Russian Chemical Reviews **68** (8) 653 – 684 (1999) © 1999 Russian Academy of Sciences and Turpion Ltd

UDC 547.241 + 547.539.15

N-Fluoro amines and their analogues as fluorinating reagents in organic synthesis

G G Furin, A A Fainzilberg

Contents

I.	Introduction	653
II.	Fluorination of organic compounds with neutral reagents (R_2NF)	654
III.	Highly efficient fluorinating reagents based on heterocyclic compounds containing a fluorine atom at the charged nitrogen atom	665
IV.	Some examples of fluorination with inorganic tetrafluoroammonium salts	677
V.	On the mechanism of fluorination with *N*-fluoroamines and their analogues	678
VI.	The effect of the solvent in fluorination reactions with *N*-fluoro amines and their analogues. Comparative reactivities of fluorinating reagents containing the N – F bonds	679
VII.	Conclusion	682

Abstract. The data on the synthesis and application in organic synthesis of fluorinating compounds containing N – F bonds are surveyed and systematised. The reagents are classified into two categories, *viz*., neutral (perfluoro-*N*-fluoropiperidine, *N*-fluoro-2-pyridone, *N*-fluorosulfonamides, *N*-fluoro-*N*-alkylamides, *N*-fluorobis(trifluoromethyl)sulfonylamine, *N*-fluorobenzo–1,3,2-dithiazole 1,1,3,3-tetroxide, *N*-fluoro sultams) and ionic reagents (*N*-fluoropyridinium, *N*-fluoroquinuclidinium and 1-alkyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane salts). A comparative analysis of the fluorinating activity of the reagents depending on their structure and the nature of the solvent is carried out taking into account theoretical calculations. The possibility of fluorination of various classes of organic compounds is discussed. The mechanisms of fluorination with N – F compounds are analysed using kinetic data. The advantages and disadvantages of *N*-fluoro amines in comparison with elemental fluorine, xenon difluoride and other fluorinating reagents are considered. The influence of the nature of the solvent on the fluorinating activity of *N*-fluoro amines and their analogues is discussed. The bibliography includes 245 references.

I. Introduction

Over almost a century, fluorination of organic and inorganic substrates with elemental fluorine has been used as the basis for the synthesis of fluorine-containing compounds. Fluorine is known to be a highly potent fluorinating reagent. However, being a strong oxidant, fluorine is aggressive against numerous organic substrates and solvents and thus does not manifest the high selectivity required in fine organic synthesis. Other plausible fluorinating reagents, such as xenon difluoride and perchloryl fluoride ($FClO_3$), have not received wide acceptance in fluoroorganic chemistry, primarily because of their high cost, although their pilot-plant syntheses have already been carried out. For example, the synthesis of $FClO_3$ is being carried out at the Russian Research Centre 'Applied Chemistry'.

The situation in this area has changed radically in the past decade. The ever increasing application of fluorine-containing compounds as biologically active compounds (first of all, of medicinal drugs) has given a strong impetus to the synthesis of a wide range of new electrophilic fluorinating reagents (fluorine 'carriers'), *viz*., the so-called *N*-fluoro reagents and fluoro compounds (*O*-fluoro reagents).

Undoubtedly, *N*-fluoroamines and their analogues belong to the most representative class of fluorine 'carriers' as regards their number, previous experience and application. A chemist engaged in synthesis will always be able to select a reagent complementary to the substrate to be fluorinated in its physical and chemical characteristics.[1 – 6]

N-Fluoro reagents surpass *O*-fluoro and *S*-fluoro reagents in stability, reliability, safety, ecological friendliness and handling convenience.[7 – 16]

In considering the wealth of knowledge concerning the chemistry of *N*-fluoro amines and their analogues, we thought it more reasonable to classify these fluorinating reagents into two groups according to the type of the fluorine – nitrogen bond in their molecule. The first group includes the so-called neutral compounds of the type R_2NF, *i.e*., the reagents in which the fluorine atom is bound to the uncharged nitrogen atom. The second group includes the reagents in which the fluorine atom is bound to the positively charged nitrogen atom.

The most popular neutral compounds are perfluoro-*N*-fluoropiperidine, *N*-fluoro-2-pyridone, *N*-fluoro carboxamides, *N*-fluoro sulfonamides, *N*-fluoro sulfonylamines (including perfluorinated compounds), *N*-fluoro(diphenylsulfonyl)amine, *N*-fluoro alkanesulfonimides, *N*-fluoro benzenesulfonimide and *N*-fluoro sultams. The most popular quaternary compounds include *N*-fluoropyridinium, *N*-fluoroquinuclidinium and 1-alkyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane salts.

Only a few *N*-fluoro-reagents are commercially available. The data on these compounds are summarised in the review by Lal *et al*.[6]

G G Furin Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, prosp. Akad. Lavrent'eva 9, 630090 Novosibirsk, Russian Federation. Fax (7-383) 235 47 47
A A Fainzilberg N D Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, 117913 Moscow, Russian Federation. Fax (7-095) 135 53 28. Tel. (7-095) 135 63 49

Received 25 February 1999
Uspekhi Khimii **68** (8) 725 – 759 (1999); translated by R L Birnova

II. Fluorination of organic compounds with neutral reagents (R_2NF)

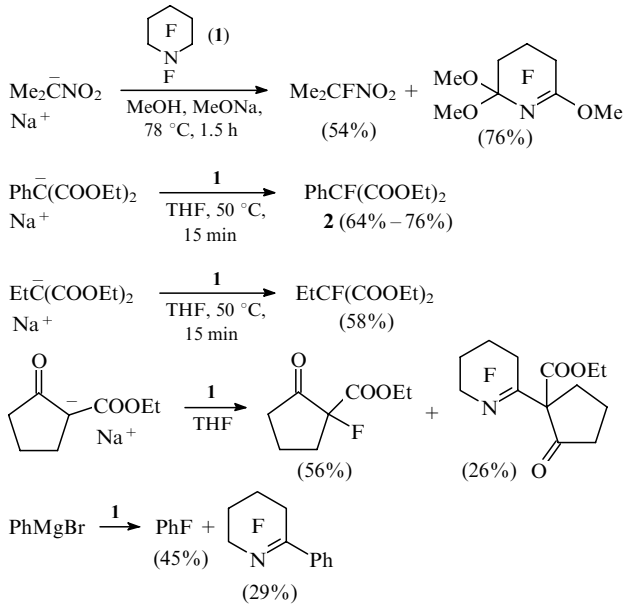
All fluorine 'carriers' of this class are derivatives of secondary amines and their heterocyclic analogues. The methods of their preparation are based on direct substitution of the hydrogen atom in the amino group, most commonly under the action of elemental fluorine. These reactions are carried out at low temperatures under flow-through or static conditions. To avoid destruction, fluorine is diluted with an inert gas (*e.g.*, to 5%–10% concentration at the beginning and to 20%–50% at the end of the reaction). Preparatively, this method is characterised by simplicity; the yields of the target products are close to quantitative, especially when the reaction is performed in the presence of sodium fluoride. Some inorganic materials routinely used for this purpose (*e.g.*, glass, quartz, polymers) are stable under these conditions, which makes it possible to use ordinary chemical equipment in conducting experiments with *N*-fluoro derivatives both in their synthesis and further use as fluorinating reagents.

All *N*-fluoro reagents are oxidants. Attempts have been undertaken [17] to establish a quantitative correlation between their efficiency as oxidants and fluorinating ability, since it is the liberation of fluorine with the cleavage of a relatively weak N–F bond that is the driving force of both oxidation and fluorination. Numerous studies of the fluorination reaction using *N*-fluoro-reagents have led to an idea of 'pseudo-positive' fluorine as an intermediate. Within the framework of this concept, strong electron-accepting substituents in a molecule of the fluorinating reagent will favour fluorination. This is characteristic of all types of reactions involving *N*-fluoro reagents, *e.g.,* substitutive fluorination, reaction with carbanions, addition to the multiple bond, *etc*.

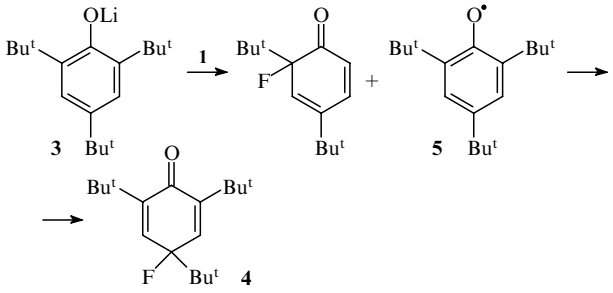
1. The use of perfluoro-*N*-fluoropiperidine

Perfluoro-*N*-fluoropiperidine (**1**) was obtained by electrochemical fluorination of pyridine or 2-fluoropyridine.[18–20] It is a liquid with a boiling point of 49.5 °C. Compound **1** compares favourably with other fluorinating reagents as regards its safety and solubility in organic solvents.

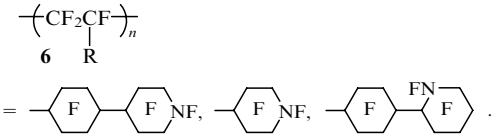
The reagent **1** is effective in fluorination of aryl anions, the Grignard reagents, 2-nitropropane sodium salt, diethyl malonate derivatives, *etc*.[21,22]



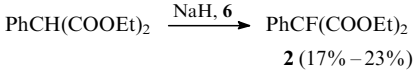
Ph_3PF_2 was obtained in the reaction with triphenylphosphine.[23] Phenols and *N,N*-dialkylanilines are fluorinated with the reagent **1** to give a mixture of *ortho*- and *para*-fluoro derivatives.[24–26] However, lithium 2,4,6-tri(*tert*-butyl)phenoxide (**3**) yields fluorinated dienone **4** under the action of the reagent **1**. It is assumed that this reaction gives rise to the stable phenoxyl radical **5**.[27]



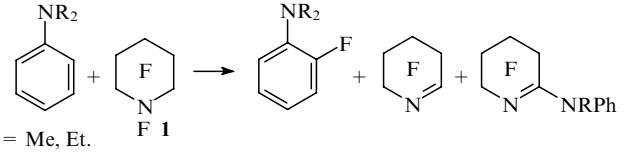
Polyfluorinated polyethylene **6** containing perfluoropiperidine rings with the N–F bond as substituents also possesses the properties of a fluorinating reagent.[27]



Fluorination of sodium diethyl phenylmalonate with the reagent **6** has been described.[27] It should be noted, however, that perfluoropiperidine (**1**) gives compound **2** in 68% yield.[27]



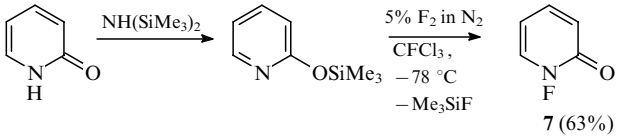
N,N-Dialkylanilines react with the reagent **1** to give fluorinated *N,N*-dialkylanilines.[24] However, perfluorotetrahydropyridine and its derivatives are by-products of this reaction.



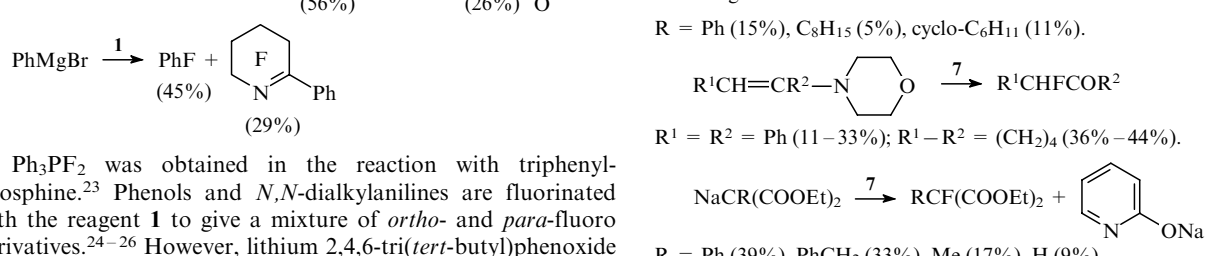
The initial step of this reaction is electron transfer from the dialkylaniline molecule to perfluoropiperidine. This was confirmed by identification of the dimethylaniline radical cation using EPR spectroscopy.[24]

2. The use of *N*-fluoro-2-pyridone

A highly efficient fluorinating reagent, *N*-fluoro-2-pyridone (**7**), was obtained by the reaction of fluorine with 2-trimethylsilyloxypyridine.[28–30]



The reagent **7** fluorodemetallates the Grignard reagents and fluorinates regioselectively sodium salts of diethyl malonate derivatives. It is also used in the synthesis of α-fluoro carbonyl compounds.[28]



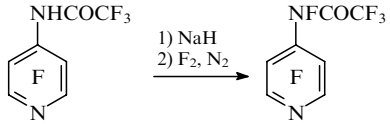
3. The use of *N*-fluoro carboxamides and *N*-fluoro sulfonamides

N-Fluoro carboxamides and *N*-fluoro sulfonamides are obtained by fluorination of the corresponding amides or sulfonamides with elemental fluorine or other fluorinating reagents. Thus fluorination of alkylamides with CF_3OF results in the corresponding *N*-fluoroalkylamides in high yields.[31]

$$R^1CONHR^2 + CF_3OF \longrightarrow R^1CONFR^2 + CF_2{=}O + HF$$

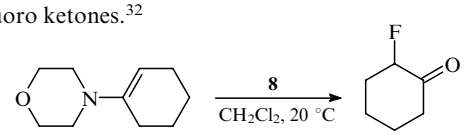
R^1	R^2	Yield (%)
$Me(CH_2)_{16}$	Me	30
Me		60
4-FC_6H_4	Me	13
H	Me	85
H		71

Direct fluorination of sodium *N*-(perfluoro-4-pyridyl)trifluoroacetamide with elemental fluorine was used to obtain the selective fluorinating reagent, *viz*., (*N*-fluoro-*N*-perfluoro-4-pyridyl)trifluoroacetamide (**8**).[32–34]



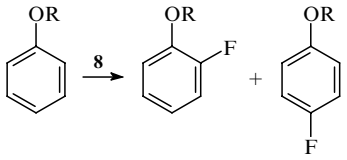
8

The reagent **8** fluorinates diethyl phenylmalonate (NaH, THF, from −10 to 20 °C) to give the fluoro derivative **6** in 66% yield.[32] The reaction with enamines results in the corresponding α-fluoro ketones.[32]



(73%)

The reactions with phenol (MeOH, 20 °C) and anisole (MeCN, 20 °C) yield mixtures of *ortho*- and *para*-isomers (in 1 : 1 and 7 : 3 ratios, respectively).[32]



R = H (91%), Me (81%).

Fluorination of sulfonamides with F_2 in the presence of KF or with a $FClO_3$–NaH mixture gives the corresponding *N*-fluoro derivatives of the type **9** (yield ~ 60%). Fluorination of *O*-acetyl-*N*-tosyl- and -*N*-mesylphenylglycinol gives the corresponding *N*-fluoro derivatives in 52% and 13% yields, respectively.[35,36]

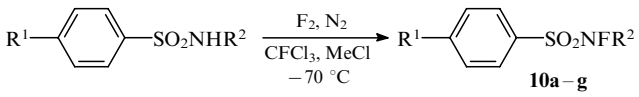
$$R^1R^2R^3CNHSO_2R^4 \longrightarrow R^1R^2R^3CNFSO_2R^4$$

9

R^1	R^2	R^3	R^4
Ph	H	CO_2Et	4-MeC_6H_4, Me, F_3C
Me	Bn	CO_2Et	4-MeC_6H_4
Ph	H	CH_2OAc	4-MeC_6H_4
Pr^i	H	CO_2Et	4-MeC_6H_4, Me, F_3C
Ph	H	Me	4-MeC_6H_4, Me, F_3C

Compounds **9** possess fluorinating ability and can be used for the synthesis of α-fluorocarbonyl derivatives from enolates (Table 1).[35,36]

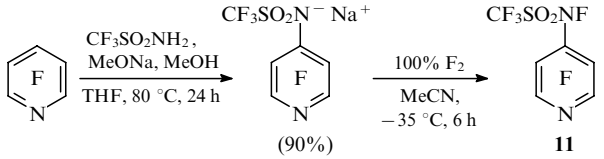
Normally, fluorination of *N*-alkyl(aryl)sulfonamides is performed in a $CFCl_3$–$CHCl_3$ mixture (1 : 1) using 1%–5% F_2 in N_2, MeOF or CF_3OF as fluorinating reagents. *N*-Fluoro sulfonamides **10a**–**g** were synthesised in this way.[37–47]



10a–**g**

Compound **10**	R^1	R^2	Yield (%)	Ref.
a	Me	Bu^t	14	37
b	Me	Me	59	37
c	Me	Bu^tCH_2	57	37
d	Me		47	37
e	Me		71	37
f	Me		11	37
g	H	Bu^t	–	47

Sulfonamide derivatives are preferably fluorinated as the corresponding salts.[48–50] Thus the fluorination of sodium perfluoro-*N*-(4-pyridyl)methanesulfonamide with elemental fluorine results in perfluoro-*N*-fluoro-*N*-(4-pyridyl)methanesulfonamide (**11**) in 89% yield.[49]

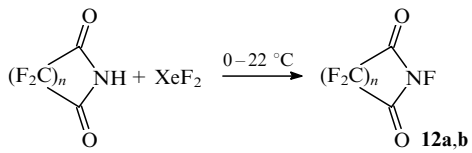


(90%) **11**

N-Perfluoroquinolyl-, -isoquinolyl and -naphthylsulfonamides were also introduced into the reaction.[49]

It is noteworthy that *N*-*tert*-butyl-*N*-fluoro-*p*-toluenesulfonamide **10a** can be obtained in 69% yield by fluorination of sodium *N*-*tert*-butyl-*p*-toluenesulfonamide with cesium fluoroxysulfate in MeCN at 0–5 °C.[51]

Perfluorosuccinimide and -glutarimide react with xenon difluoride to give the corresponding *N*-fluoro imides **12a**,**b** in good yields.[52,53] The fluorination is performed at 0–20 °C in the absence of the solvent or at 0 °C in dichlorodifluoromethane for 24 h. These compounds represent easily distillable liquids, which are stable upon 24-h storage in quartz glassware under nitrogen. The fluorination of sodium phthalimide with cesium fluoroxysulfate in acetonitrile gives *N*-fluorophthalimide in 48% yield.[45]

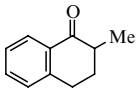
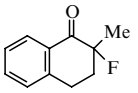
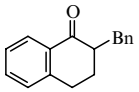
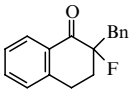
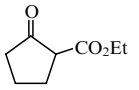
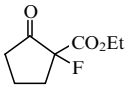
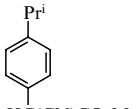
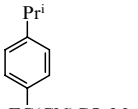


12a,**b**

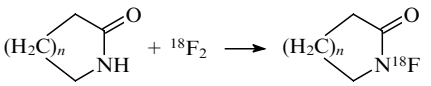
n = 2 (**a**, 55%–65%), 3 (**b**, 50%–60%).

Satyamurthy *et al*.[54] used the reaction of solutions of lactams with 100% fluorine for the synthesis of *N*-fluoro lactams **13** labelled with ^{18}F. However, the yields of *N*-fluoro lactams **13a**–**c** are rather low. Higher yields could be obtained by fluorination of solutions of lactams in Freon with fluorine diluted with neon.[53]

Table 1. Fluorination of organic compounds with *N*-fluorosulfonamides in THF.[35, 36]

Substrate	Fluorinating reagent **9**				Reaction conditions		Reaction product	Yield (%)	Enantiomeric excess (%)
	R^1	R^2	R^3	R^4	base	T/°C			
	Ph	H	Me	4-MeC_6H_4	LDA [a]	−40 to −20		10	40
	Ph	H	Me	4-MeC_6H_4	KHMDS [b]	−40 – 0		46	46
	Ph	H	Me	Me	LDA	−40 – 0		11	20
	Ph	H	Me	4-MeC_6H_4	LDA	−4 to −20		3	46
	Ph	H	Me	Me	LDA	−40 – 0		4	6
	Ph	H	Me	4-MeC_6H_4	NaH	0 – 20		20	14
	Ph	H	Me	Me	NaH	0		6	30
$PhCOCH(Me)CO_2Et$	Ph	H	Me	4-MeC_6H_4	NaH	0	$PhCOCF(Me)CO_2Et$	21	18
	Ph	H	Me	Me	NaH	0	$PhCOCF(Me)CO_2Et$	21	6
	Pr^i	H	CO_2Et	Me	NaH	20		6	6

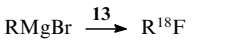
[a] LDA is lithium diisopropylamide; [b] Potassium bis(trimethylsilylamide).



13a – e

Compound **13**	*n*	Yield (%)	Radiochemical yield (%)
a	1	76	41
b	2	61	33
c	3	79	42
d	4	71	48
e	5	33	19

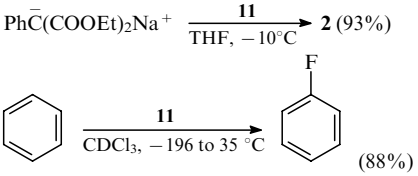
N-Fluorolactams **13** can be used for the synthesis of fluoro derivatives labelled with ^{18}F. They react with the Grignard reagents, however, the yields of the reaction products are low.[54]

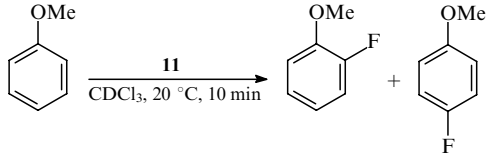


Reagent	**13a**	**13b**	**13c**	**13c**	**13c**	**13c**	**13d**
R	Ph	Ph	Ph	4-MeC_6H_4	1-naphthyl	cyclo-C_6H_{11}	Ph
Yield (%)	1 – 2	8	20	30	51	19	19

Controlled fluorination of aromatic compounds and derivatives of malonic acid with *N*-fluoro lactams of the type **13** and with *N*-fluoro sulfonamides **10** and **11** can be used for the synthesis of aromatic fluoro derivatives and fluorinated malonates.

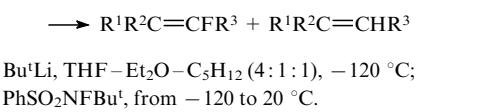
Thus sulfonamide **11** fluorinates sodium diethyl phenylmalonate, benzene and anisole (a mixture of *ortho*- and *para*-fluoroanisoles is formed in 3 : 1 ratio and in 98% yield).[49] *N*-Fluorobenzenesulfonamide reacts with anisole (4 h, 150 °C) to yield a mixture of 57% 2-fluoroanisole and 37% 4-fluoroanisole.[53, 54]





The data on fluorination of several compounds with substituted *N*-fluorotoluenesulfonamides **10a, c, d** are presented in Table 2.[37]

The halogen atoms in alkenyl iodides can be selectively substituted by the fluorine using *N*-fluorobenzenesulfonamide, *via* intermediate lithium derivatives. The yields of the resulting fluorides are rather high, although in some cases alkenes are formed in large amounts. The results of fluorination of alkenyl iodides are presented in Table 3.[47]



(*a*) Bu^tLi, THF – Et_2O – C_5H_{12} (4 : 1 : 1), −120 °C;
(*b*) $PhSO_2NFBu^t$, from −120 to 20 °C.

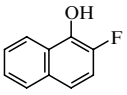
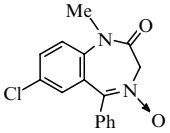
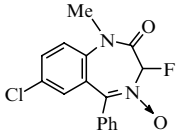
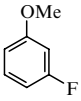
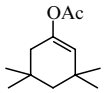
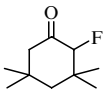
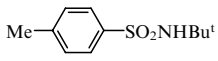
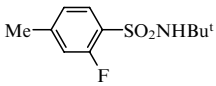
4. Fluorinating reagents based on *N*-fluoro sulfonylamines

N-Fluoro imides have found much wider application in organic synthesis than *N*-fluoro amides. The methods for preparing *N*-fluorobis[alkyl(aryl)sulfonyl]amines are based on direct fluorination of the corresponding bisalkyl(aryl)sulfonylamines (1% – 3% F_2 in Ar or XeF_2). Fluorinated products are obtained in up to 70% yields.[55]

N-Fluorodisulfonylamines of the type $CF_3SO_2NFSO_2R$ (R is perfluoroalkyl, cycloalkyl, aralkyl or aryl) are obtained by fluorination of the corresponding imides with elemental fluorine at −20 °C.[56 – 64] Thus treatment of $(CF_3SO_2)_2NH$ with F_2 at 22 °C gives *N*-fluorobis(trifluoromethylsulfonyl)amine (**14a**) in 95% yield. *N*-Fluorodisulfonylamines **14b – e** and imides **15** were synthesised in a similar way.[59]

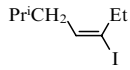
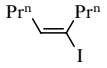
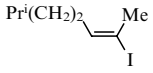
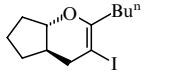
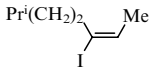
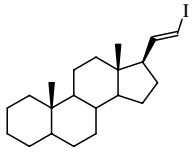
The fluorination is performed with elemental fluorine diluted with nitrogen in solvents ($CHCl_3$, $CFCl_3$, HF, fluorohydrocarbons, MeCN) at 80 – 135 °C in the presence of NaF or CaF_2.

Table 2. Fluorination of organic compounds with *N*-fluorosulfonamides **10**.[37]

Substrate	Base	Reagent	Solvent	T /°C	Reaction product	Yield (%)
$PhCH(COOEt)_2$	NaH	A	THF	20	$PhCF(COOEt)_2$	81
$MeCH(COOEt)_2$	NaH	A	PhMe, THF	20	$MeCF(COOEt)_2$	53
PhMgCl		B	Et_2O	20	PhF	50
Me_2CHNO_2	$Bu^n_4N^+OH^-$	B	PhMe, PhH	−20	Me_2CFNO_2	83–87
	KH	B	THF	20		60
	KH	B	PhMe, THF	−50		52
$PhCOCH_2CHMe_2$	KH	C	Et_2O	20	$PhCOCHFCHMe_2$	81
$Me(CH_2)_{13}MgBr$		C	PhMe, Et_2O	−78	$Me(CH_2)_{13}F$	15
$Ph_2CHCOOH$	Bu^nLi	C	PhMe, THF	−50	$Ph_2CFCOOH$	69
	Bu^nLi	C	PhMe, THF	20		24
	KH	C	PhMe, THF	−50		81
	KH	C	PhMe, THF	−50		31
	MeLi	C	PhMe, THF	−20		35
	Bu^nLi	C	PhMe, THF	20		55

Note. A, *N*-fluoro-*N*-neopentyl-*p*-toluenesulfonamide (**10c**); B, *N*-*tert*-butyl-*N*-fluoro-*p*-toluenesulfonamide (**10a**); C, *exo*-*N*-fluoro-2-norbornyl-*p*-toluenesulfonamide (**10d**).

