Russian Chemical Reviews **79** (4) 259 – 283 (2010) © 2010 Russian Academy of Sciences and Turpion Ltd

DOI 10.1070/RC2010v079n04ABEH004091

The selectivity problem in electrophilic fluorination of aromatic compounds

G I Borodkin, V G Shubin

Contents

I.	Introduction	259
II.	Reagents and mechanism of electrophilic fluorination	259
III.	Fluorination of benzene derivatives	261
IV.	Fluorination of bi- and polycyclic aromatic compounds	270
V.	Fluorination of heteroaromatic compounds	273
VI.	Fluorination of organoelement compounds	277
VII.	Fluorination of fullerenes	279
VIII.	Conclusion	280

Abstract. Data on electrophilic fluorination of aromatic, heteroaromatic and organoelement compounds are generalized and analyzed. The attention is focused on the factors determining the selectivity of fluorine atom substitution for hydrogen in the aromatic ring. The bibliography includes 188 references.

I. Introduction

Fluorinated aromatic derivatives represent an important class of organic compounds, which find a broad range of practical applications as drugs (antibiotics, analgesics, antiseptic agents, antidepressants, antitumour agents, *etc.*),[1–19] pesticides,[5,10,11,20–22] liquid crystals,[4–6,11,23,24] dyes,[4] materials for electronics,[25–27] polymers,[28] cancer diagnostics agents.[29] Fluoroaromatic derivatives are key intermediates in the synthesis of various (including practically useful) organic compounds by nucleophilic substitution, polymerization and other reactions.[2–4,28]

Fluorine is the most electronegative element, while the van der Waals radius of the fluorine atom does not exceed much that of hydrogen; this largely determines its unique effect on the properties of organic molecules.[12,15,30–33] Usually, the introduction of a fluorine atom into the aromatic ring considerably changes the physical and biological properties and reactivity of organic compounds.[4–7,12,22] These changes especially concern increase in the stability, lipophilicity and biological activities of organic compounds, which is important for pharmaceutical and agrochemical industries.[32,33] The fluoro-containing drug analogues metabolized to give compounds toxic for the body are used as bioisosteric drug mimetics.[6,12,31,32]

This review deals with the problem of selectivity of the electrophilic fluorination of aromatic, heteroaromatic and organoelement compounds with an aryl fragment. Despite the numerous reviews and monographs published in recent years[4–64] that consider the methods of synthesis and the properties of fluoroaromatic compounds, the selectivity problem in the electrophilic fluorination has still received little attention. This review covers the literature published during the last 10 to 15 years. Earlier publications are mentioned only whenever necessary to understand the considered problem and to elucidate new trends in this field.

II. Reagents and mechanism of electrophilic fluorination

Throughout many decades, gaseous fluorine served as the reagent for fluorination of aromatic compounds (Refs 4–6, 16, 34, 38–42). However, this reagent is hazardous, highly reactive and corrosive with respect to many materials; therefore, it is used most often as a mixture with inert gas (N_2, He). Owing to high reactivity, fluorine does not possess selectivity needed for the synthesis. Even the use of polar solvents (or Lewis acids) at low temperatures does not result in selective fluorination of arenes.

The presence of Brønsted or Lewis acids in the reaction mixture should result in polarization of the F–F bond, electrophilic substitution of fluorine for a hydrogen atom being the most probable mechanism of arene fluorination. In the case of using oxygen-containing solvents or acids, formation of compounds with the O–F bonds acting as electrophiles may be expected.[65]

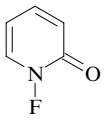
$$F{-}F \longrightarrow \overset{\delta+\ \delta-}{F\cdots F\cdots HOY} \longrightarrow YO{-}F$$

G I Borodkin, V G Shubin N N Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, prosp. Akad. Lavrentieva 9, 630090 Novosibirsk, Russian Federation. Fax (7-383) 330 97 52, tel. (7-383) 330 93 86, e-mail: gibor@nioch.nsc.ru (G I Borodkin), tel. (7-383) 330 76 51, e-mail: vshubin@nioch.nsc.ru (V G Shubin)

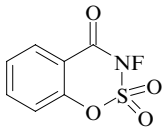
Received 16 July 2009
Uspekhi Khimii **79** (4) 299 – 324 (2010); translated by Z P Svitanko

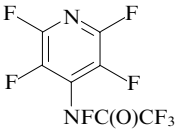
During the last 50–60 years, a number of oxygen-containing fluorinating agents have been proposed ($FClO_3$, AcOF, CF_3OF, $CsSO_4F$).[5–7, 16, 38, 40, 43, 44] However, most of them are not sufficiently stable and moreover toxic. Xenon difluoride is a fairly reactive fluorinating agent but it is also rather toxic and expensive.[5–7, 45, 46] Both XeF_2 and most OF reagents are potent oxidants, which complicates the electrophilic aromatic fluorination.[6] In recent years a broad range of new electrophilic fluorinating agents, NF reagents, have been developed and have started to be widely used in the fluorination of aromatic compounds (Refs 5–7, 10, 11, 16, 40–42, 47–64). Reagents with the N–F bonds are beneficial over OF and SF reagents as regards stability, environmental safety and handling safety, which accounts for their extensive use. As neutral reagents for introducing a fluorine atom into the aromatic ring, compounds **1**–**8** have been proposed.

$(RSO_2)_2NF$
1a–c
R = Ph (**a**), CF_3 (**b**), C_4F_9 (**c**)

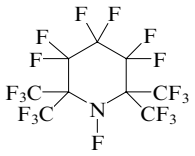

2

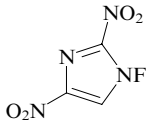

3


4


5

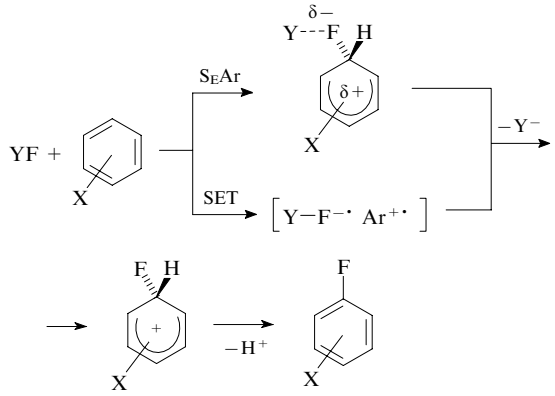

5


7


8

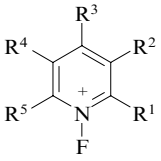
As a rule, pyridinium and quaternary ammonium cations used as salts with the BF_4^-, TfO^- and other anions or zwitter-ions (*e.g.*, reagents **9**–**17**) are more reactive NF reagents.

Since fluorine is the most electronegative element, the formation of the F^+ cation is thermodynamically extremely unfavourable (the formation enthalpy in the gas phase ΔH_f is 1757 kJ mol^{-1}).[6] Therefore, the formation of this cation during electrophilic aromatic fluorination is unlikely. Molecular fluorine and other fluorinating reagents are to be considered as sources of 'pseudopositive' or 'electrophilic' fluorine (see reviews [36, 54]). Therefore, two variants of fluorine atom transfer to the arene are mainly considered in the electrophilic fluorination of aromatic compounds, namely, nucleophilic substitution at fluorine (polar mechanism, S_EAr) and single-electron transfer with involvement of radical cation (SET mechanism).[6, 35, 37, 38, 40, 45, 54, 60]

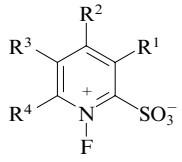


Y = F, Alk_2N, *etc.*

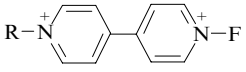
From comparison of experimental rate constants for fluorination of 1-naphthyllithium, potassium 2-methyl-3,4-dihydronaphtholate-1 and some other compounds by 3,3-dimethyl-2-fluoro-2,3-dihydro-1,2-benzoisothiazole 1,1-dioxide with the values calculated from standard redox potentials (E°) using the Marcus theory, it was concluded [66, 67] that the polar S_EAr mechanism is preferred. High substrate selectivity of mesitylene (Mes) and durol (Dur) fluorination with the reagent

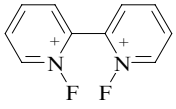

9a–n

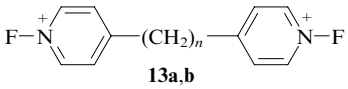
$R^1 = R^2 = R^3 = R^4 = R^5 = H$ (**a**);
R^1 = Me, $R^2 = R^3 = R^4 = R^5 = H$ (**b**);
$R^1 = R^3 = R^5$ = Me, $R^2 = R^4 = H$ (**c**);
$R^2 = R^4$ = Me, $R^1 = R^3 = R^5 = H$ (**d**);
$R^3 = NO_2$, $R^1 = R^2 = R^4 = R^5 = H$ (**e**);
R^3 = CN, $R^1 = R^2 = R^4 = R^5 = H$ (**f**);
$R^2 = R^4 = CF_3$, $R^1 = R^3 = R^5 = H$ (**g**);
$R^1 = R^5 = CO_2Me$, $R^2 = R^3 = R^4 = H$ (**h**);
$R^1 = SO_3^-$, $R^2 = R^3 = R^4 = R^5 = H$ (**i**);
$R^2 = SO_3^-$, $R^1 = R^3 = R^4 = R^5 = H$ (**j**);
$R^3 = SO_3^-$, $R^1 = R^2 = R^4 = R^5 = H$ (**k**);
$R^1 = R^5$ = Cl, $R^2 = R^3 = R^4 = H$ (**l**);
$R^2 = R^4$ = Cl, $R^1 = R^3 = R^5 = H$ (**m**);
$R^1 = R^2 = R^3 = R^4 = R^5$ = Cl (**n**)

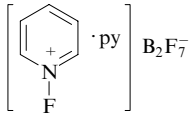

10a–i

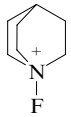
$R^1 = R^3 = R^4 = H$, R^2 = Me (**a**);
$R^1 = R^3 = R^4 = H$, R^2 = Et (**b**);
$R^1 = R^3 = R^4 = H$, $R^2 = Bu^t$ (**c**);
$R^1 = R^2 = R^3 = H$, R^4 = Me (**d**);
$R^1 = R^2 = R^4 = H$, $R^3 = CF_3$ (**e**);
R^1 = Cl, $R^3 = CF_3$, $R^2 = R^4 = H$ (**f**);
$R^1 = R^3 = H$, $R^2 = R^4$ = Me (**g**);
$R^1 = R^3 = H$, $R^2 = R^4 = CF_3$ (**h**);
$R^1 = R^2 = R^3 = H$, $R^4 = CF_3$ (**i**)

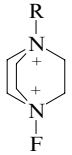

11a–c
R = Me (**a**), F (**b**), BF_3^- (**c**)

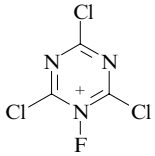

12


13a,b
n = 2 (**a**), 3 (**b**)


14


15


16a–e
R = Me (**a**), Pr^n (**b**), CH_2Cl (**c**), OH (**d**), F (**e**)


17

(**16c**)$(BF_4)_2$ (F-TEDA·BF_4, Selectfluor) (80 °C, $k_{Mes}:k_{Dur}$ = 6–10) or **1a** (NFSI) (105 °C, $k_{Mes}:k_{Dur}$ = 3.4) also indicates that the reaction follows the polar mechanism.[68,69] Conversely, in some studies dealing with fluorination of aromatic compounds with NF reagents, reasons are given supporting the SET mechanism[70–75] assuming a very short (10^{-13}–10^{-15} s) life span of the radical cation–fluorine atom pair.[60] In this case, according to Jencks, reasons pro or contra the SET mechanism become meaningless.[76] (Note that the SET mechanism has been substantiated for fluorination of alkenes and organometallic compounds.[77,78]) A common feature of the considered mechanisms (SET and S_EAr) is the formation of σ-complex or the Wieland complex, which is converted to fluorinated aromatic derivative upon proton elimination. In the general case, various fluorination mechanisms are possible depending on the nature of the fluorinating reagent, aromatic compound and reaction conditions. Some specific features of the fluorination mechanism of aromatic compounds that affect the process selectivity are discussed below.

III. Fluorination of benzene derivatives

1. Fluorination of monosubstituted benzenes

Fluorination of monosubstituted benzene derivatives with fluorine or fluorine–inert gas mixtures has most often low selectivity.[79–85] The effects of the solvent nature, various additives and reaction conditions for the liquid-phase fluorination of PhX (X = H, Me, OH, CO_2H) were studied (Table 1).

The predominant formation of the *meta*-isomer in the case of benzoic acid and *ortho*-, *para*-isomers for phenol and toluene confirms the electrophilic character of the reaction. The *ortho*-/*para*-isomer ratio depends little on the solvent nature, temperature, excess of F_2 with respect to the starting

Table 1. Fluorination of monosubstituted benzenes PhX with fluorine gas as a F_2–N_2 mixture.

X	F_2 (vol.%)	Solvent	Temperature /°C	Ratio of the products XC_6H_4F (%)			S[a]	Overall yield (%)[b]	Ref.
				ortho	*meta*	*para*			
Me	6.5	$CHCl_3$[c]	−45	60	0	40	1.50	(74)	79
	3.3	MeOH[d]	−40	36	0	64	0.56	(29)	79
	3.3	MeOH[e]	−40	53	0	47	1.13	(40)	79
	5.0	CF_3CH_2OH	−37	59	0	41	1.44	(33)	79
	5.0	CF_3CH_2OH	−37	56	0	44	1.27	(91)	79
	4.8	CF_3CO_2H	−12	61	0	39	1.56	(36)	79
	10	MeCN[f]	–	56	11	33	1.70	–	80
	1.0	MeCN[f]	20	53	16	31	1.71	12	81
	2.5	MeOH[f]	20	61	11	28	2.18	11	81
CO_2H	5.5	$CF_3CH_2OH-H_2O$	−10	20	80	0		(26)	79
	5.5	CF_3CO_2H	−15	31	69	0		(53)	79
	9.5	MeOH	−40	29	71	0		(30)	79
OH	4.3	$CHCl_3$	−62	61	0	39	1.56	(77)	79
	3.9	MeOH[d]	−40	64	0	36	1.78	(72)	79
	5.2	CF_3CH_2OH	−30	60	0	40	1.50	(77)	79
	5.5	CF_3CO_2H	15	61	0	39	1.56	(50)	79
	3.0	H_2O	−2	56	0	44	1.27	(73)	79
	3.0	H_2O[d]	−3	63	0	37	1.70	(75)	79
	5	CH_2Cl_2	−78	52	0	48	1.08	(58)	82
	5	$CH_2Cl_2-BCl_3$	−78	21	0	79	0.27	(100)	82
	5	$CH_2Cl_2-AlCl_3$	−78	27	0	73	0.37	(100)	82
NH_2	10	H_2SO_4	20	29	39	31	0.94	(74)	83
	10	CF_3SO_3H	20	27	40	33	0.82	(59)	83
	10	$CF_3SO_3H-B(OTf)_3$	20	25	40	35	0.71	(62)	83
	10	$CF_3SO_3H-SbF_5$ (4%)	20	23	44	33	0.70	(61)	83
F	10	$CFCl_3-CF_3SO_3H$ (5%)	−30	18	0	82	0.22	(93)	84
	10	$CFCl_3-CF_3SO_3H-BF_3$	−25	26	0	74	0.35	(78)	84
	10	$CFCl_3-CF_3CO_2H$ (10%)	−20	27	0	73	0.37	(76)	84
	10	$MeCN-CF_3CO_2H$ (10%)	−30	40	0	60	0.67	(71)	84
Cl	5	$CFCl_3-CH_2Cl_2$	−78	39	9	52	0.75	(9.5)	82
	5	$CFCl_3-CH_2Cl_2-BCl_3$	−78	21	5	74	0.28	(62)	82
	5	$CFCl_3-CH_2Cl_2-AlCl_3$	−78	52	20	28	1.86	(39.9)	82
CHO	5	$CFCl_3$	−78	0	100	0		(2.2)	82
	5	$CFCl_3-BCl_3$	−78	0	100	0		(2.1)	82
	10	MeCN	0	11	65	24	0.46	(48)	85
$CH(OCH_2)_2$	5	$CFCl_3$	−78	74	0	26	2.85	(19.7)	82
	5	$CFCl_3-BCl_3$	−78	58	0	42	1.38	(41.7)	82
NO_2	5	$CFCl_3-BCl_3$	−78	0	100	0		(5)	82

[a] S is the *ortho*- : *para*-isomer ratio; [b] degree of conversion is given in parentheses; [c] in the presence of 2.6% of 2,4-dinitrophenol; [d] with addition of 9% KOH; [e] in the presence of 3.2% of KOH; [f] in a microreactor.

substrate, degree of conversion, or additives (2,4-dinitrophenol or other). In the fluorination of toluene in MeOH, the highest fraction of *para*-isomer (*ortho* : *para* = 0.56) was attained for F_2 : PhMe ratio of 0.5 in the presence of 9.2% KOH.[79] The authors noted an increase in the yield of monofluorinated products following a decrease in the F_2 : substrate ratio and along the following series of polar solvents: $CFCl_3 < CHCl_3 < MeOH < CF_3CH_2OH < CF_3CO_2H$.

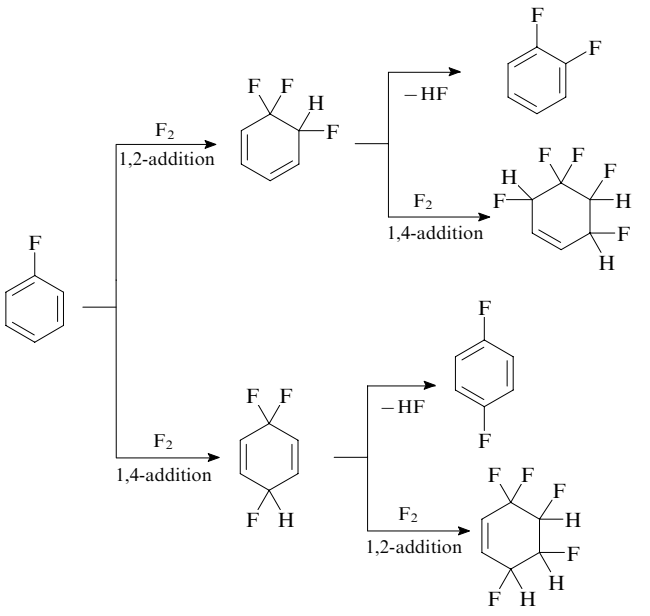
The fluorination of aniline with a F_2-N_2 mixture in strong acids (H_2SO_4, CF_3SO_3H) yields mainly *m*-fluoroaniline, which is caused by transformation of the NH_2 group to the electron-withdrawing NH_3^+ substituent directing the electrophile to enter the *meta*-position.[83] The addition of Lewis acids does not change considerably the reaction selectivity (see Table 1).

