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[3,3]-Sigmatropic rearrangements as a method of organofluorine synthesis

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Abstract. Literature data on [3,3]-sigmatropic rearrangements of organofluorine compounds are surveyed and described systematically in terms of the type of substances and intermediates involved in the rearrangements. The characteristic features of these reactions are considered as a function of the structure of the isomerising molecules and the positions in the latter of fluorine atoms and fluorine-containing substituents. The possibilities arising from the use of the [3,3]-sigmatropic rearrangements for the specific synthesis of fluorine-containing compounds belonging to particular classes are assessed. The bibliography includes 180 references.

I. Introduction

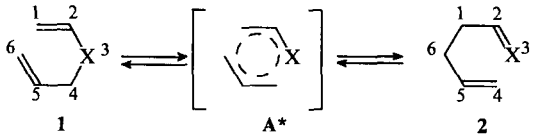
The [3,3]-sigmatropic rearrangements, which include the Claisen and Cope rearrangements, as well as their different modifications (Carroll, Ireland–Claisen, Johnson–Claisen, etc. rearrangements) and their numerous versions based on unsaturated compounds with hetero- and functional-group substituents constitute one of the most important synthetic methods in modern organic chemistry.

This type of intramolecular rearrangements was discovered by Claisen[1] in 1912 in relation to the thermal transformations of the allyl ethers of phenol and 2-naphthol into the corresponding *C*-allyl derivatives. Later similar reactions were investigated for a large number of substituted allyl (propargyl) aryl ethers, which made it possible to develop high-temperature synthesis of a wide variety of unsaturated aryl-substituted aliphatic substances (see the relevant reviews[2–4]).

The extension of the Claisen rearrangement to aliphatic and alicyclic systems (ethers, sulfides, and amines) as well as heteroaromatic compounds and the discovery of the Cope rearrangement[5] and its modifications converted the [3,3]-sigmatropic reactions into a universal method for the specific construction of the carbon skeletons of compounds containing multiple bonds in the 1,5-positions relative to one another. The principal advances in the last two decades of the study of the Claisen and Cope rearrangements have been described in a number of reviews[6–13] and numerous data on hetero-[3,3]-sigmatropic rearrangements are available in other reviews.[14–18]

The [3,3]-sigmatropic rearrangements are irreplaceable in the syntheses of many substances with a complex structure. For example, effective methods for the synthesis of polyenes have been developed on the basis of consecutive [3,3]-sigmatropic rearrangements,[13] while certain versions of the Cope aza-rearrangement have been used to synthesise the previously unavailable nitrogen-containing polycyclic systems.[17, 18] However, the importance of these reactions is mainly associated with the total synthesis of polyfunctional unsaturated compounds, the preparation of which by other methods usually involves several stages.

The extensive synthetic possibilities of the [3,3]-sigmatropic reactions are responsible for the continued interest in the theoretical aspects of these reactions. In accordance with the ideas of Woodward and Hoffman,[19] the [3,3]-sigmatropic rearrangements are assigned to the class of unimolecular pericyclic reactions. They take place as thermal concerted processes in accordance with the general **1** → **2** mechanism predominantly via a six-centre quasi-aromatic transition state of type **A***.



1 **A*** **2**

X = CH_2, O, S, Se, NH.

The most preferred pathway in these reactions involves a supra-suprafacial formation of the transition state **A*** in the chair form.[6, 13, 19] This is the reaction for the high effectiveness of the stereochemical control of the rearrangements, which frequently lead to the enantioselective formation of a C–C bond. By virtue of this, they are widely used in asymmetric synthesis,[20, 21] primarily for the preparation of biologically active natural products and their analogues.[22–26]

The formation of the transition state **A*** in the aliphatic Claisen rearrangement (in contrast to the purely carbon systems) is accompanied by an appreciable charge separation,[27] i.e. is a charge-controlled process, which leads to extensive possibilities for controlling it. Thus the rate of the [3,3]-sigmatropic reactions increases by 2–6 orders of magnitude in the presence of polar solvents or catalysts stabilising the zwitter-ionic or ionic states of the intermediates.[9, 10] The principal reagents generating anions

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derived from the initial substrates exert an even stronger influence. For example, the rate of the sigmatropic shift in the Cope oxy-rearrangement increases by a factor of $10^{10}-10^{17}$ if the reaction intermediate is the anion formed when the substrate is acted upon by metal hydrides.[28] A similar acceleration is observed in the carbanionic Claisen rearrangements[29-32] and in all these reactions the temperature of the rearrangement is reduced sharply. A similar but less marked effect may be produced by substituents at the multiple bonds of allyl vinyl ethers **1**, which enhance the π-donor properties of the 'vinyl' and/or the π-acceptor properties of the 'allyl' fragments.[29, 33-35] Thus the [3,3]-sigmatropic rearrangements, which had been previously considered as hard thermal processes, can be achieved as soft chemo-, regio-, and stereo-selective transformations of 1,5-diene systems.

The mild conditions and the high rate of the reactions are especially characteristic of the relatively little investigated [3,3]-sigmatropic rearrangements of fluorine-containing unsaturated compounds. The anomalous behaviour of aliphatic fluoro-compounds in reactions of this type was first described in 1967 by Krespan in the paper "Negative substituents in the Claisen rearrangements".[36] The unexpected results of this study, which has since become classical, have served as a powerful stimulus to the more extensive use of [3,3]-sigmatropic rearrangements of compounds of the organofluorine series. It was shown subsequently[37] that not only the specific features of the electronic effects of the fluorine atoms and the fluoroalkyl groups but also the special nature of the double bond in the fluorinated olefins, which tends to combine with fluorine and alkoxide ions to form carbanions, exerts a significant influence on the conditions and nature of the reactions of the fluorine-containing substrates.

The rearrangements of the allyl and propargol ethers of polyfluorophenols polyfluorocycloenols, and aliphatic polyfluorophenols as well as the esters of the polyfluorocarboxylic acids and polyfluoroallyl ethers have been investigated. However, until recently there were no surveys of data concerning the [3,3]-sigmatropic rearrangements as a method of organofluorine synthesis. In the reviews published recently,[37, 38] only individual aspects of the problem are considered which emphasises still further its timeliness.

