Some tendencies in application of reagents containing O-F bonds in organic synthesis

G.G.Furin

Novosibirsk Institute of organic chemistry named after N.N.Vorozhtsov, Siberian branch of the Academy of Science

9, Lavrentev ave., Novosibirsk, 630090, Russia

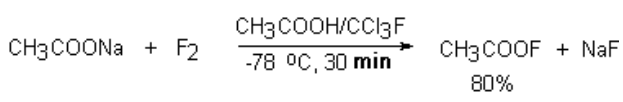
Fax: 8-3832-344752 E-mail: ***furin@nioch.nsc.ru***

This paper summarizes and systemizes up-to-date information on synthesis of organofluorine compounds of different classes with use of new reagents as fluorine carriers including organic compounds containing O-F bonds (hypofluorites of perfluorinated alcohols and carbonic acids) and cesium fluorooxysulfate. Fluorinating ability of these reagents is comparatively analyzed in dependence on their structure and the solvent nature. A feasibility to fluorinate unsaturated organic, heterocyclic and hetero-organic compounds is discussed. Matters of a mechanism of fluorination with compounds containing O-F bonds are examined. Specific features of carrying out the processes of fluorination, their merits and demerits in comparison with reactions using elemental fluorine, xenon difluoride and other fluorinating agents are revealed. Availability of methyl- and tret-butylhypofluorites as reagents able to introduce the alkoxy- group into unsaturated organic compounds and their opportunities are shown. Examples of application of HOF/MeCN system as an oxidizer of unsaturated compounds to carry out processes of epoxidation and hydroxylation of olefins are under review. This oxidizer advantages, its specific peculiarities and application in organic synthesis are discussed.

Contents

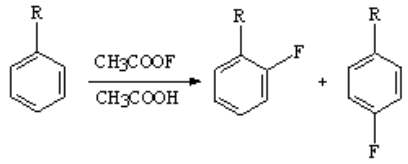
5.2. Fluorinating properties of acetylhypofluorite and trifluoroacetylhypofluorite.

Acetylhypofluorite synthesized for the first time by S.Rozen and collaborators has become a very popular electrophilic fluorinating reagent [57].



The complete characteristic of this compound is given in [146]. It is used to introduce ^{18}F isotope into molecules of different compounds used as objects for positron-emissive tomography. In syntheses acetylhypofluorite is used as a solution in dimethylformamide, acetonitrile, dimethylsulfoxide at low temperatures but the concentration of the fluorinating agent is low (1 mmole).

In the fluorination of aromatic compounds containing electron-donating substituents under action of CH_3COOH mainly the hydrogen atoms in ortho-position are replaced with fluorine while the hydrogen atoms in *para*-position are replaced negligibly [57,147,148].



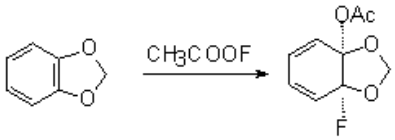
R = OMe, OH, NH_2, NHAc, Me, H, Cl

Thus, anisole gives ortho- and para-fluoroanisoles in 85% yield in a ratio of 9:1 [57]. 1,3-Dimethoxybenzene under action of acetylhypofluorite is convereted into a mixture of two products: 1-fluoro-2,4-dimethoxybenzene (40%) and 1,5-difluoro-2,4-dimethoxybenzene (55%) (see table 14).

Table 14. *Reactions of aromatic compounds with acetylhypofluorite*

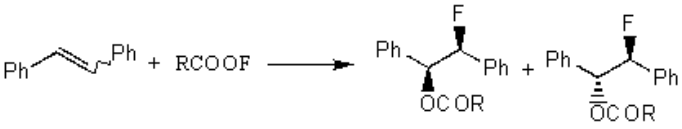
Initial substrate	Reaction products	Yield, %	References
$C_6H_5OCH_3$	2-$FC_6H_4OCH_3$	85	133
	4-$FC_6H_4OCH_3$	8	
$C_6H_5OCH_3$	2-$FC_6H_4OCH_3$	77	135
	4-$FC_6H_4OCH_3$	8	
$C_6H_5OCH_3$	2-$FC_6H_4OCH_3$	64	135,136
	4-$FC_6H_4OCH_3$	21	
1,3-$(CH_3O)_2C_6H_4$	3-CH_3O-4-$FC_6H_3OCH_3$	39	133
	3-CH_3O-4,6-$F_2C_6H_2OCH_3$	55	
	2,4,-$(CH_3O)_2$ -1,5,-$F_2C_6H_2$	46	
$C_6H_5OC_2H_5$	2-$FC_6H_4OC_2H_5$	46	133
	4-$FC_6H_4OC_2H_5$	6	
$C_6H_5NHCOCH_3$	2-$FC_6H_4NHCOCH_3$	44	135,136
	4-$FC_6H_4NHCOCH_3$	22	
$C_6H_5NHCOCF_3$	2-$FC_6H_4NHCOCF_3$	57	133
$C_6H_5NHCOBu$-t	2-$FC_6H_4NHCOBu$-t	52	133
3-$CF_3C_6H_4NHCOCH_3$	2-CF_3-6-$FC_6H_3NHCOCH_3$	62	133
C_6H_5OH	2-FC_6H_4OH	45	135,136
	4-FC_6H_4OH	30	
$C_6H_5NH_2$	2-$FC_6H_4NH_2$	3,5	136
	4-$FC_6H_4NH_2$	2,5	
C_6H_5Cl	2-FC_6H_4Cl	5	136
	4-FC_6H_4Cl	15	
$C_6H_5CH_3$	2-$FC_6H_4CH_3$	8	135,136
	3-$FC_6H_4CH_3$	1	
	4-$FC_6H_4CH_3$	4	

Polycylic aromatic compounds are fluorinated with acetylhypofluorite stereoselectively enough. So, 1-methoxynaphthaline gives a mixture of 1-methoxy2-fluoro- and 1-methoxy-4-fluoronaphthalines in a ratio of 6:1 in 70% yield. 2-Methoxynaphthaline gives 1-fluoro-2-methoxynaphthaline in 65% yield and 6-methoxynaphthaline is converted to 5-fluoro-6-methoxyquinoline in 75% yield.6-Methoxy-1-tetralone is converted to 5-fluoro-6-methoxy-1-tetralone (53%) and 5,7-difluoro-6-methoxy-1-tetralone (13%) [149]. The fluorination reaction proceeds by way of addition-elimination that was experimentally confirmed by separation of adduct 6 produced in the fluorination of piperonal 7 with acetylhypofluorite [57].



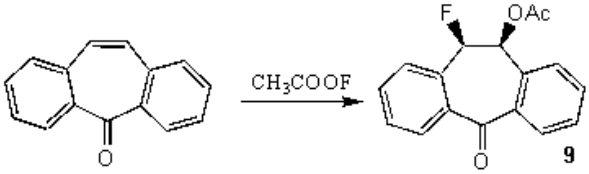
7 **6**

If a molecule contains a double bond together with a benzene ring, the double bond is first subjected to fluorination and addition of acetylhypofluorite to the multiple bond proceeds stereoselectively. So the reaction of *cis*-stilbene with CF3(CF2)6COOF gives a mixture of *erythro*- and *threo*-1-fluoro-perfluorostannoyloxyenanes [44]. Stereospecificity of fluoroacetoxylation was shown in the reactions of *cis*- and *trans*-stilbenes with acetylhypofluorite and trifluoroacetylhypofluorite [150].



Olefine	Reagent	R	Yield, %	
			syn-	*anti*-
(E)-	CH_3COOF	Me	50	7
	CH_3COOF	CF_3	100	0
(Z)-	CH_3COOF	Me	11	51
	CH_3COOF	CF_3	0	100

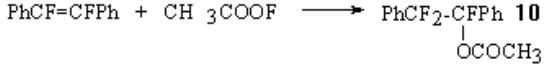
5H-Dibenzo[a,d]cyclohepten-5-one gives under action of this reagent syn-product [31].



8 **9**

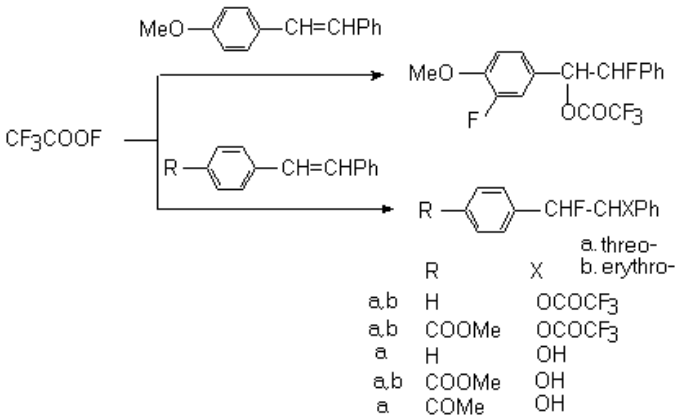
55 %

The reaction of 1,2-difluoro-1,2-diphenylethylene with CH_3COOF also gives product **10** , adduct of fluorine and the acetoxy-group [151].

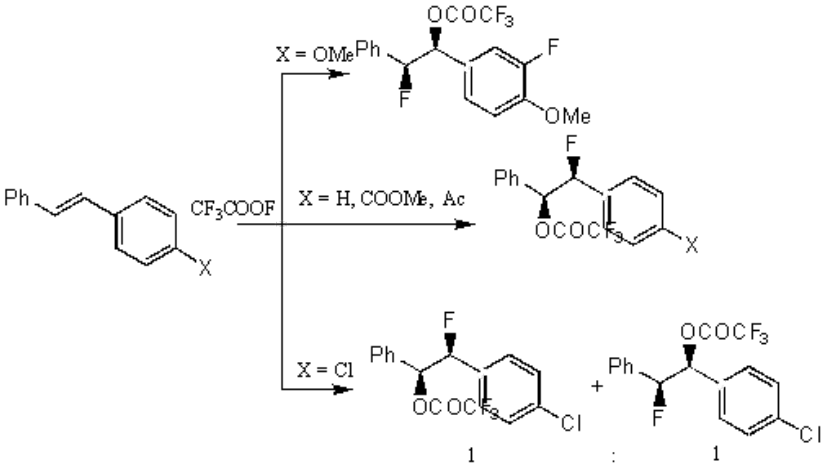


Acylhypofluorites produced by fluorination of elemental fluorine of appropriate salts of perfluorinated carbonic acids turned out to be effective catalysts for polymerization of fluoro-olefins [152]. For example, polymerization of tetrafluoroethylene catalyzed by perfluorooctanoyl hypofluorite gives perfluoro-2-butyltetrahydrofurane and polyfluoro(tetrafluoroethylene) (89% yield) [152].

When a benzene ring contains an electron-donating group, for example the methoxy-group, the addition of trifluoroacetylhypofluorite to the multiple bond also takes place together with fluorination of the benzene ring.

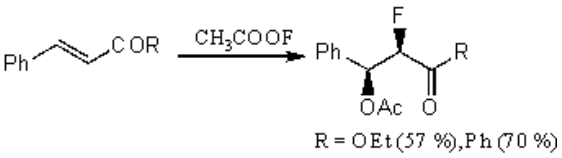


Regioselective fluorination of phenyl-substituted alkenes containing substituents of different nature is described in [39].

