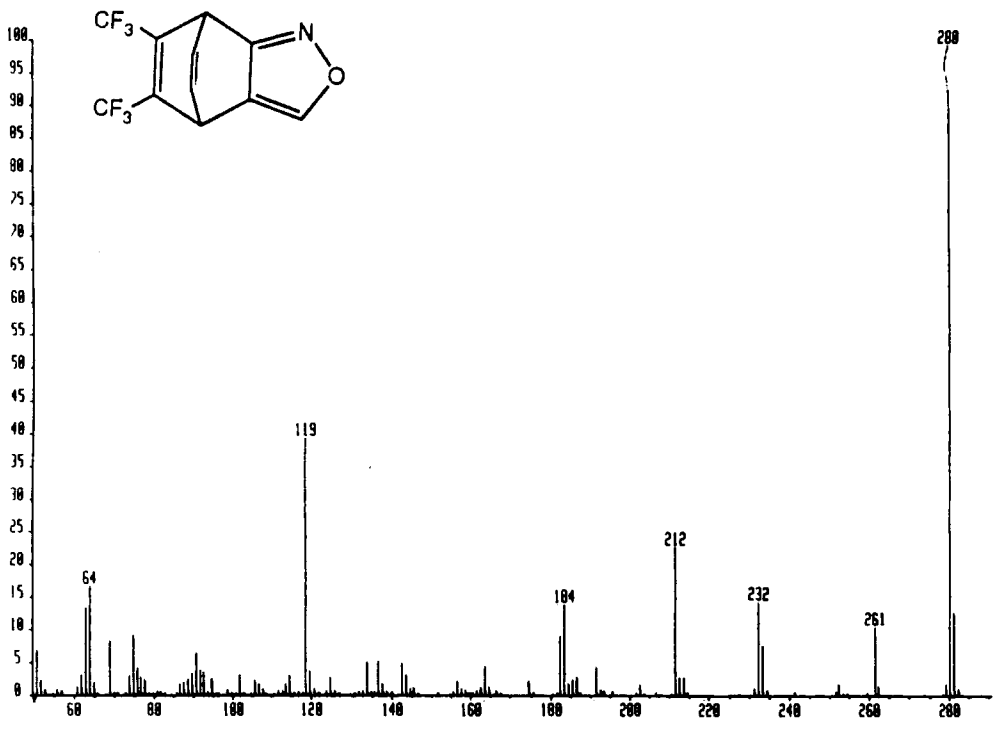
Mass	% Base
50.96	13.28
51.97	2.71
52.97	4.58
53.96	0.32
53.99	0.28
54.97	6.31
55.96	0.80
56.98	5.34
57.96	0.83
58.96	5.76
59.96	0.58
60.95	0.97
61.96	3.88
62.96	11.80
63.97	2.24
64.98	7.72
65.98	3.72
66.97	2.15
67.96	2.45
68.96	10.61
69.97	2.35
70.95	2.25
71.97	0.36
72.94	1.39
73.95	1.71
74.94	9.06
75.95	1.10
76.96	12.35
77.97	1.87
78.97	3.98
79.95	0.62
80.95	4.27
81.96	0.67
82.96	5.63
83.96	1.57
84.97	0.72
85.95	0.24
86.93	1.39
87.94	2.29
88.94	12.41
89.95	1.27
90.96	2.15
91.94	0.42
92.95	1.00
93.95	5.67
94.95	21.54
95.95	16.57
96.94	42.61
97.95	2.86
98.94	1.75
99.94	0.39
100.94	4.24
101.95	0.29
102.95	1.93
104.94	4.74
105.94	0.84
106.95	3.41
107.95	0.88
108.94	15.62
109.95	1.09
110.95	4.15
111.94	1.01
112.93	4.51
113.93	8.09
114.94	34.58
115.95	4.18
116.92	8.77
117.93	0.84
118.92	1.24
119.93	0.79
120.93	1.54
121.95	0.37
122.92	7.23
123.93	1.15
124.92	3.15
125.92	1.38
126.93	35.19
127.94	16.76
128.94	1.36
129.93	0.66
130.93	1.57
131.92	1.01
132.92	5.26
133.93	2.50
134.93	3.54
135.92	1.11
136.90	13.60
137.91	1.43
138.57	0.23
138.91	0.53
139.93	0.74
140.90	3.43
141.91	0.75
142.91	16.37
143.92	12.79
144.90	28.45
145.91	100.00
146.91	9.51
147.92	0.89
148.89	8.37
149.89	1.75
150.91	0.80
152.93	0.86
153.91	0.41
154.90	8.78
155.90	1.36
156.91	0.63
157.90	0.36
158.91	2.48
159.92	2.79
160.90	2.12
161.90	1.33
162.90	8.85
163.91	1.10
164.88	73.08
165.88	6.05
166.90	0.58
170.89	3.80
171.90	0.88
172.89	2.83
173.89	7.46
174.89	11.13
175.90	1.59
176.88	3.24
177.89	0.45
178.89	2.90
184.91	0.21
186.88	0.27
188.89	0.58
190.88	6.10
191.89	2.62
192.89	0.23
194.87	0.95
195.87	21.24
196.89	1.84
197.89	0.22
202.89	0.36
203.89	1.03
205.90	0.54
221.89	0.23

EI+ M.Wt. 281 No. 37.



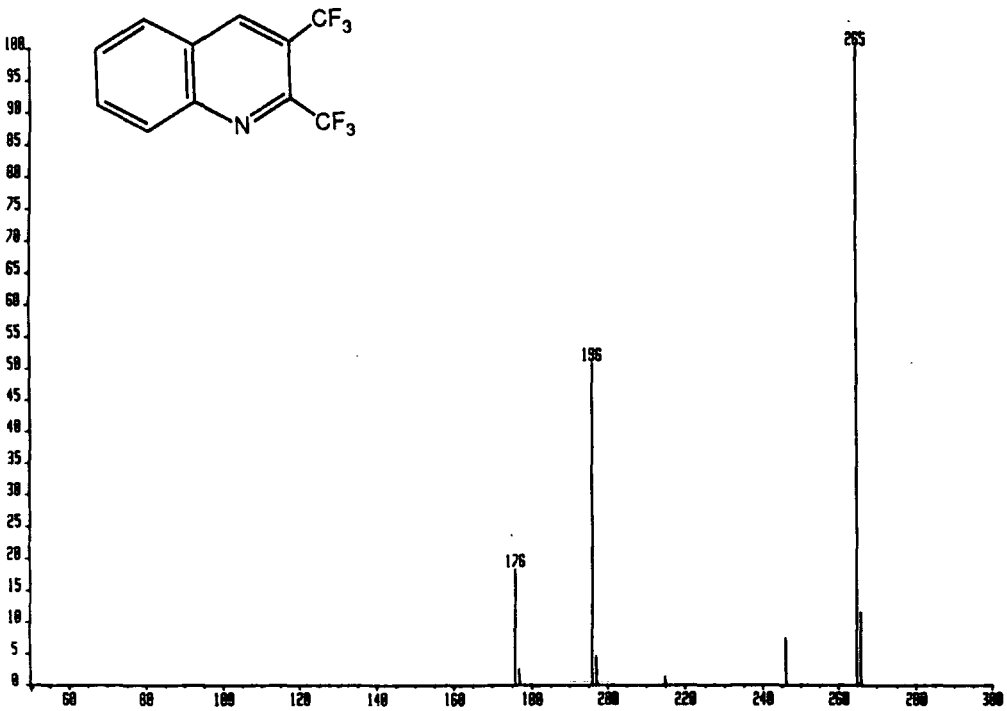
Mass	% Base
50.86	7.89
51.86	0.97
56.84	0.81
60.83	1.61
61.83	6.96
62.84	16.47
63.84	4.61
64.84	0.68
67.82	0.30
68.79	16.40
69.81	0.29
72.81	0.45
73.80	2.85
74.80	5.27
75.81	4.64
76.82	3.61
77.81	0.44
79.79	0.29
80.78	1.17
81.78	0.40
82.29	0.30
84.78	0.33
85.77	1.08
86.78	3.38
87.78	4.50
88.79	17.07
89.78	1.78
90.79	0.86
91.26	0.22
91.77	0.89
92.74	2.29
93.75	0.38
94.77	1.65
95.77	0.45
96.73	0.89
97.75	0.62
98.75	2.09
99.75	1.24
100.76	1.95
101.76	0.76
103.75	0.25
104.73	0.30
105.73	0.62
106.74	3.71
107.75	5.94
108.75	0.29
110.73	0.28
111.72	0.54
112.73	0.41
113.74	2.84
114.74	3.13
115.73	0.41
116.71	0.46
117.71	0.43
118.72	3.47
119.71	0.41
122.69	0.49
123.69	0.81
124.69	0.73
125.71	1.44
126.71	1.35
129.67	0.20
130.68	0.40
131.68	1.00
132.70	0.44
133.70	27.98
134.70	2.73
135.68	4.70
136.67	3.84
137.67	2.95
138.68	1.22
142.66	1.27
143.65	3.82
144.66	1.98
145.66	2.41
146.62	0.42
148.63	0.71
149.63	0.32
155.63	0.68
156.63	3.96
157.63	5.68
158.64	0.51
162.61	1.07
163.62	11.36
164.63	12.89
165.63	1.26
166.61	2.03
167.61	0.31
168.61	0.54
174.59	0.37
175.60	12.19
176.60	1.32
181.58	0.53
182.57	3.97
183.58	100.00
184.58	10.22
185.57	22.24
195.56	23.22
196.56	2.52
202.55	1.24
210.52	0.53
211.53	17.65
212.53	2.23
213.53	1.21
214.54	0.44
231.49	0.37
232.49	3.32
233.49	0.87
245.48	1.12
251.47	0.40
252.46	5.94
253.47	0.53
261.44	4.28
262.45	0.60
264.43	9.10
265.42	1.18
280.38	82.10
281.39	10.18
282.39	0.66