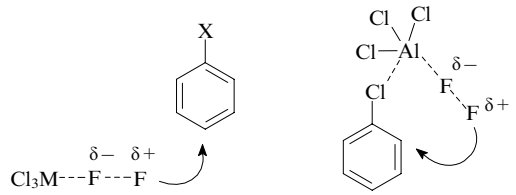
The use of a microreactor for toluene fluorination with a 2.5% F_2-N_2 mixture in MeCN or MeOH did not result in a higher selectivity either: the ratio of *o*-, *m*- and *p*-fluorotoluene isomers was 3.8 : 1 : 2.1 or 5.3 : 1 : 2.4, respectively.[81] The increase in the fluorine content in the gas phase to 50% results in considerable increase in the fraction of the *para*-isomer (*ortho* : *para* $\approx$ 1 : 4).[80]

The possibility of formation *ortho*- and *para*-isomers through the addition of fluorine to the aromatic ring followed by elimination of HF was considered. This mechanism is supported by the following data: fluorination of fluorobenzene gives addition products along with substitution products (Scheme 1).[84]

Notably, fluorination of fluoro- and chlorobenzene with a F_2-N_2 mixture gives in most cases predominant amount of *para*-substituted products (see Table 1). This is attributable to high electronegativity of fluorine and chlorine atoms, which deactivate to a higher extent the neighbouring *ortho*-position of the aromatic ring by the inductive effect and by the 'back donation' effect.[84] In the fluorination of chlorobenzene and phenol with a F_2-N_2 mixture in the presence of BCl_3, the fraction of the *para*-isomer was much higher than of the *ortho*-isomer, which was attributed to an increase in the effective volume of the electrophilic system $F\cdots F\cdots BCl_3$.[82] The replacement of the Lewis acid BCl_3 by $AlCl_3$ in the case of phenol also resulted in the predominance of the *para*-isomer, whereas in the fluorination of chlorobenzene, the proportion of the *ortho*-substituted product increases; this was explained by higher degree of coordination of $AlCl_3$ to the chlorine atom of the substrate as compared with BCl_3;[82] obviously, F_2 involved in the reaction is coordinated, thus increasing the probability of the *ortho*-attack.

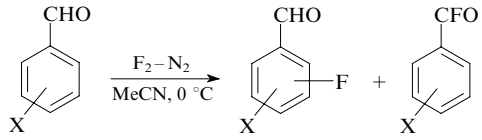
Scheme 1





X = OH, Cl; M = B, Al.

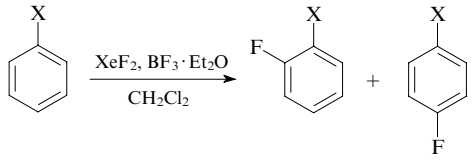
Fluorination of benzaldehyde derivatives with a F_2-N_2 mixture has low selectivity and affords a mixture of fluorobenzaldehydes and benzoyl fluoride.[85]



X = H, 3-CF_3, 3-CHO, 3-CN, 3-NO_2, 4-Me, 4-OMe, 4-CF_3, 4-CN.

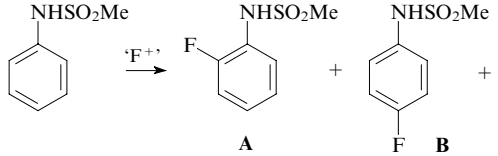
When electron-withdrawing substituents are present in the ring, benzoyl fluorides are mainly formed, while in the case of electron-releasing substituents, fluorination involves mainly the aromatic ring. The ratio of fluorination products does not change significantly when the reaction is carried out in a flow microreactor system.[85]

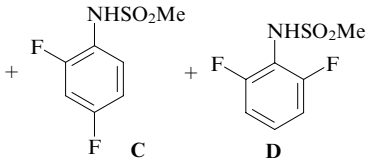
The fluorination of monosubstituted benzenes with electron-releasing substituents with XeF_2, like fluorination with fluorine gas, yields predominantly *ortho*- and *para*-substituted products,[86, 87] which is in line with the electrophilic nature of the reaction.



X	Product ratio (%)	
	ortho	*para*
Bn	45	55
Ph	53	47
PhO	38	62

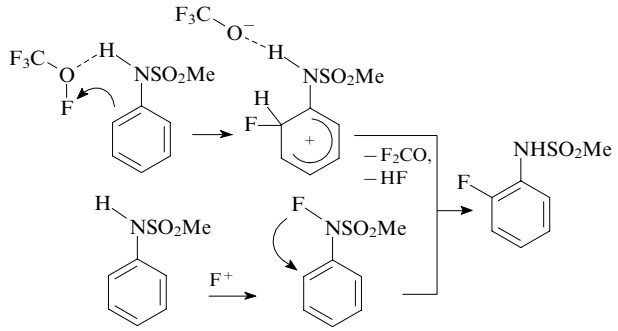
Note a number of early examples of using OF reagents to attain high selectivity. Thus fluorination of *N*-phenylmethanesulfonylamide with CF_3OF and $CF_2(OF)_2$ in CF_3CO_2H is mainly directed to the *ortho*-position.



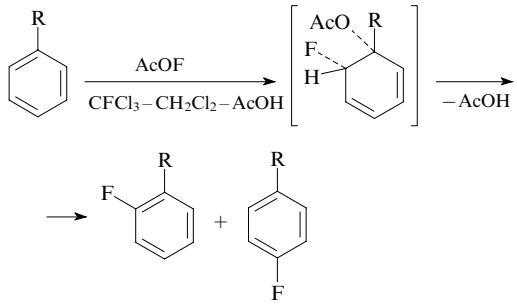


'F^+' = CF_3OF: yields 60% (**A**), 18% (**B**), 4% (**C**), 4% (**D**);
'F^+' = $CF_2(OF)_2$: yields 38% (**A**), 12% (**B**), 10% (**C**), 1% (**D**).

This can be attributed to hydrogen bonding between the oxygen atom of the OF reagent and the $NHSO_2Me$ group.[88] The mechanism involving the intermediate formation of *N*-phenyl-*N*-fluoromethanesulfonylamide cannot be ruled out.



Similarly, treatment of anisole and acetanilide with AcOF gives mainly *ortho*-substituted products; the authors explained this by assuming that the reaction follows the 'addition–elimination' mechanism.[89]



R	Yield (%)	
	ortho	*para*
MeO	77	8
NHAc	55	8

Analysis of the data of fluorination of monosubstituted benzenes with NF reagents has shown that the use of these

Table 2. Fluorination of monosubstituted benzenes PhX with NF reagents.

X	Reagent	Solvent	Temperature /°C	Time	Ratio of the products XC_6H_4F (%)			*S*	Overall yield (%) (see [a])	Ref.
					ortho	*meta*	*para*			
Me	**1a**	PhMe	Δ	216 h	65	7	28	2.32	19	90
	(**16c**)$(BF_4)_2$	MeCN	Δ	16 h	75	0	25	3.00	80	91
	(**16c**)$(BF_4)_2$	$CF_3SO_3H-CH_2Cl_2$	Δ	24 h	68	0	32	2.12	89	92
	(**16c**)$(BF_4)_2$	MeCN [b]	150	30 min	71	0	29	2.45	53	93
Bn	**1b**	MeCN	22	36 h	70	0	30	2.33	(95)	94
	1b	CH_2Cl_2	22	36 h	71	0	29	2.45	(63)	94
	1c	MeCN	22	36 h	76	0	24	3.17	(94)	94
	1c	CH_2Cl_2	22	36 h	71	0	29	2.49	(34)	94
	(**16c**)$(BF_4)_2$	MeCN	80	48 h	76	0	24	3.17	13	74
	(**16c**)$(BF_4)_2$	$MeCN-PhNO_2$	80	48 h	72	0	28	2.57	14	74
	(**16c**)$(BF_4)_2$	CF_3CO_2H	60	4 h	64	0	36	1.78	(66)	74
Ph	**1b**	MeCN	22	40 h	64	0	36	1.78	(90)	94
	1b	CH_2Cl_2	22	40 h	60	0	40	1.50	(63)	94
	1c	MeCN	22	40 h	70	0	30	2.33	(97)	94
	1c	CH_2Cl_2	22	40 h	63	0	37	1.70	(28)	94
	(**9l**)BF_4	MeCN	70	24 h	60	0	40	1.50	53	95
	(**16c**)$(BF_4)_2$	MeCN	70	97 h	78	0	22	3.55	77	95
	(**16c**)$(BF_4)_2$	$MeCN-PhNO_2$	70	97 h	78	0	22	3.55	73	95
	(**16c**)$(BF_4)_2$	CF_3CO_2H	60	4 h	83	0	17	4.88	69	95
	(**16d**)$(BF_4)_2$	MeCN	70	96 h	77	0	23	3.35	50	95
OH	**5**	MeOH	20	overnight	~50	0	~50	~1	91	96
	9i	$(CH_2Cl)_2$	100	84 h	99	0	<1	>99	(85)	97
	9j	$(CH_2Cl)_2$	100	264 h	66	0	34	1.94	(57)	97
	10a	$(CH_2Cl)_2$	100	24 h	98	0	<2	>49	(81)	97
	10e	$(CH_2Cl)_2$	100	18 h	98	0	<2	>49	(71)	97
	10f	$(CH_2Cl)_2$	100	1.5 h	99	0	<1	>99	(85)	97
	10h	$(CH_2Cl)_2$	100	0.05 h	96	0	4	24.0	(81)	97
	10h	CH_2Cl_2	Δ	2 h	98	0	2	49.0	(88)	97
	10h	CH_2Cl_2	20	13 h	99	0	1	99.0	(87)	97
	10h	MeCN	40	3 h	76	0	24	3.17	(82)	97

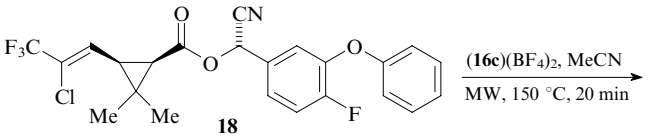
Table 2 (continued).

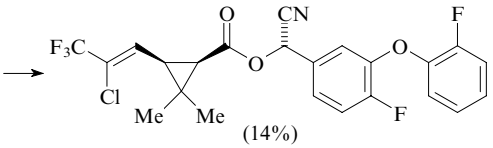
X	Reagent	Solvent	Temperature /°C	Time	Ratio of the products XC_6H_4F (%)			*S*	Overall yield (%) (see [a])	Ref.
					ortho	*meta*	*para*			
OH	**10h**	$(CF_3)_2CHOH$	5	0.25 h	80	0	20	4.00	(83)	97
	10h	$CF_3SO_3H-CH_2Cl_2$	20	2.5 h	79	0	21	3.76	(88)	97
	(**12**)$(BF_4)_2$	MeCN	Δ	8 h	54	0	46	1.17	77	98
	(**12**)$(BF_4)_2$	MeCN (NaOTf)	Δ	5 h	58	0	42	1.38	80	98
	(**16a**)$(OTf)_2$	MeOH	20	overnight	~60	0	~40	~1.5	85	99
	(**13b**)$(OTf)_2$	MeOH	20	15 h	~60	0	~40	~1.5	52	100
	(**16c**)$(BF_4)_2$	MeCN [b]	150	60 min	67	0	33	2.03	24	93
	(**16e**)$(BF_4)_2$	HCO_2H	20	15 min	71	0	29	2.45	48	71
MeO	**1a**	see [c]	100	24 h	58	5	37	1.57	33	90
	1a	MeCN [b]	150	10 min	50	0	50	1.00	4	93
	4	see [c]	150	5 h	56	0	44	1.27	77	101
	(**9a**)OTf	MeCN [b]	150	10 min	50	0	50	1.00	2	93
	(**9a**)OTf	$(ClCH_2)_2$	120	18 h	36 [d]	–	–		(72)	64
	(**9c**)OTf	$(ClCH_2)_2$	147	10 h	42 [d]	–	–		(68)	64
	(**9m**)OTf	$(ClCH_2)_2$	83	18 h	49	0	51	0.96	(65)	64
	(**9l**)OTf	CH_2Cl_2	40	7 h	50	0	50	1.00	(71)	64
	(**9n**)OTf	CH_2Cl_2	20	15 min	49	0	51	0.95	(91)	64
	(**9l**)BF_4	MeCN	70	3 h	64	0	36	1.78	56	95
	10h	CH_2Cl_2	Δ	29.5 h	39	0	61	0.64	(80)	97
	(**11a**)$(OTf)_2$	MeCN	80	15 h	~50	0	~50	~1.0	55	100
	(**12**)$(BF_4)_2$	MeCN	Δ	9 h	59	0	41	1.44	76	98
	(**12**)$(BF_4)_2$	MeCN [b]	150	10 min	56	0	44	1.27	21	93
	(**15**)BF_4	MeCN	90	overnight	52	0	48	1.08	21	102
	(**15**)PF_6	MeCN	90	overnight	54	0	46	1.17	23	102
	(**15**)(FSO_3)	MeCN	90	overnight	50	0	50	1.00	20	102
	(**15**)F	MeCN	90	overnight	50	0	50	1.00	10	102
	(**15**)OTf	MeCN	90	overnight	60	0	40	1.50	26	102
MeO	(**16a**)$(OTf)_2$	MeCN	40	13 h	~50	0	~50	~1.0	72	99
	(**15**)BF_4	MeCN	90	overnight	52	0	48	1.08	21	102
	(**16c**)$(BF_4)_2$	MeCN	70	3 h	60	0	40	1.50	47	95
	(**16c**)$(BF_4)_2$	$MeCN-PhNO_2$	70	3 h	58	0	42	1.38	55	95
	(**16c**)$(BF_4)_2$	CF_3CO_2H	50	2.5 h	58	0	42	1.38	42	95
	(**16c**)$(BF_4)_2$	MeCN [b]	150	10 min	60	0	40	1.50	32	93
	(**16d**)$(BF_4)_2$	MeCN [b]	150	10 min	62	0	38	1.63	42	93
	(**16d**)$(BF_4)_2$	MeCN	70	3 h	60	0	40	1.50	58	95
	(**16c**)$(BF_4)_2$	$CF_3SO_3H-CH_2Cl_2$	Δ	12 h	45	0	55	0.82	99	92
	(**16e**)$(SbF_6)_2$	MeCN	20	15 min	60	0	40	1.50	57	71
	(**16c**)$(BF_4)_2$	[emim][CF_3SO_3]	80	15 h	47	0	53	0.89	54	68
	(**16c**)$(BF_4)_2$	[emim][CF_3SO_3] [e]	80	15 h	47	0	53	0.89	12	68
	(**16c**)$(BF_4)_2$	[emim][BF_4]	80	15 h	43	0	57	0.75	40	68
	(**16c**)$(BF_4)_2$	[bmim][PF_6]	80	15 h	48	0	52	0.92	41	68
	(**16d**)$(CF_3SO_3)_2$	[emim][CF_3SO_3]	80	15 h	56	0	44	1.27	29	68
	14	[emim][CF_3SO_3]	80	15 h	54	0	46	1.17	11	68
	(**17**)BF_4	$MeNO_2$	−20→20	–	33	0	67	0.49	–	103
PhO	(**9l**)BF_4	MeCN	70	24 h	41	0	59	0.69	72	95
	(**16c**)$(BF_4)_2$	MeCN	70	24 h	44	0	56	0.79	65	95
	(**16c**)$(BF_4)_2$	$MeCN-PhNO_2$	70	24 h	44	0	56	0.79	73	95
	(**16c**)$(BF_4)_2$	CF_3CO_2H	50	4 h	41	0	59	0.69	68	95
	(**16d**)$(BF_4)_2$	MeCN	70	24 h	47	0	53	0.89	62	95
F	(**16c**)$(BF_4)_2$	$CF_3SO_3H-CH_2Cl_2$	Δ	36 h	23	0	77	0.30	87	92
Cl	(**17**)BF_4	$MeNO_2$	70	~6 h	30	9	61	0.49	–	103
	(**16c**)$(BF_4)_2$	$CF_3SO_3H-CH_2Cl_2$	Δ	36 h	69	0	31	2.23	87	92
NHAc	**1a**	see [c]	100	18 h	62	0	38	1.63	40	90
	(**16a**)$(OTf)_2$	MeOH	70	4 min	~62	0	~38	~1.6	80	99
$NHCO_2Et$	**10h**	$(CH_2Cl)_2$	Δ	2 h	87	0	13	6.69	(87)	97
NO_2	(**17**)BF_4	$MeNO_2$	70	~6 h	29	71	0		–	103

Note. emim is 1-ethyl-3-methylimidazolium, bmim is 1-butyl-3-methylimidazolium. [a] The yield of fluorination products, the value in parentheses is the degree of conversion; [b] using microwave irradiation; [c] without a solvent; [d] the yield of the *ortho*-isomer is indicated, while the yield of the *para*-isomer was not determined due to superimposition of impurity signals in the NMR spectrum; [e] with addition of dicyclohexane-24-crown-8.

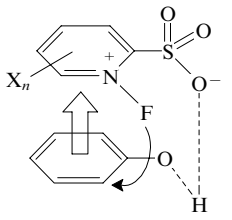
reagents does not increase significantly the selectivity in both cases. Thus in the case of toluene and chlorobenzene, the ranges of variation of the selectivity factor S ($S = ortho : para$) for the NF reagents are 2.1 – 3.0 and 0.5 – 2.2, respectively (Table 2); these do not differ much from these values for the fluorination of these compounds with molecular fluorine without additives (KOH, 2,4-dinitrobenzene) (1.3 – 2.2, 0.3 – 1.9) (see Table 1). The fluorination of fluorobenzene with (**16c**)$(BF_4)_2$ (like that with fluorine) affords *p*-difluorobenzene as the major product (see Table 1, 2), which is attributable to high electronegativity of fluorine, which deactivates to a higher extent the neighbouring *ortho*-position of the aromatic ring.[84] In the chlorobenzene fluorination with (**17**)BF_4, the relative fraction of the *meta*-isomer is nearly the same as for the use of F_2, which attests to its higher activity (see Tables 1, 2).

Anisole fluorination with (**16c**)$(BF_4)_2$ has shown that the use of ionic liquids (instead of MeCN) or microwave radiation does not change significantly the process regioselectivity (see Table 2). Nevertheless, fluorination of insecticide **18** with this reagent assisted by microwave irradiation (MW) is fairly selective being directed to the *ortho*-position relative to the OR group of the less substituted aromatic ring.[93]



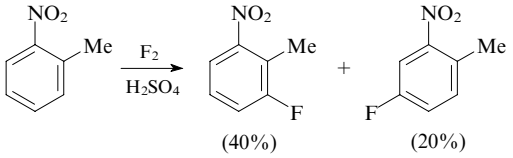


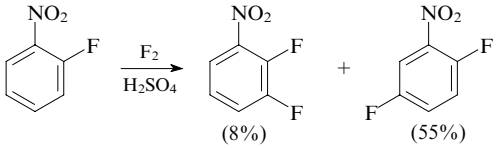
High regioselectivity was attained by treatment of phenol with NF reagents **9i**, **10f**,**h**. The fluorination occurs almost completely to the *ortho*-position ($ortho : para \geqslant 99$), which was explained by hydrogen bonding between the SO_3^- fragment of the reagent and the phenol OH group in the transition state, the ring orientation in the transition state being determined by the donor-acceptor interaction.[97]



2. Fluorination of disubstituted benzenes

The selectivity of electrophilic fluorination of disubstituted benzenes depends on the nature of substituents in the ring (Tables 3 – 5). Thus fluorination of *o*-nitrotoluene with molecular fluorine in H_2SO_4 yields a mixture of 3-fluoro- and 5-fluoro-2-methylnitrobenzenes in 2 : 1 ratio, while for 2-fluoronitrobenzene, the reaction gives mainly 2,5-difluoronitrobenzene.[36]





The low fraction of 3-substituted product in the latter case is apparently due to high electronegativity of fluorine, which deactivates more efficiently the neighbouring *ortho*-position of the aromatic ring.[84] Similarly, fluorination of 1,2-difluorobenzene gives predominantly 1,2,4-trifluorobenzene (Table 3).

Fluorination of 1,3-disubstituted benzenes containing electron-releasing or electron-withdrawing groups under their concerted influence is mainly directed to positions 4 and 5, respectively (Table 3, 5).

In the fluorination of (*E*)- and (*Z*)-β-fluoromethylene-*m*-tyrosines with AcOF in CF_3CO_2H – AcOH, both the benzene ring and the double bond are involved in the reaction.[108, 109]

Table 3. Fluorination of 1,2- and 1,3-disubstituted benzenes C_6H_4XY with a $F_2 - N_2$ mixture (10 vol.% F_2).

