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INTERNAL PERFLUOROOLEFINS IN A SYNTHESIS OF FLUOROORGANIC COMPOUNDS

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ABSTRACT

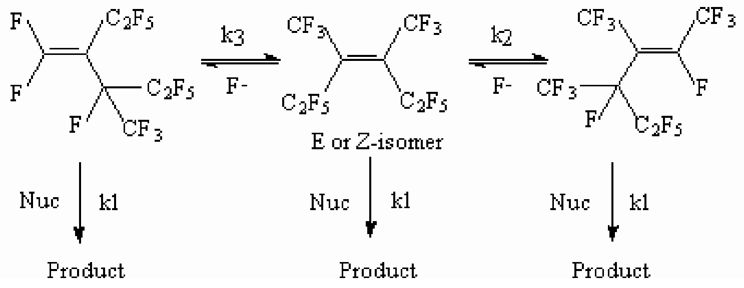
Experimental data in the last decade on the synthesis of fluoroorganic compounds by the reaction of internal perfluoroolefins with nucleophilic reagents and a direct fluorination with elementary fluorine or electrochemical fluorination of the most important classes of organic compounds have been generalized 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 carbcations 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.

CONTENTS

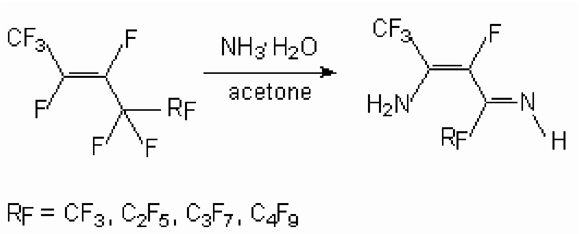
2.3.The specific interaction of N-nucleophilic reagents with the internal perfluoroolefins containing fluorine atoms at carbon-carbon double bond.

In the chemistry of fluoroorganic compounds, a special role is played by reactions of perfluoroolefins with nitrogen-containing mono- and di-nucleophilic reagents [83], allowing to obtain various intermediate product for a synthesis of materials of various purposes, including numerous classes of heterocyclic compounds.

For terminal perfluoroolefins the nucleophilic reagent unequivocally attacks atom of carbon at terminal double bond C=C with formation of perfluoroolefins, which contain entered functional group at double bond. At the same time for internal perfluoroolefins these reactions go ambiguously. Enamines and imines of the corresponding ketones are not obtained during interaction of primary amines with internal perfluoroolefins, containing a fluorine atom at double bond It is caused by a tautomerizing proceeding in systems, containing double bond C=C and substituent with NH-group, which to a great extent depends on the structure and character of the perfluorinated substituents at double bond and thermodynamic factor. Besides, it is necessary to take into account the fact that the isomerization of internal perfluoroolefins under the influence of a fluoride- ion of another structure in many cases generates perfluoroolefins containing mobile fluorine atom at double bond. In these processes the alkylamine shows properties of the active catalyst for isomerization of internal perfluoroolefins to terminal ones. Here, the main role is played by a ratio of speeds of the reactions between these isomers and nucleophilic by-reagent. We would like to demonstrate it by the example of reactions between the isomeric tetramer tetrafluoroethylene and methylic alcohol [84]. The constants of speeds of these reactions make a following number $k_3 > > k_2 > > k_1$ [85].

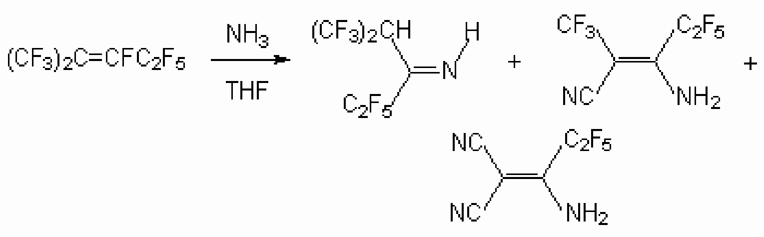


The reactions of internal perfluoroolefins with aqueous ammonia usually include vinylic replacement, enamine - imine isomerization and dehydrofluorination. It was shown that the imine-enamines (or products of their further transformations) give exclusive β-diimines with high yields in all cases [86].

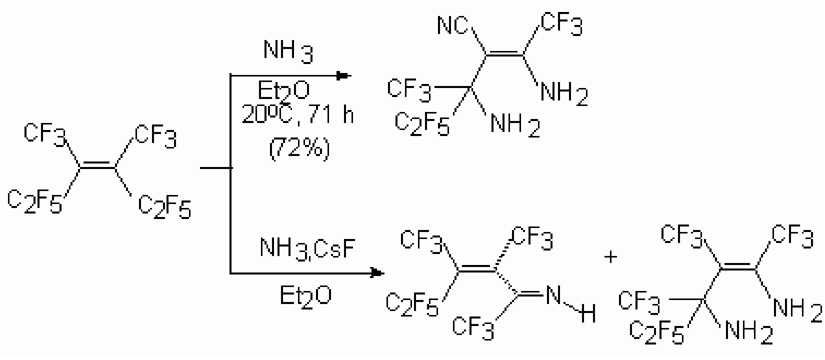


For example, the interaction of ammonia and tert-perfluoropent-2-ene results the nitrogen analogue β-diketone [83], and reaction with perfluorobut-2-ene yields 3-amino-2,4,4,4-tetrafluoro-2-butenenitrile [87]. The same transformations are also characteristic for nucleophilic reagents having NH_2 group and they widely involved in obtaining the results at a synthesis of heterocyclic compounds with the use of internal perfluoroolefins. We would like to specify some of them: reaction perfluoropent-2-ene and ethylenediamine described by Saloutin with co-workers [88,89], reaction perfluoro-2-methylpent-2-ene with amides of benzoic acid [89] and hydrazone [90] (Ikeda and others), reaction acetamide with perfluoro-2-methyl-pent-2-ene described German with co-workers [91].

