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Triethylamine Trishydrofluoride in Synthesis

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Abstract. Triethylamine trishydrofluoride is a highly versatile fluorinating agent without the disadvantages of liquid hydrogen fluoride or other mixtures of HF with bases. The main types of fluorination using this reagent are reviewed: Nucleophilic substitutions, reactions using this reagent as nucleophilic partner in electrophilic additions, electrofluorinations and deprotection of silylethers.

Fluorinated organic materials – both analogues of naturally occurring compounds and synthetic substances – gain a continuously growing interest by organic chemists, biochemists, medicinal chemists, material scientists and others because of its unique chemical properties and biological activity. Hence, there is an enormous demand of synthetic methods for such compounds. Although there exist plenty of different procedures to introduce fluorine substituents into organic molecules, there are only a few which can be handled easily and safely in an ordinary organic chemistry laboratory. One of these is triethylamine trishydrofluoride ($Et_3N{\cdot}3HF$)[1] as a source of nucleophilic fluoride.

After this reagent was formed in situ for epoxide ring openings [1], Franz synthesized this complex about 15 years ago as a distillable oily liquid [2]. $Et_3N{\cdot}3HF$ has important advantages over the most other HF-based fluoride sources: The reagent is less corrosive compared to other mixtures of HF with organic bases and can be handled in usual borosilicate glassware up to temperatures of about 150 °C and it is soluble in polar protic and aprotic solvents and in organic substrates of different kind [2].

There are mainly five types of application for $Et_3N{\cdot}3HF$:

1. Nucleophilic substitutions
1.1. Halogens or hydroxyl groups (via esters)
1.2. Epoxide ring openings to fluorohydrins
1.3. Balz-Schiemann reaction
2. Nucleophilic partner in electrophilic additions
2.1. Halofluorinations
2.2. Sulfenyl- and selenenylfluorinations
3. Electrofluorinations of activated positions in organic compounds
3.1. Benzylic positions
3.2. Thioethers
3.3. Thioacetals and hydrazones
3.4. Olefins
3.5. Aromatic compounds
4. Nucleophilic substitutions of halogen atoms with fluorine in organo phosphorus compounds
5. Deprotection of silylethers

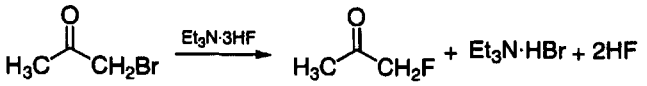
1 Nucleophilic Substitutions

1.1 Halogens or Hydroxyl Groups (via Esters)

Usually nucleophilic substitutions of ordinary alkyl halides with fluoride are not favored. Thus, after 122 h refluxing of 2-bromooctane with two equivalents of $Et_3N{\cdot}3HF$ and one equivalent of Et_3N in acetonitrile only 48 % (GC) of 2-fluorooctane was formed [3]. Mesylate is a much better leaving group yielding 90% (GC) of the fluoro compound starting from the mesylate of octan-2-ol and from 1-mesyloxy-3-phenylpropane 100% (GC) of the 1-fluoro compound was obtained [3]. However compounds with activated carbon-halogen bonds can easily be substituted. In this way by heating

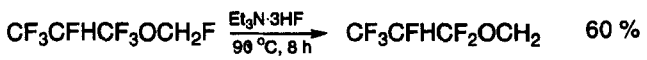
[1]) Very recently a review on the same topic appeared; M. A. McClinton, Aldrichimca Acta **28** (1995) 31.

bromoacetone (**1**) with $Et_3N{\cdot}3HF$ to 110–115 °C and simultaneous addition of Et_3N (to bind HBr and the elevating HF to form again $Et_3N{\cdot}3HF$) fluoroacetone (**2**) is formed in 90% yield [2].



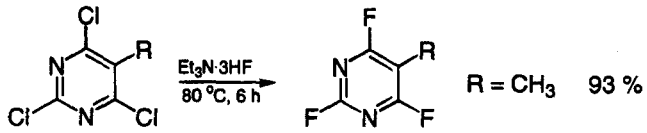
1 **2**

Also from α-(chloromethyl)-pentafluoropropyl ether (**3**) on heating with $Et_3N{\cdot}3HF$ the corresponding fluoro compound **4** has been obtained in good yield [4].



3 **4**

2,4,6-Trifluoro-1,3-diazines **6** were prepared by treating the trichloropyrimidines **5** with $Et_3N{\cdot}3HF$ at room temperature and heating the mixture for 6 h at 80 °C [5].

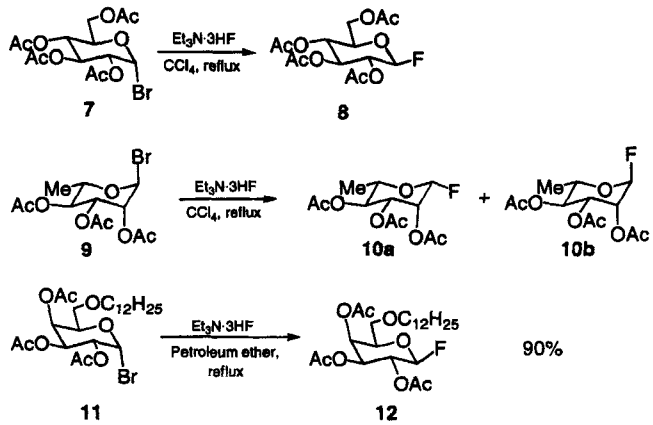


5 **6**

R = H, Alkyl

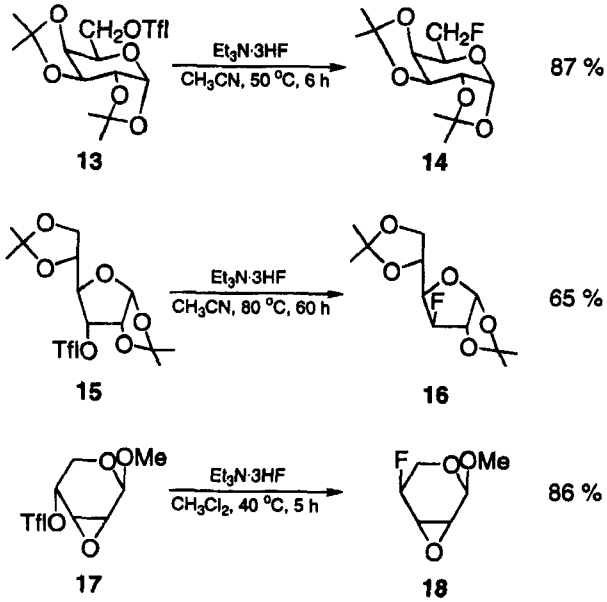
In a similar way cyanuric chloride was transformed into cyanuric fluoride, from phosgene difluorophosgene, from oxalylchloride oxalylfluoride and from dichlorosulfane sulfur tetrafluoride were obtained [2].

In sugar chemistry the reagent has been extensively used to introduce fluorine substituents. Nucleophilic substitutions with inversion of the configuration of α-bromine substituents at the anomeric centre with fluorine were effectively realized by refluxing of **7** with a large excess of $Et_3N{\cdot}3HF$ in a two-phase system with CCl_4 to give **8** [6].

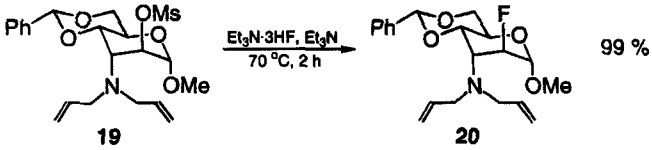


Several similar transformations of other protected α-bromo sugars [5] and protected sugar analogues like **9** and **11** [7,8] have been realized.

Related substitutions were successfully used also for the synthesis of primary or secondary sugar fluorides. In this way the triflate **13** gave 87% of **14** and the triflates **15** and **17** gave the corresponding fluorides **16** and **18** with complete inversion of the configuration in 65% and 86% yield, respectively, and without opening of the expoxide in the case of **17** [9].



Retention of the configuration has also been obtained in the substitution of the mesylate **19** with $Et_3N{\cdot}3HF$ to yield **20** by intermediary neighbouring group participation of the nitrogen functionality [10].

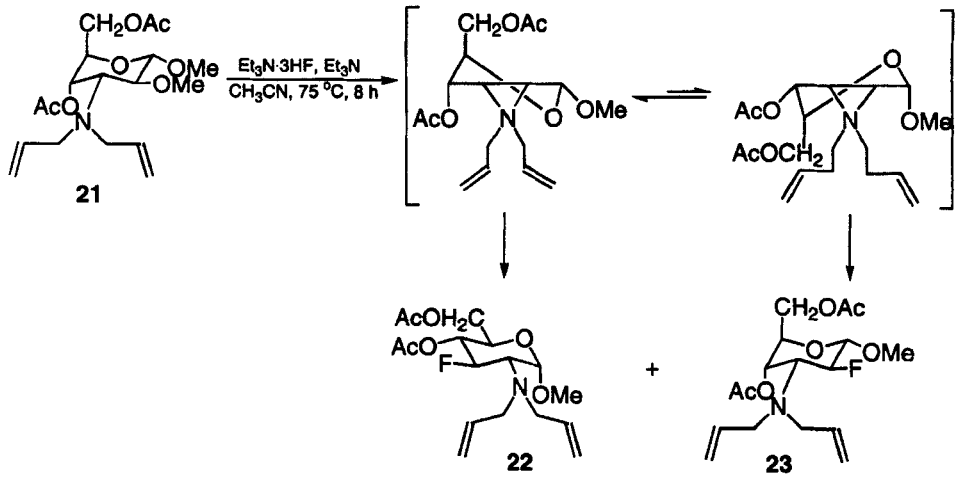


19 **20**

Partial retention of the configuration, but mainly rearrangement, caused as well by intermediary participation of a bis-allylamino group, gave the fluorides **22** and **23** (7:1) by treatment of **21** with $Et_3N{\cdot}3HF$ [11].