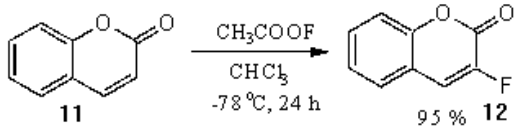


Acetylhypofluorite gives addition products to a multiple bond whereas trifluoroacetylhypofluorite fluorinates a benzene ring containing the methoxy group [31,39].

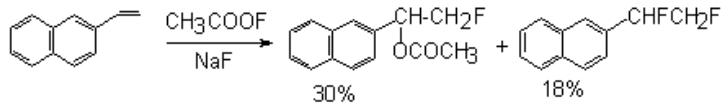
The reactivity of acetylhypofluorite is very sensitive to the organic molecule structure. Thus, olefins containing electron-deficient groups are fluorinated regio- and stereoselectively whereas cyclohexanone and ethylcrotonate do not react at -75^{o}C.



2H- Chromene-2-one (coumarin) **11** reacts with acetylhypofluorite at a low temperature to give 4-acetoxy-3-fluoro-3,4-2H-chromene-2-one **12** [39].

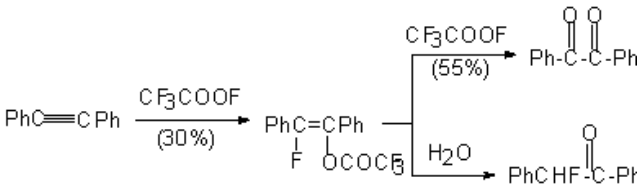


2-Vinyl-2-naphthalene under action of CH_3COOF reagent gives a mixture of 1-fluoro-1-acetoxy-2-naphthylethane [30].

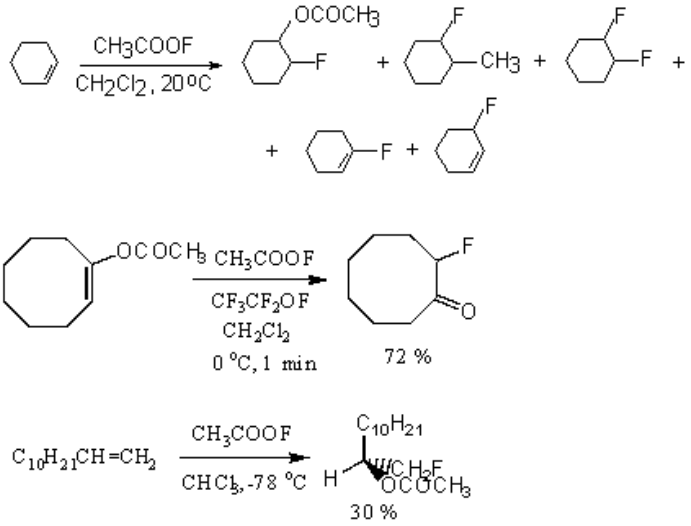


Diphenylacetylene with CF_3COOF gives at first an addition product to the triple bond which is converted in hydrolysis to fluoro-phenylacetophenone whereas in the excess of the fluorinating agent

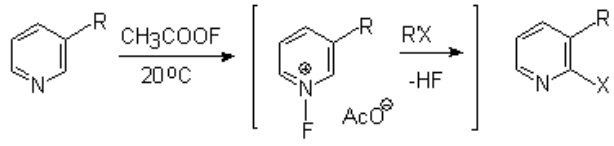
α-diketone is formed [31].



Acetylhypofluorite reacts with other unsaturated compounds under mild conditions (-70 – -80°C in $CHCl_3$ or in a mixture of CH_3COOH-$CFCl_3$ to form products of fluoroacetoxylation and fluorination. For example, the reaction of cyclohexene with CH_3COOF in CH_2Cl_2 at room temperature results in *cis*-1-acetoxy-2-fluorocyclohexane (in 33% yield) together with mono- and difluoro derivatives [153,154]. 1-Dodecadecene is converted to 2-acetoxy-1-fluorododecane in 30% yield [31].

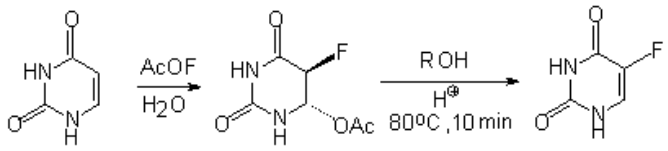


Acetylhypofluorite can be used not only for introduction of fluorine atoms into a heterocyclic ring but also as a reagent to obtain 2-substituted compounds, pyridine for example [155-158]. This functionality depends on the substituent nature in the pyridine ring. In the authors' opinion, basicity of pyridine derivatives, solvent, space effects, strength of the C-Hal bond affect the way of these reactions. Thus, in the reaction of pyridine with acetylhypofluorite in a mixture of CH_2Cl_2 and CH_2Br_2 a mixture of 3-chloropyridine and 3-bromopyridine is formed in a ratio of 1:1 (there are two competitive factors: a smaller volume of CH_2Cl_2 and the strength of the C-Cl >C-Br bonds). At the same time in a solution of chlorobromomethane the same mixture is formed, but in a ratio of 2:3 (here the main role plays the fact that the C-Cl bond is more strong than the C-Br bond) [156].



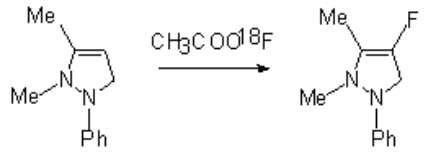
R	R'X	**Yield** ,%
H	CH_2Cl_2	70
4-Me	CH_2Cl_2	70
3-Me	CH_2Cl_2	15
3-Cl	CH_2Cl_2	80
3-PhO	CH_2Cl_2	80
3-COOMe	CH_2Cl_2	60
3-Cl	CH_2Br_2	80
4-MeO	CH_2Br_2	60
4-Me	CH_2Cl_2	60
H	CH_2Br_2	60

Uracil and cytosine under action of acetylhypofluorite in acetic acid [159-163] form a product of addition of fluorine and acetoxy-group to the multiple bond whereas in water 4-hydroxy-5,5-difluoro-derivative is formed[164-166]. The following influence of the alcohols in the presence of a catalytic amount of the acid



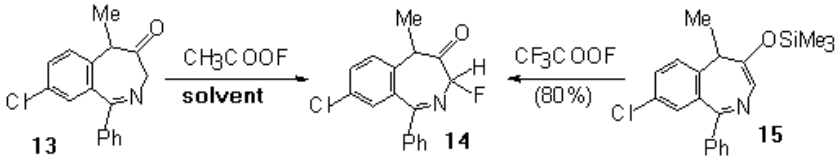
R = Me, Et, Pr, Bu, t-Bu, i-Pr

Antipyrine under the influence of CH_3COOF gives fluoro-derivative [160].



A similar picture has place for nucleotides based on uracil and cytosine. In this case the formation of the adduct (*syn*-isomer) points to a mechanism including intermediate generation α-fluorocarbcation [166].

The fluorination of diazepane **13** with acetylhypofluorite results in 3-fluorodiazepate **14** in a low yield (15-21%) whereas 3-trimethyl-siloxy diazepane **15** under action of trifluoroacetylhypofluorite gives fluoro derivative in 80% yield [72,168].



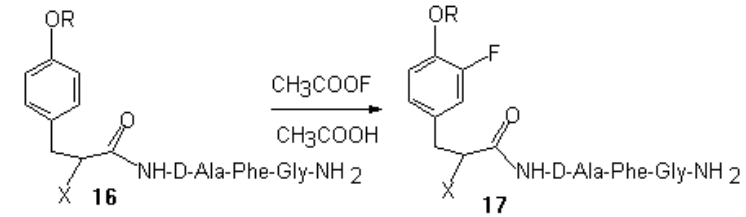
Solvent:

CH3COOH (15%)

CH3Cl (21%)

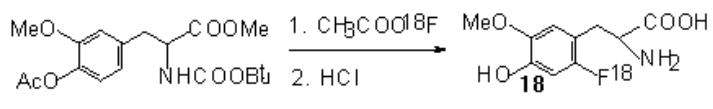
CFCl3 (18%)

Such natural compounds as 3-methoxy-4-hydroxy-L-phenylalanine **16** in the reaction of fluorination with acetylhypofluorite gives at 20°C a mixture of 2-, 5- and 6-fluoro derivatives 17 [156]. At the same time biologically active peptides containing the tyrosine ring give exclusively 2-fluoroderivative [156,169]. A mixture of 2-,4- and 6-fluoroderivatives is formed in a ratio of 36:11:52 in case of fluorination with m-tyrosine reagent labeled with ^{18}F isotope [170].

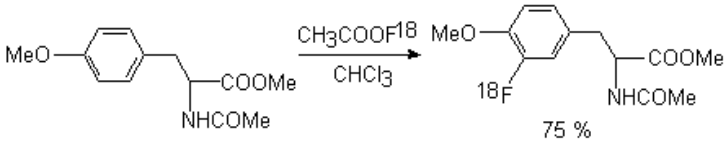


R = X = H
R = Bzl, X = BOC
R = H, X = BOC

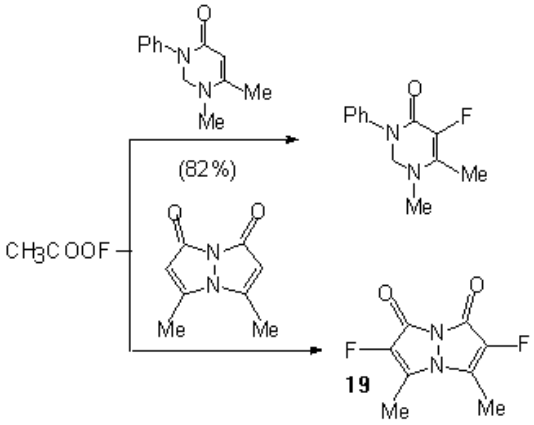
An important value for medicine have 2-fluoro- and, particularly, 6-fluoro-L-dopamine **18** labeled with ^{18}F isotope [171-175] which are produced by fluorination using $CH_3COO^{18}F$.



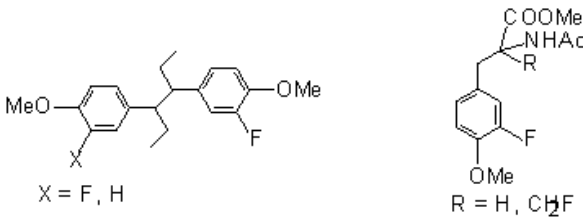
Although the radiochemical yield does not exceed 25%, this reaction has found practical application.