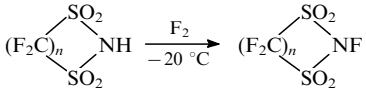
Table 3. Fluorination of alkenyl iodides with *N*-*tert*-butyl-*N*-fluorobenzenesulfonamide.[47]

Alkenyl iodide	Yield (%)		Alkenyl iodide	Yield (%)	
	fluoride	alkene		fluoride	alkene
$n\text{-}C_6H_{13}CH{=}CHI$	71	15		88	7
$PhCH{=}CHI$	76	10			
	85	3		83	7
	75	12		74	8
	75	12		80	13

Syvret *et al*. have proposed to use lithium derivatives instead of free imides.[62]

$$R^1SO_2NHR^2 \xrightarrow[-20\ ^\circ C]{F_2} R^1SO_2NFR^2$$
14a–e

$R^1 = CF_3$: $R^2 = SO_2CF_3$ (**a**, 95%), $SO_2C_4F_9$ (**b**, 96%), $SO_2C_6F_{13}$ (**c**, 93%), Me (**d**, 11%); $R^1 = C_4F_9$, $R^2 = SO_2C_6F_{13}$ (**e**, 88%).


15

n = 2 (77%), 3 (61%), 4 (86%).

N-Fluorobis(methylsulfonyl)amine (**16**) was obtained in 90% yield by fluorination of bis(methylsulfonyl)amine with elemental fluorine ($F_2 : N_2 = 1 : 9$) in acetonitrile in the presence of NaF (−40 °C).[34]

$$(MeSO_2)_2NH \xrightarrow{F_2 \text{ in } N_2} (MeSO_2)_2NF$$
16

Other *N*-fluorobis[alkane(arene)sulfone]amides[33,64,65] and *N*-fluorobenzo-1,3,2-dithiazine 1,1,3,3-tetroxide [commonly referred to as *N*-fluoro-*o*-benzodisulfonimide (NFOBS)][66,67] have been synthesised in a similar way. Water or water–organic solvent mixtures can be used as a reaction medium.[64] The best results are attained through the use of sodium salts of the corresponding sulfonimides.[34,65,67]

The reagent **14a** obtained by the scheme given below (total yield 76% with respect to trifluoromethanesulfonyl fluoride) is the most reactive among other *N*-fluorodisulfonylamines.[59] This compound has a boiling point at 90–91 °C, is thermally stable, can be stored in glassware and is a highly efficient fluorinating agent which has many applications. The same scheme was used to obtain the reagent **14a** labelled with ^{18}F (45% radiochemical yield).[68]

$$F_3CSO_2F \xrightarrow{a,\,b} F_3CSO_2NHNa \xrightarrow{c} F_3CSO_2NNaSiMe_3 \xrightarrow{d} (F_3CSO_2)_2NNa \xrightarrow{e} (F_3CSO_2)_2NH \xrightarrow{f} (F_3CSO_2)_2NF$$

14a

(*a*) NH_3 (liquid), −78 °C; (*b*) NaOMe, MeOH (95%); (*c*) $(Me_3Si)_2NH$, Δ (92%); (*d*) F_3CSO_2F, THF, 100 °C, autoclave (98%); (*e*) H_2SO_4, sublimation *in vacuo* (93%); (*f*) 100% F_2, metal tube, from −196 to 22 °C (95%).

N-Fluorobis(phenylsulfonyl)amine (**17**) often referred to as *N*-fluorobenzenesulfonimide was obtained in 70% yield by fluorination of bis(phenylsulfonyl)amine with fluorine diluted with nitrogen, in acetonitrile or in a $CHCl_3-CFCl_3$ mixture in the presence of sodium fluoride at −40 °C.[69–71] The structure of compound **17** was confirmed by X-ray diffraction analysis.[71]

$$(PhSO_2)_2NH \xrightarrow{a \text{ or } b} (PhSO_2)_2NF$$

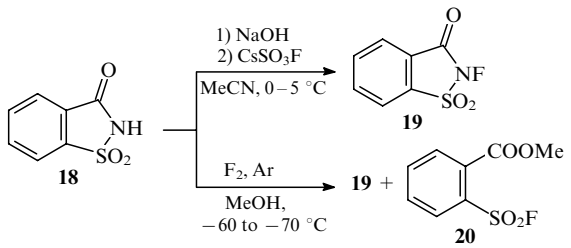
17

(*a*) 10% F_2 in N_2, NaF, MeCN, −40 °C; (*b*) 10% F_2 in N_2, NaF, $CHCl_3-CFCl_3$ (1 : 1), −40 °C.

N-Fluorobis(phenylsulfonyl)amine (**17**) is a white crystalline powder, which is soluble in the majority of organic solvents (ether, THF, CH_2Cl_2, MeCN, PhMe). It is convenient in handling, non-hygroscopic and storage-stable. This reagent can be used for fluorination of carbanions, enolates and enol esters as well as for the preparation of fluorinated intermediates used in the production of medicinal drugs.

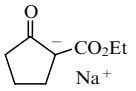
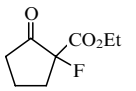
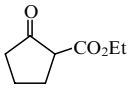
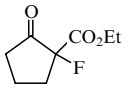
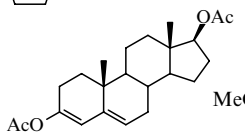
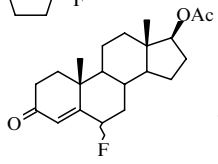
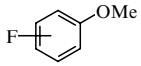
Fluorination of the sodium salt of saccharin **18** with cesium fluoroxysulfate in acetonitrile at 0–5 °C gives the *N*-fluoro derivative **19** in 69% yield. Treatment of compound **18** with fluorine in methanol at −60 °C (−70 °C) gives methyl *o*-fluorosulfonylbenzoate **20** formed by the opening of the heterocycle and the fluoro derivative **19**.[40]

An analogue of compound **19**, 3-fluorobenzo-1,2,3-oxathiazin-4-one 2,2-dioxide (**21**), is prepared by treatment of sodium salt

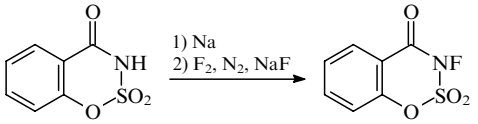


of benzo-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide in acetonitrile with dilute fluorine in the presence of sodium fluoride (−40 °C).[33,34,63] The reagent **21** is a rather stable crystalline compound, which manifests high fluorinating ability and is used for fluorination of various compounds including carbanions, steroids and aromatic compounds.[34,63] Examples of these reactions are given in Table 4.

Table 4. Fluorination of organic compounds with 3-fluorobenzo-1,2,3-oxathiazin-4-one 2,2-dioxide (**21**).[34]

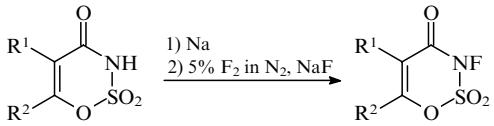
Starting compound	Reaction conditions[a]			Reaction product	Yield (%)
	solvent	*T* /°C	*t* /h		
PhMgBr	THF	20	4	PhF	5
$PhC^-(CO_2Et)_2Na^+$	THF	20	4	$PhCF(CO_2Et)_2$ (**2**)	52
	THF	20	0.5		77
	n-C_6H_{14}	65	8		66
	MeCN	20	4		59
PhOMe	MeCN	150	5		77[b]

[a] Sodium bis(trimethylsilyl)amide (NaHMDS) was used to generate the enolates and salts. [b] The *ortho* : *para* ratio is 56 : 44.



21 (88%)

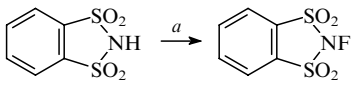
Substituted *N*-fluoro-1,2,3-oxathiazin-4-one 2,2-dioxides **22a**,**b** are prepared in a similar way.[65]



22a,**b**

R^1 = H, R^2 = Me (**a**); R^1 = Me, R^2 = Me (**b**).

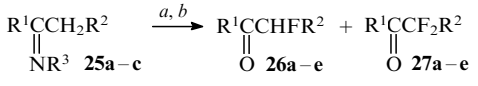
Treatment of benzo-1,3,2-dithiazole 1,1,3,3-tetroxide (**23**) with nitrogen-diluted fluorine at −40 °C gives *N*-fluorobenzo-1,3,2-dithiazole 1,1,3,3-tetroxide (**24**)[66,67,72] as a white crystalline powder. Its structure was confirmed by X-ray diffraction analysis.[71]



23 **24** (90%)

(*a*) 10% F_2 in N_2, NaF, $CFCl_3-CHCl_3$, −40 °C.

Electrophilic fluorination of imines **25a**–**c** with *N*-fluorobis(trifluoromethylsulfonyl)amine (**14a**) yields mono- (**26a**–**e**) and difluoroketones (**27a**–**e**); the imine anions were generated by treatment with bases.[73]



25a–**c** **26a**–**e** **27a**–**e**

(*a*) **14a**, CH_2Cl_2, Na_2CO_3, 22 °C; (*b*) H_3O^+.

Direct fluorination of imines with $(CF_3SO_2)_2NF$ (**14a**) gives α-monofluoro and α,α-difluoro ketones without preliminary generation of anions.[74–76] The results of fluorination are listed in Table 5.[73] Enamines react in a similar way. Thus 1-morpholino-1-

Table 5. Synthesis of fluoro ketones by fluorination of imines **25** with the reagent **14a**.[73]

Compounds **25**–**27**	R^1	R^2	R^3	**14a** : **25** Ratio	Yield of **26** (%)	Yield of **27** (%)
a	Ph	H	Pr^n	2.4 : 1	0	82
				1 : 3	33	15
b	4-MeC_6H_4	H	Pr^n	2.4 : 1	0	83
				1 : 3	36	16
c	Ph	Me	Pr^n	2.4 : 1	0	58
				1 : 3	38	17
d	4-$MeOC_6H_4$	H	Bu^n	2.4 : 1	0	70
				1 : 3	26	17
e	4-BrC_6H_4	H	Bu^n	2.4 : 1	0	78
				1 : 3	30	16

phenylpropene reacts with compound **14a** to give α-fluoropropiophenone after hydrolysis. Fluorination of imines and enamines with the reagent **14a** can be regarded as an alternative route to α-fluoro ketones, which are usually synthesised from the corresponding enolates. Mild reaction conditions and high yields of the final products make this procedure very promising.

The reagent **14a** proved to be efficient in fluorination of lithium enolates of esters, amides, ketones, β-diketones and β-oxo esters (enolates are prepared by treatment with lithium diisopropylamide in THF). The fluorination is fairly selective at 22 °C and results in monofluoro derivatives.[75]

$$R^1R^2CHCOX \xrightarrow[2)\ \mathbf{14a},\ THF,\ 22\ ^\circ C]{1)\ LDA} R^1R^2CFCOX$$

X	R^1	R^2	Yield (%)
OCH_2Ph	H	H	76
OEt	H	OEt	63
OEt	H	Ph	71
OEt	Me	Ph	83
OEt	Et	Ph	70
NPr^i_2	H	Ph	87
NPr^i_2	Me	Ph	85
NPr^i_2	Et	Ph	70
Ph	H	H	86
Me	Ph	Ph	81

The synthesis of α,α-difluoro derivatives requires 2 equiv. of the reagent **14a** and more drastic conditions.[60, 66, 75–77]

The nature of substituents at the carbonyl group of ketones has no appreciable influence on the yields of the monofluorinated derivatives, which are normally high. Esters are also smoothly fluorinated with this reagent (Table 6).[76]

$$R^1COCH(R^3)COR^2 \xrightarrow[CH_2Cl_2,\ 22\ ^\circ C]{\mathbf{14a}} \begin{cases} \xrightarrow{R^3 = H} R^1COCF_2COR^2\ \mathbf{29} \\ R^1COCF(R^3)COR^2\ \mathbf{28} \end{cases}$$

Lithium diethyl 2-nitromalonate is fluorinated with high yield in the treatment with $(CF_3SO_2)_2NF$ (**14a**) in THF.[60, 76]

The fluorination of β-diketones, β-oxo esters and β-oxoamides with the reagent **14a** in non-polar solvents results in the formation of α-monofluoro or α,α-difluoro derivatives. Thus ethyl 2-chloroacetoacetate,[74] ethyl 2-acetoxyacetoacetate[78] and 3-chloro-2,4-pentanedione[79] are fluorinated with the reagent **14a** in chloroform in quantitative yields. Fluorination of benzoylacetone in CH_2Cl_2 gives 90% of 1-benzoyl-1,1-difluoroacetone, whereas in a CH_2Cl_2–H_2O system the monofluoro derivative is obtained in 93% yield (see Table 6).[76]

Fluorination of α-oxo esters can also occur in the absence of bases. These compounds generate fluoro derivatives with practically quantitative yields upon treatment with equimolar amounts of the reagent **14a**.[74]

Table 6. Fluorination of 1,3-dicarbonyl compounds $[R^1COCH(R^3)COR^2]$ with the reagent **14a**.[76]

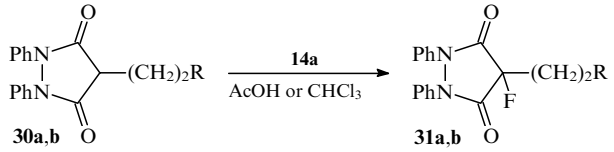
R^1	R^2	R^3	Reagent : substrate ratio	Solvent	*t* /h	Yield (%)[a] **28**	Yield (%)[a] **29**
Me	Me	Me	1 : 1	CH_2Cl_2	7	91	
Me	Me	OEt	1 : 1	CH_2Cl_2	7	83	
Me	Me	H	2 : 1	CH_2Cl_2	3		54
Me	OEt	H	2 : 1	CH_2Cl_2	20		80
Ph	Me	H	2 : 1	CH_2Cl_2	24		90
Ph	Me	H	2 : 1	CH_2Cl_2–H_2O	11	93	
Ph	OEt	H	2 : 1	CH_2Cl_2	24		96
Me	OEt	H	1.5 : 1	CH_2Cl_2–H_2O	8	86	
p-$NO_2C_6H_4$	OEt	H	1.5 : 1	CH_2Cl_2–H_2O	11	94	
Pr^i	OEt	H	1.3 : 1	CH_2Cl_2–H_2O	14	91	
OMe	OMe	H[b]	1 : 1	THF	5	78	
OEt	OEt	Ph[b]	1 : 1	THF	3	92	

[a] After separation by chromatography on SiO_2. [b] Sodium enolate was used.

$$R^1R^2CHCOCOOR^3 \xrightarrow{\mathbf{14a}} R^1R^2CFCOCOOR^3$$

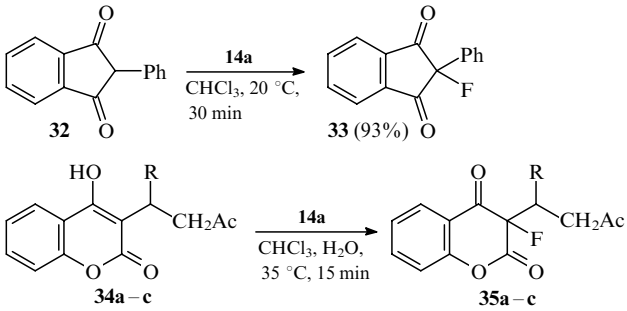
R^1	R^2	R^3	Yield (%)
Me	Me	Et	95
Me	Et	H	95
H	Me	H	95

4-Substituted *N,N*-diphenylpyrazolidine-3,5-diones **30a**,**b** are fluorinated with 1 equiv. of the reagent **14a** in acetic acid or in $CHCl_3$ to give 4-n-butyl-4-fluoro-1,2-diphenylpyrazolidine-3,5-dione (**31a**) and 4-fluoro-1,2-diphenyl-4-[(2-phenylsulfinyl)ethyl]pyrazolidine-3,5-dione (**31b**).[77]



R = Et (**a**, 95%), SOPh (**b**, 90%).

The fluorination of 2-phenylindane-1,3-dione (**32**) with the reagent **14a** in acetic acid at 20 °C gives 2-fluoro-2-phenylindane-1,3-dione (**33**).[42] In fluorination of substituted 4-hydroxycoumarins **34a**–**c** with the reagent **14a**, the fluorine atom also occupies the α-position relative to the carbonyl group to give compounds **35a**–**c** in high yields.[42]



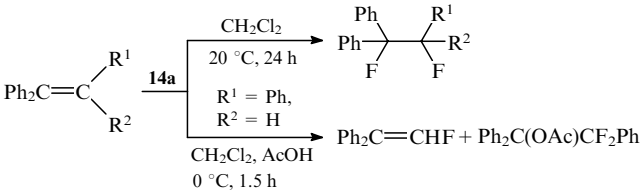
R = H (**a**, 91%), Ph (**b**, 92%), 4-ClC_6H_4 (**c**, 90%).

The fluorination of 4-hydroxy-3-(3-oxobutyl)coumarin **34a** in a chloroform–water mixture (5 min, 35 °C) gives the corresponding fluoro derivative **35a** (which represents a mixture of diastereomers) in a quantitative yield.[58] 3-Fluoro-3-(1-phenyl-3-oxobutyl)-

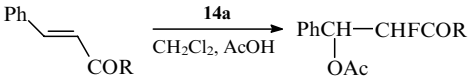
2*H*-benzopyran-2,4-dione and 3-fluoro-3-[1-(4-chlorophenyl)-3-oxobutyl]-2*H*-benzopyran-2,4-dione are prepared in a similar way. The highly selective fluorination of heterocyclic compounds with the reagent **14a** is better carried out in polar solvents, *e.g.,* 2,2,2-trifluoroethanol or nitromethane.[73]

N-Fluorobis(trifluoromethylsulfonyl)amine (**14a**) reacts with some activated aromatic compounds such as toluene, anisole and acetanilide, resulting in the *ortho*- and *para*-substituted products.[65] Monofluoro derivatives are predominantly formed at the ArH : **14a** ratio of 2 : 1. As for nitrobenzene, chlorobenzene or acetophenone, they cannot be introduced into this reaction.[59, 65, 69, 70]

The reagent **14a** is effective in reactions with alkenes to give addition products of fluorine at the multiple bond. If a CH_2Cl_2 – acetic acid mixture is used, the latter enters into the reaction to give acetoxy and hydroxyfluoro derivatives (these reactions were described, *e.g.,* with styrene and *trans*-β-methylstyrene).[80]



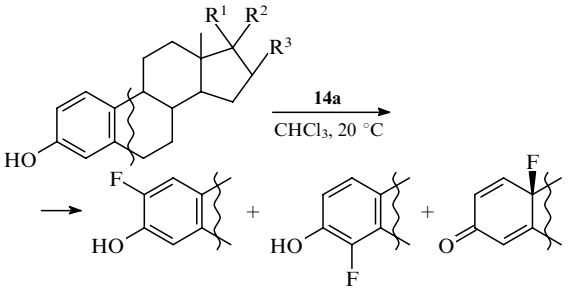
The reagent **14a** reacts with α,β-unsaturated carbonyl compounds in AcOH to give β-acetoxy α-fluoro ketones.[80]



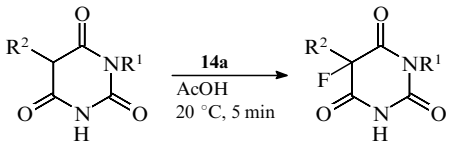
R	Me	Ph	OMe
Yield (%)	71	58	69
erythro : *threo* Ratio	4 : 6	4 : 6	1 : 1

Uracil does not react with $(CF_3SO_2)_2NF$ (**14a**) at 22 °C in AcOH, presumably due to its poor solubility, whereas at 45 °C this reaction is completed in 12 h to give a difluoro derivative.[80] 1,3-Dimethyluracil is much more reactive and gives a difluoro derivative in the reaction with 2 equiv. of $(CF_3SO_2)_2NF$ (**14a**) at 22 °C (yield 85%); 1 equiv. of the reagent **14a** gives 1,3-dimethyl-5-fluorouracil.[80]

N-Fluorodisulfonylamine (**14a**) is effective in fluorination of various steroids. Thus fluorination of estra-1,3,5-trien-3-ols in $CHCl_3$ gives *ortho*- and *para*-fluorinated products. If acetic acid is used as a solvent, fluorine selectively occupies the *para*-position to give 10β-fluoro-1,4-estradien-3-one derivatives in high yields.[61]



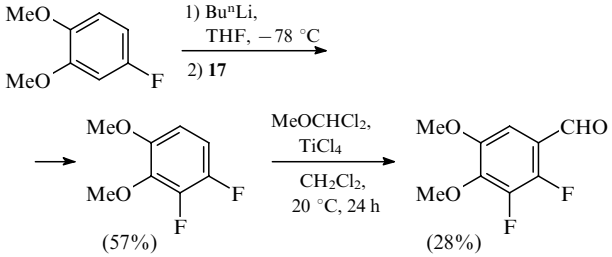
The fluorination of a suspension of 2,4,6-trihydroxypyrimidine in acetic acid with 1 equiv. of $(CF_3SO_2)_2NF$ (**14a**) at room temperature results in a monofluoro derivative, whereas a 5,5-difluoro derivative is obtained in high yield with 2 equiv. of the reagent.[77] This method was used for the synthesis of a wide range of fluorinated pyrimidinetriones.[77]



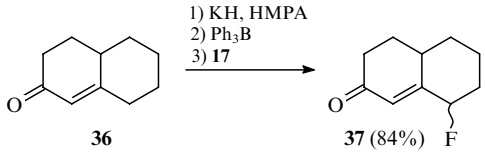
R^1	H	Me	Et	Bu^n	Ph	OMe	Me	Et	Ph
R^2	H	H	H	H	H	H	Me	Me	Me
Yield (%)	88	92	89	90	91	90	92	83	91

Along with reagent **14a**, other *N*-fluoro imides, *e.g., N*-fluorobis(phenylsulfonyl)amine (**17**) or *N*-fluorobenzo-1,3,2-dithiazole 1,1,3,3-tetroxide (**24**) are used for fluorination of various classes of organic compounds. Some examples are given in Table 7.

The reagent **17** is more efficient than the reagent **24** in fluorination of organometallic compounds and highly stabilised anions (see Table 7). Under the action of the reagent **17** (100 °C, 18 h), acetanilide gives a mixture of isomeric fluoroacetanilides, the yields of the *ortho*- and *para*-isomers being 25% and 15%, respectively.[65] Fluorination of metallated aromatic and heteroaromatic compounds with the reagent **17**, which is accompanied by the formation of *ortho*-fluoro derivatives, is used in the synthesis of valuable biologically active compounds, *e.g.,* fluoro- and difluoroveratric aldehydes.[74, 81, 82]



Base-catalysed formation of enolates, subsequent complexation with boron compounds and fluorination of the latter with the reagent **17** is a novel method for the synthesis of γ-fluorinated α,β-unsaturated ketones.[83–85] Thus the reaction of the reagent **17** with a carbanion generated from 4,4*a*,5,6,7,8-hexahydronaphthalen-2(*3H*)-one (**36**) in the presence of triphenylborane gave the fluoro derivative **37**.[84]



The enolate prepared from 10-methyl-1(9)-octal-2-one upon treatment with KH in a HMPA – THF mixture in the presence of triphenylborane gives a fluoro derivative with the reagent **17** in the α : β ratio of 1 : 8.6 (yield 84%).[85]

Yet another example of efficient fluorination with this reagent in the presence of 2-phenylbenzo[1.3.2]dioxaborol is the synthesis of γ-fluorinated steroid enones. Thus the fluoro derivative **39** was prepared from compound **38**.[84]

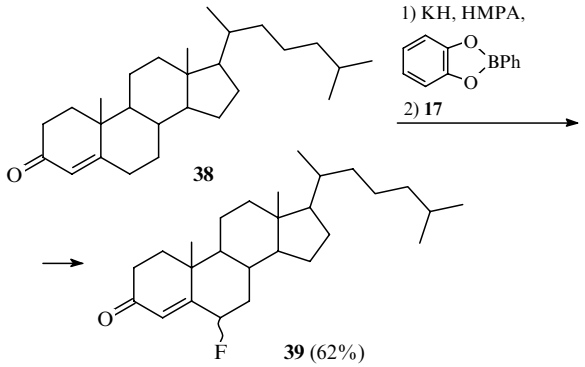
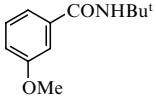
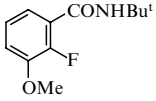
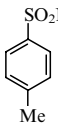
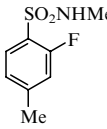
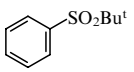
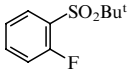
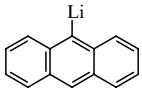
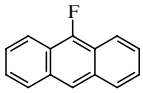
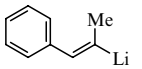
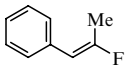
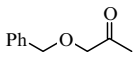
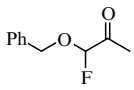
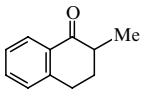
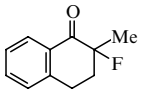
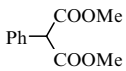
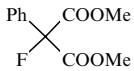
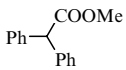
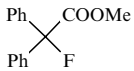
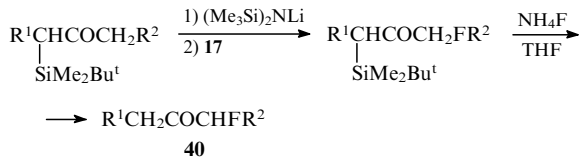


Table 7. Fluorination with the reagents **17** and **24**.