EI+ M.Wt. 281 No. 38.



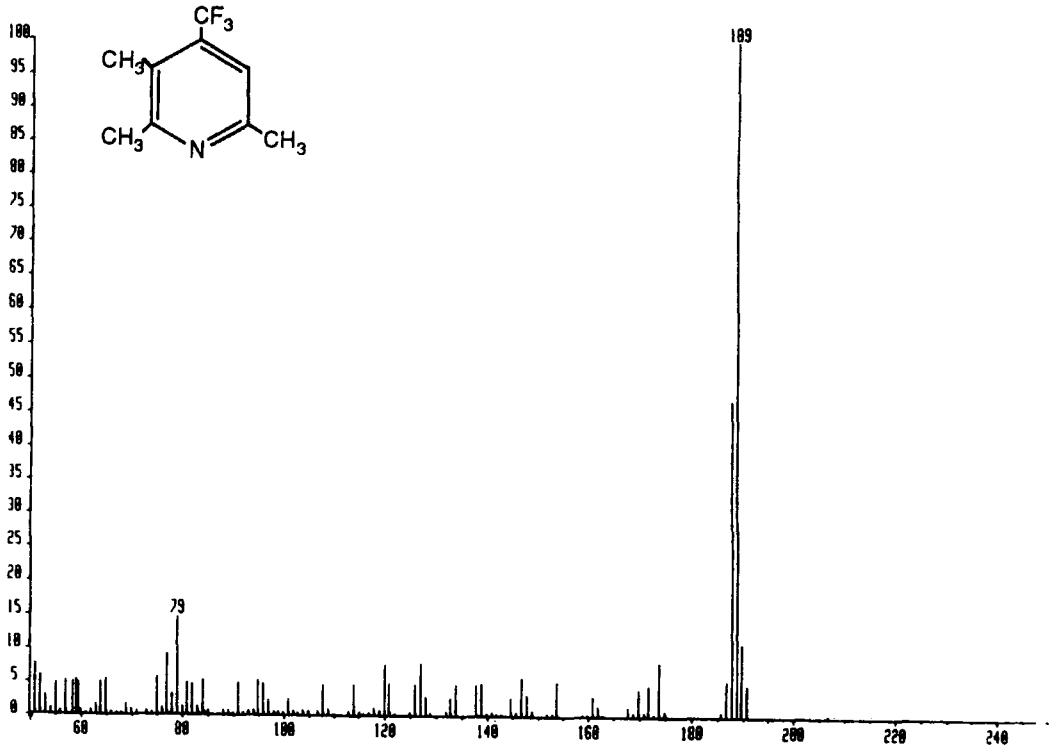
Mass	% Base
50.85	6.74
51.85	2.31
52.83	0.69
55.83	0.90
56.84	0.55
60.82	1.20
61.82	2.99
62.83	13.36
63.83	16.56
64.83	1.89
68.79	8.15
69.80	0.24
70.79	0.26
72.80	0.33
73.79	3.09
74.79	9.12
75.80	4.03
76.81	2.78
77.80	2.24
78.79	0.36
80.77	0.57
81.77	0.42
85.75	0.26
86.76	1.69
87.77	1.91
88.78	2.35
89.77	3.31
90.77	6.34
91.76	3.72
92.73	3.45
93.75	0.42
94.76	2.40
98.73	0.71
99.72	0.29
100.74	0.22
101.75	2.98
102.75	0.23
104.72	0.21
105.72	2.25
106.74	1.72
107.74	0.86
108.73	0.22
111.71	0.60
112.71	0.58
113.72	1.74
114.73	3.00
115.73	0.29
116.70	0.46
117.71	0.36
118.71	39.19
119.71	3.58
120.70	0.88
121.70	0.26
123.68	0.57
124.67	2.60
125.70	0.48
130.67	0.38
131.66	0.45
132.67	0.60
133.68	4.99
134.69	0.43
135.67	0.52
136.66	5.14
137.66	1.62
138.67	0.53
140.15	0.43
142.64	4.90
143.64	3.04
144.64	0.88
145.65	1.02
151.64	0.26
155.61	0.51
156.62	2.07
157.62	0.89
158.62	0.83
161.61	0.60
162.61	1.14
163.61	4.36
164.62	1.21
166.61	0.55
174.55	2.17
175.57	0.34
181.58	0.28
182.57	8.97
183.57	13.86
184.58	1.71
185.57	2.23
186.56	2.78
187.55	0.36
191.55	4.25
192.54	0.74
193.53	0.56
195.54	0.43
201.53	0.26
202.55	1.54
206.52	0.25
211.51	22.53
212.52	2.67
213.51	2.58
214.51	0.29
231.47	1.07
232.47	14.28
233.48	7.63
234.49	0.79
241.46	0.42
251.44	0.61
252.45	1.60
253.44	0.21
259.43	0.28
261.43	10.33
262.43	1.33
279.33	1.62
280.37	100.00
281.37	12.62
282.38	0.88

EI$^+$ M.Wt. 265 No. 39.



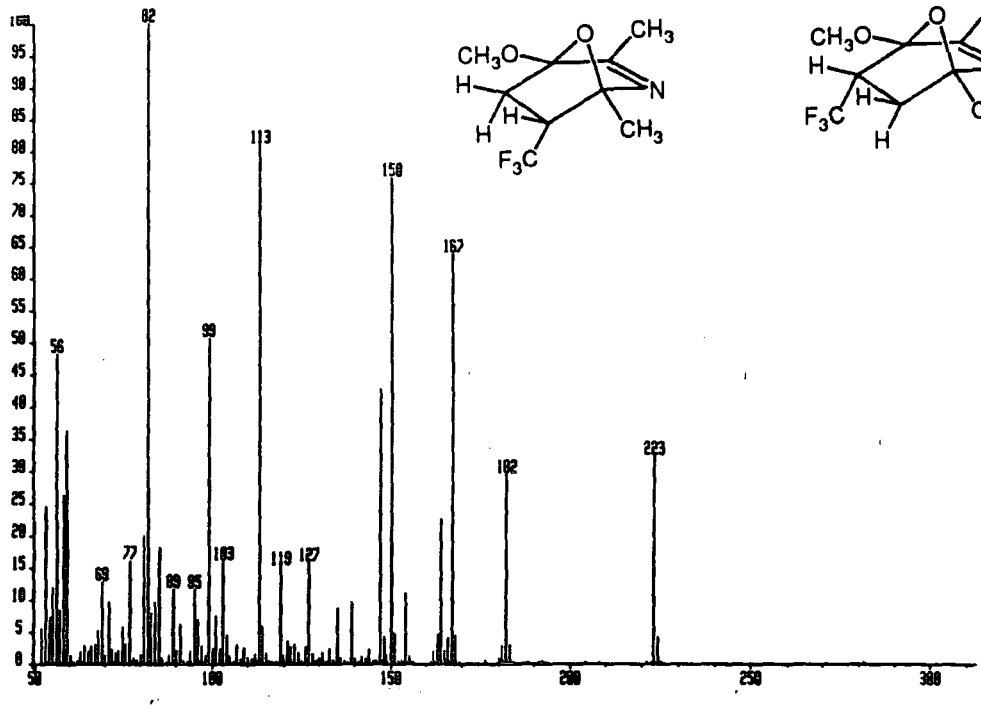
MSEC Mass	% Base
176.01	18.13
177.01	2.49
196.00	50.69
197.01	4.35
215.01	1.19
245.99	7.33
264.98	100.00
265.99	11.35

EI+ M.Wt. 189 No. 40.