1-X	Y	Medium	Temperature /°C	Product yield (%)			Conversion (%)	Ref.
				4-F	5-F	6-F		
F	2-F	$CFCl_3 - CF_3SO_3H$	−25	13 [a]	–	–	94	84
Me	2-NO_2	H_2SO_4	–	20	–	40	see [b]	36
F	2-NO_2	H_2SO_4	–	55	–	8	see [b]	36
	3-F	$CFCl_3 - CF_3SO_3H$	−15	18 [a]	–	–	94	84
CF_3	3-CHO	MeCN	0	–	24 [c]	–	38	85
CN	3-CHO	MeCN	0	–	23 [c]	–	34	85
NO_2	3-CHO	MeCN	0	–	15 [c]	–	39	85

[a] Apart from the 4-F-product, 2% of 1,2,4,5-tetrafluorobenzene was found; [b] reaction conditions and conversion are not indicated in the literature source; [c] the yields of the isolated product with respect to the crude product mixture are given; fluorination products at the formyl group predominated.

Table 4. Fluorination of 1,4-disubstituted benzenes C_6H_4XY with a F_2-N_2 mixture (10 vol.% F_2).

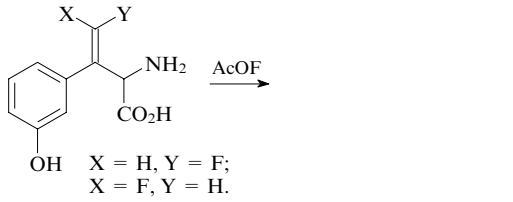
1-X	4-Y	Medium	Temperature /°C	Product yield (%)		Conversion (%)	Ref.
				2-F	2,6-F_2		
F	CO_2H	HCO_2H	20	52	3	79	65
	CO_2H	H_2SO_4	20	39	5	92	65
OH	NO_2	HCO_2H	10	70	8	75	104
OMe	NO_2	HCO_2H	10	50	20	100	104, 105
NHAc	NO_2	HCO_2H	10	60	8	100	104
Me	NO_2	HCO_2H	10	50	traces	63	104
F	NO_2	HCO_2H	10	53	traces	36	104
Cl	NO_2	HCO_2H	10	44	traces	47	104
OH	NO_2	H_2SO_4	10	24	8	30	104
OMe	NO_2	H_2SO_4	10	50	11	63	104
Me	NO_2	H_2SO_4	10	81	2	75	104
	NO_2	$HCO_2H-MeCN$ [a]	0–5	60–78 [b]	–	44–77	39
F	NO_2	H_2SO_4	10	75	10	87	104
Cl	NO_2	H_2SO_4	10	65	–	64	104
OMe	CO_2Me	H_2SO_4	10	31	10	23	104
Me	CHO	H_2SO_4	10	60	–	74	104
	CHO	MeCN	0	73 [c]	12	58	85
OH	CN	HCO_2H	10	64	10	84	104
OMe	CN	HCO_2H	10	35	10	90	104
NHAc	CN	HCO_2H	10	66	10	86	104
Me	CN	HCO_2H	10	60	< 5	86	104
F	CN	HCO_2H	10	40	traces	67	104
OH	CF_3	HCO_2H	10	12	22	100	104
	Ac	HCO_2H	10	41	7	83	104
	CO_2H	HCO_2H	10	55	20	50	104
	CO_2Me	HCO_2H	10	28	17	100	104
	Br	HCO_2H	10	22	4	90	104
	Cl	HCO_2H	10	18	13	100	104
OMe	NO_2	HCO_2H	10	50	19	100	104
	CN	HCO_2H	10	35	10	90	104
	CHO	H_2SO_4	–	60	–	–	36
	CHO	MeCN	0	79	12	66	85
	Ac	HCO_2H	–	65	–	–	36
OMe	CO_2Me	HCO_2H	10	51	9	92	104
	Br	HCO_2H	10	43	15	92	104
	Cl	HCO_2H	10	49	7	80	104
	Me	HCO_2H	10	53	< 5	48	104
CN	CHO	MeCN	0	see [d]	–	44	85

[a] In a microreactor; [b] the yield of the crude product; [c] apart from the 2-F-isomer, 3-F-isomer was formed (12% relative to the major product) but it was not isolated; [d] 12% of the 3-F-product was isolated.

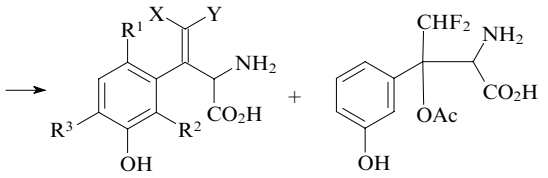
Table 5. Fluorination of 1,2- and 1,3-disubstituted benzenes C_6H_4XY with NF reagents in MeCN.

1-X	Y	Reagent	Temperature /°C	Reaction time	Product yields (%)			Overall yield (%)	Ref.
					2-F	4-F	4,6-F_2		
Me	2-Me	(**16c**)$(BF_4)_2$	Δ	16 h	49 [a]	29	17 [a]	95	91
	3-Me	(**16c**)$(BF_4)_2$	Δ	16 h	23	42	23	88	91
OH	3-OH	(**16c**)$(BF_4)_2$	Δ	12 h	–	–	–	see [b]	106
	3-OH	(**12**)$(BF_4)_2$	Δ	< 5 min	3	72	10	85	98
OMe	3-OMe	(**11c**)BF_4	20	20 h	0	52	0	52	100
	3-OMe	(**11a**)$(OTf)_2$	see [c]	see [c]	0	40	0	40	100
	3-OMe	**1a** [d]	85–90	1–8 h	0	73	15	88	107
	3-OMe	(**16c**)$(BF_4)_2$ (see [d])	85–90	1–8 h	0	78	13	91	107

[a] In this case, these are 3-F- and 3,6-F_2-products; [b] isomer mixture; the yield and conversion are not indicated; [c] kept at 20 °C for 15 h and then at 60 °C for 20 h; [d] the reaction was carried out without a solvent.



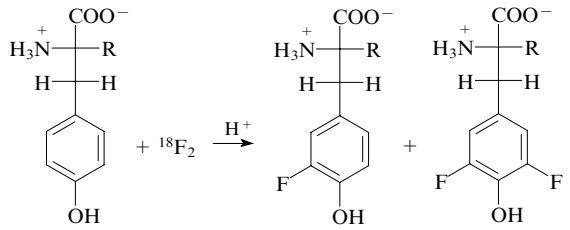
X = H, Y = F;
X = F, Y = H.



X = H, Y = F: $R^1 = F, R^2 = R^3 = H$;
$R^1 = R^3 = H, R^2 = F$;
$R^1 = R^2 = F, R^3 = H$;
X = F, Y = H: $R^1 = F, R^2 = R^3 = H$;
$R^1 = R^3 = H, R^2 = F$;
$R^1 = R^2 = F, R^3 = H$;
$R^1 = R^2 = H, R^3 = F$.

The fluorination of *m*-tyrosine with F_2O in H_2O or HCO_2H furnishes a mixture of 2-, 4- and 6-fluoro-*m*-tyrosines in 33 : 20 : 47 or 26 : 8 : 66 ratio, respectively.[110] When the acids AcOH, CF_3CO_2H or CF_3SO_3H are used as the solvents, no 4-fluoro derivative is produced, while the fraction of 6-fluoro isomer increases to reach 91% for CF_3SO_3H.[110]

The electrophilic fluorination of 1,4-disubstituted benzenes with a F_2-N_2 mixture or NF reagents is mainly directed to the *ortho*-position relative to more potent electron-releasing group out of the two groups present in the ring (Table 4, 6). This regularity holds for the fluorination of L-tyrosine and L-α-methyltyrosine with molecular fluorine in the presence of various acids (HCO_2H, CF_3CO_2H, HF, $HF-BF_3$); for all acids except for HF, minor amounts of difluorinated products are formed together with monofluorinated products.[113]



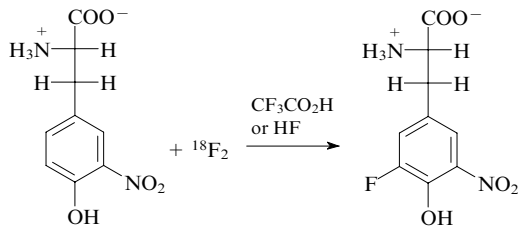
R = H, Me.

3-Nitro-L-tyrosine is also fluorinated in the *ortho*-position to the OH group.[114]

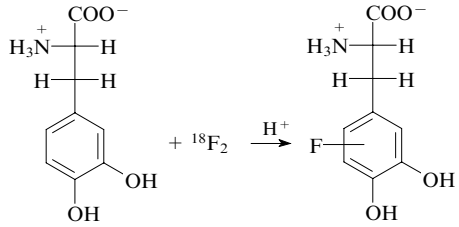
Table 6. Fluorination of 1,4-disubstituted benzenes C_6H_4XY with NF-reagents.

1-X	4-Y	Reagent	Solvent	Temperature /°C	Time	Product ratio (%)			Overall yield (%)	Ref.
						2-F	3-F	other		
Me	Me	(**16c**)$(BF_4)_2$	MeCN	Δ	16 h	67	0	33 [a]	97	91
OH	Cl	(**12**)$(OTf)_2$	$(CH_2Cl)_2$	82	20 h	100	0	0	40	111
	CO_2Me	(**12**)$(OTf)_2$	$(CH_2Cl)_2$	82	20 h	100	0	0	50	111
	Me	(**16c**)$(BF_4)_2$	MeCN	Δ	2 h	34	0	66 [b]	55	112
	Me	(**16d**)$(BF_4)_2$	MeCN	Δ	2 h	41	0	59 [b]	53	112
	Me	(**16c**)$(BF_4)_2$	MeOH	Δ	2 h	100	0	0	52	112
	Me	(**16d**)$(BF_4)_2$	MeOH	Δ	2 h	100	0	0	60	112
	Pr^i	(**16c**)$(BF_4)_2$	MeCN	Δ	2 h	40	0	60 [b]	78	112
	Pr^i	(**16d**)$(BF_4)_2$	MeCN	Δ	2 h	47	0	52 [b]	87	112
	Pr^i	(**16c**)$(BF_4)_2$	MeOH	Δ	2 h	62	0	38 [b]	84	112
	Pr^i	(**16d**)$(BF_4)_2$	MeOH	Δ	2 h	67	0	33 [b]	88	112
	Pr^i	(**9l**)BF_4	MeCN	Δ	2 h	100	0	0	22	112
	Bu^t	(**16c**)$(BF_4)_2$	MeCN	Δ	2 h	60	0	40 [c]	84	112
	Bu^t	(**16d**)$(BF_4)_2$	MeCN	Δ	2 h	61	0	39 [c]	92	112
	Bu^t	(**9l**)BF_4	MeCN	Δ	2 h	63	0	36 [c]	43	112
	Bu^t	(**16c**)$(BF_4)_2$	MeOH	Δ	2 h	81	0	19 [c]	83	112
	Bu^t	(**16d**)$(BF_4)_2$	MeOH	Δ	2 h	90	0	10 [c]	91	112
	Bu^t	(**9l**)BF_4	MeCN	Δ	2 h	63	0	36 [c]	43	112
	Bu^t	**1a**	see [d]	85	4 h	~100	0	0	55	107
	tert-C_8H_{17}	(**16c**)$(BF_4)_2$	MeCN	Δ	2 h	88	0	12 [c]	55	112
	tert-C_8H_{17}	(**16c**)$(BF_4)_2$	MeOH	Δ	2 h	88	0	12	60	112
OMe	Me	(**16c**)$(BF_4)_2$	[emim][CF_3SO_3]	80	15 h	93	6	1 [e]	51	68
OEt	Bu^t	**1a**	see [d]	85	4 h	~100	0	0	52	107
OMe	Cl	(**16c**)$(BF_4)_2$	[emim][CF_3SO_3]	80	15 h	95	0	5 [e]	50	68
	F	(**16c**)$(BF_4)_2$	[emim][CF_3SO_3]	80	15 h	~100	0	0	23	68
Me	Me	(**16c**)$(BF_4)_2$	[emim][CF_3SO_3]	80	15 h	~100	0	0	48	68
	Me	(**16c**)$(BF_4)_2$	[emim][BF_4]	80	15 h	~100	0	0	22	68
	NO_2	(**16c**)$(BF_4)_2$	[bmim][BF_4]	80	15 h				0	68
	NO_2	(**16c**)$(BF_4)_2$	[bmim][CF_3SO_3]	80	15 h				0	68

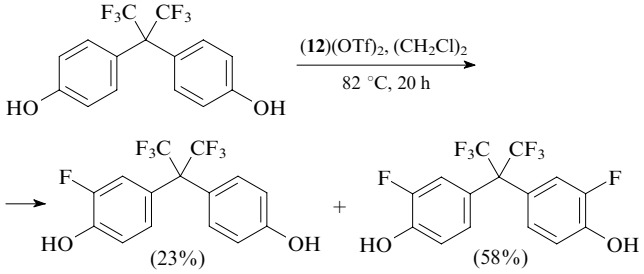
[a] 1,4-Dimethyl-2,5-difluorobenzene; [b] 4-Y-4-fluorocyclohexa-2,5-dienone; [c] 4-fluorophenol; [d] the reaction was carried out without a solvent; [e] 1-X-4-Y-2,6-difluorobenzene.



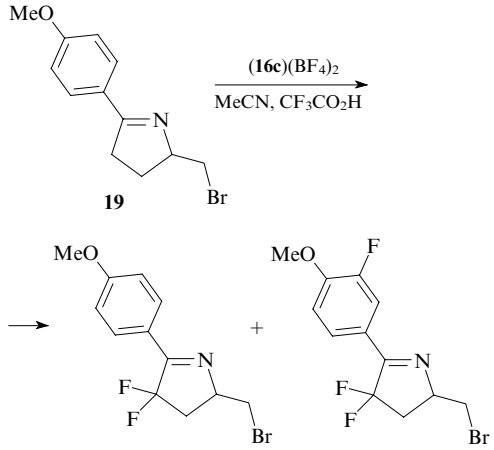
The direction of fluorination of 3,4-dihydroxyphenyl-L-alanine with molecular fluorine is considerably dependent on the medium acidity: the use of CF_3CO_2H, HCO_2H or a $CF_3CO_2H-AcOH$ mixture gives 2- and 5-fluoro derivatives as the major products, while in the presence of HF or $HF-BF_3$, 2- and 6-fluoro isomers are formed.[115]



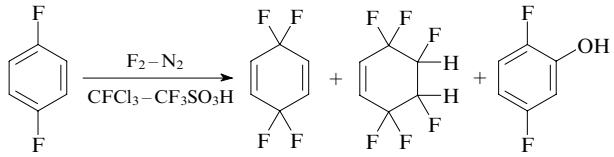
The fluorination of bis(4-hydroxyphenyl)bis(trifluoromethyl)methane with (**12**)$(OTf)_2$ also gives rise to mono- and disubstituted products with the fluorine atom in the *ortho*-position relative to the electron-releasing group OH.[111]



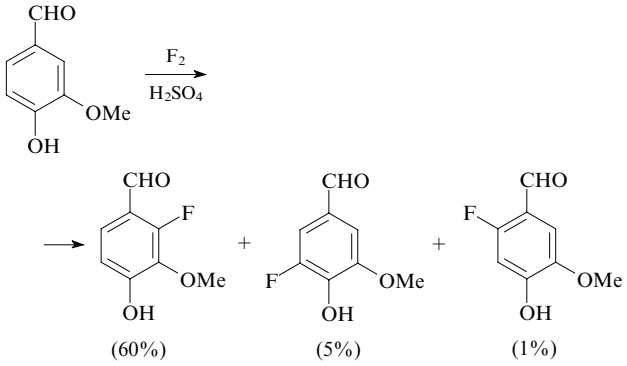
The fluorination of dihydropyrrole derivative **19** with (**16c**)$(BF_4)_2$ in MeCN in the presence of CF_3CO_2H affords a mixture of di- and trifluorinated products in 57 : 43 ratio.[116]



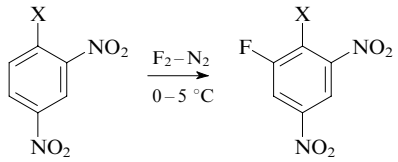
In the fluorination of *p*-difluorobenzene with a F_2-N_2 mixture in $CFCl_3-CF_3SO_3H$, the addition rather than substitution reaction is the predominant route, because the *para*-position of the substrate is occupied by the fluorine atom.[84]



An unexpected result came from fluorination of vanillin with a F_2-N_2 mixture in H_2SO_4: the reaction proceeded selectively being directed mainly to position 2 rather than 5, *i.e.*, to the *ortho*-position relative to the electron-withdrawing formyl group.[36, 117]

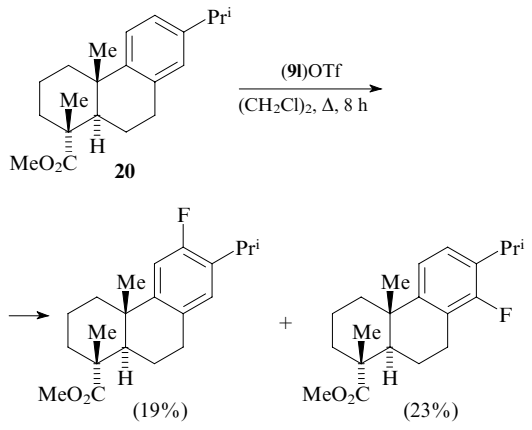


Similarly, the low-temperature fluorination of 1-X-2,4-dinitrobenzenes (X = Me, Cl) with a F_2-N_2 mixture in HCO_2H or $HCO_2H-MeCN$ using a microreactor was performed selectively.[37, 39]



X = Me (70%), Cl (97%).

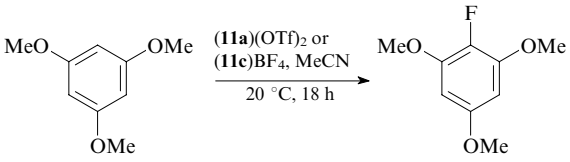
Conversely, fluorination of methyldehydroabietate (**20**) with (**9l**)OTf is non-selective and gives fluorinated products in moderate yields.[64]



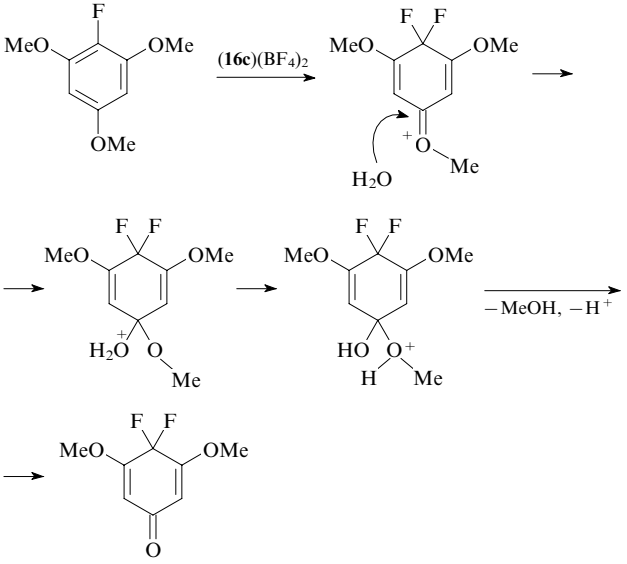
3. Fluorination of tri- and tetrasubstituted benzenes

The fluorination of mesitylene with NF reagents **1a** or (**16c**)$(BF_4)_2$ in MeCN, $CF_3SO_3H-CH_2Cl_2$ or ionic liquid [bmim][PF_6] proceeds selectively yielding 2-fluoromesitylene.[68, 92, 118, 119]

The monofluoro derivative is formed as the major product in the fluorination of 1,3,5-trimethoxybenzene with (**11a**)$(OTf)_2$ and (**11c**)BF_4 (yields 50% and 61%, respectively).[100]

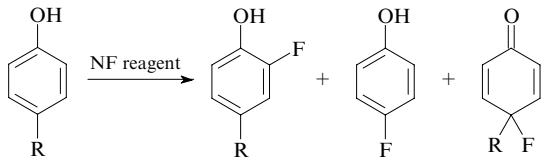


Meanwhile, fluorination of 1,3,5-trimethoxybenzene with equimolar amount of (**16c**)$(BF_4)_2$ gives, in addition to 1,3,5-trimethoxy-2-fluorobenzene, the demethylation product, namely, 3,5-dimethoxy-4,4-difluorocyclohexa-2,5-dien-1-one (yields 62% and 26%, respectively) even under mild conditions (from −40 to 20 °C).[120] As the (**16c**)$(BF_4)_2$: ArH molar ratio increases to 2, the yield of the demethylation product increases to 51%; the use of water as the solvent increases the yield (63%). The specific effect of water was attributed to its participation in the reaction as a nucleophile.