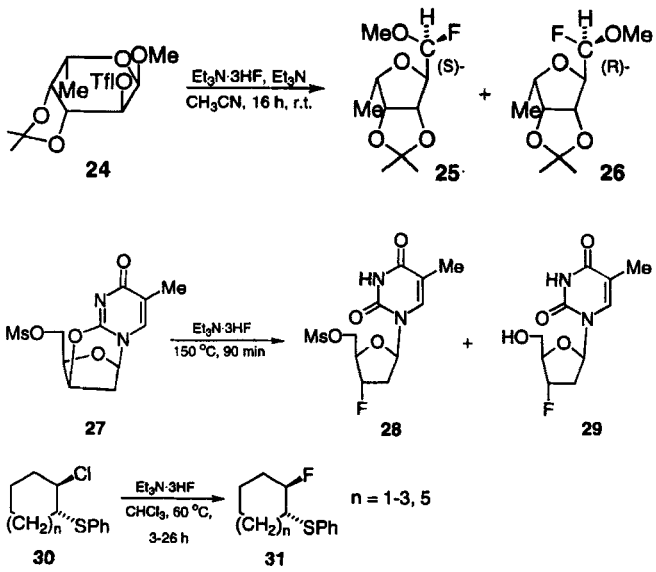
Ring contraction occurred in the reaction with $Et_3N{\cdot}3HF$ in acetonitrile and some additional amount of Et_3N of the methyl hexopyranoside **24** bearing the leaving group in 2-position to form a 1:3 mixture of epimers **25** and **26** [12].

Several similar examples were described in the literature [7,13]. Moreover, nucleophilic substitution of a 2,3'-anhydronucleoside was realized under very harsh conditions. By heating **27** with neat $Et_3N{\cdot}3HF$ to 150



°C for 90 min a mixture of 19% of **28** and 5% of the demesylated **29** was formed [14].

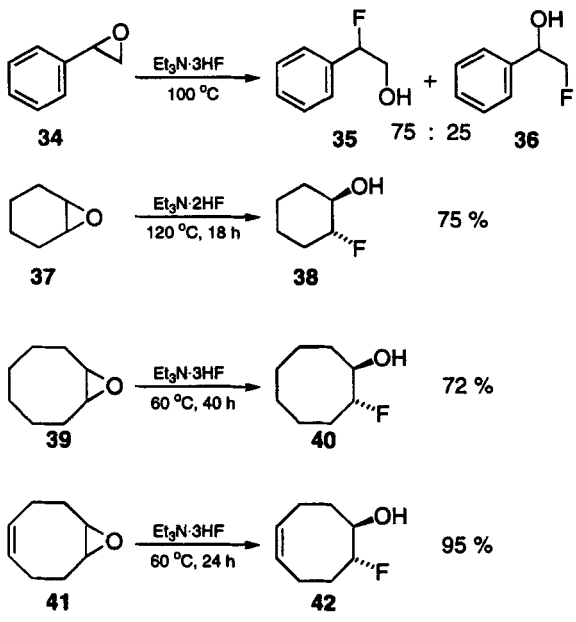
Neighbouring group participation of a sulfur function to form an intermediary episulfonium ion is responsible for the nucleophilic displacement of chlorine by fluorine with retention of the configuration in several ß-chloroalkyl-phenylthio ethers **30** with 80–96% yield [15].



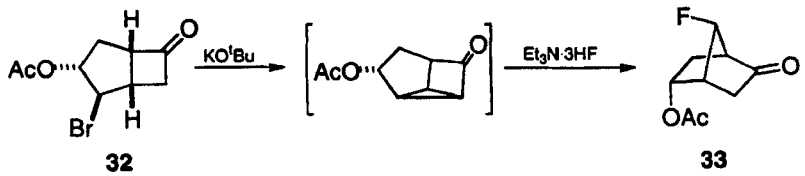
As part of a synthetic strategy twoards fluorinated carbocyclic analogues of nucleosides treatment of 3-acetoxy-2-bromobicyclo[3.2.0]heptan-6-one (**32**) with potassium *tert.*-butoxide followed by $Et_3N{\cdot}3HF$ gave fluoroketone **33** likely via HF addition to a highly strained intermediary cyclopropane [16].

1.2 Epoxide Ring Openings to Fluorohydrins

The first application of $Et_3N{\cdot}3HF$, formed in situ, was the ring opening of activated epoxides like **34** to form fluorohydrins **35** and **36** in 60% yield [1].

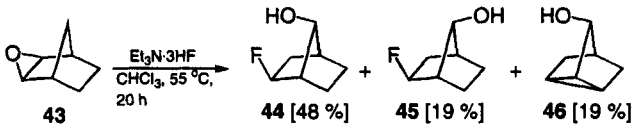


Opening of cyclohexene oxide (**37**) needs a more nucleophilic reagent $Et_3N{\cdot}2HF$, and heating for 18 h at 120 °C was necessary to form **38** [1]. For ring opening of not activated epoxides like **39** [17] or **41** [18] with $Et_3N{\cdot}3HF$ long reaction time is necessary to form the



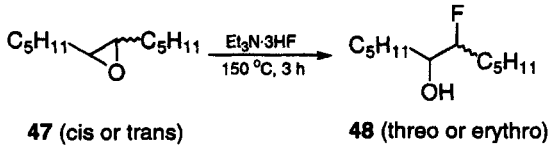
1,2-fluorohydrins **40** or **42**, respectively, without transannular hydrogen shift or transannular participation of the second double bond which was obtained using the more acidic Py·9HF (Olah's reagent).

By contrast, refluxing of exo-norbornene oxide (**43**) with $Et_3N{\cdot}3HF$ in chloroform for 20 h gave no 1,2-fluorohydrin, but two products of an intermediary Wagner-Meerwein rearrangement **44** and **45** and nortricyclanol (**46**) [19].

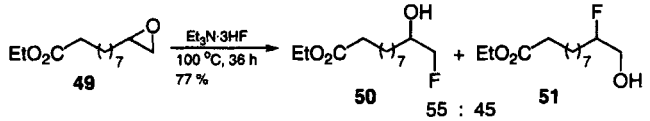


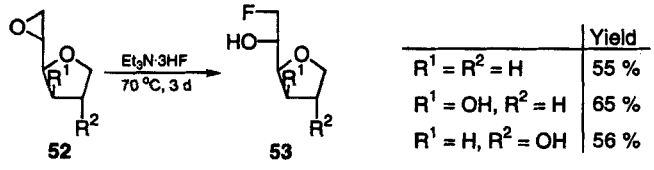
Mainly rearranged fluorohydrins were also formed in reactions of carvomenthene oxide, limonene oxide and α- and ß-pinene oxides with Et_3N/nHF reagent prepared in situ [20].

From the epoxides of *cis*- and *trans*-dodec-6-ene **47** on heating with $Et_3N{\cdot}3HF$ to 150 °C for 3 h the corresponding *threo*- or *erythro*-7-fluorododecan-6-ols **48** were obtained in 81% and 82% yield, respectively, in a highly stereoselective ring opening [21].



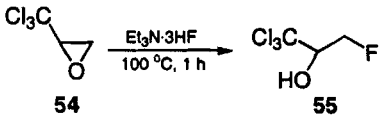
Terminal epoxides like **49** on reaction with $Et_3N{\cdot}3HF$ gave mixtures of the regioisomeric fluorohydrins **50** and **51** bearing fluorine slightly predominant in primary position. Addition of more amine (Et_3N or other tertiary or secondary amines) shifted the product ratio towards the main compound **50** [22].



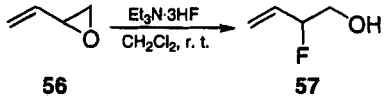


In an analogous way 5,6-epoxyhexonolactones **52** were also transformed selectively into the corresponding primary fluorides **53** [23].

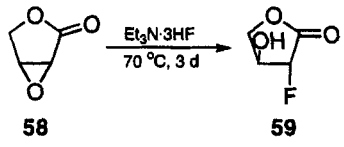
However, the regioselectivity is also dependent on functional groups attached to the epoxide ring. From trichloropropene oxide (**54**) only the primary fluorine compound **55** was formed in 76% isolated yield [24].



Contrary to saturated terminal epoxides vinyl oxiranes like **56** can be opened using $Et_3N{\cdot}3HF$ under much milder conditions to form the corresponding quite unstable fluorohydrins like **57** bearing the fluorine substituent in allylic position [25].

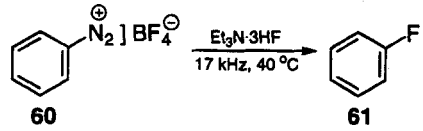


The ring opening of different analogues of sugar epoxides was shown to proceed much more selective using $Et_3N{\cdot}3HF$ compared to other HF-amine complexes. 2,3-Anhydro-L-erythrono-1,4-lactone (**58**) gave the regioisomer **59** exclusively after three days at 70 °C [26].



1.3 Balz-Schiemann Reaction

The Balz-Schiemann reaction, the traditional method for the synthesis of fluoroaromatics from arenediazonium tetrafluoroborates, is much more effective in the presence of $Et_3N{\cdot}3HF$ and ultrasonic irradiation. Benzenediazoniumtetrafluoroborate (**60**) and equimolar amounts of $Et_3N{\cdot}3HF$ in Freon 113 with sonication for 8 h at 40 °C gave 92–95% of fluorobenzene (**61**) [27].