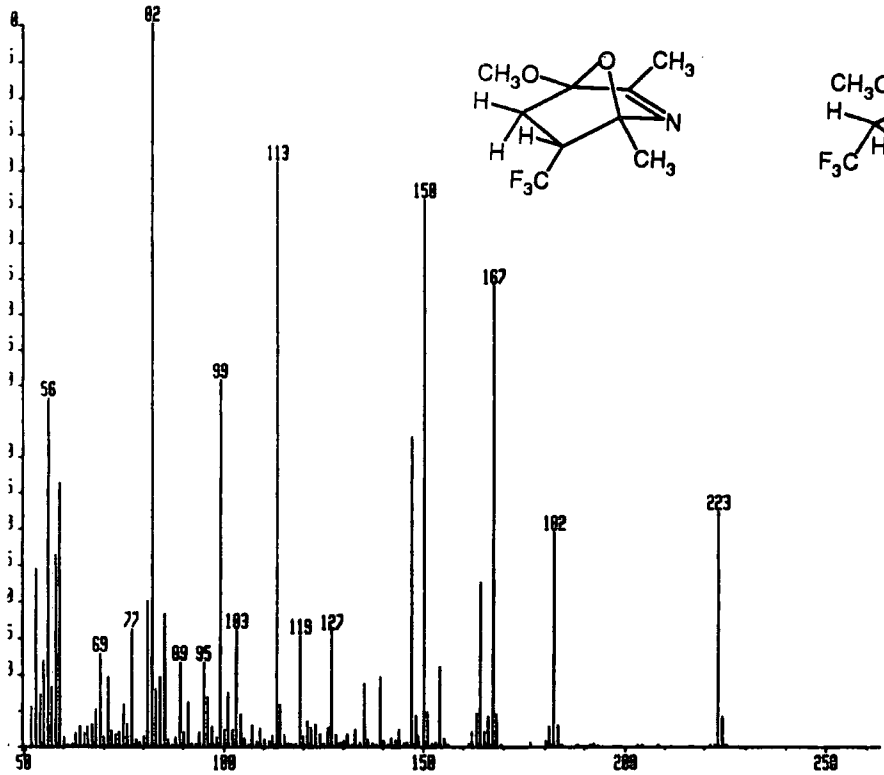
50.90	7.55	93.88	0.77	151.75	0.29
51.91	5.83	94.84	5.08	152.76	0.35
52.92	2.69	95.86	4.52	153.77	4.93
53.92	0.97	96.86	2.14	159.75	0.21
54.94	4.64	97.87	0.47	160.76	2.82
55.94	0.52	98.82	0.40	161.77	1.34
56.90	4.93	99.83	0.24	167.77	1.26
58.41	4.84	100.83	2.31	168.78	0.46
58.91	5.18	101.84	0.61	169.79	3.94
59.42	4.76	102.85	0.25	170.79	0.49
59.91	0.55	103.86	0.71	171.76	4.54
61.89	0.55	104.87	0.64	173.75	8.02
62.89	1.57	106.82	0.64	174.76	0.72
63.89	4.78	107.85	4.50	185.74	0.66
64.90	5.33	108.85	0.94	186.86	5.11 F
65.90	0.28	112.82	0.55	187.73	46.94 F
68.86	1.50	113.80	4.60	188.75	100.00 F
69.89	0.68	114.83	0.51	189.75	10.87
70.89	0.43	116.83	0.32	190.75	4.55
72.89	0.45	117.85	1.01		
73.87	0.34	118.83	0.75		
74.86	5.57	119.86	7.59		
75.87	0.99	120.84	4.67		
76.88	9.07	124.81	0.41		
77.38	0.20	125.77	4.57		
77.89	2.98	126.80	7.86		
78.89	14.52	127.81	2.70		
79.89	1.18	128.82	0.37		
80.88	4.63	131.78	0.62		
81.89	4.60	132.79	2.64		
82.86	1.29	133.82	4.54		
83.87	5.19	137.84	4.54		
84.37	0.26	138.83	4.68		
84.88	0.40	139.78	0.30		
87.84	0.81	140.80	0.53		
88.85	0.68	144.76	2.50		
90.88	4.71	145.76	0.46		
91.88	0.36	146.77	5.55		
92.89	0.57	147.78	3.05		
		148.78	0.82		

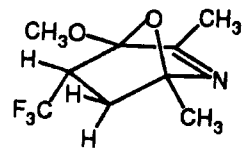
EI$^+$ M.Wt. 223 No. 41.



Mass	% Base		Mass	% Base	
52.10	3.24		112.25	1.08	
53.11	9.06		113.25	1.74	
54.11	3.60		119.21	35.43	
55.11	9.11		120.22	2.01	
56.14	36.97		121.21	2.31	
57.12	4.27		122.22	3.07	
58.13	20.94		123.21	2.73	
59.12	22.32		124.23	1.21	
60.13	1.08		127.25	11.78	
63.12	1.30		135.27	8.81	
64.13	1.82		139.25	1.18	
65.14	1.71		142.25	1.34	
66.15	2.51		144.28	4.06	
67.16	2.39		147.25	100.00	FO
68.17	3.35		148.26	8.51	
69.13	9.05		149.27	1.17	
71.16	4.17		164.32	10.55	
72.17	1.74		166.29	2.29	F
73.18	1.57		167.28	73.18	F
75.14	3.62		168.29	4.71	
76.15	1.81		181.30	1.08	
77.16	11.14		182.31	27.94	
80.19	1.15		183.32	1.79	
81.18	2.71	F	208.34	0.18	
82.23	100.00	FO	223.39	17.35	
83.21	9.43		224.40	1.84	
84.20	6.70		225.40	0.06	
85.21	1.97				
89.18	1.90				
91.18	7.98				
94.22	1.24				
95.19	7.95				
96.16	4.77	F			
97.21	1.74	F			
98.23	1.09				
99.24	34.83				
100.24	1.92				
101.20	4.82				
102.21	1.76				
103.22	10.54				
104.22	1.93				

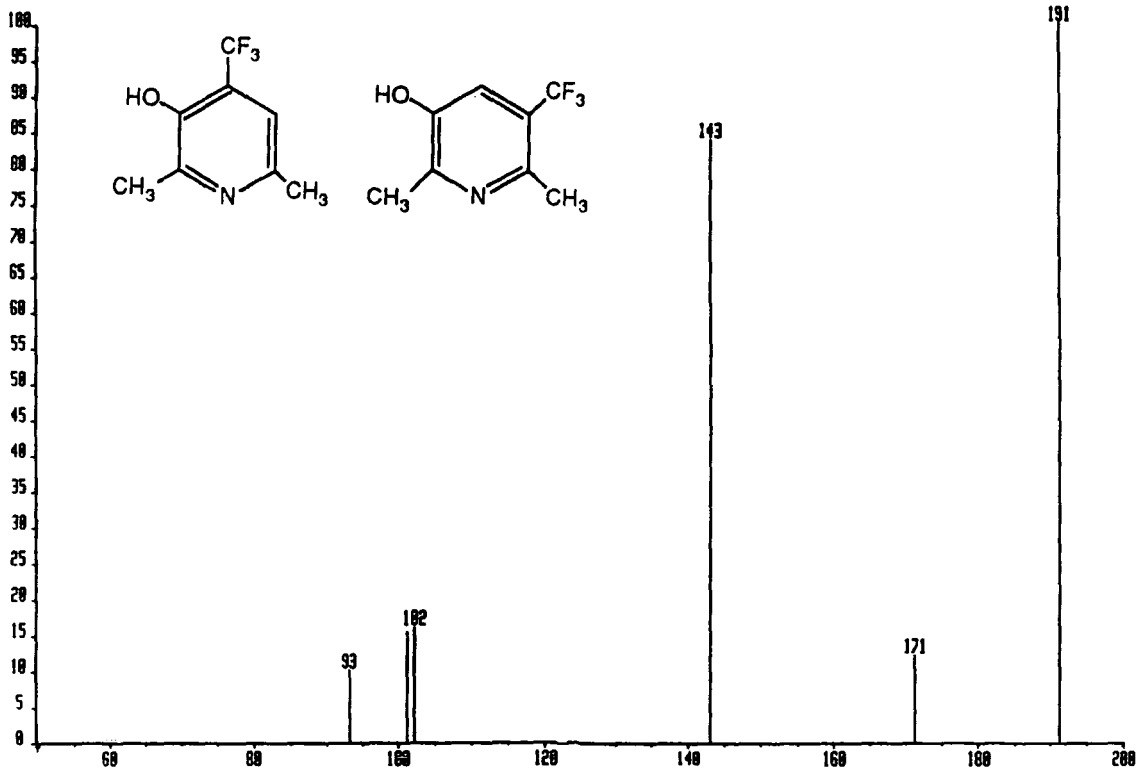
EI$^+$ M.Wt. 223 No. 42.