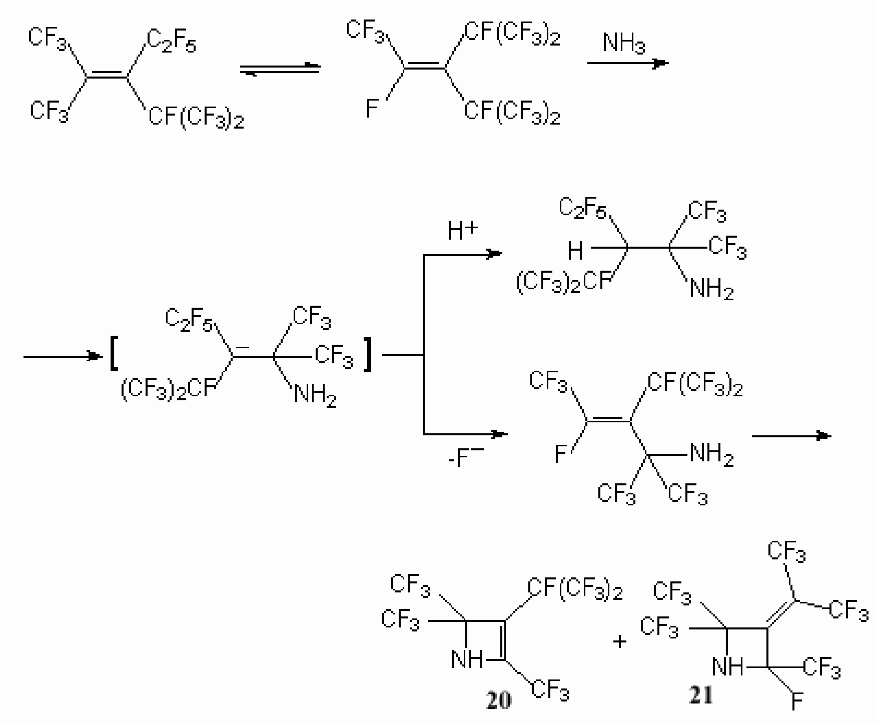
It was shown by authors of [80,92], that the reaction perfluoro-2-methylpent-2-ene with waterless ammonia in a tetrahydrofuran produced the mixture of products, in which there are two compounds with internal double bond containing CN-group alongside with a product of replacement of fluorine atom at double bond (ketenimine). Probably, it can be explained by comparable speeds of two reactions: replacing of fluorine vinylic atom and subsequent dehydrofluorination, resulting polyamination products.



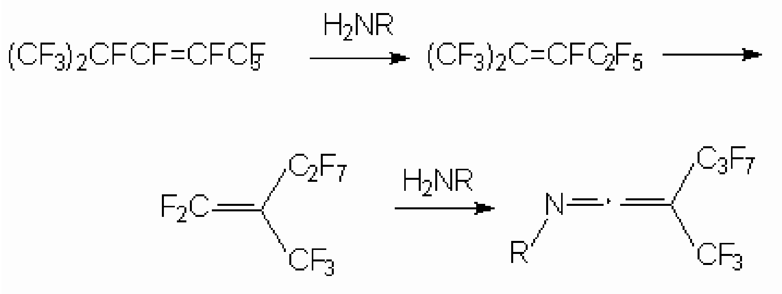
At the reaction of perfluoro-3,4-dimethylhex-3-ene with an ammonia water the products containing NH_2 and CN groups at internal double bond was obtained whereas during reaction with a waterless ammonia the complex mixture of fluorine atom replacement on NH_2 group products is formed [84].



At the reaction of hexafluoropropylene trimer (perfluoro-2-methyl-3-isopropyl-2-pentene) with ammonia the mixture of products 2-aminoperfluoro-2-methyl-3-isopropyl-3-hydropentane and 4-aminoperfluoro-4-methyl-3-isopropylpent-2-ene is formed, whose the heating results two azetines (20) and (21) [93]. The treatment of the mixture of these compounds with triethylamine excess (20 °C, 1 month) gave two

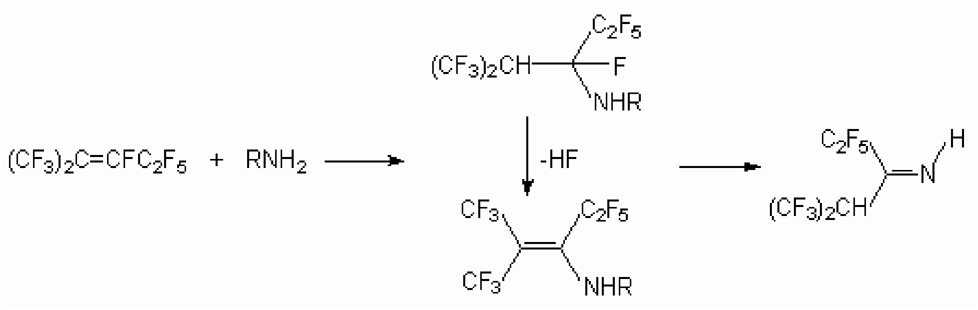


A similar situation happens under the influence of ammonia water on perfluoro-2-ethyl-2-methyl-pent-2-ene [84]. Previously it was shown that when perfluoro-4-methylpentene-2 reacted with nucleophilic reagents (with amines, for example) [94] the isomerization into perfluoro-2-methyl-2-pentene or perfluoro-2-methyl-1-pentene was observed. This is the result of amines interaction with these olefins and (sometimes) their mixture.