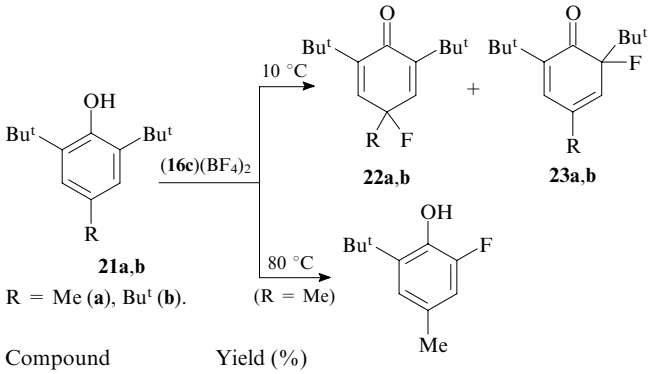
The fluorination of 2,4,6-trimethoxytoluene with (**16c**)$(BF_4)_2$ in MeCN proceeds in a similar way (the yield of 4-methyl-3,5-dimethoxy-4-fluorocyclohexa-2,5-dien-1-one is 81%).[120]

The fluorination of phenols is often accompanied by the formation of ketones. Thus on treatment of 4-R-phenols with the tetrafluoroborates of cations **9l** and **16c**,**d**, the *ortho*-substitution is accompanied by the *ipso*-substitution or *ipso*-addition to give 4-fluorophenol and 4-R-4-fluorocyclohexa-2,5-dienone; the fraction of *ortho*-substituted product tends to increase with increase in the bulk of the substituent R and the fraction of *ipso*-addition product decreases when acetonitrile is used as the solvent (see Table 6).[112]



R = Me, Pr^i, Bu^t, *tert*-C_8H_{17}.

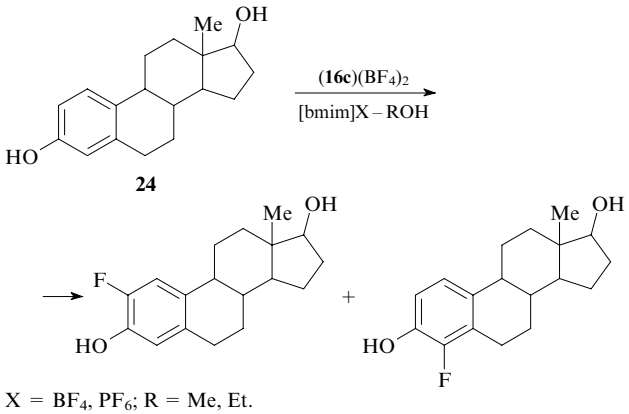
The fluorination of substituted phenols **21a**,**b** with (**16c**)$(BF_4)_2$ under kinetic control conditions also affords ketones **22**, **23**, whereas under thermodynamic control conditions for R = Me, fluorodealkylation takes place.[73]



R = Me (**a**), Bu^t (**b**).

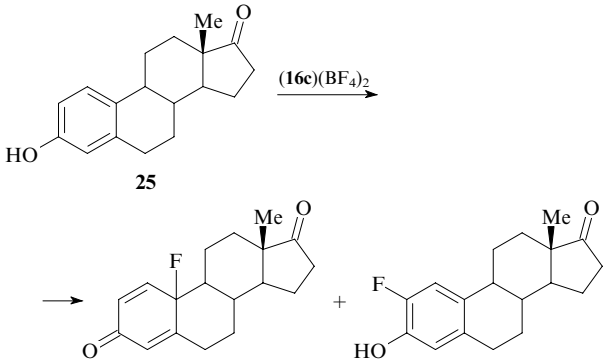
Compound	Yield (%)
22a	44
22b	20
23a	56
23b	80

Using a [bmim]X – MeOH or [bmim]X – EtOH mixture (X = BF_4, PF_6) and the reagent (**16c**)$(BF_4)_2$, it is possible to carry out selective fluorination of diol **24** giving rise to *ortho*-substituted products in ~8 : 1 ratio.[121]

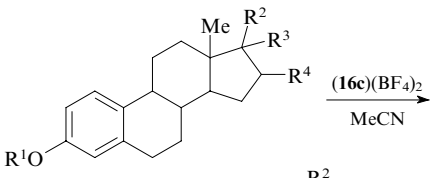


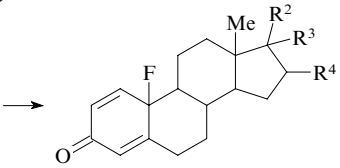
X = BF_4, PF_6; R = Me, Et.

Conversely, the reaction of estrone (**25**) with (**16c**)$(BF_4)_2$ in water[122] or without a solvent[123, 124] occurs mainly as oxidative addition of the fluorine atom in the *para*-position to the hydroxyl group.

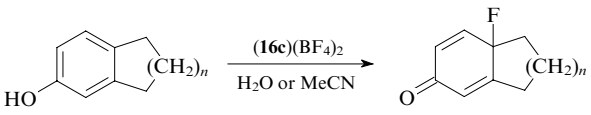


Fluorination of other steroids in MeCN (Ref. 125) and of hydroxy indane and tetrahydronaphthalene derivatives in MeCN[125] and in water[122] occurs in a similar way.



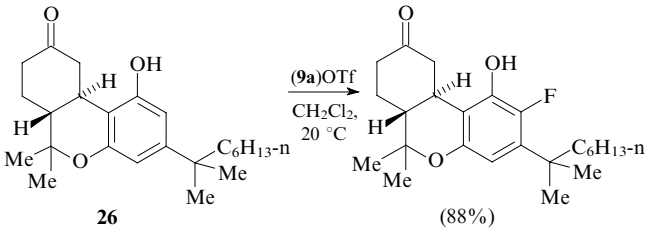


$R^1 = R^4 = H$, $R^2 + R^3 = O$;
$R^1 = R^3 = R^4 = H$, $R^2 = OH$;
$R^1 = R^4 = H$, $R^2 = OH$, $R^3 = C_2H$;
$R^1 = Me$, $R^2 + R^3 = O$, $R^4 = H$;
$R^1 = Me$, $R^2 = OH$, $R^3 = C_2H$, $R^4 = H$;
$R^1 = R^3 = H$, $R^2 = R^4 = OH$.



$n = 1, 2$.

A high selectivity was attained in the fluorination of nabilone (**26**) with salt (**9a**)OTf.[126]

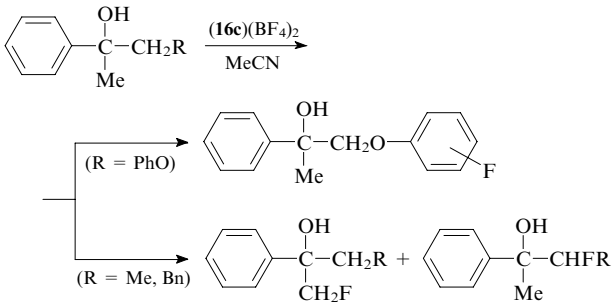


26 (88%)

4. Side reactions at the side chain

In some cases, the fluorine substitution for the hydrogen atom in the aromatic ring is accompanied by side-chain fluorination. The reaction of alkyl aryl ketones with (**16d**)$(BF_4)_2$ in MeOH affords α-fluoro ketones in a nearly quantitative yield, whereas in MeCN, aromatic hydrogen is displaced by fluorine (Table 7).[127]

Similarly, 1-R-2-hydroxy-2-phenylpropanes (R = Me, Bn, PhO) are fluorinated with (**16c**)$(BF_4)_2$ to give vicinal fluorohydrins for R = Me, Bn, whereas in the case of R = PhO, fluorination involves only the phenoxy group to give mainly the *ortho*-isomer (*ortho* : *para* = 1.8).[128]

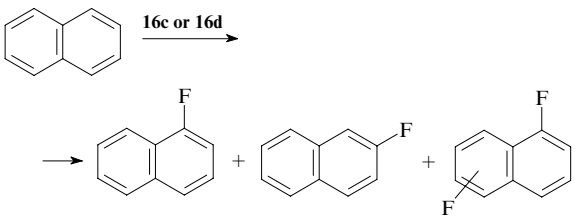


R = Me, Bn, PhO.

IV. Fluorination of bi- and polycyclic aromatic compounds

In recent years, the interest in the use of molecular fluorine and OF reagents for the fluorination of bicyclic and polycyclic aromatic compounds has considerably decreased, while NF reagents have found extensive use.[27, 38, 44, 47]

In the naphthalene fluorination with the tetrafluoroborate of cation **16c** or **16d**, the formation of 1-fluoronaphthalene is accompanied by the formation of noticeable amount of 2-fluoronaphthalene and difluorination products (Table 8).



The introduction of electron-releasing substituents in position 1 of naphthalene leads to predominant displace-

Table 7. Fluorination of some alkyl aryl ketones with reagent (**16d**)$(BF_4)_2$.[127]

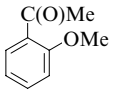
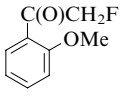
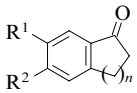
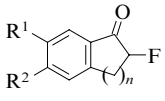
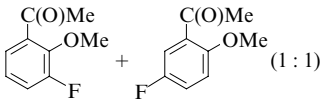
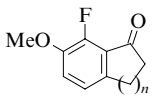
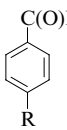
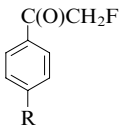
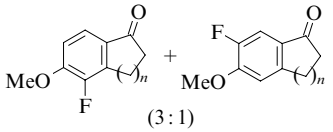
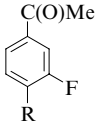
Starting ketone	Solvent	Products	Starting ketone	Solvent	Products
	MeOH		 $R^1 = H$, $R^2 = OMe$; $R^1 = OMe$, $R^2 = H$; $n = 1, 2$.	MeOH	
	MeCN	 (1 : 1)		MeCN	 ($R^1 = OMe$, $R^2 = H$)
 $R = OH, OMe$	MeOH				 (3 : 1) ($R^1 = H$, $R^2 = OMe$)
	MeCN				

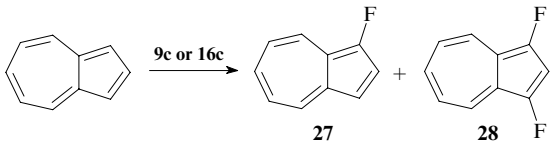
Table 8. Fluorination of naphthalene and its 1-derivatives $C_{10}H_7X$ with NF reagents.

X	Reagent	Solvent	Temperature /°C	Time	Product ratio (%)				Overall yield (%) [a]	Ref.
					1-F	2-F	4-F	other		
H	(**16c**)$(BF_4)_2$	[emim][CF_3SO_3]	80	15 h	91	7	0	2 [b]	88	68
	(**16c**)$(BF_4)_2$	CF_3CO_2H	70	4 h	75	25	0	0	75	129
	(**16c**)$(BF_4)_2$	$CF_3SO_3H-CH_2Cl_2$	Δ	12 h	60	40	0	0	100	92
	(**16d**)$(BF_4)_2$	MeCN	80	30 min	90	< 2	0	8 [c]	82	130
Me	(**16d**)$(BF_4)_2$	MeCN	80	3 h		22	68	10 [d]	65	130
	(**16c**)$(BF_4)_2$	[bmim][PF_6]	80	15 h		21	53	11[e], 15[f]	23	68
OH	**10h**	CH_2Cl_2	20	5 min		95	0	5 [g]	66	97
	(**16a**)$(OTf)_2$	MeOH	20	1 h		~67	~33	0	~100	99
	(**16c**)$(BF_4)_2$	MeCN	20	3 h		49	41	10 [g]	100	131
	(**16d**)$(BF_4)_2$	MeCN	80	10 min		45	42	13 [g]	80	130
OMe	(**16d**)$(BF_4)_2$	MeCN	80	15 min		48	48	4 [g]	85	130
	1a	CH_2Cl_2 [h]	20	12 h		43	57	0	31	132
OPr^i	(**16d**)$(BF_4)_2$	MeCN [b]	80	10 min		68	30	2 [g]	85	130
F	(**16d**)$(BF_4)_2$	MeCN	80	3 h		15	85	0	65	130

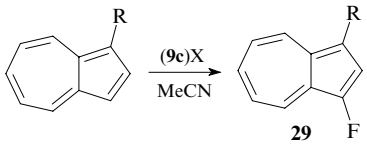
[a] Overall yield of fluorinated products; [b] 1,8-difluoronaphthalene; [c] 1,4-difluoronaphthalene; [d] 1-methyl-2,4-difluoronaphthalene; [e] 1-methyl-5-fluoronaphthalene; [f] 1-methyl-8-fluoronaphthalene; [g] 2,2-difluoro-1(*2H*)-naphthalenone; [h] in the presence of 20% $ZrCl_4$.

ment of the 2- and 4-hydrogen atoms in the aromatic ring (see Table 8).

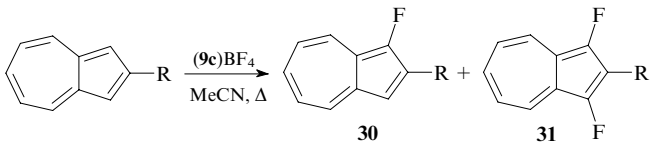
The fluorination of azulene and its derivatives with NF reagents is directed to positions 1 and 3 of the five-membered ring, the yield of fluorinated products (for example, **27**–**31**) being considerably dependent on the nature of substituents.[133, 134]



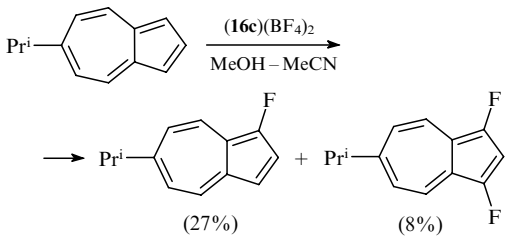
NF reagent	Yield (%)	
	27	**28**
(**9c**)OTf	24	7
(**16c**)$(BF_4)_2$	34	3

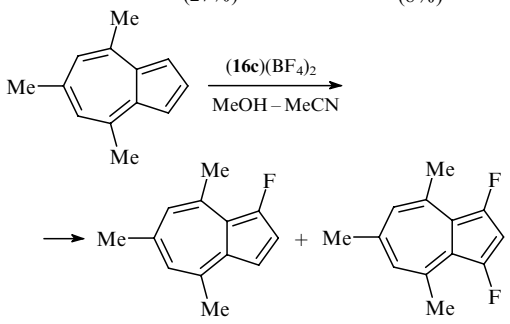


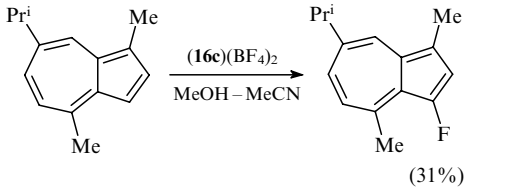
X	R	Yield (%)
BF_4	Me	5
BF_4	Ph	16
OTf	CHO	21
OTf	CO_2Me	19



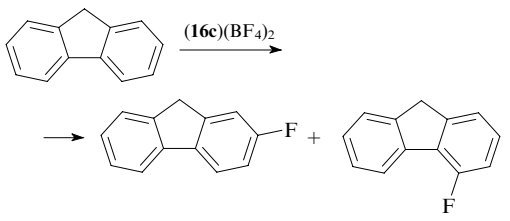
R	Yield (%)	
	30	**31**
Me	41	13
Ph	33	7





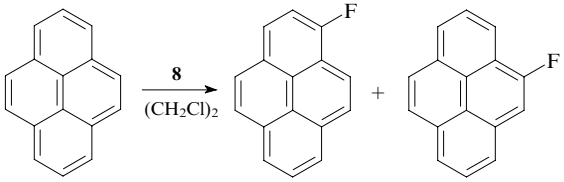


Fluorene is fluorinated with (**16c**)$(BF_4)_2$ in MeCN or CF_3CO_2H to give 2- and 4-fluorofluorenes in 1.6 : 1 or 1.2 : 1 ratio, respectively, which corresponds to a larger coefficient of electron density at C(2) (0.39) than at C(4) (0.278) in its HOMO.[74]

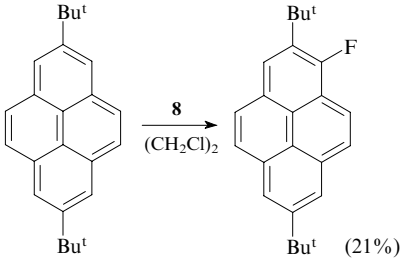


Fluorene fluorination with XeF_2 in CH_2Cl_2 in the presence of a catalytic amount of $BF_3 \cdot Et_2O$ also provides 2- and 4-fluorofluorenes in 2 : 1 ratio.[87]

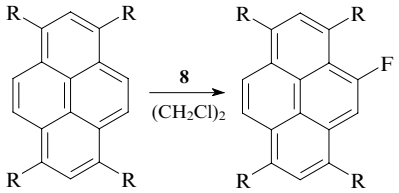
Phenanthrene is fluorinated fairly selectively with (**16c**)$(BF_4)_2$ (Ref. 129) and (**16d**)$(BF_4)_2$ (Ref. 130) in CF_3CO_2H or MeCN at position 9, whereas pyrene is converted, on treatment with **16d**, to a mixture of 1-fluoro- and 4-fluoropyrenes, the selectivity becoming higher upon a decrease in temperature (63 : 22 at 80 °C and 93 : 7 at 5 °C).[130] Note that the use of reagent **8** for fluorination of pyrene and a number of its derivatives ensures high selectivity even at ~80 °C.[135] Fluorination of other polycyclic arenes with this reagent is non-selective (for product yields and isomer ratios, see below).[135]



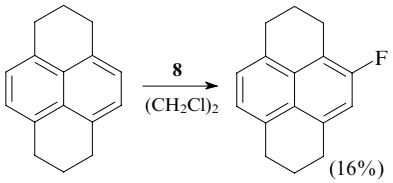
(23%, 9 : 1)



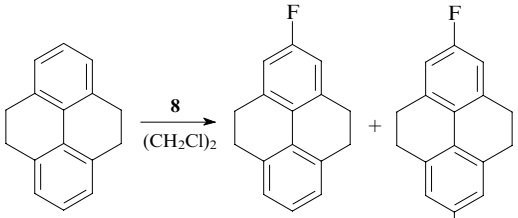
(21%)



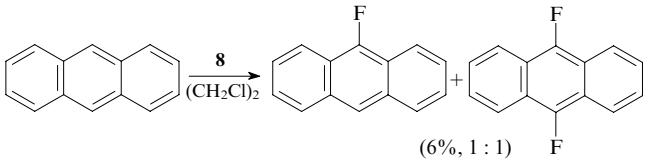
R = Pr^i (18%), cyclo-C_5H_9 (13%).