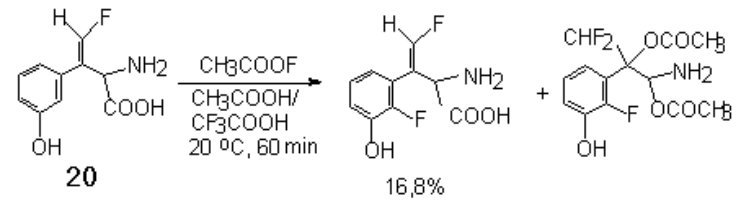
Dimethylphenylisopyrazolone containing an ethylene fragment under the influence of acetylhypofluorite gives a product of fluoroacetoxylation in 82% yield [176] . The following elimination of the acetic acid fragments leads to 4-fluorodimethylphenyl - isopyrazolone. The fluorination of bimane with acetylhypofluorite under the same conditions forms difluoroderivative **19** [177]. But in $CHCl_3$-$MeNO_2$ system (2:1) a mixture of mono- and difluoro derivatives is formed [161].



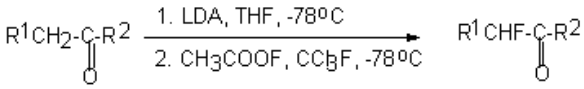
Biologically interesting compounds including fluorohexesestrol, different steroids and fluorotyrosine can be readily obtained using CH_3COOF [177].



Fluorination of (Z)-fluoromethene-m-tyrosine **20** with CH_3COOF reagent gives monofluoro- and difluoroderivatives at the expense of fluorine introduction into the benzene ring whereas the fluorination of (E)-isomer affects only the double bond [178,179]. Phenylalanine and (3,4-dihydroxyphenyl)-L-alanine give mainly 2-fluoro-substituted products labeled with ^{18}Fisotope [179]. This is a potential method to introduce ^{18}F isotope without using fluorine gas.

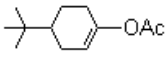
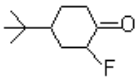
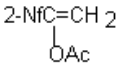
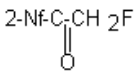
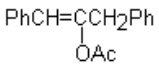
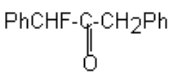
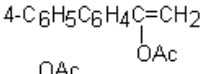
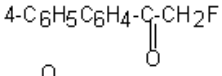
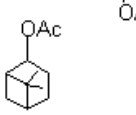
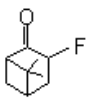
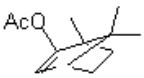
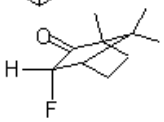


α,β-Unsaturated carbonyl compounds under action of acetylhypofluorite give α-fluoro-β-acetoxycarbonyl compounds[180]. Ketones, containing a methene fragment under the influence of CH_3COOF give α-fluoroketones [170]. Some examples of synthesis of α-fluorocarbonyl compounds are given in Table 15.These processes are characterized by high yields and regiospecificity of the fluorination.



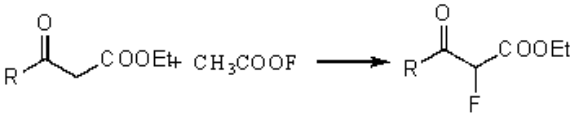
R^1	R^2	Yield, %
Ph	H	75
C_4H_9	C_3H_7	54
2-naphthyl	H	55

Table 15. *Results of the reactions of acetates of enols with acetylhypofluorite*

Initial substrate	Reaction product	Yield, %	References
		trans 43 cis 29	171,172
		45	171,172
		50	171
		62	171
		80	171
		65	171

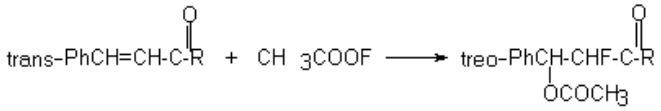
Obviously, β-diketones under the influence of this reagent give monofluoro- and difluoro-derivatives [181].

Enoles of acetates, oxo ethers, nitroalkenes and sodium salts of different ethers are successfully fluorinated affecting the carbon atom in the α-position at the carbonyl group. This approach appeared a convenient enough method to produce α-fluorine-containing ketones [180,181].



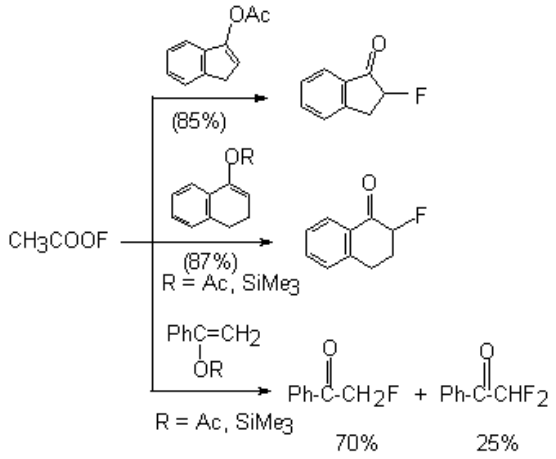
R = Me (72 %), OEt (65 %)

Elimination of acetic acid results in formation of α-fluorine-containing unsaturated ketones [170] , among which there is a number of biologically active compounds.

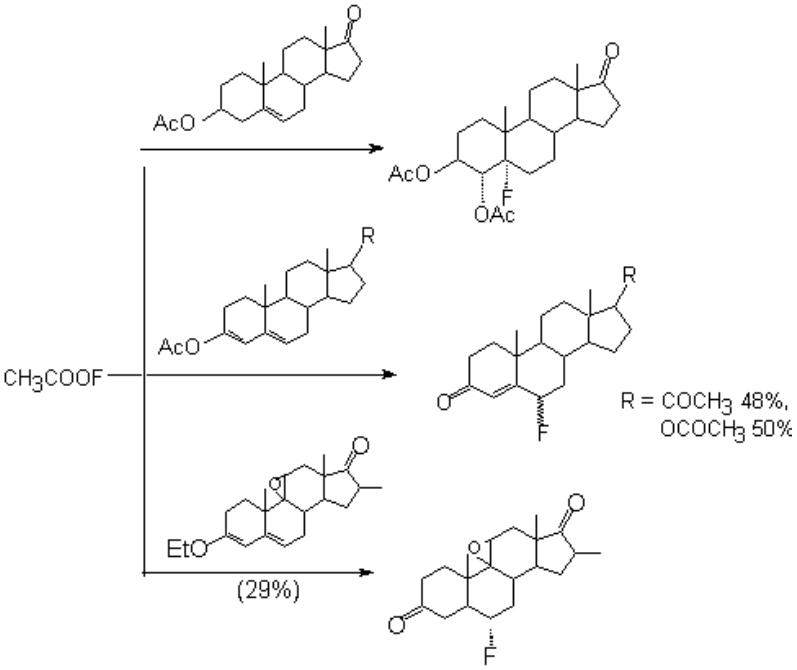


R = Ph (70%), OC_2H_5 (57%)

Enolate of tetralone acetate and its trimethylsylil ether under the influence of CH_3COOF reagent give 2-fluorotetralone [30,45]. It is more convenient to use for these purposes acetates of enoles. Thus, acetates of enoles of indanone, tetralone and acetophenone and also trimethylsylil ether of acetophenone under mild conditions give appropriate α-fluoro-derivatives of ketones [30]. The presence of the benzene ring in the substrate molecule does not influence the reaction result. It is possible to use trimethylsylil ethers as well [174].



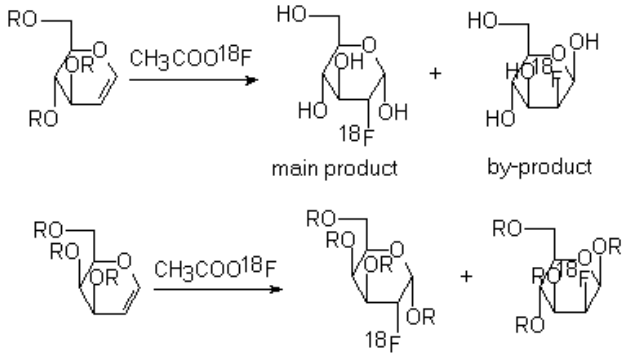
It is also used for selective introduction of a fluorine atom into steroids.



Various steroids can be introduced in the reaction with CH_3COOF and CF_3COOF to form mainly a product of addition to the multiple bond of *syn*- configuration [31,43].

Acetylhypofluorite fluorinates sugars containing the multiple bond. So, acetylhypofluorite with 3,4,6-tri-O-acetyl-D-glucose gives two isomeric 2-desoxy-2-fluoro-D-glucoses [83,182-188]. In nonpolar solvents ($CFCl_3$,CCl_4) the yield of products of fluorination of sugars is approximately 4% whereas in polar solvents (CH_3COOH,CH_3OH, DMF) it is slightly higher (ac. 20%) [189]. A substituent at hydroxy-groups does not affects much the yield of the fluorination product [189].

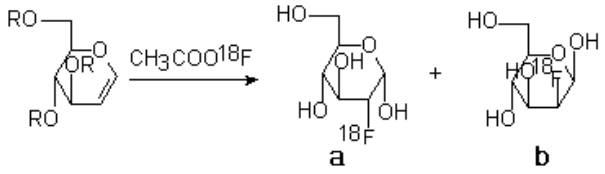
It should be noted that this method is used to introduce ^{18}F isotope into sugars [32,151,190-194]. That extends significantly the limits of application of the new fluorinating agent in biology. The demand in sugars with ^{18}F isotope has been an additional stimulus to study in detail possibilities of this reagent taken into account its availability and easiness in handling.



[^{18}F]Fluoro-2-deoxyglucose is formed in the first case and [^{18}F]fluorogalactopyranose in the second case .

Table 16 shows the results of fluorination of 3,4,6-tri-O-acetyl-D-glucose with different fluorinating reagents [183]. This is the basis of syntheses of biochemical compounds [182,195-197]. There was described the synthesis of 2-desoxy-2[^{18}F]-fluoro-D- galactose in 20% yield from galactose under the influence of CH3COOF reagent labeled with ^{18}F isotope [195]. This product may be used for control of selectivity and effectiveness of chemotherapy of tumours in tomography to diagnose diseases.

Table 16. *Results of the fluorination of 3,4,6-tri-O-acetyl-D-glucose*



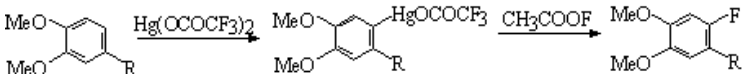
Fluorinating reagent	Solvent	Temperature, °C	Yield of the products,%	
			a	b
CH_3COOF	$CFCl_3$	-78	95	5
CH_3COOF	CH_3COOH	20	82	18
F_2	$CFCl_3$	-78	80	20
CF_3OF	$CFCl_3$	-78	81	19
XeF_2/BF_3	Et_2O/C_6H_6	20	93	7

Acetylhypofluorite was found to be a regioselective fluorinating agent with regard to hetero-organic compounds and their fluorodemetalation takes place. So, aryl derivatives of mercury [198], tin[199],silicon [200,201], germanium [199] under action of this reagent are converted to fluoro derivatives of benzene. The nature of the substituent in the aryl fragment is of great importance reflecting on the yield of the target product (see the data of Table 17) [202,203].

