

INTERNAL PERFLUOROOLEFINS IN A SYNTHESIS OF FLUOROORGANIC COMPOUNDS

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ABSTRACT

Experimental data in the last decade on the synthesis of fluoroorganic compounds by the reaction of internal perfluoroolefins with nucleophilic reagents and a direct fluorination with elementary fluorine or electrochemical fluorination of the most important classes of organic compounds have been generalized and synthesized. This overview covers the principles governing the orientation and reactivity of fluorinated alkenes towards nucleophiles, fluoride ion as a nucleophile and reactions with nitrogen-, oxygen- and sulfur-centred nucleophiles. It has been demonstrated that the reaction of internal perfluoroolefins with N-nucleophilic reagents issues in the production of terminal perfluoroolefins whose interaction leads to the formation of enamines. Factors which affect the stability and reactivity of these compounds are discussed as examples of their application for the preparation of partially fluorinated organic compounds containing N-, O-, P- and S-atoms. This treatment summarized new experimental data, as well as their theoretical description, on the use of C-nucleophiles and C-carbcations from internal perfluoroolefins in the synthesis of fluoroorganic compounds. Examples of application of the perfluorinated carbocations to the synthesis of perfluorinated olefins, cyclic systems and oxygen-containing heterocyclic compounds are considered. The mechanisms of these transformations are discussed. A new approach to the generation of the stable perfluorinated alkylradicals from internal perfluoroolefins is discussed and experimental data are given on its reaction with the varies substances. The overview discusses the modern methods for the fluorination of elementary fluorine internal perfluoroolefins and their derivatives. The problems related to the production of high quality perfluorinated organic materials are analyzed. We have also set out the trends in the development of methods and technology for obtaining fluoroorganic compounds. Instances of the practical application of various perfluorinated substances in industry and medicine are given, rational techniques for producing them are suggested and trends in the development of this technology are considered.

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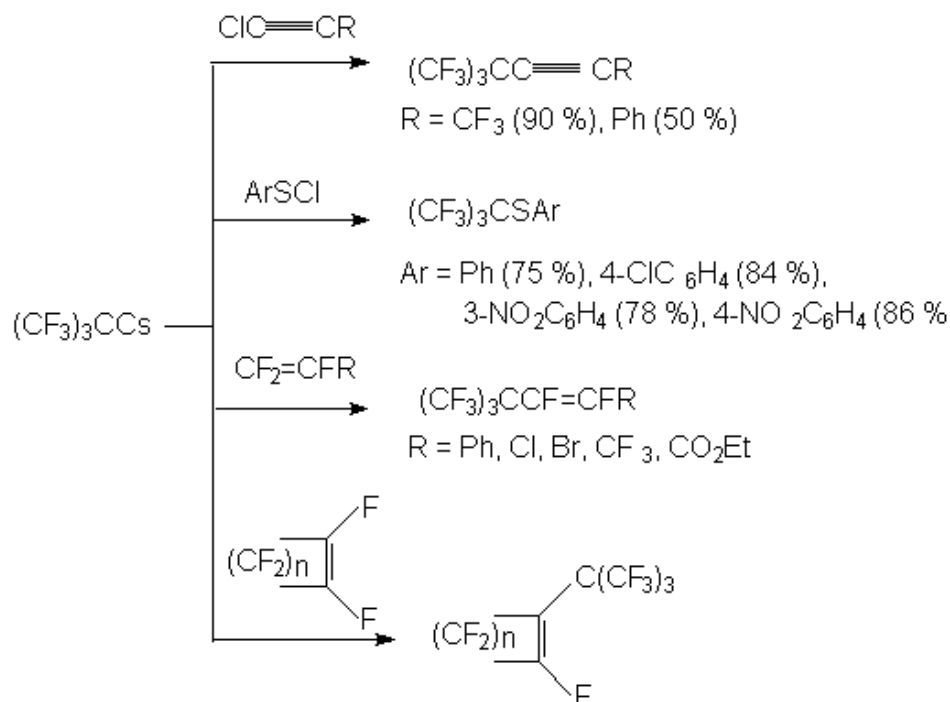
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2.4. Fluoride ion as a catalyst in generating C-nucleophile from perfluoroolefins and its interaction with electrophiles.

The significant part of internal perfluoroolefins reactions are the processes with intermediate generation of a C - carbanion. There are different ways of such carbanions generation. First way is based on the reaction between internal perfluoroolefins and fluoride-ion. The structure of carbanion after interaction can be both changed and unchanged. The key step is the opportunity of isomerization to more thermodynamically stable olefin. Second way is based on a generation of C - carbanion during decomposition of intermediate compound which receive in the reaction of some nucleophiles (phosphines, for example) with internal perfluoroolefins.

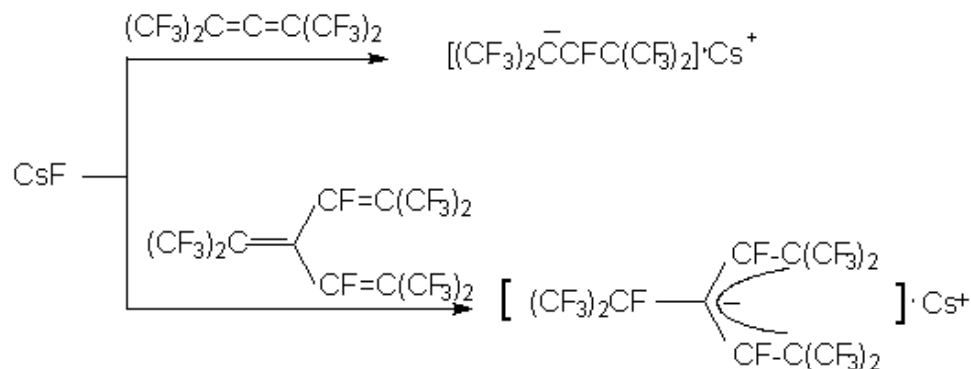
The formation of carbanions in the reaction of fluoride ion with fluorinated alkenes [127] is a very simple way to the introduction of perfluorinated groups into organic molecules and especially into aromatic systems [128-130].

It is known that the fluoride-ion in aprotic bipolar solvents has high nucleophilicity and therefore it is capable to attack the double bond of internal perfluoroolefin with formation of primary C-carbanion [124,131]. Perfluoroisobutylene reacts with CsF and $(\text{CF}_3)_3\text{CCs}$ is formed [132]. Perfluoro-2-methylpent-2-ene reacts with CsF in diglyme and $(\text{CF}_3)_2(\text{C}_3\text{F}_7)\text{CCs}$ is formed [133]. 1-Chloroacetylenes containing a strong electron-acceptor substituent react with $(\text{CF}_3)_3\text{CCs}$ and the formation of acetylenes derivatives take place [132]. $(\text{CF}_3)_3\text{CCs}$ reacts with arylsulfenylchlorides in acetonitrile with perfluoroalkylarylsulfide formation [134]. The reaction with fluoroolefins gave 50-84 % of $(\text{CF}_3)_3\text{CCF}=\text{CFR}$. Analogous reaction with perfluorocyclobutene and -cyclopentene gave 75-89 % of cycloalkene derivatives [135].