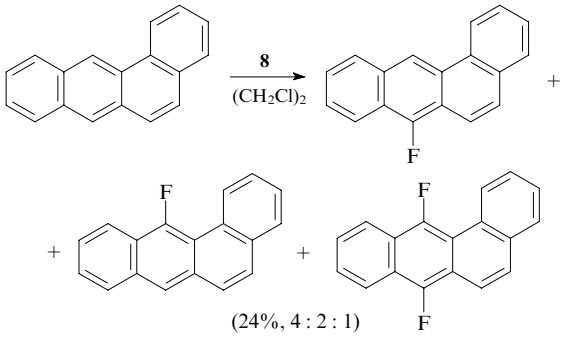
(16%)



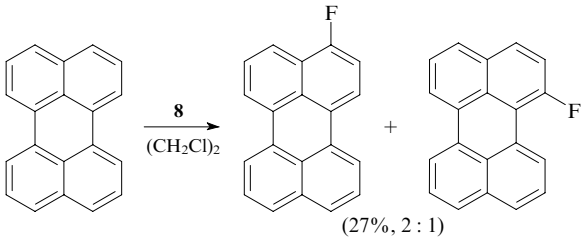
(12%, 3 : 1)



(6%, 1 : 1)

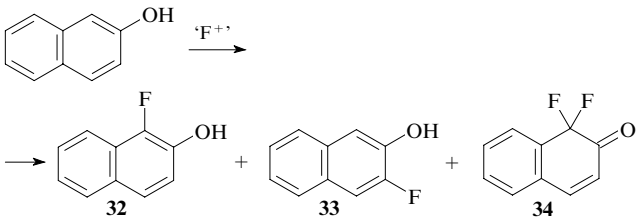


(24%, 4 : 2 : 1)



(27%, 2 : 1)

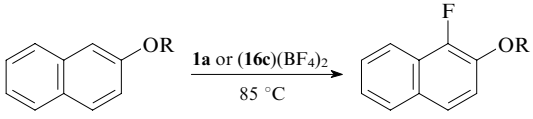
The fluorination of 2-naphthol with NF-reagents gives products **32**, **33** and is usually accompanied by the formation of ketone **34** (Table 9).



Using 2-naphthol and the reagent (**16c**)$(BF_4)_2$ in 1 : 1,1 ratio in a [bmim]X – MeOH or [bmim]X – EtOH mixture (X = BF_4, PF_6), one can selectively obtain naphthol **32** (yield > 94%), while the amounts of ketone **34** and naphthol **33** are relatively small (< 3%).[121] An increase in the (**16c**)$(BF_4)_2$: 2-naphthol ratio to 2.1 : 1 in the same solvent mixture affords mainly ketone **34** (> 97%).[121]

In liquid CO_2, fluorination of 2-naphthol with the reagent (**12**)$(BF_4)_2$ does not proceed due to low solubility of the fluorinating reagent.[111] The addition of NaOTf induces salt exchange, thus increasing the solubility of the fluorinating reagent, and results in the formation of ketone **34** in a high yield (see Table 9). The variation of the anions X^- in the salts with cation **15** has almost no influence on the ratio of mono- and difluorinated products obtained from 2-naphthol (see. Table 9).[102]

The fluorination of 2-naphthol ethers with **1a**, (**16c**)$(BF_4)_2$ without a solvent was carried out rather selectively giving no corresponding ketone.[107]



R = Et, Pr^i.

NF reagent	R	Yield (%)
16c	Et	61
1a	Et	67
16c	Pr^i	52
1a	Pr^i	55

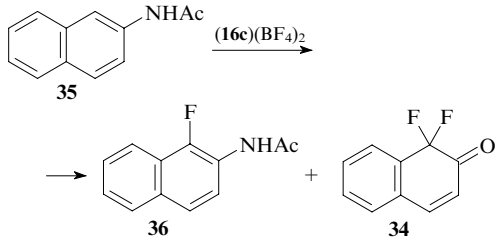
Table 9. Fluorination of 2-naphthol with NF reagents at room temperature.

Reagent	Solvent	Reaction time	Product ratio (%) [a]		Overall yield (%)	Ref.
			I	II		
(**12**)$(OTf)_2$	MeCN	12 h	35	65	85	111
	CO_2	12 h	10	90	99	111
(**12**)$(BF_4)_2$	CO_2	12 h			0	111
	CO_2 [b]	12 h	traces	95 [c]	95	111
	HCO_2H	10 min	77	23	79	98
(**11a**)$(OTf)_2$	MeCN [d]	15 h	100	0	60	100
(**15**)BF_4	MeCN	overnight	~67	~33	90	102
(**15**)PF_6	MeCN	overnight	~67	~33	94	102
(**15**)SO_3F	MeCN	overnight	~67	~33	88	102
(**15**)OTf	MeCN	overnight	~67	~33	92	102
(**16c**)$(OTf)_2$	MeOH	30 min	~67	~33	~100	99
(**16c**)$(BF_4)_2$	MeCN	3 h	73	27	100	131
	H_2O [e]	30 min	0	100	78	122
(**16e**)$(BF_4)_2$	HCO_2H–MeOH	15 min	57	43	67	71

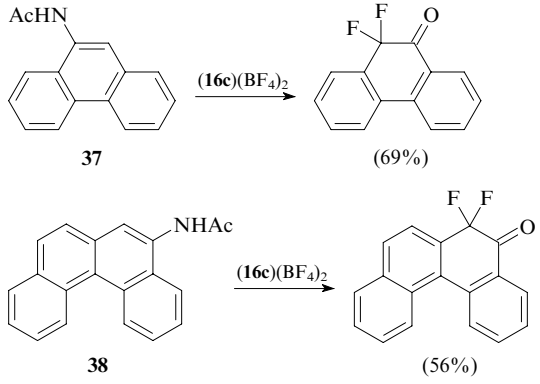
[a] I is 1-fluoro-2-naphthol, II is 1,1-difluoro-1-(2*H*)-naphthalenone; [b] with addition of NaOTf; [c] yield of fluorinated products; [d] at 80 °C; [e] at 60 °C.

The $ZrCl_4$-catalyzed fluorination of 2-methoxynaphthalene with **1a** affords 2-methoxy-1-fluoronaphthalene; an increase in the amount of the catalyst (20 mol.%, 50 mol.% and 100 mol.%) entailed an increase in the product yield (28%, 43% and 70%, respectively).[132]

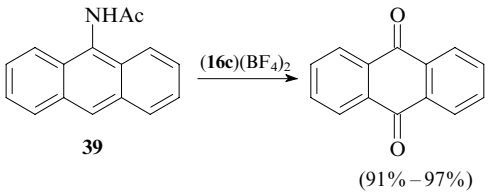
The fluorination of 2-acetylaminonaphthalene (**35**) with the reagent (**16c**)$(BF_4)_2$ in a [bmim]X–MeOH or [bmim]-X–EtOH mixture (X = BF_4, PF_6), as in the case of 2-naphthol, is fairly selective giving predominantly product **36** (>96%) for the ratio (**16c**)$(BF_4)_2$: substrate = 1.1 or ketone **34** (>95%) when the NF reagent is present in a twofold excess.[121]



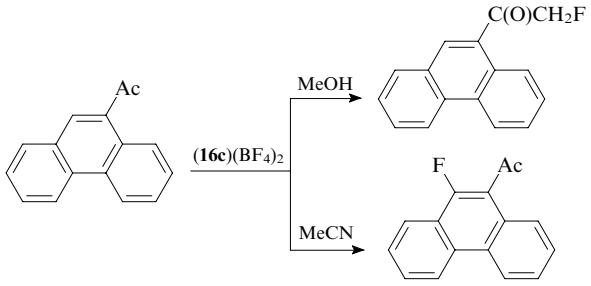
The fluorination of phenanthrene derivatives **37** and **38** with (**16c**)$(BF_4)_2$ in a [bmim]X–MeOH or [bmim]X–EtOH mixture (X = BF_4, PF_6) furnishes the corresponding fluoroketones.[121]



Under analogous conditions, anthracene **39** is converted to anthraquinone in a high yield.[121]



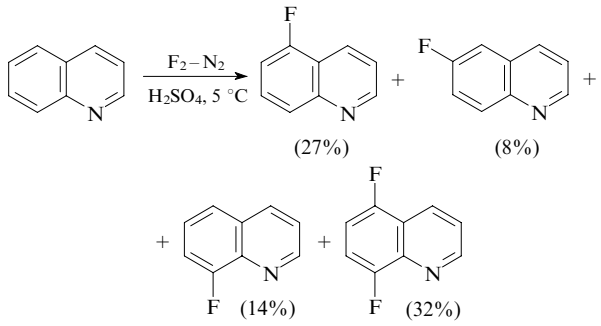
In the case of alkyl aryl ketones, the fluorine substitution for the hydrogen atom in the ring is accompanied by side-chain fluorination. For example, the reaction of 9-acetylphenanthrene with (**16d**)$(BF_4)_2$ in MeOH affords α-fluoro ketone in a high yield, whereas in MeCN a hydrogen atom of the ring is displaced.[127]



V. Fluorination of heteroaromatic compounds

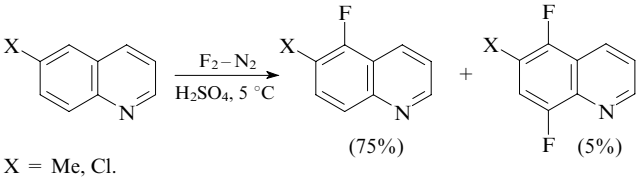
Since nitrogen and oxygen are more electronegative than carbon, the electrophilic fluorination of six-membered N- and O-heteroaromatic compounds is hampered and is usually performed by potent electrophilic reagents [F_2, XeF_2, (**16c**)$(BF_4)_2$, *etc.*); as a rule, the fluorine atom enters the aromatic ring free from heteroatom.

Indeed, fluorination of quinoline with a F_2–N_2 mixture in acid medium produces 5-, 6-, 8-fluoroquinolines and 5,8-difluoroquinoline.[136]



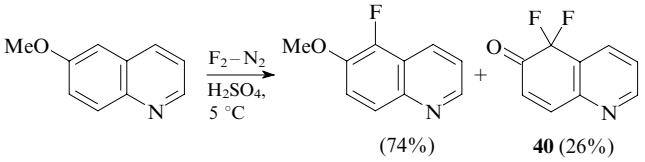
The variation of the nature of the medium (conc. H_2SO_4 and a concentrated H_2SO_4–perfluorophenanthrene mixture) and the excess of F_2 in the fluorination of quinoline with a 10% F_2-N_2 mixture changes the ratio of the isomeric products, but the reaction selectivity still remains low.[136] Similarly, low selectivity is observed for the fluorination of 2-chloro-, 4-methyl-, 2,7-dimethyl- and 4,7-dichloroquinoline with this mixture.[136]

Meanwhile, 6-X-quinolines (X = Me, OMe, Cl) are fluorinated more selectively and mainly in position 5, irrespective of the electron-releasing properties of the substituents.[136, 137]

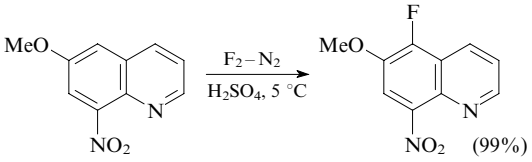


X = Me, Cl.

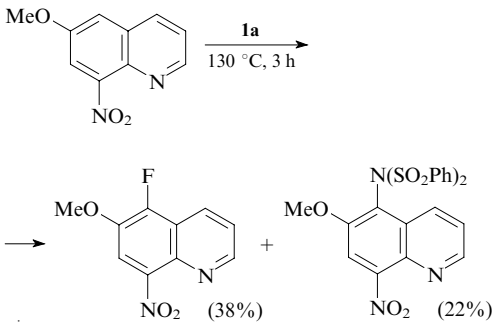
In the case of 6-methoxyquinoline, apart from the product of fluorine atom substitution for the hydrogen atom, ketone **40** is formed.[137] The yield of this product increases when an excess of F_2 is used.[136, 137]



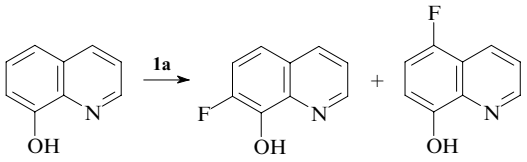
Fluorination of 6-methoxy-8-nitroquinoline under the same conditions gives almost quantitatively the corresponding 5-fluoro derivative.



However, fluorination of 6-methoxy-8-nitroquinoline with reagent **1a** without a solvent is evidently accompanied by nucleophilic displacement of fluorine from the initially formed 6-methoxy-8-nitro-5-fluoroquinoline.[138]

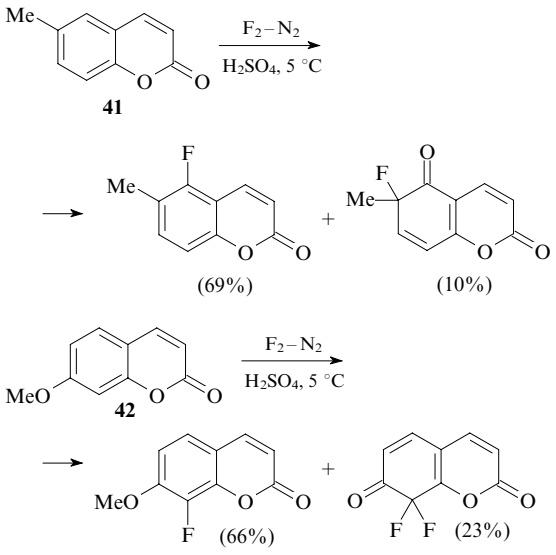


However, the reaction of 8-hydroxyquinoline with this reagent without a solvent affords only fluorination products.[139]



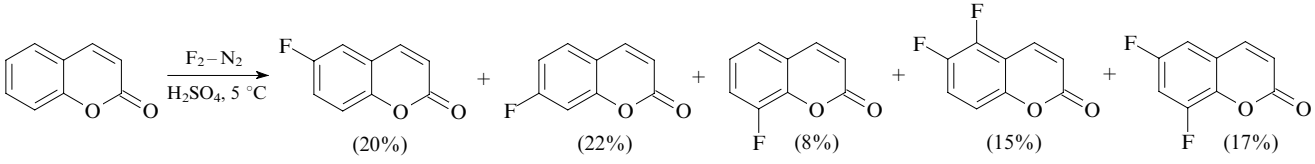
The fluorination of coumarin with a F_2-N_2 mixture in acid medium mainly involves the benzene ring and affords a complex mixture of products (Scheme 2).[140]

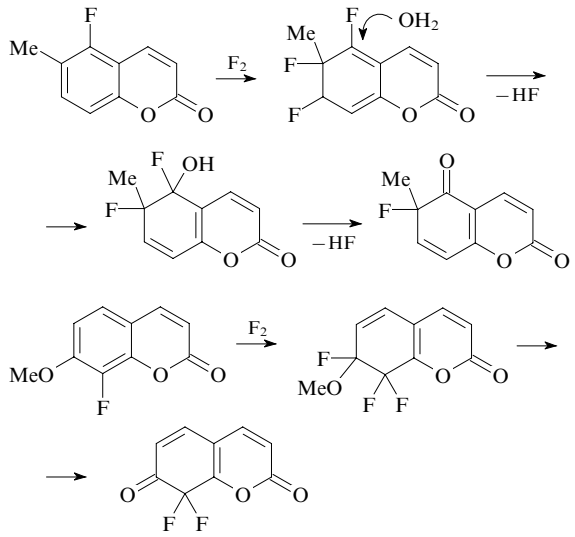
The fluorination of 6-methyl- (**41**) and 7-methoxycoumarins (**42**) is more selective yielding a minor amount of diketones.[140]



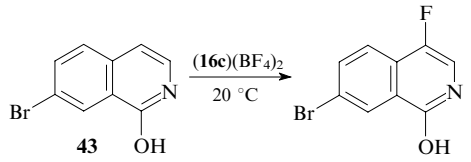
As the F_2 : **42** molar ratio increases from 5 to 10, the yield of diketone considerably increases (to 72%).[140] The mechanism of diketone formation can be represented as follows.[140]

Scheme 2

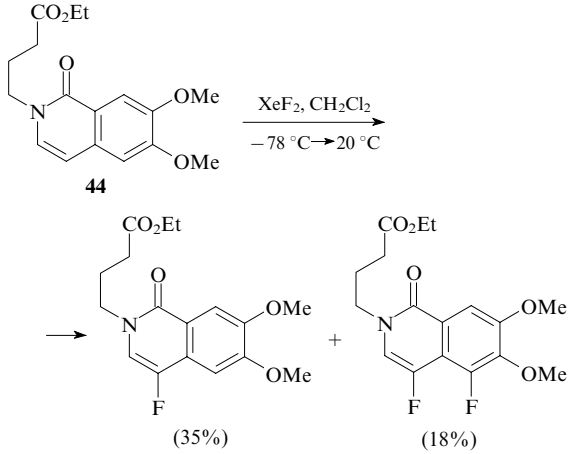




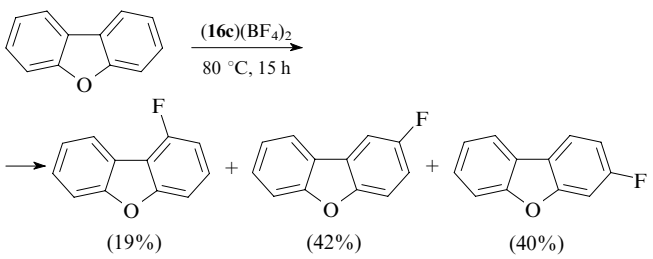
When a strong electron-releasing group is present in the heterocycle, hydrogen atom displacement occurs in this ring. For instance, fluorination of isoquinoline **43** with (**16c**)$(BF_4)_2$ is directed only to position 4 of the nitrogen-containing ring, the yields of the target product being higher in a MeCN–MeOH mixture at room temperature than on refluxing in MeCN (100% and 45%, respectively).[141]



During fluorination of isoquinoline derivative **44** with xenon difluoride, both rings are involved in the reaction to give both mono- and difluoro derivatives.[142]

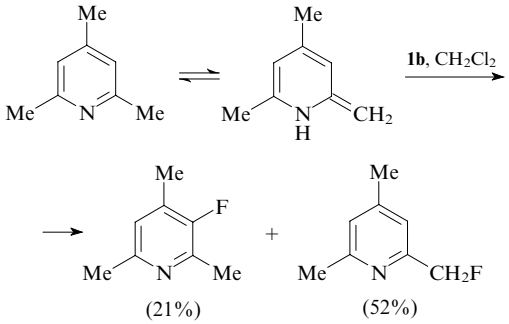


The regioselectivity of dibenzofuran fluorination with (**16c**)$(BF_4)_2$ in the ionic liquid [emim]OTf is low.[68]

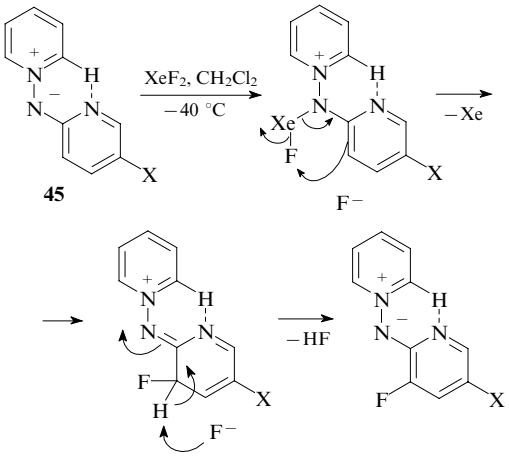


A similar situation is observed for fluorination of dibenzofuran with this reagent also in other solvents (MeCN, MeCN–$PhNO_2$, MeCN–CH_2Cl_2, MeCN–MeOH, MeCN–CF_3CO_2H, CF_3CO_2H)[95] under microwave radiation[93] or for fluorination with XeF_2.[87]

The electrophilic fluorination of collidine with reagent **1b** in the ring is accompanied by displacement of a hydrogen atom of the methyl group affording 4,6-dimethyl-2-fluoromethylpyridine, which reduces the reaction selectivity.[143] Presumably, this product appears as a result of formation of the enamine form of the substrate during fluorination.