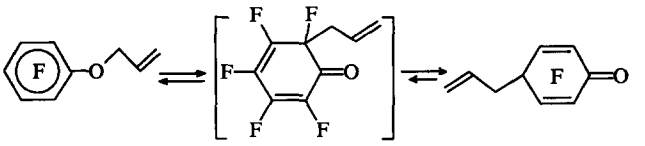
In the present review, an attempt is made for the first time to survey fully and to give systematic account of data on the [3,3]-sigmatropic reactions of fluorine-containing compounds and to assess the possibilities and prospects of their use for the specific synthesis of new organic derivatives of fluorine.

The review is not concerned with the Cope rearrangements (see the relevant communications[38-43]), because studies on the thermodynamic, kinetic, and stereochemical effects of fluorine and the trifluoromethyl group in these reactions are of no preparative value.

II. Rearrangements of polyfluoroaryl ethers

Allyl(propargyl) aryl and allyl heteroaryl ethers and sulfides fully or partly fluorinated in the aromatic ring as well as the corresponding phenyl trifluoromethyl ethers and phenyltrifluoromethylamines have now been involved in the Claisen rearrangement or its different versions. The most interesting results have been obtained in the study of the rearrangements of compounds with aromatic perfluoro-fragments in the gas phase and in solutions. The characteristic features of these reactions were elucidated in an excellent series of studies by Brooke[44-53, 56-60] in relation to perfluorinated phenyl, 2-naphthyl, 2-, 3-, and 4-pyridyl, quinolin-2(4)-yl, and pyrimidin-4-yl ethers.

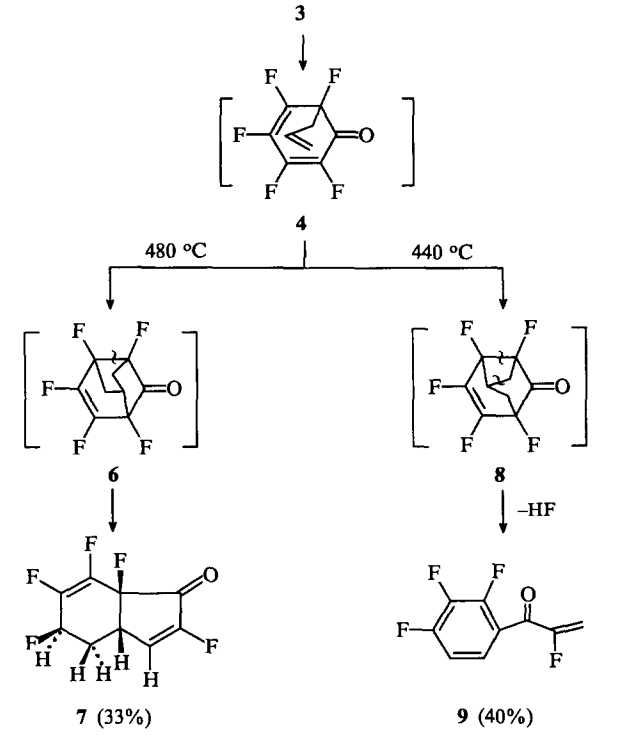
In contrast to allyl phenyl ether,[6, 54] heating of allyl pentafluorophenyl ether **3** in the gas phase at 137–141 °C (for 13 days) or at 365 °C leads to the *para*-rearrangement product 4-allylpentafluorocyclohexa-2,5-dien-1-one **5** and not to the expected *ortho*-rearrangement product the 2,4-dien-1-one **4**.[44, 45]



3 **4** **5**

The yield of compound **5** increases from 10% to 32% with increase in temperature. The absence of the dienone **4** among the reaction products is associated with its low thermodynamic stability, its ability to undergo reversible isomerisation to the ether **3**, and also its tendency to undergo side reactions.[45]

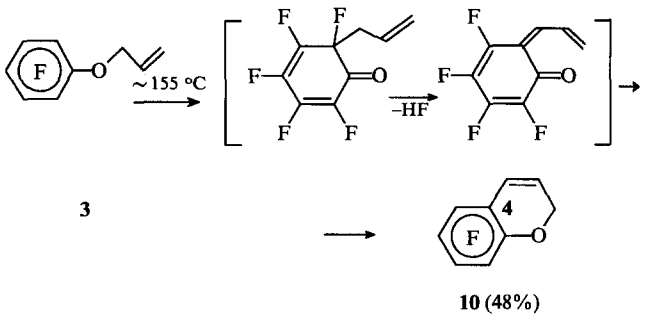
Indeed, the gas-phase pyrolysis of compound **3** at 440 °C–480 °C in a quartz tube filled with siloxane fibre affords either pentafluorotetrahydroinden-1-one **7**[46] or 1'-fluorovinyl 2,3,4-trifluorophenyl ketone **9** mixed with compound **7** as the main product.[47] Their appearance is explained by the alternative transformations of the dienone **4** into the intermediate tricycloketones **6** and **8**, which are formed as the stereoisomeric adducts as a result of the intramolecular Diels–Alder [4 + 2]-cycloaddition.[46, 47]



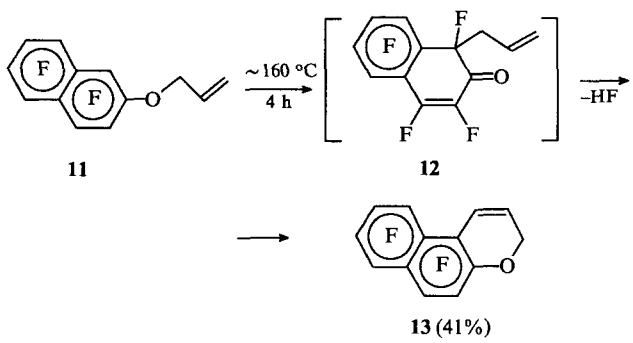
Under these conditions (480 °C), the dienone **5** is also converted into compound **7** in 28% yield, which demonstrates the reversibility of the rearrangements **4** ⇄ **5** under severe conditions.[46]

It was possible to isolate the tricyclic ketone **8** after the low-temperature (137–141 °C and 13 days) thermolysis of compound **3** in the gas phase.[48] This compound, which is the first carbocyclic Diels–Alder adduct obtained in the rearrangement of an allyl aryl ether, was characterised by spectroscopic methods and by conversion into a hemihydrate,[48] which was subsequently obtained also from compound **3** but without the intermediate isolation of compound **8**.[45]

Another type of reaction of the ether **3** take place in the liquid phase (DMF, refluxing, 4 h) in the presence of potassium fluoride.[49] In this case, the temperature of the rearrangement of the ether **3** is appreciably reduced compared with the temperature of the isomerisation of the allyl phenyl ether,[6, 54] while the primary *ortho*-rearrangement product **4** undergoes successive dehydrofluorination and intramolecular electrocyclisation to tetrafluoro-2*H*-1-benzopyran **10**.