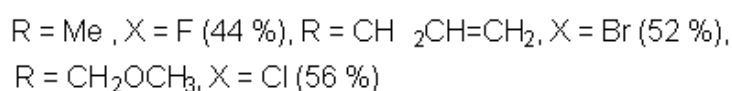


The various forms of alkaline metals fluorides [136], including their complexes with crown-ethers [137,138], $(\text{Me}_2\text{N})_3\text{S}^+ \cdot \text{Me}_3\text{SiF}_2^-$ ("TASF") [139,140] (Table 2), salt of a perfluorocyclobutene with a triethylamine [143,144] and others are used as sources of a fluoride-ion.

Perfluoroallen and perfluorinated α -bis(isobutenyl)-isobutylene react with CsF in absolute diglyme and salts is formed [145]. These salts are thermally very stable.



The salt $[(\text{CF}_3)_2\text{CCFC}(\text{CF}_3)_2]^- \cdot \text{Cs}^+$ reacts with compounds having mobile halogen atom at elevated temperature [145]:



The nature of a source of ion and nature of a solvent are extremely important for stability of these C-anions and cesium and the "TAS" cation (i.e. $\{\text{Me}_2\text{N}\}_3\text{S}^+$) are the most effective. The "TAS" cation has especial value, because the starting material $\text{TAS}^+ \cdot \text{Me}_2\text{SiF}_2^-$ is soluble in various organic solvents. Examples of stable anions are shown in Table 2.

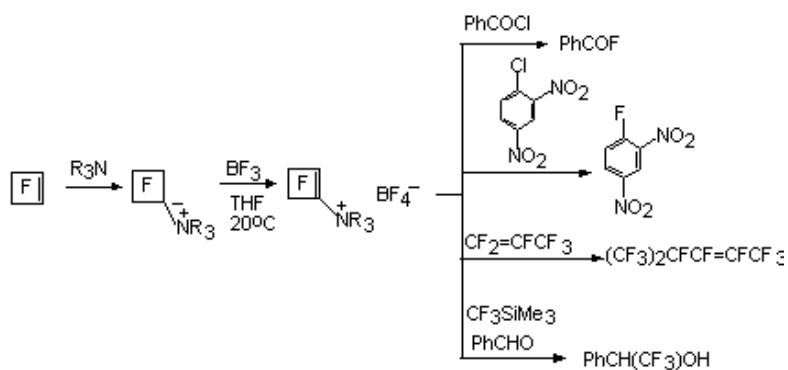
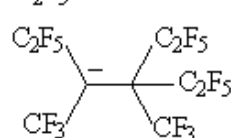
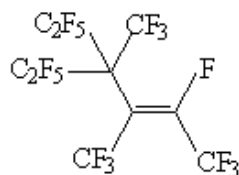
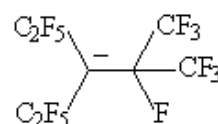
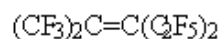
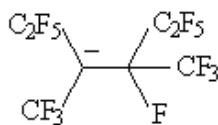
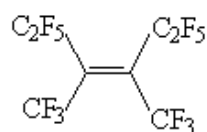
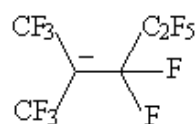
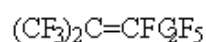
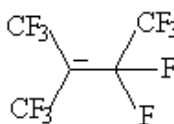
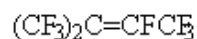
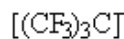
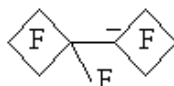
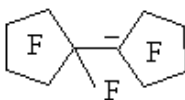
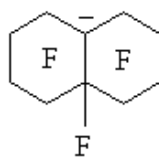
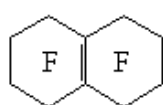


Table 2. Salts obtained as the result of the reaction $(\text{Me}_2\text{N})_3\text{S}^+ \text{Me}_3\text{SiF}_2^-$ or CsF with perfluoroolefins [141,142].

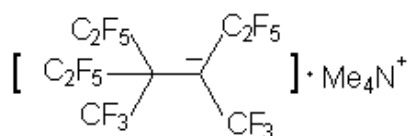
Olefins

Salt*

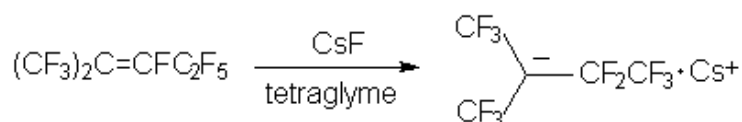


* Cation $(\text{Me}_2\text{N})_3\text{S}^+$ or Cs^+

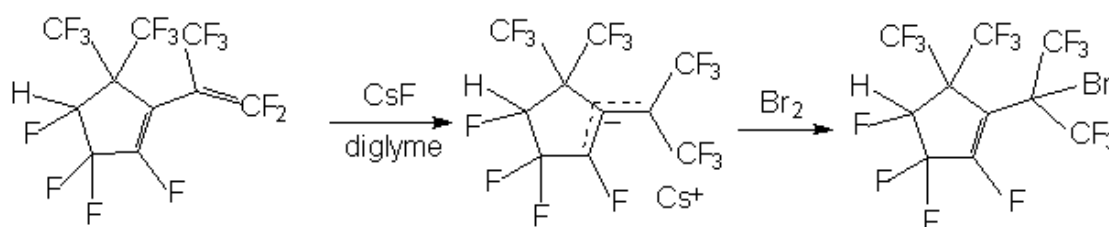
Perfluoro-4-ethyl-3,4-dimethylhexan-3-yl tetramethylammonium carbanion was prepared as a stable salt from the pentamer tetrafluoroethylene and Me_4NF in acetonitrile. The reaction is fast and quantitative [146].



Reaction of perfluoro-2-methylbut-2-ene with cesium fluoride in tetraglyme gave the stable carbanion [29]. This ion is analogous to the polyfluoro-t-butyl anion that was described previously in [122,129].



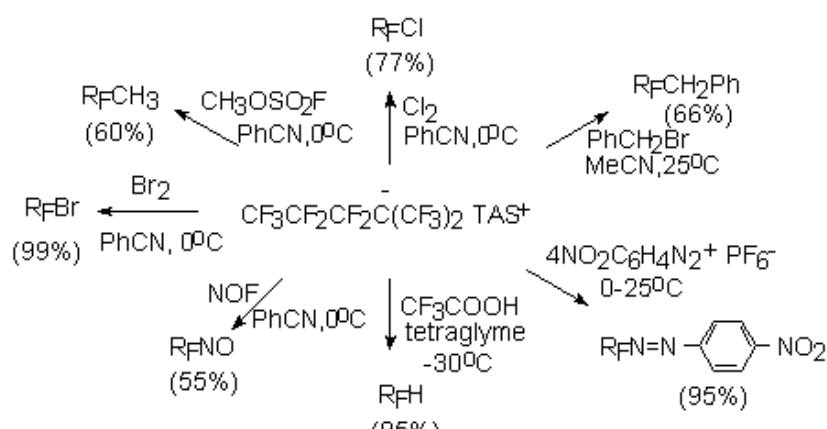
Reaction of 1(pentafluoropropyl-2-enyl)-3H-decafluoro-2,2-dimethylcyclopentene with cesium fluoride gave a stable allyl anion [29]. This is the first example of observable fluorinated carbanion where a fluorine atom is formally directly attached to a charged site, although more charge probably resides on the $(\text{CF}_3)_2\text{C}^-$ site. Thus, when these ion was treat by bromine, 1-(2-bromohexafluoro-2-propyl)-3-hydrofluoro-2,2-dimethyl-cyclopentene was formed, i.e. bromine attack of $(\text{CF}_3)_2\text{C}^-$ site took place.