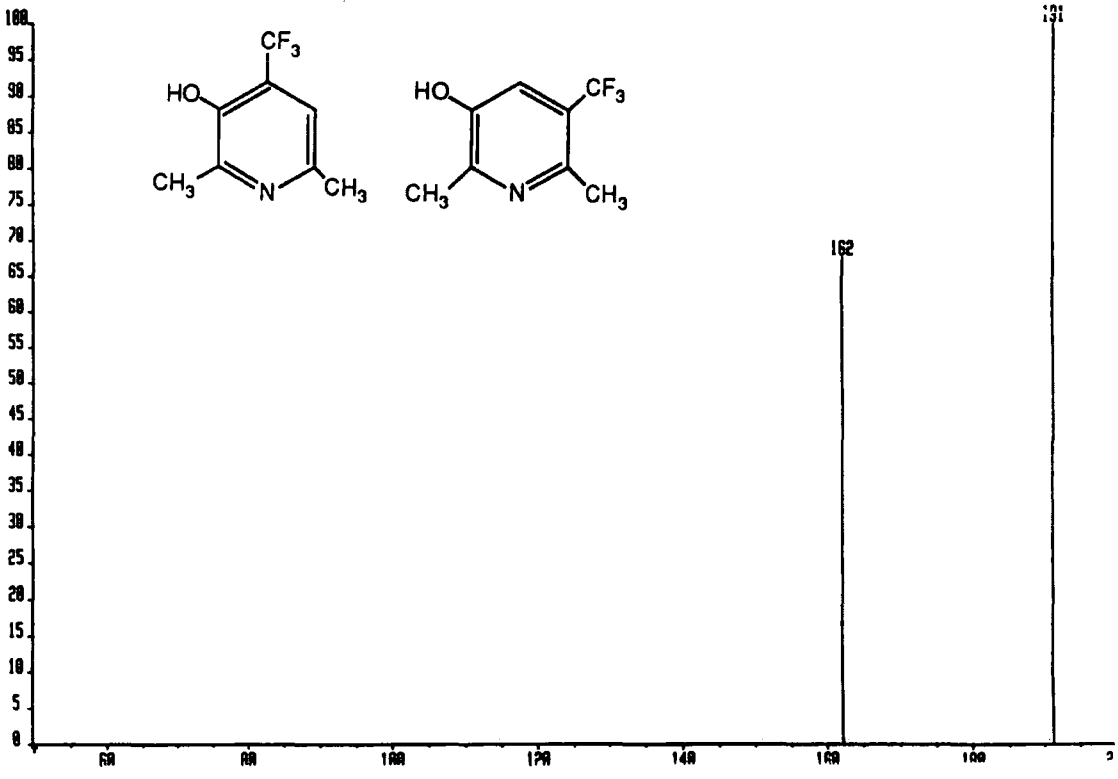
Mass	% Base
52.10	5.39
53.11	24.38
54.12	7.10
55.12	11.85
56.14	48.02
57.12	8.22
58.13	26.23
59.12	36.22
60.13	1.26
63.12	1.88
64.13	2.71
65.14	1.77
66.15	2.69
67.16	2.97
68.17	5.16
69.13	12.69
70.15	1.42
71.17	9.55
72.17	2.10
73.18	1.64
74.17	1.91
75.14	5.80
76.15	3.05
77.16	16.00
80.20	1.42
81.18	20.05
82.21	100.00
83.20	7.93
84.20	9.60
85.22	18.13
88.17	1.15
89.18	11.52
90.19	1.97
91.18	6.03
94.22	1.97
95.19	11.47
96.20	6.86
97.18	2.78
98.22	1.28
99.24	50.59
100.24	2.24
101.20	7.45
102.20	2.26
103.22	15.97
104.22	4.39
105.21	1.13
107.22	2.84
109.22	2.46
112.25	1.49
113.25	81.12
114.25	5.76
115.24	1.52
119.21	15.10
120.22	1.32
121.21	3.47
122.21	2.52
123.21	3.10
124.22	1.70
126.28	2.56
127.25	15.75
128.25	1.55
131.23	1.66
133.25	2.31
135.26	8.68
139.25	9.62
142.27	1.02
144.28	2.22
147.25	42.72
148.26	4.25
149.07	1.43
150.28	75.84
151.28	4.62
154.31	10.93
155.32	1.11
162.30	1.97
163.31	4.62
164.32	22.61
165.31	1.93
166.30	4.06
167.28	63.89
180.29	4.37
181.30	2.76
182.31	29.35
183.32	2.85
203.34	0.08
204.36	0.13
208.38	0.17
221.31	0.11
222.42	0.17
222.71	0.07
222.92	0.06
223.38	32.25
224.39	4.16

EI+ M.Wt. 191 No. 43.



Mass	% Base
93.17	10.07
101.14	15.44
102.15	16.11
143.20	83.89
171.21	12.08
191.22	100.00

EI^+ M.Wt. 191 No. 44.



Mass	% Base
162.21	67.62
191.22	100.00

APPENDIX 4

COLLOQUIA AND CONFERENCES

APPENDIX 4

UNIVERSITY OF DURHAM

Board of studies in chemistry

COLLOQUIA, SEMINARS, AND LECTURES GIVEN BY INVITED SPEAKERS

OCTOBER 1987 TO OCTOBER 1990

(A)

(those attended are marked *)

15.10.87 Dr. M.J. Winter (University of Sheffield), 'Pyrotechnics (Demonstration Lecture)'.

22.10.87 Prof. G.W. Gray (University of Hull), 'Liquid Crystals and their Applications'.

29.10.87 * Mrs. S. van Rose (Geological Museum), 'Chemistry of Volcanoes'.

5.11.87 Dr. A.R. Butler (University of St. Andrews), 'Chinese Alchemy'.

12.11.87 Prof. D. Seebach (E.T.H. Zurich), 'From Synthetic Methods to Mechanistic Insight'.

19.11.87 * Dr. J. Davidson (Herriot-Watt University), 'Metal Promoted Oligemerisation Reactions of Alkynes'.

19.11.87 Prof. P.G. Sammes (Smith, Kline and French), 'Chemical Aspects of Drug Development'.

26.11.87 Dr. D.H. Williams (University of Cambridge), 'Molecular Recognition'.

3.12.87 Dr. J. Howard (I.C.I. Wilton), 'Liquid Crystal Polymers'.

10.12.87 Dr.C.J. Ludman (University of Durham), 'Explosives'.

16.12.87 Mr. R.M. Swart (I.C.I.), 'The Interaction of Chemicals with Lipid Bilayers'.

21.1.88 * Dr. F. Palmer (University of Nottingham), 'Luminescence (Demonstration Lecture)'.

28.1.88 Dr. A. Cairns-Smith (University of Glasgow), 'Clay Minerals and the Origin of Life'.

11.2.88 Prof. J.J. Turner (University of Nottingham), 'Catching Organometallic Intermediates'.

18.2 88 Dr. K. Borer (University of Durham Industrial Research Laboratories), 'The Brighton Bomb A Forensic Science View'.

25.2.88 Prof. A. Underhill, (University of Bangor), 'Molecular Electronics'.

3.3.88 Prof. W.A.G. Graham (University of Alberta, Canada), 'Rhodium and Iridium Complexes in the Activation of Carbon-Hydrogen Bonds'.