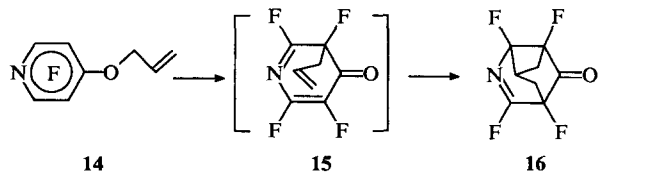
Allyl heptafluoro-2-naphthyl ether **11** is similarly converted into 5,6,7,8,9,10-hexafluoro-2*H*-napththopyran **13** in the KF/sulfolan system.[49]



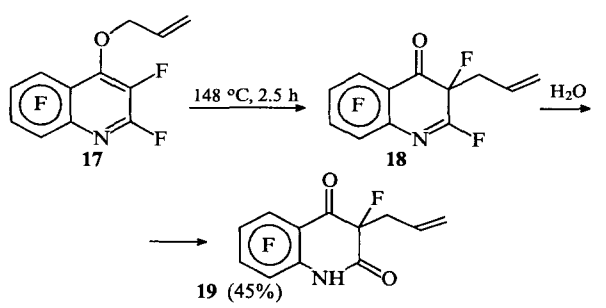
However, at 135 °C in xylene the ether **11** isomerises smoothly, in 64% yield, to the *ortho*-rearrangement product 1-allylheptafluoronaphthalen-2-one **12**, which is stable, in contrast to compound **4**.[50]

The structural rearrangements occurring in the [3,3]-sigmatropic rearrangements of allyl tretralfluoropyridyl and allyl hexafluoroquinolinyl ethers are in many respects similar to the reactions of allyl perfluoroallyl ethers examined above. The mode of these reactions is determined primarily by the position of the allyloxy-group relative to the nitrogen atom and they occur as a rule under milder conditions than the rearrangements of the non-fluorinated analogues.[6, 12]

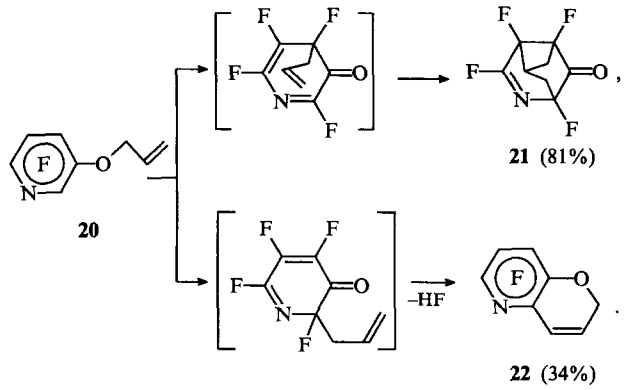
Thus the low-temperature gas-phase thermolysis (138 °C, 10 h) of allyl tetrafluoro-4-pyridyl ether **14** leads to the tricyclic ketone **16** in a yield up to 25%. This compound is formed as a result of the stabilisation via the [4 + 2]-cycloaddition of the product **15** of the *ortho*-rearrangement.[51]



On the other hand, when allyl hexafluoroquinolin-4-yl ether **17** is refluxed in *o*-xylene the stable product of the *ortho*-rearrangement is produced—the quinolinone **18**, which readily hydrolyses to the dione **19** during isolation.[52]

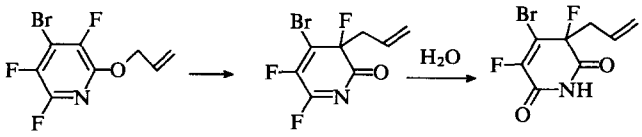


Allyl tetrafluoro-3-pyridyl ether **20** is converted under conditions more severe than for the ether **14** (gas phase, 185 °C, 113 h), into the tricyclic ketone **21**,[51] whilst heating in sulfolan in the presence of KF (nickel flask, 184 °C, 4 h) leads to its conversion into 6,7,8-trifluoro-2*H*-pyranopyridine **22**.[49]



The opposite direction of migration of the allyl group in the [3,3]-sigmatropic shift in the second reaction is explained by the strong influence of the protophilic solvent.[49]

It is of interest to note that, in contrast to the ethers **14** and **20**, the rearrangement of allyl 4-bromo-3,5,6,-trifluoro-2-pyridyl ether **23** is completed, even after prolonged heating in the gas phase (160 °C, 139 h), by the formation of the stable product **24** of the *ortho*-C-migration of the allyl group, which is hydrolysed during isolation to 3,4-dehydropiperidinedione **25**. The degree of conversion of the ether **23** is 38%.[51]

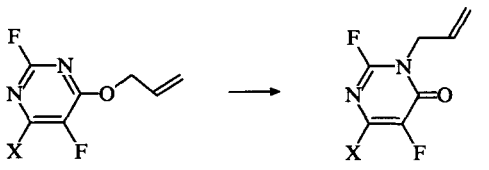


The formation of the *N*-allyl-substituted product was not detected in this reaction.

Nevertheless the migration of the allyl group exclusively to the nitrogen atom is characteristic of the thermal reactions of allyl hexafluoroquinolin-2-yl and allyl hexafluoroisoquinolin-1-yl ethers in tetralin (212 °C, 48 h). These rearrangements result in the formation of fluorine-containing *N*-allylquinolinone **26** and *N*-allylisoquinolinone **27** in satisfactory yields.[52]



The rearrangements of allyl polyfluoropyrimidin-4-yl ethers **28** take place with much more difficulty. The products **29** of the [3,3]-sigmatropic shifts were obtained from the ethers **28** in 53%–67% yields only at 440–475 °C under the conditions of gas-phase pulsed pyrolysis.[53]



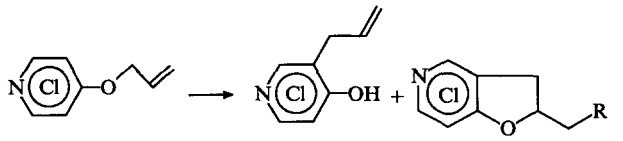
28 29

X = H, F, OMe.