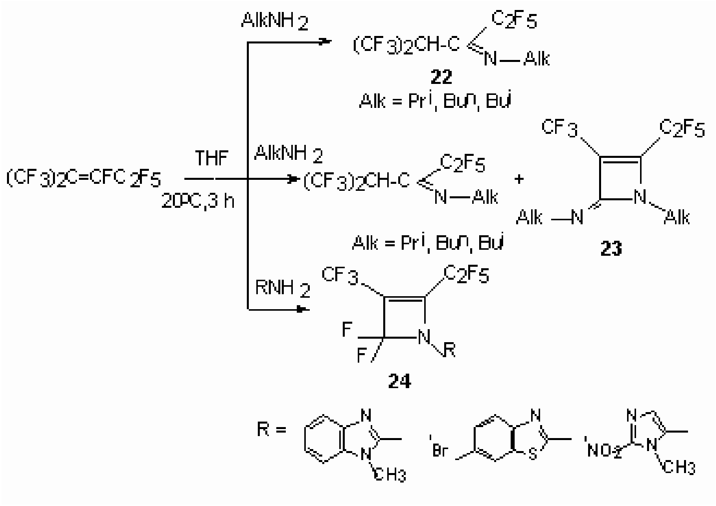
The reaction of perfluoro-2-methylpent-2-ene with primary alkylamines proceeds with formation of 1,4-connection-N-replaced imine products of the corresponding ketone (22). So, the interaction of two equivalents of a propylamine (butylamine, isobutylamine, *tert*-butylamine, ethylamine, cyclohexylamine) with equivalent of perfluoro-2-methylpent-2-ene gives the products of 1,4-connection (ratio sin- and anti-isomers 1:1) [95]. If the triethylamine use as basis alongside with compound (22) the formation of N-alkylamino derivatives perfluoro-2-ethyl-3-methylazete (23) takes place. The yield of last grows from 5 % up to 25 % if instead of perfluoro-2-methyl-pent-2-ene was used the salt of this olefin with a triethylamine (reception of salt is described in [96]).

If to use primary amines with low base, that reduces their catalytic activity in isomerization processes involving internal perfluoroolefins, the main product of reaction being the product of connection on double bond, whose valid enamine-imine rearrangement turns to a imine-enamine [97].

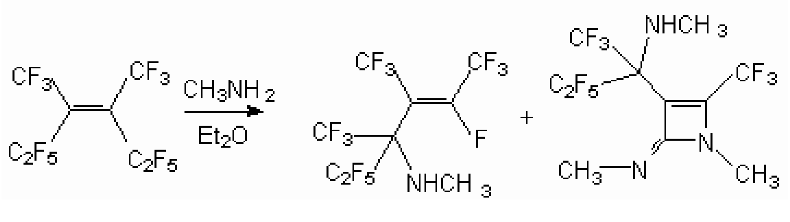


The primary amines with low base reduce catalytic activity in isomerization processes of internal perfluoroolefin to terminal, which results in exclusive attack of an N-nucleophile on the atom of carbon at internal double bond.

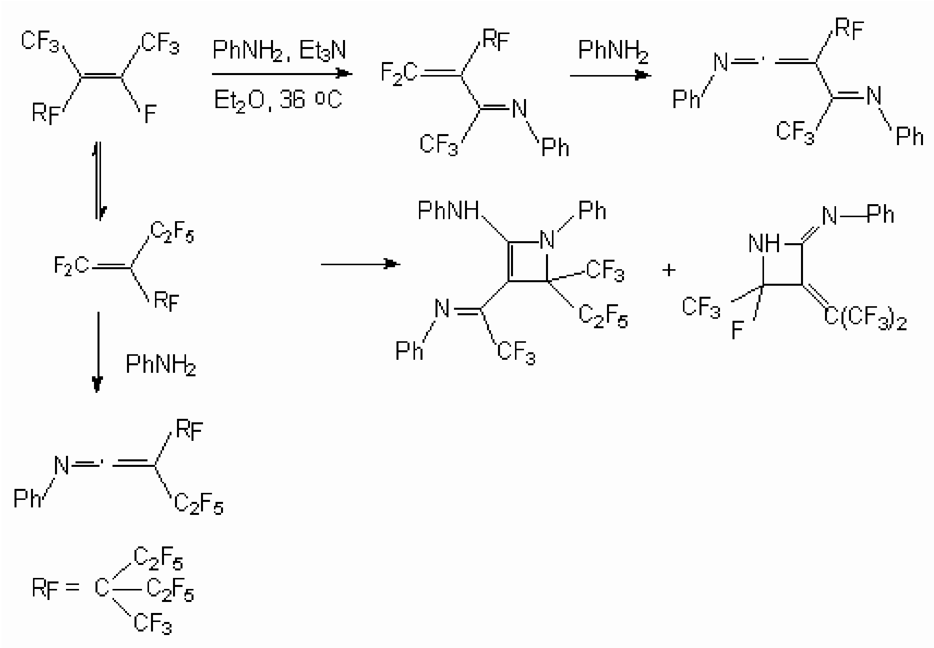
At the same time the reaction of perfluoro-2-methylpent-2-ene with 2-amino derivatives- 1-methylbenzimidazole and 6-bromobenzthiazole give the extreme products of internal double bond adduction (23). The subsequent treatment of these compounds by K_2CO_3 results the formation of the azetine derivative (24). These data specify the essential influence of the nature of the substituent at NH_2 group of amine on the direction of the course of processes involving internal perfluoroolefins.