7.4.88 Prof. M.P. Hartshorn (University of Canterbury, New Zealand), 'Aspects of Ipso-Nitration'.

18.4.88 Prof. C.A. Nieto de Castro (University of Lisbon and Imperial College), 'Transport Properties of Non-polar Fluids'.

25.4.88 * Prof. D. Birchall (I.C.I Advanced Materials), 'Environmental Chemistry of Aluminium'.

27.4.88 * Dr. J.A. Robinson (University of Southampton), 'Aspects of Antibiotic Biosynthesis'.

27.4.88 Dr. R. Richardson (University of Bristol), 'X-Ray Diffraction from Spread Monolayers'.

28.4.88 Prof. A. Pines (University of California, Berkeley, U.S.A.), "Some Magnetic Moments".

11.5.88 Dr. W.A. McDonald (I.C.I. Wilton), 'Liquid Crystal Polymers'.

8.6.88 Prof. J.-P. Majoral (Universite Paul Sabatier), 'Stabilisation by Complexation of Short-Lived Phosphorus Species'.

29.6.88 * Prof. G.A. Olah (University of Southern California), 'New Aspects of Hydrocarbon Chemistry'.

6.10.88 * Prof. R. Schmutzler (University of Braunschweig), 'Fluorophosphines Revisited - New Contributions to an Old Theme'.

18.10.88 * Dr. J. Dingwall (Ciba Geigy), 'Phosphorus-containing Amino Acids: Biologically Active Natural and Unnatural Products'.

18.10.88 Dr. C.J. Ludman (Durham University), 'The Energetics of Explosives'.

21.10.88 Prof. P. von Rague Schleyer (University of Erlangen), 'The Fruitful Interplay Between Calculational and Experimental Chemistry'.

27.10.88 * Prof. W.C. Rees (Imperial College), 'Some Very Heterocyclic Compounds'.

9.11.88 * Dr. G. Singh (Teesside Polytechnic), 'Towards Third Generation Anti-Leukaemics'.

10.11.88 Prof. J.I.G. Cadogan (B.P. Research), 'From Pure Science to Profit'.

16.11.88 Dr. K.A. McLauchlan (University of Oxford), 'The Effect of Magnetic Fields on Chemical Reactions'.

24.11.88 Dr. R.W. Walker and Dr. R.R. Baldwin (University of Hull), 'Combustion - Some Burning Problems'.

1.12.88 * Dr. R. Snaith (University of Cambridge), 'Egyptian Mummies - What, Where, Why and How ?' (*)

9.12.88 Dr. C. Jaeger (Friedrich-Schiller University GDR), 'NMR investigations of Fast Ion Conductors of the NASICON Type'.

25.1.89 * Dr. L. Harwood (University of Oxford), 'Synthetic Approaches to Phorbols Via Intramolecular Furan Diels-Alder Reactions: Chemistry Under Pressure

26.1.89 Prof. K.R. Jennings (University of Warwick), 'Chemistry of the Masses'.

2.2.89 Prof. L.D. Hall (Addenbrookes' Hospital), 'NMR - A Window to the Human Body'.

9.2.89 * Prof. J. Baldwin (University of Oxford), Recent advances in the bioorganic chemistry of biosynthesis

13.2.89 * Prof. R.R. Schrock (M.I.T.), 'Recent Advances in Living Metathesis'.

15.2.89 Dr. A.R. Butler (St. Andrews University), 'Cancer in Linxiam: The Chemical Dimension'.

16.2.89 Prof. J.B. Aylett (Queen Mary College), 'Silicon-based Chips: The Chemists Contribution'.

22.2.89 Dr. G. MacDougall (Edinburgh University), 'Vibrational Spectroscopy of Model Catalytic Systems'.

23.2.89 * Dr. B.F.G. Johnson (University of Cambridge), 'The Binary Carbonyls'.

1.3.89 Dr. R.J. Errington (University of Newcastle-upon-Tyne), 'Polymetalate Assembly in Organic Solvents'.

9.3.89 Dr. I. Marko (Sheffield University), 'Catalytic Asymmetric Osmylation of Olefins'.

15.3.89 Dr. R. Aveyard (University of Hull), 'Surfactants at your Surface'.

20.4.89 Dr. M. Casey (University of Salford), 'Sulphoxides in Stereoselective Synthesis'.

27.4.89 * Dr. D. Crich (University College London), 'Some Novel Uses of Free Radicals in Organic Synthesis'.

3.5.89 Dr. P.C.B. Page (University of Liverpool), 'Stereocontrol of Organic Reactions Using 1,3-dithiane-1-oxides'.

10.5.89 Prof. P.B. Wells (Hull University), 'Catalyst Characterisation and Activity'.

11.5.89 Dr. J. Frey (Southampton University, 'Spectroscopy of the Reaction Path: Photodissociation Raman Spectra of NOCl'.

16.5.89 Dr. R. Stibr (Czechoslovak Academy of Sciences), 'Recent Developments in the Chemistry of Intermediate-Sited Carboranes'.

17.5.89 Dr. C.J. Moody (Imperial College), 'Reactive Intermediates in Heterocyclic Synthesis'.

23.5.89 Prof. P. Paetzold (Aachen), 'Iminoboranes XB≡≡NR: Inorganic Acetylenes ?'.

15.6.89 Prof. J. Pola (Czechslovak Academy of Sciences), 'Carbon Dioxide Laser Induced Chemical Reactions - New Pathways in Gas-Phase Chemistry'.

17.10.89 Dr. F. Palmer (Nottingham University), 'Thunder and Lightning.

25.10.89 Prof. C. Floriani (University of Lausanne, Switzerland) Molecular Aggregates - A bridge between Homogenous and Hetrogenous Systems.

9.10.89 * Prof. N.N. Greenwood (University of Leeds) Novel Cluster Geometries in Metalloborane Chemistry.

10.10.89 Prof. J.E. Bercaw (California Institute Of Technology) Synthetic and Mechanistic Approaches to Zieger-natta Polymerisation of Olefins.

13.10.89 * Dr. J. Becher (Odense University) Synthesis of New Macrocyclic Systems using Heterocyclic Building Blocks.

16.11.89 Dr. D. Parker (Durham University) Macrocycles, Drugs and Rock 'n' roll.

29.11.89 Prof. D.J. Cole-Hamilton (St. Andrews University) New Polymers from Homogeneous Catalysis.

30.11.89 Dr. M.N. Hughes (Kings College, London) A bug's Eye View of the Periodic Table.

4.12.89 Dr. D. Graham (B.P. Reserch Centre) How Proteins Absorb to Interfaces.

6.12.89 Dr. R.L. Powell (ICI) The Development of CFC Replacements.

7.12.89 * Dr. A. Butler (St Andrews University) The Discovery of Penicillin: Facts and Fancies

13.12.89 Dr. J. Klinowski (Cambridge University) Solid State NMR Studies of Zeolite Catalysis.

15.12.89 * Prof. R. (Universitat Munchen) Recent Mechanistic Studies Of [2+2] Additions

24.1.90 * Dr. R.N. Perutz (York University) Plotting the Course of C-H Activation With Organometallics

31.1.90 Dr. U. Dyer (Glaxo) Synthesis and conformation of C-Glycosides.

1.2.90 Prof. J.H. Holloway (University of Leicester) Noble Gas Chemistry

7.2.90 Dr. D.P. Thompson (Newcastle University) The Role of Nitrogen in Extending Silicate Crystal Chemistry.

8.2.90 Rev. R. Lancaster (Kimbolton Fireworks) Fireworks- Principles and Practice.

12.2.90 Prof. L. Lunazzi (University of Bologna) Applications of Dynamic NMR to the Study of Conformational Enantiomerism.

14.2.90 Prof. D. Sutton (Simon Fraser University Vancouver B.C.) Synthesis and Applications of Dinitrogen and Diazo Compounds of Rhenium and Iridium.

15.2.90 Prof. L. Crombie (Nottingham University) the chemistry of Cannabis and Khat.

21.2.90 Dr. C. Bleasdale (Newcastle University) The Mode of Action of some Anti-tumor Agents.

22.2.90 Prof. D.T. Clark (ICI Wilton) Spatially Resolved Chemistry (using Natures Paradigm in the Advanced Materials Arena).