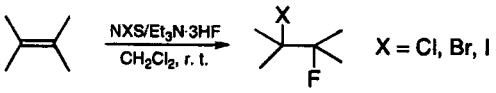
2 Nucleophilic Partner in Electrophilic Additions

2.1 Halofluorinations

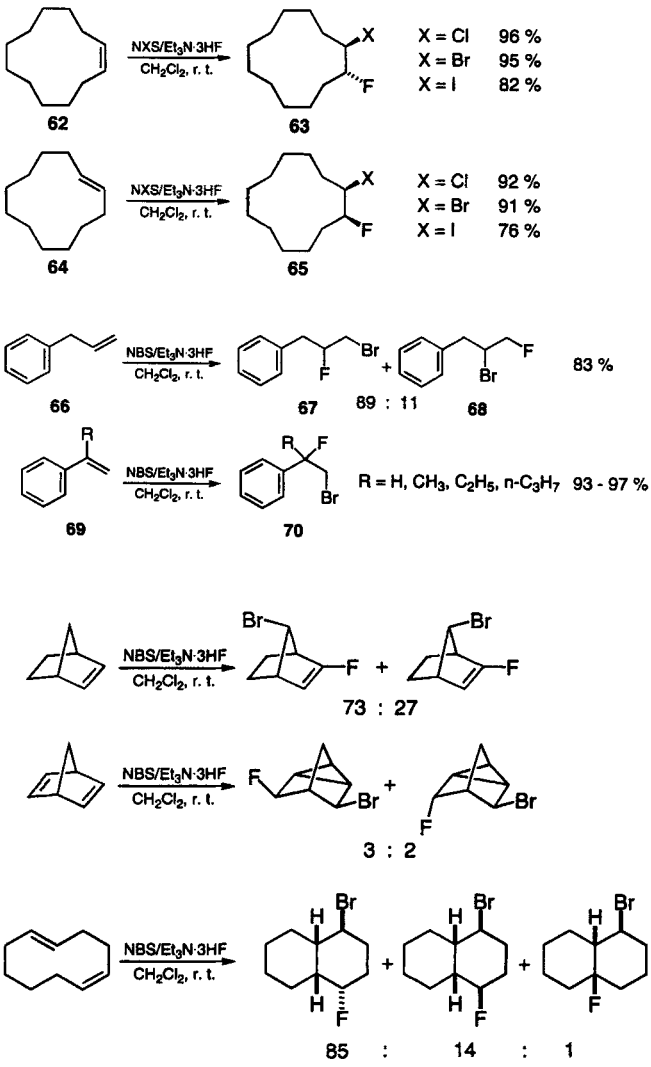
Halofluorinations as well as selenenyl- or sulfenylfluorinations (cf. chapter 2.2) of unsaturated hydrocarbons allow the introduction of a fluoride atom under much milder conditions and usually more selective than direct hydrofluorination. Moreover, the ß-halo, ß-thio, or ß-seleno substituents are very useful functionalities for

elimination or substitution reactions [28].

The combination of a source of an electrophilic halogen (like N-halosuccinimides) and $Et_3N{\cdot}3HF$ is a very convenient and effective reagent for the halofluorination of alkenes [29].

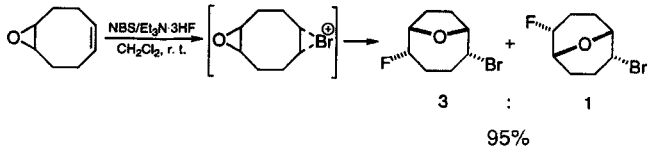


The addition of the halofluorides like "BrF" proceeds stereospecifically giving *trans*-2-fluoro-1-halo-cycloalkenes like **63** from *cis*-cycloalkenes like **62** or *cis*-2-fluoro-1-halo-cycloalkanes like **65** from *trans*-cycloalkenes like **64**. Moreover, the addition is regioselective according to the Markovnikov rule as shown for bromofluorinations to allyl benzene (**66**) and α-alkylstyrenes **69** to form the products **67** and **68** and **70**, respectively, in very good yields [30].



Such reactions occur in hydrocarbon systems where Wagner-Meerwein-type rearrangements or transannular π-participations are possible [29, 31].

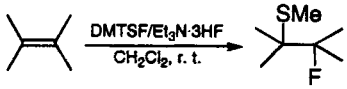
Meanwhile several other types of ethylenic compounds such as long chain terminal [32] and symmetric [33] alkenes, terminal allylic alcohols [34], vinyl oxiranes [35], methallyl derivatives [36], and ω-unsaturated fatty acids [37] and enol esters [38] have been bromofluorinated using this method.



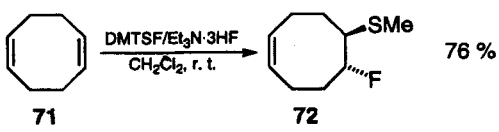
If an oxirane is placed in transannular position to a double bond in an eight membered ring on bromofluorination transannular O-participation occurs prior to the introduction of the fluoride ion [39].

2.2 *Sulfenyl- and Selenenyl Fluorinations*

The combination of $Et_3N{\cdot}3HF$ with electrophilic sulfur or selenium reagents gives rise to sulfenylfluorinations or selenenylfluorinations. In this way the electrophilic *anti*-1,2-addition of the elements of methane- sulfenyl fluoride to carbon-carbon double bonds by a one-pot reaction of dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF) and $Et_3N{\cdot}3HF$ with various types of alkenes was used for the synthesis of ß-fluoroalkyl methyl thioethers [40].

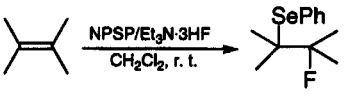


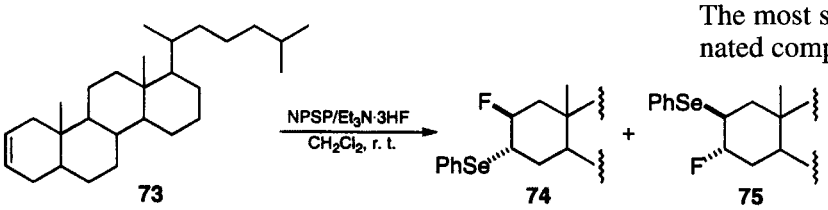
This reaction is stereospecific like the halofluorinations: From *cis*-cycloalkenes *trans*-1-fluoro-2-(methylthio) cycloalkanes are formed while *trans*-cycloalkenes give the *cis*-products, always in good yields [40]. With unsymmetrical alkenes, these reactions proceed regioselectively to produce mainly Markovnikov-oriented flu- oroalkyl thioethers. With norbornadiene exclusively *exo*-attack of the electrophile on one of the double bonds and subsequent transannular participation of the second π-bond gives rise to two isomeric 3,5-disubstituted nortricyclanes, while starting with the medium-sized (*Z,Z*)-cycloocta-1,5-diene (**71**) only 1,2-addition to **72** and no transannular π-participation has been observed [40].



In contrast, the reaction of the monoepoxide of this diene gives in addition to the simple 1,2-adduct also transannular oxygen participation producing oxybicyclic compounds (analogous to the bromofluorination) [40].

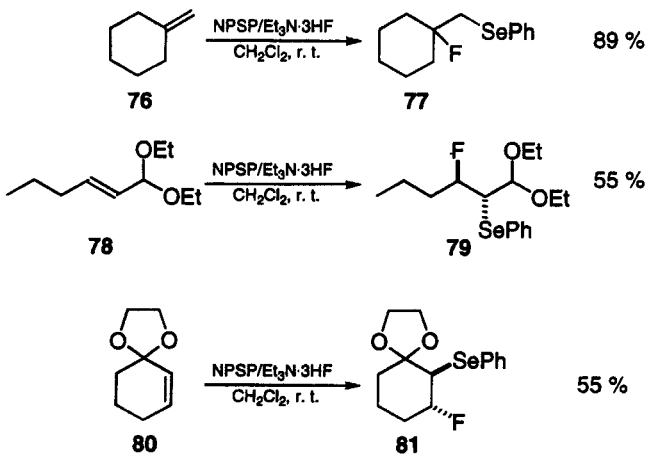
Phenylselenofluorinations of various kinds of alkenes and alkynes were realized in good yields using N-phenylselenophthalimide (NPSP) combined with $Et_3N{\cdot}3HF$. Again the reactions occur as *anti*-1,2-additions forming ß-fluoroalkyl phenylseleno ethers from alkenes [41].





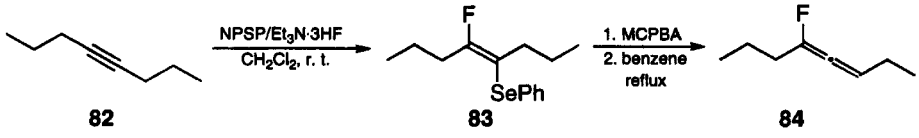
From 5α-cholest-2-ene (**73**) a mixture of two trans-configurated regioisomers **74** and **75** were formed in a ratio of 3 : 2.

Acid sensitive olefins like methylene cyclohexane (**76**) yield the corresponding 1,2-adducts like **77** without rearrangement prior to the addition of the elements of PhSeF and also acetals of α,ß-unsaturated aldehydes like **78** or ketones like **80** give the 1,2-addition products **79** or **81**, respectively, bearing the electrophile next to the acetal function [41].



Moreover, the formal addition of the elements of PhSeF across triple bonds is most successful with symmetric alkynes giving ß-fluoroalkenyl phenylselenoethers. With unsymmetric alkynes mixtures of regioisomers are formed while terminal acetylenes yield unpleasant mixtures of at least five products with 1-fluoro-1,2-(diphenylseleno)-1-alkenes as the main components [41].

This reaction has been used as a key step in a new synthesis of a fluoroallene. From 4-octyne (**82**) first the corresponding *trans*-phenylseleno vinylfluoride **83** is formed in 80% yield which after oxidation and elimination gives the fluoroallene **84** [42].



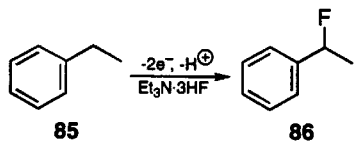
3 Electrochemical Fluorinations of Activated Positions

The most simple procedure for the synthesis of fluorinated compounds is the direct fluorination. However, chemical methods using elemental fluorine or CF_3OF, XeF_2, DAST or N-fluoro compounds are often dangerous, difficult to handle, or very costly [43].