Substrate	Reagent	Reagent : substrate ratio	Temperature /°C	Time /h	Reaction product	Yield (%)	Ref.
	**17**	22 : 1	150	5		100 [a]	65
	17	1 : 1	100	24		33 [a]	65
	**17**	2 : 1	100	18		40 [b]	65
	**17**	50 : 1	100	216		19 [c]	65
	**17**	2 : 1	−78 [d]	6–7		56	74
	**17**	2 : 1	−78 [d]	6–7		62	74
	24	2 : 1	−78 [d]	6–7		0	74
	**17**	2 : 1	−40 [d]	6–7		74	74
	24	2 : 1	−40 [d]	6–7		70	74
	**24**	2 : 1	−40 [d]	6–7		71	74
	**17**	2 : 1	−78 [d]	6–7		74	74
	24	2 : 1	−78 [d]	6–7		30	74
	**17**	1 : 1	20	24		46	65
	**17**	1 : 1.2	−78	20		76	65
	**17**	1 : 3	105	20		40	65
	**17**	1 : 1.2	−78 [e]	20		47	65
EtCOPh	**17**	1 : 1.2	−78 [e]	20	MeCHFCOPh	85	65
	**17**	1 : 1.15	−95 [e]	20		50	65
	**17**	1 : 1.2	0 [f]	20		47	65
	**17**	1 : 1.3	−78 [g]	20		82	65

[a] The *ortho* : *meta* : *para* ratio is 58 : 5 : 37. [b] The *ortho* : *para* ratio is 62 : 38. [c] The *ortho* : *meta* : *para* ratio is 65 : 7 : 28. [d] The organolithium derivative was generated previously by treatment with Bu^nLi in THF. [e] The lithium derivative was generated previously by treatment with LDA in THF. [f] The potassium derivative was generated previously by treatment with KH in Et_2O. [g] The potassium derivative was generated previously by treatment with KHMDS in THF.

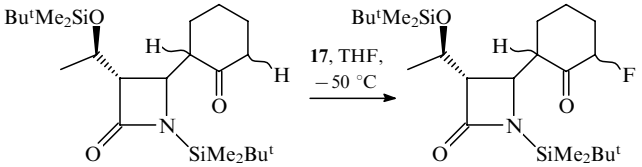
The fluorination of lithium enolates of silylated ketones with the reagent **17** gives α-fluoro ketones **40** in high yields. The silyl group is eliminated by treatment with ammonium fluoride.[86]



R^1	R^2	Yield (%)	Configuration of **40**
Et	Et	97	*S*
Pr	Pr	97	*S*
Et	$PhCH_2$	95	*R*
	$(CH_2)_3$	99	*R*
	$(CH_2)_4$	99	*R*

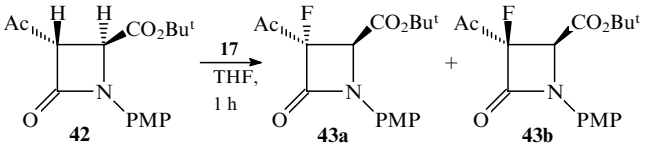
Synthesis of α-fluoro ketones with the reagent **17** has also been described by Padova *et al.*[87]

The fluorinating reagent **17** was used for introducing fluorine into a molecule containing an azetidinone fragment.[88] Compound **41** is an intermediate in the synthesis of new antibiotics.



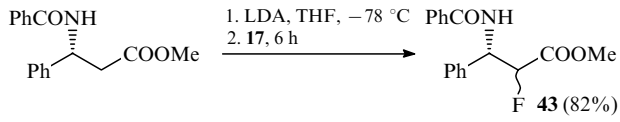
41 (95%)

The fluorination of the azetidinone derivative **42** with the reagent **17** results in a mixture of stereoisomeric 3-fluoroazetidinones **43a**,**b** (yield 70%). The isomer ratio depends on temperature, *e.g.*, at 20 °C the **43a** : **43b** ratio is 85 : 15, whereas at −15 °C it is 95 : 5.[88]



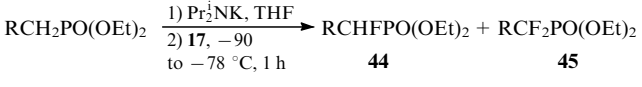
PMP is polymethylenepyridine.

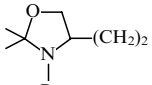
Compound **17** is a very convenient reagent for diastereoselective fluorination of optically active substances. Thus the fluorination of a dianion generated from (−)-methyl 3-benzamido-3-phenylpropionate gives compound **43** with the *anti* : *syn* diastereomer ratio of 35 : 65.[89]



Treatment of methyl phenylacetate with *N*-fluorodisulfonylamine **17** in the presence of hexamethyldisilazane in THF (1 h, −78 °C) yields methyl difluorophenylacetate.[90]

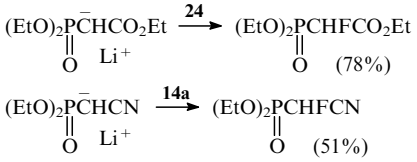
Fluorination of alkylphosphonate anions with the reagent **17** results in monofluoro **44** and difluoro derivatives **45**.[78, 79, 91, 92]



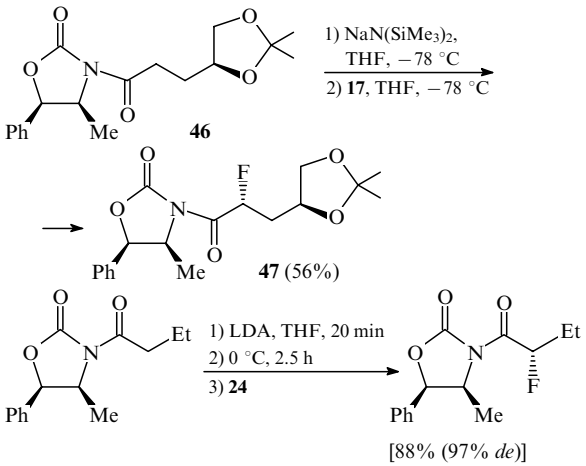
R	Yield of **44** (%)	Yield of **45** (%)
H	11	66
Bu	48	70
Me	45	66
	54	61

Boc is *tert*-butoxycarbonyl.

Other *N*-fluorinating agents can also be used for preparing monofluoro derivatives of alkylphosphonates.[72, 91]

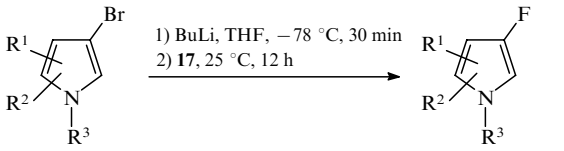


Sodium enolate obtained by treatment of compound **46** with sodium bis(trimethylsilyl)amide is fluorinated with the reagent **17** to give the monofluoro derivative **47**.[92] This method was also used for the synthesis of other fluoro derivatives of oxazolidinone.[93]



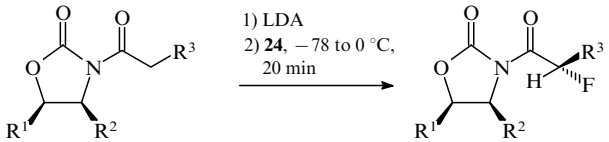
[88% (97% *de*)]

Treatment with the reagent **17** of lithium derivatives of functionalised pyrroles **48** prepared from bromides **48** results in the fluoro derivatives **49**.[94]



R^1, R^2 = Ar, Alk, CN; R^3 = CH_2OEt, $SiPr^i_3$.

N-Fluorobenzo-1,3,2-dithiazole 1,1,3,3-tetroxide (**24**) is effective in fluorination of enolates and carbanions (Table 8).[72] It is also used for stereoselective fluorination of chiral lithium enolates.[66]

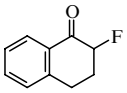
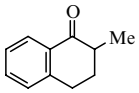
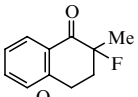
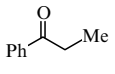
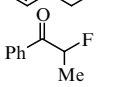
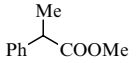
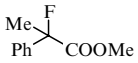
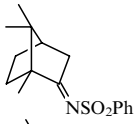
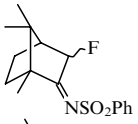
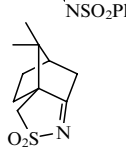
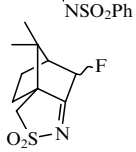
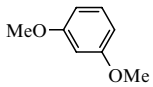
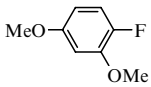


R^1	R^2	R^3	Yield (%)	*de* (%)[a]
Ph	Me	Bu^n	88	97
H	Pr^i	Bu^n	85	96
Ph	Me	Bu^t	86	96
H	Pr^i	Bu^t	80	97
Ph	Me	$PhCH_2$	84	89
Ph	Me	Ph	86	86

[a] The diastereomer ratio was determined on the basis of GLC and ^{1}H NMR data.

Fluorination of 1,3-dicarbonyl compounds with the imide **24** results in α-fluoro derivatives in yields up to 95%.[72] The reaction of the imide **24** with anisole results in a mixture of 2-, 3- and 4-fluoroanisoles (total yield ~ 100%, the isomer ratio is 58 : 5 : 39, respectively).

Table 8. Fluorination of ketone enolates and carbanions with *N*-fluorobenzo-1,3,2-dithiazole 1,1,3,3-tetroxide (**24**).[72]

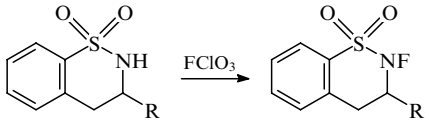
Substrate [a]	Time /h	Reaction product	Yield (%)
	1 [b]		80
	2 [b]		100
	2 [c]		87
	2 [b]		65
	4 [c]		60–65
	2 [d]		45
	4 [e]		60
PhMgBr	4 [e]	PhF	80

[a] KHDMS, lithium bis(trimethylsilyl)amide (LiHDMS) and LDA were used to generate enolates and salts. [b] The fluorinating reagent was added to the enolate at 0 °C with subsequent warming to 20 °C. [c] After addition of the fluorinating reagent, the mixture was heated to 20 °C. [d] The fluorinating reagent was added to the enolate at −78 °C with subsequent warming to 0 °C. [e] The substrate was added to the fluorinating reagent at 0 °C.

5. The use of *N*-fluoro sultams

N-Fluoro sultams are obtained in high yields by the reaction of nitrogen-diluted fluorine (10% F_2 in N_2) with the corresponding sultams or their derivatives (direct fluorination in $CHCl_3$–$CFCl_3$ (1 : 1), 1 h, −40 °C, in the presence of NaF powder[35,95–100]). *N*-Fluro sultams are colourless crystalline compounds that are thermally stable and may be stored without decomposition for a sufficiently long period of time.

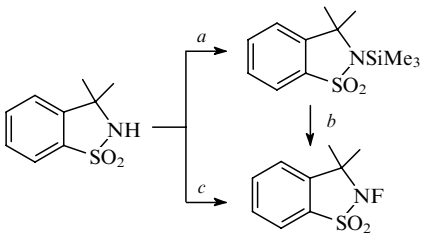
The fluorinating reagents **50a**–**d** were obtained by fluorination of the corresponding NH derivatives with $FClO_3$.[101] Their structure was confirmed by X-ray diffraction analysis.[71]



50a–**d**

R = Pr^i (**a**), Bu^t (**b**), cyclo-C_6H_{11} (**c**), Ph (**d**).

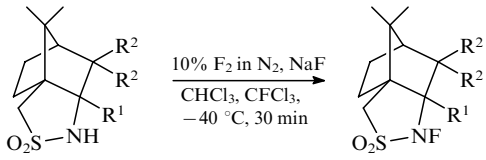
Yet another effective fluorinating reagent of this type is *N*-fluoro-3,3-dimethyl-2,3-dihydro-1,2-benzothiazole 1,1-dioxide (**51**).[98–107] It is prepared using two main approaches, *viz.,* fluorination (10% F_2 in N_2) of *N*-trimethylsilyl-3,3-dimethyl-2,3-dihydro-1,2-benzothiazole 1,1-dioxide (yield 49%[105]) and direct fluorination of the NH derivative in the presence of NaF. In the latter case, the yield of compound **51** reaches 74%.[105]



51

(*a*) $(Me_3Si)_2NH$, Δ, 95%; (*b*) 10% F_2 in N_2, $CFCl_3$, $CHCl_3$, −40 °C, 49%; (*c*) 10% F_2 in N_2, NaF, $CFCl_3$, $CHCl_3$, −40 °C, 74%.

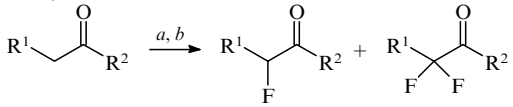
N-Fluoro sultams **52a**–**c** on the basis of bicyclo[2.2.1]heptane are synthesised in a similar way.[95–99]



52a–**c**

Compound **52**	R^1	R^2	Configuration	Yield (%)
a	H	Cl	(+)	80
b	H	H	(−)	75
c	Me	H	(+)	80

N-Fluoro-3,3-dimethyl-2,3-dihydro-1,2-benzothiazole 1,1-dioxide (**51**) is effective in fluorination of enolates and carbanions generated by strong bases.[105] The reaction is carried out in THF and yields a mixture of monofluoro and difluoro ketones (Table 9).



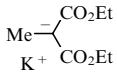
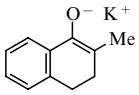
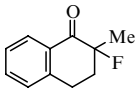
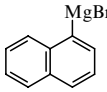
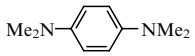
(*a*) B^-, THF, −78 °C; (*b*) **51**, THF, from −78 to 20 °C.

Table 9. Fluorination of carbonyl compounds with *N*-fluoro-3,3-dimethyl-2,3-dihydro-1,2-benzothiazole 1,1-dioxide (**51**).[105]

R^1	R^2	Base	**51** : substrate ratio	Mono : difluoro ketone ratio	Total yield (%)
Ph	MeO	LDA	(1.3–1.6) : 1	95 : 5	40
		LiHMDS	(1.3–1.6) : 1	>98 : 2	33
		NaHMDS	(1.3–1.6) : 1	70 : 30	36
		KHMDS	(1.3–1.6) : 1	53 : 47	27
		KHMDS	(1.3–1.6) : 1	64 : 36	23
Ph	MeO	KHMDS	(2.6–3.6) : 1	2 : 98	53
Me	Ph	LDA	1.1 : 1	97 : 3	53
		LiHMDS	1.1 : 1	95 : 5	66
		NaHMDS	1.1 : 1	78 : 22	56
		NaHMDS	1.1 : 1	>95 : 5	49
		KHMDS	1.1 : 1	50 : 50	40
		KHMDS	1.1 : 1	65 : 35	49
Me	Ph	KHMDS	(2.6–3.6) : 1	5 : 95	64
Me	$PhCH_2O$	LiHMDS	(1.3–1.6) : 1	>98 : 2	<10
		KHMDS	(1.3–1.6) : 1	90 : 10	58
		KHMDS	(2.6–3.6) : 1	33 : 67	27
Me	NPr^i_2	LDA	(1.3–1.6) : 1	>98 : 2	20
		KDA [a]	(1.3–1.6) : 1	>98 : 2	47
		KDA [a]	(2.6–3.6) : 1	54 : 46	42

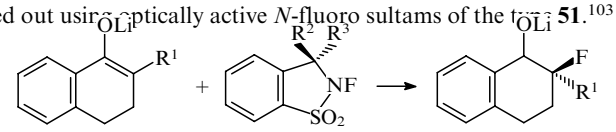
[a] KDA is potassium diisopropylamide.

Table 10. Rate constants for fluorination of some organic nucleophiles with the *N*-fluoro sultam **51**.[108]

Substrate	E°_{Nu} (see [a])	Solvent	T /°C	k_{exp} /litre mol^{-1} s^{-1}	k_{calc} [b] /litre mol^{-1} s^{-1}	Reaction product	Yield (%)
	1.6	$Cl(CH_2)_2Cl$	60	$\ll 10^{-6}$ (see [c])	6.3×10^{-24}		no reaction
	0.34	Et_2O	0	$>8\times10^{-2}$	5×10^{-15}	$MeC(F)(CO_2Et)_2$	94
	−0.39	THF	−78	3.2×10^{-2}	3×10^{-15}		80 [d]
	−0.34	THF	−75	1.9×10^{-2}	1.2×10^{-7}		72 [d]
	−0.29	THF, Et_2O	0	6.8×10^{-2}	1.4×10^{-7}	see [e]	17
	0	MeCN	0	1.3×10^{-3}	2×10^{-5}	see [f]	0

[a] For the reagent **51**, $E^{o} = -0.12$. [b] Calculated for the SET process. [c] The reaction rate is too small to be measured. [d] No other reaction products were found. [e] 62% of naphthalene and 12% of naphthyltetrahydrofuran were isolated. [f] The fluorinated products were not characterised.

Enantioselective fluorination of lithium enolates can be carried out using optically active *N*-fluoro sultams of the type **51**.[103]



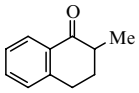
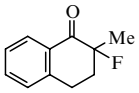
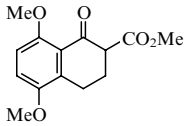
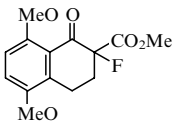
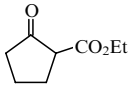
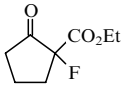
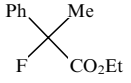
R^1 = Me (80% *ee*), Et (72% *ee*), Bn (86% *ee*); R^2 = Me, R^3 = Pr^i.

The rate of this reaction depends on the nature of the metal and the solvent. Thus propiophenone reacts with *N*-fluoro sultam **51** at −78 °C, its sodium derivative reacts from −60 °C to −40 °C, whereas the lithium derivative of propiophenone reacts only at temperatures above −40 °C.

The rate constants of the fluorination of various compounds with the reagent **51** are listed in Table 10.[108]

N-Fluoro sultams **52a**–**c** have found application as enantioselective fluorinating reagents (Table 11).[95, 96, 99] The fluorination of enolates was carried out using 1.5 equiv. of the reagents **52a**,**b**. The ratio of enantiomers was determined by NMR spectroscopy with the use of a shift-reagent.[95, 96]

Table 11. Asymmetric fluorination of enolates with *N*-fluorosultams **52a**,**b**.[95, 96]

Substrate	Fluorinating reagent	Base	Solvent	T /°C	Reaction product	*ee* (configuration) (%)	Yield (%)
	**52b**	LDA	THF	−78 to 20		35	< 5
	52a	LDA	THF	−78		10(*S*)	49
	52a [a]	NaHMDS	THF	−78 to 0		67(*S*)	41
	52a [a]	NaHMDS	THF	−78		65(*S*)	40
	52a	NaHMDS	THF	−78 to 0		75(*R*)	40
	52a	NaHMDS	THF	−78		65(*R*)	50
	**52b**	NaH	Et_2O	0 to 20		25	28
	52a	NaH	Et_2O	0 to 20		46	> 95
	52a	NaHMDS	THF	−78 to 0		26	57
	**52b**	NaH	Et_2O	0 to 20		70	63
	52a	NaH	Et_2O	−78 to 0		34	59
$PhCH(Me)CO_2Et$	**52b**	LDA	THF	−78 to 20		35	< 10
	52a	LDA	THF	−78		29	62
	52a	NaHMDS	THF	−78		33	54

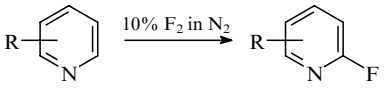
[a] 0.8 Equiv. of the reagent **52a** was used.

III. Highly efficient fluorinating reagents based on heterocyclic compounds containing a fluorine atom at the charged nitrogen atom

Synthesis of fluorinating reagents in which the fluorine atom is bound to the charged nitrogen atom of a heterocycle is one of the most fruitful ideas in the chemistry of organofluorine compounds. Two groups of reagents are mainly used, *viz.*, *N*-fluoropyridinium and *N*-fluoroquinuclidinium derivatives. This type of compounds (they are commonly referred to as charged or quaternary) are characterised by high reactivity which surpasses that of neutral reagents of the type R_2NF. The interest in these compounds is also due to the possibility to vary their structures to match a specific synthetic problem. Therefore, these reagents can be used for fluorination of a vast variety of substrates. It is not accidental that only charged fluorine 'carriers' have rapidly found industrial application.

1. Fluorination with *N*-fluoropyridinium salts

N-Fluoropyridinium salts are structurally the simplest and most readily available fluorine carriers of the type $(R_3NF)^+X^-$. Direct fluorination of pyridine and its derivatives with nitrogen-diluted fluorine (10% F_2 in N_2) in $CF_2ClCFCl_2$ results mainly in 2-fluoropyridines.[109]

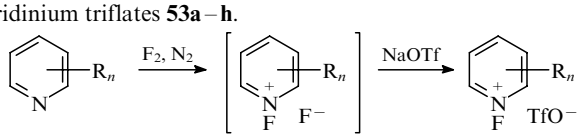


Substrate	*T* /°C	Reaction product	Yield (%)
4-MeC_5H_4N	−25	2-F-4-MeC_5H_3N	31
4-EtC_5H_4N	−25	2-F-4-EtC_5H_3N	32
4-$Pr^iC_5H_4N$	−25	4-F-4-$Pr^iC_5H_3N$	47
4-$PhCH_2C_5H_4N$	−25	2-F-4-$CH_2PhC_5H_3N$	25
3,5-$Me_2C_5H_3N$	0	2-F-3,5-$Me_2C_5H_2N$	37
3,5-$Cl_2C_5H_3N$	25	2-F-3,5-$Cl_2C_5H_2N$	46
4-AcC_5H_4N	0	2-F-4-AcC_5H_3N	26
4-$MeOOCC_5H_4N$	0	2-F-4-$MeOOCC_5H_3N$	61

Earlier studies of Meinert and Cech [110,111] showed that the fluorination of pyridine with a F_2N_2 mixture in $CFCl_3$ at −80 °C results in a pyridine–fluorine complex, *viz.*, *N*-fluoropyridinium fluoride. This compound manifests fluorinating activity at low temperatures (particularly, with respect to uracil and some chloro alkenes). It is very unstable and is decomposed explosively at temperatures above −2 °C. In practice, fluorination with *N*-fluoropyridinium fluoride can be carried out only at temperatures below −20 °C, which restricts the applicability of the method.

Attempts to replace the fluoride ion by other, less nucleophilic anions were undertaken aimed at obtaining stable *N*-fluoropyridinium salts. These studies are well documented.

Fluorination of pyridine and its derivatives in the presence of trifluoromethanesulfonic acid salts [112–122] in aqueous acetonitrile [123] or in polyfluorinated alcohols [124] results in *N*-fluoropyridinium triflates **53a**–**h**.



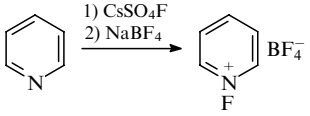
53a–**h**

R_n = H (**a**, 80%), 2-Me (**b**, 60%), 2,4,6-Me_3 (**c**, 49%), 3,5-Me_2 (**d**, 73%), 4-NO_2 (**e**, 86%), 3,5-$(CF_3)_2$ (**f**, 68%), 4-CN (**g**, 94%), 2,6-$(COOMe)_2$ (**h**, 72%).

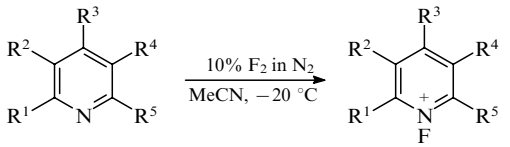
The salts **53** represent stable crystalline compounds which decompose without explosion only at, and above, melting points. They are soluble in organic solvents and do not react with glass. This class of fluorinating reagent has found wide application, particularly in fluorination of steroids, sugars and other natural compounds.

The range of stable fluorinating reagents on the basis of pyridine has been considerably extended [125–128] owing to employment of salts (other than triflates) containing non-nucleophilic anions (BF_4^-, PF_6^-, SbF_6^-) in their synthesis. This method was used for the preparation and characterisation (by ^{19}F NMR) (see Refs 129–131) of numerous *N*-fluoropyridinium salts with different substituents in the pyridine ring and counterions. Thus the fluorination of pyridine with dilute fluorine ($F_2 : N_2 = 1 : 4$) in the presence of trifluoromethanesulfonic acid in MeCN results in *N*-fluoropyridinium triflate (**53a**) in 97% yield.[131]

Other fluorinating reagents, *e.g.*, cesium fluoroxysulfate, can be used instead of fluorine.[133] Thus the reaction of pyridine with cesium fluoroxysulfate in acetonitrile (0–5 °C) in the presence of $NaBF_4$ results in stable *N*-fluoropyridinium tetrafluoroborate in 48% yield.



Internal pyridinium salts **54a**–**j** were synthesised by introduction of sulfo groups into the pyridinium ring.[125,134–136]

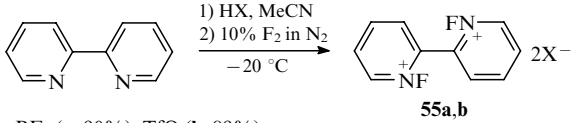


54a–**j**

Compound **54**	R^1	R^2	R^3	R^4	R^5	Solvent	*T* /°C	Yield (%)
a	Me	H	Me	H	SO_3^-	MeCN : H_2O (10 : 1)	−20	88
b	H	H	Me	H	SO_3^-	MeCN : H_2O (10 : 1)	−20	92
c	H	H	Et	H	SO_3^-	MeCN	−20	79
d	H	H	Bu^t	H	SO_3^-	MeCN : H_2O (20 : 1)	−20	84
e	H	H	Me	H	SO_3^-	MeCN : H_2O (10 : 1)	−20	65
f	H	CF_3	H	H	SO_3^-	MeCN	−20	90
g	H	CF_3	H	Cl	SO_3^-	MeCN	−10	88
h	CF_3	H	CF_3	H	SO_3^-	MeCN	−40	95
i	H	H	H	SO_3^-	H	$(CF_3)_2CHOH$	0	87
j	H	H	SO_3^-	H	H	$(CF_3)_2CHOH$	0	74

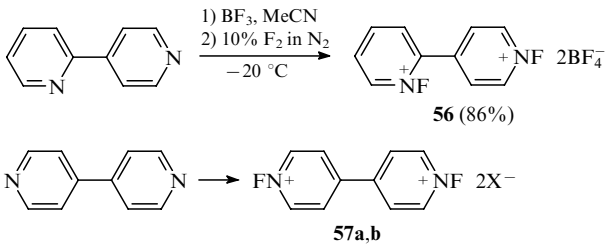
The reaction is normally performed in MeCN; however, polyfluorinated alcohols $H(CF_2)_nCH_2OH$ (n = 2, 3, 4) can also be used as solvents. This approach was used to prepare *N*-fluoropyridinium-3-sulfonates (**54i**,**j**) (yields 87% and 74%, respectively).[137,138] Compounds **54** belong to the most potent fluorinating reagents. After completion of fluorination, the internal salts are converted into pyridinium sulfonates, which are readily soluble in water but poorly soluble in organic solvents, which facilitates the isolation of the target fluorination products and their separation from the products of degradation of the fluorinating reagent.

Umemoto *et al.*[139–142] synthesised *N*,*N*′-difluorobipyridinium salts by fluorination of bipyridine complexes with Lewis or Brønsted acids with nitrogen-diluted molecular fluorine (10% F_2 in N_2). The molecule of these salts has two mutually activating cationic centres.