¹³C and ¹⁹F NMR spectra were measure in solution down to -95 °C. These results with combination of semi-empirical quantum chemical calculations show that the decision could be made between the occurrence of a planar sp² or a tetrahedral inverting carbon at the carbanion site. It is seems from DNMR-data a planar existing rather than a tetrahedral carbanion, where the lone pair is not stereo active.

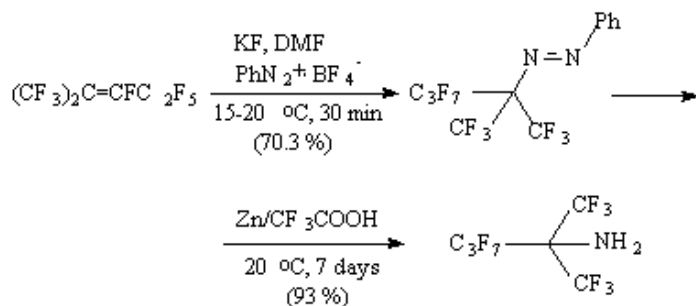
Perfluoroalkyl groups stabilize this carbanion and the following reactions are possible: 1) isomerization of double bond; 2) reaction with electrophile; 3) reaction with initial when a high nucleophilic mobil fluorine atom at double bond take place.

It should be note, that it is not necessary to generate steady tertiary perfluoro-carbanion during the reaction of perfluoroolefine with a fluoride of metal. Reaction generates enough intermediate C-carbanion in situ. Tertiary fluorinated carbanions, generated from corresponding unsaturated precursors, react with variety electrophiles. The examples of reactions of C-carbanion generated from perfluoro-2-methylpent-2-ene are given in Scheme [124,141,147,148].

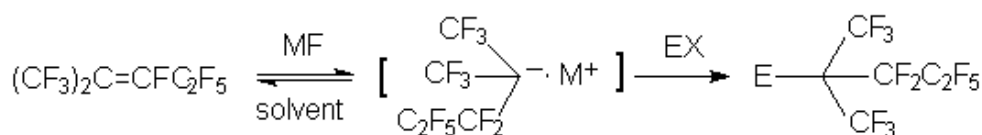


Recent methodology [149] has revealed, that solvent employment may be avoided, when use the organic base, such as trimethylamine. Such compounds are uses in situ as very active fluoride-ion sources. This methodology simplifies the procedure of product isolation.

This C - carbanion reacts with diazonium salt of aniline, giving diazonium compounds, which are used for producing of a primary amine with spatially complicated perfluoroalkyl substituent [119].



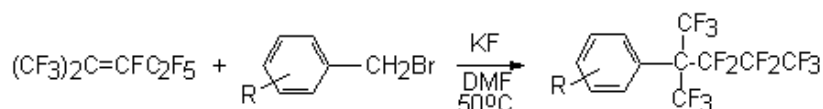
It is reported that perfluoro-2-methylpent-2-ene react with fluoride ion with perfluoro-t-carbanion formation. Under appropriate conditions, this carbanion reacts with specific electrophile with addition products formation. The probable reaction pathway is shown in Scheme.



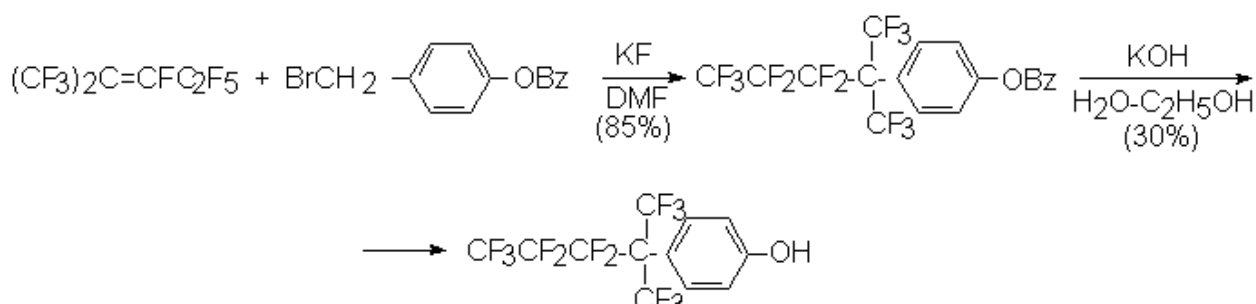
RX = PhCH₂Br [149,150]

RX [146], R = Me, Et, Pr, Bu, CH₂CH=CH₂; x = Cl, Br

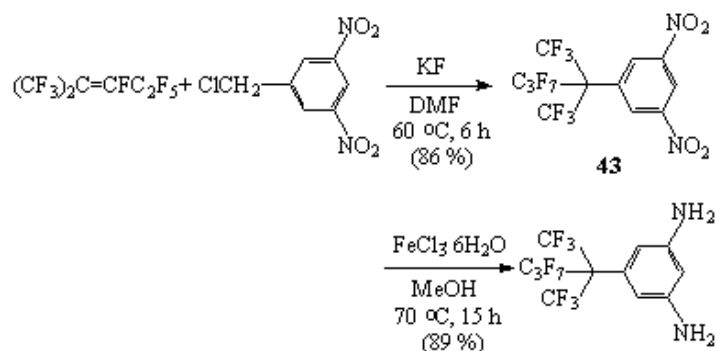
These carbanions are the active nucleophiles and also very active alkylation reagents. So, various benzylbromides (RC₆H₄CH₂Br (R = H, p-, m-, o-CN, p-, m-, o-NO₂, p-, m-CH₂Br)) easily react with perfluoro-2-methylpent-2-ene in bipolar aprotic solvents at KF presence or with iodides of alkaline metals. The yield of products of bromine replacement is more than 70 %. This method is used for production industrial oil for hydraulic liquids in electronic branch and for surface-active substances production [150-152].