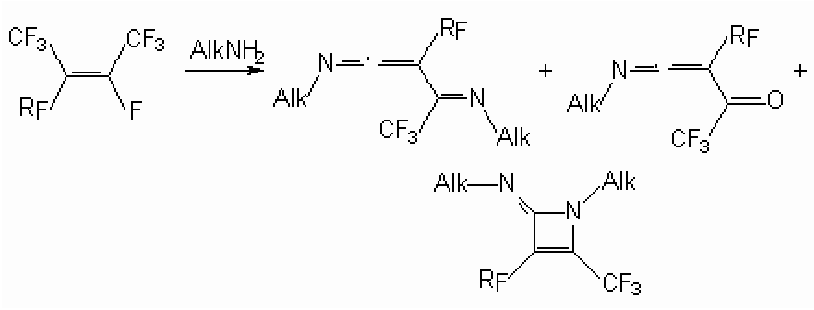
N-Alkylamino derivatives 2-azete also were received by the reactions between alkylamines RNH_2 (R = Me, Et, n-Bu) and perfluoro-2,5-dimethyl-3-ethylpent-2-ene [93] or (R = n-Bu) perfluoro-3,4-di-methylhex-3-ene [98], and hexamethyldisilazane with perfluoro-2-methylpent-2-ene [99].



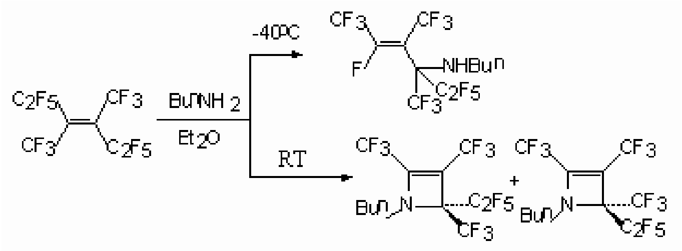
Reactions of condensation of the tetramer and pentamer of tetrafluoroethylene with aniline in 1:1 (or 1:2, 1:3) mol ratio to produce the main disubstituent product (25) and a small quantity of azetidine [100,101].



As a result of the influence on a pentamer tetrafluoroethylene by primary amines, for example, t-butylamine, methylamine, three products was observed: imine ketenimine, carbonylketimine, azetidine [102].



Tetramer tetrafluoroethylene at the lowered temperatures with a *tert*-butylamine [45] and methylamine [103] gives a product of connection on double bond, whereas at heating derivative of azetine are formed (26).



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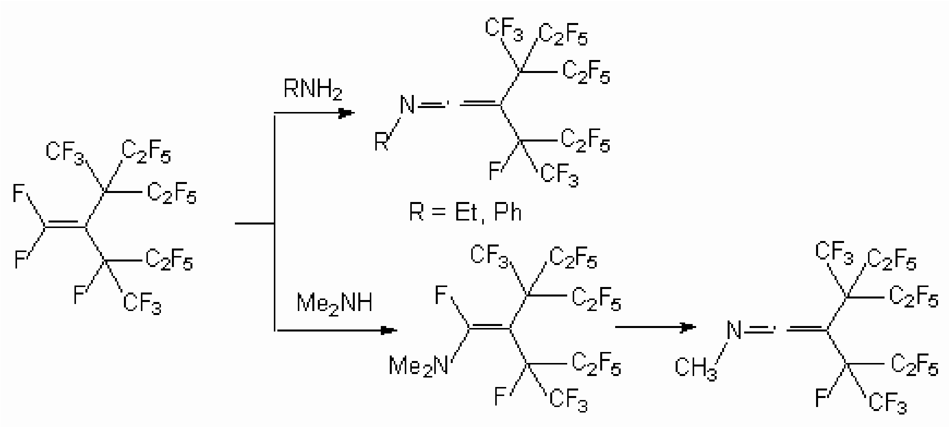
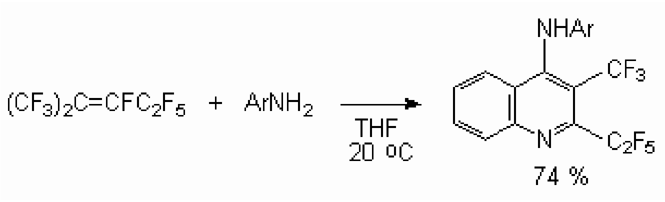
Hexamer tetrafluoroethylene with primary ($EtNH_2$ and $PhNH_2$) and secondary (Me_2NH) amines produce ketenimine [104,105].



The reaction of perfluoro-2-methylpent-2-ene with aniline is not results products of fluorine atom replacement at double bond, but a heterocyclic compound is observed (27) [106].



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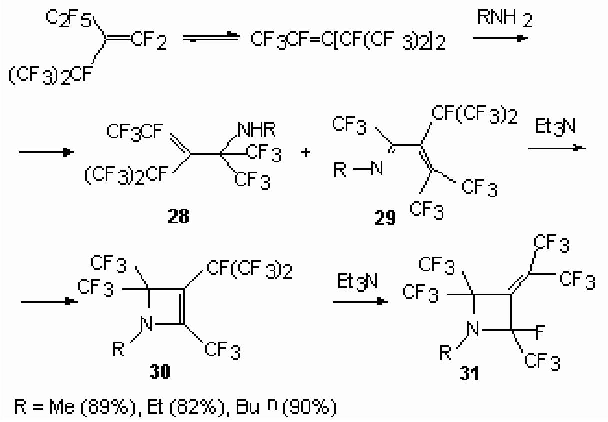
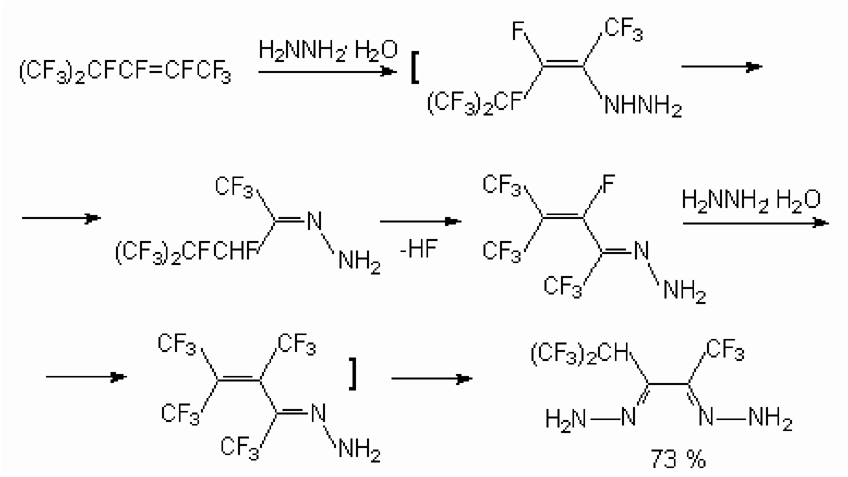
Trimer of a hexafluoropropylene react with primary amines, giving originally products of double bond addition (28) and (29), which under heating or at Et_3N presence turns to derivative of azetine (30) [93]. It should be note, azetine isomerizate to azetidine under the treatment of Et_3N or anhydrous CsF in acetonitrile (31)