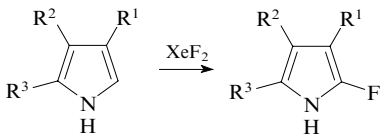


High regioselectivity observed for the reaction of tricyclic compounds **45** with XeF_2 is apparently achieved through binding of this reagent to the nitrogen atom bearing a negative charge.[144]



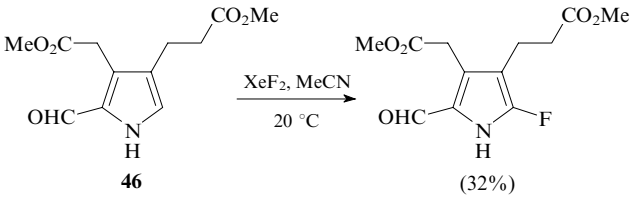
X = H, Cl, Br, I.

The electrophilic fluorination of pyrrole and its derivatives occurs most often at position 2 in moderate yields. For example $ZrCl_4$-catalyzed fluorination of pyrrole with *N*-fluorobis(phenylsulfonyl)amine in CH_2Cl_2 gives rise to 2-fluoropyrrole in a 53% yield.[132] When pyrrole derivatives react with XeF_2 in MeCN or CH_2Cl_2, fluorination is also directed to position 2 and results in 25%–54% yields.[145]



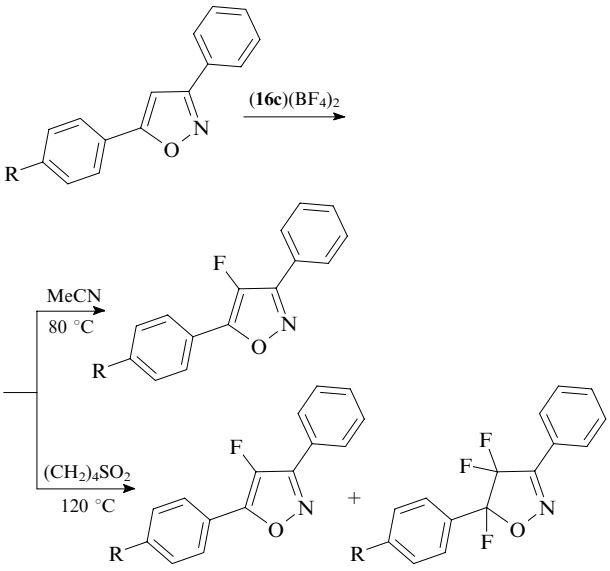
$R^1 = R^2 = H$: R^3 = CHO, CO_2Bn, $C(O)NMe_2$, $C(O)CCl_3$;
$R^1 = CH_2CO_2Me$, $R^2 = (CH_2)_2CO_2Me$, $R^3 = CO_2Bn$;
$R^1 = (CH_2)_2CO_2Me$, $R^2 = CH_2CO_2Me$: R^3 = CHO, CO_2Bn.

Xenon difluoride proved to be the best in the series of reagents including **9a**, *N*-fluoro-*N*-propyl-*p*-toluenesulfonylamide, XeF_2 as regards fluorination of pyrrole derivative **46**.[146]



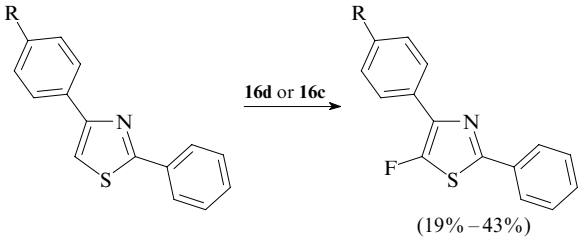
46 (32%)

The fluorination of 3,5-diarylisoxazoles with the reagent (**16c**)$(BF_4)_2$ in MeCN or sulfolane occurs in position 4; at high temperatures, the substitution reaction is accompanied by trifluorination of the isoxazole ring.[147]



R = H, Me, OMe, CF_3, Br.

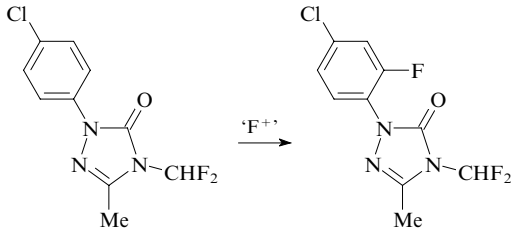
It was shown that (**16d**)$(BF_4)_2$ (Accufluor) is a more efficient reagent than (**16c**)$(BF_4)_2$ (Selectfluor) for introducing a fluorine atom into the 2,4-diarylthiazole ring; however, the yields of fluorinated products are relatively low.[148]



(19%–43%)

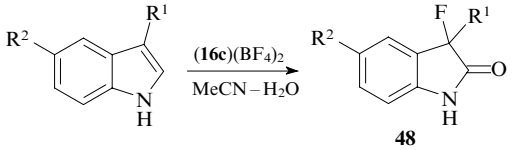
R = H, Me, OMe, NO_2, Br.

Compound **47** is fluorinated with various electrophilic reagents into the benzene ring at the *meta*-position to the chlorine atom.[149] The highest selectivity was attained on treatment with the reagents XeF_2, $CF_2(OF)_2$, CF_3CO_2F and CF_3OF (100%, 98%, 93% and 93%, respectively), while the lowest selectivity was observed with the use of fluorine gas (44%–66%), which is in line with the usual 'activity–selectivity' relationship.



47

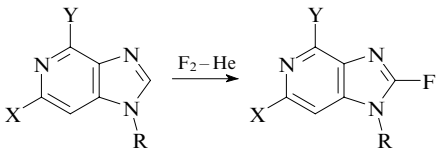
Treatment of 3-methylindole with (**16c**)$(BF_4)_2$ in MeCN, MeCN–H_2O, MeCN–MeOH, MeCN–CF_3CH_2OH afforded oxindole **48**, the highest yield (71%) being attained using a threefold excess of the fluorinating reagent and a MeCN–H_2O mixture (1 : 1).[150] The yield of oxindole **48** increases to 88%–99% when the ionic liquid [bmim]X–MeOH or [bmim]X–EtOH (X = BF_4, PF_6) is used as the solvent.[151] The fluorination of 3,5-disubstituted indoles, tryptophans, tryptamines and serotonin with the reagent (**16c**)$(BF_4)_2$ also leads to 3-fluoro-substituted products.[150, 152]



48

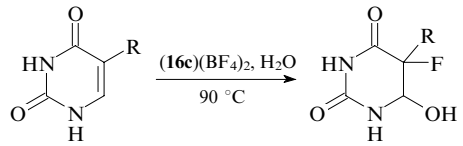
R^2 = H: R^1 = Me, CH_2CO_2Me, $(CH_2)_2CO_2Me$, $(CH_2)_3CO_2Me$, $(CH_2)_2OAc$, $(CH_2)_3OAc$, $(CH_2)_4OAc$, $(CH_2)_2NPhth$, $(CH_2)_2CH(NHAc)CO_2Me$, $(CH_2)_2CH[NH(p\text{-}NO_2C_6H_4CO_2)]CO_2Me$, $CH_2C(CO_2Me)NHAc$, $CH_2C(CO_2Me)NH(CO_2Bu^t)$, $CH_2C(CO_2Me)NH(CO_2Bn)$, $CH_2C(CO_2Me)NHC(O)CF_3$, $CH_2C(CO_2Bu^t)NHAc$, $CH_2C(CO_2Me)N(CO_2Bu^t)_2$; R^1 = $(CH_2)_2NPhth$, R^2 = OAc; HNPhth is phthalimide.

The substituted purines (X = H, NHAc) are fluorinated with a F_2–He mixture in $CHCl_3$, MeCN or EtOH in position 8, the yields of the fluorination products being dependent on the nature of substituents X and Y (X = NH_2, Y = OH: 7%–10%; X = H, NHAc; Y = OH, NH_2: 25%–30%).[153–155]

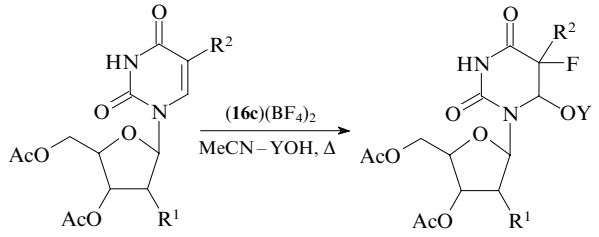


R = β-D-ribofuranosyl, X = NH_2: Y = OH, NH_2; X = NHAc, Y = OH: R = 2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl, (2-acetoxyethoxy)methyl; R = (2-hydroxyethoxy)methyl, X = NH_2, Y = OH; R = 2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl: X = H, Y = OH; X = H, Y = NH_2.

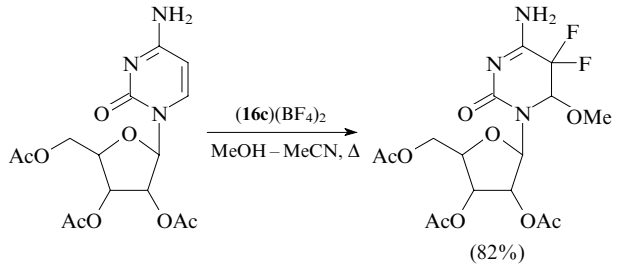
In an aqueous solution of uracil with (**16c**)$(BF_4)_2$, a stereoisomeric mixture of fluorohydrins is formed with the ratio *trans* : *cis* = 8 : 1; the reaction involves the participation of water.[156] Fluorination of thymine, 2′,3′,5′-triacetyluridins and other pyrimidine bases with this reagent occurs in a similar way.[156]



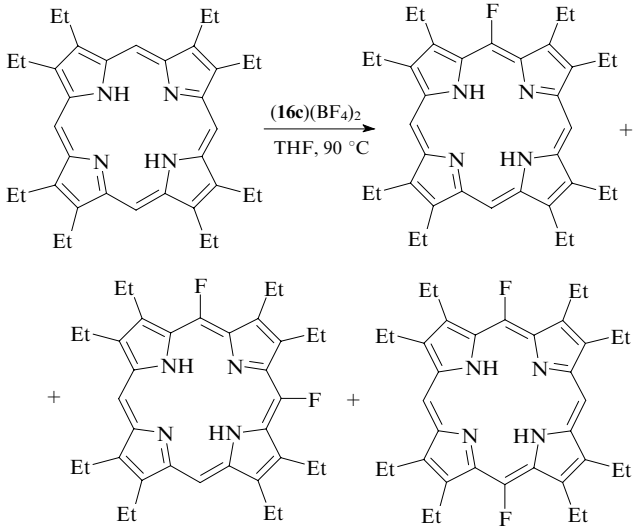
R = H (82%), Me (95%).



R^1	R^2	Y	Product yield (%)
OAc	H	H	80
OAc	H	Me	85
OAc	H	Ac	82
H	Me	H	96



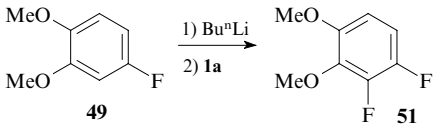
The octaethylporphin fluorination with the reagent **(16c)**$(BF_4)_2$ in THF is non-selective and gives 5-fluorooctaethylporphin (16%) as well as 5,10- and 5,15-difluorooctaethylporphins (33%).[157]

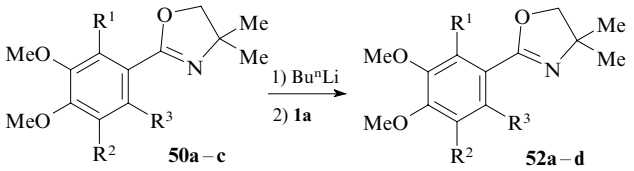


VI. Fluorination of organoelement compounds

One way of selective fluorination of aromatic and heteroaromatic compounds is preliminary introduction of an organoelement group or metal atom into a particular position of the molecule followed by their displacement by a fluorine atom. In this Section, we first consider the substitution of a fluorine atom for the hydrogen atom through intermediate formation of an organoelement compound. As a rule, this method provides for fairly selective fluorination without isolation of the organoelement intermediate. Organolithium compounds obtained by direct displacement of the hydrogen atom from the aromatic ring are often used for this purpose.

The Bu^nLi metallation of 1,2-dimethoxybenzene derivatives **49**, **50** followed by treatment with **1a** results in fluorinated derivatives **51**, **52** in moderate yields (33% – 65%); in the case of substrate **50c**, two products are formed, **52c** and **52d**.[158]

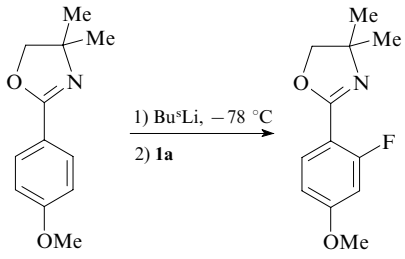


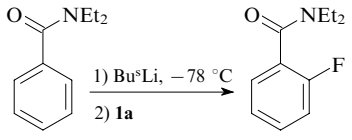


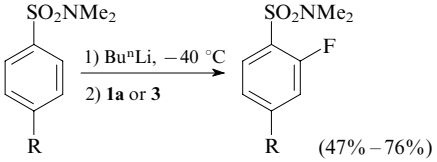
$R^1 = R^2 = R^3 = H$ (**a**);
$R^1 = F$, $R^2 = R^3 = H$ (**b**);
$R^1 = R^2 = H$, $R^3 = F$ (**c**).

$R^1 = F$, $R^2 = R^3 = H$ (**a**);
$R^1 = R^3 = F$, $R^2 = H$ (**b**);
$R^1 = H$, $R^2 = R^3 = F$ (**c**);
$R^1 = R^3 = F$, $R^2 = H$ (**d**).

Treatment of aromatic compounds containing oxazolidine, amide or sulfamide group with Bu^nLi or Bu^sLi followed by fluorination with NF reagents results in displacement of the hydrogen atom located in the *ortho*-position to this functional group by the fluorine atom.[159]

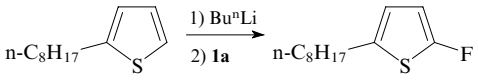




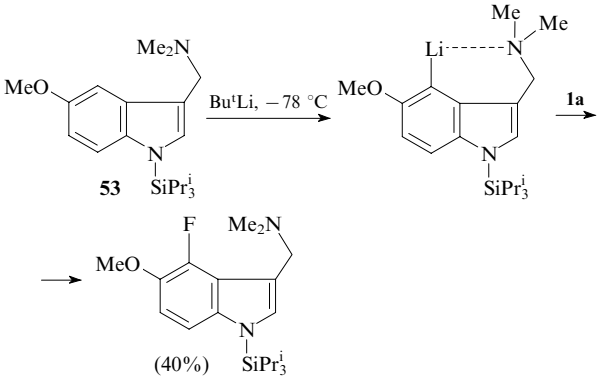


R = Me, MeO.

Treatment of 2-octylthiophene with Bu^nLi and then with reagent **1a** yielded 5-fluoro-2-octylthiophene.[160]

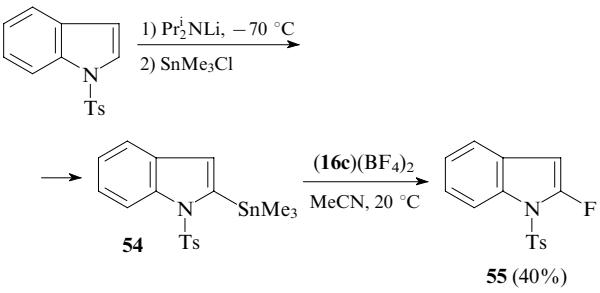


The reaction of Bu^tLi with substituted gramine **53** affords the 4-lithium derivative, which then reacts with reagent **1a** to give the desired fluoro derivative.[161]

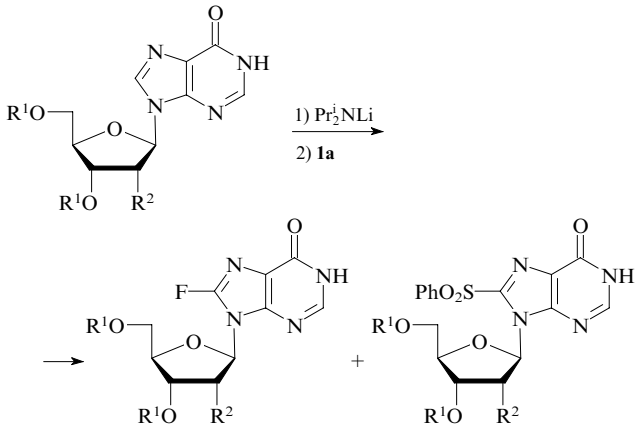


Note that the use of reagent **(16c)**$(BF_4)_2$ instead of **1a** in this process does not result in a fluorination product.

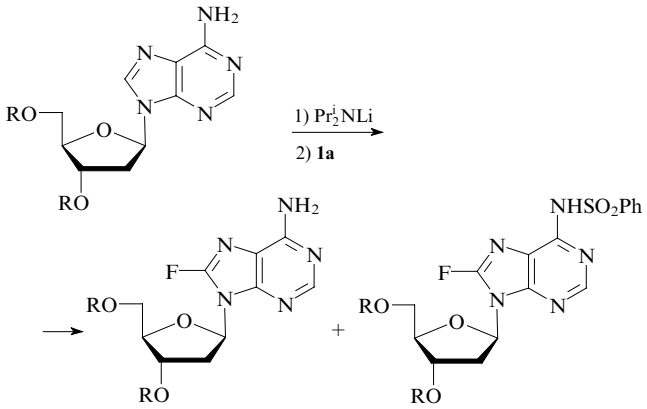
The metallation of 1-(4-toluenesulfonyl)indole with lithium diisopropylamide followed by treatment of the lithium derivative with trimethylstannyl chloride gives rise to compound **54**, which is readily fluorinated by reagent **(16c)**$(BF_4)_2$ being converted to substituted indole **55**.[162]



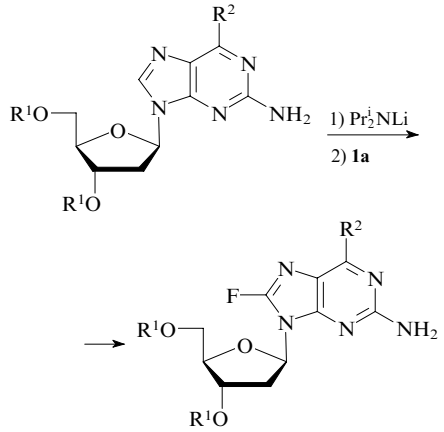
Pre-metallation of nucleosides with lithium diisopropylamide followed by treatment with reagent **1a** gives the corresponding 8-fluoronucleosides in relatively low yields (14%–34%).[163] The fluorination is accompanied by the formation of the corresponding phenylsulfonyl derivatives (6%–21%).



R^1 = Bu^tMe_2Si: R^2 = H, Bu^tMe_2SiO.