Electrochemical fluorinations, on the contrary, are a very good alternative because they can be done in one step under safe conditions using cheap chemicals [44]. However, electrochemical partial fluorinations sometimes lack selectivity or give low yield because of the low nucleophilicity of fluoride ions in solvating solvents or because of solvent participation. $Et_3N{\cdot}3HF$ has two major advantages in this respect: It can be used as the electrolyte and simultaneously as the source of fluoride ions. The reagent is stable against oxidation and it is a good solvent for several organic substrates (sometimes no additional solvent is needed). Moreover, it can be recycled by simple distillation without change of the initial $Et_3N{\cdot}3HF$ ratio [1, 45].

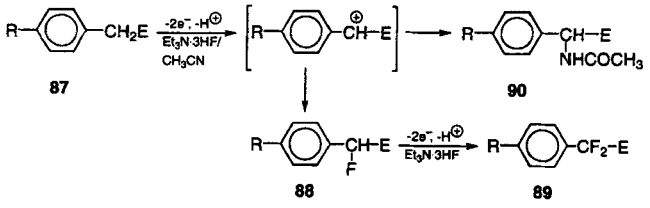
3.1 Benzylic Positions

The electrochemical oxidation of ethylbenzene (**85**) in neat $Et_3N{\cdot}3HF$ at 63% conversion gave 42% of 1-fluoro-1-phenylethane (**86**) [45].



The anodic oxidation of benzylic nitriles, carboxylic acid esters, sulfonic acid esters and ketones **87** in the presence of $Et_3N{\cdot}3HF$ in acetonitrile yields the corresponding monofluorides **88** or difluoro compounds **89** depending on the electrode potential. Best results are obtained with p-substituted aromatics like p-chloro or p-methoxy derivatives, which stabilize the intermediates. In some cases acetamides **90** are formed as minor products [46].

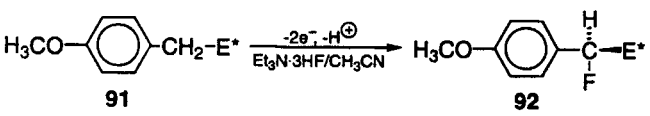
The monofluoro compounds **88** or the difluoro compounds **89**, respectively, are usually obtained in 30–70% yield [44]. Replacing acetonitrile with sulfolane as the solvent the formation of acetamide by-products is prevented. However, parallel fluorination of the aromatic nucleus is obtained under these conditions [47].



R = H, p-Cl, p-OCH_3
E = $COCH_3$, $COC_6H_4OCH_3$, $CO_2C_2H_5$, CN, $SO_3C_2H_5$

In reactions of compounds with two different benzylic positions in neat $Et_3N{\cdot}3HF$ the chemoselectivity is difficult to direct by different electrode potentials, giving usually mixtures of mono- or difluorinated products [48].

A diastereoselective fluorination of the benzylic position is possible using a chiral, non racemic auxiliary as the ester alcohol component . Best diastereoselectivity was found for the phenylmenthyl ester **91** to give the (S)-enantiomer of the benzylic fluoro compound **92** in 65% chemical yield and 60% *de* [49].

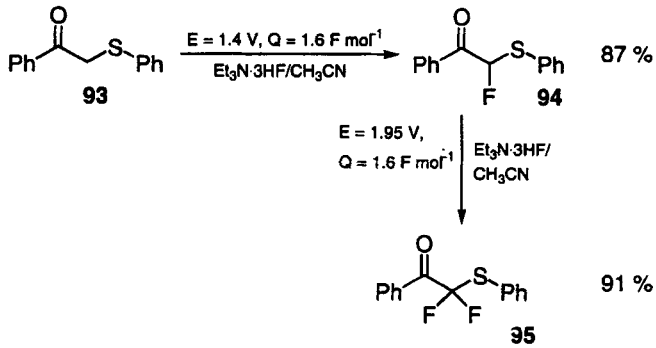


3.2 Thioethers

Highly selective anodic fluorination of activated α-positions has been also obtained in sulfides, selenides, and heterocycles including ß-lactams [50].

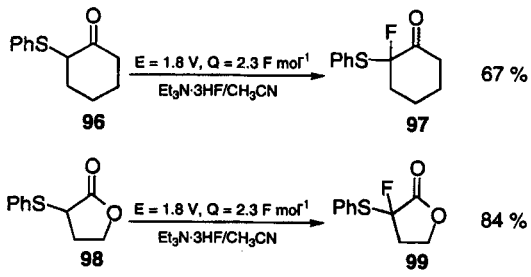
Constant potential electrolysis of activated sulfides on a platinum electrode in the presence of excess $Et_3N{\cdot}3HF$ in acetonitrile gave the corresponding α-fluoro compounds in 50–87% yield. In this way, e.g. from **93** the fluorinated phenylsulfide **94** was obtained in 85% yield [51].

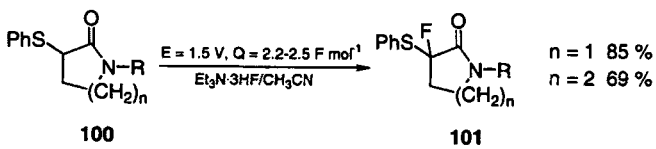
However, **94** contains another susceptible proton which can be substituted by a fluorine atom. By increasing the potential during the electrolysis, the difluoro compound **95** was isolated in 91% yield [51].

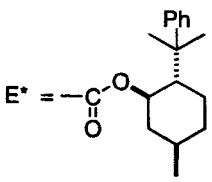


Other α-phenylthiocarbonyl compounds like ketone **96** or γ-lactone **98** have been monofluorinated to give the products **97** and **99**, respectively, in good yields [52].

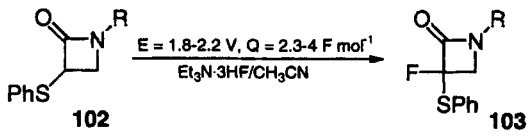
Recently the successful electrochemical monofluorination of α-phenylsulfenyl lactams **100** has been reported to give **101** in good yields [53].





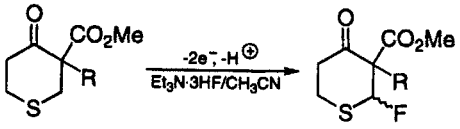


Moreover, α-phenylsulfenyl ß-lactams **102** were regioselectively monofluorinated giving **103** in high yields (65–92%) and with good current efficiencies using the analogous protocoll [54].



R = Et, i-Pr, n-Bu, t-Bu, cyclohexyl, Bzl

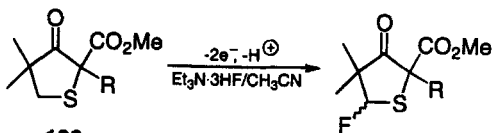
The first successful anodic fluorination of sulfur-containing heterocycles has been reported by Fuchigami et al. [55]. The 4-thiacyclohexanones **104** provide the fluorinated diastereomers **105** in low or reasonable yields and with moderate to high diastereoselectivity.



104 **105**

a R = Me yield 7 % (100 % de)
b R = Bzl 49 % (44 % de)

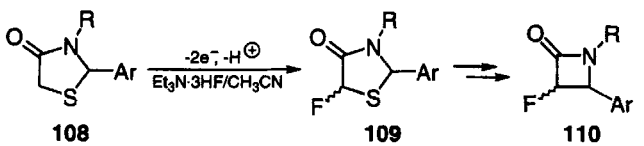
The related reaction takes also place in thiolanone derivatives **106** to yield the corresponding *cis/trans*-isomeric fluoro compounds **107** which exhibit *in vitro* human type II phospholipase A_2 inhibitory activity [56].



106 **107**

a R = Me 2.1 V, 5.1 F mol^{-1} yield 74 % (48 % de)
b R = Bzl 2.4 V, 8.2 F mol^{-1} 71 % (22 % de)

Recently also the anodic monofluorination of 4-thiazolidinones **108** gave the corresponding *cis/trans* isomeric α-fluoro compounds **109** with moderate to good yields, but low diastereomeric excess [57].



108 **109** **110**

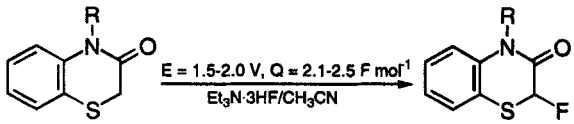
Ar = Ph, naphthyl
R = H, Me, i-Pr, Ph, Bn

Oxidation of **109** to the corresponding sulfones and thermal extrusion of SO_2 provides monofluorinated ß-lactams **110** [57].

Furthermore, several 2H-1,4-benzothiazin-3(4H)-one derivatives **111** with protected nitrogen were effectively monofluorinated to form **112** under the same conditions [53].

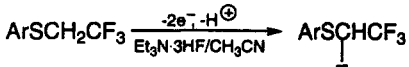
Analogously, different aryl 2,2,2-trifluoroethyl sulfides **113** were α-fluorinated in acetonitrile solution of $Et_3N{\cdot}3HF$ at a platinum electrode with constant potential to give **114** in 25–56% yield [58].

The α-monofluorination of phenyl sulfides bearing other electron-withdrawing groups is also successful [58, 59]. Simple alkyl phenylsulfides like **115** can be



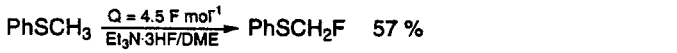
111 **112**

R = COPh 77 %
R = i-Pr 88 %
R = Me 68 %

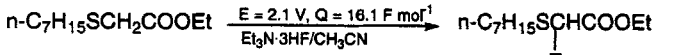


113 **114**

Ar = Ph, p-MeC_6H_4, p-$MeOC_6H_4$, p-ClC_6H_4, $PhCH_2$



115 **116**



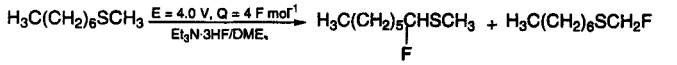
117 **118**

electrochemically monofluorinated to form **116**, best in DME solution [60].