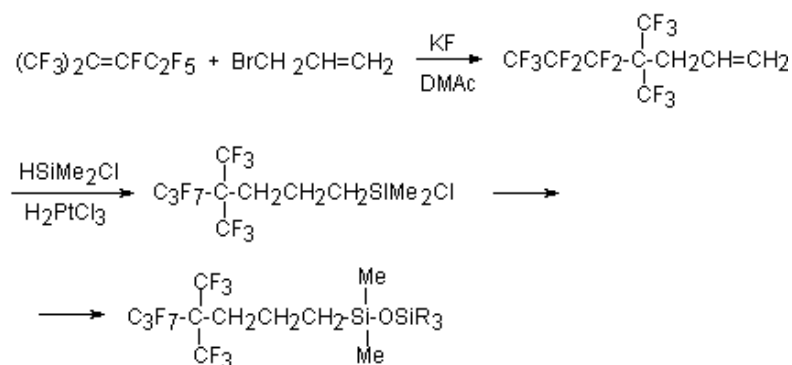
Esters of *para*-(bromomethyl)phenylbenzoate reacts in DMF (50-60 °C; 20 hours, 85 % yield) giving the product of replacement, which further is hydrolyzed by KOH treatment in ethyl alcohol- water mixture to oxy-derivative (**42**) (yield 30 %) [153].



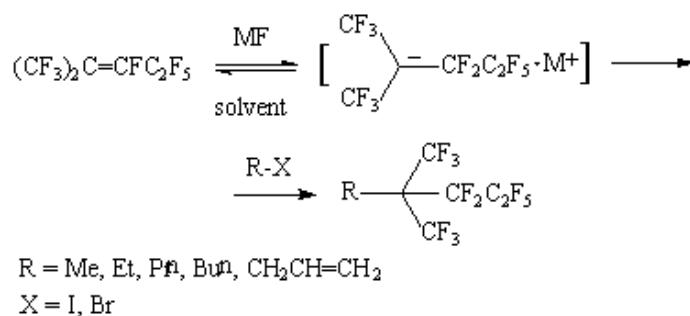
Benzylchlorides react too. So, 3,5-dinitrobenzyl chloride in DMF at 60 °C reacts with a dimer of a hexafluoropropylene, giving a product of replacement of atom of chlorine (**43**) [154]. This compound is used as an intermediate product in synthesis of aromatic diamines.



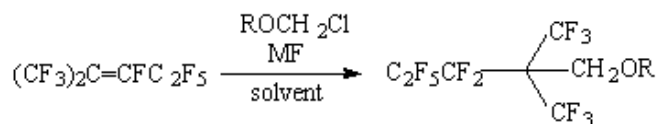
The reaction with benzylbromide results the formation of a product of bromine replacement, which react with dimethylchlorosilane with adducts formation. It contains active bond Si-Cl. Such compounds (for example, 1,1-H-, 2,2-H-) are used for creation of chromatography phases for 3,3-H- tridecafluoro (4,4-dimethylheptyl) silicon (Fluotix 120 N (A)) [155].



Halogen alkyl also is effective in the given processes, that allow to produce the partially fluorinated paraffins for various purpose [147].

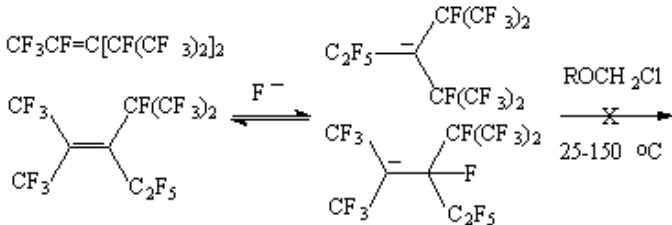


Chloromethyl ethers react with dimers of a hexafluoropropylene with partially fluorinated ethers formation [142].

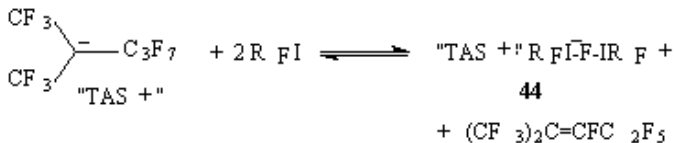


R = C₈H₁₇ (90%), Ph (81%), PhCH₂ (82%), CH₂CH=CH₂ (50%), CH₂=CH(CH₂)₈ (86%), CH₂=CHCH₂OCH₂CH₂(85%)

At the same time, the reaction with trimer of a hexafluoropropylene is not observed even when temperature was increased up to 150 °C. It shows that the essential influence of shield of anionic center by the spatial substituents take place.



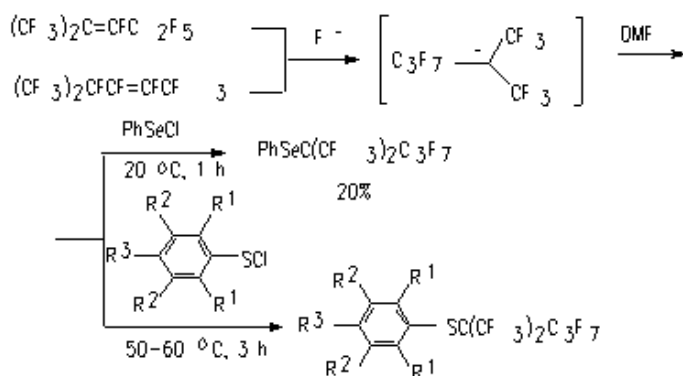
At the same time the reactions of C-carbanion with perfluoroalkyl iodides yield the fluoride-bridged products **44** [156].


$$R_F = C_6F_5I \text{ (86\%)}, I(CF_2)_4I \text{ (86\%)}, C_6F_{13}I \text{ (76\%)}, I(CF_2)_2I, I(CF_2)_8I, I(CF_2)_{10}I$$

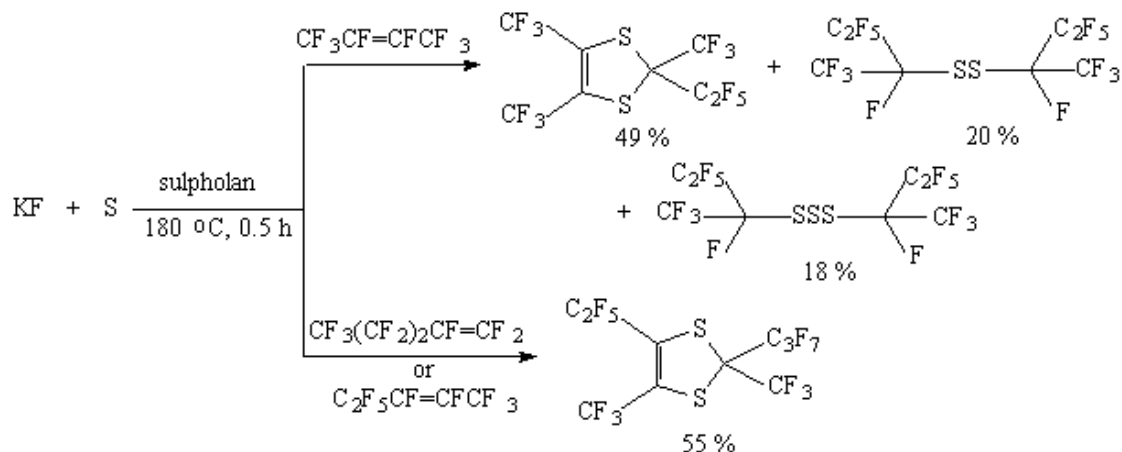
The high mobility of chlorine in arylsulphenylchloride and arylselenenylchloride allows to develop the method of producing of partially fluorinated arylperfluoroalkyl-sulphides and - selenides [157,158], which can be employed as fungicides and insecticides. When dimers of perfluoropropylene is stirred with KF in DMF at 50-60 °C the perfluoro(1,1-dimethylbutanide) anion is generated. It smoothly reacts with arenesulfenyl chloride and the corresponding arylperfluoro(1,1-dimethylbutyl)sulfines with 58-86 % yields are produced [157].