The probability of the migration of the allyl group to the N(3) atom in this reaction proved significantly higher than that of the migration to the C(5) atom, which made it possible to develop on its basis a new approach to the preparative synthesis of derivatives of 5-fluorouracil and barbituric acid.[53]

Evidently the features of the [3,3]-sigmatropic rearrangement of allyl perfluoroaryl and allyl polyfluoroheteroaryl ethers noted above can be explained primarily by the high $+E$ contributions of the fluorine atoms to the aromatic and conjugated cyclohexa-2,4-diene systems and also by the reaction conditions. These factors are responsible, in the first place, for the enhancement of the π-donor properties of the aryl fragment and hence for the appreciably milder, compared with the non-fluorinated analogues, conditions in the Claisen rearrangement, which is completed (in aprotic solvents) by the formation of stable *ortho*-rearrangement products — bicyclic 2-aryl ketones incapable of isomerising to the corresponding *ortho*-hydroxyallyl derivatives. In the second place, they are responsible for the higher probability of the stabilisation of the intermediate 2,4-dienones either (in the gas phase) via the intramolecular [4 + 2]-cycloaddition or (in protophilic media) via dehydrofluorination, with subsequent electrocyclisation.

By virtue of the influence of the fluorine atoms, the Claisen rearrangements of aromatic polyfluoro-compounds and the subsequent reactions of the *ortho*-rearrangement products are unique. Even chlorine, which is very close to fluorine as regards the electromeric contribution, is incapable of altering quite so radically the traditional modes of these reactions. Thus allyl tetrachloro-4-pyridyl ether **30** isomerises under conditions more severe than in the case of compound **14** (sulfolan, 190 °C, 1.5 h).[55] The product of the *ortho*-rearrangement of the ether **30** does not exhibit a tendency to undergo any of the transformations examined above and is stabilised by a homolytic mechanism with formation of a mixture of allyl-2,5,6-trichloro-4-hydroxypyridine **31** and fluoropyridines **32**.

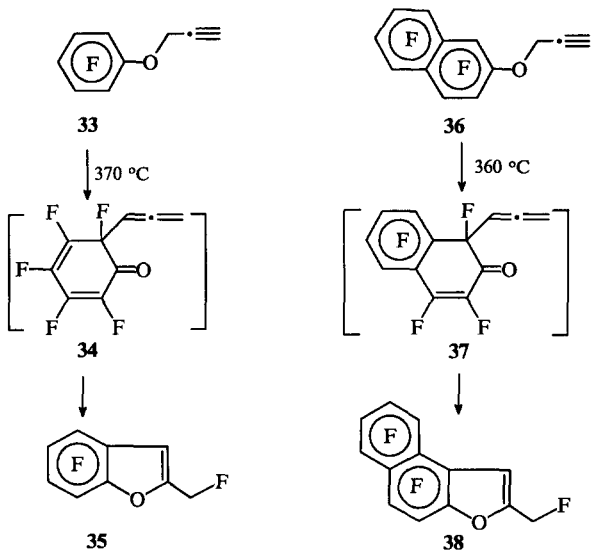


30 31 (26%) 32 (16.5%)

R = H, Cl.

The data obtained by Brooke and coworkers[56-60] in the study of the rearrangements of pentafluorophenyl propargyl ether **33** and heptafluoro-2-naphthyl propargyl ether **36** confirm the strong influence of the perfluoroallyl groups on the nature of the [3,3]-sigmatropic shift. The gas-phase pyrolysis of the ethers **33** and **36** at 360–370 °C leads to tetrafluorobenzofuran **35**[56] and hexafluoronaphthofuran **38**[57, 58] in 8% and 43% yields respectively. The polyfluorofuranes are formed as a result of the electrocyclisation of the intermediate *ortho*-rearrangement products **34** and **37** accompanied by the [1,4]-fluorotropic shift.

In solutions, these rearrangements occur already at 140 °C–150 °C, the structure of the final products being determined under these conditions by the nature of the solvents employed. The maximum selectivity in the formation of compounds **35** (yield 17%) and **38** (yield 81%) is observed in solution in Khladon 113 [Freon 113].[58] In solvents of the π-donor type (benzene, *p*-xylene),



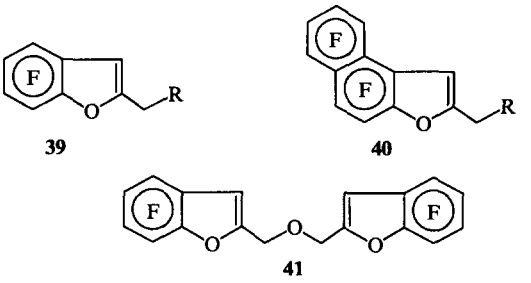
33 36

370 °C 360 °C

34 37

35 38

the products of the incorporation of the solvents into the molecules of the annelated furans **39** and **40** are formed together with compounds **35** and **38**.[56] In addition an appreciable amount (11%–18%) of the ether **41** is formed from the ether **33** in Khladon 113 and benzene.[58, 59]



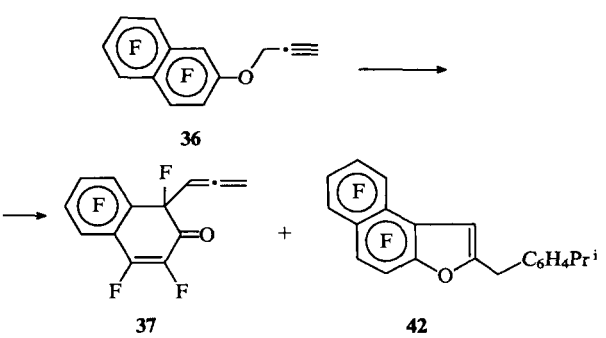
39 40

41

For **39**: R = Ph (28%), 2,5-$Me_2C_6H_3$ (21%);
For **40**: R = Ph (64%), 2,5-$Me_2C_6H_3$ (73%).

When the ether **33** is isomerised in *N*,*N*-diethylaniline (153 °C, 134 h), the latter solvent is also incorporated into the structure of the final furan, but numerous products of side reactions of the initial compound are mainly formed in the given reaction.[60] On the other hand, the rearrangement of the fluorine-free phenyl propargyl ether in boiling *N*,*N*-diethylaniline proceeds relatively smoothly and affords 2*H*-1-benzopyran (yield 2%) as the main product, formed on cyclisation of the intermediate products of the *ortho*-rearrangement.[6]

Interesting results have been obtained in the study of the rearrangement of the ether **36** in isopropylbenzene (155 °C, 24 h),[59] where the naphthalenone **37**, which is a stable compound, was isolated in 10% yield together with the naphthofuran **42**.