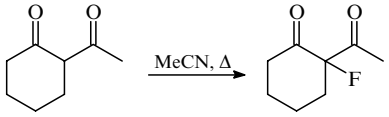
55a,**b**

X = BF_4 (**a**, 90%), TfO (**b**, 89%).



Compound **57**	Reaction conditions		Yield (%)
	1st step	2nd step	
a	TfOH, MeCN	10% F_2 in N_2, 20 °C	89
b	BF_3, MeCN	10% F_2 in N_2, 0 °C	96
a	LiOTf, MeCN	10% F_2 in N_2, $CFCl_3$, $CHCl_3$, −35 °C	67

The reagents **53**, **55**–**57** differ in their fluorinating ability as can be exemplified in the reactions with 2-acetylcyclohexanone.[139]



Fluorinating reagent	**53a**	**55b**	**56**	**57a**
t /h	19	0.1	2	5
Yield (%)	79	85	78	87

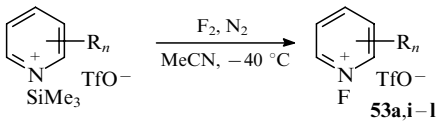
Compound **55b** turned out to be the most reactive among other compounds tested. 1,1′-Difluoro-2,2′-bipyridinium bis(tetrafluoroborate) (**55a**) can be regarded as one of the most efficient reagents for industrial manufacture of fluorine-containing compounds by virtue of its high reactivity, high (in comparison with other reagents) content of the active fluorine and ease of synthesis.[139] Bis(tetrafluoroborate) **55a** efficiently fluorinates compounds containing an active methylene group as well as aromatic and other compounds.[140]

Some *N*-fluorinating reagents, *e.g.*, *N,N′*-difluoro-2,2′-bipyridinium (**55b**) and *N*-methyl-*N′*-fluoro-4,4′-bipyridinium (**58**) bistriflates and *N,N′*-difluoro-2,2′-bipyridinium (**57a**) bistetrafluoroborate, proved to be very convenient reagents for fluorination of various types of organic compounds (Tables 12 and 13).[142, 143]

The introduction of readily polymerisable groups into the pyridine ring of the reagents **55**–**57** allows one to obtain polymers with molecular masses above 500 000 Daltons. The latter are used as electrolytes (*i.e.*, as an active cathode mass) in batteries and as solid fluorinating agents.[137]

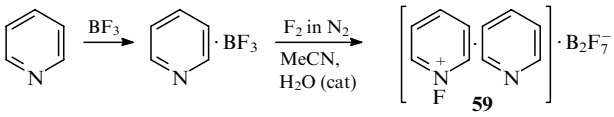
Among quaternary (charged) fluorinating reagents, pyridinium salts present the greatest interest for investigators; therefore, the methods for their synthesis are permanently improved and the areas of application are extended.

Thus yet another approach to the preparation of fluorinating reagents on the basis of pyridinium salts consists in fluorination of the corresponding *N*-trimethylsilyl derivatives with fluorine in MeCN.



R_n = H (**a**, 78%), 3-Cl (**i**, 79%), 3,5-Cl_2 (**j**, 55%), 2-CO_2Me (**k**, 69%), 2,3,4,5,6-Cl_5 (**l**, 67%).

The fluorination of the pyridine–BF_3 complex with nitrogen-diluted elemental fluorine (20% F_2 in N_2) in MeCN or CCl_4 at room temperature results in the heptafluorodiborate of a pyridine–*N*-fluoropyridinium complex (**59**) rather than *N*-fluoropyridinium tetrafluoroborate, which is also an efficient fluorinating reagent.[115, 118–121]



2,6-Dichloropyridine gives *N*-fluoro-2,6-dichloropyridinium tetrafluoroborate upon fluorination with elemental fluorine in a BF_3–HF–H_2O–MeCN system at −15 °C (yield 76%). The effect of temperature on the fluorination of pyridine with elemental fluorine in a CF_3SO_3H–MeCN system was estimated by Nukui.[143] At −20 °C, the yield of *N*-fluoropyridinium triflate was 92% after 30 days and at 40 °C it was 99%. Polyfluorinated secondary alcohols (RR′CHOH, where R,R′ are C_1–C_4 fluoroalkyl) are used as solvents in the synthesis of the salts.[134]

The fluorinating ability of *N*-fluoropyridinium salts depends not only on the nature of the substituent in the pyridine ring, but also on the nature of the counterion. The effect of the latter on the efficiency of fluorination of 1-trimethylsilyloxycyclohexene with *N*-fluoropyridinium salts has been studied by Umemoto *et al.*[134]

Table 12. Fluorination of aromatic compounds with *N,N′*-difluorobipyridinium derivatives **57b** and **58** (in MeCN).[142]

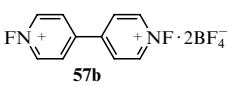
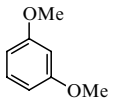
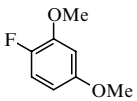
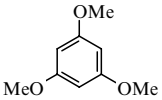
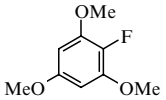
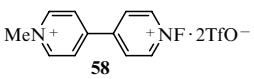
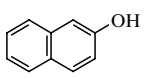
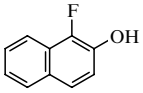
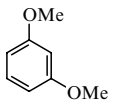
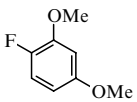
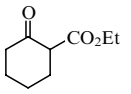
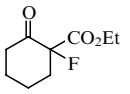
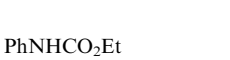
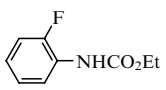
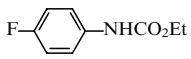
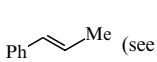
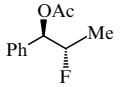
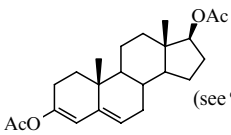
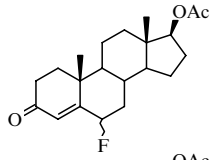
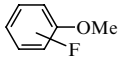
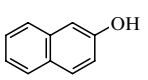
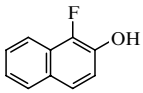
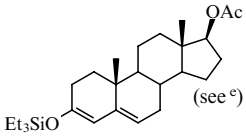
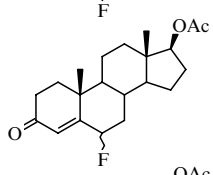
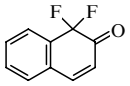
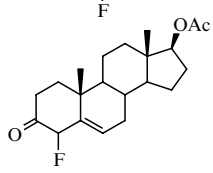
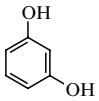
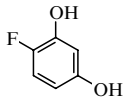
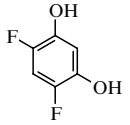
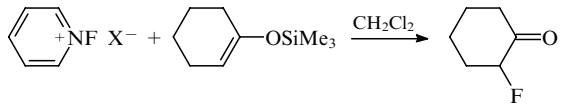
Fluorinating reagent	Substrate	*T* /°C	*t* /h	Reaction products	Yield (%)
 **57b**		20	20		52
		20	18		61
 **58**		80	15		60
	PhOMe	80	15	2- and 4-FC_6H_4OMe	55
		20	15		40
		60	20		40

Table 13. Fluorination of organic compounds with the reagent **55b** (in MeCN).[143]

Substrate	*T* /°C	*t* /h	Reaction product	Yield (%)	Substrate	*T* /°C	*t* /h	Reaction product	Yield (%)
	boiling	8		76		boiling	48		48
$AcCH(Me)CO_2Et$	"	8	$AcCF(Me)CO_2Et$	73					32
$PhCOCH_2COPh$ [a]	"	48	$PhCOCHFCOPh$, $PhCOCF_2COPh$	10, 76					
 (see [b])	"	0.25		51	 (see [e])	70	0.15		82 [f]
PhOMe	"	9		73 [c]					
 (see [d])	20	0.15		61	 (see [e])	20	0.5		46 [g]
				18					19
	boiling	< 0.1		72					
				10					

[a] In the presence of 20 mol. % of TfOH. [b] The reaction was carried out in AcOH. [c] The 2-F : 4-F : 2,4-F_2 ratio is 6.5 : 4.6 : 1. [d] The reaction was carried out in HCO_2H. [e] 50 mol. % of $NaHCO_3$. [f] The α : β ratio is 1 : 1.7. [g] The α : β ratio is 1 : 1.4.

The best results were obtained with *N*-fluoropyridinium triflates. They manifest high regio- and stereoselectivity in fluorination of aromatic compounds, compounds containing activated methylene groups, the Grignard reagents, sodium salts of CH-acids, vinyl acetates, enolates, alkyl and silyl enol ethers, organic sulfides, enamides, alkenes, *etc*.

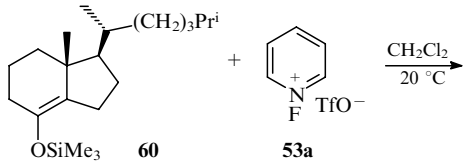


X	*T* /°C	Time/h	Yield (%)
CF_3SO_3	20	7	87
BF_4	20	72	traces
BF_4	36	64	1
SbF_6	36	8	23
ClO_4	36	19	0

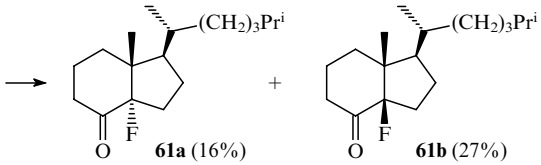
Some examples of fluorination of organic compounds with *N*-fluoropyridinium triflates are given in Table 14.[144]

The regioselective fluorination of enol esters and ethers with *N*-fluoropyridinium salts leads to α-fluorocarbonyl compounds.[114] A modified general fluorination procedure has been proposed which consists in the conversion of a carbonyl compound into enol trimethylsilyl ether or enol acetate which is subject to fluorination.

α-Fluorinated carbonyl compounds are convenient as starting compounds in fine organic syntheses.[130, 144–147] Thus the fluorination of the silyl ether **60** with the reagent **53a** yields a mixture of α- and β-fluoro ketones **61a**,**b**.[116, 148]



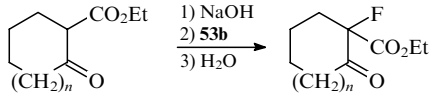
60 **53a**



61a (16%) **61b** (27%)

N-Fluoropyridinium salts containing the BF_4^-, SbF_6^- or PF_6^- counterions give 2-fluoropyridines in good yields upon treatment with bases (Et_3N, Pr^i_2NH, Py, MeONa, Bu^tOK, MeCOONa, Bu^n_4NF) at room temperature.[141, 149, 150]

On heating with *N*-fluoro-2,4,6-trimethylpyridinium triflate (**53b**) in the presence of NaOH, ethyl 2-oxocyclohexanecarboxylate is converted into ethyl 1-fluoro-2-oxocyclohexanecarboxylate (yield 84%). Five- and seven-membered cyclic fluorinated β-oxo esters are obtained in a similar way.[123, 151]



$n = 0-2$.

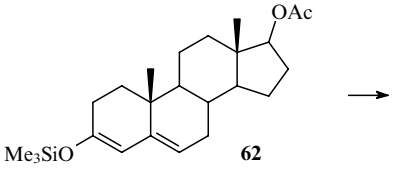
Fluoro derivatives with a predetermined position of the fluorine atom can be synthesised using reagents of the type **53** or **54** for fluorination of steroids under various reaction condi-

Table 14. Fluorination of organic compounds with *N*-fluoropyridinium triflates **53a**,**b**,**j**,**l**.[144]

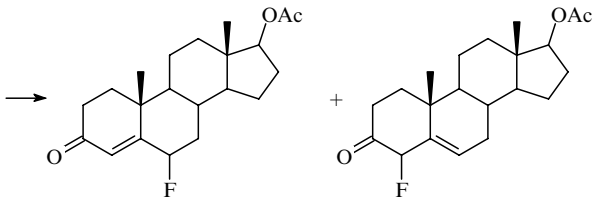
Fluorinating reagent	Substrate	Solvent	T /°C	t /h	Reaction product	Yield (%)
53a	PhOH	CH_2Cl_2	100	24		75 [a]
	1-naphthol	CH_2Cl_2	36	22	2-fluoro-1-naphthol (**A**) 4-fluoro-1-naphthol (**B**) 2,2-difluoro-1(2*H*)naphthalenone (**C**)	56 [b]
	$4\text{-}NO_2C_6H_4OH$	CH_2Cl_2	20	17	$2\text{-F-}4\text{-}NO_2C_6H_3OH$	65
	$PhCH=C(OEt)(OSiMe_3)$	CH_2Cl_2	20	2	$PhCHFCO_2Et$	65
	$n\text{-}C_7H_{15}CH=C(OSiMe_3)Me$	CH_2I_2	20	2	$n\text{-}C_7H_{15}CHFCOMe$	72
	$PhCH=C(OSiMe_3)_2$	CH_2Cl_2	20	2	$PhCHFCO_2H$	68
53b	$n\text{-}C_{12}H_{25}MgCl$	Et_2O	0	0.5	$n\text{-}C_{12}H_{25}F$	75
	PhMgCl	THF	0	0.5	PhF	58
	$Na^+[CH(CO_2Et)_2]^-$	THF	0	0.1	$FCH(CO_2Et)_2$	73
	$Na^+[MeC(CO_2Et)_2]^-$	THF	0	0.2	$MeCF(CO_2Et)_2$	78
	$Na^+[PhC(CN)_2]^-$	THF	0	0.2	$PhCF(CN)_2$	71
	$Na^+[PhSO_2CHCO_2Et]^-$	THF	0	0.2	$PhSO_2CF_2CO_2Et$ (**D**) $PhSO_2CHFCO_2Et$ (**E**)	53 [c]
	$Na^+[ClC(CO_2Et)_2]^-$	THF	0	0.2	$ClCF(CO_2Et)_2$	86
	$CH_2(COPh)_2$ (see [d])	CH_2ClCH_2Cl	60	18	$CF_2(COPh)_2$	88
	$MeCOCH_2CO_2Et$ (see [d])	CH_2ClCH_2Cl	60	24	$MeCOCHFCO_2Et$ (**F**) $MeCOCF_2CO_2Et$ (**G**)	81 [e]
	$CH_2(CO_2Et)_2$ (see [d])	CH_2ClCH_2Cl	60	48	$CHF(CO_2Et)_2$	80
53j	$4\text{-}ClC_6H_4OH$	CH_2ClCH_2Cl	20	23	$2\text{-F-}4\text{-}ClC_6H_3OH$	54
	2-naphthol	CH_2Cl_2	20	26	1-fluoro-2-naphthol (**J**) 1,1-difluoro-2(1*H*)-naphthalenone (**K**)	95 [f]
	$4\text{-}HOC_6H_4CO_2Me$	$CH_2ClCHCl_2$	20	40	$3\text{-F-}4\text{-}HOC_6H_3CO_2Me$	53
53l	PhNHCOMe	CH_2Cl_2	20	48	$2\text{-}FC_6H_4NHCOMe$ (**H**) $4\text{-}FC_6H_4NHCOMe$ (**I**)	51 [g]
	$PhCH=CH_2$	AcOH	20	1	$PhCH(OAc)CH_2F$	72
		$AcOSiMe_3$	20	72	$PhCH(OAc)CH_2F$	56
		$MeOSiMe_3$	20	120	$PhCH(OMe)CH_2F$	54
		$EtOSiMe_3$	20	432	$PhCH(OEt)CH_2F$	29
	trans-$PhCH=CHMe$	AcOH	20	0.3	$PhCH(OAc)CHFMe$	80 [h]
	$PhCH=CHMe$ (see [i])	AcOH	20	1	$PhCH(OAc)CHFMe$	80 [h]
	$Ph(Me)C=CH_2$	AcOH	20	0.08	$Ph(CH_2F)C=CH_2$	25
		Pr^iOH	20	0.16	$PhC(Me)(OPr^i)CH_2F$	70
		CH_2Cl_2	20	0.08	$Ph(CH_2F)C=CH_2$	73
	$Me(CH_2)_6C(OSiMe_3)=CH_2$	CH_2Cl_2	20	3	$Me(CH_2)_5CHFCOMe$	42
	$Me(CH_2)_5CH=C(OSiMe_3)Me$	CH_2Cl_2	20	3	$Me(CH_2)_5CHFCOMe$	58
	cyclo-$C_6H_{11}(OSiMe_3)C=CHMe$	CH_2Cl_2	20	10	cyclo-$C_6H_{11}COCHFMe$	61

[a] The *ortho*:*para*:*meta* ratio is 9 : 3 : 1. [b] The **A** : **B** : **C** ratio is ~ 8 : 2 : 1. [c] The **D** : **E** ratio is ~ 1 : 12. [d] The fluorination was performed in the presence of 0.4 equiv. of $ZnCl_2$. [e] The **F** : **G** ratio is ~ 6 : 1. [f] The **J** : **K** ratio is ~ 8 : 1. [g] The **H** : **I** ratio is ~ 1 : 1. [h] The *threo* : *erythro* ratio is 1 : 1. [i] The *trans* : *cis* ratio is 1 : 1.

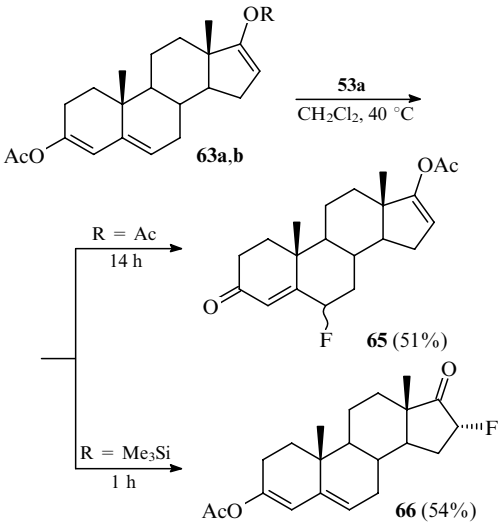
tions.[130, 144, 146, 147] Oxo steroids are preliminarily converted into *O*-silyl enol ethers.[146, 147] In the case of α,β-unsaturated oxo steroids, these are to be first converted into trimethylsilyl enol ethers. The choice of a fluorinating reagent makes it possible to selectively synthesise a required isomer. Thus the reagent **54a** predominantly fluorinates the trimethylsilyl ether **62** at position 6, whereas the reagent **53a** leads to 6- and 4-fluoro derivatives in comparable yields.



62

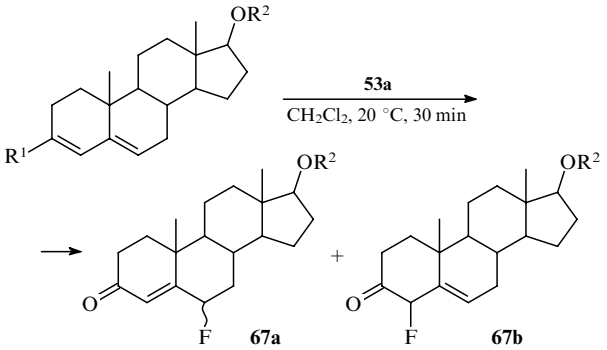


Fluorination of 3,17-diacetoxyandrosta-3,5,16-triene (**63a**) with *N*-fluoropyridinium triflate (**53a**) occurs selectively and yields compound **65** with the fluorine atom in position 6. The corresponding silyl ether **63b** is selectively fluorinated into ring *D* to yield compound **66**.[100, 117, 152–154]



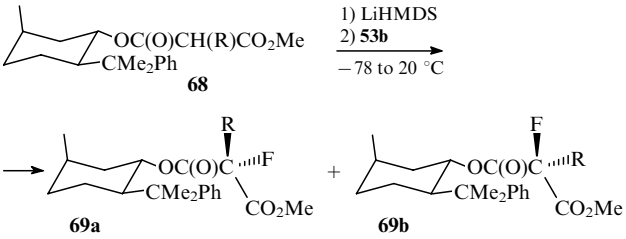
3,17β-Diacetoxyandrosta-3,5-diene is converted into a mixture of 6α- and 6β-fluoro-17β-acetoxytestosterones (total yield ~ 81%) upon treatment with the reagent **53a** in acetic acid (3 h, 77 °C).[155]

The stereo- and regioselectivity of fluorination of steroids with the reagent **53a** have been studied.[115, 116, 143]



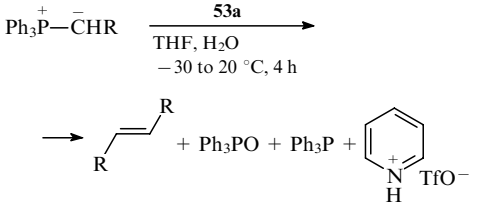
R^1	R^2	Yield (%) (α : β ratio)	
		67a	**67b**
OEt	H	26 (2 : 3)	27
OAc	Ac	72 (1 : 2)	0
$OSiMe_3$	$SiMe_3$	41 (1 : 3)	18
—N O	H	0	46

The reagent **53b** was used for stereoselective introduction of fluorine into the α-position relative to the carbonyl group of compound **68**. The ratio of enantiomers **69a**,**b** depends on the size of the substituent R.[154, 155]



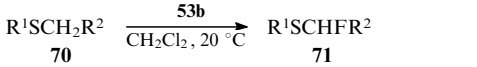
R	Yield (%)	**69a** : **69b** ratio
Me	87	79 : 21
Et	96	67 : 33
Pr	95	67 : 33
Bu	–	38 : 62
$PhCH_2$	88	62 : 38

The use of reagents **53a**,**b** is not confined to fluorination reactions; they can also be used in the synthesis of *trans*-alkenes. Thus treatment of the Wittig reagents with *N*-fluoropyridinium triflate **53a** makes it possible to obtain the corresponding *trans*-alkenes under mild conditions and in acceptable yields.[156]



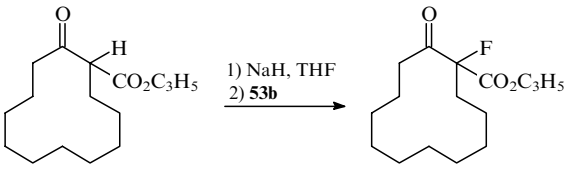
R = COOEt (51%), COPh (50%), COMe (44%), 2-$NO_2C_6H_4$ (47%), 4-$NO_2C_6H_4$ (55%), 4-$MeOC_6H_4CO$ (81%), 4-$NO_2C_6H_4CO$ (71%).

The reaction of sulfides **70** with *N*-fluoro-2,4,6-trimethylpyridinium triflate (**53b**) yields sulfides **71** fluorinated at the methylene group.[157]



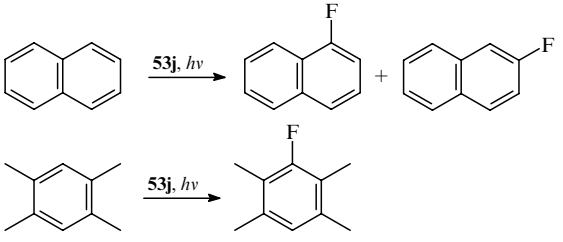
R^1	R^2	*t* /h	Yield (%)
Ph	H	4	85
4-ClC_6H_4	H	8	87
n-$C_{12}H_{25}$	H	17.5	44
Me	CO_2Et	8	46
Ph	CO_2Me	23	45
$PhCH_2$	H	0.5	77
$MeO_2CCH(NHCOCF_3)(CH_2)_2$	H	7.5	39

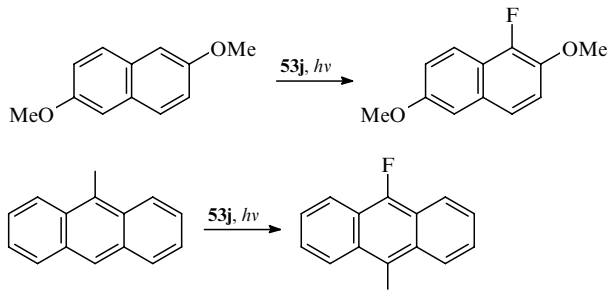
Fluorination of β-oxo acid allyl ester **72** with *N*-fluoro-2,4,6-trimethylpyridinium triflate (**53b**) affords the α-fluoro derivative **73** in 84% yield.[158]



N-Fluoro-3,5-dimethylpyridinium triflate (**53c**) and other salts with a substituted pyridine ring fluorinate aromatic compounds. Thus benzene is fluorinated with *N*-fluoro-2,6-dimethoxycarbonylpyridinium triflate to fluorobenzene (yield 56%); *N*-(ethoxycarbonyl)aniline gives a mixture of the corresponding 2- and 4-fluoro derivatives (yields 60% and 27%, respectively). Phenylurethane also yields fluorination products in positions 2 (47%) and 4 (32%) of the aromatic ring. The fluorination of anisole results in a mixture of *o*- and *p*-fluoroanisoles which points to the electrophilic nature of the fluorination reaction.[129, 132, 158–161] The value of the electrochemical reducing potential ($E_p^c = -0.66$ V) of the *N*-fluoropyridinium cation also indicates that this cation is a strong electrophile.[162]

Bockman *et al.*[160] studied fluorination of aromatic compounds with 3,5-dichloro-*N*-fluoropyridinium triflate **53j** on irradiation with UV light.



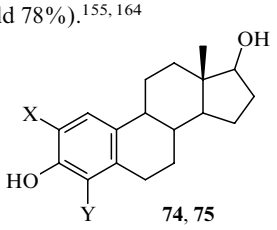


N-Fluoropyridinium sulfonates manifest high selectivity in fluorination of activated aromatic compounds. Thus fluorination of phenol, naphthol, *O*-trimethylsilylphenol and phenylurethane with the reagent **54j** results in the predominant formation of the corresponding *ortho*-isomers: for phenol, the conversion is 88% and the *ortho* : *para* ratio is 40 : 1; the *ortho* : *para* ratio for *O*-trimethylsilylphenol is 34 : 1; and 1-naphthol gives 63% of 2-fluoro-1-naphthol.[114, 129]

Chloro- and bromophenols as well as *N*-acylhalogenoaniline are fluorinated with *N*-fluoropyridinium salts with high selectivity to give high yields of *ortho*-fluorination products. Thus the reaction of 4-chlorophenol with 2-chloro-6-trichloromethyl-*N*-fluoropyridinium tetrafluoroborate in $ClCH_2CHCl_2$ (3 h, 45 °C) gives 4-chloro-2-fluorophenol in 68% yield.[162]

N-Fluoropyridinium triflates[155, 163, 164] along with acetylhypofluorite[165] are used for fluorination of biologically active compounds. Thus a mixture of 2-fluoro-17β-estradiol (**74**) and 4-fluoro-17β-estradiol (**75**) (total yield 60%) was obtained by fluorination of 17β-estradiol in CH_2Cl_2–MeCN (9 : 1) (12 h, 20 °C) with the reagent **53j**.