28.2.90 Dr. R.K. Thomas (Oxford University) Neutron Reflectometry from surfaces.

1.2.90 Dr. J.F. Stoddart (Sheffield University) Molecular Lego.

8.3.90 * Dr. A.K. Cheetham (Oxford University) Chemistry of Zeolite Cages.

21.4.90 Dr. I. Powis (Nottingham University) Spinning off in a huff: Photodissocation of methyl iodide.

23.3.90 Prof. J.M Bowman (Emory University) Fitting Experiment with theory in Ar-OH.

9.7.90 * Prof. L.S. German (USSER Academy of Sciences Moscow)
New Synthesis of Fluoroaliphatic Chemistry: Recent Advances in the Chemistry of Fluorinated Oxiranes.

9.7.90 * Prof. V.E. Platonov (USSER Academy of Sciences Novosibirsk)
Polyfluoroindanes: Synthesis and Transformation

9.7.90 * Prof. I.N. Rozhkov (USSER Academy of Sciences Moscow)
Reactivity of perfluoroalkyl Bromides.

(B) Conferences attended

1. 21st Sheffield Symposium on "Modern Aspects of Sterochemistry" Sheffield 16.12.87

2. Gradute Symposium Durham, 16.4.88

3. 9th European Symposium on Fluorine Chemistry, Leicester, 4.9.1989

4. 23rd Sheffield Symposium on "Modern Aspects of Sterochemistry" Sheffield 1.12.89

(C) First year induction course, October 1987

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

1. Departmental organisation.
2. Safety matters.
3. Electrical appliances and infra-red spectroscopy.
4. Chromatography and microanalysis.
5. Atomic absorptiometry and inorganic analysis.
6. Library facilities.
7. Mass spectroscopy.
8. Nuclear magnetic resonance spectroscopy.
9. Glassblowing technique.

REFERENCES

REFERENCES

1. R. Filler and Y. Kobayashi, *"Biomedicinal Aspects of Fluorine Chemistry"*, Elsevier, Amsterdam 1982.

2. R. Filler in *"Fluorine-The First Hundred Years"*, ed. R.E. Banks, D.W.A. Sharp, and. J.C.Tatlow, Elsevier, Amsterdam, 1986, pp361-374.

3. G.T. Newbold in *"Organofluorine Chemicals and their Indrustral Application"*, ed. R.E. Banks, Ellis Horwood Ltd, Chichester, 1979, pp169-87.