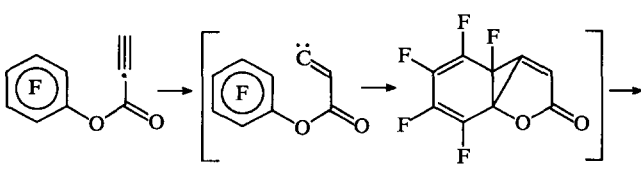
36

37 42

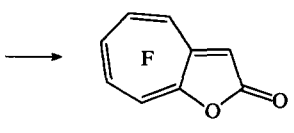
The appearance of the naphthalenone among the reaction products indicates that the [3,3]-sigmatropic shift is of the usual type in perfluoroaryl propargyl ethers and is accompanied by the inversion of the propargyl group and the acetylene–allene rearrangement. At the same time, the stability of compound **37** suggests that compound **35** and **38–42** would not necessarily be formed solely from the products of the *ortho*-rearrangement of compounds **34** and **37**.[56] Their synthesis is probably ensured also by another pathway — directly from the type A* transition state of the reaction. This mode of reaction is associated with the thermodynamically favourable homolytic cleavage of the C–F aromatic bond and a subsequent [1,4]-fluorotropic shift. At any rate, the involvement of arene solvents of the π-donor type (and apparently of traces of moisture) in the formation of the furans **39–42** can be explained solely by a free-radical mechanism of the reactions.

Pentafluorophenyl ethers containing fragments related to the allyl propargyl groups are also capable of undergoing rearrangements, being converted into exotic products under these conditions.

Under the conditions of vacuum pyrolysis (640 °C, 0.01 Torr), pentafluorophenyl propiolate **43** is transformed into 4,5,6,7,8-pentafluoro-2*H*-cycloheptatrieno[*b*]furan-2-one **46**.[61a] The formation of compound **46** is attributed[61a] not to [3,3]-sigmatropic shift[61b] but to the thermal acetylene–methylenecarbene rearrangement[61c] leading to the generation of the carbene **44** in the first stage. The subsequent intramolecular conversion of the pentafluorophenyl group into a cyclopropane derivative and rearrangement of the intermediate oxatricyclodecanone **45** with ring expansion afford the furanone **46** in 8% yield.



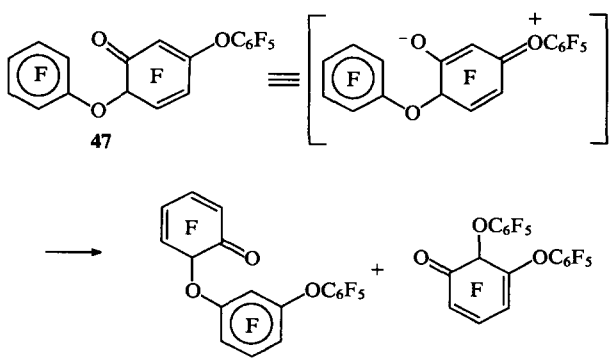
43 **44** **45**



46

When phenyl propiolate is used as the initial compound in this reaction, the yield of the corresponding furanone reaches 45%.[61b]

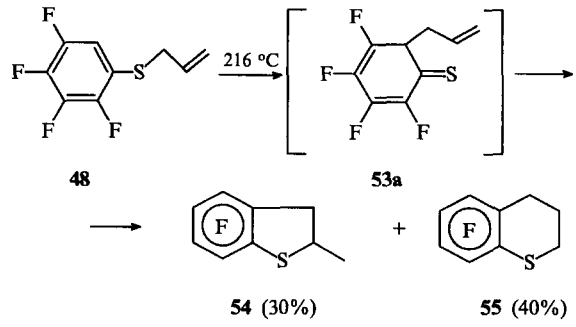
It is believed[62] that the O–O′ migration of the C_6F_5 group in the molecule of perfluoro-3,6-diphenoxycyclohexa-2,4-dien-1-one **47** takes place via a mechanism involving the [3,3]-sigmatropic rearrangement under exceptionally mild conditions (CCl_4, 50 °C, 3.5 h). The authors suggest[62] that this reaction is favoured by the appreciable charge separation in the initial compound **47** with the localisation of the excess electron density on the carbonyl oxygen.



47

The Claisen thio-rearrangement has been investigated by Brooke and coworkers[49, 63] in relation to allyl 2,3,4,5-tetrafluoro-phenyl sulfide **48**, allyl 2,3,5,6-tetrafluorophenyl sulfide **49**, allyl pentafluorophenyl sulfide **50**, pentafluorophenyl propargyl sulfide **51**, and heptafluoro-2-naphthyl propargyl sulfide **52**.[64]

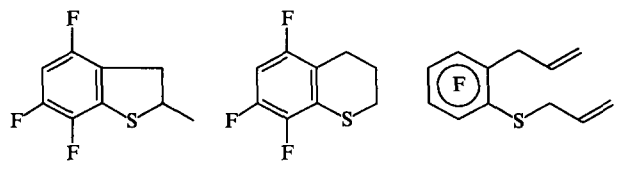
The rearrangement of the sulfide **48** proceeds smoothly in boiling *N*,*N*-diethylaniline with the intermediate formation of the 2,4-diene-1-thione **53a**, which cyclises, after a [1,3]-prototropic shift, to the dihydrobenzothiophene **54** and the dihydrobenzothiopyran **55**.[63]



48 **53a**

54 (30%) **55** (40%)

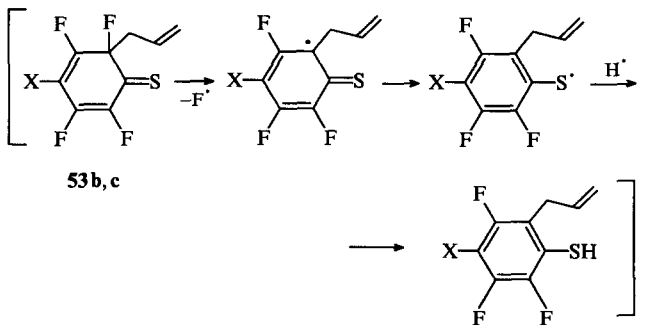
The thiophene **56** and the thiopyran **57** were obtained under the same conditions from the sulfide **49** in 5% and 12% respectively. The reaction of sulfide **50** in *N*, *N*-diethylaniline, which led to the isolation of compounds **54** and **55** in an overall yield of 7% and of the sulfide **58** (yield 8%) is just as ambiguous.[63]



56 **57** **58**

Furthermore, the rearrangements of the sulfides **49** and **50** result in the formation of appreciable amounts of ethyl polyfluorophenyl sulfides, which indicates the dominant role of *N*,*N*-diethylaniline in the side reactions.