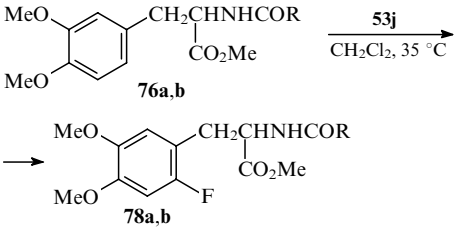
Estrol upon fluorination with *N*-fluoropyridinium triflate also yields a mixture of 2- and 4-fluoro derivatives (ratio 2.5 : 1, total yield 78%).[155, 164]



74, **75**

74: X = F, Y = H;
75: X = H, Y = F

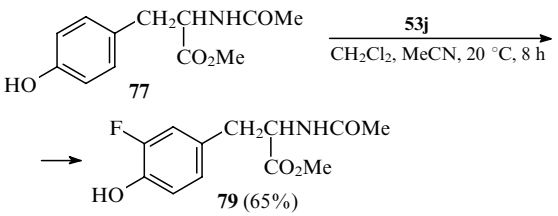
Fluorination of dopamine derivatives **76a**,**b** and the dopamine analogue **77** with 3,5-dichloro-*N*-fluoropyridinium triflate (**53j**) proceeds under mild conditions and results in the corresponding fluoro derivatives **78a**,**b** and **79**.[163]



76a,**b**

78a,**b**

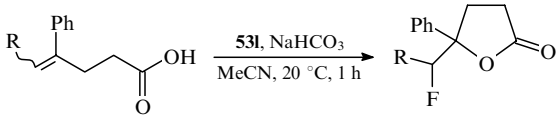
R = CF_3 (**a**, 20%), Me (**b**, 30%).



77

79 (65%)

Pentachloro-*N*-fluoropyridinium triflate (**53l**) proved to be efficient in fluorination of unsaturated acids containing a phenyl substituent in positions 4 or 5 leading to fluorinated γ- and δ-lactones.[166]



R	Yield (%)	Diastereomer ratio
H	69	
(*Z*)-Et	72	2.1 : 1
(*E*)-Et	51	1 : 2.4

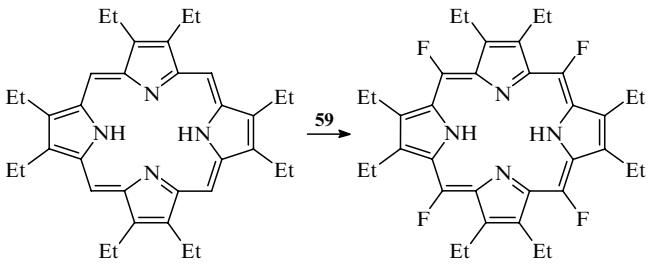
N,*N*′-Difluoro-2,2′-bipyridinium- (**55b**) and *N*,*N*′-difluoro-4,4′-bipyridinium triflates (**57a**) react with 2-acetylcyclohexanone in boiling acetonitrile to give 2-acetyl-2-fluorocyclohexanone (yields 85% and 87%, respectively).[167] The reagent **57a** is more efficient in this case.

Treatment with *N*-fluoropyridinium salts was used for electrophilic fluorination of azulene and its derivatives.[168] Relatively low yields of fluorination products (14%–40%) are due to side reactions. In addition, a prominent role is played by the solvent. For example, the reaction of azulene with *N*-fluoro-4-methylpyridinium triflate **53b** in acetonitrile or CH_2Cl_2 gives a mixture of mono- (yields 12% and 3%, respectively) and difluoro derivatives (yields 17% and 5%, respectively). In dichloroethane, the yield of the monofluoro derivative is increased to 24%.[168]

The heptafluoroborate of the *N*-fluoropyridinium pyridine complex (**59**) proved to be an excellent fluorinating reagent in the synthesis of monofluoro derivatives of various classes (Table 15).[115] The reagent **59** is highly selective; the reactions occur under mild conditions.[129, 136–140, 145]

More complex compounds can also be subject to selective fluorination without oxidation and decomposition. Highly selective *meso*-fluorination of porphyrins is effected with 2,6-dichloro-*N*-fluoro-pyridinium, 3,5-dichloro-*N*-fluoropyridinium and pentachloro-*N*-fluoropyridinium triflates.[153] This reaction is carried out in acetonitrile or hexafluorobenzene as solvents and K_2CO_3 or $SrCO_3$ as bases. The yield of the fluorinated product is low. For example, the tetrafluoro derivative **80** is obtained in 20% yield on boiling of octaethylporphyrin for 2 days in hexafluorobenzene.[153]

Salts of *N*-fluoropyridinium and its derivatives have obvious advantages over other fluorinating reagents. They are stable, transportable and fit for long-term storage without any deterioration of their properties; besides, they are explosion-proof and non-toxic. The fluorination is performed under mild conditions and is not accompanied by side reactions, which is especially important for steroids, sugars and other biologically active compounds.

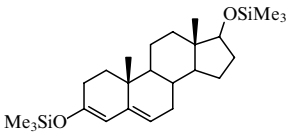
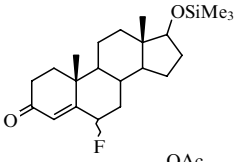
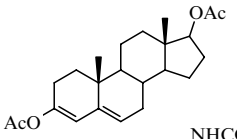
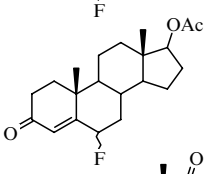
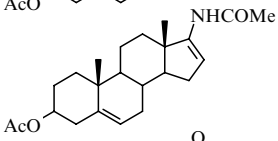
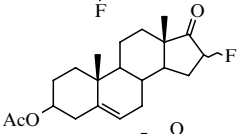
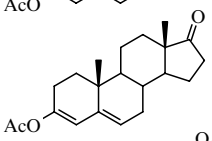
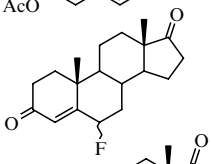
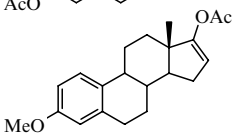
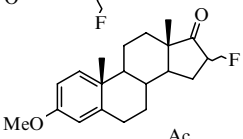
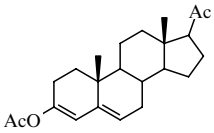
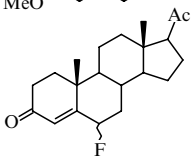
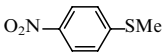
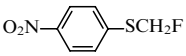
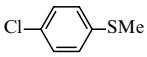
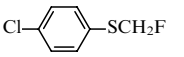
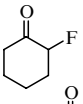
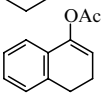
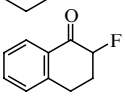
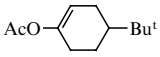
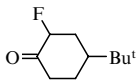
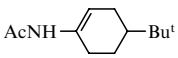
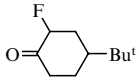


80

2. *N*-Fluoroquinuclidinium and 4-alkyl-1-fluoro-1,4-diazoniabicyclo[2.2.2]octane salts

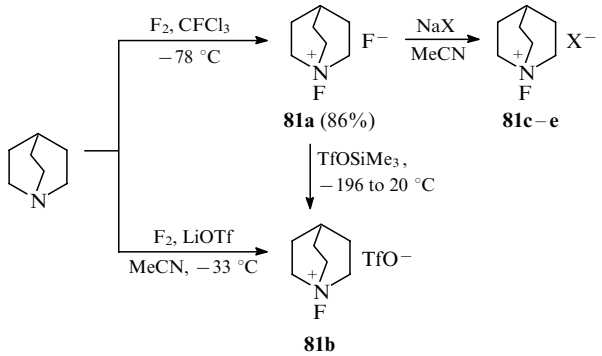
Like *N*-fluoropyridinium salts, *N*-fluoroquinuclidinium salts belong to the most efficient fluorinating reagents of the *N*-fluoroamine series. The main method for their synthesis is direct fluorination of the corresponding NH-precursors.[132, 169–176] *N*-

Table 15. Fluorination with the complex *N*-fluoropyridinium – pyridine (**59**) heptafluorodiborate in MeCN.[115]

Substrate	*T* /°C	*t* /h	Reaction product	Yield (%)
	25	18		88
	80	5		57
	40	48		96
	25	120		82
	25	72		69
	80	18		38
	25	120		82
	40	72		68
	80	10		23
	40	96		60
	80	5		39
	40	72		99
	80	6		87
	40	72		46
	80	36		36
	25	18		45
	25	18		26
	0	1		37
	80	18		61
	80	18		62 [a]
	25	48		93 [b]

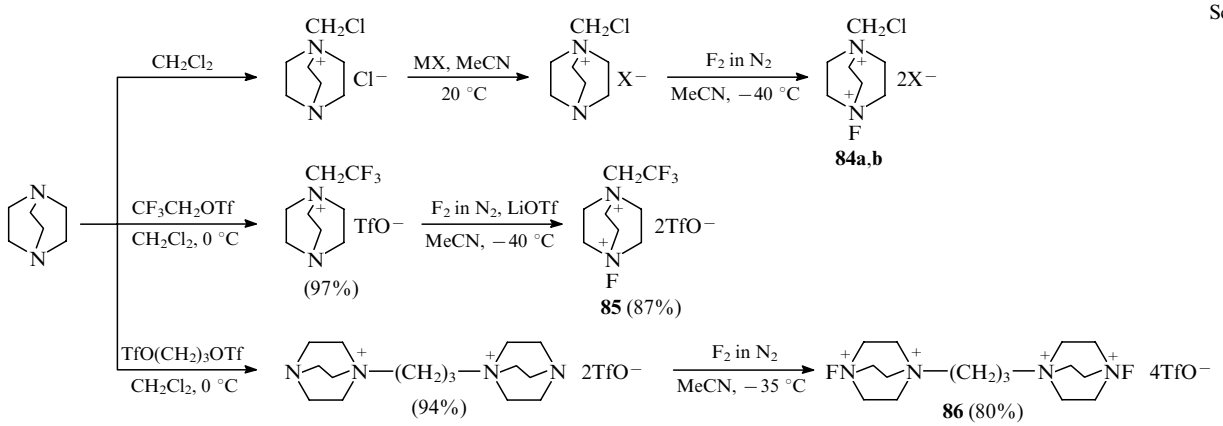
[a] The *cis* : *trans* ratio is 3 : 1. [b] The *cis* : *trans* ratio is 4 : 1.

Fluoroquinuclidinium fluoride (**81a**) was obtained in 83% – 89% yield by direct fluorination of quinuclidine with 10% F_2 in $CFCl_3$ at −78 °C.[169, 171, 175, 176] Later, preparation of *N*-fluoroquinuclidinium salts with other counterions was performed by fluorination of quinuclidine in the presence of the corresponding salts (the Umemoto method). With LiOTf, *N*-fluoroquinuclidinium triflate (**81b**) was obtained in 88% yield (fluorination in MeCN at −33 °C). The salts **81a**,**b** are non-hygroscopic compounds soluble in water and polar organic solvents;[17] they are non-explosive and convenient for experimenting in glassware. The synthetic procedure is simple and gives high yields of target products.



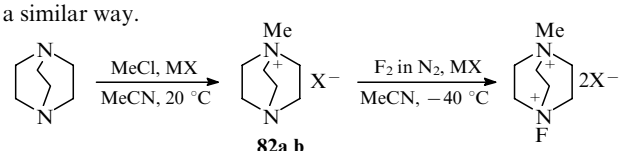
X = BF_4 (**c**, 63%), CF_3CO_2 (**d**, 72%), n-$C_3F_7CO_2$ (**e**, 47%).

Scheme 1



M = Li, Na; X = TfO (**a**), BF_4 (**b**).

The fluorination of 1-alkyl-1-azonia-4-azabicyclo[2.2.2]octane salts with elemental fluorine in the presence of alkali metal salts gives 4-alkyl-1-fluoro-1,4-diazoniabicyclo[2.2.2]octanes. Thus treatment of a mixture of 1-methyl-1-azonia-4-azabicyclo[2.2.2]octane (**82a**) and lithium triflate with elemental fluorine in acetonitrile (3 h, −35 °C) leads to 1-fluoro-4-methyl-1,4-diazoniabicyclo[2.2.2]octane triflate (**83a**) in 88%–94% yield.[167,176–182] The tetrafluoroborate **83b** is prepared in a similar way.



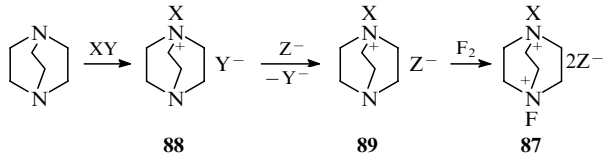
M = Li, Na.

X	Compounds **82**, **83**	Yield of **82** (%)	Yield of **83** (%)
TfO	**a**	86	84
BF_4	**b**	98	94

1,4-Diazabicyclo[2.2.2]octane *N*-oxide can also be used as a starting compound. Its reaction with elemental fluorine in acetonitrile in the presence of $BF_3 \cdot Et_2O$ or HBF_4 at 0 °C results in 75% of *N*-hydroxy-1-azonia-4-azabicyclo[2.2.2]octane tetrafluoroborate.[183]

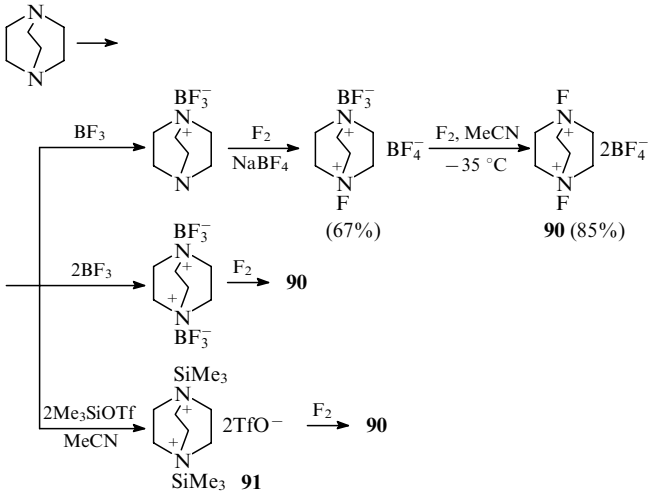
The *N*-fluoro derivatives **84a**,**b** and **85** containing one fluorine atom and the bisfluoro derivative **86** have been synthesised in which two bicyclic fragments are linked through a trimethylene bridge (Scheme 1).[182–187] The structure of some of these salts has been confirmed by X-ray diffraction analysis. Thus the length of the N–F bond in compounds **84a** and **84b** is 1.406 and 1.37(2) Å, respectively.[185]

Preparation of 1-fluoro-1,4-diazoniabicyclo[2.2.2]octanes **87** containing various functional groups at the second nitrogen atom involved treatment of 1,4-diazabicyclo[2.2.2]octane with reagents XY containing the corresponding functional group X and a good leaving group Y. In intermediates **88**, the anion Z is substituted for the leaving group Y. Then the salts **89** are fluorinated with elemental fluorine in inert solvents.[183,188]

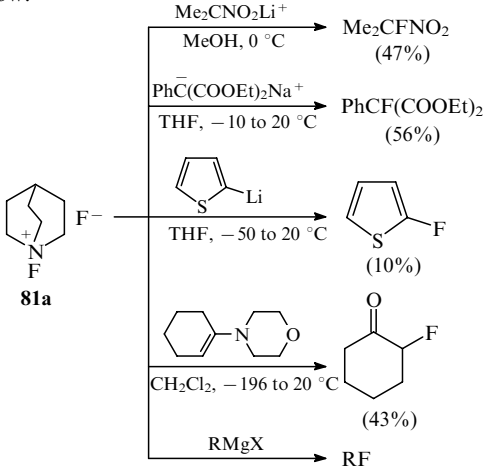


X = OH, OR, OCOR, SO_3, SO_2R, NO_2, NO, $P(O)(OR)_2$;
Z = FSO_3, BF_4, PF_6, ClO_4, R_FSO_3.

The attempts to synthesise 1,4-difluoro-1,4-diazoniabicyclo[2.2.2]octane salts have long been unsuccessful. The synthesis of the reagent **90** could be carried out by fluorination of 1,4-diazabicyclo[2.2.2]octane with elemental fluorine in acetonitrile in the presence of BF_3 and PF_5 or in acetone in the presence of BF_3.[169] Later, polyfluorinated alcohols [*e.g.*, $(CF_3)_2CHOH$)] and sulfuric acid were used as fluorination media (yield > 80%). Yet another convenient approach to the synthesis of the reagent **90** is the fluorination of the trimethylsilyl derivative **91**.[179,180,182,187]



Reagents of the type **81** efficiently fluorinate carbanions, the Grignard reagents and aromatic compounds.[17,166,169,175,181,182,188–191] Some examples of fluorination of organic compounds with the reagent **81a** are given below:[176]

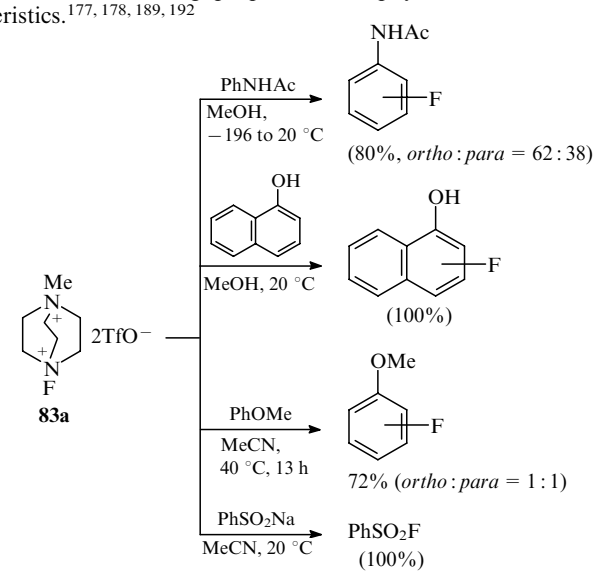


R = Ph, X = Br (26%); R = cyclo-C_6H_{11}, X = Cl (20%).

Fluorobenzene is formed in 22% yield upon reaction of the reagent **81a** with phenyltrichlorosilane.[169]

$$PhSiCl_3 \xrightarrow[THF,\ -50\ ^\circ C]{\mathbf{81a}} PhF \quad 22\%$$

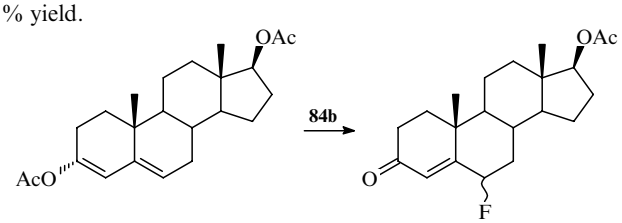
Such popular reagents as 1-fluoro-4-methyl-1,4-diazoniabicyclo[2.2.2]octane bistriflate (**83a**) and 4-chloro-1-fluoromethyl-1,4-diazoniabicyclo[2.2.2]octane bistetrafluoroborate (**84b**) (commercial names, F-TedaBF$_4$ or Selectfluor^{TM}) possess excellent fluorinating properties and physicochemical characteristics.[177, 178, 189, 192]



The reagents **83a**,**b** and **84b** are highly efficient reagents for introducing fluorine into steroids, aromatic compounds, CH-acids and sulfides containing α-hydrogen atoms. These reactions occur under mild conditions and give high yields of fluorination products.[132, 177, 178]

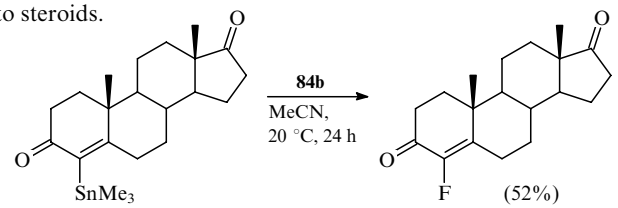
As a rule, fluorination of oxo steroids is performed using acetates or trimethylsilyl derivatives of the corresponding enols as substrates.[192, 193] The yields and regioselectivity can be rather high. Fluorination of hydrocortisone, prednisolone and other oxo steroids with the reagent **84b** gives 6- or 16-monofluoro derivatives under extremely mild conditions.[132]

Reaction of 3,17β-diacetoxyandrosta-3,5-diene with the reagent **84b** in a mixture of acetic acid and 1,2-dichloroethane (3 h, 77 °C) yields a mixture of 6α- and 6β-fluoro derivatives in 81% yield.



The advantages of the reagents **84b** over other fluorinating reagents are illustrated in Table 16.

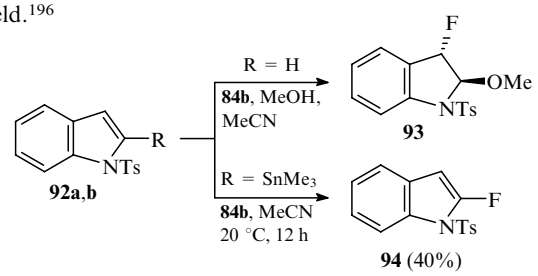
Fluorination of Δ^4- and $\Delta^{1,4}$-3-oxo steroids with the reagent **84b** normally gives a mixture of 4- and 6-fluoro derivatives. The presence of a trimethylstannyl group at the multiple bond of the steroid allows the introduction of fluorine atoms under mild conditions and in a more selective manner. The yields of 4-fluoroandrost-4-ene-3,17-dione and 17-*O*-benzoyl-4-fluorotestosterone prepared by this method are about 50% and the results obtained are not much lower than those obtained with cesium fluoroxysulfate [194] which is potentially explosive.[195] Fluorination with the reagent **84b** can be used for introducing the isotope ^{18}F into steroids.



Fluorodestannylation with reagent **84b** is rather widely used in stereospecific syntheses of complex fluoroalkenes.[184]

$$R^1R_2C{=}CHSnBu_3 \xrightarrow[MeCN,\ 80\ ^\circ C]{\mathbf{84b}} R^1R^2C{=}CF_2$$

Fluorination of 1-tosylindole **92a** with the reagent **84b** in MeCN – MeOH leads to 3-fluoro-2-methoxy-1-tosyl-2,3-dihydroindole **93** in 48% yield.[196] The *trans*-arrangement of the substituents in the reaction product has been confirmed by X-ray diffraction analysis. In this case, the reaction occurs as conjugated vicinal fluoromethoxylation. The substitution of fluorine for the trimethylstannyl group in the derivative **92b** occurs under the action of reagent **84b** in acetonitrile to give compound **94** in 21% yield.[196]

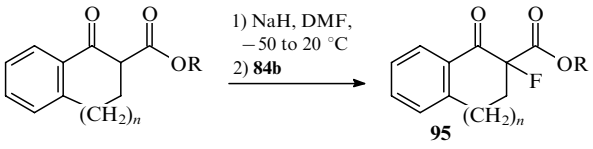


R = H (**a**), Me_3Sn (**b**).

Some other reactions of this kind are documented.[41, 177, 178, 197, 198]

The fluorination of ethyl 1-indanone-2-carboxylate and methyl 5,7-difluoro-1-indanone-2-carboxylate with the reagent **84b** leads to ethyl 2-fluoro-1-indanone-2-carboxylate (yield 80%) and methyl 2,5,7-trifluoro-1-indanone-2-carboxylate (yield 83%).[192]

The fluorination of methyl and menthyl 1-tetralone-2-carboxylates and 1-indanone-2-carboxylates with the reagent **84b** affords the corresponding α-fluoro esters **95** in high yields.[199]



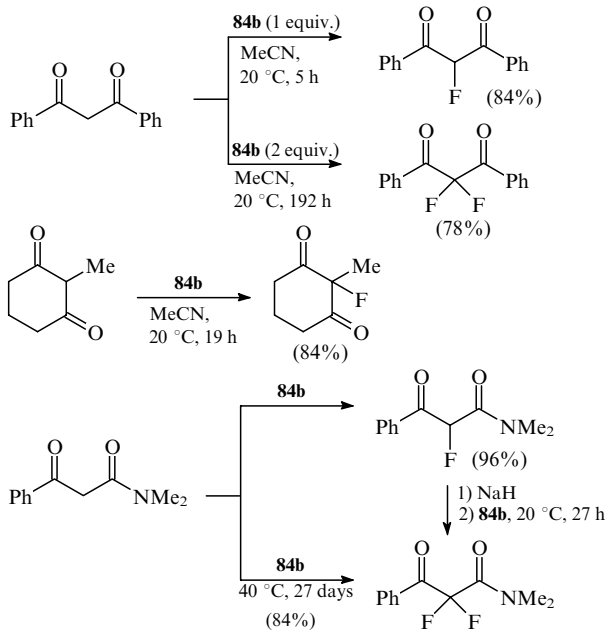
n = 0, 1; R = Me, menthyl.

The oxidation of hydroxy compounds was studied in order to determine the activity of fluorine in the fluorinating reagents **17**, **59** and **84b**. It was found [200] that the reagent **84b** quantitatively oxidises hydroquinone to *p*-benzoquinone (2 h, 25 °C). The yield of *p*-benzoquinone upon treatment with the reagent **17** is low (30%), whereas the reagent **59** does not react with hydroquinone under these conditions.

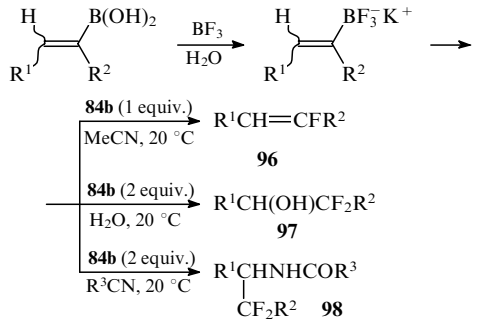
Treatment of acyclic and cyclic 1,3-diketones, β-oxo esters and β-oxo amides with the reagent **84b** results in the corresponding mono- and difluoro compounds.[189, 190] Selective fluorination of β-dicarbonyl compounds with the reagent **84b** is used to obtain biologically active compounds.[188]

Table 16. Fluorination of 3,17β-diacetoxyandrosta-3,5-diene.