4. J.T. Welch, *Tetrahedron*, 1987, 43, 3123.

5. K.A. Hassal, *"The Chemistry Of Pesticides"*, Macmillan Press Ltd, 1982, 162.

6. T.H. Maugh, *Science*, 1981, 214, 1225.

7. G. Balz and G. Schiemann, *Chem. Ber.*, 1927, 60, 1186.

8. J.P. Feraris and G. Sallo, *J. Chem. Soc. Chem. Commun.*, 1978, 992.

9. A. Roe, *Org. React.*, 1949, 5, 193.

10. H. Suschitzky, *Advan. Fluorine Chem.*, 1965, 4, 1.

11. G.M. Bennett, G.L. Brooks, and S. Gladstone, *J. Chem. Soc.*, 1935, 1821.

12. C. Niemann, A.A. Benson, and J.F. Mead, *J. Am. Chem. Soc.*, 1941, 63, 2204.

13. M.F.W. Dunker, E.B. Starkey, and G.L. Jerkins, *J. Am. Chem. Soc.*, 1936, 58, 2308.

14. G. Schiemann and R. Pillarskey, *Chem. Ber.*, 1929, 62, 3035.

15. E. Wilke-Dorfurt and G. Balz, *Chem. Ber.*, 1927, 60, 115.

16. A. Roe and H.L. Fleishmann, *J. Am. Chem. Soc.*, 1947, 69, 509.

17. G. Schiemann, *J. Prakt. Chem.*, 1934, 97,140.

18. M.A. Goldberg, E.P. Ordas, and G. Garsch, *J. Am. Chem. Soc.*, 1947, 69, 260.

19. A. Roe and G.F. Hawkins, *J. Am. Chem. Soc.*, 1949, 69, 2443.

20. B.L. Zenitz and W.H. Hartung, *J. Org. Chem.*, 1946, 11, 444.

21. H. Hopff and G. Valkanas, *J. Chem. Soc.*, 1963, 1925.

22. G.B. Bachman and T. Hokamo, *J. Am. Chem. Soc.*, 1957, 79, 4370.

23. E.D. Bergman, S. Berkovic, and R. Ikan, *J. Am. Chem. Soc.*, 1956, 78, 6007.

24. A. Roe and G.F. Hawkins, *J. Am. Chem. Soc.*, 1949, 71, 1785.

25. J.S. Moilliet B.P., 2,173,188/1987.

26. P. Osswald and O. Scherer, G.P., 600, 706/1933. CA. 28, P7260.

27. R.L. Ferm and C.A. van der Werf, *J. Am. Chem. Soc.*, 1950, 72, 4809.

28. W. Presott, *Chem. Ind.*, 1978, 56

29. L. Dolby-Glover, *Chem. Ind.*, 1986, 518.

30. R.D. Chambers, "*Fluorine in Organic Chemistry*", Wiley Interscience, New York, 1973.

31. M.Hudlicky, "*Chemistry of Organic Fluorine Compounds*", 2nd Edn, Ellis Horwood, Chichester, 1976.

32. G. Filler, *J. Chem. Soc.*, 1965, 6264.

33. K. Seisaku, S. Ryuji, F. Yutaka, and M. Masshi, *Asahi Garasu Kenkyn Hokoku*, 1985, 5, 85. CA. 1987, 107, 6848g.

34. J.H. Clark and D.K. Smith, *Tetrahedron Lett.*, 1985, 26, 2233.

35. M.R.C. Gerstenberger and A. Haas, *Agnew. Chem. Int. Ed.*, 1981, 20, 647.

36. H. Moissan, *Ann. Chim. Phys.*, 1891, 19, 272.

37. H. Moissan, "*Das Fluoro und Seine Verbindungen*", Verlag. M. Kroyn, Berlin, 1900, p236.

38. F. Cacace, P. Giacomello, and A.P. Wolf, *J. Am. Chem. Soc.*, 1980, 102, 3511.

39. W.D. Bancroft and N.C. Jones, *Trans. Am. Electrochem. Soc.*, 1929, 183.

40. W.D. Bancroft and S.F. Whearty, *Proc. Nat. Acad. Sci. U.S.*, 1931, 17, 183.

41. W. Brockemüller, *Ann. Chem*, 1933, 20, 506.

42. W.S. Calcott and A.F. Benning, U.S.P., 2, 013, 030/1935.

43. H.W. Daudt, W. Del, and H.M. Parmelee, U.S.P., 2, 013, 035/1935.

44. J.H. Simons, U.S.P., 2, 447, 717/1948.

45. H. Meinert, *Z. Chem.*, 1965, 5, 64.

46. R.E. Eibeck, M. Van der Puy, U.S.P., 4, 786, 733/1988.

47. M. Van der Puy *Tetrahedron Lett.*, 1987, 28, 255.

48. F. Cacace, P. Giacomello, and A.P. Wolf, *J. Am. Chem. Soc.*, 1980, 102, 3511.

49. F. Cacace, and A.P.Wolf, *J. Am. Chem. Soc.*, 1978, 100, 3639.

50. R.O.C. Norman and R. Taylor *"Electrophilic Substitution in Benzenoid Compounds"*, Elsevier, Amsterdam 1965.

51. C.K. Ingold *"Structure and Mechanisms in Organic Chemistry"* Cornell University Press, Ithica, New York, 1955.

52. V. Grakauskas, *J. Org. Chem.*, 1969, 34, 2835.

53. V. Grakauskas, *J. Org. Chem.*, 1970, 35, 723.

54. L.C. Sams, T.A. Reames, and M.A. Durrance, *J. Org. Chem.*, 1978, 43, 2273.

55. S. Misaki, *J. Fluorine Chem.*, 1981, 17, 159.

56. S. Misaki, *J. Fluorine Chem.*, 1982, 21, 191.

57. S. Misaki, *Chem. Express*, 1986, 11, 683.

58. G. Firnau, R. Chirakai, and G.S.Garnet, *J. Nucl. Med.*, 1984, 25, 1228.

59. R. Dagani, *Nature*, 1988, 26.

60. K.O. Christe, *J. Fluorine Chem.*, 1983, 22, 519.

61. K.O. Christe, *J. Fluorine Chem.*, 1984, 25, 269.

62. M.M. Cartwright and A.A. Wolf, *J. Fluorine Chem.*, 1984, 25, 263.

63. R.H. Hesse, *Isreal J. Chem.*, 1978, 17, 60.

64. S. Rozen, *Acc. Chem. Res.*, 1988, 21, 307.

65. M.J. Fivolt, R.T. Olozak, and R.F. Mundnenke, *J. Org. Chem.*, 1985, 23, 4577.

66. D.H.R. Barton, A.K. Ganguly, R.H. Hesse, S.M. Loo, and M.M. Pecker, *J. Chem. Soc. Chem. Commun.*, 1968, 806.

67. J.A.C. Allision and G. Cady, *J. Am. Chem. Soc.*, 1974, 39, 2120.

68. M.J. Fivolt, *U.S.P.*, 4, 766, 243/1988.

69. T.B. Patrick, G.L. Cantrell, and C.Y. Chang, *J. Am. Chem. Soc.*, 1979, 101, 7434.

70. J. Leroy and C. Wakselman, *J. Chem. Soc. Perkin. Trans.* 1, 1978, 1224.

71. J. Airey, D.H.R. Barton, R.H. Hesse, and M.M. Decker, *An. Quim.* 1974, 70, 871

72. M.J. Fivolt, *U.S.P.*, 4, 449, 024/1985.

73. D.H.R. Barton, *U.S.P.*, 3, 687, 943/1972.

74. G.H.Cady and K.B.Kellog, *J.Am.Chem.Soc.*, 1653, 75, 2501.

75. O. Lerman and S. Rozen, *J. Am. Chem. Soc.*, 1979, 101, 2782.

76. O. Lerman and S. Rozen, *J. Org. Chem.*, 1980, 45, 672.

77. S. Rozen and Y. Menahem, *J. Fluorine Chem.*, 1980, 16, 19.

78. S. Rozen and Y. Menahem, *Tetrahedron Lett.* 1979, 725.

79. G.K. Mulholl and R.E. Ehrenkauler, *J. Org. Chem.*, 1986, 51, 1482.

80. J.H. Prager and P.G. Thompson *J. Am. Chem. Soc.*, 1965, 87, 231.

81. O. Lerman and S. Rozen, *J. Org. Chem.*, 1980, 45, 4122.

82. W.E. Barnette, R.C. Whealand, and W. Middleton, *J. Org. Chem.*, 1985, 50, 3698.

83. A.E. Feiring, *J. Org. Chem.*, 1985, 50, 3269.

84. O. Lerman, Y. Tor, S. Rozen, and D. Hebel, *J. Org. Chem.*, 1981, 46, 4629.

85. O. Lerman, S. Rozen, and D. Hebel, *J. Org. Chem.*, 1984, 49, 806.

86. O. Lerman, S. Rozen, and M. Kol, *J. Chem. Soc. Chem. Commun.*, 1981, 443.

87. D. Hebel, K.L. Kirk, L.A. Cohen, and V.M. Labroo, *Tetrahedron Lett.*, 1990, 31, 619.

88. S. Rozen and D. Hebel, *J. Org. Chem.*, 1990, 55, 2621.

89. F. Fichter and K. Humpert, *Helv. Chim. Acta.*, 1926, 9, 602.

90. E.A. Appleman, L.J. Basile, and R.C. Tompson, *J. Am. Chem. Soc.*, 1979, 101, 3384.

91. S. Stavber and M. Zupan, *J. Org. Chem.*, 1985, 50, 3609.

92. E.H. Appleman, C.D. Auther, D. Ip, and R. Winans, *J. Am. Chem. Soc.*, 1981, 103, 1964.

93. S. Stavber and M. Zupan *J. Chem. Soc. Chem. Commun.*, 1981, 148.

94. S. Stavber and M. Zupan, *J. Fluorine Chem.* 1981, 17, 597.

95. S. Stavber and M. Zupan, *J. Org. Chem.*, 1985, 50, 3609.

96. E.H. Applemann, L.J. Basile and R. Hayatsie, *Tetrahedron*, 1984, 40, 189.

97. T.B. Patrick and D.L. Darling, *J. Org. Chem.*, 1986, 51, 3242.

98. S. Stavber and M. Zupan, *Tetrahedron lett.*, 1990, 31.

99. G.C. Coates and K. Wade, *Organometallic Compounds* Methuen & Co. L.t.d, London 1967.

100. M.J. Adam, B.D. Pate, and J.R. Thomas, *J. Chem. Soc. Chem. Commun.* 1981, 733.

101. M.J. Adam, B.D. Pate, and J.R. Thomas, *Can. J. Chem.*, 1982, 61, 658.

102. M.J. Adam, B.D. Pate, and J.R. Thomas, *J. Fluorine Chem.*, 1984, 25, 329.

103. G.W.M. Viesser, J.D.M. Herschied, G. Brinkman, A. Hoehstra, *J. Lab. Comp. & Radiopharm.*, 1984, VOL *XXI* 1185.

104. M.J. Adam, B.D. Pate, and J.R.Thomas, *J. Lab. Comp.& Radiopharm.*, 1984, Vol XXI, 1227.

105. H.H. Coenen, S.M. Moelien, *J. Fluorine Chem.*, 1987, 36, 63.

106. R.D. Chambers, M.R. Bryce, and S.T. Mullin, and A. Perkin, *J. Fluorine Chem.* 1984, 26, 533.

107. R.D. Chambers, M.R. Bryce, S.T. Mullin, and A. Perkin *Bull. Soc. Chem. France*, 1986, 930.

108. R.D. Chambers, M.R. Bryce, S.T. Mullin, and A. Perkin *J. Chem. Soc. Chem. Commun.*, 1986, 1623.

109. R.E. Banks and G.E. Williams, *Chem. Ind.*, 1964, 1864.

110. R.E. Banks, W.M. Cheng, and R.H. Haszeldine, *J. Chem. Soc.*, 1962, 3407.

111. V.R. Polishchuck, B.Ya. Medvidev, N.N. Bubnov, L.S. Germain, and I.L. Knunyants, *Izv. Akad. Nauk. SSSR Ser. Khim.*, 1972, 2805.