In contrast to the thione **53a**, the *ortho*-rearrangement products **53b** and **53c**, formed initially from the sulfides **49** and **50** respectively, undergo subsequently reductive defluorination. The homolysis of the aliphatic C–F bond is favoured by the biradical nature of the thiocarbonyl group in compounds **53b** and **53c** and by the presence of a highly electron-donating solvent in the reaction sphere.[63]

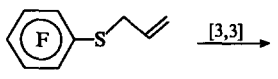


53b,c

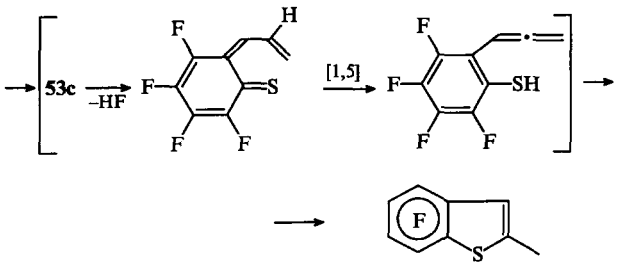
X = H (b), F (c).

On heat treatment of the sulfide **50** in the KF-sulfolan system (nickel flask, 192 °C, 22 h), the reaction proceeds via a different pathway.[49] In this case, only 4,5,6,7-tetrafluoro-2-methylbenzo-[*b*]thiophene **59** was isolated in 9% yield from a complex mixture of final products. According to Brooke,[49] the intermediate **53c** is

initially dehydrofluorinated, the process being accompanied by the [1,5]-migration of the vinyl hydrogen atom to the terminal heteroatom.

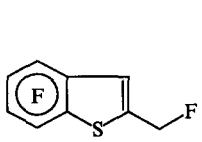


50

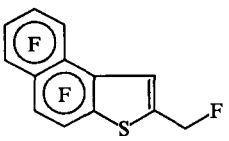


59

The rearrangements of the perfluoroaryl propargyl sulfides **51** and **52** in Khladon 113 at 160–180 °C lead to the thiophene **60** and **61** in 13% and 14% yields respectively.[64] Evidently, as in the case of perfluoroaryl propargyl ethers, these reactions are accompanied by a [1,4]-fluorotropic shift.



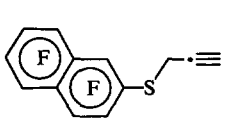
60



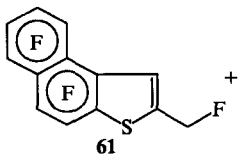
61

In the gas phase at 360 °C, the yield of the thiophene **61** reaches 81%.

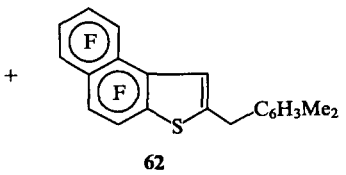
The thermal reactions of the sulfide **52** in *p*-xylene make it possible to obtain either mainly the thiophene **61** (nickel flask, yield 61%) or exclusively the product **62** of incorporation of *p*-xylene (glass bulb, yield up to 85%), depending on the material of the reactor.[64]



52



61



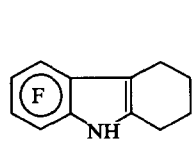
62

The mode of the rearrangement of the sulfide **52** probably depends on the ability of the reactor wall to sorb fluorine atoms, which determines the probability of the involvement of the arene in the transformation of the reaction intermediate.

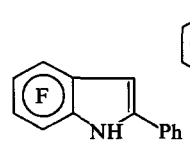
The Cope 3,4-diaza-rearrangement, which is a key stage in the Fischer synthesis of indoles,[17] has been investigated in relation to 2,3,4,5-tetrafluorophenyl-, pentafluorophenyl-, and heptafluoro-2-naphthylhydrazones.[65–67]

On refluxing in concentrated hydrochloric acid, cyclohexanone tetrafluorophenylhydrazone is converted smoothly into 5,6,7,8-tetrafluoro-1,2,3,4-tetrahydrocarbazole **63** (yield 50%), while acetophenone tetrafluorophenylhydrazone in converted on heating (215 °C) with $ZnCl_2$ into tetrafluoro-2-phenylindole **64** in 15% yield.[65]

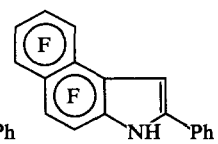
The indole **64** is the main product (yield 12%) also on refluxing acetophenone pentafluorophenylhydrazone in tetralin (208 °C) in the absence of any catalyst or condensing agents.[66] The non-catalysed thermolysis of acetophenone heptafluoro-2-naphthylhydrazone is more effective under the same conditions: the product of this reaction — hexafluoro-2-phenylbenzo[*e*]indole **65** — was isolated in 37% yield.[66] The corresponding fluorinated indoles were obtained by a similar procedure from the pentafluorophenyl- and heptafluoro-2-naphthyl-hydrazones of various aldehydes and ketones.[67] It has been noted[67] that the presence of a fluorine atom in the *ortho*-position relative to the nitrogen atom in the initial hydrazones accelerates their conversion into products of the Fischer reaction. The formation of polyfluoroindoles is apparently formally associated under these conditions with the reductive defluorination of the primary products of the *ortho*-rearrangement.



63

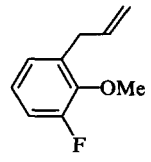


64

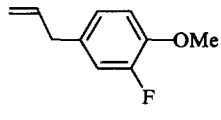


65

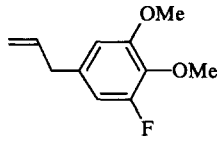
The [3,3]-sigmatropic rearrangements of the partly fluorinated allyl aryl ethers have been less investigated. It has been shown[68a] that allyl 2-fluorophenyl ether is converted in *N*-methylpyrrolidinone (195 °C, 3.5 h) preferentially into the *ortho*-rearrangement product **66** with an admixture of the *para*-rearrangement product **67**. On the other hand, heat treatment of allyl 2-fluoro-6-methoxyphenyl ether does not lead to its isomerisation, but in the presence of Lewis acids as the catalysts a mixture of the *para*-isomer **68** and the *meta*-isomer **69** is formed from this ether even at −20 °C, the latter compound being an unusual product of the Claisen rearrangement.[68b] All the compounds obtained in the above studies[68a, 68b] were isolated in the form of the corresponding methyl ethers.