Reagent	T /°C	t /h	Yield (%)	The α : β ratio
$FClO_3$	20	1	58	1 : 3
CF_3OF	−70		38	1 : 3
$CF_3C(O)ONa$, F_2	−78	0.25	70	3 : 5
$MeC(O)OF$	−78	0.25	61	1 : 2
53a	40	10	71	1 : 2
84b	20	0.15	95	2 : 3

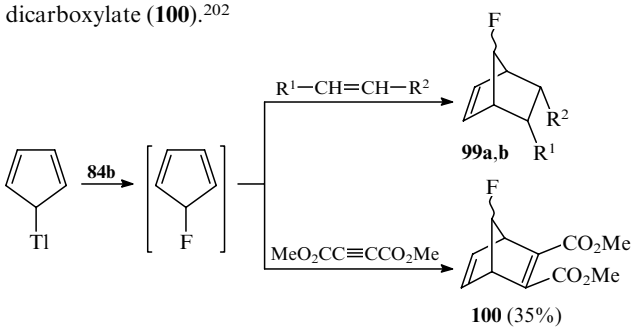


Petasis *et al.*[201] have developed a new procedure for the synthesis of alkenyl fluorides **96**, substituted alcohols **97** and difluoroalkylamides **98**, which is based on fluorination of alkenylboric acids with the reagent **84b** in the presence of boron trifluoride.



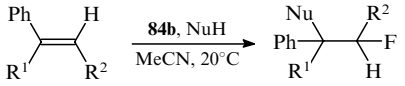
R^1	R^2	Yield of **96** (%)	*E*:*Z* ratio	Yield of **97** (%)	R^3	Yield of **98** (%)
Ph	H	89	1 : 1	69	Me	82
					Et	62
4-MeC_6H_4	H	87	1 : 1	71	Me	68
Ph	Ph	71	5.8 : 1	58	Me	77
Bu	H	58	1 : 1			
4-ClC_6H_4	H			67	Me	81
Ph	Me			75		

The reaction of the tetrafluoroborate **84b** with cyclopentadienylthallium affords 5-fluorocyclopentadiene, which was not isolated but its formation was confirmed by identification of cycloaddition products to acrylates **99a**,**b** and dimethyl acetylenedicarboxylate (**100**).[202]



R^1 = Cl, R^2 = CN (**a**, 18%); R^1 = H, R^2 = CO_2Me (**b**, 17%).

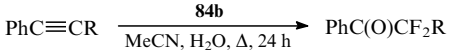
Fluorination of unsaturated compounds with the reagent **84b** occurs in accordance with the Markownikoff rule. The reaction begins with the addition of the pseudo-positive fluorine to the multiple bond and generation of an intermediate carbocation. Its outcome depends on the presence of other nucleophiles in the system. Thus the tetrafluoroborate **84b** reacts with styrene, α-methylstyrene and stilbene in MeCN in the presence of H_2O, AcOH and MeOH, which are involved into the reaction.[7, 203, 204]



R^1	R^2	Nu	Yield (%) (*erythro* : *threo* ratio)
H	H	OH	48
Me	H	OMe	98
Me	H	OH	89
Me	H	OAc	65
Me	H	F	66
H	Ph	OMe	75 (72 : 28)
H	Ph	OH	86 (69 : 31)
H	Ph	OAc	77 (60 : 40)
H	Ph	F	65 (66 : 34)

As can be seen from the data of Table 17, the rate of methoxyfluorination of substituted alkenes increases with a decrease in their ionisation potential which is in favour of the ionic mechanism of the reaction.

In the fluorination of phenylacetylenes with the tetrafluoroborate **84b** in aqueous acetonitrile, the addition of fluorine to the triple bond is accompanied by the addition of water. This reaction occurs with high regioselectivity and yields α,α-difluoroketones. It was shown that the nature of the alkyl substituent in phenylacetylenes influences only the fluorination rate without any effect on the yield of the final products.[197, 198, 205]



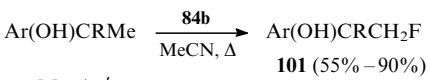
R	k_{rel}	Yield (%)
H	< 0.01	36
Me	1	51
Bu^t	0.63	48
Ph	0.56	51

The reagent **84b** was also used for fluorination of tertiary alcohols. In this case, substitution of fluorine for the hydrogen atom of the methyl group occurs to give β-fluoroalkanols **101**.

Table 17. Relative rates of methoxyfluorination of some alkenes with the reagent **84b** in MeCN.[203]

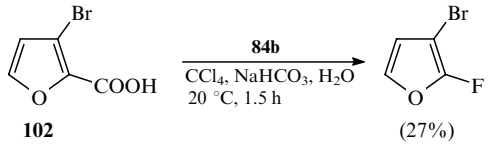
Alkene	*k* [a]	*IP* /eV
2-Phenylprop-1-ene	0.64	8.40
trans-1-Phenylprop-1-ene	0.54	8.36
1,1-Diphenylethylene	1.00	8.24
1,1-Diphenylpropene	8.60	8.14
Indene	0.47	8.40
1,2-Dihydronaphthalene	0.63	8.26
1-Phenylcycloheptene	29.0	7.92
3-Phenyl-1*H*-indene	27.8	7.73
1,2-Dihydro-4-phenylnaphthalene	32.2	7.67
1-Phenyl-6,7-benzocyclohept-1-ene	11.3	7.91

[a] Hereinafter *k* is the relative reaction rate constant with respect to that of 1,1-diphenylethylene.

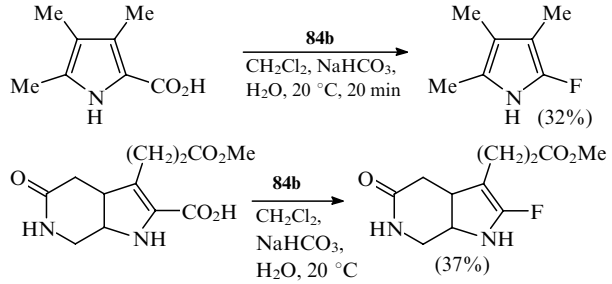


R = Me, Ar′.

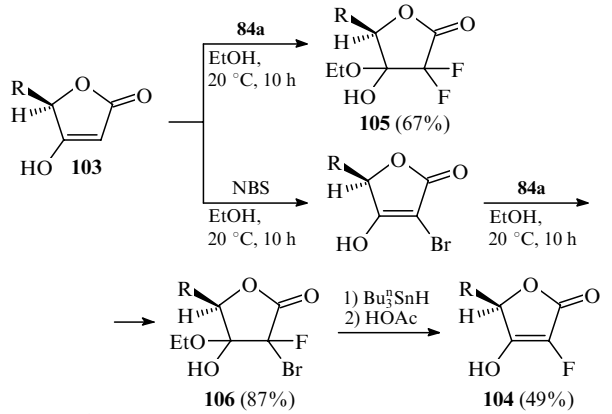
Reaction of the reagent **84b** with some carboxylic acids can occur as fluorodecarboxylation. The possibility of synthesis of fluoro derivatives from the corresponding carboxylic acids is especially important in the furan and pyrrole series. Until very recently, fluorinated furans and pyrroles were not considered to be readily accessible compounds, although they have always attracted attention as starting compounds for the synthesis of fluorinated analogues of natural bactericides. In this particular case, fluorinated reagents with the N–F bond proved to be more efficient than other reagents, in the first place, the elemental fluorine. For example, the reaction of 3-bromofuran-2-carboxylic acid (**102**) with the reagent **84a** in a biphasic system aqueous CCl_4–$NaHCO_3$ yields 3-bromo-2-fluorofuran.[206]



Pyrrole-2-carboxylic acids containing electron-donor substituents give the corresponding 2-fluoropyrroles upon treatment with the reagent **84b** (yields 32%–47%).

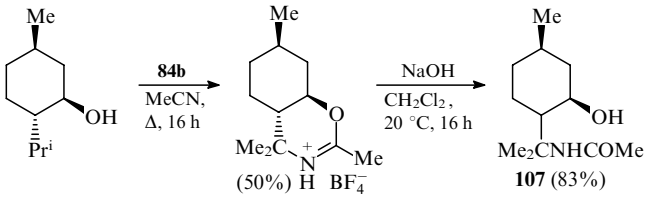


Tetronic acid derivatives attract attention in connection with the presence of its fragment in some natural biologically active compounds. Direct fluorination of 2-deoxy-L-ascorbic acid (**103**) with the reagent **84b** afforded only traces of the 2-fluoro derivative **104**.[207, 208] When the reaction is performed in ethanol, a product of fluorine and the ethoxy group addition to the double bond (compound **105**) is formed. Compound **104** could only be obtained by treatment of the bromofluoro derivative **106** with tributyl-tin hydride (yield 49%).

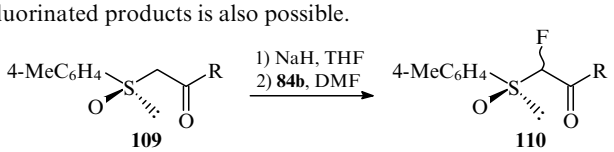


R = HO  ; NBS is *N*-bromosuccinimide.

In the reaction of (–)-menthol with the reagent **84b** in acetonitrile, the hydrogen atom at the tertiary exocyclic carbon atom is selectively substituted by fluorine. Presumably, the further course of this reaction involves the substitution of the fluorine atom with participation of the solvent. Subsequent saponification leads to the reaction product **107**.[209]

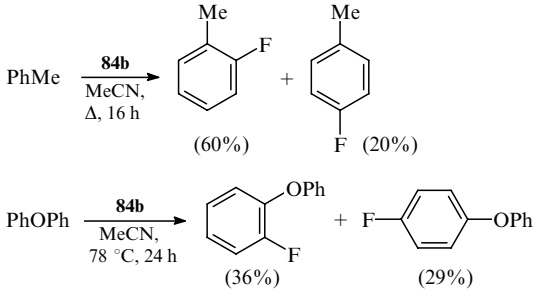


Fluorination of chiral β-oxo sulfoxides **109** with the compound **84b** resulted in a mixture of diastereoisomeric α-monofluoro chiral compounds **110**.[210] The formation of α,α-difluorinated products is also possible.



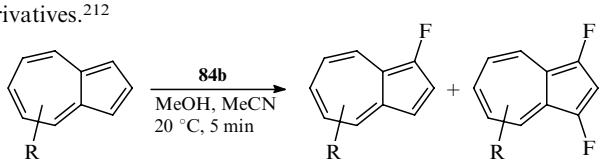
R	Me	Ph	2-pyridyl	4-pyridyl	CH_2F	CHF_2	CF=CHPh
Conversion (%)	60	48	84	73	90	70	87
Yield (%)	80	23	82	52	23	19	70

Benzene derivatives containing electron-donor substituents are fluorinated with the reagent **84b**.[7, 147, 188, 198, 199] The fact that fluorine occupies the *ortho*- or *para*-position testifies to the electrophilic nature of the reagent.



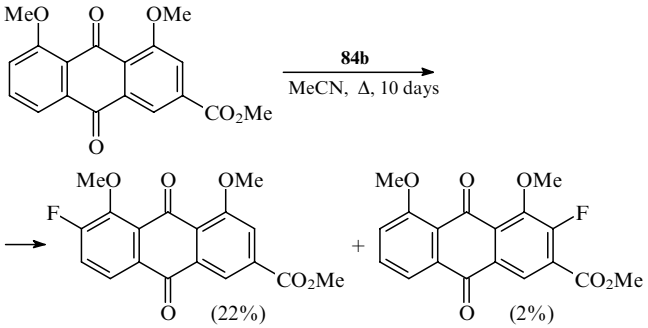
Fluorination with the reagent **84b** can be accompanied by oxidation of functional groups. For example, substituted benzyl alcohols and aromatic aldehydes give the corresponding benzaldehydes or benzoic acids.[211]

Polycyclic aromatic compounds (biphenyl, naphthalene, anthracene, phenanthrene) and their derivatives give monofluoro derivatives.[174, 198] The fluorination of azulene and its derivatives with the reagent **84b** affords a mixture of mono- and difluoro derivatives.[212]

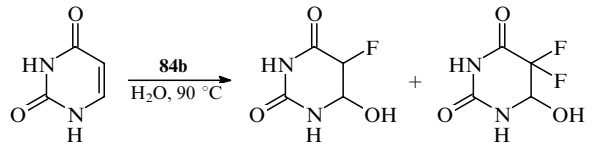


R	Yield of the monofluoro derivative (%)	Yield of the difluoro derivative (%)
H	34	3
6-Pri	27	8
4,6,8-Me3	12	2

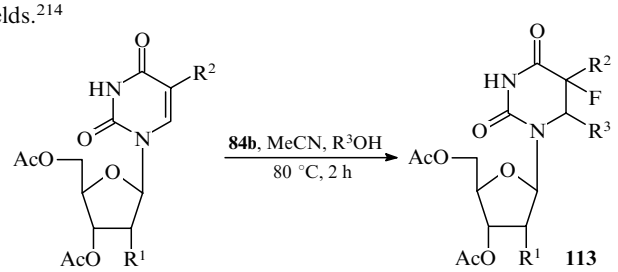
Regioselective fluorination of anthraquinone derivatives with the reagent **84b** presents interest for the synthesis of biologically active compounds.[213]



Reactions of the reagent **84b** with uracil, thymidine and nucleosides in the presence of an external nucleophile occur as conjugated addition. Thus 5-fluoro- (**111**) and 5,5-difluoro-6-hydroxy-5,6-dihydroxyuracils (**112**) were obtained from uracil.[214]

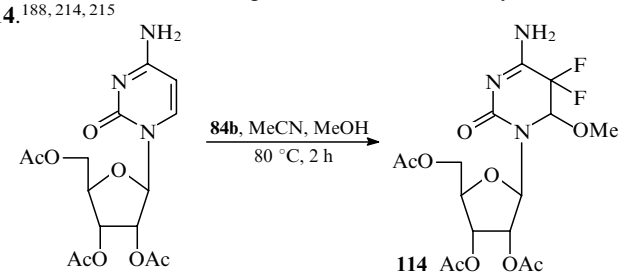


Uracil and thymidine derivatives give compounds **113** in high yields.[214]

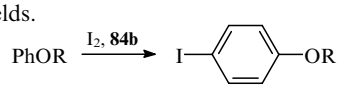


R^1	R^2	R^3	Yield of **113** (%)
OAc	H	OH	80
OAc	H	OMe	85
OAc	H	OAc	82
H	Me	OH	96

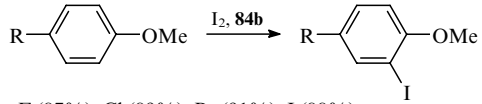
2′,3′,5′-Tri-*O*-acetylcytidine is fluorinated in MeCN in the presence of methanol to give the difluoromethoxy derivative **114**.[188,214,215]



The reagent **84b** is used in iodination of aromatic compounds.[216] Thus treatment of alkylphenyl ethers and *para*-substituted anisoles with iodine in the presence of an equimolar amount of the reagent **84b** affords monoiodo derivatives in high yields.

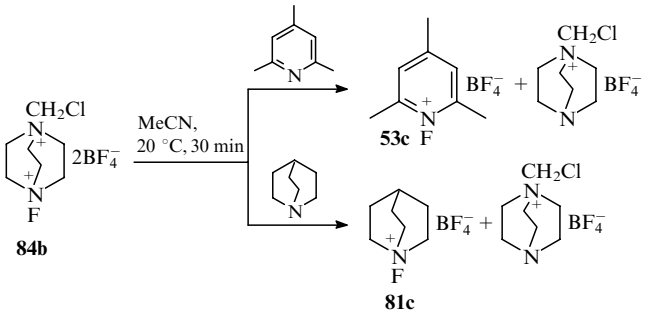


R = Me (89%), $PhCH_2$ (90%), Ph (80%).



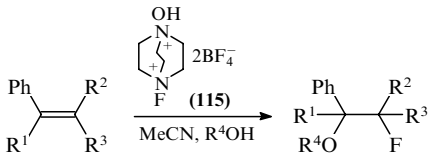
R = F (87%), Cl (89%), Br (91%), I (88%), Ac (90%), CHO (85%), Bu^t (92%).

N-Fluoroquinuclidinium (**81c**), *N*-fluoropyridinium (**53a**) and *N*-fluoro-2,4,6-trimethylpyridinium (**53c**) tetrafluoroborates were obtained in sufficiently high yields by fluorination of the corresponding bases with the reagent **84b**.[217]



Properties of 1-fluoro-4-hydroxy-1,4-diazoniabicyclo[2.2.2]-octane bistetrafluoroborate (**115**) (commercial names, NFTh and Accufluor™) are similar to those of the reagent **84b**. This compound fluorinates the same substrates in high yields and with high stereoselectivity. The reagent **115** can be obtained by fluorination of 1,4-diazabicyclo[2.2.2]octane *N*-oxide with elemental fluorine in acetonitrile at 8 °C in the presence of $BF_3 \cdot Et_2O$ and HBF_4 (yield 75%).[183,218] This fluorinates naphthalene to 1-fluoronaphthalene, phenanthrene to 9-fluorophenanthrene and pyrene to 1-fluoropyrene [219] but is less stable. It was shown [206,220] that the stability of fluorinating reagents in water, acetonitrile, alcohols and aqueous alkali decreases in the following order: **17** > **84b** > **115**.

Fluorination of unsaturated compounds with the reagent **115** in the presence of alcohols occurs as the conjugated vicinal fluoroalkoxylation; the formation of monofluoro derivatives occurs with high regioselectivity (Table 18).[221]



Treatment of alkenes with the reagent **115** in acetonitrile results in the corresponding fluorinated amides.[222]

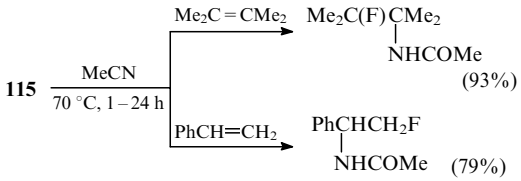
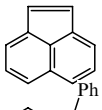
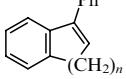


Table 18. Fluorination of substituted styrenes with the reagent **115**.[221]

R^1	R^2	R^3	R^4	T /°C	t /min	Yield (%)	k
H	H	H	H	80	60	90	
			Me	80	60	92	< 0.001
Me	H	H	H	35	60	93	
			Me	35	60	93	0.89
			Ac	35	60	90	
Ph	H	H	H	35	30	95	
			Me	35	30	95	1.00
			Ac	35	30	93	
Ph	Ph	H	H	35	30	98	
			Me	35	30	97	2.5
			Ac	35	30	95	
Ph	Ph	Ph	H	80	60	96	
			Me	80	60	96	0.24

Table 19. The stereochemistry of methoxyfluorination of cyclic alkenes with the reagent **115**.[221]

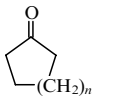
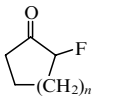
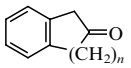
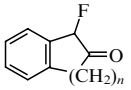
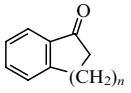
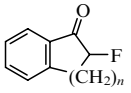
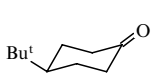
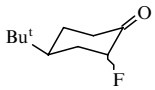
Alkene	*T* /°C	*t* /min	Yield (%)	The *syn* : *anti* ratio
	35	60	92	60 : 40
	35	10	89	53 : 47
	22	5	96	73 : 27
	35	5	96	59 : 41
$n = 1$	35	30	95	25 : 75
	80	45	95	25 : 75
$n = 2$	22	5	97	40 : 60
$n = 3$	35	10	96	1 : 100

The stereochemical features of fluoroalkoxylation were studied with cyclic compounds containing a multiple bond as examples (Table 19).[221]

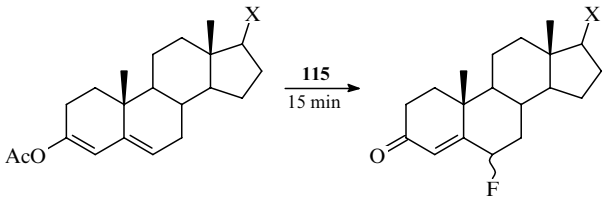
The bistetrafluoroborate **115** is a highly efficient regioselective reagent for the fluorination of ketones (Table 20).[223]

Treatment of *N*-acetylaniline with the reagent **115** leads to a mixture of *o*- and *p*-fluoro-*N*-acetylanilines (67 : 33); 4-*tert*-butyl-1-trimethylsilyloxycyclohexene gives a mixture of *cis*- and *trans*-4-*tert*-butyl-2-fluorocyclohexanones (10 : 1), while anisole in acetonitrile at 20 °C gives a mixture of *o*- and *p*-fluoroanisoles (1 : 2.4) (total yield 83%). Some steroids give monofluoro derivatives under extremely mild conditions.[224–226]

Table 20. Direct fluorination of ketones with the reagent **115**.[223]

Substrate		*t* /h [a]	Product	Yield (%) [b]
	$n = 1$	8		80 (70)
	$n = 2$	8		92 (84)
	$n = 3$	8		85 (78)
	$n = 4$	8		85 (78)
	$n = 1$	1		88 (80)
	$n = 2$	0.5		81 (75)
		8		82 (72)
	$n = 1$	8		95 (88)
	$n = 2$	8		95 (88)
	$n = 3$	8		90 (82)
		2		85
Bu^n_2CO		12	$Bu^nCOCHFPr^n$	91 (81)
$C_6H_{13}COMe$		10	$C_5H_{11}CHFCOMe$	86 (78)
PhCOMe		48	$PhCOCH_2F$	33 (23)
$PhCOCH_2Me$		30	PhCOCHFMe	88 (80)
$PhCOCHMe_2$		12	$PhCOCFMe_2$	83 (74)

[a] Reaction conditions: 2 mmol of ketone, 2.2 mmol of the reagent **115** in MeCN (30 ml), 80 °C. [b] The yield was calculated from the ^{19}F NMR spectroscopy data for a mixture of reaction products prior to workup. The isolated yields are given in parentheses.



(89%, α : β = 1 : 2.2)

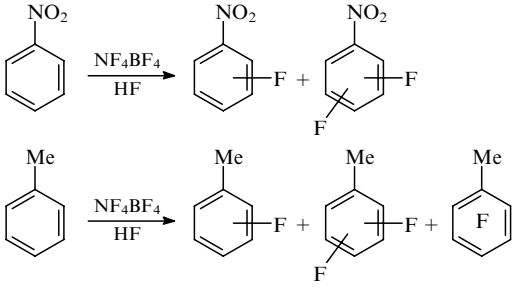
X = $COCH_2OAc$.

The reactivities of the fluorinating reagents **84b**, **115** and *N*-fluoro-2,6-difluoropyridinium tetrafluoroborate in the fluorination of dibenzofuran, diphenyl ether and biphenyl were found to be similar. *ortho*-Isomers are predominant in the reaction products.[174]

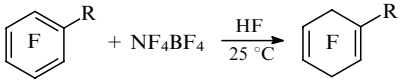
IV. Some examples of fluorination with inorganic tetrafluoroammonium salts

Inorganic tetrafluoroammonium salts (*e.g.*, NF_4BF_4, NF_4SbF_6) are formal analogues of organic *N*-fluoro derivatives.

Christe *et al.*[227, 228] showed that NF_4BF_4 fluorinates benzene and its derivatives in anhydrous HF to give fluorinated products.

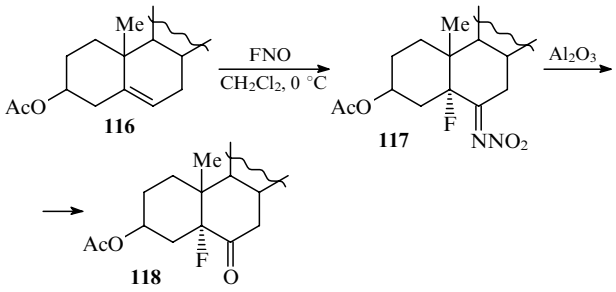


The fluorination of nitrobenzene results in substitution of both the hydrogen atoms of the benzene ring (the predominant formation of the *meta*-isomer testifies to electrophilic substitution) and the nitro group, resulting in fluorobenzene. The reaction of tetrafluorobenzene, pentafluorobenzene and hexafluorobenzene with NF_4BF_4 gives perfluorocyclohexadienes, *i.e.*, in this case, fluorine adds to the multiple bonds.[227–229]

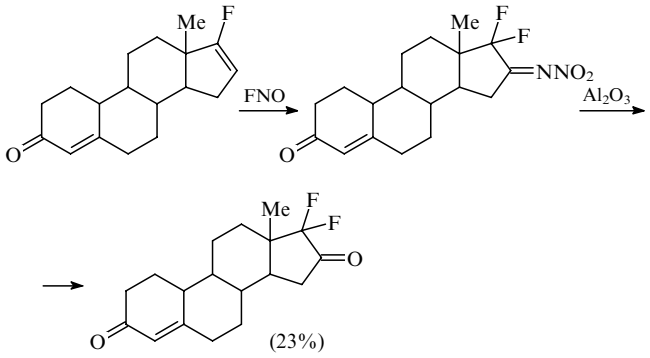


R = H, F.

Among inorganic fluorinating reagents, nitrosyl fluoride is worthy of note. This compound is a low-boiling highly toxic gas, and its application as a fluorinating reagent is very limited. Nitrosyl fluoride was used for fluorination of cholesteryl acetate **116** to give 5α-fluoro-6-nitroimine **117** in high yield. The latter was further converted into the corresponding ketone **118**.[230]



Fluorination of steroidal vinyl fluorides with nitrosyl fluoride leads to α,α-difluoro ketones *via* the intermediate nitroimines.[231, 232]

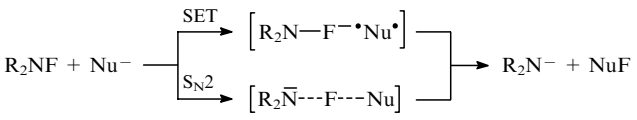


Prakash *et al.*[233, 234] proposed to use the Olah reagent (hydrogen fluoride in pyridine) for the activation of nitrosyl fluoride. This results in a highly active fluorinating reagent which fluorinates many organic compounds. Thus the fluorination of ketoximes and thioacetals affords the corresponding *gem*-difluoro derivatives, while alkynes and alkenes are fluorinated to tetrafluoro- and trifluoroalkanes in sufficiently high yields. Interestingly, fullerene C_{60} is polyfluorinated with nitrosyl fluoride. Treatment of alkyl phenyl sulfides with this reagent affords products of substitution of the hydrogen atoms of the alkyl group by fluorine atoms.[233, 234]

V. On the mechanism of fluorination with *N*-fluoroamines and their analogues

The experimental data concerning the use of *N*-fluoroamines and their analogues in organic synthesis altogether suggest that these compounds are electrophilic fluorinating agents. Inasmuch as the formation of F^+ is a thermodynamically very unfavourable process and this species is very unstable and can be detected only by spectral methods in the gas phase, the formation of F^+ in fluorination is hardly probable.[132, 184] This contradiction has led to an idea of specific polarisation of the N–F bond with the appearance of a partial positive charge on the fluorine atom, *i.e.*, the concept of 'pseudo-positive' fluorine. However, the idea that *N*-fluorinating reagents are the sources of 'pseudo-positive' or 'electrophilic' fluorine does not contribute any rationale to the real mechanism of fluorination. However, *N*-fluoro reagents can also be regarded as sources of the fluorine radical the existence of which is established (see Ref. 175). The oxidising properties of *N*-fluorinating reagents, particularly their ability to displace iodine from inorganic iodides (this reaction is of analytical importance) is attributed to the electrophilic nature of the fluorine radical.