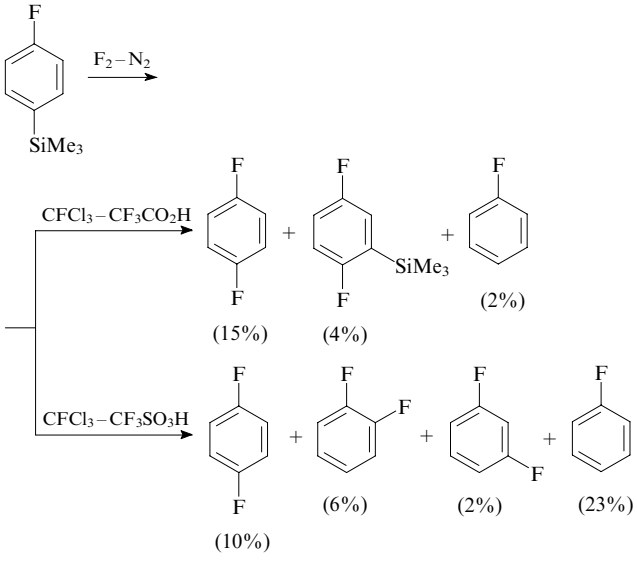


R = Bu^tMe_2Si.



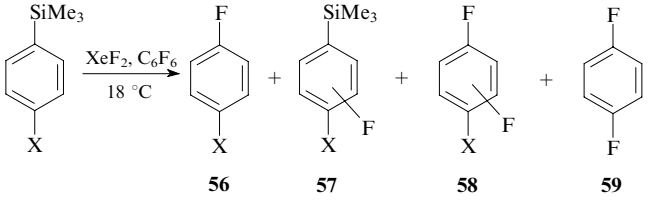
R^1 = Bu^tMe_2Si: R^2 = OMe, OBn.

When an organoelement group SiR_3 or SnR_3 is present in the aromatic ring, the reaction with a fluorinating reagent results in displacement of this group by the fluorine atom. For example, fluorination of (4-fluorophenyl)trimethylsilane with a F_2-N_2 mixture in $CF_3CO_2H-CFCl_3$ gives 1,4-difluorobenzene, resulting from *ipso*-substitution of the trimethylsilyl group, as the major product.[164] The fluorination of the substrate with the same F_2-N_2 mixture in the presence of a stronger acid (CF_3SO_3H) affords products devoid of the trimethylsilyl group, obviously, as a result of *ipso*-substitution of the proton for this group; apart from

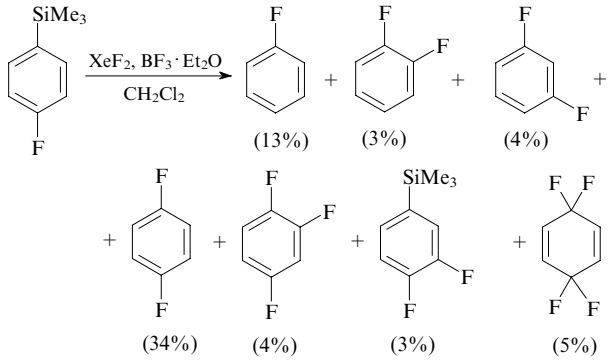


p-difluorobenzene, this reaction produces the *ortho*- and *meta*-isomers and fluorobenzene. Presumably, (2,5-difluorophenyl)trimethylsilane is formed upon the 1,2-shift of the trimethylsilyl group.

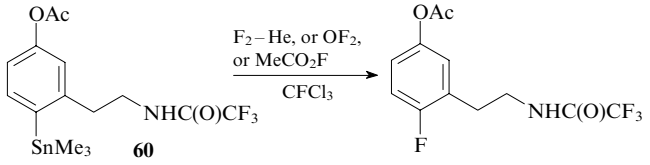
The major route of the reaction of aryltrimethylsilanes with XeF_2 or XeF_2 in $BF_3 \cdot Et_2O$ is *ipso*-substitution of the $SiMe_3$ group, as indicated, in particular, by the yields of products **56**–**59**.[165,166]



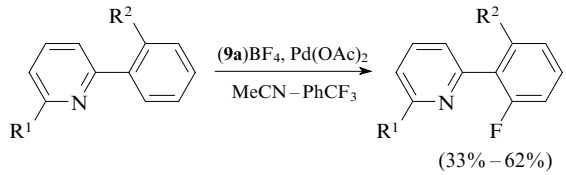
X	Yield (%)			
	56	**57**	**58**	**59**
H	65	0	0	35
Bu^t	86	8	6	
OMe	61	39	0	
Cl	82	12	6	



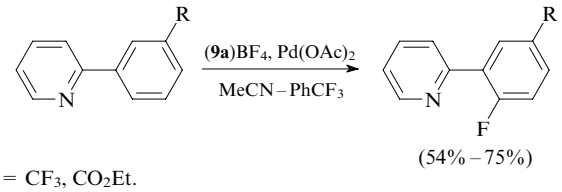
On treatment with a F_2–He mixture, OF_2 or $MeCO_2F$, phenethylamine derivative **60** undergoes *ipso*-substitution of the $SnMe_3$ group.[167]



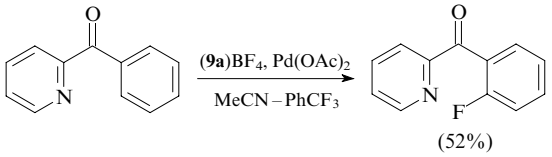
A catalytic method for fluorination of benzene derivatives containing a pyridine ring as a substituent using reagent (**9a**)BF_4 and $Pd(OAc)_2$ catalyst has been proposed.[168]



R^1 = H: R^2 = Me, OMe, CF_3, Cl; R^1 = OMe, R^2 = F.



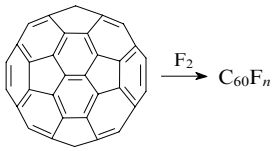
R = CF_3, CO_2Et.



It is noteworthy that it is the *ortho*- hydrogen atom relative to the pyridyl fragment that is displaced in all cases; the authors interpreted this fact by considering preferred formation of the five-membered palladacyclic intermediate. The C–H bond activation by palladium may also proceed through a six-membered palladacyclic intermediate if the formation of the five-membered ring is impossible.[168]

VII. Fluorination of fullerenes

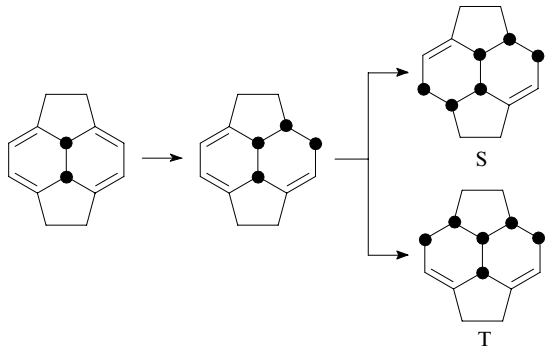
Fullerene fluorination is evidently the fluorine addition reaction, which is most often non-selective.[169,170] Treatment of C_{60} fullerene with F_2 at a temperature of 20–120 °C produces a set of fullerenes of variable composition $C_{60}F_{36-42}$ (Ref. 170). Treatment with F_2 in the presence of HF induced a similar reaction, which gave fluorofullerenes with composition ranging from $C_{60}F_{38-40}$ (70 °C) to $C_{60}F_{48}$ (315 °C).[171] The composition of the products of fullerene fluorination with molecular fluorine considerably depends on the reaction temperature; as the temperature increases from 237 to 397 and 487 °C, the number of fluorine atoms (n) in the $C_{60}F_n$ mixture successively decreases from 32–42 to 14–34 and 2–18, respectively.[172]



The reasons for the lack of selectivity in the fluorination of fullerenes with molecular fluorine or other fluorinating agents have been considered in reviews[169,170,172–176] and are concerned, first of all, with the specific properties of this substrate. The poor solubility of fullerene in solvents that are inert against molecular fluorine dictates the necessity to perform fluorination under heterogeneous conditions.[175] Moreover, fluorine gas affects first of all the surface layer of fullerene and to a lesser extent penetrates to the deeper layers of the sample; as a result, the reaction mixture contains both high-fluorinated and low-fluorinated fullerenes together with the starting fullerene.[175] The presence of equivalent reaction sites in fullerenes makes the formation of a complex mixture of fluorinated products highly probable.[169–177]

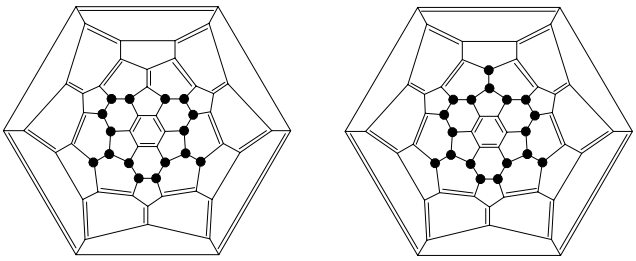
The presence of 'short' and 'long' bonds (1.40 and 1.45 Å) in C_{60} fullerene is indicative of a relatively low degree of aromaticity; initially, in the fluorination with molecular fluorine, the 1,2-addition of fluorine to the 'short' bond in the area of which the π-electron density is higher is more probable.[169] Further conjugated addition of

F_2 may occur according to either S or T variant, resulting in the corresponding set of isomers (the F positions are shown with black circles).[169]



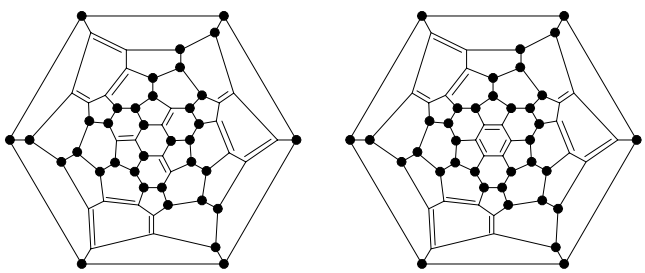
The existence of $C_{60}F_2$ was first reliably confirmed by ^{13}C and ^{19}F NMR and IR spectroscopy and mass spectrometry.[178] Treatment of C_{60} fullerene with K_2PtF_6 at 470 °C afforded a product mixture comprising $C_{60}F_2$, $C_{60}F_4$, $C_{60}F_6$, $C_{60}F_8$, $C_{60}F_7CF_3$ $C_{60}F_2O$; by HPLC, compound $C_{60}F_2$ was isolated from this mixture in a low yield (< 1%).[178, 179] The T-type positions of 6 out of the 8 F atoms in $C_{60}F_8$ were confirmed by 2D ^{19}F NMR data and quantum chemical calculations.[180]

The selectivity of fluorination is considerably affected by the degree of aromaticity of the fluorinated fullerenes formed. The compounds $C_{60}F_{10}$ and $C_{60}F_{14}$ have not been isolated and their existence as discrete species has not been confirmed by mass spectrometry.[169] Apparently, this is due to higher degree of aromaticity of the subsequent more fluorinated fullerenes $C_{60}F_{16}$, $C_{60}F_{18}$ caused by lower strain and higher electron delocalization in the latter compounds.[169]

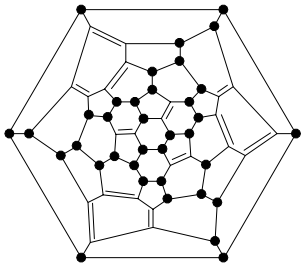


$C_{60}F_{16}$ $C_{60}F_{18}$

It was shown by X-ray diffraction analysis that the $C_{60}F_{18}$ molecule has a planar aromatic six-membered ring, which increases its aromatic nature.[181] Similarly, the isolation of compounds from $C_{60}F_{26}$ to $C_{60}F_{34}$ is hampered, as the $C_{60}F_{36}$ molecule has a higher aromaticity.[169] The $C_{60}F_{36}$ fullerene is a mixture of three isomers with C_3, T and C_1 symmetry incorporating several planar aromatic rings.[169]



C_3 T



C_1

The selectivity of fullerene fluorination with molecular fluorine can be increased by using metal fluorides on which it is believed to be chemisorbed. In the presence of MnF_2, molecules $C_{60}F_{18}$, $C_{60}F_{36}$ were predominantly formed,[182] and the reaction carried out in a closed reactor under elevated pressure gave fluorinated fullerene $C_{60}F_{48}$ in a high yield.[183]

In the solid-state fluorination of C_{60} fullerene with metal fluorides, the selectivity is largely determined by the nature of the fluorinating reagent. The reactions with MnF_3 afford mainly $C_{60}F_{36}$, while the use of K_2PtF_6 results in $C_{60}F_{18}$ as the major product.[184, 185]

The fluorination of C_{60} fullerene with xenon difluoride in CH_2Cl_2 is non-selective, giving rise to a large set of fluorinated fullerenes $C_{60}F_{6-44}$ and $C_{60}F_{60}$.[170, 186]

A large number of isomers are also formed in the fluorination of C_{70}, C_{76}, C_{78} and C_{84} fullerenes. The structures of some of them were determined by ^{19}F NMR spectroscopy: $C_{70}F_{34}$, $C_{70}F_{36}$ (6 isomers), $C_{70}F_{38}$ (7 isomers), $C_{70}F_{40}$ (4 isomers), $C_{70}F_{42}$, $C_{70}F_{44}$, $C_{76}F_{36}$, $C_{76}F_{38}$, $C_{76}F_{40}$ (4 isomers), $C_{76}F_{42}$, $C_{76}F_{44}$, $C_{78}F_{38}$, $C_{78}F_{42}$, $C_{82}F_{44}$, $C_{84}F_{40}$ (2 isomers) and $C_{84}F_{44}$.[169, 187, 188]

VIII. Conclusion

The material presented in the review clearly demonstrates that the problem of selective introduction of a fluorine atom into aromatic and heteroaromatic compounds is far from being solved. Fluorination selectivity depends on the structural details of the substrate, fluorinating reagent and reaction conditions. Molecular fluorine is most reactive among the fluorinating reagents; however, the selectivity is usually low. In recent years, Brønsted and Lewis acids have been employed to increase the selectivity of fluorination of aromatic and heteroaromatic compounds by the F_2–inert gas system. It was hypothesized that interaction of Lewis acid with the F_2 molecule results in polarization of the latter and, hence, increases the reaction selectivity. High selectivity can be attained owing to the formation of substrate–reagent complexes with a specific structure. Thus fluorination of phenols with *N*-fluoropyridinium 2-sulfonates proceeds almost completely to the *ortho*-position owing to hydrogen bonding between the SO_3^- and OH groups. One method for increasing the selectivity of fluorine atom substitution for the hydrogen atom is pre-metallation of the aromatic or heteroaromatic compound provided that metallation can be performed selectively. Further progress in the development of methods for selective introduction of the fluorine atom in aromatic compounds requires, evidently. more profound investigation of the electrophilic fluorination mechanism, search for new systems of specific external action on the reagent or substrate, which would provide for development of targeted synthetic routes to fluoroaromatic compounds, in particular, to practically valuable products.

This review was prepared with the support of the Russian Foundation for Basic Research (Project No. 07-03-00475-a) and Division of Chemistry and Material Science of the RAS (Project 5.1.4).