If nucleophilic reagent has two nucleophilics centers, the intramolecular nucleophilic cyclization is possible. Thus, at the reaction of perfluoro-2-methylpent-2-ene with ethylene-diamine in the Et_3N (THF medium) 5-pentafluoroethyl-6-trifluoromethyl-7-fluoro-2,3-dihydro-1H,1,4-diazepine is formed [61]. It is necessary to note that the imine and terminal double bond is formed, and the atom of nitrogen is the second nucleophilic center. This double bond undergoes the further intramolecular nucleophilic cyclization.

At the reaction of hydrazine-hydrate with perfluoro-4-methylpent-2-ene only replacement of fluorine atoms at double bond is observed and the bis-hydrazone 1,1,1,5,5,5-hexafluoro-4-trifluoro-methyl-2,3-pentane-dione and (32) is formed [107,108]. The process involves a number steps: nucleophilic substitution of the vinyl fluorine atom, isomerization of intermediate enehydtazine, dehydrofluorination of the mono-hydrazone and further treatment by second equivalent of hydrazine hydrate [109].



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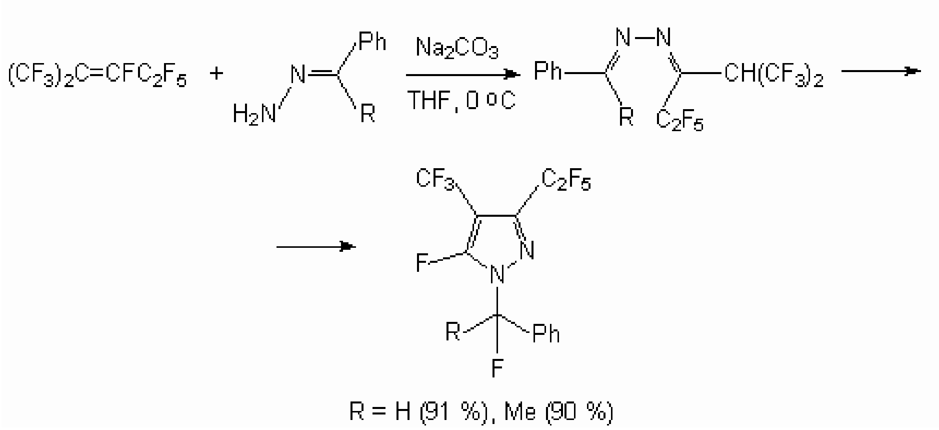
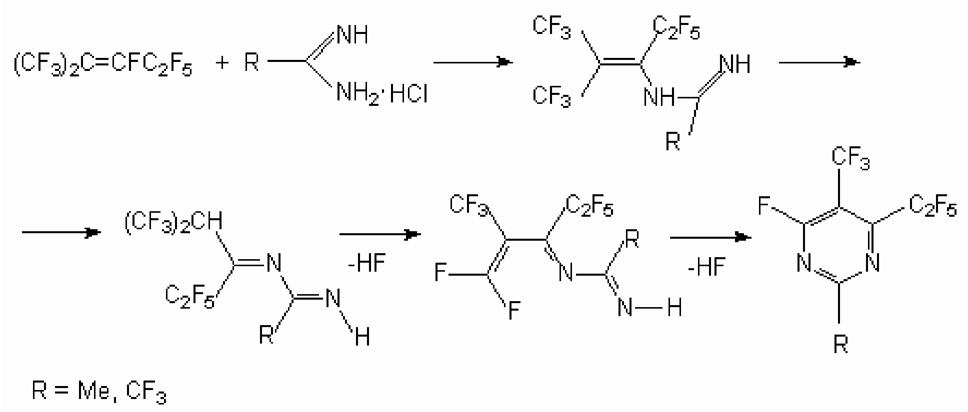
When internal perfluoroolefin reacts with hydrazones a appropriate ketenimine is formed, which further in conditions of reaction is transformed into a cyclic product [90].



In the reaction of perfluoro-2-methylpent-2-ene with hydrochloride acet- and trifluoroacetamidine at presence of NaOH and triethylbenzylammonium chloride the product of substitution of fluorine at double bond is formed. The product is unstable and further prototropion isomerization [see 103], dehydration and cyclization [110] is observed. The derivatives of 4-fluoropyrimidine are produced as a result of reaction.