Table 17. *Reaction of hetero-organic compounds with acetylhypofluorite*

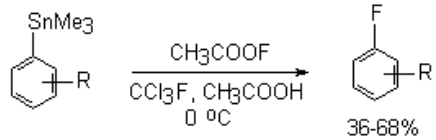
Initial subtrate	Reaction product	Yield,%	References
4-$CH_3OC_6H_4HgOCOCH_3$	4-$CH_3OC_6H_4F$	65	185,186
4-$CH_3OCOHgC_6H_4NHCOCH_3$	4-$FC_6H_4NHCOCH_3$	60	185,186
2-HOC_6H_4HgCl	2-HOC_6H_4F	53	185,186
4-HOC_6H_4HgCl4	4-HOC_6H_4F	47	185,186
C_6H_5HgCl	C_6H_5F	55	185,186
$C_6H_5HgOCOCH_3$	C_6H_5F	58	185,186
4-$NH_2C_6H_4HgOCOCH_3$	4-$NH_2C_6H_4F$	4	185,186
3-$NH_2C_6H_4HgOCOCH_3$	3-$NH_2C_6H_4F$	19	185,186
4-$CH_3OC_6H_4SnBu_3$	4-$CH_4OC_6H_4F$	78	189
4-$CH_3C_6H_4SnBu_3$	4-$CH_3C_6H_4F$	72	189
3-$CH_3C_6H_4SnBu_3$	3-$CH_3C_6H_4F$	71	189
$C_6H_5SnBu_3$	C_6H_5F	72	189
4-$FC_6H_4SnBu_3$	1,4-$F_2C_6H_4$	73	189
$C_6H_5SiMe_3$	C_6H_5F	10	189
4-$CH_3C_6H_4SiMe_3$	4-$CH_3C_6H_4F$	13	189
4-$CH_3OC_6H_4SiMe_3$	4-$CH_3OC_6H_4F$	9	189
4-$CH_3COC_6H_4SiMe_3$	4-$CH_3COC_6H_4F$	6	189
4-$CH_3COOC_6H_4SiMe_3$	4-$CH_3COOC_6H_4F$	16	189
$K_2[C_6H_5SiF_5]$	C_6H_5F	20	190,191
$K_2[C_6H_5CH_2SiF_5]$	$C_6H_5CH_2F$	6	190,191
K_2[4-$CH_3C_6H_4SiF_5$]	4-$CH_3C_6H_4F$	18	190,191
4-$CH_3OC_6H_4SnMe_3$	4-$CH_3OC_6H_4F$	66	192
4-$CH_3C_6H_4GeMe_3$	4-$CH_3C_6H_4F$	16	192
$C_6H_5SnMe_3$	C_6H_5F	68	192
$C_6H_5GeMe_3$	C_6H_5F	9	192
$C_6H_5SiMe_3$	C_6H_5F	4	192

R = L- è D-$CH_2CH(NHCOCF_3)COOEt$,



$CH_3CH_2NHCOCF_3$, CH_2COOEt, CHO

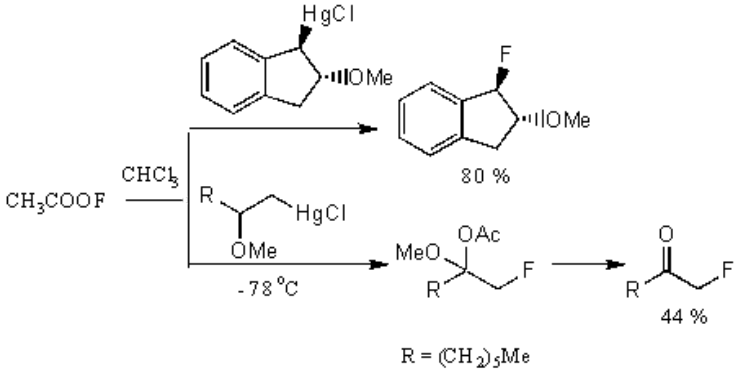
The simplicity of carrying out the process and high enough regioselectivity allows introducing ^{18}F isotope by this method. So, direct introduction of fluorine or of fluorine labeled with^{18}F isotope by the influence of CH_3COOF is carried out with aromatic derivatives of tin or mercury derivatives [147,198,204].



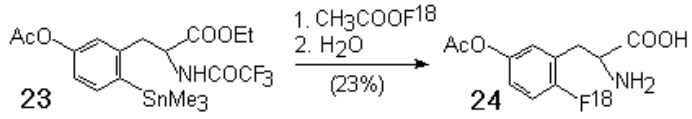
R = H, CH_3, OCH_3, Cl, CF_3

The solvent is of great importance in fluorodemetalation. Fluorodestannylation of phenyltrimethylstannane with CH_3COOF at 0^oC results in fluorobenzene: 68.2% in $CFCl_3$, 65.5% in CCl_4, 14.5% in CH_2Cl_2. It follows from Table 17 that the yield of of fluorobenzene decreases in the series Sn>Ge>Si derivatives. Fluoroaromatic compounds are also formed in reactions of CH_3COOF with organic derivatives of germanium [199], silicon [206], arylpentafluorosilicates [201].

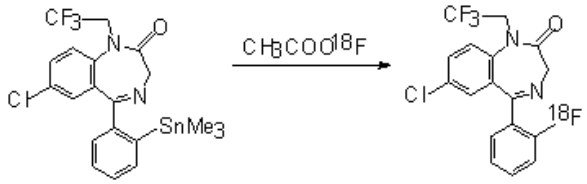
Vicinal fluoro- and methoxy- derivatives are formed regioselectively in high yields in fluorination of saturated mercury derivatives with CH_3COOF in chloroform medium [205].



Regioselectivity of fluorination with CH_3COOF was used for introduction of ^{18}F isotope into derivatives of L-m-tyrosine **23**. Here the C-Si bond is affected and the fluorine atom is introduced in the benzene ring. Removal of protective functions at amino- and carboxyl groups by a plain hydrolysis results in appropriate aminoacids **24** [207].

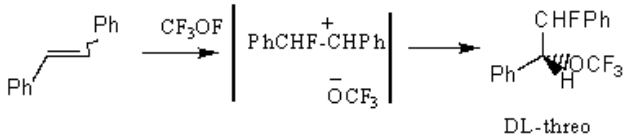


This way has been realized for fluorine introduction into the benzene ring and other heterocyclic compounds, for example for benzodiazepine [208].



5.3. Application of perfluoroalkyl hypofluorites as fluorinating reagents.

For hypofluorites, derivatives of perfluorinated aliphatic alcohols, two groups of processes are typical: the addition to the multiple bond and substitutive fluorination. In early reviews [10,189,202,209] these reactions were described in detail. But the high toxicity of trifluoromethylhypofluorite kept a check on the research of this reagent for a long time and only the last 20 years they have been drawn attention. The processes were studied with a purpose of a preparatory way to introduce fluorine into different cyclic compounds instead of elemental fluorine reacting more hard. The processes of addition to unsaturated substrates consist in the addition of F and OCF_3 elements to the multiple bond (spontaneously in the absence of sources of initiation) together with the fluorination of the latter. In the interaction of CF_3OF with olefins the formation of adducts of fluorine and trifluoromethoxysilyl group to the multiple bond takes place [210-213].The stereochemistry of the addition is exclusively of syn character that points to the electrophilic nature of the reagent. The course of the process is supposed to be vβ-carbcation.

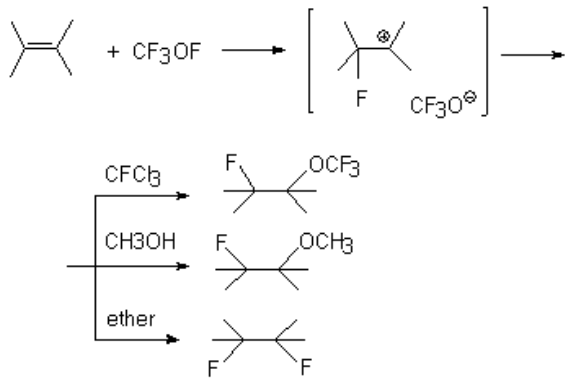


Homolytic dissociation of the O-F bond is caused by heating or light. Addition of hypofluorites ROF to unsaturated centers is a well-known method to produce organofluoric compounds. Usually the reaction is carried out at low temperatures. Hypofluorites are strong oxidizers and may cause explosions when contact with organic molecules. A medium in which the process is carried out influences the character of the reaction products also. So, the carrying out of the process with CF_3OF in alcohols results in the formation of derivatives containing the fluorine atom and alkoxyl group whereas products of addition of F and OCF_3 are formed in non-polar solvents. The OCF_3 group can be subjected to conversion to the OH-

group when the process is carried out in water and to the splitting off under the influence of bases with the reagent of the multiple bond.

We are reviewing reactions of CF_3OF with olefins selectively : we are interested mainly in demonstrative examples to clarify the chemistry of interaction of the O-F reagents with unsaturated centers. In this respect CF_3OF ($CsSO_4F$ as well) is an unsurpassed object. Synthetic ability of CF_3OF as a fluorinating agent , an exotic agent for most of laboratories, is surpassed to a considerable extent by such available reagents as acylhypofluorites, trifluoroacetylhypofluorite and $CsSO_4F$.

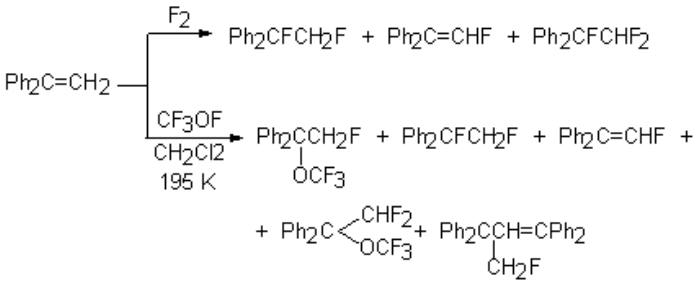
Interesting data were obtained in reactions of CF_3OF with *trans*- and *cis*-stilbenes: a mixture of *threo/erythro*- isomers in a ratio of 1:5 is formed with *trans*-stilbene , whereas under the same conditions *cis*-stilbene gives a mixture of *threo/erythro*- isomers in a ratio of 5:1 [36]. Stereospecificity of the addition and a certain dependence of the results on the solvent nature allow supposing that in the first stage the multiple bond of the reagent is attacked together with generation of the carbcation which further conversions depend on the reaction conditions and nature of substituents. The carbcation is stabilized in inert solvents by a reaction with the CF_3O-anti-ion. Such solvents as diethyl ether, for example, promote the reaction of this carbcation with fluoride ion to form a difluoro-derivative . In the presence of a stronger electron donor comparing with CF_3OF in the system , the nucleophile of the medium is added to the carbcation. Regioselectivity of fluorination of many olefins points to the reality of intermediate formation of fluorocarbene ion.



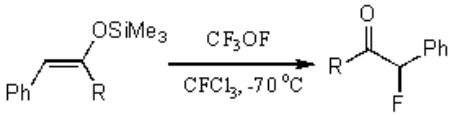
Fluorine-containing olefins react with CF_3OF in high yield but with low stereo- and regioselectivity even at temperatures of +20- +75^oC to give adducts of, for example, hexafluoropropylene [214-219].

The thermal gas-phase reaction of tetrachloroethylene at 41-71oC results in trifluoromethyl-1,1,2,2-tetrachloro-2-fluoroethyl ether (97.7-99.5% yield) [220].