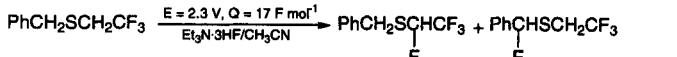
Even the aliphatic thioether **117** having a methylene group activated by a carboxylic function gave the monofluoro derivative **118** in 70% isolated yield [58].

And also *n*-heptyl methylsulfide (**119**) exhibiting any electron-withdrawing group underwent fluorination rather effectively in DME to give a mixture of **120** and **121** [60].

Thioethers with two different activated α-methylene positions gave mixtures of isomers fluorinated in α or α' position, respectively. For example, **122** gave the isomers **123** and **124** in good overall yield [60].



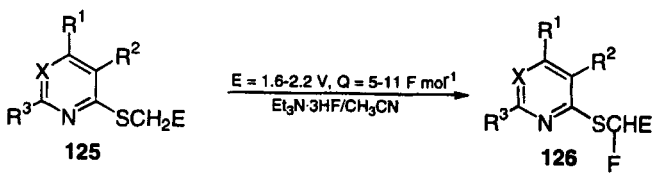
119 **120** [22 %] **121** [31 %]



122 **123** [51 %] **124** [30 %]

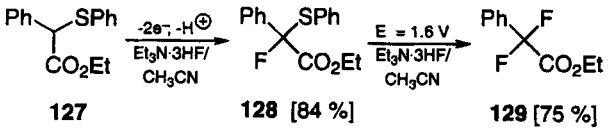
Furthermore, thioethers **125** bearing a nitrogen containing heterocycle at one side and an activated methylene function at the other have been selectively monofluorinated electrochemically in the presence of $Et_3N{\cdot}3HF$ to give **126** [61].

Phenyl sulfides bearing two substituents at the α-carbon can readily be fluorinated in constant-potential electrolysis on platinum electrode in acetonitrile solution of $Et_3N{\cdot}3HF$. For example **127** was fluorinated giving **128** with 84 % yield [62].



125 126

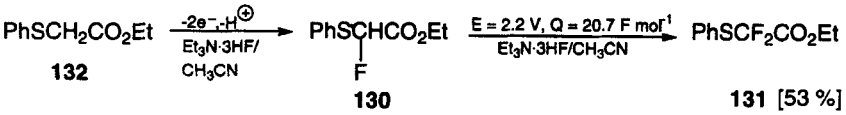
R¹	R²	R³	X	E	yield [%]
H	H	H	CH	CN	76
H	H	H	CH	COOEt	76
H	H	H	N	COOEt	55
CH_3	CN	CH_3	CH	CN	55
CH_3	CN	CH_3	CH	COOEt	45



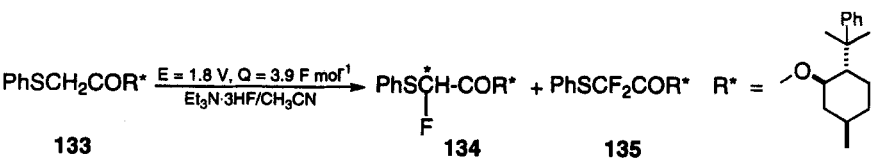
127 128 [84 %] 129 [75 %]

At a potential of 1.6 V in the presence of $Et_3N{\cdot}3HF$ the carbon-sulfur bond of **128** is cleaved and the intermediary formed fluorocarbenium ion is fluorinated to give the difluoro compound **129** [62].

On the other hand a similar procedure was applied to the synthesis of α,α-difluorosulfides. From monofluoride **130** the difluoride **131** was formed in 53 % yield. **131** could also be obtained directly by anodic fluorination of ethyl (phenylthio)acetate (**132**) [58].

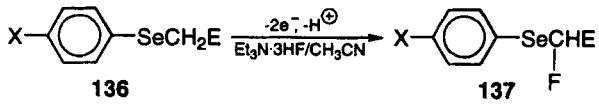


132 130 131 [53 %]



133 134 135

Similar to the diastereoselective electrofluorination of α-(p-methoxyphenyl)acetates **87** bearing enantiopure auxiliaries [49] the analogous α-phenylsulfenyl-acetates **133** bearing the same auxiliaries yield optically active compounds **134**, however, with much lower diastereoselectivity compared to the reactions of compounds **91**. This is explained by the different reaction mechanisms [2] [63]. Difluorides **135** were found as by-products [63].

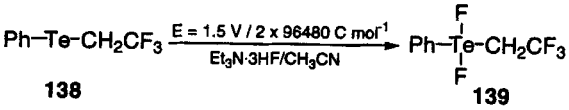


136 137

X = H, Cl, OMe
E = CN, CO_2Et, $CONH_2$

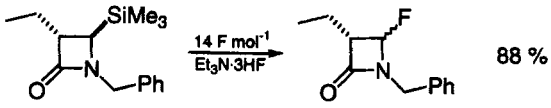
Analogous to the monofluorinations of phenylsulfides also phenylseleno ethers **136** bearing activated methylene groups give the corresponding α-fluorinated derivatives **137** in 51–81% yield [3] [64].

In contrast, the corresponding tellurides like **138** and several similar phenyltelluro compounds with or without activating groups did not give α-fluorination at the methylene group, but the tellurium has been difluorinated giving **139** in 86% yield [66].



138 139

The electrochemical procedure has also been used for substitution of substituents other than H-atoms with fluoride. Anodic oxidation of 4-trimethylsilylazetidin-2-ones **140** in the presence of $Et_3N{\cdot}3HF$ gives 4-fluoroazetidin-2-ones **141** in high yields under very mild conditions [67].



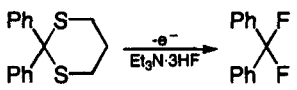
140 141 (m.d. 1 : 1)

3.3 Thioacetals and Hydrazones

From 2,2-diphenyl-1,3-dithiane **142** on electrofluorination the geminal difluoride **143** is formed in good yield [62].

[2]) A Pummerer-type mechanism has been suggested recently for the reactions of sulfides [60] instead of an ECEC-mechanism proposed earlier for the reactions of phenylacetates [46].

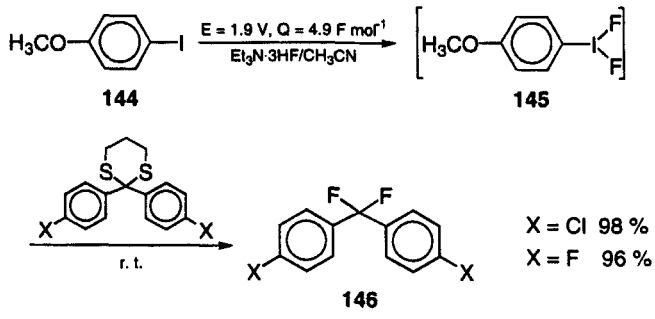
[3]) Interestingly it was noted that electrochemical α-methoxylations of phenylthio ethers or phenylseleno ethers bearing activated methylene groups were much more effective in the presence of $Et_3N{\cdot}3HF$/MeOH compared to the related reactions without the HF/amine reagent [59, 65]. This was suggested to be a proof for the Pummerer-type electrochemical fluorination of phenylsulfides [59].



142 143

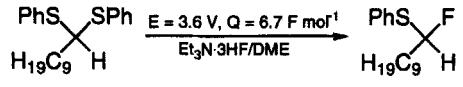
Several similar compounds including even dithioacetals of aliphatic and alicyclic ketones have been transformed in this way to the corresponding gem. difluorides [68].

Recently Fuchigami and Fujita reported the electrosynthesis of hypervalent p-nitro- and p-methoxyiodobenzene difluorides and the latter, **145**, has been used as a mediator (0.05 or 0.2 equivalents) for indirect anodic gem. difluorination of dithioacetales to form **146** [69].



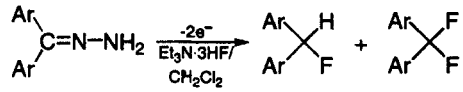
144 145 146

On the contrary, in diphenyl dithioacetals only one C-S bond is selectively cleaved. The diphenyldithioacetal **147** gave solely the monofluoride **148** in 54% yield [68].



147 148

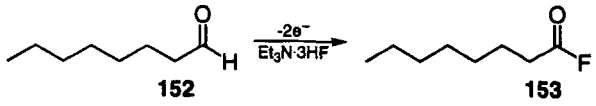
Similarly the electrochemical reaction of diarylketone hydrazones **149** in the presence of $Et_3N{\cdot}3HF$ in CH_2Cl_2 solution gives mainly the monofluorinated compounds **150** and some traces of the difluorides **151** [66].



149 150 151

Ar	current density mA cm^{-2}	150	151
Ph	1.3	95	3
p-ClC_6H_4	1.3	40	0
p-FC_6H_4	1.3	63	8
p-MeC_6H_4	1.3	16	1

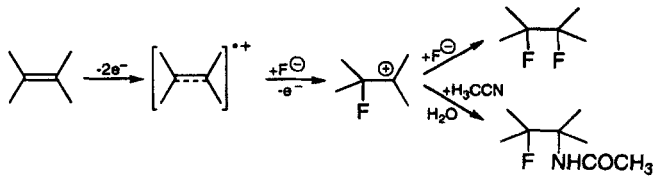
Selective electrochemical oxidation of aliphatic aldehydes like **152** in neat $Et_3N{\cdot}3HF$ or in acetonitrile solution leads to the corresponding acylfluorides, e.g. octanoyl fluoride **153** in 23% or 42% yields, respectively. However, a more acidic fluorinating agent, namely $Et_3N{\cdot}5HF$ gave even better yields (66–89%) for **153** and several other aliphatic aldehydes [71].