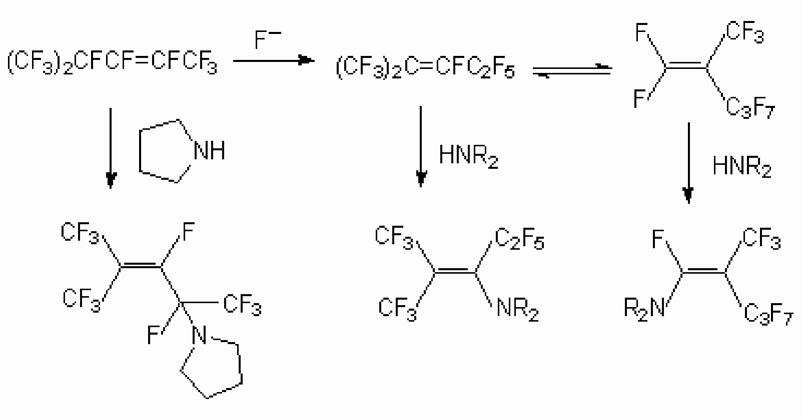
When secondary amines react with internal perfluoroolefins a products of replacement of a fluorine at internal double bond is not observed. [111]. The matter of a fluorine replacement orientation is based on the preliminary process of internal perfluoroolefins isomerization to terminal ones. [112, 113].

Internal perfluoroolefins also was formed as a products (by replacement of fluorine atom at double bond) from corresponding terminal olefins, which was produced by isomerization of internal perfluoroolefins under fluoride ion influence [94,112,114,115]

At the same time, the available data do not confirm the conclusions that for a number of secondary amines were received mixture two isomeric products or exclusively products of replacement of fluorine atom at internal or terminal double bonds [94,112,114,115]. The replacement's analysis of influence of a secondary amine structure, based on orientation of a fluorine in internal perfluoroolefins, allow to formulate a conclusion about a uniform way of reactions involving internal and terminal perfluoroolefins, excluding preliminary isomerization of internal to terminal perfluoroolefins [116] . It is likely that the key moment of these reactions are the transformations of an intermediate carbanion generated by attack of an N-nucleophile reagent with any structure on carbon atom at internal double bond. Energetically and stericaly factors add the opportunities of formation of intermediate compounds with double bond and determine the direction of transformations of initial olefin.

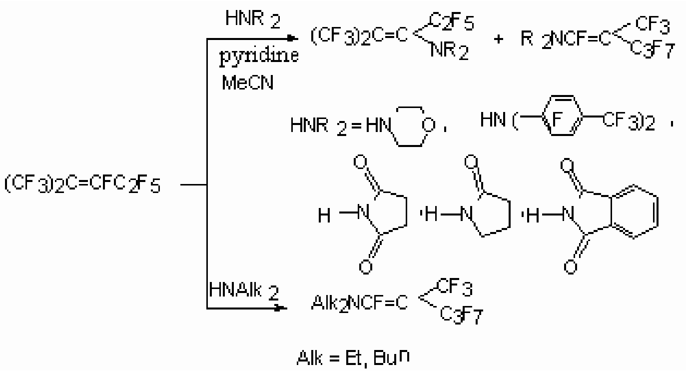
The interaction of a hexafluoropropylene dimers with secondary amines goes ambiguously : with a diethylamine - exclusively to enamine terminal perfluoroolefins [84,94], whereas with a pyperidine - to enamine received from internal perfluoroolefins [106, 113]. Orientation under action of another secondary amines is ambiguous too [112]. However, more detailed study this reaction [113] was performed, which show that the formation of two isomeric enamines actually took place: 1-[3,3,3-trifluoro-1(pentafluoroethyl)-2-(trifluoroethyl)-1-propenyl]-pyperidine and 1-[1,3,3,4,4,5,5,5-octafluoro-2-(trifluoromethyl)-1-pentenyl]pyperidine at the ratio 1:2.07 (1:6.69 in [112]). With increasing of the size of a cyclic amine (pyrrolidine, the pyperidine, cycloheptylamine) the increasing of yield of enamine is observed. Enamine formed by elimination of a fluorine from terminal olefin (a ratio of these enamines 1:0.82, 1:6.69, 1:8.09 as shown in [112]). The authors of works [112,113] explain the results by isomerization of internal perfluoroolefins to terminal ones under influence of trialkylamines or a fluoride-ion with subsequent replacement of fluorine atom at terminal double bond.

The similar path is revealed also for reactions of cyclic amines with perfluoro-4-methylpent-2-ene [112] and dialkylamines with perfluoropent-2-ene [117]. At the same time, the authors of work [117] have shown (on the example of reaction between perfluoro-2-methyl-pent-2-ene and pyperidine) that probably exclusive replacement of a fluorine at double bond of internal perfluoroolefins take place, resulting the formation of the corresponding enamine.



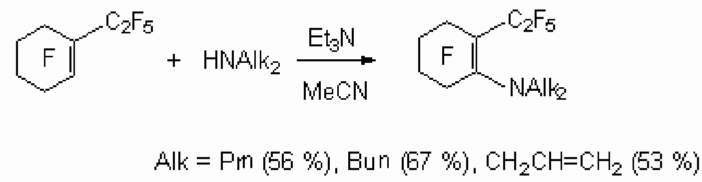
For hexafluoropropylene trimer analogous situation take place too [114].

As it is shown in [116], at the reaction between perfluoro-2-methylpent-2-ene and morpholine in absolute acetonitrile medium at presence of equimolary amount of pyridine or triethylamine (used for linkage of hydrogen fluoride) 1-[3,3,3-trifluoro-1(pentafluoro-ethyl)-2-(trifluoromethyl)-1-propenyl]-morpholine and 1-[octafluoro-2-(trifluoromethyl)-1-pente-nyl]-morpholine are formed at the ratio of 1:3.49.