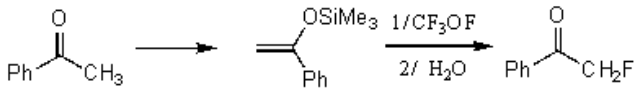
The reaction with 1,1-diphenylethylene is demonstrative for comparison between CF_3OF and F_2 [221,222].



When CF_3OF reacts with trimethylsilyl ethers of ketone enoles, ethers of carbonic acids, only the carbon atom in the α-position at the carbonyl group is affected and the yield of the reaction products is , as a rule, high enough (70-90%) [69-71].

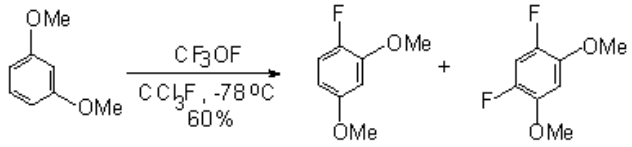


R = H, Ph, OEt, NMe2



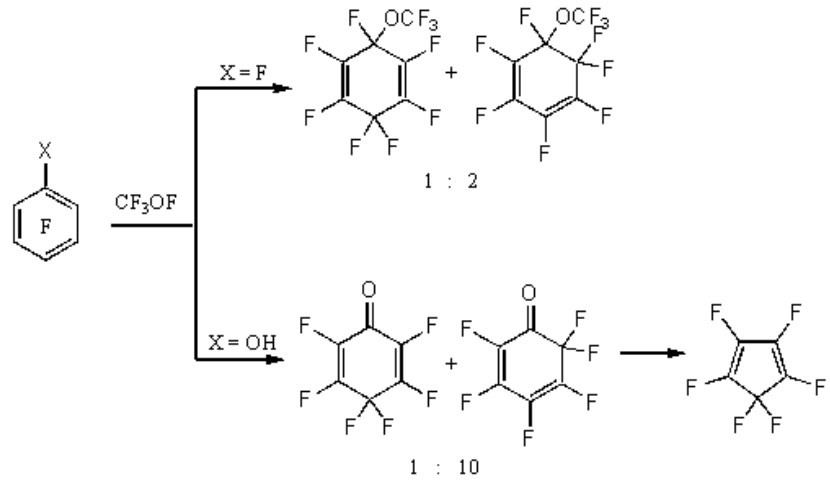
The fluorination process of aromatic and heterocyclic compounds under subjection to reagents of the hypofluorite class, perfluoroalkylhypofluorites, proceeds rather smoothly affecting the carbon atoms of the benzene ring. Thus, aniline and its N-substituted ones at 0^{o}C for 2 hours give *ortho*- and *para*-fluoroanilines in a yield over 60% [223]. Aprotic non-polar solvents increase the share of *ortho*-ispmers. For N-substituted aniline the reactivity is determined by the substituent nature at the nitrogen atom. The following activity series has been found: $PhNHSO_2CH_3$> $PhNHCOCF_3$ ≈ $PhNHCOCl$ ≈ $PhNHSO_2CF_3$.

The fluorination of phenol with CF_3OF affects the *ortho*- and *para*-positions of the benzene ring [214]. The ratio of the isomers makes possible to describe formally the influence of CF_3OF reagent as an electrophilic process. 2,6-Dimethylphenol under the influence of CF_3OF in $CFCl_3$ gives 6-fluoro-2,6-dimethylcyclohexa-2,4-dienone [224] dimer. 1,3-Dimethoxy-benzene subjected to fluorination gives mono- and difluoro derivatives [57,225].

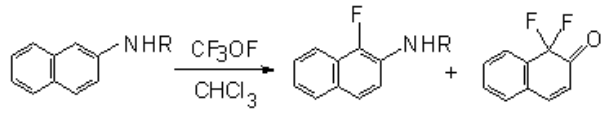


The reaction of CF_3OF with 2,6-dimethoxyacetophenone results in 2,6-dimethoxy-3-fluoroacetophenone (48% yield) [225].

The absence of hydrogen atoms in the benzene ring results in the process of addition to the multiple bond. So, the interaction of hexafluorobenzene with CF_3OF under mild conditions gives a mixture of isomeric polyfluorinated cyclohexadienes [226]. CF_3OF possesses oxidative properties that results in its reaction with pentafluorophenol in formation of hexafluorocyclohexadienone which gives hexafluorocyclopentadiene under thermolysis [226,227].

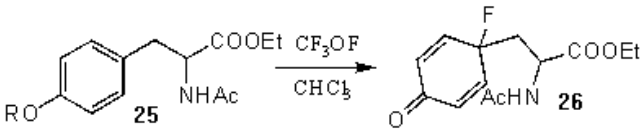


The fluorination of ethyl N-acetyl-L-tirosinate **25** at -22^{o}C in chloroform gives product **26** of addition to the benzene ring [228,229].

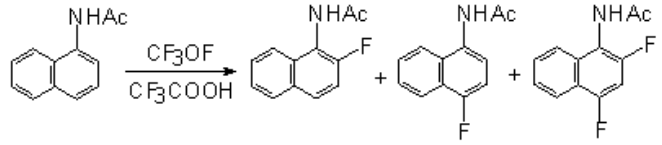


R = H, CH_3CO

In the interaction of CF_3OF with aromatic polycyclic compounds, containing functional groups, together with direct fluorination there may be transformation of functional groups and fluorination of the product of that transformation. So, the interaction of CF_3OF with naphtylamine or N-acetyl-β-naphtylamine brings to mono-fluoro-derivative and appropriate difluoroketo compound [230]. β-Naphtol reacts similarly. [231]

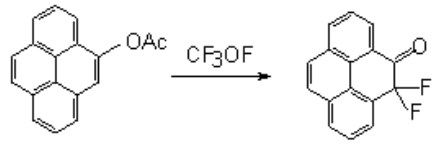


These processes are suppressed when trifluoroacetic acid is used as a solvent [224]. In this case mono- and difluoro-derivatives are formed.

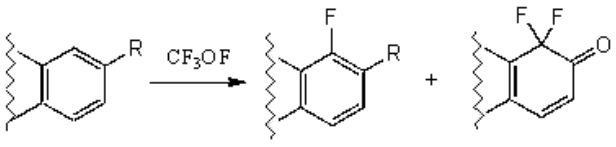


Chlorofrm, $CFCl_3$ and acetone play the same role as solvents [224]. Thus, N-acetyl-2-naphtyl amine gives 1-fluoro-N-acetyl-2-naphtyl amine in them. Difluoro-derivatives are formed in the excess of CF_3OF.

The presence in a polycyclic unsaturated system of substituents containing oxygen atoms, OAc for example, results in replacement of the hydrogen atom in the α-position at this group. In this case the formation of difluoro-derivatives is also possible [232].

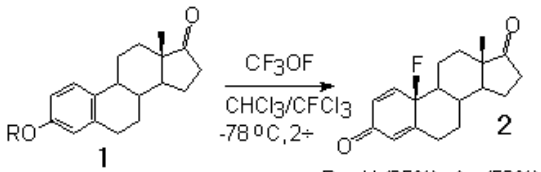


It is also typical for derivatives of naphthaline, anthracene and pyrene. Their reactions with CF_3OF at –78°C give monofluoro- and difluoro-derivatives which ratio depends on the substituent nature and structure of the aromatic molecule [230-234].



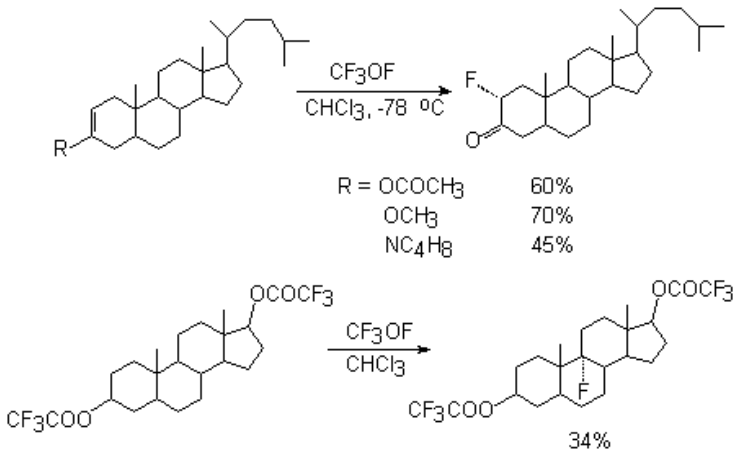
R = NH_2, NHAc, OH, AcO

Natural compounds containing a benzene ring or a multiple bond also are subjected to fluorination [72,128,235-237]. Regio- and stereoselective addition of fluorine and trifluoromethoxy group to the multiple bond is obvious enough in the example of the reaction of CF_3OF with steroids. For example, derivatives of oestrone **1** react with CF_3OF to form 9β-fluoro19-norandrosterone-1,4-diene-3,17-dione **2** [224].

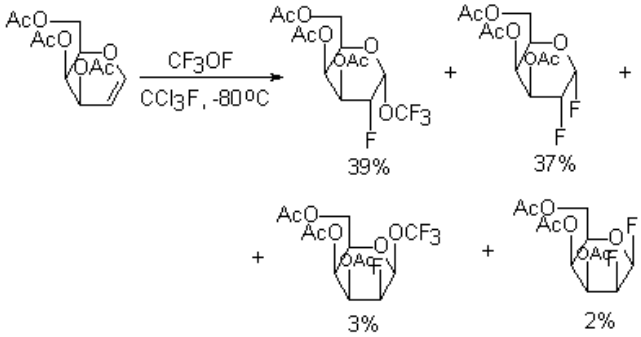


R = H (65%), Ac (50%)

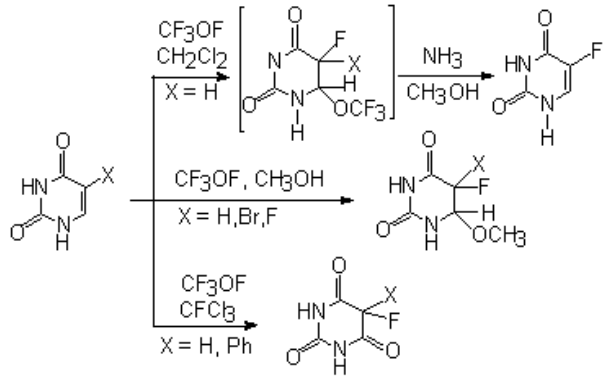
Another examples are given in [71,128,235].



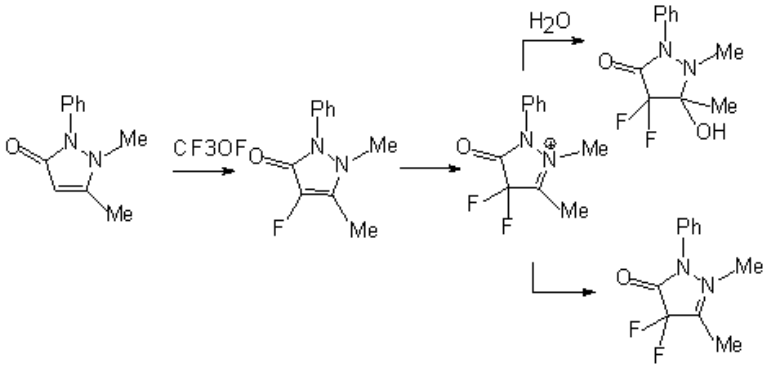
The reaction of CF_3OF with sugars results in the formation of adduct of fluorine and trifluoromethoxy-group, and also two fluorine atoms [238,239]. For example, 2-desoxy-2-fluorolactose and 2-desoxy-2-fluorodisaccharide were produced [240]. The prevailing formation of *syn*-isomers should be noted [240-246].