It is known that perfluoro-4-methylpent-2-ene undergo isomerization into thermodynamically more stable perfluoro-2-methylpent-2-ene in the presence of fluoride ion [159].

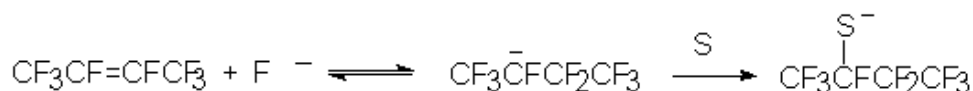
This method can be more effective as alternative method of reception of important intermediate products.

[illegible]

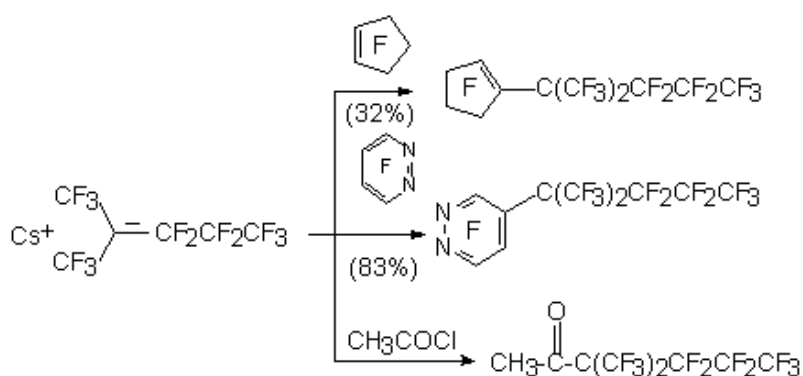
H H Me 60
 Me H Me 86
 Me Me H 80
 Me Me Me 59
 H H Cl 58



The formation of products of reaction is possible to explain by an intermediate generation of a S-anion and further transformation of this S-anion.

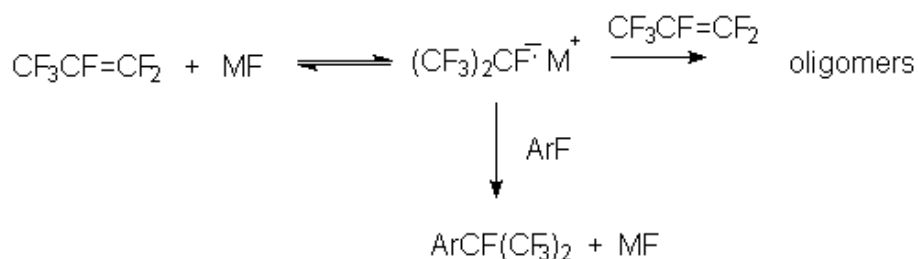


Cesium salt perfluoro-2-methylpent-2-ene in bipolar aprotic solvents reacts with a perfluoro-cyclopentene, tetrafluoropyridazine and fluorine atom replacing at double bond takes place. With acetylchloride the products of replacement of halogen are observed [124]:

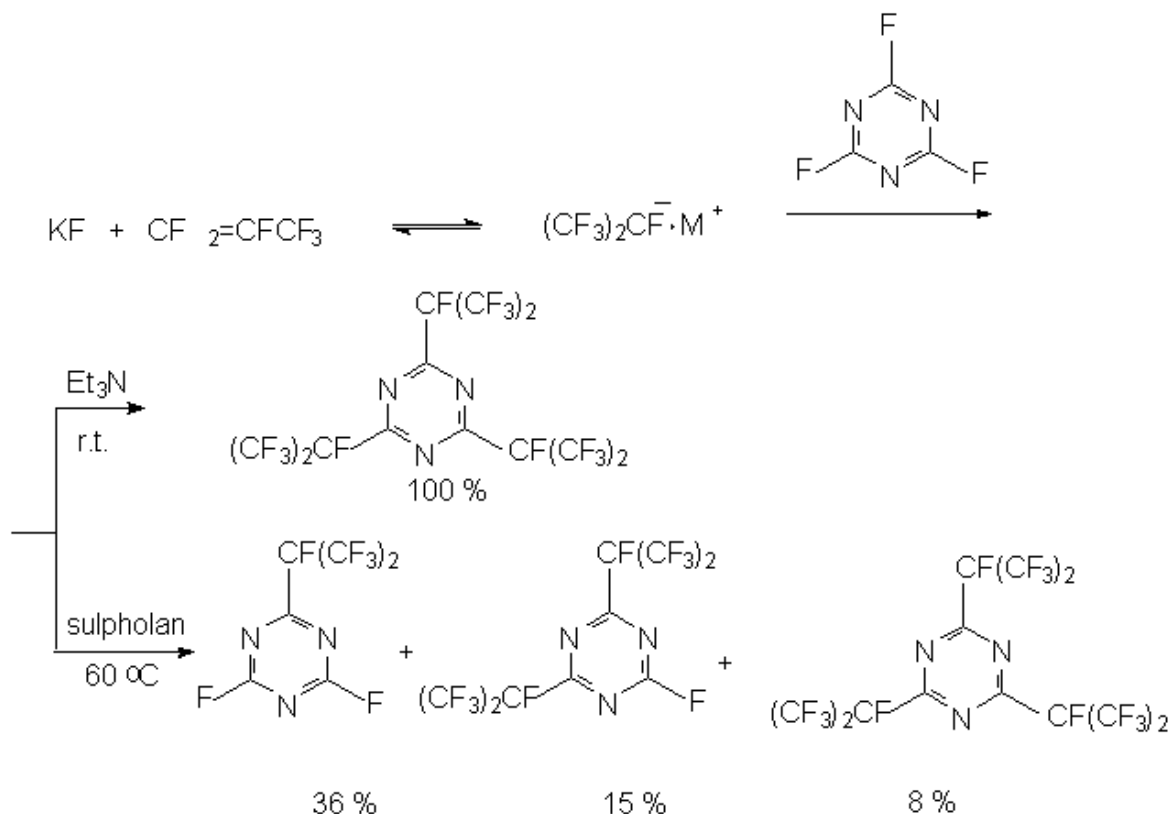


The reactions of carbanions with activated perfluoroaromatic systems were limited in scale because the difficulties of isolation of product from the high-dipolar aprotic solvents took place. Previously was believed that they were the essential component for these processes. The authors of [161] described a simple isolation technique when perfluorinated solvents were used. They also very effective in mixtures with aprotic solvents.