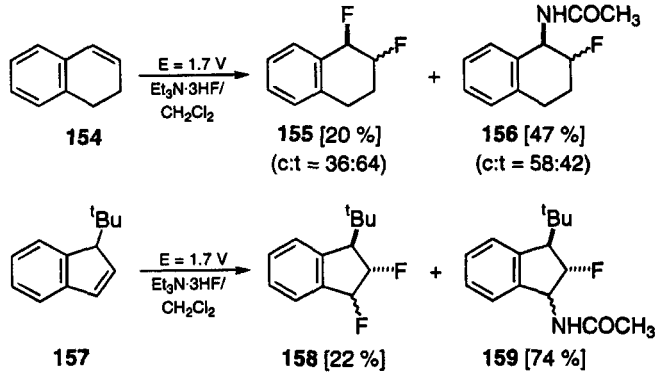
152 153

3.4 Olefins

The anodic oxidation of double bonds in the presence of fluorinating agents yields mixtures of *cis/trans* isomeric vicinal difluorides and products of solvent incorporation.



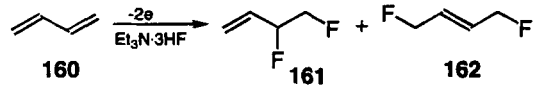
1,2-Dihydronaphthalene **154**, indene and 3-*tert*-butylindene **157** in acetonitrile solution of $Et_3N{\cdot}3HF$ give mixtures of diastereomeric difluorides **155** or **158** and the respective N-(ß-fluoroalkyl)acetamides **156** or **159**, while in methylene chloride the difluorides **158** (44:56) were formed in 67% yield [72].



154 155 [20 %] (c:t = 36:64) 156 [47 %] (c:t = 58:42)

157 158 [22 %] 159 [74 %]

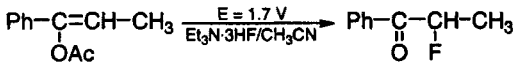
The electrofluorination of other alkenes like styrene, stilbene, 2,3-dimethylbut-2-ene or 2-methyl-2-butene with neat $Et_3N{\cdot}3HF$ leads to the corresponding vicinal difluorides in 22–51% yield and from butadiene **160** a 1:2 mixture of 1,2- and 1,4-products **161** and **162** is formed [73].



160 161 162

When enol esters are oxidized electrochemically in the presence of $Et_3N{\cdot}3HF$ after basic work up α-fluoroketones are produced in moderate yields. In this man-

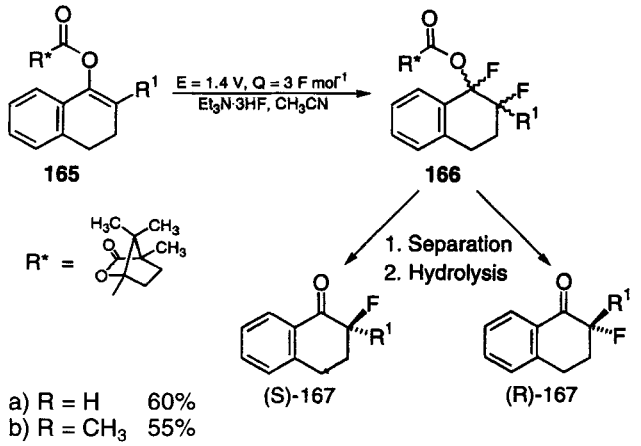
ner from **163** the α-fluoroketone **164** has been prepared in 65% yield [74].



163 **164**

Analogously, the enol acetates derived from acetophenone, benzylphenyl ketone, isopropylphenyl ketone, benzyl methyl ketone and tetralone give the corresponding α-fluoroketones [74].

From the sterically very hindered and optically active enol camphanate of α-tetralone **165a** and its ß-methyl derivative **165b** on electrofluorination gave a mixture of four diastereomers **166** in equal quantities, that means without asymmetric induction.



a) R = H 60%
b) R = CH_3 55%

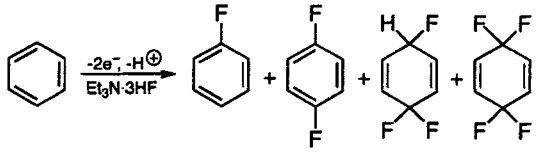
After chromatographic separation the diastereomers **166** on mild hydrolysis are transformed to the optically active ß-fluoro-α-decalones **167** in 65–70% chemical yield and >95% enantiomeric excess [75].

Moreover, the electrofluorination of vinyl sulfides gave vicinal difluorides in relatively attractive chemical yields, which in some cases are accompanied by geminal difluorides and some amount of fluorinated acetamides resulting from solvent participation. At higher potential a trifluorinated sulfide **170** was obtained in a one pot transformation of 2-(phenylthio)styrene (**168**) via the difluoride **169**. Other examples are described too [76].

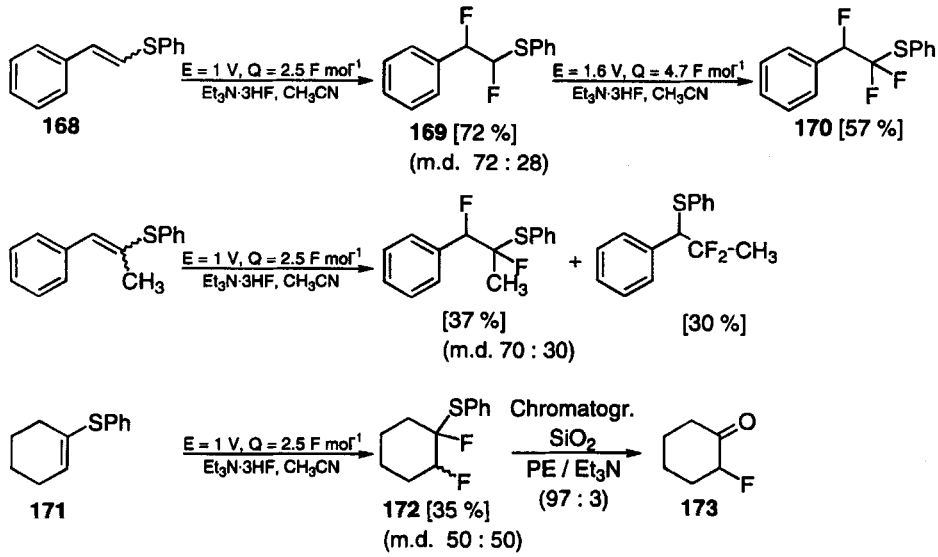
α,ß-Difluorosulfides of this type are sensitive to acids and bases and, therefore one diastereoisomer of (1,2-difluoro-cyclohexyl)-phenylthio ether (**172**) (obtained from **171**) on chromatography (SiO_2) in the presence of small amounts of triethylamine gave α-fluorocyclohexanone (**173**) [76].

3.5 Aromatic Compounds

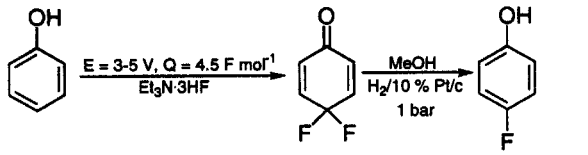
Selective monofluorination of aromatic compounds is difficult to achieve at high conversions because the ionization potentials of educts and products are very similar (e.g. benzene 9.25 eV, fluorobenzene 9.21 eV, p-difluorobenzene 9.15 eV). Consequently, benzene at a conversion of 86% on electrochemical oxidation in neat $Et_3N{\cdot}3HF$ yields a mixture of compounds shown below [45]. Better selectivity has been observed in acetonitrile solution [77]. Chlorobenzene and naphthalene produce mixtures of fluorinated compounds [45].



18 % 6 % 20 % 4 %

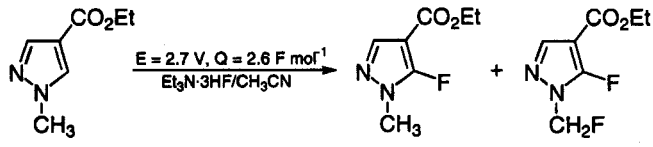


In the related reaction of phenol (**174**) 20% of 4,4-difluorocyclohexadienone (**175**) has been isolated, which on hydrogenation yielded 90% of 4-fluorophenol (**176**) [45].



174 **175** [20 %] **176** [90 %]

Also heteroaromatic compounds have been monofluorinated on a similar way. The anodic oxidation of ethyl 1-methylpyrazole-4-carboxylate (**177**) in acetonitrile solution of $Et_3N{\cdot}3HF$ produces a 93:7 mixture of **178** and **179** in 29% isolated overall yield [78].



177 **178** **179**

4 Nucleophilic Substitutions of Halogen Atoms with Fluorine in Organophosphorus Compounds

Triethylamine trishydrofluoride ($Et_3N{\cdot}3HF$) has been used for different substitutions of halogenides with fluoride at trivalent or pentavalent organophosphorus compounds. The reaction of triethylphosphite (**180**) or phosphorus trichloride with excess $Et_3N{\cdot}3HF$ in acetonitrile at room temperature gives 95% of triethylammonium-hydrido-pentafluorophosphate (**181**) [79].

$$P(OEt)_3 \xrightarrow[CH_3CN]{Et_3N\cdot 3HF} \overset{\oplus}{Et_3NH}\ \overset{\ominus}{HPF_5} + 3\ EtOH$$

180 **181**

Treatment of PCl_5 with $Et_3N{\cdot}3HF$ and additional Et_3N in acetonitrile yields triethylammoniumhexafluorophosphate (**182**) nearly quantitatively, while in the analogous reaction using a secondary amine for neutralization of the acidic fluorinating agent mainly (> 90 %) $PF_5{\cdot}HNEt_2$ is formed [80].

$$PCl_5 + 2\ Et_3N{\cdot}3HF + 4\ Et_3N \xrightarrow[CH_3CN]{} \overset{\oplus}{Et_3NH}\overset{\ominus}{PF_6} + 6\ Et_3NHCl$$

182

$$PCl_5 + {}^5/_3\ Et_3N{\cdot}3HF + {}^{13}/_3\ HNEt_2 \longrightarrow PF_5{\cdot}HNEt_2 + {}^5/_3\ Et_3NHCl + {}^{13}/_3\ Et_2NH_2Cl$$

By reaction of PCl_5 with $Et_3N{\cdot}3HF$ and a secondary or tertiary amine in the presence of ethanol or phenol the formation of the corresponding ammonium ethoxy (or phenoxy) pentafluorophosphate **183** is obtained in 39% and 68% yield, respectively [80].

$$PCl_5 + {}^5/_3\ Et_3N{\cdot}3HF + {}^{13}/_3\ Et_3N + ROH \longrightarrow \overset{\oplus}{Et_3NH}(RO)\overset{\ominus}{PF_5} + 5\ Et_3NHCl$$

183

The product **183** (R=Et) has been formed in 80% yield as well by oxidation of triethylphosphite (**180**) with CCl_4 in the presence of $Et_3N{\cdot}3HF$, Et_3N and EtOH in acetonitrile solution [81].