As a matter of fact, the mechanistic studies of fluorination available are aimed at establishing whether this occurs as single-electron transfer (SET), nucleophilic substitution at the fluorine atom (S_N2) or both.



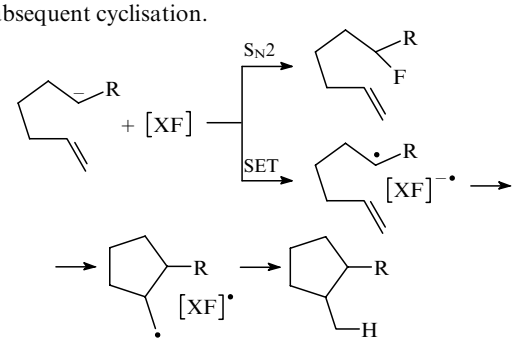
In considering the mechanism of fluorination, one should take into account that *N*-fluorinating reagents comprise two groups of compounds, which differ basically in their structures, *viz.*, R_2NF and $[R_3NF]^+A^-$. In addition, the role of nucleophiles can be played by compounds of various classes (*e.g.,* aromatic, unsaturated, organometallic, *etc.*), whereas the term 'fluorination' embraces various types of reactions (substitution, addition, *etc.*).

Hence, all the plausible mechanisms of fluorination can in general be realised. The mechanism established in a specific study may be true only for the particular group of *N*-fluorinating reagents and substrates and for the particular reaction types that had been studied.

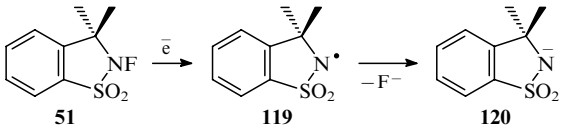
Differding *et al.*[106, 108, 235, 236] who studied the fluorination of various substrates with *N*-fluoro sultam **51** attempted to distinguish between S_N2 and SET mechanisms. To this end, they compared experimental rate constants with those calculated theoretically within the single-electron transfer theory. These calculations were based on the known standard redox potentials, E°, and Marcus rearrangement energies for both reactants.

As can be seen from Table 10, the values of experimental constants are by many orders of magnitude higher than might be expected based on the electron transfer concept, *i.e.*, the reaction does not occur as a single-electron transfer. Correspondingly, the S_N2 mechanism is realised in this case.

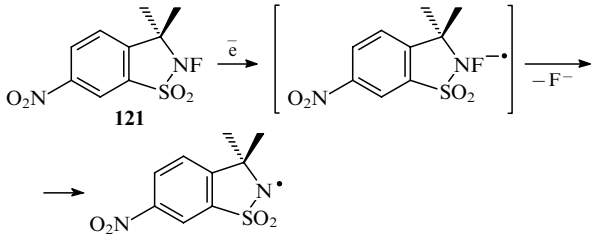
The reaction of an ester enolate (derived from citronellate) with *N*-fluoro reagents leads exclusively to the products of electrophilic fluorination at the carbon atom of the carbanion centre. This finding provides additional support in favour of the S_N2 mechanism.[108, 235] If the reaction proceeded as a single-electron transfer, the substrate would undergo oxidation with subsequent cyclisation.



However, there are literature data in favour of the SET mechanism. This process is partly realised in fluorination with XeF_2, which is known to react by a radical mechanism. The electrochemical reduction of *N*-fluoro sultam **51** results in electron transfer, which is accompanied by simultaneous cleavage of the N–F bond with elimination of the fluoride anion and reduction of the reagent **51** to the radical **119** and further to the amide anion **120**.[106, 108, 235]



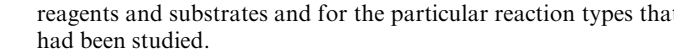
The electrochemical reduction of *N*-fluoro sultam **121** containing a nitro group in the benzene ring yields a radical anion as an intermediate.



According to Differding *et al.*,[235] this step is characteristic of compounds showing high electron affinity.

It should be noted that reactions of *N*-fluoro sultam **51** with nucleophiles (see Table 10) follow the S_N2 mechanism.

In studies of photochemical electrophilic fluorination of aromatic compounds[160, 161] it was concluded that the reaction occurs through the initial formation of a donor-acceptor complex, since the UV spectra contain absorption bands characteristic of a charge transfer complex (CTC).



The excitation energy, $h\nu_{CTC}$, is correlated with the ionisation potential of the aromatic donor. With a decrease in *IP*, $h\nu_{CTC}$ decreases favouring the electron transfer, as a result of which the substrate becomes potentially more reactive in electrophilic fluorination where the complex is converted into the final reaction products.

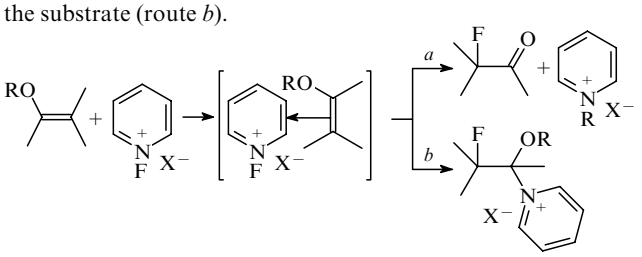
A mechanism involving the formation of CTC was also proposed by Des Marteaux *et al.*[80] who studied fluorination with $(CF_3SO_2)_2NF$ (**14a**).

The study into the single-electron transfer mechanism carried out by Umemoto *et al.* (see Ref. 144) was based primarily on the analysis of the composition of fluorination products. The concept of the single-electron transfer, which implies the formation of the fluorine radical, was used for rationalisation of various fluorination processes, *viz.*, reactions of *N*-fluoropyridinium salts with anions, neutral substrates, the Grignard reagents, alkenes, aromatic compounds, *etc.*

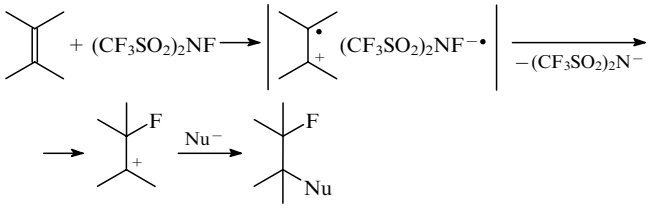
According to Umemoto, three different mechanisms can be realised in the fluorination of unsaturated compounds, *viz.*, a single-electron transfer, classical electrophilic addition and a purely radical mechanism.

In accordance with one of these schemes, the first step of this reaction envisages the formation of a π-complex between the fluorinating reagent and the enol ester/ether.

Further reactions can follow two different routes, *viz.*, transfer of fluorine to the substrate and transfer of the radical R to the pyridinium salt (route *a*) and the addition of the pyridinium salt to the substrate (route *b*).



Fluorination can also occur through the intermediate formation of a radical cation from the unsaturated system and radical anion from the fluorinating reagent.



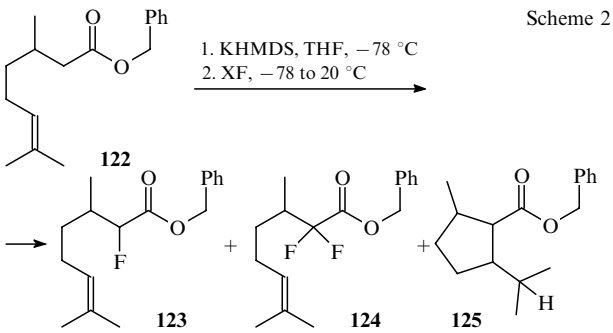
It should be noted that the experimental data currently available do not contradict these schemes. Thus the regio- and stereoselectivity of alkene fluorination fits well into the mechanism of formation of a fluoro carbocation as an intermediate species.[7, 79, 175] Alkenes in which the intermediate carbocation cannot be stabilised by substituents (*e.g.*, oct-1-ene or cyclohexene) do not react with the fluorinating reagent **84b**. As expected, polar solvents that favour the formation of a complex between the substrate and the fluorinating reagent facilitate fluorination.

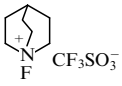
The generation of intermediate radical species from fluorinating reagents is confirmed by the formation of products of their reaction with the radicals present in the system. The formation of radical anions is confirmed by their capture with 1,4-benzoquinone.

The introduction of electron traps suppresses the conversion of alkenes. Thus the conversion of *trans*-β-methylstilbene in the reaction with $(CF_3SO_2)_2NF$ decreases from 100% to 80% in the presence of 1,4-dinitrobenzene

The fluorination of benzyl citronellate (**122**) with *N*-fluorinating reagents gives a mixture of α-mono- (**123**) and α,α-difluoro derivatives (**124**), which points to the electrophilic nature of the reagent, whereas the reaction with XeF_2 affords the cyclic product **125** typical of radical fluorination (Scheme 2).[235]

Scheme 2



Fluorinating reagent	Yield (%) [a]			
	123	**124**	**125**	**122**
51	59 (43)	28 (18)	0	< 10 (4)
17	21 (21)	31 (31)	0	20 (20)
	64 (45)	23 (18)	0	13 (6)
XeF_2	11 (10)	3 (3)	10 (6)	10 (10)

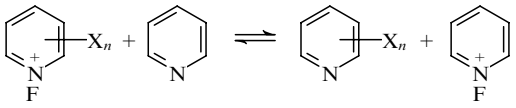
[a] The figures in parentheses refer to the yields of the isolated compound.

VI. The effect of the solvent in fluorination reactions with *N*-fluoro amines and their analogues. Comparative reactivities of fluorinating reagents containing the N – F bonds

Despite the evident role of the medium in fluorination reactions, the data accumulated in this area have not yet been adequately generalised and analysed in the literature. Systematic studies in this field have been undertaken comparatively recently by Solkan and Fainzilberg.[237–239]

A programme for quantum-chemical calculations aimed at quantitation of various effects of the solvent (the effect of solvation, in particular) on the thermodynamic parameters of the fluorination reaction was elaborated. This programme utilises both the point dipole model and the polarising continuum model in the framework of semi-empirical quantum-chemical methods (MNDO, AM-1, MNDO-PM3).

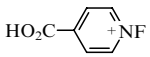
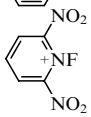
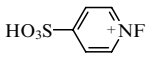
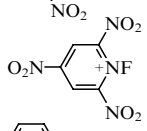
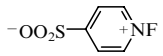
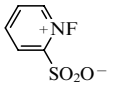
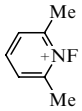
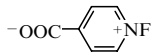
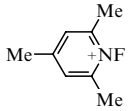
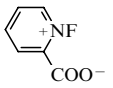
The studies [237, 239] were carried out with *N*-fluoropyridinium salts, which are readily available compounds. Their fluorinating ability varies over a wide range depending on the electronic and steric characteristics of substituents (NO_2, SO_2F, CF_3, CO_2Me, F, Cl, Br, Me, CO_2H, SO_2OH, CO_2^-, SO_3^-) whose position and number can be varied. Unsubstituted pyridine was selected as a substrate.



The reaction of *N*-fluoropyridinium salts with non-substituted pyridine is convenient because it allows comparison of the reactivities of fluorine carriers both with each other and with that of a classical fluorinating reagent such as the *N*-fluoropyridinium cation. If the enthalpy of the reaction is negative, a given fluorine carrier surpasses *N*-fluoropyridinium in the fluorinating ability; in the case of positive enthalpy, it is inferior to the latter.

In order to establish the criterion of fluorinating activity (the thermal effect, ΔH) of an exchange reaction in the gas phase, ΔH(g), and in polar solvents, ΔH(s), the authors calculated the corresponding enthalpies of formation of the reactants with account of the solvent effect within the framework of the point

Table 21. Thermodynamic parameters of the fluorination of pyridine with *N*-fluoropyridinium salts.[237]

Fluorinating reagent	ΔH(g) /kcal mol^{-1}	ΔH(s) /kcal mol^{-1}	Fluorinating reagent	ΔH(g) /kcal mol^{-1}	ΔH(s) /kcal mol^{-1}
	16.0	10.6		7.9	5.8
	31.9	26.9		8.1	7.6
	43.1	36.8		−76.4	35.8
	−2.6	0.4		−91.6	24.7
	−4.9	0.9		−79.0	38.9
	−7.6	0.9		−101.1	22.0

dipole model [ΔH_f(g) and ΔH_f(s)]. The results of this study are summarised in Table 21.[237,239]

An analysis of experimental data[237,239] and some results presented in Table 21 allow the following conclusions about the role of solvation in fluorination with *N*-fluoropyridinium salts.

1. In strongly polar solvents, the ΔH(s) values are higher (CO_2Me, Cl, Br, Me) or lower (NO_2, F, CF_3, SO_2F) than those in the gas phase.

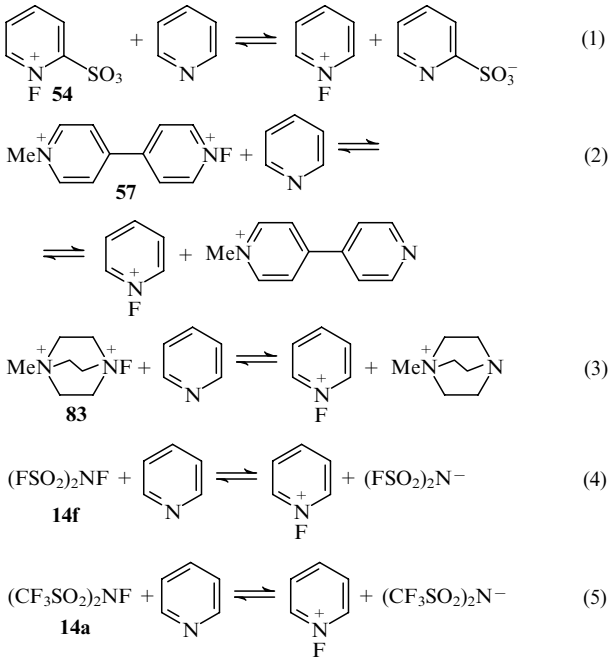
2. The additivity of the substituent effects holds to considerable extent.

3. The largest increase in ΔH in the transition from the gas to the liquid phase is observed for internal *N*-fluoropyridinium salts containing the CO_2^- and SO_3^- groups as substituents. In the latter case, the effect is so strong that it can be attributed to the crucial role of solvation in the fluorination reaction.

However, the fluorinating ability of *N*-fluoropyridinium salts containing uncharged substituents in the ring depends on the number of substituents and their electronic effects rather than on the solvation effect. In order to increase the fluorinating activity of a compound containing uncharged substituents up to the level of internal *N*-fluoropyridinium salts, it is necessary to introduce not less than three electron-accepting nitro groups into the molecule (see Table 21). Hence, the introduction of a substituent able to form an internal salt into *N*-fluoropyridinium salt and the use of polar solvating solvents is a simpler procedure, which enhances the fluorinating activity of the reagent.

Solkan and Fainzilberg[240] have established the activation barriers for the reaction of *N*-fluoropyridinium salts with pyridine. These calculations made it possible to select the most plausible transition states and to calculate the activation energies (E_a) in a highly polar solvent. Comparison of E_a values and enthalpies of fluorination in solutions ΔH(s) has revealed their nearly linear dependence, *e.g.*, an increase in the heat of reaction by 3 kcal mol^{-1} was accompanied by the decrease in the activation barrier by $\sim$ 1 kcal mol^{-1}. Thus, the heats of fluorination reactions can be used in estimation of the corresponding activation energies without determination of the structure of the transition state.

Other types of *N*-fluoro derivatives extensively employed in recent synthetic studies have also been studied.[239] The calculations were performed by a semi-empirical quantum-chemical method (MNDO-PM3) using a polarising continuum model.[241] The thermal effects of analogous reactions were calculated for comparative assessment of fluorinating activities of various fluorine carriers in solvents of different polarities.



The calculation of enthalpies of formation of the reagents and the reaction products in the gas phase [ΔH(g)] and in solution [ΔH(s)] is an indispensable step in the calculation of ΔH. In the latter case, the calculations of the Gibbs energy of solvation were carried out for charged molecules. The results of these studies are summarised in Table 22.

As can be seen from these data, the fluorination reactions (1)–(5) are exothermic even if solvents of medium polarity ($\varepsilon = 10$) are used. This implies that the reagents **14a**,**f**, **54**, **57** and **83** surpass *N*-fluoropyridinium in fluorinating activity. An increase in the solvent polarity results in manifestation of difference in the behaviour of compounds **14a**,**f**, **54** and **57a**, **83**. For the

Table 22. The thermal effects of fluorination of pyridine [reactions (1)–(5)] with *N*-fluoro derivatives in solvents of different polarity.[237]

Reaction	$-\Delta H$(s) /kcal mol^{-1}			
	$\varepsilon = 10$	$\varepsilon = 20$	$\varepsilon = 30$	$\varepsilon = 78$
(1)	−14.7	−21.9	−24.7	−27.8
(2)	−17.6	−13.6	−12.2	−10.4
(3)	−45.7	−40.4	−38.6	−36.4
(4)	−14.5	−21.3	−23.6	−26.6
(5)	−29.7	−36.1	−38.4	−41.2

former two compounds, the thermal effect of fluorination increases with an increase in the dielectric constant of the solvent and decreases for the latter two compounds. Such a behaviour of compounds **57a** and **83** seems to be due to their structural features, since both of them are dications.

Compounds **83** and **14a** were the most reactive among other fluorine carriers tested as can be judged from the thermal effects of the fluorination reaction listed in Tables 21 and 22. However, according to Solkan and Fainzilberg[237,238] the choice of an 'absolute champion' among fluorinating reagents is problematic, since their reactivities depend on reaction conditions, first of all, on the nature and polarity of the solvent.

On the whole, the approach to the study of the solvent effects in fluorination reactions[237–240] holds great promise, for the information it provides is comprehensive. This approach makes it possible: (*i*) to obtain the main thermodynamic characteristics of the fluorination reaction, *viz*., its thermal effect, which serves as a basis for quantitative evaluation of the fluorinating activity of fluorine carriers in various solvents; (*ii*) to determine the values of heats of solvation for all reactants (the starting compounds and reaction products); (*iii*) to perform comparative analysis of heats of reaction in order to evaluate the differences in fluorination rates for various reagents and in different solvents. The use of this approach which takes account of the contribution of solvation to the thermodynamic mechanism of the fluorination reaction is equally efficient both in predicting the optimum conditions for a reaction (the choice of a fluorinating reagent, solvent, *etc*.) and in the design of new fluorine carriers.

As can be seen from the material presented in this section, taking account of the contribution of the solvent has in fact opened a way to the creation of a versatile scale for quantitation of relative reactivities of *N*-fluoro derivatives. Estimation of this contribution increases the accuracy of prognosis, for it brings them closer to the real experimental conditions. Evidently, the kinetic estimates are more reliable but the kinetic characteristics can hardly be obtained for all currently known reagents. In this context, a demand arose to elaborate a criterion for estimating fluorinating activity with a relatively simple procedure.

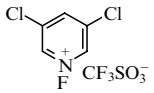
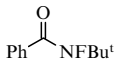
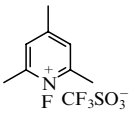
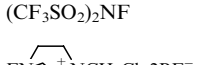
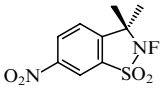
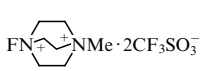
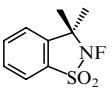
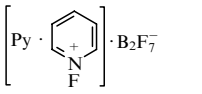
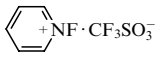
Until recently, electrochemical reduction at the N–F bond was in fact the only general approach to the quantitative estimation of the fluorinating activity of *N*-fluoro reagents, the electrochemical reduction potential being the main criterion. Papers devoted to this problem are scarce, since electrochemical reduction is a methodologically complicated procedure. Therefore, these studies were carried out with a limited number of *N*-fluoro reagents and the results were poorly reproducible.

The values of electrochemical reduction potentials for several *N*-fluoro reagents are summarised in Table 23.[242,243]

Since the values of E_{redox} are poorly reproducible due to the differences in the experimental protocols of electrochemical studies, their application for quantitative estimation of fluorinating activity is problematic. According to Differding and Bersier,[243] $(PhSO_2)_2NF$, which is analogous to *N*-fluoroquinuclidinium, is one of the most reactive fluorinating reagents of the given series, while Gilicinski *et al*.,[242] assign it to the least reactive reagents, which ranks far below *N*-fluoroquinuclidinium.

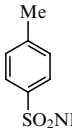
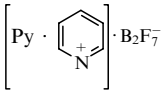
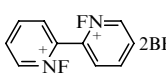
It is of note that $E_{1/2}$ seems to be a more reliable criterion than E_{redox}. According to recent data,[244] in some cases it is difficult to

Table 23. The values of the redox potential, E_{redox}, and the half-wave potential, $E_{1/2}$, for several fluorinating reagents.[a]

Reagent	E_{redox}	$E_{1/2}$	Ref.	Reagent	E_{redox}	$E_{1/2}$	Ref.
	−0.10	+0.38	243		−1.53	−1.48	243
$(PhSO_2)_2NF$	−0.78	–	242				
	−0.54	+0.16	243				
	−0.37	–	242		−1.58	−0.53	243
	−0.63	+0.085	243				
	−0.65	−0.21	243	$(CF_3SO_2)_2NF$	+0.18	–	242
					−0.04	–	242
	−0.75	−0.23	243		−0.04	–	242
	−1.21	−0.31	243		−0.34	–	242
$4\text{-}MeC_6H_4SO_2NFMe$	−2.10	–	242		−0.47	–	242
	−1.44	−0.50	243				
	−1.52	−1.30	243	$4\text{-}MeC_6H_4SO_2NFPr^n$	−2.10	–	242

[a] In MeCN relative to the standard calomel electrode.

Table 24. Some commercially available *N*-fluoro reagents.

Reagent	Properties			Manufacturer
	state of aggregation	B.p. /°C	M.p. /°C	
	liquid	49	–	FLCHEM [a]
	white crystalline substance	–	266 – 268	FLCHEM [a]
	the same	–	185 – 187	ALD,[b] FLCHEM,[a] PCR [c]
	"	–	234 (dec.)	ALO, [b] APCI, [d] FLCHEM,[a] JANCHIM [e]
	50% of reagent on Al_2O_3	–	–	ALD-SGL [f]
	white crystals	(see [g])	42 – 44	ALD,[b] PCR [c]
$(PhSO_2)_2NF$	the same	–	114 – 116	ALD,[b] PCR,[c] FLCHEM,[a] ALD-SGL [f]
	dark crystals	–	196 – 197	ALD,[b] PCR,[c] FLCHEM,[a] ALD-SGL [f]
	white crystals	–	166 – 168	AP-SC [h]

[a] FLCHEM — Fluorochem Ltd, Wesley St., Old Glossop, Derbyshire, SK 13 9RY UK; [b] ALD — Aldrich Chemical Company, Milwaukee, WI 53201 USA; [c] PCR — PCR Inc., Gainesville, FL 32602 USA; [d] APCI — Air Products and Chemicals Inc., Allentown, PA 18195-1501 USA; [e] JANCHIM — Janssen Pharmaceuticalaan, 3, 2440 Geel, Belgium; [f] ALD-SGL — Allied-Signal Inc., Buffalo, NY 14210 USA; [g] B.p. 90 °C (0.01 Torr); [h] AP-SC — Apollo Scientific Ltd, SK4 1RS, Cheshire, UK.

determine E_{redox} with a sufficiently high degree of reliability because of broad maxima on the electrochemical wave curves. Differding and Bersier [243] also hold this viewpoint and offer an original approach to the estimation of the fluorinating ability of *N*-fluoro reagents. This approach is based on a semi-empirical quantum-chemical calculation of the 'reductant couple' (the original term introduced by the authors), $\Delta H_f^\circ(R_3N) - \Delta H_f^\circ(R_3N^+F^-)$; however, a consistent scale of relative reactivities could be obtained only for structurally related compounds, *e.g.*, of the pyridinium series.[245]

On the whole, all presently known attempts to create scientific grounds for comparative quantitative assessment of the fluorinating activity of various *N*-fluoro reagents are represented by the examples described in this section. A wealth of quantitative estimates is scattered over numerous synthetic papers which mainly emphasise the crucial role of the *N*-fluorinating reagent structure on fluorination.

VII. Conclusion

The data surveyed in this review demonstrate the intensive development of the chemistry of fluorine carriers in the past decades. Fluorination with *N*-fluoro reagents has stimulated the research in the field of fluorine chemistry as a whole and provided a basis for fine organic synthesis, the synthesis for organofluorine compounds of medicinal purposes, in particular. A technology for the production of a series of fluorine carriers has been developed by leading chemical companies of the USA, Great Britain and Japan. The main characteristics of some commercially available *N*-fluoro reagents are given in Table 24.