112. V.R.Polishchuck and L.S. Germain, *Tetrahedron Lett.*, 1972, 5169.

113. R.E. Banks and E. Tsiliopoulas, *J. Fluorine Chem.*, 1986, 34, 281.

114. S.T. Purrington and W.A. Jones, *J. Org. Chem.*, 1983, 48, 761.

115. S.T. Purrington and W.A.Jones, *J. Fluorine Chem.*, 1984, 26, 43.

116. D.D. DesMarteau, H.N. Huang, S. Singh, S.S. Witz, and S. Zuberi, *J. Am. Chem. Soc.*, 1987, 109, 7194.

117. D.D. DesMarteau, U.S.P. 4,697, 011/1987.

118. W.E. Barnette, *J. Am. Chem. Soc.*, 1984, 106, 452.

119. W.E. Barnette, U.S.P., 4,479, 901/1984.

120. R.E. Banks and A. Khazaei, *J. Fluorine Chem.*, 1990, 46, 297.

121. R.E. Banks, R.A. Du Boisson, and E. Tsiliopoulas, *J. Fluorine Chem.*, 1986, 32, 461.

122. R.E. Banks, R.A. Du Boisson, and E. Tsiliopoulas, *J. Chem. Soc. Perkin 1.*, 1988, 2805.

123. R.E. Banks and I. Shaeif, *J. Fluorine Chem.*, 1988, 41, 297.

124. T. Umemato and G. Tomizaura, *Bull. Chem. Soc. Jpn.*, 1986, 59, 3625.

125. T. Umemato and G. Tomita, *J. Fluorine Chem.*, 1986, 27, 3271.

126. T. Umemato and G. Tomizaura, *J. Fluorine Chem.*, 1987, 28, 2705.

127. T. Umemato, K. Kawada, and G. Tomizaura, *J. Fluorine Chem.*, 1986, 27, 4465.

128. T. Umemato, E.P., 0204, 535/1986.

129. T. Umemato, J.P., 62, 26264/1987.

130. T. Umemato, J.P., 62, 207228/1987.

131. T. Umemato, J.P., 62, 207229/1987.

132. T. Umemato, J.P., 62, 207230/1987.

133. T. Umemato, J.P., 63, 295610/1987.

134. J.L. Weeks, C.L. Chernick and M.S. Matheson, *J. Am. Chem. Soc.*, 1962, 84, 4612.

135. S.M. Williamson, *Inorg. Syn.*, 1968, 11, 147.

136. M.J. Shaw, R. Filler, and H.H. Hayman, *J. Am. Chem. Soc.*, 1970, 92, 6498.

137. M.J. Shaw, R. Filler, and H.H. Hayman, *J. Org. Chem.*, 1971, 36, 2917.

138. M.J. Shaw, J.A. Weil, R. Filler, and H.H. Hayman, *J. Am. Chem. Soc.*, 1970, 92, 5096.

139. S.P. Anand, L.A. Quaterman, H.H. Hayman, K.G. Migliorese, and R. Filler, *J. Org. Chem.*, 1975, 40, 807.

140. M. Zupan and A. Pollak, *J. Org. Chem.*, 1975, 40, 3795.

141. E.D. Bergmann, H. Selig, C.H. Lin, M. Rabinovitz and I. Agrnat, *J. Org. Chem.*, 1975, 40, 3793.

142. S.P. Anand, L.A. Quaterman, H.H. Hayman, K.G. Migliorese, and R. Filler, *J. Org. Chem.*, 1975, 40, 3796.

143. S.P. Anand and R. Filler, *J. Fluorine Chem.*, 1976, 7, 184.

144. M. Zupan and A. Pollak, *J. Fluorine Chem.*, 1976, 7, 443.

145. R. Filler, *Israel J. Chem.*, 1978, 17, 71.

146. B. Sket and M. Zupan, *J. Org. Chem.*, 1978, 43, 835.

147. B. Sket and M. Zupan, *Bull. Chem. Soc. Japn.*, 1981, 54, 279.

148. S. Stavber and M. Zupan, *J. Org. Chem.*, 1981, 46, 300.

149. S. Stavber and M. Zupan, *J. Org. Chem.*, 1983, 48, 222.

150. "*Comprehensive Organometallic Chemistry*" ed. G. Wilkinson, Pergamon Press, Oxford., 1982, vol2, p979.

151. D. Habich and F. Effenberger, *Synthesis*, 1979, 841.

152. P. Bourgeois and R. Calas, *J. Organometallic Chem.*, 1975, 84, 165.

153. H.A. Clark, A.F. Gordon, C.W. Young, and M.J. Hunter, *J. Am. Chem. Soc.*, 1951, 73, 3798.

154. G. Eaborn, "*Organosilicon Compounds*", Butterworths Scientific Publications, London 1960.

155. J.L. Speier, *J. Am. Chem. Soc.*, 1952, 75, 2930.

156. W.A. Sheppard and C.M. Sharts, "*Organic Fluorine Chemistry*", W.A. Benjamin, Inc., New York, 1969, p20.

157. S. Rozen, *Acc. Chem. Res.*,1988, 21, 307

158. L.M. Stock and H.C. Brown, "*Advances in Physical Organic Chemistry*" ed. V. Gold, Academic, New York, 1963, Vol. 1 p35-154.

159. R. Breslow, A. Adams, M. Brandi, T. Guo, and J. Hunger, *J. Heterocyclic Chem.*, 1987, 24, S-43.

160. E. Differding and R.W. Lang, *Tetrahedron Lett.*, 1988, 29, 6087.

161. N.M. Kelly, Ph.D. Thesis, University of Durham, 1978.

162. B. Grievson, Ph.D. Thesis, University of Durham, 1983.

163. S.L. Jones, Ph.D. Thesis, University of Durham, 1987.

164. A.P. Swales, Ph.D. Thesis, University of Durham, 1989.

165. *"Free Radicals"* ed. J.K. Kochi, Wiley Interscience, New York, 1973.

166. I. Fleming, *"Frontier Orbitals and Organic Chemical Reactions"*, Wiley Interscience, London, 1976.

167. J.D. Roberts and M.C. Caserio, *"Basic Principles of Organic Chemistry"*, W.A. Benjamin, Inc., Menlo Park, California, 1977.

168. W.A. Sheppard and C.M. Sharts, *"Organic Fluorine Chemistry"*, W.A. Benjamin, Inc., New York, 1969, P298.

169. M. Hudlicky, *"Chemistry of Organic Fluorine Compounds"*, 2nd Edition, Ellis Horwood, Chichester, 1976, p416.

170. R.L. Mayhew and F. Grosser, *U.S.P.* 3404147/1968, *Chem. Abstr.*, 1969, 70, 19926y.

171. V. Dedek, M. Barta, and J. Fikar, *Czech.P.*, 154 140/1974, *Chem. Abstr.*, 1975, 82, 56874y.

172 L. Bankofer and H. Dickopp, *Chem. Ber.*, 1968, 101, 2585.

173. V. Grakauskas and K. Baum, *J. Org. Chem.*, 1970, 35, 1545.

174. N. Satyamurthy, G.T. Bida, M.E. Phelps, and J.R. Barrio, *J. Org. Chem.*, 1990, 55, 3373.

175. G.M. Trenholme, R.L. Williams, R.E. Desjardine, H. Frisher, P.E. Carson, K.H. Rieckmann, and C.J. Canfield, *Science*, 1975, 190, 792.

176. eg. D.J. Burton and D.M. Wiemers, *J. Am. Chem. Soc.*, 1986, 108, 832.

177. eg. G.A.Boswell, W.C. Ripka, R.M. Schribner, and C.W. Tullock, *Org. React.*, 1974, 21, 1.

178. eg. J.H. Brown, C.W. Suckling, and W.B. Whally, *J. Chem. Soc.*, 1949, 95.

179. T.J. Barton and E. Kline, *J. Organomet. Chem.*, 1972, 42, C21

180. C.G. Krespan, B.C. McKusick, and T.L. Cairns, *J. Am. Chem. Soc.*, 1961, 83, 3428.

181. H.C. Harris, R.J. Harder, and G.N. Sausan, *J. Org. Chem.*, 1960, 25, 633

182. H.C. Brown, H.L. Gewanter, D.H. White, and W.G. Woods, *J. Org. Chem.*, 1960, 25, 634

183. C.K. Krespan, *J. Am. Chem. Soc.*, 1961, 83, 3434

184. C.D. Weis, *J. Org. Chem.*, 1962, 27, 3693

185. H.N.C. Wong, *Synthesis*, 1984, 787

186. A.W. McCulloch and A.G. McInnes, *Can. J. Chem*, 1974, 52, 143

187. I.J. Turchi and M.J.S. Dewer, *Chem. Rev.*, 1975, 75, 389.

188. M.Ya. Korpeiskii and V.L. Florent'ev, *Russ. Chem. Rev.*, 1969, 38, 540.

189. A.L. Henne and W.G. Finnegan, *J. Am. Chem. Soc.*, 1949, 71, 298.

190. W.R. Hasek, W.C. Smith, and V.A. Engel, *J. Am. Chem. Soc.*, 1960, 82, 543.

191. H.N.C. Wong, *Acc. Chem. Res.*, 1989, 22, 145.

192. J.E. McMurry and M.P. Fleming, *J. Org. Chem.*, 1975, 40, 2555.

193. R.D. Chambers and A.J. Palmer, *Tetrahedron*, 1969, 25, 4217

194. S. Matsubara, H. Matsuda, T. Hamatani, and M. Schlosser, *Tetrahedron*, 1988, 44, 2855.

195. W.P. Norris and W.G. Finnegan, *J. Org. Chem.*, 1966, 31, 3293.

196. M. Wilk and A. Hchwab, *Liebigs Ann. Chem.*, 1966, 149, 698.

197. I. Ojima, M. Yatabe, and T. Fuchikomi, *J. Org. Chem.*, 1982, 47, 2051.

198. W. McBee, C.G. Hsu, and O.R. Pierce, *J. Am. Chem. Soc.*, 1955, 77, 915.

199. G.Ya. Kondrateva and K. Chzhi-Khen, *Zh. Obs. Khimi.*, 1962, 32, 2348.

200 R.E. Banks, F. Cuthbertson, and W.K.R. Musgrave, *Anal. Chim. Acta.*, 1955, 13, 442.

201. A.J. Gordon and R.A. Ford, "*The Chemist Companion*", Wiley Interscience, London, 1972.

202. B.F. Karararaev, A.A. Spryskov, and A.G. Zarkhorov *Izv. Vyssh. Ucheb. Zaved. Kim. Kim. Keknol.*, 1970, 13, 995.