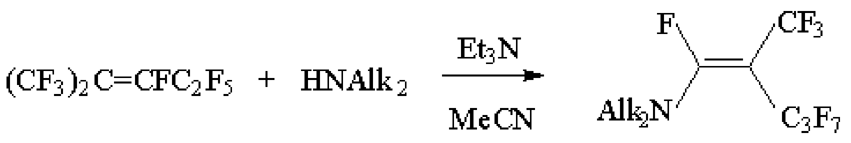


In the reaction between perfluoro-2-methylpent-2-ene and 1-N,N-di-(4-trifluoromethyl-2,3,5,6-tetrafluorophenyl)amine at the presence of a triethylamine two enamines - 3-N,N-di-(4-tri-fluoromethyl-2,3,5,6-tetrafluorophenyl)aminoperfluoro-2-methylpent-2-ene and 1-N,N-di-(4-trifluoromethyl-2,3,5,6-tetrafluorophenyl)aminoperfluoro-2-methylpent-1-ene at the ratio of 1:3 also turn out. At the same time the interaction between perfluoro-2-methylpent-2-ene and pyrrolidone, syccine-imide and phalimide at the presence of triethylamine results extremely the products of replace-ment of fluorine atom at internal double bond of perfluoroolefins: accordingly in N-(perfluoro-2-methylpent-3-yl)cycinamide, N- (perfluoro-2-methylpent-3-yl) phthalimide and 1-[3,3,3-tri-fluoro-1-pentafluoroethyl)-2-trifluoromethyl-1-propenyl]-pyrrolidone [118].Thus, with decreasing of base strength of a used amine, their catalytic activities in process of isomerization of internal perfluoroolefins to terminal decrease too and issue the formation of a product of replacement of a fluorine atom at internal double bond.

As was shown [112,115 earlier], the reaction of perfluoro-2-methylpent-2-ene with diethylamine or dibutylamine (at the presence of a triethylamine in acetonitrile) resulted the formation of 1-N,N-dietylaminoperfluoro-2-methylpent-1-ene and 1-N,N-dibutylamino-perfluoro-2-methyl-pent-1-ene, whereas with dipropylamine and diallylamine at presence Et_3N an enamine derivative from terminal perfluoroolefins was observed [115].



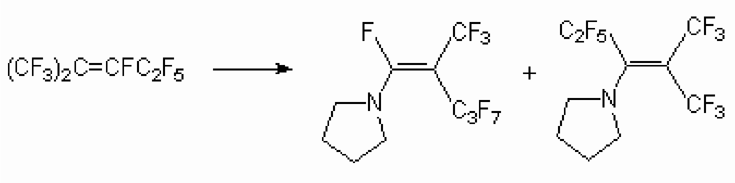
Upon the influence of diallylamine on a hexafluoropropylene trimer, only the product (23) is obtained .



Alk = Bu^n (51 %), Pr ^{n} (64 %), CH $_2$CH=CH$_2$ (53 %)

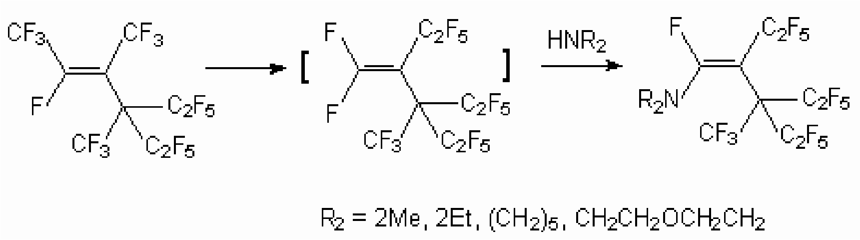
$$CF_3CF{=}C[CF(CF_3)_2]_2 + HN(CH_2CH{=}CH_2)_2 \xrightarrow[MeCN]{Et_3N} \underset{\mathbf{23}}{(CH_2{=}CHCH_2)_2NCF{=}CFCF[CF(CF_3)_2]_2}$$

At the action of bis (dimethylamino)methane and N, N-diethylamino-trimethylsilane on perfluoro-2-methylpent-2-ene an extremely product of replacement of fluorine atom also is formed [119]. It is known [120-122], that given olefin isomerizate to terminal ones under the influence of fluoride-ion. At the same time these authors has observed, that the pyrolidine with perfluoro-2-methylpent-2-ene gave a mixture of two enamines (34) and (35).

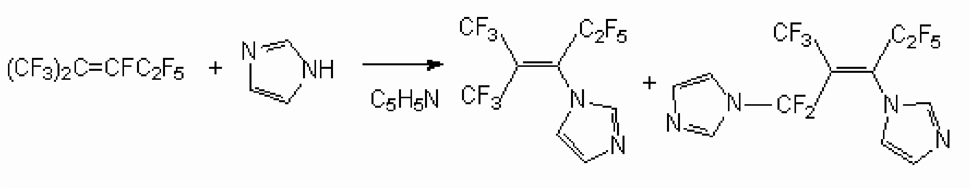


	34		**35**
Dioxane	80	:	20
Diethyl ether	70	:	30
DMF	70	:	30

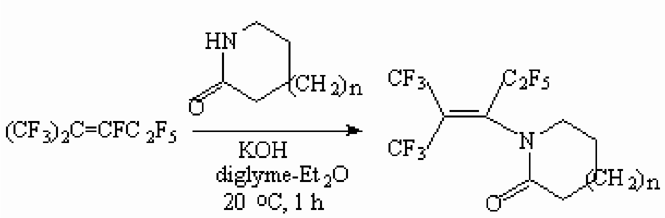
The products of replacement of fluorine atom at internal double bond and terminal olefins is not observed in the reaction of tetrafluoroethylene pentamer with dimethylamine, diethylamine, morpholine or pyperidine [102].