References

1. *Chemistry of Organic Fluorine Compounds II. ACS Monograph 187* (Eds M Hudlicky, A E Pavlath) (Washington, DC: American Chemical Society, 1995)
2. G G Furin, in *New Fluorinating Agents in Organic Synthesis* (Eds L German, S Zemskov) (Berlin: Springer, 1989) p. 34
3. N Isikava (Ed.) *Soedineniya Ftora* (Fluorine Compounds) (Translated into Russian, Moscow: Mir, 1990)
4. T Umemoto *J. Synth. Org. Chem.* **50** 338 (1992)
5. R E Banks *J. Fluor. Chem.* **87** 1 (1998)
6. G S Lal, G P Pez, R G Syvret *Chem. Rev.* **96** 1737 (1996)
7. G S Lal *J. Org. Chem.* **58** 2791 (1993)
8. V Murtagh *Perform. Chem.* **6** 35 (1991); *Ref. Zh. Khim.* 5 Zh 388 (1993)
9. K Kawada, K Nukui *Kagaku to Kogyo (Tokyo)* **46** 1730 (1993); *Chem. Abstr.* **120** 77 096 (1994)
10. W Han *Diss. Abstr. Int. B* **53** 6304 (1993); *Chem. Abstr.* **121** 157 197 (1994)
11. R Bohlmann *Org. Synth. Highlights II* 243 (1995); *Chem. Abstr.* **125** 166 844 (1996)
12. L Strekowski, A S Kiselyov *Adv. Heterocycl. Chem.* **62** 1 (1995)
13. J A Wilkinson *Chem. Rev.* **92** 505 (1992)
14. R E Banks *Spec. Chem.* **17** 252 (1997); *Chem. Abstr.* **128** 34 366 (1998)
15. M Zupan, S Stavber *Trends Org. Chem.* **5** 11 (1995); *Chem. Abstr.* **126** 305 272 (1997)
16. S Stenson *Chem. Eng. News.* **69** 691 (1991); *Ref. Zh. Khim.* 11 N 129 (1992)
17. G P Pez, A G Gilicinski, R G Syvret, G S Lal *J. Fluor. Chem.* **58** 140 (1992)
18. T C Simon, F W Hoffman, R B Beck, H V Holler, T Katz, R J Koshar, E R Larsen, J E Mulvaney, K E Paulson, F E Rogers, B Singleton, R E Sparks *J. Am. Chem. Soc.* **79** 3429 (1957)
19. R E Banks, W M Cheng, R N Haszeldine *J. Chem. Soc.* 3407 (1962)
20. R E Banks, A E Ginsberg, R N Haszeldine *J. Chem. Soc.* 1740 (1961)
21. I V Vigalok, G G Petrova, S G Lukashina *Zh. Org. Khim.* **19** 1347 (1983) [a]
22. R E Banks, V Murtagh, E Tsiliopoulos *J. Fluor. Chem.* **52** 389 (1991)
23. R E Banks, R N Haszeldine, R Hatton *Tetrahedron Lett.* 3993 (1967)
24. V P Polishchuk, B Ya Medvedev, N N Bubnov, L S German, I L Knunyants *Izv. Akad. Nauk SSSR, Ser. Khim.* 2805 (1972) [b]
25. V R Polishchuk, L S German *Tetrahedron Lett.* 5169 (1972)
26. O Dutt Gupta, R L Kirchmeier, J M Shreeve *J. Am. Chem. Soc.* **112** 2383 (1990)
27. R E Banks, E Tsiliopoulos *J. Fluor. Chem.* **34** 281 (1986)
28. S T Purrington, W A Jones *J. Org. Chem.* **48** 761 (1983)
29. S T Purrington, W A Jones *J. Fluor. Chem.* **26** 43 (1984)
30. H Gershon, J A A Renwick, W K Wynn, R D'Ascoli *J. Org. Chem.* **31** 916 (1966)
31. D H R Barton, R H Hasse, M M Pechet, H T Toh *J. Chem. Soc., Perkin Trans. 1* 732 (1974)
32. R E Banks, M K Besheesh, E Tsiliopoulos *J. Fluor. Chem.* **78** 39 (1996)
33. BRD P. 4 408 681; *Chem. Abstr.* **124** 55 990 (1996)
34. I Cabrera, W K Appel *Tetrahedron* **51** 10205 (1995)
35. A Satoh, N Shibata, Y Takeuchi, in *The 15th International Symposium on Fluorine Chemistry (Abstracts of Reports), Vancouver, 1997* P(I) 39
36. A Satoh, N Shibata, Y Takeuchi, in *The 20th Japanese Symposium on Fluorine Chemistry (Abstracts of Reports), Nagoya, 1996* O-16, p. 20

37. W E Barnette *J. Am. Chem. Soc.* **106** 452 (1984)
38. US P. 4 479 901; *Chem. Abstr.* **102** 113 537 (1985)
39. US P. 3 917 688; *Chem. Abstr.* **84** 30 714 (1976)
40. M Seguin, J C Adenis, C Michaud, J J Basselier *J. Fluor. Chem.* **15** 201 (1980)
41. J Foropoulos, D D DesMarteau *Inorg. Chem.* **23** 3720 (1984)
42. D D DesMarteau, M Witz *J. Fluor. Chem.* **52** 7 (1991)
43. R E Banks, J C Tatlow *J. Fluor. Chem.* **33** 71 (1986)
44. BRD P. 2 332 430; *Chem. Abstr.* **80** 108 209 (1974)
45. J Leroy, F Dudragne, J C Adenis, C Michaud *Tetrahedron Lett.* 2771 (1973)
46. R Bohlmann *Nachr. Chem. Tech. Lab.* **38** 40 (1990)
47. S H Lee, J Schwartz *J. Am. Chem. Soc.* **108** 2445 (1986)
48. R E Banks, A Khazei *J. Fluor. Chem.* **46** 297 (1990)
49. US P. 5 227 493; *Chem. Abstr.* **119** 203 432 (1993)
50. A Khazei, V Murtagh, I Sharif, R E Banks *J. Fluor. Chem.* **45** 167 (1989)
51. A A Gakh, S V Romaniko, B I Ugrak, A A Fainzilberg *Tetrahedron* **47** 7447 (1991)
52. Yu L Yagupol'skii, T I Savina *Zh. Org. Khim.* **17** 1330 (1981) [a]
53. V Grakauskas, K Baum *J. Org. Chem.* **35** 1545 (1970)
54. N Satyamurthy, G T Bida, M E Phelps, J R Barrio *J. Org. Chem.* **55** 3373 (1990)
55. N N Aleinikov, N V Kondratenko, S A Kashtanov, A D Kuntzevich *J. Fluor. Chem.* **58** 141 (1992)
56. Jpn. Appl. 6 226 264; *Chem. Abstr.* **106** 213 414 (1987)
57. BRD P. 4 313 664; *Ref. Zh. Khim.* 1 N 149P (1996)
58. US P. 4 828 764; *Ref. Zh. Khim.* 12 N 334P (1990)
59. S Singh, D D DesMarteau, S S Zuberi, M Witz, H-N Huang *J. Am. Chem. Soc.* **109** 7194 (1987)
60. Z-Q Xu, D D DesMarteau, Y Gotoh *J. Fluor. Chem.* **58** 71 (1992)
61. W T Pennington, G Resnati, D D DesMarteau *J. Org. Chem.* **57** 1536 (1992)
62. R G Syvret, R E Banks, H M Marsden, V Murtagh, in *American Chemical Society Thirteenth Winter Fluorine Conference (Abstracts of Reports), St. Petersburg, FL, 1997* Vol. 11, p. 17
63. BRD P. 4 313 664; *Chem. Abstr.* **122** 132 608 (1995)
64. WO PCT 94 08 955; *Chem. Abstr.* **122** 191 006 (1995)
65. E Differding, H Ofner *Synlett* 187 (1991)
66. F A Davis, W Han *Tetrahedron Lett.* **32** 1631 (1991)
67. F A Davis, W Han *Tetrahedron Lett.* **33** 1153 (1992)
68. N Satyamurthy, G T Bida, M E Phelps, J R Barrio *Appl. Radiat. Isot.* **41** 733 (1990); *Chem. Abstr.* **113** 230 771 (1990)
69. US P. 5 254 732; *Chem. Abstr.* **120** 134 027 (1994)
70. US P. 5 478 964; *Ref. Zh. Khim.* 5 N 111P (1995)
71. D Nalewajek, A Poss, J Ziller, F A Davis, W Han, in *The 15th International Symposium on Fluorine Chemistry (Abstracts of Reports), Vancouver, 1997* P(I) 30
72. F A Davis, W Han, C K Murphy *J. Org. Chem.* **60** 4730 (1995)
73. W Ying, D D DesMarteau, in *American Chemical Society Thirteenth Winter Fluorine Conference (Abstracts of Reports), St. Petersburg, FL, 1997* Vol. 11, p. 18
74. W Ying, D D DesMarteau, Y Gotoh *Tetrahedron* **52** 15 (1996)
75. G Resnati, D D DesMarteau *J. Org. Chem.* **56** 4925 (1991)
76. Z-Q Xu, D D DesMarteau, Y Gotoh *J. Chem. Soc., Chem. Commun.* 179 (1991)
77. G Resnati, D D DesMarteau *J. Org. Chem.* **57** 4281 (1992)
78. S E Demark, N Chatani, S V Pansare *Tetrahedron* **48** 2191 (1992)
79. E Differding, R O Duthaler, A Krieger, G M Rmegg, C Schmit *Synlett* 395 (1991)
80. D D Des Marteau, Z-Q Xu, M Witz *J. Org. Chem.* **57** 629 (1992)
81. V Snieckus, F Beaulieu, K Mohri, W Han, C K Murphy, F A Davis *Tetrahedron Lett.* **35** 3465 (1994)
82. J-Y Nie, K L Kirk *J. Fluor. Chem.* **74** 297 (1995)
83. US P. 5 478 964; *Ref. Zh. Khim.* 5 N 111P (1998)
84. A J Poss, G A Shia *Tetrahedron Lett.* **36** 4721 (1995)
85. A J Poss, G A Shia, in *The 12th Winter Fluorine Conference (Abstracts of Reports), St. Petersburg, FL, 1995* P28, p. 52
86. D Enders, M Potthoff, G Raabe, J Runsink *Angew. Chem., Int. Ed. Engl.* **36** 2362 (1997)
87. A Padova, S M Roberts, D Donati, C Marchioro, A Perboni *Tetrahedron* **52** 263 (1996)
88. J-P Genet, J-O Durand, S Roland, M Savignac, F Jung *Tetrahedron Lett.* **38** 69 (1997)
89. F A Davis, R E Reddy *Tetrahedron. Asymmetry* **5** 955 (1994)
90. Jpn. Appl. 09 110 729; *Chem. Abstr.* **127** 33 997 (1997)
91. Z-Q Xu, D D DesMarteau *J. Chem. Soc., Perkin Trans. 1* 313 (1992)
92. M A Siddiqui, V E Marquez, J S Driscoll, J J Barchi Jr *Tetrahedron Lett.* **35** 3263 (1994)
93. F A Davis, P V N Kasu *Tetrahedron Lett.* **39** 6135 (1998)
94. K D Barnes, Y Hu, D A Hunt *Synth. Commun.* **24** 1749 (1994)
95. F A Davis, P Zhou, C K Murphy *Tetrahedron Lett.* **34** 3971 (1993)
96. E Differding, R W Lang *Tetrahedron Lett.* **29** 6087 (1988)
97. K Auer, E Hungerbuhler, R W Lang *Chimia* **44** 120 (1990)
98. F A Davis, P Zhou, B C Chen *Phosphorus Sulfur Silicon Relat. Elem.* **115** 85 (1996)
99. F A Davis, P Zhou, C K Murphy, G Sundarababu, H Qi, W Han, R M Przeslawski, B-C Chen, P J Carroll *J. Org. Chem.* **63** 2273 (1998)
100. E Differding, W Frick, R W Lang, P Martin, C Schmit, S Veenstra, H Greuter *Bull. Soc. Chim. Belg.* **99** 647 (1990)
101. Eur. P. 311 086; *Chem. Abstr.* **112** 118 805 (1990)
102. E Differding *J. Fluor. Chem.* **45** 99 (1989)
103. Jpn. Appl. 09 249 653; *Chem. Abstr.* **127** 262 674 (1998)
104. E Differding, R W Lang *Helv. Chim. Acta* **72** 1248 (1989)
105. E Differding, G M Rüegg, R W Lang *Tetrahedron Lett.* **32** 1779 (1991)
106. C P Andrieux, E Differding, M Robert, J M Saveant *J. Am. Chem. Soc.* **115** 6592 (1993)
107. T Suzuki, N Shibata, Y Takeuchi, in *The 21st Fluorine Conference of Japan (Abstracts of Reports), Sapporo, 1997* O-26, p. 34
108. E Differding, M Wehrli *Tetrahedron Lett.* **32** 3819 (1991)
109. M van Der Puy *Tetrahedron Lett.* **28** 255 (1987)
110. H Meinert *Z. Chem.* **5** 64 (1965)
111. H Meinert, D Cech *Z. Chem.* **12** 292 (1972)
112. T Umemoto, K Tomita *Tetrahedron Lett.* **27** 3271 (1986)
113. T Umemoto, K Harasawa, G Tomizawa, K Kawada, K Tomita *Bull. Chem. Soc. Jpn.* **64** 1081 (1991)
114. T Umemoto, G Tomizawa *J. Org. Chem.* **60** 6563 (1995)
115. A J Poss, M van Der Puy, D A Nalewajek, G A Shia, W J Wagner, R L Frenette *J. Org. Chem.* **56** 5962 (1991)
116. W G Dauben, L J Greenfield *J. Org. Chem.* **57** 1597 (1992)
117. T Umemoto, K Tomita, K Kawada *Org. Synth.* **69** 129 (1990)
118. Jpn. P. 62 181 230; *Chem. Abstr.* **108** 55 132 (1988)
119. US P. 5 086 190; *Ref. Zh. Khim.* 24 H 122 (1994)
120. Jpn. P. 07 233 097; *Chem. Abstr.* **124** 29 615 (1996)
121. US P. 4 935 519; *Chem. Abstr.* **114** 42 579 (1991)
122. V Reydellet-Casey, D J Knoechel, P M Herrinton *Org. Process Res. Dev.* **1** 217 (1997); *Chem. Abstr.* **126** 251 284 (1997)
123. Jpn. P. 07 188 173; *Chem. Abstr.* **123** 256 533 (1995)
124. Jpn. P. 0 873 434; *Chem. Abstr.* **125** 33 484 (1996)
125. Jpn. P. 399 062; *Ref. Zh. Khim.* 5 H 102 (1993)
126. Jpn. P. 09 255 657; *Chem. Abstr.* **127** 318 888 (1997)
127. Eur. P. 204 535; *Chem. Abstr.* **107** 77 638 (1987)
128. US P. 5 336 772; *Ref. Zh. Khim.* 12 N 115P (1994)
129. T Umemoto, K Harasawa, G Tomizawa *J. Fluor. Chem.* **53** 369 (1991)
130. Jpn. P. 07 247 235; *Chem. Abstr.* **124** 145 600 (1996)
131. Jpn. P. 05 125 050; *Chem. Abstr.* **119** 180 672 (1993)
132. R E Banks, S N Mohialdin-Khaffaf, G S Lal, L Sharif, R G Syvret *J. Chem. Soc., Chem. Commun.* 595 (1992)
133. A A Gakh, S V Romaniko, A A Fainzil'berg, K G Nikitin *Izv. Akad. Nauk SSSR, Ser. Khim.* 1936 (1991) [b]
134. T Umemoto, K Kawada, K Tomita *Tetrahedron Lett.* **27** 4465 (1986)
135. Jpn. P. 08 188 573; *Chem. Abstr.* **125** 221 594 (1996)
136. US P. 5 081 249; *Ref. Zh. Khim.* 19 R 116P (1993)
137. T Umemoto, K Adachi, M Nagayoshi, G Tomizawa, in *The 20th Japanese Symposium on Fluorine Chemistry (Abstracts of Reports), Nogoya, 1996* P-27, p. 47
138. WO PCT 9 612 702; *Chem. Abstr.* **125** 119 500 (1996)
139. T Umemoto, M Nagayoshi, K Adachi, G Tomizawa *J. Org. Chem.* **63** 3379 (1998)
140. T Umemoto, M Nagayoshi, in *The 2nd International Conference 'Chemistry, Technology and Application of Fluorocompounds' (Abstracts of Reports), St. Petersburg, Russia, 1997* P3-42, p. 160
141. T Umemoto, G Tomizawa, H Hachisuka, M Kitano *J. Fluor. Chem.* **77** 161 (1996)

142. R E Banks, M K Besheesh, S N Mohialdin-Khaffaf, I Sharif *J. Fluor. Chem.* **81** 157 (1997)
143. K Nukui *J. Synth. Org. Chem., Jpn.* **53** 64 (1995)
144. T Umemoto, S Fukami, G Tomizawa, K Harasawa, K Kawada, K Tomita *J. Am. Chem. Soc.* **112** 8563 (1990)
145. Jpn. P. 62 207 228; *Chem. Abstr.* **109** 22 344 (1988)
146. G Tomizawa, T Umemoto *J. Fluor. Chem.* **54** 205 (1991)
147. Eur. P. 470 669; *Chem. Abstr.* **116** 193 897 (1992)
148. M Ihara, T Kai, N Taniguchi, K Fukumoto *J. Chem. Soc., Perkin Trans. 1* 2357 (1990)
149. T Umemoto, G Tomizawa *J. Org. Chem.* **54** 1726 (1989)
150. T Umemoto, G Tomizawa *Tetrahedron Lett.* **28** 2705 (1987)
151. Jpn. P. 0 753 456; *Chem. Abstr.* **123** 111 590 (1995)
152. T Umemoto *Rev. Heterocycl. Chem.* **10** 123 (1994)
153. Jpn. P. 0 559 059; *Chem. Abstr.* **119** 138 983 (1993)
154. M Ihara, N Taniguchi, T Kai, K Satoh, K Fukumoto *J. Chem. Soc., Perkin Trans. 1* 221 (1992)
155. Jpn. P. 08 092 278; *Chem. Abstr.* **125** 86 977 (1996)
156. A S Kiselyov *Tetrahedron Lett.* **35** 8951 (1994)
157. T Umemoto, G Tomizawa *Bull. Chem. Soc. Jpn.* **59** 3625 (1986)
158. I Shimizu, H Ishii *Tetrahedron* **50** 487 (1994)
159. M Sato, N Kitazawa, C Koneko *Heterocycles* **33** 105 (1992)
160. T M Bockman, K Y Lee, J K Kochi *J. Chem. Soc., Perkin Trans. 2* 1581 (1992)
161. Y Chung, B F Duerr, T A McKelvey, P Nanjappan, A W Czarnik *J. Org. Chem.* **54** 1018 (1989)
162. K Y Lee, J K Kochi *J. Chem. Soc., Perkin Trans. 2* 1011 (1992)
163. D Hebel, K L Kirk *J. Fluor. Chem.* **47** 179 (1990)
164. P C B Page, F Hussain, J L Maggs, P Morgan, B K Park *Tetrahedron* **46** 2059 (1990)
165. D Hebel, O Lerman, S Rozen *Bull. Soc. Chim. Fr.* 861 (1986)
166. M Okada, Y Nakamura, H Horikawa, T Inoue, T Taguchi *J. Fluor. Chem.* **82** 157 (1997)
167. G S Lal, R G Syvret *J. Fluor. Chem.* **54** 208 (1991)
168. T Ueno, H Toda, M Yasunami, M Yoshifuji *Bull. Chem. Soc. Jpn.* **69** 1645 (1996)
169. R E Banks, R A DuBoisson, W D Morton, E Tsiliopoulos *J. Chem. Soc., Perkin Trans. 1* 2805 (1988)
170. Eur. P. 692 479; *Chem. Abstr.* **124** 261 086 (1996)
171. R E Banks, I Sharif *J. Fluor. Chem.* **41** 297 (1988)
172. R E Banks, I Sharif *J. Fluor. Chem.* **55** 207 (1992)
173. US P. 5 086 178; *Ref. Zh. Khim.* 24 H 121 (1994)
174. M Zupan, J Iskra, S Stavber *Tetrahedron* **52** 11341 (1996)
175. R E Banks, R A DuBoisson, E Tsiliopoulos *J. Fluor. Chem.* **32** 461 (1986)
176. R E Banks, M K Besheesh *J. Fluor. Chem.* **76** 161 (1996)
177. R E Banks, M K Besheesh, S N Mohialdin-Khaffaf, I Sharif *J. Chem. Soc., Perkin Trans. 1* 2069 (1996)
178. R E Banks, M K Besheesh, S N Khaffaf, I Sharif *J. Fluor. Chem.* **54** 207 (1991)
179. US P. 5 473 065; *Ref. Zh. Khim.* 21 N 140P (1997)
180. US P. 5 086 178; *Chem. Abstr.* **116** 194 355 (1992)
181. Eur. P. 657 457; *Chem. Abstr.* **123** 83 392 (1995)
182. WO PCT 97 06 170; *Chem. Abstr.* **126** 212 164 (1997)
183. WO PCT 95 17 404; *Chem. Abstr.* **124** 8844 (1996)
184. D P Matthews, S C Miller, E T Jarvi, J S Sabol, J R McCarthy *Tetrahedron Lett.* **34** 3057 (1993)
185. R E Banks, R G Pritchard, I Sharif *Acta Crystallogr., Sect. C* **49** 1806 (1993)
186. T Umemoto, M Nagayoshi *Bull. Chem. Soc. Jpn.* **69** 2287 (1996)
187. US P. 5 367 071 SShA; *Chem. Abstr.* **122** 314 589 (1995)
188. G S Lal, in *Fluorine in Agriculture* (Ed. R E Banks) (Manchester, 1995) Paper 16
189. R E Banks, N J Lawrence, A L Popplewell *J. Chem. Soc., Chem. Commun.* 343 (1994)
190. R E Banks, M K Besheesh *J. Fluor. Chem.* **74** 165 (1995)
191. S Stavber, M Zupan *J. Chem. Soc., Chem. Commun.* 149 (1994)
192. J Y Godard *Fluorine in Medicine in the 21st Century* (Ed. R E Banks) [Manchester: Chemserve (UMIST), 1994] Paper 10
193. J Wang, A I Scott *J. Chem. Soc., Chem. Commun.* 2399 (1995)
194. H F Hodson, D J Madge, D A Widdowson *J. Chem. Soc., Perkin Trans. 1,* 2965 (1995)
195. N S Zefirov *Encyclopedia of Reagents for Organic Synthesis* (Eds L.A.Paquett *et al.*) (New York: Wiley, 1995) Vol. 2, p. 1046
196. H F Hodson, D J Madge, A N Z Slawin, D A Widdowson, D J Williams *Tetrahedron* **50** 1899 (1994)
197. M Zupan, J Iskra, S Stavber *J. Org. Chem.* **60** 259 (1995)
198. M Zupan, J Iskra, S Stavber *J. Fluor. Chem.* **70** 7 (1995)
199. D S Brown, B A Marples, P Smith, L Walton *Tetrahedron* **51** 3587 (1995)
200. M Zupan, J Iskra, S Stavber *Bull. Chem. Soc. Jpn.* **68** 1655 (1995)
201. N S Petasis, A K Yudin, I A Zavialov, G K S Prakash, G A Olah *Synlett* 606 (1997)
202. M A McClinton, V Sik *J. Chem. Soc., Perkin Trans. 1* 1891 (1992)
203. S Stavber, T Sotler-Pecan, M Zupan *Bull. Chem. Soc. Jpn.* **69** 169 (1996)
204. S Stavber, T Sotler-Pecan, M Zupan *Tetrahedron Lett.* **35** 1105 (1994)
205. S Stavber, M Zupan *Synlett* 693 (1996)
206. A K Forrest, P J O'Hanlon *Tetrahedron Lett.* **36** 2117 (1995)
207. P Ge, K L Kirk *J. Fluor. Chem.* **84** 45 (1997)
208. P Ge, K L Kirk *J. Org. Chem.* **62** 3340 (1997)
209. R E Banks, N J Lawrence, M K Besheesh, A L Popplewell, R G Pritchard *J. Chem. Soc., Chem. Commun.* 1629 (1996)
210. A Arnone, P Bravo, M Frigerio, G Salani, F Viani, M Zanda, C Zappala *J. Fluor. Chem.* **84** 79 (1997)
211. R E Banks, N J Lawrence, A L Popplewell *Synlett* 831 (1994)
212. R S Muthyala, R S H Liu *J. Fluor. Chem.* **89** 173 (1998)
213. M Brunavs, C P Dell, W M Owton *J. Fluor. Chem.* **68** 201 (1994)
214. G S Lal, W Pastore, R Pesaresi *J. Org. Chem.* **60** 7340 (1995)
215. G S Lal *Synth. Commun.* **25** 725 (1995)
216. M Zupan, J Iskra, S Stavber *Tetrahedron Lett.* **38** 6305 (1997)
217. M Abdul-Ghani, R E Banks, M K Besheesh, I Sharif, R G Syvret *J. Fluor. Chem.* **73** 255 (1995)
218. US P. 5 631 372; *Ref. Zh. Khim.* 14 N 98P (1997)
219. S Stavber, M Zupan *Chem. Lett.* 1077 (1996); *Chem. Abstr.* **126** 59 714 (1997)
220. M Zupan, M Papez, S Stavber *J. Fluor. Chem.* **78** 137 (1996)
221. S Stavber, M Zupan, A J Poss, G A Shia *Tetrahedron Lett.* **36** 6769 (1995)
222. S Stavber, T Sotler-Pecan, M Papez, M Zupan *Chem. Commun. (Cabmridge)* 2247 (1996); *Chem. Absrt.* **126** 18 627 (1997)
223. S Stavber, M Zupan *Tetrahedron Lett.* **37** 3591 (1996)
224. A J Poss, G A Shia *Chem. Eng. News.* **73** 45 (1995); *Ref. Zh. Khim.* 10 Zh 260 (1996)
225. A J Poss, G A Shia *Chim. Oggi.* **13** 47 (1995); *Chem. Abstr.* **124** 259 915 (1996)
226. US P. 5 606 084; *Ref. Zh. Khim.* 14 N 127P (1998)
227. K O Christe, C J Schack, R D Wilson *J. Fluor. Chem.* **8** 541 (1976)
228. C J Schack, K O Christe *J. Fluor. Chem.* **18** 363 (1981)
229. US P. 343 033; *Chem. Abstr.* **97** 215 716 (1982)
230. G A Boswell *Chem. Ind.* 1929 (1965)
231. US P. 3 634 466; *Chem. Abstr.* **76** 99 924 (1972)
232. US P. 3 629 301; *Chem. Abstr.* **76** 86 012 (1972)
233. G K S Prakash, C York, G A Olah, in *International Chemical Congress of Pacific Basin Societies (Abstracts of Reports), Honolulu, 1995* Inorg. 7, No 349
234. C York, G K S Prakash, G A Olah *Tetrahedron* **52** 9 (1996)
235. E Differding, G M Rüegg *Tetrahedron Lett.* **32** 3815 (1991)
236. L Eberson *Electron Transfer Reactions in Organic Chemistry* (Berlin: Springer, 1987)
237. V N Solkan, A A Fainzil'berg *Zh. Org. Khim.* **30** 1143 (1994) [a]
238. V N Solkan, A A Fainzil'berg *Zh. Org. Khim.* **32** 977 (1996) [a]
239. V N Solkan, A A Fainzil'berg *Zh. Org. Khim.* **32** 1153 (1996) [a]
240. V N Solkan, A A Fainzil'berg *Zh. Org. Khim.* **34** 1157 (1996) [a]
241. K Burshtein *J. Mol. Struct. (Teorchem.)* **23** 195 (1987)
242. A G Gilicinski, G P Pez, R G Syvret, G S Lal *J. Fluor. Chem.* **59** 157 (1992)
243. E Differding, P M Bersier *Tetrahedron* **48** 1595 (1992)
244. L G Feoktistov, A A Fainzil'berg, G P Girina *Elektrokhimiya* (1999) (in the press) [c]
245. H Hochisuka, M Kitano *J. Fluor. Chem.* **54** 206 (1991)

[a] — *Russ. J. Org. Chem. (Engl. Transl.)*
[b] — *Russ. Chem. Bull. (Engl. Transl.)*
[c] — *Russ. J. Electrochem. (Engl. Transl.)*