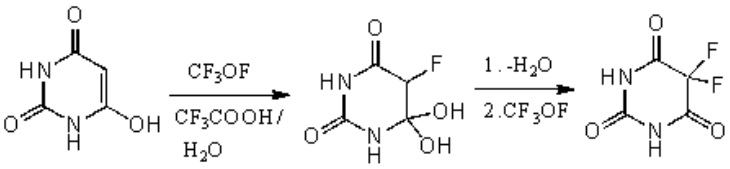
Fluorination of heterocyclic compounds with CF_3OF may proceed with affecting heteroatom and without it. In case of uracil and its derivatives, fluorination of the multiple bond takes place [238,247-257].



The reaction of 2,3-dimethyl-1-phenyl-3-pyrazoline-5-one with CF_3OF in a system of CF_3COOH-acetone (1:50 at room temperature) results in two products: 4,4-difluoro-3-hydroxy-2,3-dimethyl-1-phenylpyrazolidine-5-one and 4,4-difluoro-3-methyl-1-phenyl-2-pyrazoline-5-one [224]. When this reaction is carried out in $CFCl_3$, then together with difluoro-derivatives also 4-fluoro-2,3-dimethyl-1-phenyl-3-pyrazoline-5-one is formed which is converted further to difluoro derivative in the excess of CF_3OF [224].

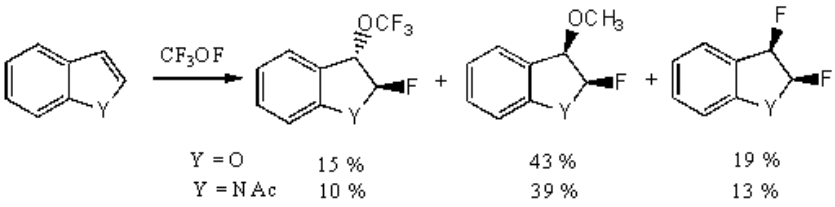


Direct fluorination with CF_3OF of different pyrimidines (uracil, cytosine, thymine etc.) at –78-25^{o}C gives fluoro-derivatives in good yields [255-257]. Barbituric acid forms difluorobarbituric acid [238,247-254].

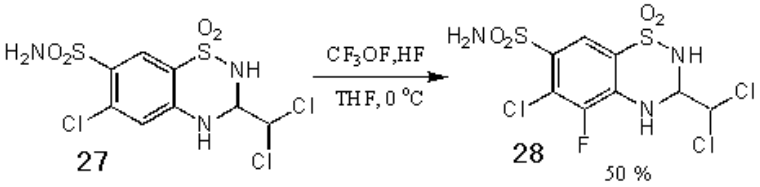


Similarly to fluorine, CF_3OF fluorinates nucleosides to give fluoro-derivatives [255-257].

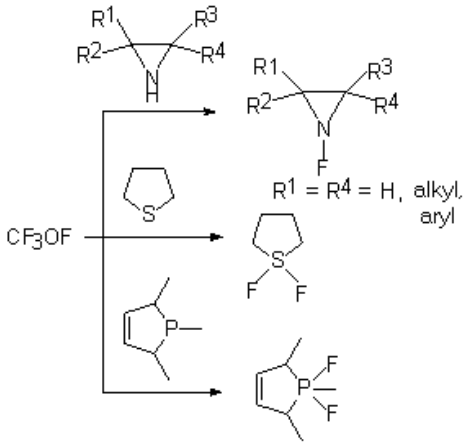
At low temperature CF_3OF fluorinates benzofuran and 1-acetylindol to give fluorine adducts and trifluoromethoxy groups [258].



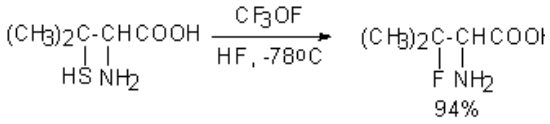
As a different example [259], trichloromethiazide **27** gives 5-fluoro-derivative **28** only in the system of tetrahydrofuran/hydrogen fluoride, whereas in the system of chloroform/acetone another two products without fluorine atoms are also formed.



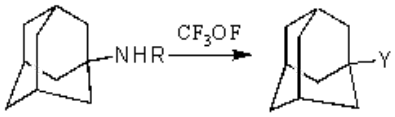
In case of aziridine, the main way of the reaction with CF_3OF is formation of N-F-derivatives [260-262]. Cyclic sulfides under mild conditions are converted to fluoro-derivatives and the fluorination affects only the sulfur atom of the cyclic system [263,264].



But it should be noted that using oxidative properties of CF_3OF in a number of cases results in replacement of sulfur-containing group with fluorine. Thus, thiols, disulfides and dithiolates form appropriate fluorides [265,266]. A similar picture is observed for heterocyclic derivatives of trivalent phosphorus [267].

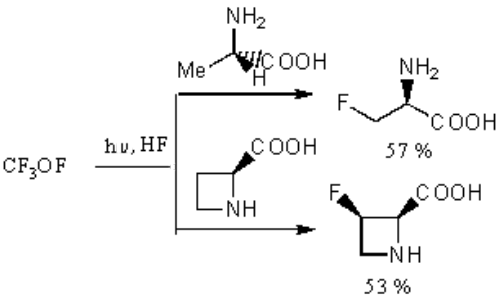


In the reaction of CF_3OF with some derivatives of amines the functionality of the system depends on the molecule structure and on the presence of substituents at amino-group [228].

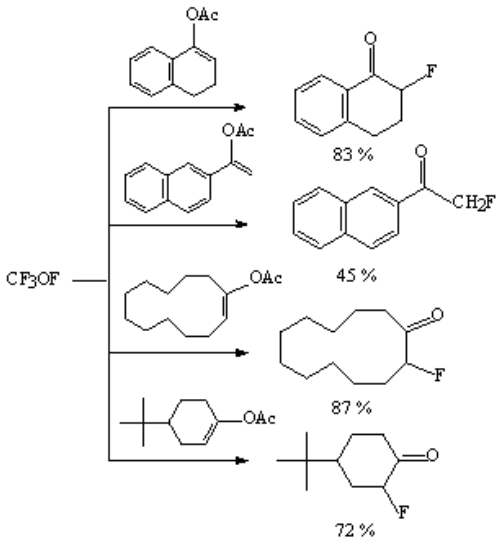


R	Ac	H
Y	NF_2	NCO
Yield, %	60	55

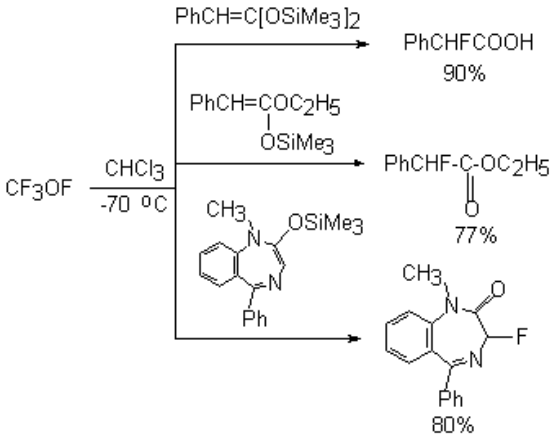
Low-temperature fluorination of different amino-acids in a solution of hydrogen fluoride gives α-fluoroamino-acids which are potential antimetabolites [268-271].



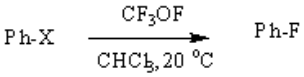
The presence of such substituents as hydroxy-, alkoxy- and acetoxy-groups at the multiple bond causes formation of α-fluoroketones under the influence of CF_3OF (in non-polar solvents, as a rule) [72,272-276].



Silyl ethers of enols behave in a similar way [72].

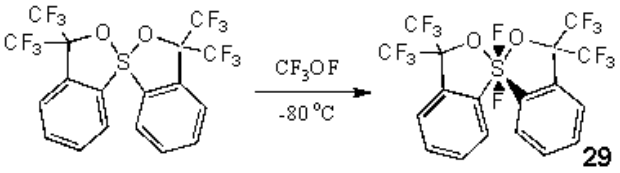


Derivatives of tin and mercury in reactions with CF_3OF form fluorobenzene in chloroforrm at room temperature [138,277].



R	$SnPh_3$	$SnMe_3$	HgPh
Yield,%	22	50	83

Some sulfuranes under the influence of CF_3OF oxidize derivatives of tetravalent sulfur to hexavalent one to give stable compounds **29** [266].



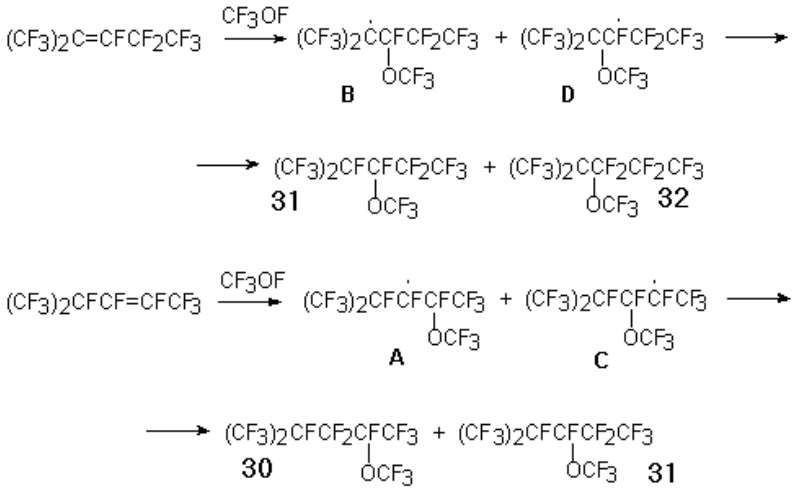
In most cases the use of perfluoroalkylhypofluorites is justified by mild conditions of fluorination processes, high selectivity and high yield of the fluorination products in comparison with using elemental fluorine. It is of great importance that these fluorinating agents may be successfully used for fluorination of a number of biologically active structures, heterocyclic compounds, amino-acids etc.. The simplest alkylhypofluorite, CF_3OF, introduces into a substrate CF_3O fragment that is easy to identify and able to be converted to the oxy-group that may be of synthetic interest. The successful study of the class of hypofluorites may be found fruitful not only for clarification of the nature of hypofluorites themselves but for the chemistry of fluorination processes with different reagents as a whole.