At the same time the reaction of azoles with perfluoro-2-methylpent-2-ene in base medium (pyridine, Et_3N) gives extremely products of replacement of fluorine atom at internal double bond: N-(perfluoro-2’-methylpent-2’-yl-3’)-imidazole and the product of further transformation: N,N-1,3-bis(imidazolyl)-perfluoro-2-methylpent-2-ene [123].



Lactames at the presence of the bases is sufficiently effective N-nucleophiles and react with perfluoro-2-methylpent-2-ene with formation of exclusively N- (perfluoroalkenyl)-lactams (36), being a product of replacement of fluorine atom at double bonα(-pyperidone (49 %), caprolactam (51 %)) [73].



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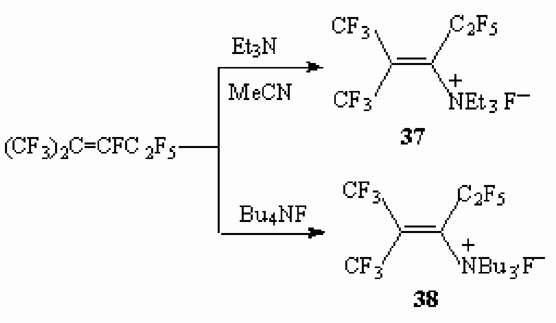
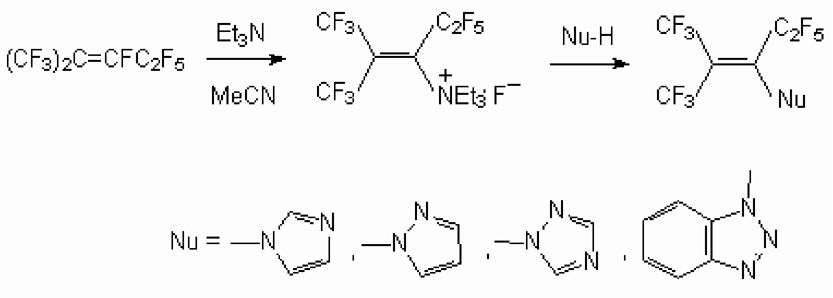
Lactames (36) are unstable in acidic medium and they ara easily hydrolyzed during the boiling with solution of HCl with formation of corresponding ketone $(CF_3)_2CH\text{-}C(O)\text{-}C_2F_5$.

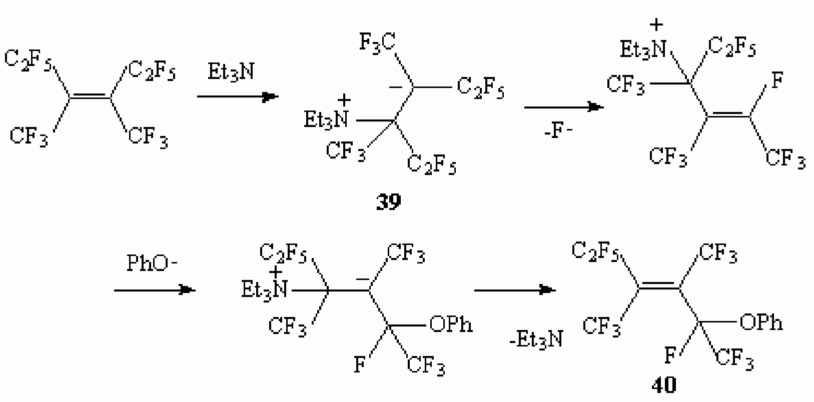
It is necessary to note, that some internal perfluoroolefins are capable to react with tertiary amines with formation the salt of trialkylammonium. So, perfluoro-2-methylpent-2-ene reacts with a triethylamine such salts possess more reactivity in comparison with corresponding internal perfluoroolefins and it is possible to carry out the reactions with nucleophilic by-reagents with low nucleophility. Thus, it is possible to receive exclusive replacements Alk_3N - group by N-nucleophilic component without influence of another centres.



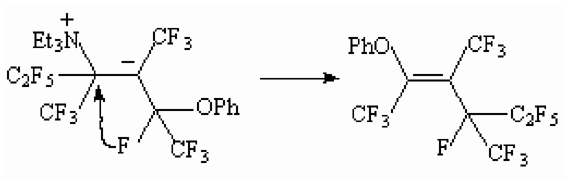
For example, similar type of salt reacts with dialkylamines at carbon atom of double bond with subsequent replacement of Alk_3N-group to dialkylamino-group [125,126]. In reactions of perfluoro-2-methylpent-2-ene with pyrazole, benzo-1,2,3-triazole and 1,2,4-triazole the temporary replacement of fluorine atom at double bond on group, for example, Et_3N (the salt (37), which was received by a method [96]), give only products of replacement of fluorine atom at internal double bond [123]. Apparently, N-nucleophile attacks C=C bond on the atom of carbon, which connect with positively charged atom of nitrogen. The salt (37) has appeared essentially more electrophility in comparison with initial internal perfluoroolefins.



This approach can be also used for olefins containing only perfluoroalkyl substituents. In this case inner salt is formed. So, the triethylamine reacts with perfluoro-3,4-dimethylhex-3-ene with initial formation of internal salt (39). The elimination a fluoride-anion from CF_2group is possible, which results a generation of double bond. The further reaction of a phenol with new double bond results a product (40) (the yield *trans*-isomer 28 %, and *cis*-isomer 37 %) [113] or compound (41) (yield 35 %).



The generation of new double bond proceeds with elimination of a triethylamine (first path) or by reason of intramolecular attack of carbon atom with NEt_3-group.



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This example show the different ways of interaction of internal perfluoroolefins with nucleophilic by-reagents.

to be continued