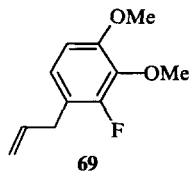
66



67



68

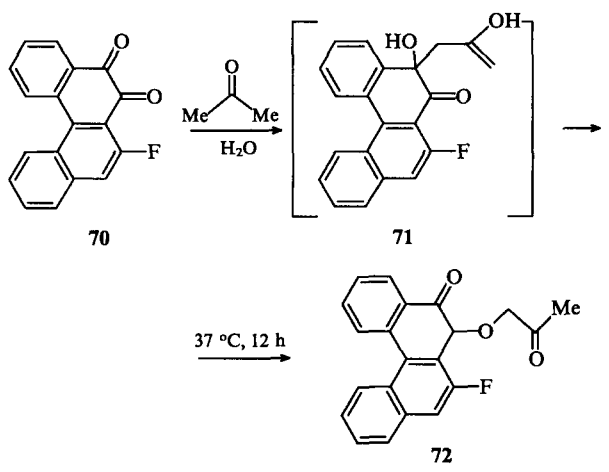


69

The rearrangement of 3-fluoro-substituted aryl penta-2′,4′-dienyl ethers takes place just as readily in the presence of $AlCl_3$ etherate.[69]

Interestingly, the presence of Lewis acids (which lower the reaction temperatures and accelerate not only the Claisen rearrangement[68b, 69] but also the Claisen retro-rearrangement[13]) is not required for the Claisen retro-rearrangement of the monofluroro-derivative of a quinone.[70] The aldol condensation of 7-fluoro-benzo[*c*]phenanthrene-5,6-quinone **70** with an excess of water-containing acetone leads to the primary formation of two regioisomeric intermediates **71** of the aldol type (one regioisomer is illustrated). The intermediate aldols **71** undergo the spontaneous

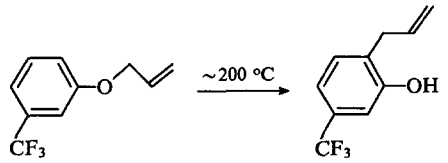
Claisen retro-rearrangement with formation of acetylmethyl ethers **72** (one regioisomer is shown).[70]



70 **71** **72**

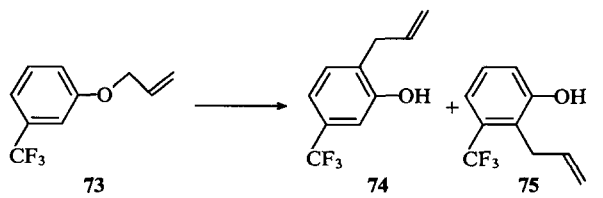
The interaction of the 7-fluoroquinone **70** with acetophenone in solution in $MeCN/H_2O$, reaching completion in the stage involving the formation of the corresponding aldol which is incapable of undergoing the Claisen retro-rearrangement, constitutes an indirect confirmation of the reaction mechanism proposed by the authors.[70]

The influence of the trifluoromethyl group in the *meta*-position relative to the allyl group in allyl phenyl and methylallyl phenyl ethers on the rate and conditions of the Claisen rearrangement has been investigated. On refluxing (without a solvent) under a CO_2 atmosphere, methylallyl 3-trifluoromethylphenyl ether does not rearrange, while allyl 3-trifluoromethylphenyl ether **73** gives rise to the *ortho*-rearrangement product **74** at a rate lower by a factor of 15 than the fluorine-free analogue.[71]



73 **74**

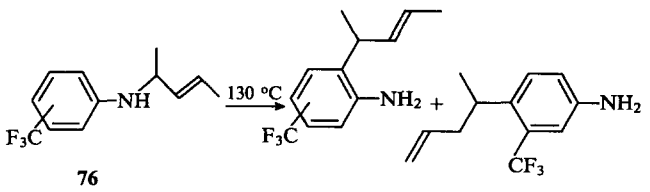
In dimethylformamide at 220 °C, the difference between the rates of rearrangement of the ether **73** and of its non-fluorinated analogue is abolished and, together with the phenol **74**, an equal amount of its regioisomer **75** is formed in an overall yield of the rearrangement products of 81%.[72a]



73 **74** **75**

A mixture of the same composition was obtained when the above reaction was catalysed by boron trichloride and under the conditions of an electric discharge, the induction of which increases, according to the authors' calculations,[73] the rate of the [3,3]-sigmatropic shift by tens of orders of magnitude.

The CF_3 group exerts a greater influence, compared with the rearrangement of the ether **73**, on the rate of the Claisen amino-rearrangement. Thus, in solution in nitrobenzene, the hydrochlorides of *N*-alkenyl-3(4)-trifluoromethyl-anilines **76** rearrange 100 times more slowly than the hydrochloride of *N*-(1-methyl-but-2-enyl)aniline.[74]



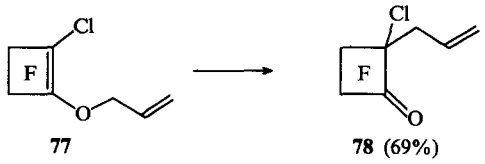
76

Thus the CF_3 group lowers the rate of isomerisation of compounds **73** and **76** similarly to other electron-accepting substituent in the *meta*-position[72a] or the *para*-position[72b] in the aromatic ring and has a negative influence on the rate of the Claisen rearrangement and on the conversion of the initial allyl aryl ethers (up to their decomposition).

III. Rearrangements of polyfluorocycloalkenyl ethers

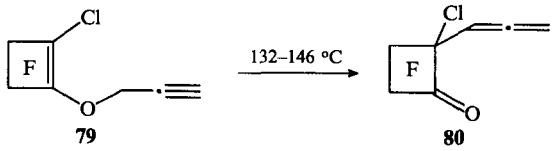
The [3,3]-sigmatropic rearrangements of compounds of this class have been investigated in relation to derivatives of polyfluorinated cyclobut-1-enols, cyclopent-1-enols, and cyclohex-1-enols as well as five-membered heterocycles with one or two heteroatoms. The sigmatropic shift in these systems takes place much more readily (at 25–150 °C) than in the case of allyl(propargyl) polyfluoroaryl ethers. The ring size, the effects of the substituents at the C(1) atom of the 'vinyl' fragment, the nature of the 'allyl' fragment of the molecule, and probably the degree of aromaticity of the ring in the initial compounds have a decisive influence on the conditions and rate of the rearrangement.