In the system $Et_2NH/CCl_4/Et_3N{\cdot}3HF$ elemental phosphorus P_4 is oxidized very fast forming $[HPF_5]^-$ as well as $Et_2NH{\cdot}PF_5$ and $(Et_2N)_2P(O)F$. In the case of simultaneous addition of alcohols $[(RO)PF_5]$, $(RO)_3PO$ and $(Et_2N)_2P(O)F$ are formed [81].

Dialkyl fluorophosphonates were prepared by fluorination of some phosphoric acid derivatives with $Et_3N{\cdot}3HF$. Thus, fluorination of $(EtO)_2P(O)ON{=}CCl_2$ with the reagent in acetonitrile gave 83.5% of $(EtO)_2P(O)F$ [82].

The reaction of phenyldichlorophosphane ($PhPCl_2$) with an equimolar amount (Cl:F = 1:1) of $Et_3N{\cdot}3HF$ did not give the expected instable $PhPF_2$, but mainly the disproportionation products $(PhP)_n$ and $PhPF_4$ [79]. With excess of $Et_3N{\cdot}3HF$ (in regard to Cl atoms) phenylhydridofluorophosphorane (**184**) was obtained [83].

$$PhPCl_2 + Et_3N{\cdot}3HF \longrightarrow PhPHF_3 + Et_3NHCl + HCl$$

184

Organyldifluorophosphanes (RPF_2) have been synthesized treating the corresponding chlorides with $Et_3N{\cdot}3HF$ in the presence of excess Et_3N [83].

$$3\ RPCl_2 + 2\ Et_3N{\cdot}3HF + 7\ Et_3N \longrightarrow 3\ RPF_2 + 3\ Et_3N + 6\ Et_3NHCl$$

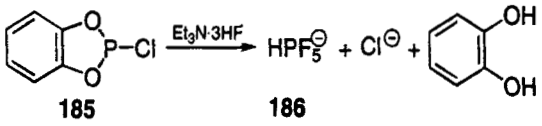
R = Ph, p-$MeOC_6H_4$, n-Bu

$$3\ R_2PCl + Et_3N{\cdot}3HF + 5\ Et_3N \longrightarrow 3\ R_2PF + 3\ Et_3N + 3\ Et_3NHCl$$

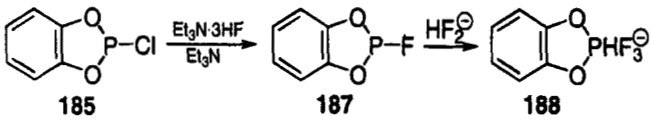
R = Ph, n-Bu, t-Bu

Reactions of cyclic phosphoric **185** or phosphonic compounds with $Et_3N{\cdot}3HF$ are strongly dependent on the stoichiometry. With excess of the acidic reagent $Et_3N{\cdot}nHF$ ($n > 1$) the pentafluorohydridophosphate **186** is formed, while by addition of more amine $Et_3N{\cdot}nHF$ ($n < 1$) and equimolar amounts of fluoride and phosphorus (F:P = 1) chlorine–fluorine exchange was obtained to form **187**. With a reagent combination (ratio $F:P \approx 3$) additionally the trifluorohydridophosphate **188** was formed [84].

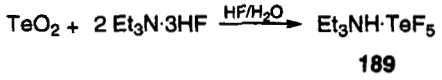
Triethylammonium pentafluorotellurate (IV) (**189**) has been prepared by the reaction of $Et_3N{\cdot}3HF$ with TeO_2 in aqueous hydrogen fluoride [85].



185 186



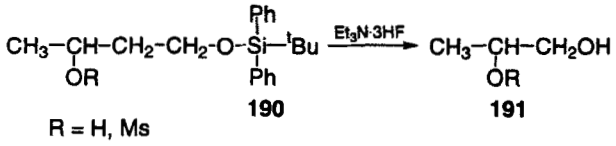
185 187 188



189

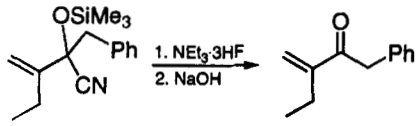
5 Deprotection of Silylethers

Triethylamine trishydrofluoride has successfully been used for the deprotection of silylethers. Treatment of the 1-*tert.*-butyldiphenylsilylether of 1,3-butanediol **190** or its 3-mesylate with this reagent gave the corresponding primary alcohols **191** with excellent yield [9].

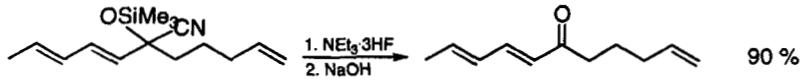


190 191

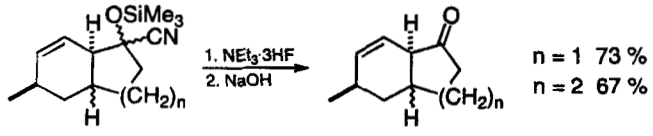
R = H, Ms



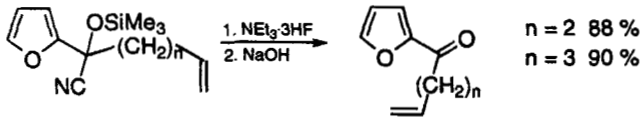
85 %



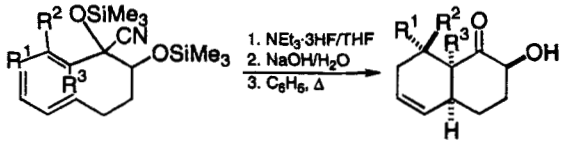
90 %



n = 1 73 %
n = 2 67 %



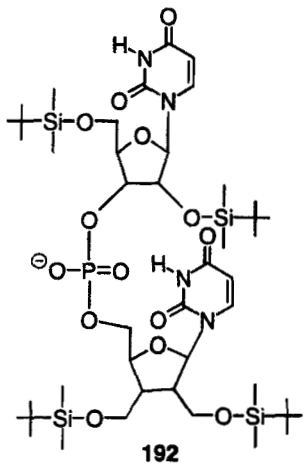
n = 2 88 %
n = 3 90 %



a) $R^1 = R^2 = H$, $R^3 = Me$
b) $R^1 = Me$, $R^2 = R^3 = H$
c) $R^1 = R^2 = Me$, $R^3 = H$

In the same way trimethylsilylated cyanohydrines derived from ketones can be desilylated [86].

The reagent has been reported to be a more efficient desilylating agent than tetrabutylammonium fluoride in deprotection of a *tert.*-butyldimethylsilylether of a synthetic t-RNA [87] and has been shown to be quite safe with respect to migration of phosphodiester linkages in



192

deprotection of silylated oligoribonucleotides like 2',5'-di-O-tert.-butyl-dimethylsilyluridine-3'-(2',3'-di-O-*tert.*-butyldimethyl-silyluridine-5'-phosphate) (**192**) as a model substrate [88].

For the deprotection of several nucleosides and nucleotides bearing disiloxane, *tert.*-butyldimethylsilyl and *tert.*-butyldiphenylsilyl groups 4–10 equivalents of $Et_3N{\cdot}3HF$ in THF were used giving the deprotected compounds in good yields [89].