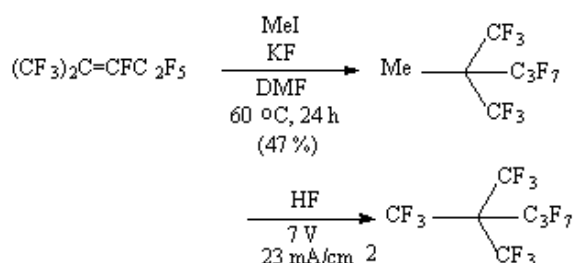
The aromatic compound are more active and there is the high probability that the perfluoroalkylation processes will be successful in comparison with oligomerization of fluorinated alkenes [149].



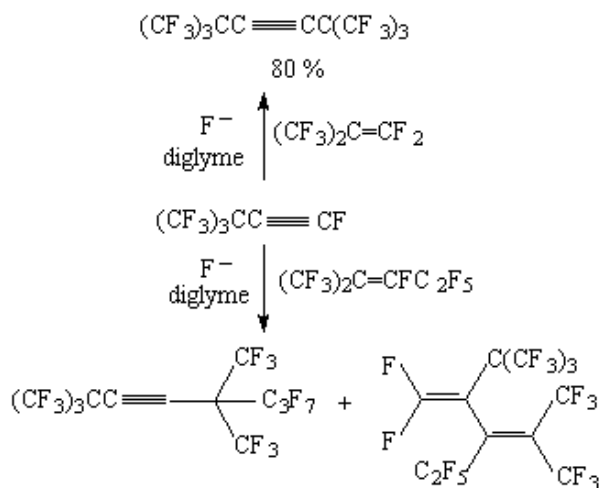
Polyfluoroalkylation of trifluoro-s-triazine is took place with hexafluoropropene and potassium fluoride in sulpholan [162] or triethylamine at the absence of a solvent [161,162].



In work [163] the way of producing of the ramified fluorocompounds based on the reaction of potassium salt of perfluoro-2-methylpent-2-ene with methyl iodide and allyl bromide is described. The subsequent of electrochemical fluorination gives the ramified completely fluorinated paraffin.

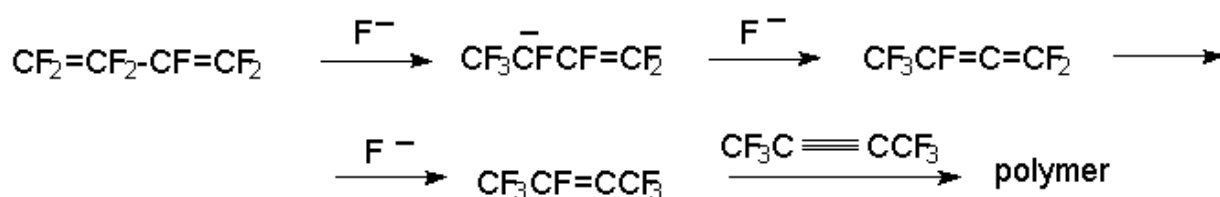
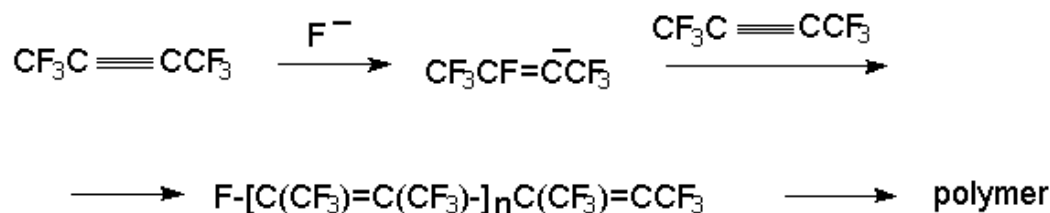


The carbanions generated by action of a fluorine-ion on perfluoroisobutylene or perfluoro-2-methylpent-2-ene react with perfluoroalkyl-derivatives of acetylene, giving a product of replacement of fluorine [164,165].

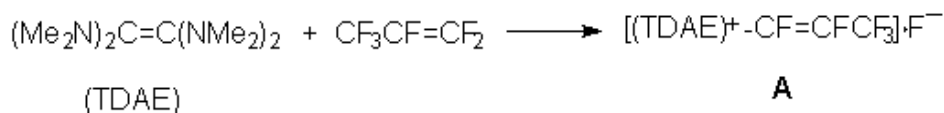


When using perfluoro-2-methylpent-2-ene the reaction pathway has two directions: the replacement atom of fluorine in ethyl by a tertiary anion and replacement vinylic atom of fluorine by anion $[(\text{CF}_3)_3\text{C}-\text{C}=\text{CF}_2]^-$.

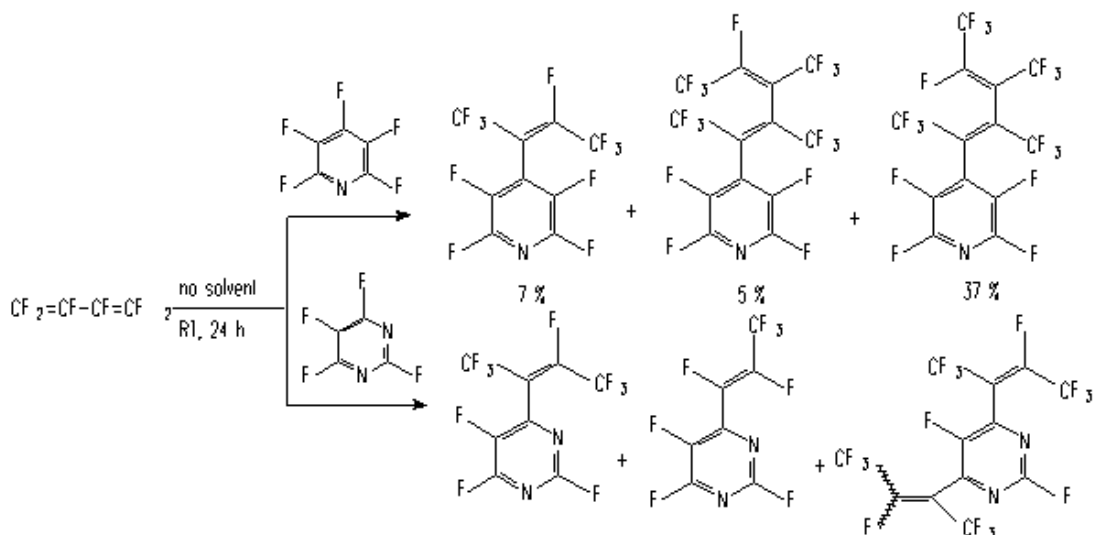
Fluoride ion reacts with hexafluorobut-2-yl and polymers are produced [166-168]. But the reaction of hexafluoro-1,3-butadiene with fluoride ion also gives a polymer [169]. It was proposed that this polymer is formed via an identical rearrangement with following polymerization.