5.4. Mechanism of fluorination with reagents containing O-F bonds.

The study and discussion of the mechanism of fluorination with fluorooxy-reagents have lasted almost the same period as this synthetic direction has existed. But the most demonstrative arguments in favor of this or that version appeared when such stable study objects as fluorooxytrifluoromethane, CF_3OF and cesium fluorosulfate,$CsSO_3OF$, became available. As it was seen from the above review, the compounds containing the O-F bonds have the reactivity close to fluorine gas and a stronger electrophilic character. Only some attempts have been done with the purpose to study the reaction mechanism of these fluorinating reagents and main investigations are at hand. Nevertheless, many authors made their suggestions about the ways of the course of the processes. The idea of electrophilic character of fluorine bound with oxygen lies in the basis of all studies.

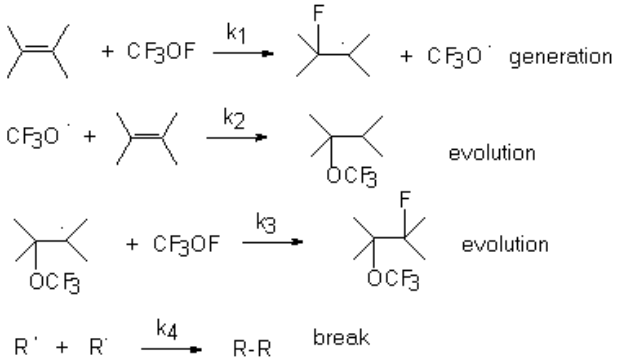
The most vital importance in the study of the mechanism of the reactions of fluorooxy-reagents has the addition of CF_3OF to unsaturated compounds. So, in papers [278-282] it was shown that perfluoro-2-methyl-2-pentene and perfluoro-4-methyl-2-pentene in the reactions with CF_3OF formed products of addition to multiple bonds of fluorine and trifluoromethoxy-group in high yield but with low regioselectivity.

of **30/31** is 24, though the ratio of **31/32** is only 2.3. Such difference may be explained by steric factors, polarity of reagents and stability of the intermediate radicals. It should be noted that carrying out the process in a cell of ESR-spectrometer at 330 and 320K made possible to obtain distinct signals of **A** and **B**radicals with super fine splitting on fluorine atoms (the authors failed to identify **C** and **D** radicals, perhaps, due to their lower stability) [278]. That is the first example of determination of intermediate particles in the reactions of olefins with CF_3OF.



A similar picture is observed under the influence of CF_3OF $X(CF_2O)_n(CF_2CF_2O)_mCF_2OF$ with other perfluoroolefins [284]. Secondary and tertiary radicals were determined in these reactions by the ESR method.

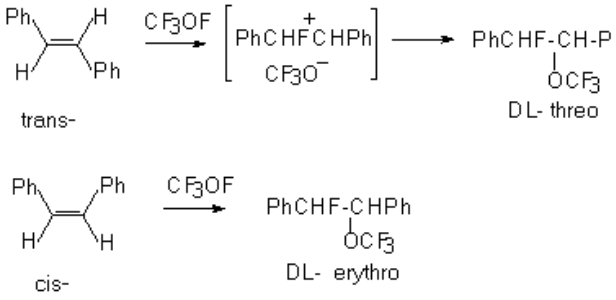
The addition of CF_3OF to “electron-deficient” olefins in non-polar solvents at low temperatures proceeds according to the radical-chain mechanism [284]. The kinetics of all stages of the chain mechanism has been investigated: generation, evolution and break of the chain (auto-initiation, the reaction of CF_3O radical with olefin to form the intermediate radical which reacts affecting the O-F bond of the reagent to give the reaction product and CF_3O radical).



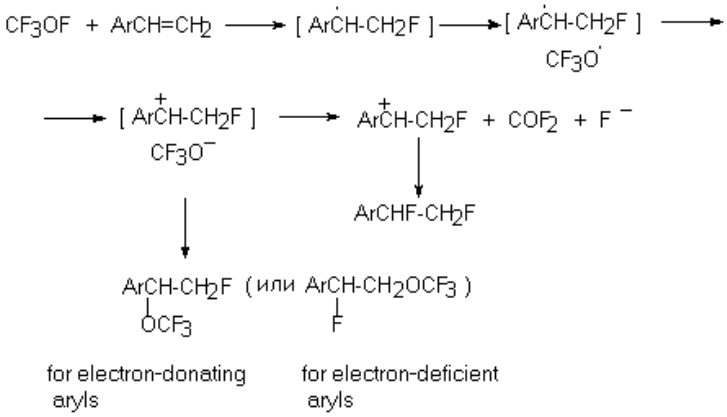
Trifluoromethoxyl radical (CF_3O) is generated at low temperature from bis(trifluoromethyl)peroxide in the presence of olefins that was determined by the ESR spectrum [285,286].

One more confirmation of the radical mechanism in the reaction of CF_3OF with unsaturated compounds was received in the study of the kinetics of the interaction of CF_3OF with perfluoropropylene [287,288] and trichloroethylene [211]. DesMarteau has noted that CF_3OF reacts with perfluorinated olefins according to the radical mechanism with low regio- and stereoselectivity in concentrated solvents or without solvents[212].

It is of interest that Barton with collaborators, one among the most competent researchers in this field of investigations, studied the interaction of the CF_3OF with unsaturated compounds and observed the reaction course as a syn-addition and have concluded that the process proceeds through the formation of α-fluorocarbcation [289].

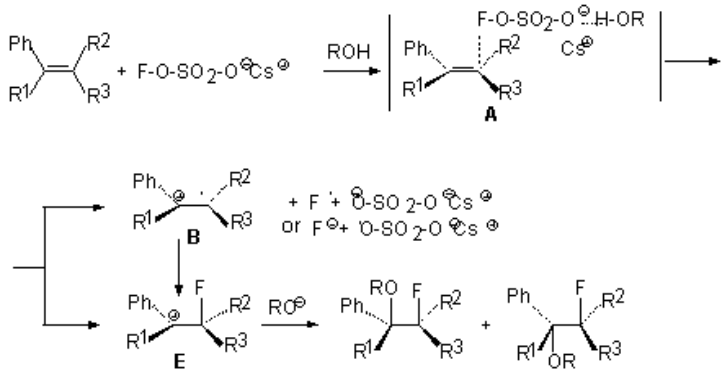


At last, the authors of papers [221,290] studying the addition of CF_3OF to aryl-olefins concluded that the process proceeded according to the radical-ion mechanism.



As we have already noted, together with CF_3OF, cesium fluorooxysulfate is a beneficial object for the study of the addition reaction mechanism . Nevertheless, there are a few purposeful studies of that kind, far less than in case of CF_3OF.

In the study by Zupan with collaborators the kinetics of the fluorination of unsaturated compounds with cesium fluorooxysulfate in methyl alcohol has been studied. The authors proposed the following process scheme [112]:



As it is seen from the scheme, the formation of carbcation E may proceed in two ways, but in both cases at first π-complex **A** is to be generated.

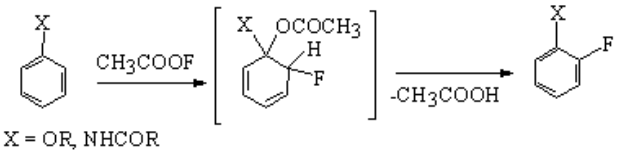
The mechanism of the fluorination of olefins with cesium fluorooxysulfate is similar. In Table 18 one can see relative rate constants of the fluorination with this reagent of various olefins to form products of methoxyfluorination [112]. As it is seen from Table 18, there is a linear dependence of the first ionization potential and the relative rate constant of the fluorination of olefins with $CsSO_4F$ (the correlation coefficient r =0.945). With decreasing the potential value the rate of the reaction of the olefin with the fluorinating agent is increasing that is in conformance with the ion mechanism of the process. In other words, the formation of carbcation **E** may proceed in two ways at least, but in both cases complex **A** has to be generated at first.

Table 18. *Comparative rate (k , relative to 1,1-diphenylethylene) of the fluorination of unsaturated compounds under the influence of $CsSO_4F$ in methyl alcohol.*

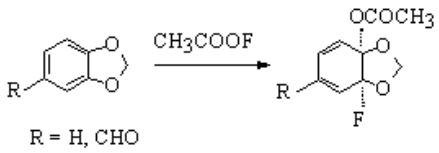
Olefin	k	IP (eV)
1,1-diphenylethane	1,00	8,24
1,1-diphenyl-1-propene	5,7	8,14
indene	0,9	8,4
1,2-dihydronaphthalene	1,6	8,26
3-phenyl-1-H-indene	15,4	7,73
4-phenyl-1,2-dihydronaphthalene	17,1	7,67
9-phenyl-6,7-dihydro-5H-benzocycloheptene	5,5	7,91

There are many synthetic studies, which have discussed the matter of the reaction mechanism with fluorooxy-compounds participation. As a rule they judge the mechanism according to the reaction products. Though the proposed schemes are not always conclusive enough and conclusions are often of a hypothetical character, they have contributed to the understanding of the matter essence.

As an example, we can refer to the study of Rosen with collaborators [150] on the reaction of acetylhypofluorite, a source of electrophilic fluorine, with aromatic compounds. They found that the compounds, containing activating substituents in the main body, gave mainly ortho-isomer as the reaction product in a yield up to 85%. The authors conclude that in the first stage the addition of CH_3COOF to the double bond of the benzene ring takes place, CH_3COOH is then eliminated with regeneration of the aromatic structure. But if the elimination stage is impossible structurally, the intermediate, CH_3COOFadduct, can be isolated.

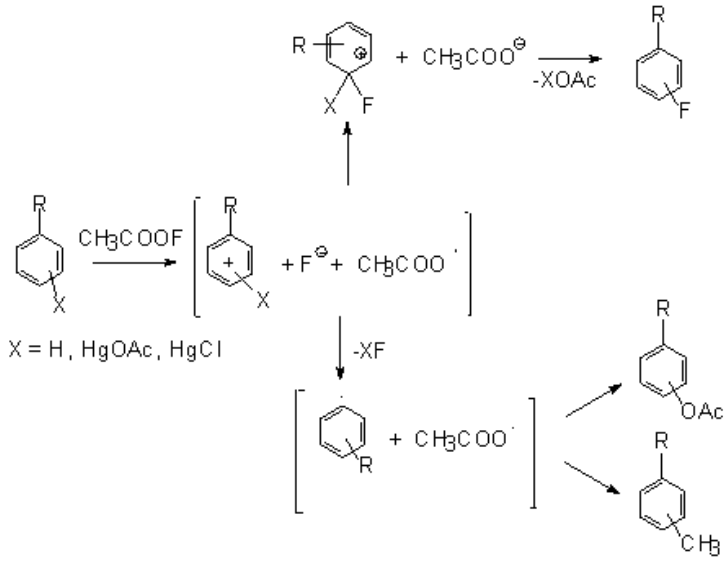


X = OR, NHCOR



R = H, CHO

Acetylhypofluorite has a higher selectivity compared with fluorine and CF_3OF and exhibits evident oxidizing properties. By virtue of that, one of possible ways of its interaction with aromatic compounds in the first stage can be one-electron oxidation of the aromatic compound to cation-radical [150]. Further conversions depend both on the nature of the substituent in the benzene ring and on the solvent used. So, if the substituent is a hetero-organic group, containing, for example, the mercury atom, then a fluoro-aromatic derivative is formed exclusively. If the substituent is NH_2, the oxidizer affects, first at all, the nitrogen atom that results in a very low yield of a fluoroaromatic derivative, whereas with OH substituent exclusively fluoroaromatic derivatives are formed and with CH_3 substituent there are formed methyl- and acetoxy-derivatives together with fluorobenzenes.