References

[1] G. Aranda, J. Jullien, J. A. Martin, Bull. Soc. Chim. Fr. **1965**, 1890; G. Aranda, J.Jullien, J. A. Martin, Bull. Soc. Chim. Fr. **1966**, 2850
[2] R. Franz, J. Fluorine Chem. **15** (1980) 423
[3] M. B. Giudicelli, D. Picq, B. Veyron, Tetrahedron Lett. **31** (1990) 6527
[4] H. Muffler, R. Franz, Ger. Offen. 2.823.969 to Hoechst AG; Chem. Abstr. **92** (1980) 197322k
[5] M. Bimmler, M. von Janta-Lipinski, P. Langer, H. Plaul, Ger. (East) DD 221.736 to Akademie der Wissenschaften der DDR; Chem. Abstr. **104** (1986) 68880h
[6] R. Miethchen, G. Kolp, D. Peters, J. Holz, Z. Chem. **30** (1990) 56
[7] R. Miethchen, G. Kolp, J. Fluorine Chem. **60** (1993) 49
[8] R. Miethchen, C. Zur, J. Prakt. Chem. **337** (1995) 159
[9] D. Picq, D. Anker, Carbohydr. Res. **166** (1987) 309
[10] D. Picq, D. Anker, J. Carbohydrate Chem. **4** (1985) 113
[11] P. Nebois, D. Picq, D. Anker, J. Carbohydrate Chem. **9** (1990) 359
[12] H. H. Baer, F. H. Mateo, L. Siemsen, Carbohydr. Res. **187** (1989) 67
[13] T. Haradahira, M. Maeda, H. Omae, Y. Yano, M. Kojima, Chem. Pharm. Bull. **32** (1984) 4758; D. Picq, I. Drivas, G. Carret, D. Anker, Tetrahedron **41** (1985) 2681
[14] M. von Janta-Lipinski, P. Langen, D. Czech, Z. Chem. **23** (1983) 325
[15] C. Saluzzo, G. Alvernhe, D. Anker, G. Haufe, J. Fluorine Chem. **47** (1990) 467
[16] A. N. Payne, S. M. Roberts, J. Chem. Soc., Perkin Trans. I **1992**, 2633
[17] G. Alvernhe, A. Laurent, G. Haufe, J. Fluorine Chem. **34** (1986) 147
[18] S. Pietz, G. Haufe, unpublished
[19] G. Gargaro, M. A. Loreto, L. Pellacani, P. A. Tardella, J. Org. Chem. **48** (1983) 2043
[20] G. Farges, A. Kergomard, Bull. Soc. Chim. Fr. **1975**, 315
[21] T. Hamatani, S. Matsubara, H. Matsuda, M. Schlosser, Tetrahedron **44** (1988) 2875
[22] A. Sattler, G. Haufe, J. Fluorine Chem. **69** (1994) 185
[23] J. Jünnemann, I. Lundt, J. Thiem, Acta Chem. Scand. **48** (1994) 265
[24] M. M. Chaabouni, A. Baklouti, Bull. Soc. Chim. Fr. **1989**, 549
[25] A. Hedhli, A. Baklouti, J. Fluorine Chem. **70** (1995) 141
[26] M. Bols, I. Lundt, Acta Chem. Scand. **44** (1990) 252
[27] A. Müller, U. Roth, S. Siegert, R. Miethchen, Z. Chem. **26** (1986) 169
[28] N. Yoneda, Tetrahedron **47** (1991) 5329; J. A. Wilkinson, Chem. Rev. **92** (1992) 505
[29] G. Haufe, G. Alvernhe, A. Laurent, Tetrahedron Lett. **27** (1986) 4449
[30] G. Alvernhe, A. Laurent, G. Haufe, Synthesis **1987**, 562
[31] G. Alvernhe, D. Anker, A. Laurent, G. Haufe, C. Beguin, Tetrahedron **44** (1988) 3551
[32] G. Haufe, G. Alvernhe, A. Laurent, O. Goj, S. Kröger, A. Sattler, Organic Syntheses, submitted for publication
[33] H. Suga, T. Hamatani, Y. Guggisberg, M. Schlosser, Tetrahedron **46** (1990) 4255
[34] I. Chehidi, M. M. Chaabouni, A. Baklouti, Tetrahedron Lett. **30** (1989) 3167
[35] A. Hedhli, A. Baklouti, J. Org. Chem. **59** (1994) 5277
[36] G. Haufe, U. Weßel, K. Schulze, G. Alvernhe, J. Fluorine Chem. **74** (1995) 283
[37] A. Sattler, G. Haufe, Tetrahedron, submitted for publication
[38] D. Limat, Y. Guggisberg, M. Schlosser, Liebigs Ann. Chem. **1995**, 849
[39] G. Haufe, G. Alvernhe, A. Laurent, J. Fluorine Chem. **46** (1990) 83
[40] G. Haufe, G. Alvernhe, D. Anker, A. Laurent, C. Saluzzo, J. Org. Chem. **57** (1992) 714
[41] C. Saluzzo, A.-M. LaSpina, D. Picq, G. Alvernhe, D. Anker, D. Wolf, G. Haufe, Bull. Soc. Chim. Fr. **131** (1994) 831
[42] C. Saluzzo, G. Alvernhe, D. Anker, G. Haufe, Tetrahedron Lett. **31** (1990) 2127
[43] Synthetic Fluorine Chemistry, G. A. Olah, R. D. Chambers, G. K. S. Prakash, Eds., Wiley, New York, 1992
[44] W. V. Childs, L. Christensen, F. W. Klink, C. F. Kolpin, in: Organic Electrochemistry, 3rd Ed., H. Lund, M. M. Baizer, Eds., Marcel Dekker, N.Y. 1991, Chapter 26; T. Fuchigami, A. Konno, Current Topics in Electrochemistry, Council of Scientific Research Integration, Ed., Research Trends: Trivandum, 1993, Vol. 2, p. 155
[45] J. H. H. Meurs, D. W. Sopher, W. Eilenberg, Angew. Chem. **101** (1989) 955; Angew. Chem. Int. Ed. Engl. **28** (1989) 927
[46] E. Laurent, B. Marquet, R. Tardivel, Tetrahedron **45** (1989) 4431
[47] E. Laurent, B. Marquet, R. Tardivel, J. Fluorine Chem. **49** (1990) 115
[48] E. Laurent, B. Marquet, R. Tardivel, Tetrahedron **47** (1991) 3969
[49] L. Kabore, S. Chebli, R. Faure, E. Laurent, B. Marquet, Tetrahedron Lett. **31** (1990) 3137
[50] T. Fuchigami, Rev. Heteroatom Chem. **10** (1994) 155
[51] T. Brigaud, E. Laurent, Tetrahedron Lett. **31** (1990) 2287
[52] T. Fuchigami, M. Shimojo, A. Konno, J. Org. Chem. **60** (1995) 3459
[53] A. Konno, W. Naito, T. Fuchigami, Tetrahedron Lett. **33** (1992) 7017
[54] S. Narizuka, T. Fuchigami, J. Org. Chem. **58** (1993) 4200
[55] S. Narizuka, A. Konno, H. Matsuyama, T. Fuchigami, J. Electrochem. Soc. Jpn. **61** (1993) 868
[56] S. Narizuka, T. Fuchigami, Bioorg. Med. Chem. Lett. **5** (1995) 1293
[57] T. Fuchigami, S. Narizuka, A. Konno, J. Org. Chem. **57** (1992) 3755
[58] T. Fuchigami, M. Shimojo, A. Konno, K. Nakagawa, J. Org. Chem. **55** (1990) 6074
[59] A. Konno, K. Nakagawa, T. Fuchigami, J. Chem. Soc., Chem. Commun. **1991**, 1027; A. Konno, T. Fuchigami, J. Appl. Electrochem. **25** (1995) 173

[60] T. Fuchigami, A. Konno, K. Nakagawa, M. Shimojo, J. Org. Chem. **59** (1994) 5937
[61] A. W. Erian, A. Konno, T. Fuchigami, Tetrahedron Lett. **35** (1994) 7245
[62] T. Brigaud, A. Laurent, E. Laurent, Phosphorus, Sulfur, and Silicon **59** (1991) 153
[63] S. Narizuka, H. Koshiyama, A. Konno, T. Fuchigami, J. Fluorine Chem. **73** (1995) 121
[64] T. Fuchigami, T. Hayashi, A. Konno, Tetrahedron Lett. **33** (1992) 3161
[65] K. Surowiec, T. Fuchigami, Tetrahedron Lett. **33** (1992) 1065
[66] T. Fuchigami, T. Fujita, A. Konno, Tetrahedron Lett. **35** (1994) 4153
[67] K. Suda, K. Hotoda, M. Aoyagi, T. Takanami, J. Chem. Soc., Perkin Trans. I **1995**, 1327
[68] T. Yoshiyama, T. Fuchigami, Chem. Lett. **1992**, 1995
[69] T. Fuchigami, T. Fujita, J. Org. Chem. **59** (1994) 7190
[70] T. Fuchigami, M. Sano, K. Jio, J. Electroanalytical Chem. **369** (1994) 255
[71] N. Yoneda, S.-Q. Chen, T. Hatakeyama, S. Hara, T. Fukuhara, Chem. Lett. **1994**, 849
[72] E. Laurent, H. Lefranc, R. Tardivel, Nouv. J. Chim. **8** (1984) 345
[73] J. H. H. Meurs, W. Eilenberg, Tetrahedron **47** (1991) 705
[74] E. Laurent, B. Marquet, R. Tardivel, H. Thiebault, Bull. Soc. Chim. Fr. **1986**, 955
[75] F. M. Ventalon, R. Faure, E. G. Laurent, B. S. Marquet, Tetrahedron Asymm. **5** (1994) 1909
[76] D. F. Andres, E. G. Laurent, B. S. Marquet, H. Benotmane, A. Bensadat, Tetrahedron **51** (1995) 2605
[77] K. Momota, M. Morita, Y. Matsuda, Electrochim. Acta **38** (1993) 619
[78] K. Makino, H. Yoshioka, J. Fluorine Chem. **39** (1988) 435
[79] L. Riesel, M. Kant, Z. Chem. **24** (1984) 382
[80] L. Riesel, M. Kant, Z. Anorg. Allg. Chem. **530** (1985) 207
[81] L. Riesel, M. Kant, Z. Anorg. Allg. Chem. **531** (1985) 73
[82] S. J. Zavorin, S. A. Lermotov, J. V. Martynov, Izv. Akad. Nauk SSSR, Ser. Khim. **1988**, 1174.
[83] L. Riesel, D. Lindemann, Z. Anorg. Allg. Chem. **603** (1991) 145
[84] L. Riesel, J. Haenel, Z. Anorg. Allg. Chem. **615** (1992) 66
[85] J. Carré, M. Siniti, J. Fluorine Chem. **60** (1993) 27
[86] U. Hertenstein, S. Hünig, H. Reichelt, R. Schaller, Chem. Ber. **119** (1986) 722; K. Fischer, S. Hünig, Chem. Ber. **119** (1986) 3344; K. Fischer, S. Hünig, Chem. Ber. **119** (1986) 2590; K. Fischer, S. Hünig, J. Org. Chem. **52** (1987) 564
[87] D. Gasparutto, T. Livache, H. Bazin, A.-M. Duplaa, A. Guy, A. Khorlin, D. Molko, A. Roget, R. Téoule, Nucleic Acids Res. **20** (1992) 5159; A.-M. Duplaa, D. Gasparutto, T. Livache, D. Molko, R. Teoule, PTC Int. Appl. WO 93 07.164 to Commissariat a l'Energie Atomique; Chem. Abstr. **119** (1993) 199176r
[88] E. Westmann, R. Strömberg, Nucleic Acids Res. **22** (1994) 2430
[89] M. C. Pirrung, S. W. Shney, D. C. Lever, L. Fallon, Bioorg. Med. Chem. Lett. **4** (1994) 1345

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