These C-anions can be trapped by some electrophiles including perfluorinated heterocycles [167,170]. Authors used caesium or potassium fluoride in aprotic solvent, e.g., sulfolan, to generate the ions. In [170] was mentioned about using of tetrakis(dimethylamino)ethane (TDAE) for the "in-situ" generation of active fluoride (e.g., possible **A**) This method has practical advantage because reactions can be conducted in the absence of solvent.

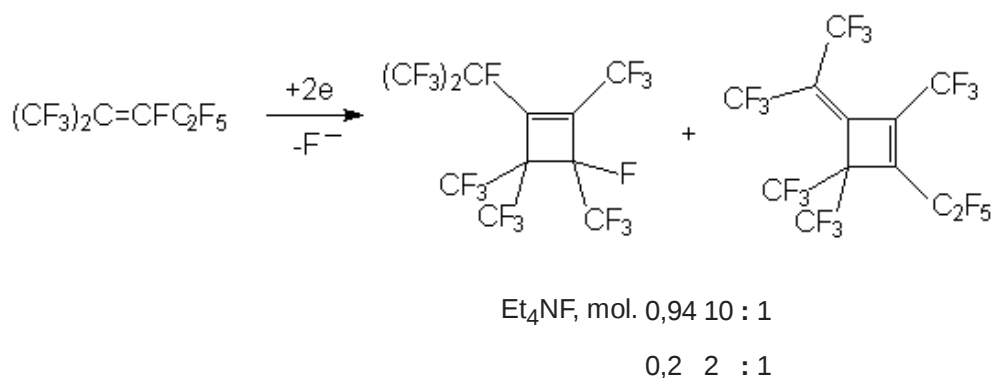


Experiments with electrophiles (pentafluoropyridine and tetrafluoropyrimidine) and TDAE as fluoride ion source were conducted. The products of reactions are shown in Scheme:

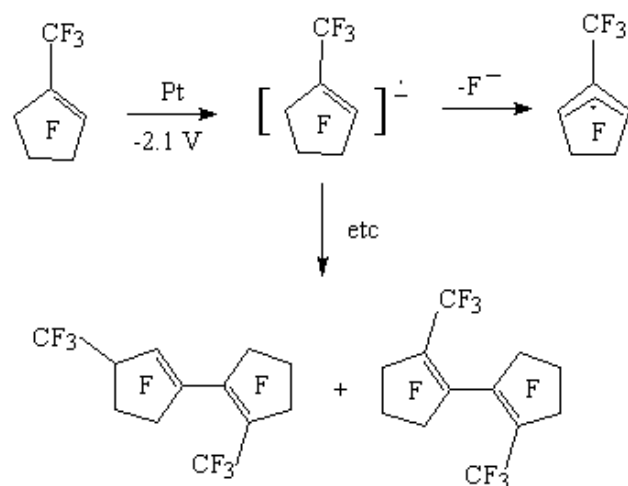


Anionic dimerization of internal perfluoroolefins under action of various sources of a fluoride-ion is widely used not only in organic synthesis, but also for a number industrial manufactures of fluoroorganic compounds. So, the dimerization of perfluoropropylene is employed in industry for producing the dimers and trimers of hexafluoropropylene [122,171,172].

It is necessary to note, that the generation of a carbanion can be also proceed during electrolysis processes (platinum electrode at presence electrolyte $\text{MeCN} \cdot \text{Et}_4\text{NF} \cdot 2\text{H}_2\text{O}$). The electrochemical reduction of some internal perfluoroolefins is accompanied by the processes of a dimerization, cyclization and defluorination of initial internal perfluoroolefins. So, the electrolysis of hexafluoropropylene dimers gives 60 % of replaced perfluorocyclobutenes [156]. The yield of dimers reduced to 30 %, when transition materials of cathode (plumbum, zinc, titane, coper amalgame) were used.



Another example is the cathode reductive dimerisation of trifluoromethyl derivative of perfluorocyclopentene [173].



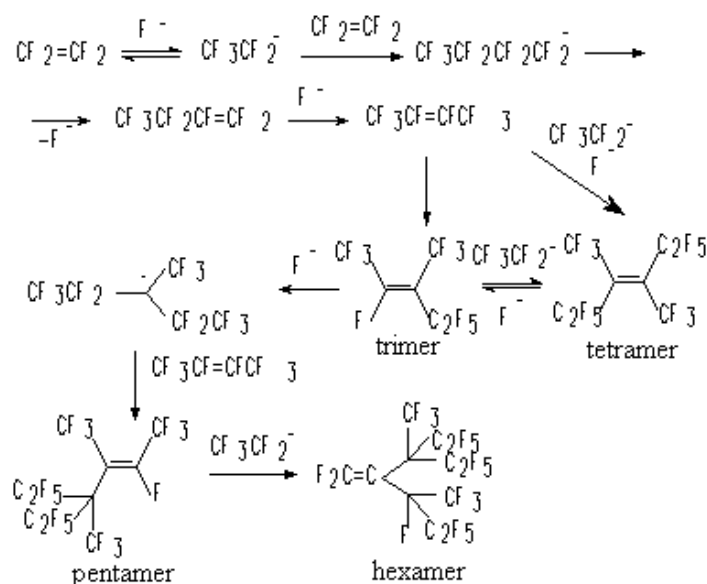
Obviously, the cathode dimerization is carried out by the radical mechanism with anion-radicals or allylic radicals recombinations, which formed after elimination of fluorine anion. However, some rules of reaction and the structure of products of reaction show that the ionic mechanism of a dimerization takes place. Apparently, the initial step of reaction is the transfer of two electrons to initial perfluoroolefin, which accompany by elimination of fluorine anion with formation of allylic anion (**45**). Further, the typical for internal perfluoroolefins reaction of cycloaddition take place: anion (**45**) is attacked by initial perfluoroolefin with replacement vinylic atom of fluorine. The dimeric product is formed as result of reaction. After that there two ways of reaction:

1) isomerization under influence of fluorine anion, resulting a perfluoro-1,3,3-trimethyl-4-ethyl-2-isopropylcyclobutene-1

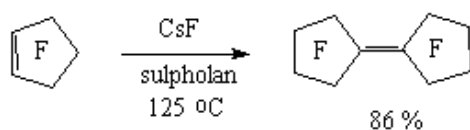
2) Further cathode reduction with formation of perfluoro-1,3,3-trimethyl-2-ethyl-4-isopropylidenecyclobutene-1.

The increasing of fluorine anion concentration in electrolyte results the reaction of dimer isomerization as main direction.