In reactions with $CsSO_4F$ the relative reactivity of mono-substituted benzenes is determined by the substituent nature [110]. The ratio of ortho/para- isomers in the fluorination with $CsSO_4F$ in the presence of catalyst is determined by r and the rate of the process itself depends on $–H_0$ function [121]. All that points that in acid catalysis the mechanism of fluorination of aromatic compounds with $CsSO_4F$ reagent corresponds most probably to electrophilic aromatic substitution. Probably, the process runs through the formation of electrophiliσ-complex generated by the initial attack of F-OSO_3- anion, in which the polarization is such that the positive charge is on the fluorine atom and readiness of elimination of thermodinamically stable O-SO_3- anion promotes the process of conversion of the intermediate complex to thσ-complex. The role of the Lewis acids is in assistance with the formation of O-SO_3- anion and in the stabilization of thσ-complex.

In the case when only $CsSO_4F$ affects an aromatic compound, at the expense of its oxidizing properties [135] there may be one-electron oxidation of the aromatic compound to the appropriate cation-radical which reacts with the fluorine radical of $CsSO_4F$ to generate thσ-complex which stabilization to aromatic system proceeds by elimination of H+. In this case the influence of the fluorine radical proceeds regioselectively and the all three isomers are formed. But one should have in mind that kinetically controlled distribution of the isomers can be changed due to thermodinamical factors (the kinetic data of the reactions of some aromatic compounds are given in Table 19)[94,110,291]. In some cases the interaction of $CsSO_4F$ with substituted aromatic compounds can be followed with splitting of the C-C_{ar} bond to form fluoro-derivatives [119].

Table 19. *Rate constants of the fluorination of benzene derivatives C_6H_5R under the influence of $CsSO_4F$ [94].*

R	k $m^{-1}s^{-1}$	R	k $m^{-1}s^{-1}$
OH	0,34	F	0,0029
OCH_3	0,55	COOMe	0,0016
CH_3	0,15	CN	$5*10^{-4}$
C_6H_5	1,2	NO_2	$8*10^{-5}$
H	0,033		

The authors of paper [127] have studied the action of $CsSO_4F$ reagent on substituted benzaldehydes that resulted in fluoroanhydrides of benzoic acid. The linear dependence between the relative fluorination rate constant arσ+ - constant of the substituent was found (the correlation coefficient was 0.9955); based on these data, r was calculated as –0.385. This value of **r** is significantly lower than that observed for the processes of oxidation of benzaldehydes with peroxymono sulfate, perbenzoic acid and N-bromobenzamide (-1.7, -1.6, -5.5 respectively). It may be proposed that here is not only oxidation but a

Deep understanding of the course of fluorination processes with use of various fluorinating agents allows more deliberate improving the existing practical important methods of fluorination and searching new effective systems for these purposes. But independently of that, the fluorinating agents containing the O-F and N-F bonds have contributed much to the development of the chemistry of fluorine organic compounds.

5.5. Comparative fluorinating ability of fluorooxy-reagents in solvents of different polarity.

A qualitative estimation of the fluorinating ability in the series of fluorooxy-reagents is not a simple task, because many of such compounds are unstable, can not be isolated individually and studied under adequate conditions. So much a fundamental theoretical approach to this problem proposed recently seems more significant. Thermodynamics of the fluorination processes has been assumed as a basis, and a qualitative criteria of the fluorinating ability of fluorooxy-reagents has been chosen as the reaction heat calculated taken into account the polarity of a solvent used for the process [292].

Quantum-chemical calculations were done by MNDO, AMI, MNDO-PM-3 methods taken into account the solvent polarity, within the frames of the model of polarizable continium developed by Tomasi.

To compare the fluorinating abilities of fluorine " carriers" of R-OF type, their interaction with pyridine, as a fluorination object, was chosen as a reference reaction. This reaction is attractive because in addition to the comparative estimation of the carriers with each other it makes possible to compare them with a classical fluorinating reagent, N-fluoropyridinium: if the reaction enthalpy is negative, then the R-OF reagent under consideration exceeds N-fluoropyridinium cation in the fluorinating ability and yields to it in this respect if the reaction enthalpy is positive.

To fluorinate the fluorinating ability of typical fluorooxy-reagents in solvents of different polarity, calculations of the heat efficiencies (ΔH_{reac} solvent) were made for the model exchange reactions (1-5).

$CF_3OF + C_5H_5N \rightarrow [C_5H_5N\text{-}F]^+ + CF_3O^-$ (1)

$CH_3COOF + C_5H_5N \rightarrow [C_5H_5N\text{-}F]^+ + CH_3COO^-$ (2)

$CF_3COOF + C_5H_5N \rightarrow [C_5H_5N\text{-}F]^+ + CF_3COO^-$ (3)

$FSO_2OF + C_5H_5N \rightarrow [C_5H_5N\text{-}F]^+ + FSO_3^-$ (4)

$CF_3SO_2OF + C_5H_5N \rightarrow [C_5H_5N\text{-}F]^+ + CF_3SO_3^-$ (5)

To calculate the heat efficiencies of these reactions in gas phase ΔH_{reac} (g) and in solvents of different polarity ΔH_{reac}(s), the formation enthalpies ΔH_f (g) of the reagents and products with complete optimization of geometry of the molecules were calculated. For charged molecular systems there was calculated free Gibbs energy ΔG (s) of formation of a system of "polarized molecule + polarization field" ,taken into account the solvent influence within the limits of PCM model at different values of the dielectric constant ε.

On the basis of the obtained values of ΔH_f (g) and ΔG (s) the target values were calculated: the heat efficiencies of fluorination reactions (1-5) in gas phase and in solvents of different polarity ΔH_{reac} (s), they are given in Table 20. The calculations were made by the authors by three quantum-chemical methods, but Table 20 represents the data only of one of them, MNDO-PM3, as the most correct one.

Table 20. *Heat efficiencies (ΔH_{reac} solvent) of exchange reactions (1-5) in solvents of different polarity (ε >1) and in gas phase (ε =1)*

Reaction	ε	ΔH_{reac} solvent kkal/mole
1	1	105,2
	10	2,6
	20	-10,6
	30	-13,5
	78,5	-16,8
2	1	121,4
	10	5,0
	20	-2,2
	30	-4,7
	78,5	-7,8
3	1	89,8
	10	-14,0
	20	-20,5
	30	-22,7
	78,5	-25,5
4	1	84,9
	10	-24,0
	20	-31,1
	30	-33,7
	78,5	-86,8
5	1	66,6
	10	-33,8
	20	-40,5
	30	-42,9
	78,5	-45,8

As it is seen from the data of Table 20, reactions under investigation (1-5) in gas phas(ε≠1), given for comparison, are very endothermi ΔH_{reac} reaches 100 kkal/mole and are positive. At transition to polar solvents, a principal change of the heat reaction efficiencies occurs: they become negative, i.e. exothermic. Even in solvents of middle polarity (the dielectric constar ε =20-30) the equilibrium of reactions (1-5) is shifted to the right-hand side, in other words, the R-OF reagents under consideration exceed N-fluoropyridinium cation in the fluorinating ability.

The comparison of the R-OF reagents with each other looks especially demonstrative : it is seen from Table 20 that according to the fluorinating ability they form the following series:

$CF_3SO_2OF > FSO_2OF > CF_3COOF > CF_3OF > CH_3COOF$

The series corresponds to the ideas of synthesis researchers about connection of the structure of the R-OF reagents with their reactivity. That is an additional evidence of reliability of the proposed thermodynamic method.

In conclusion, one should take into account the variation of the Gibbs curves (Fig.1) directly connected with the solvation effect : already within a range (ε= 30-40 the dependence (ΔGε' degenerates , i.e. the solvation reaches saturation. Obviously , the solvents with such dielectric constant can be acceptable enough for fluorination.

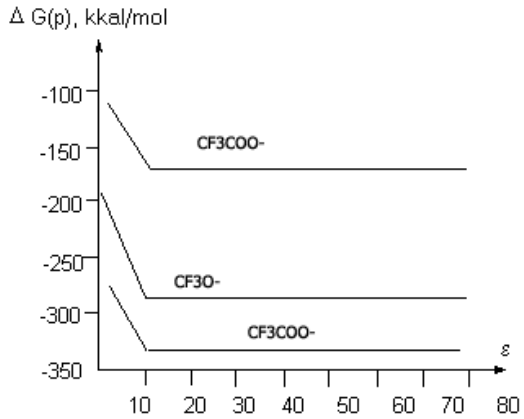


Figure1.*Dependence of the Gibbs free energy (taken into acoount the solvent influence) on the dielectric constant of the solvent (calculated within the limits of MNDO method).*

As a whole, the results of the calculations of the heat efficiencies have clearly demonstrated the change of the fluorinating ability of the R-OF reagents in a form convenient for comparison in dependence on the solvent polarity. This method is the most fruitful and to some extent is unique for estimation of the fluorinating ability of the R-OF reagents and their comparison with each other.

CONCLUSION

Usually the choice of a fluorinating agent is made taken into account its availability, selectivity of the fluorination, readiness of the process course and equipment, safety of handling. It is customary to compare these factors with elemental fluorine using, because its use is the most efficient process of production of organofluorine compounds. But the high reactivity of elemental fluorine requires application of special methods that increases significantly the cost of the target products.

This paper reviews examples of application of compounds containing the O-F bonds as effective fluorinating agents. Their abilities for selective fluorination of different classes of compounds have been shown and compared. The combination of potential electron properties and steric effects is typical when hydrogen atoms are replaced with fluorine in organic molecules and is widely used in organic chemistry. Besides, in addition to the direct method of fluorination with elemental fluorine, new fluorinating reagents have appeared, which sometimes have some advantages compared with elemental fluorine and conventionally used hydrogen fluoride and fluorides of transition metals. The new fluorinating reagents do not replace the existing ones produced commercially but supplement with them. More over, a number of them have been produced on an industrial scale that makes possible their widespread study. At the same time their practical application allows changing economic factors and environment of production of fluorine-containing materials. Widespread investigations in this field have become a basis for creation of materials perspective for new technique and medicine and great technological efforts of these studies have promoted complete use of elemental fluorine in organic synthesis.

On the whole, there has been formulated a task of application of fluorinating agents not only for realization of the fluorination processes but for their application for different synthetic purposes. In our review we gave some new areas of application of compounds containing the O-F bonds for processes of oxidation and generation of reactive electrophilic particles.

We assume that the analysis of the existing data and some formulated conclusions will be useful not only for chemists working in the fluorine chemistry, but also for experts using new materials in their work and solving new complex technical tasks. The presented review on the chemistry of compounds containing the O-F bonds places at disposal of experts in this important and dynamically developing field a possibility to become familiar with the new ideas, the latest achievements and results of the investigations and also with unsolved problems.

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