References

1. M D Mashkovskii *Lekarstvennye Sredstva* (Pharmaceutical Drugs) Vols 1, 2 (Moscow; Novaya Volna, 2002)
2. A T Soldatenkov, N M Kolyadina, I V Shendrik *Osnovy Organicheskoi Khimii Lekarstvennykh Veshchestv* (Foundations of Organic Chemistry of Drugs) (Moscow: Mir, 2003)
3. D Lednicer *Strategies for Organic Drug Synthesis and Design* (New York; Wiley, 1998)
4. *Organofluorine Chemistry. Principles and Commercial Applications* (Eds R E Banks, B E Smart, J C Tatlow) (New York: Plenum, 1994)
5. T Hiyama *Organofluorine Compounds: Chemistry and Applications* (Berlin: Springer, 2000)
6. P Kirsch *Modern Fluoroorganic Chemistry. Synthesis, Reactivity, Applications* (Weinheim: Wiley-VCH, 2004)
7. K Uneyama *Organofluorine Chemistry* (Oxford: Blackwell, 2006)
8. L A Mitscher *Chem. Rev.* **105** 559 (2005)
9. W R Dolbier *J. Fluorine Chem.* **126** 157 (2005)
10. R E Banks *J. Fluorine Chem.* **87** 1 (1998)
11. R Salvatore *Chem. Today* **22** 57 (2004)
12. S Purser, P R Moore, S Swallow, V Gouverneur *Chem. Soc. Rev.* **37** 320 (2008)
13. G Giannini *Med. Chem. Rev.* **1** 47 (2004)
14. C Isanbor, D O'Hagan *J. Fluorine Chem.* **127** 303 (2006)
15. F M D Ismail *J. Fluorine Chem.* **118** 27 (2002)
16. K L Kirk *Org. Process Res. Dev.* **12** 305 (2008)
17. J-P Bégué, D Bonnet-Delpon *J. Fluorine Chem.* **127** 992 (2006)
18. K L Kirk *J. Fluorine Chem.* **72** 261 (1995)
19. I Ojima *ChemBioChem.* **5** 628 (2004)
20. F A Macías, J M Siqueira, N Chinchilla, D Marín, R M Varela, J M G Molinillo *J. Agric. Food Chem.* **54** 9843 (2006)
21. Y Kagoshima, T Konosu *J. Fluorine Chem.* **127** 643 (2006)
22. P Jeschke *ChemBioChem.* **5** 571 (2004)
23. M Hird *Chem. Soc. Rev.* **36** 2070 (2007)
24. F Guittard, E T de Givenchy, S Geribaldi, A Cambon *J. Fluorine Chem.* **100** 85 (1999)
25. F Babudri, G M Farinola, F Naso, R Ragni *Chem. Commun.* 1003 (2007)
26. J-i Nishida, Y Yamashita *J. Synth. Org. Chem. Jpn.* **66** 515 (2008)
27. T Okazaki, K K Laali, in *Advances in Organic Synthesis: Modern Organofluorine Chemistry — Synthetic Aspects* Vol. 2 (Eds Atta-ur-Rahman, K K Laali) (Bentham Sci. Publ., 2006) p. 353
28. H R Kricheldorf, O Nuyken *Handbook of Polymer Synthesis* (New York: Marcel Dekker, 2005)
29. P L Jager, R Chirakal, C J Marriott, A H Brouwers, K P Koopmans, K Y Gulenchyn *J. Nucl. Med.* **49** 573 (2008)
30. D O'Hagan *Chem. Soc. Rev.* **37** 308 (2008)
31. K Mikami, Y Itoh, M Yamanaka *Chem. Rev.* **104** 1 (2004)
32. H-J Böhm, D Banner, S Bendels, M Kansy, B Kuhn, K Müller, U Obst-Sander, M Stahl *ChemBioChem.* **5** 637 (2004)
33. B E Smart *J. Fluorine Chem.* **109** 3 (2001)
34. K O Christe, in *Houben-Weyl E10. Organo-Fluorine Compounds. Methods of Organic Chemistry* (Eds B Baasner, J C Hagemann) (Stuttgart: Thieme, 2000) p. 176
35. R D Chambers, J Hutchinson, G Sandford *J. Fluorine Chem.* **100** 63 (1999)
36. J S Moilliet *J. Fluorine Chem.* **109** 13 (2001)
37. G Sandford *J. Fluorine Chem.* **128** 90 (2007)
38. S Rozen, in *Advances in Organic Synthesis: Modern Organofluorine Chemistry — Synthetic Aspects* Vol. 2 (Eds Atta-ur-Rahman, K K Laali) (Bentham Sci. Publ., 2006) p. 3
39. P Löb, H Löwe, V Hessel *J. Fluorine Chem.* **125** 1677 (2004)
40. G G Furin, G P Gambaretto *Direct Fluorination of Organic Compounds* (Padova: Coop. Libr. Ed. University of Padova, 1996)
41. I Pravst, M Zupan, S Stavber *Curr. Org. Chem.* **13** 47 (2009)
42. *Handbook of Reagents for Organic Synthesis. Fluorine-Containing Reagents* (Ed. L A Paquette) (Chichester: Wiley, 2007)
43. M Zupan, in *Houben-Weyl E10. Organo-Fluorine Compounds. Methods of Organic Chemistry* (Eds B Baasner, J C Hagemann) (Stuttgart: Thieme, 2000) p. 270
44. S Rozen *Chem. Rev.* **96** 1717 (1996)
45. M A Tius *Tetrahedron* **51** 6605 (1995)
46. B Zajc, in *Advances in Organic Synthesis: Modern Organofluorine Chemistry — Synthetic Aspects* Vol. 2 (Eds Atta-ur-Rahman, K K Laali) (Bentham Sci. Publ., 2006) p. 61
47. J A Wilkinson. *Chem. Rev.* **92** 505 (1992)
48. L Strekowski, A S Kiselyov *Adv. Heterocycl. Chem.* **62** 1 (1995)
49. G S Lal, G P Pez, R G Syvret *Chem. Rev.* **96** 1737 (1996)
50. B Xu, S-Z Zhu *Youji Huaxue* **18** 202 (1998); *Chem. Abstr.* **129** 53909 (1998)
51. J J Hart, R G Syvret *J. Fluorine Chem.* **100** 157 (1999)
52. R E Banks, M K Besheesh, N J Lawrence, D J Tovell *J. Fluorine Chem.* **97** 79 (1999)
53. S D Taylor, C C Kotoris, G Hum *Tetrahedron* **55** 12431 (1999)
54. G G Furin, A A Fainzil'berg *Usp. Khim.* **68** 725 (1999) [*Russ. Chem. Rev.* **68** 653 (1999)]
55. G G Furin, in *Houben-Weyl E10. Organo-Fluorine Compounds. Methods of Organic Chemistry* (Eds B Baasner, J C Hagemann) (Stuttgart: Thieme, 2000) p. 432
56. V Gouverneur, B Greedy *Chem.–Eur. J.* **8** 767 (2002)
57. H Ibrahim, A Togni *Chem. Commun.* 1147 (2004)
58. K M Dawood *Tetrahedron* **60** 1435 (2004)
59. R P Singh, J M Shreeve *Acc. Chem. Res.* **37** 31 (2004)
60. P T Nyffeler, S G Durón, M D Burkart, S P Vincent, C-H Wong *Angew. Chem., Int. Ed.* **44** 192 (2005)
61. A S Kiselyov *Chem. Soc. Rev.* **34** 1031 (2005)
62. T M Klapötke *J. Fluorine Chem.* **127** 679 (2006)
63. S Stavber, M Zupan, in *Advances in Organic Synthesis: Modern Organofluorine Chemistry — Synthetic Aspects* Vol. 2 (Eds Atta-ur-Rahman, K K Laali) (Bentham Sci. Publ., 2006) p. 213
64. T Umemoto, in *Advances in Organic Synthesis: Modern Organofluorine Chemistry — Synthetic Aspects* Vol. 2 (Eds Atta-ur-Rahman, K K Laali) (Bentham Sci. Publ., 2006) p. 159
65. R D Chambers, C J Skinner, J Hutchinson, J Thomson *J. Chem. Soc., Perkin Trans. 1* 605 (1996)
66. E Differding, M Wehrli *Tetrahedron Lett.* **32** 3819 (1991)
67. C P Andrieux, E Differding, M Robert, J-M Saveant *J. Am. Chem. Soc.* **115** 6592 (1993)
68. K K Laali, G I Borodkin *J. Chem. Soc., Perkin Trans. 2* 953 (2002)
69. R V Andreev, G I Borodkin, V G Shubin *Zh. Org. Khim.* **45** 1483 (2009) [a]
70. T Umemoto, S Fukami, G Tomizawa, K Harasawa, K Kawada, K Tomita *J. Am. Chem. Soc.* **112** 8563 (1990)
71. T Umemoto, M Nagayoshi *Bull. Chem. Soc. Jpn.* **69** 2287 (1996)
72. T M Bockman, K Y Lee, J K Kochi *J. Chem. Soc., Perkin Trans. 2* 1581 (1992)
73. S Stavber, M Jereb, M Zupan *J. Phys. Org. Chem.* **15** 56 (2002)
74. J Iskra, M Zupan, S Stavber *Org. Biomol. Chem.* **1** 1528 (2003)
75. P Kralj, M Zupan, S Stavber *J. Org. Chem.* **71** 3880 (2006)
76. W P Jencks *Acc. Chem. Res.* **13** 161 (1980)
77. X Zhang, Y Liao, R Qian, H Wang, Y Guo *Org. Lett.* **7** 3877 (2005)
78. S Piana, I Devillers, A Togni, U Rothlisberger *Angew. Chem., Int. Ed.* **41** 979 (2002)
79. L Conte, G P Gambaretto, M Napoli, C Fraccaro, E Legnaro *J. Fluorine Chem.* **70** 175 (1995)
80. K Jähnisch, M Baerns, V Hessel, W Ehrfeld, V Haverkamp, H Löwe, Ch Wille, A Guber *J. Fluorine Chem.* **105** 117 (2000)
81. N de Mas, A Günther, M A Schmidt, K F Jensen *Ind. Eng. Chem. Res.* **42** 698 (2003)

82. S T Purrington, D L Woodard *J. Org. Chem.* **56** 142 (1991)
83. J P Alric, B Marquet, T Billard, B R Langlois *J. Fluorine Chem.* **126** 661 (2005)
84. P L Coe, A M Stuart, D J Moody *J. Chem. Soc., Perkin Trans. 1* 1807 (1998)
85. R D Chambers, G Sandford, J Trmcic, T Okazoe *Org. Process Res. Dev.* **12** 339 (2008)
86. Yu L Yagupolski, in *Houben-Weyl E10. Organo-Fluorine Compounds. Methods of Organic Chemistry* (Eds B Baasner, J C Hagemann) (Stuttgart: Thieme, 2000) p. 228
87. M Zupan, J Iskra, S Stavber *J. Org. Chem.* **63** 878 (1998)
88. M J Fifolt, R T Olczak, R F Mundhenke *J. Org. Chem.* **50** 4576 (1985)
89. O Lerman, Y Tor, D Hebel, S Rozen *J. Org. Chem.* **49** 806 (1984)
90. E Differding, H Ofner *Synlett* 187 (1991)
91. G S Lal *J. Org. Chem.* **58** 2791 (1993)
92. T Shamma, H Buchholz, G K S Prakash, G A Olah *Israel J. Chem.* **39** 207 (1999)
93. G W Bluck, N B Carter, S C Smith, M D Turnbull *J. Fluorine Chem.* **125** 1873 (2004)
94. J Zhang, D D DesMarteau *J. Fluorine Chem.* **111** 253 (2001)
95. M Zupan, J Iskra, S Stavber *Tetrahedron* **52** 11341 (1996)
96. R E Banks, M K Besheesh, E Tsiliopoulos *J. Fluorine Chem.* **78** 39 (1996)
97. T Umemoto, G Tomizawa *J. Org. Chem.* **60** 6563 (1995)
98. T Umemoto, M Nagayashi, K Adachi, G Tomizawa *J. Org. Chem.* **63** 3379 (1998)
99. R E Banks, M K Besheesh, S N Mohialdin-Khaffaf, I Sharif *J. Chem. Soc., Perkin Trans. 1* 2069 (1996)
100. R E Banks, M K Besheesh, S N Mohialdin-Khaffaf, I Sharif *J. Fluorine Chem.* **81** 157 (1997)
101. I Cabrera, W K Appel *Tetrahedron* **51** 10205 (1995)
102. R E Banks, M K Besheesh *J. Fluorine Chem.* **76** 161 (1996)
103. R E Banks, M K Besheesh, W Fraenk, T M Klapötke *J. Fluorine Chem.* **124** 229 (2003)
104. R D Chambers, J Hutchinson, M E Sparrowhawk, G Sandford, J S Moilliet, J Thomson *J. Fluorine Chem.* **102** 169 (2000)
105. R D Chambers, C J Skinner, J Thomson, J Hutchinson *J. Chem. Soc., Chem. Commun.* 17 (1995)
106. J T Link, B Sorensen, J Patel, M Grynfarb, A Goos-Nilsson, J Wang, S Fung, D Wilcox, B Zinker, P Nguyen, B Hickman, J M Schmidt, S Swanson, Z Tian, T J Reisch, G Rotert, J Du, B Lane, T W von Geldern, P B Jacobson *J. Med. Chem.* **48** 5295 (2005)
107. G Stavber, M Zupan, S Stavber *Tetrahedron Lett.* **48** 2671 (2007)
108. G Laćan, N Satyamurthy, J R Barrio *J. Org. Chem.* **60** 227 (1995)
109. G Laćan, N Satyamurthy, J R Barrio *J. Fluorine Chem.* **74** 211 (1995)
110. B B Azad, R Ashique, R Chirakal, G J Schrobilgen *J. Fluorine Chem.* **129** 22 (2008)
111. K Adachi, Y Ohira, G Tomizawa, S Ishihara, S Oishi *J. Fluorine Chem.* **120** 173 (2003)
112. I Pravst, M P Iskra, M Jereb, M Zupan, S Stavber *Tetrahedron* **62** 4474 (2006)
113. N Vasdev, R Chirakal, G J Schrobilgen, C Nahmias *J. Fluorine Chem.* **111** 17 (2001)
114. N Vasdev, R Chirakal, R Ashique, G J Schrobilgen, K Gulenchyn *J. Fluorine Chem.* **121** 9 (2003)
115. R Chirakal, N Vasdev, G J Schrobilgen, C Nahmias *J. Fluorine Chem.* **99** 87 (1999)
116. R Surmont, G Verniest, F Colpaert, G Macdonald, J W Thuring, F Deroose, N De Kimpe *J. Org. Chem.* **74** 1377 (2009)
117. WO 9824740; *Chem. Abstr.* **129** 67597 (1998)
118. G I Borodkin, P A Zaikin, V G Shubin *Tetrahedron Lett.* **47** 2639 (2006)
119. G I Borodkin, P A Zaikin, M M Shakirov, V G Shubin *Zh. Org. Khim.* **43** 1460 (2007) [a]
120. R E Banks, M K Besheesh, R W Gurski, N J Lawrence, A J Taylor *J. Fluorine Chem.* **96** 129 (1999)
121. M R P Heravi *J. Fluorine Chem.* **129** 217 (2008)
122. G Stavber, M Zupan, M Jereb, S Stavber *Org. Lett.* **6** 4973 (2004)
123. G I Borodkin, P A Zaikin, V G Shubin, in *7-ya Vserossiiskaya Konferentsiya 'Khimiya Ftora', Moskva, 2006* (The 7th All-Russian Conference 'The Fluorine Chemistry', Moscow, 2006) P-04
124. P A Zaikin, G I Borodkin, V G Shubin, in *The 15th European Symposium on Fluorine Chemistry. Book of Abstracts, Prague, 2007* p. 273
125. S Stavber, M Jereb, M Zupan *Synlett* 1375 (1999)
126. M A Tius, J K Kawakami, W A G Hill, A Makriyannis *J. Chem. Soc., Chem. Commun.* 2085 (1996)
127. S Stavber, M Jereb, M Zupan *Chem. Commun.* 1323 (2000)
128. S Stavber, M Zupan *J. Chem. Soc., Chem. Commun.* 149 (1994)
129. M Zupan, J Iskra, S Stavber *J. Fluorine Chem.* **70** 7 (1995)
130. S Stavber, M Zupan *Chem. Lett.* **25** 1077 (1996)
131. M Zupan, J Iskra, S Stavber *Bull. Chem. Soc. Jpn.* **68** 1655 (1995)
132. Y Zhang, K Shibatomi, H Yamamoto *Synlett* 2837 (2005)
133. T Ueno, H Toda, M Yasunami, M Yoshifuji *Bull. Chem. Soc. Jpn.* **69** 1645 (1996)
134. R S Muthyala, R S H Liu *J. Fluorine Chem.* **89** 173 (1998)
135. K K Laali, M Tanaka, F Forohar, M Cheng, J C Fetzer *J. Fluorine Chem.* **91** 185 (1998)
136. R D Chambers, D Holling, G Sandford, A S Batsanov, J A K Howard *J. Fluorine Chem.* **125** 661 (2004)
137. R D Chambers, D Holling, G Sandford, H Puschmann, J A K Howard *J. Fluorine Chem.* **117** 99 (2002)
138. P M O'Neill, R C Storr, B K Park *Tetrahedron* **54** 4615 (1998)
139. R V Andreev, G I Borodkin, V G Shubin, in *Osnovnye Tendentsii Razvitiya Khimii v Nachale XXI Veka (Tez. Dokl. Mezhdunar. Konf.), St Peterburg, 2009* [Basic Tendencies of Development of Chemistry in Beginning of the 21st Century (Abstracts of Reports of the International Conference), St Petersburg, 2009)] p. 323
140. D Holling, G Sandford, A S Batsanov, D S Yufit, J A K Howard *J. Fluorine Chem.* **126** 1377 (2005)
141. D A Price, K James, S Osborne, G W Harbottle *Tetrahedron Lett.* **48** 7371 (2007)
142. Q Chao, L Deng, H Shih, L M Leoni, D Genini, D A Carson, H B Cottam *J. Med. Chem.* **42** 3860 (1999)
143. W Ying, D D DesMarteau, Y Gotoh *Tetrahedron* **52** 15 (1996)
144. A G de Viedma, V Martínez-Barrasa, C Burgos, M L Izquierdo, J Alvarez-Builla *J. Org. Chem.* **64** 1007 (1999)
145. J Wang, A I Scott *Tetrahedron Lett.* **35** 3679 (1994)
146. J Wang, A I Scott *Tetrahedron* **50** 6181 (1994)
147. C E Stephens, J A Blake *J. Fluorine Chem.* **125** 1939 (2004)
148. T F Campbell, C E Stephens *J. Fluorine Chem.* **127** 1591 (2006)
149. R G Syvret, W J Casteel, G S Lal, J S Goudar *J. Fluorine Chem.* **125** 33 (2004)
150. Y Takeuchi, T Tarui, N Shibata *Org. Lett.* **2** 639 (2000)
151. J Baudoux, A-F Salit, D Cahard, J-C Plaquevent *Tetrahedron Lett.* **43** 6573 (2002)
152. T Fujiwara, B Yin, M Jin, K L Kirk, Y Takeuchi *J. Fluorine Chem.* **129** 829 (2008)
153. J R Barrio, M Namavari, M E Phelps, N Satyamurthy *J. Am. Chem. Soc.* **118** 10408 (1996)
154. J R Barrio, M Namavari, M E Phelps, N Satyamurthy *J. Org. Chem.* **61** 6084 (1996)
155. US P. 6262254; *Chem. Abstr.* **130** 81795 (1999)
156. G S Lal, W Pastore, R Pesaresi *J. Org. Chem.* **60** 7340 (1995)
157. Jpn. P. 2008100993; *Chem. Abstr.* **148** 495680 (2008)
158. J-Y Nie, K L Kirk *J. Fluorine Chem.* **74** 297 (1995)
159. F A Davis, W Han, C K Murphy *J. Org. Chem.* **60** 4730 (1995)
160. E Dvornikova, M Bechcicka, K Kamieńska-Trela, A Krdwczyński *J. Fluorine Chem.* **124** 159 (2003)
161. Y Hayakawa, M Singh, N Shibata, Y Takeuchi, K L Kirk *J. Fluorine Chem.* **97** 161 (1999)
162. H F Hodson, D J Madge, A N Z Slawin, D A Widdowson, D J Williams *Tetrahedron* **50** 1899 (1994)
163. A K Ghosh, P Lagisetty, B Zajc *J. Org. Chem.* **72** 8222 (2007)
164. A M Stuart, P L Coe, D J Moody *J. Fluorine Chem.* **88** 179 (1998)
165. A P Lothian, C A Ramsden *Synlett* 753 (1993)

166. V V Bardin, H J Frohn *J. Fluorine Chem.* **90** 93 (1998)
167. M Namavari, N Satyamurthy, J R Barrio *J. Fluorine Chem.* **74** 113 (1995)
168. K L Hull, W Q Anani, M S Sanford *J. Am. Chem. Soc.* **128** 7134 (2006)
169. R Taylor *J. Fluorine Chem.* **125** 359 (2004)
170. O V Boltalina *J. Fluorine Chem.* **101** 273 (2000)
171. O V Boltalina, L N Sidorov, V F Bagryantsev, V A Seredenko, A S Zapol'skii, J M Street, R Taylor *J. Chem. Soc., Perkin Trans. 2* 2275 (1996)
172. L N Sidorov, O V Boltalina *Usp. Khim.* **71** 611 (2002) [*Russ. Chem. Rev.* **71** 535 (2002)]
173. R Taylor *Izv. Akad. Nauk, Ser. Khim.* 852 (1998) [b]
174. O V Boltalina, N A Galeva *Usp. Khim.* **69** 661 (2000) [*Russ. Chem. Rev.* **69** 609 (2000)]
175. R Taylor *Chem. – Eur. J.* **7** 4075 (2001)
176. A Yu Lukonin, V Yu Markov, O V Boltalina *Vestn. Mosk. Univ., Ser. 2, Khim.* **42** 3 (2001) [c]
177. R Taylor, G J Langley, J H Holloway, E G Hope, A K Brisdon, H W Kroto, D R M Walton *J. Chem. Soc., Perkin Trans. 2* 181 (1995)
178. O V Boltalina, A Yu Lukonin, J M Street, R Taylor *Chem. Commun.* 1601 (2000)
179. O V Boltalina, A D Darwish, J M Street, R Taylor, X-W Wei *J. Chem. Soc., Perkin Trans. 2* 251 (2002)
180. J P B Sandall, P W Fowler *Org. Biomol. Chem.* **1** 1061 (2003)
181. I S Neretin, K A Lyssenko, M Yu Antipin, Yu L Slovokhotov, O V Boltalina, P A Troshin, A Yu Lukonin, L N Sidorov, R Taylor *Angew. Chem., Int. Ed.* **39** 3273 (2000)
182. N S Chilingarov, A V Nikitin, J V Rau, I V Golyshevsky, A V Kepman, F M Spiridonov, L N Sidorov *J. Fluorine Chem.* **113** 219 (2002)
183. A V Kepman, V F Sukhoverkhov, A Tressaud, C Labrugere, E Durand, N S Chilingarov, L N Sidorov *J. Fluorine Chem.* **127** 832 (2006)
184. O V Boltalina, A Ya Borschevskii, L M Sidorov, J M Street, R Taylor *Chem. Commun.* 529 (1996)
185. O V Boltalina, V Yu Markov, R Taylor, M P Waugh *Chem. Commun.* 2549 (1996)
186. J H Holloway, E G Hope, R Taylor, G J Langley, A G Avent, T J Dennis, J P Hare, H W Kroto, D R M Walton *J. Chem. Soc., Chem. Commun.* 966 (1991)
187. R Taylor, A K Abdul-Sada, O V Boltalina, J M Street *J. Chem. Soc., Perkin Trans. 2* 1013 (2000)
188. O V Boltalina, T V Avakyan, V Yu Markov, T S J Dennis, A K Abdul-Sada, R Taylor *J. Phys. Chem. B* **103** 8189 (1999)

[a] — *Russ. J. Org. Chem. (Engl. Transl.)*
[b] — *Russ. Chem. Bull., Int, Ed. (Engl. Transl.)*
[c] — *Moscow Univ. Chem. Bull. (Engl. Transl.)*