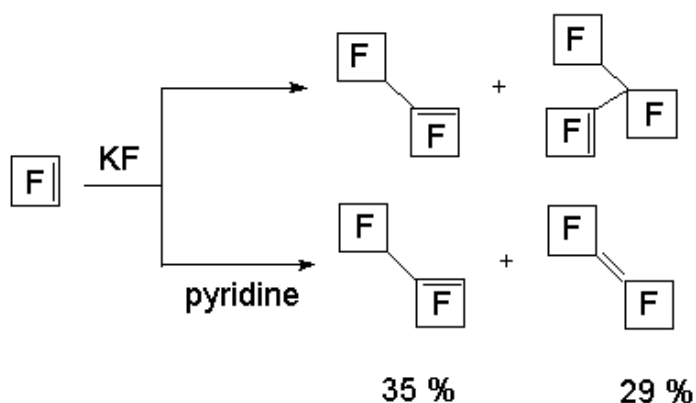
Oligomerization of internal perfluoroolefins and perfluorocycloolefins under influence of fluorine-ion is well known process [174,175]. So, oligomerization of tetrafluoroethylene gives a complex mixture of products (See Scheme) .



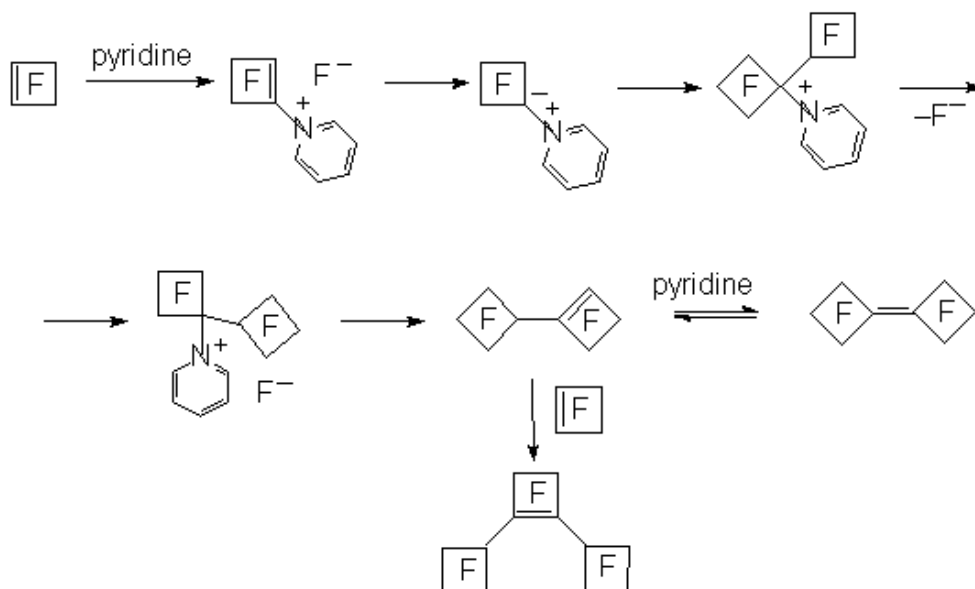
Oligomerization of perfluorocycloalkenes proceeds similarly. As a rule, a mixture of dimers is formed and the reactions are more sensitive to conditions of their realization. So, perfluorobicyclophenylene is formed from perfluorocyclopentene and CsF in sulpholane at 125 °C [176].



The yield of dimer in the reaction of perfluorocyclobutene with KF raise when use pyridine as a solvent [176-179].

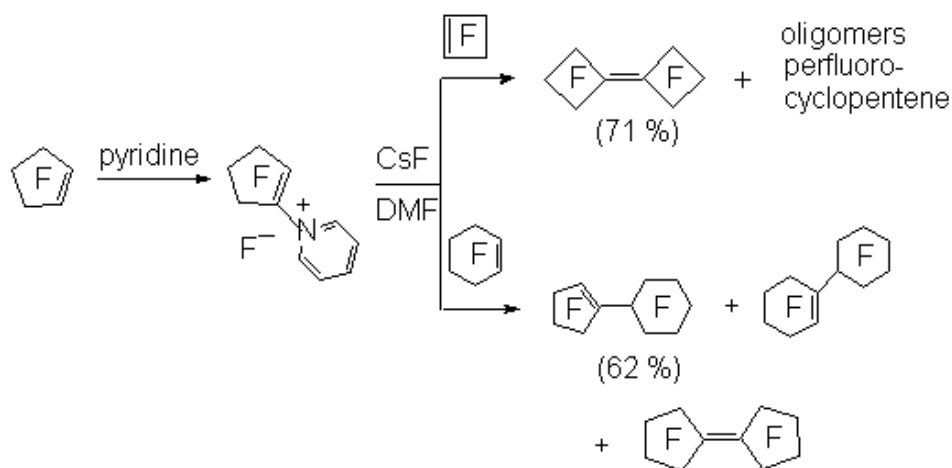


The first step of perfluorocyclobutene reaction in pyridine is the formation of the salt, which contains active cyclobutylylic anion [178,180]. At perfluorocyclobutene excess (or addition to reaction mixture another internal perfluoroolefin) the reaction of replacement of fluorine atom at double bond take place.

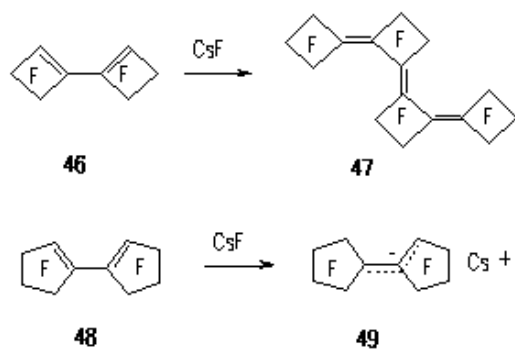


The ratio between mono- and di-replaced products depends on the amount of a pyridine. So, if mole ratio initial olefin: pyridine was 15:1 the yield of the mono replaced products was 64 %, whereas at ratio 9:1 -only 21 %.

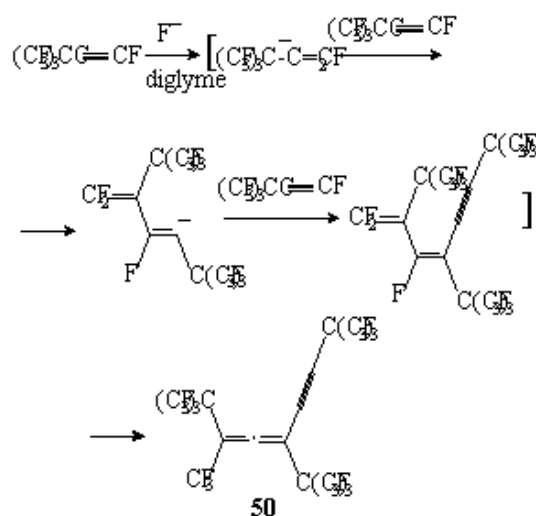
Others perfluorocycloolefins react similarly too [181,182].



These processes are the base of a synthesis of a number new dienes from perfluorocyclobutene and -pentene [182]. However, oligomerization was not always observed when CsF was used. So, if diene **(46)** transformed to **(47)** [183,184], the diene **(48)** under influence of CsF gave only corresponding salt **(49)** [185].



In the reaction between fluorine-ion and perfluoro-*tert*-butylacetylene the formation of trimer **50** was observed [165].



Highly fluorinated alkenes are generally very electron-deficient species and therefore susceptible to attack a wide range of nucleophiles.

to be continued