In the series of ally(propargyl) cycloalkenyl ethers, the polyfluorocyclobutenyl ethers enter into the Claisen rearrangement with the greatest difficulty. Thus allyl 2-chlorotetrafluorocyclobut-1-enyl ether **77**[75] is converted at an appreciable rate into chlorotetrafluorocyclobutanone **78** only at 120–130 °C.[36] The reaction is completed in 8 h.



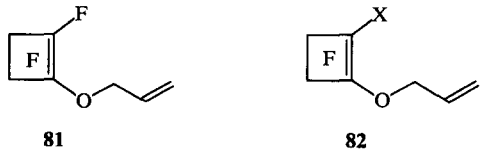
77 **78** (69%)

The propargyl ether **79** isomerises with much greater difficulty. Under these conditions, the [3,3]-sigmatropic shift is accompanied by the acetylene–allene rearrangement and the formation of the cyclobutanone **80** in 55% yield.[36]



79 **80**

The presence of the fluorine atom and other electron-donating substituents at the C(1) atom apparently hardly lowers the thermodynamic stability of allyl polyfluorocyclobutenyl ethers. Thus allyl perfluorocyclobutenyl ether **81** and the 2X-substituted ether **82** synthesised from it distil without change at a reduced pressure and temperature up to 75 °C.[76]



81 **82**

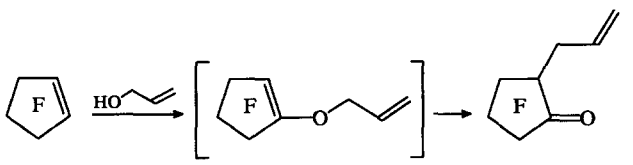
X = H, OMe, NEt_2 .

Ring expansion leads to appreciably milder conditions and acceleration of the Claisen rearrangement. Allyl 2-chlorohexafluorocyclopent-1-enyl ether **83** isomerises smoothly to the cyclopentanone **84** even at 95 °C.[77]



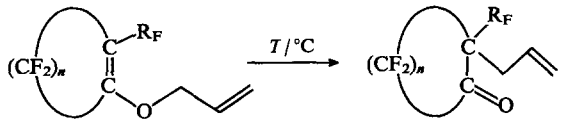
83 **84**

Allyl perfluorocyclopentenyl ether **86**, formed in the reaction of perfluorocyclopentene **85** with allyl alcohol in the presence of KOH, probably rearranges under similar conditions. After the reaction mass had been heated for a short time up to 106 °C, only the product of the rearrangement of the ether **86**—2-allylperfluorocyclopentanone **87**—was isolated from it.[36]



85 **86** **87** (35%)

The influence of ring size and of the perfluoroalkyl groups at the C(1) atom on the conditions and rate of the rearrangement of allyl ethers **88** has also been investigated.[78, 79] An appreciable increase in the rate and a decrease in the temperature of the reaction in parallel with a decrease in ring strain were noted. The yield of 2-allylperfluorocycloalkanones **89** is 90%–94%.[78, 79] The bulky perfluoroethyl group hinders the [3,3]-sigmatropic shift. The equal half-reaction times ($\tau_{1/2}$ = 1.0–1.5 h at 100 °C) for the cyclopentenyl ether **88b** and the cyclohexenyl ether **88c** have been attributed to the inhibiting effect of the C_2F_5 group, which compensates for the increase in the rate of the rearrangement on passing from the five-membered to the six-membered ring.[78, 79]

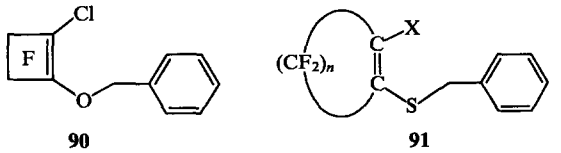


88 **89**

Compound	n	R_F	T/°C
a	2	C_2F_5	130
b	3	CF_3	100
c	4	C_2F_5	100

It is noteworthy that benzyl ethers (sulfides) derived from polyfluorocycloenols do not enter into the Claisen rearrangement, in contrast to allyl ethers. All the attempts to subject the rearrangement of the benzyl ether **90** to radical or anionic catalysis, including those under photolytic conditions, were unsuccessful.[36]

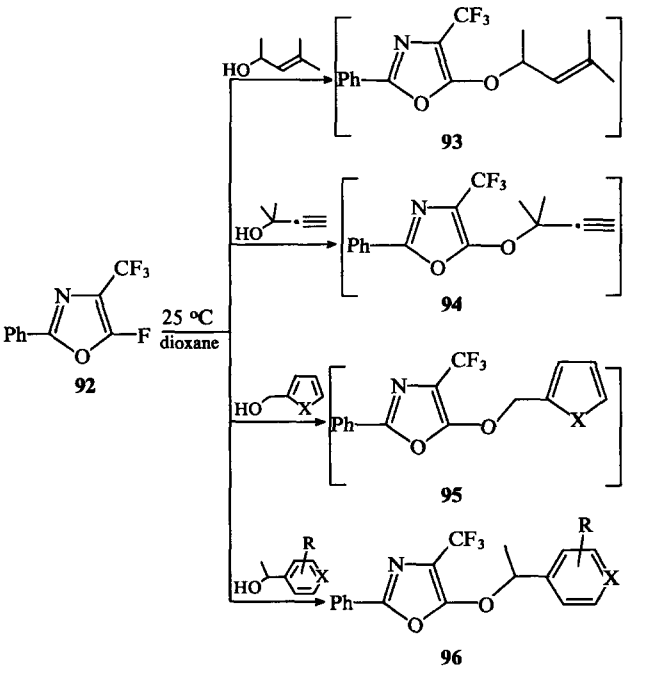
Benzyl polyfluorocycloalkenyl sulfides **91**, formed in the reactions of the corresponding cycloalkenes with toluene-α-thiol in the presence of triethyl-amine, are evidently just as stable.[80]



90 **91**

n = 2, X = F; n = 3, X = CF_3; n = 4, X = Cl.

Unexpected results were obtained by Burger and coworkers[81–86] in the study of the reactions of polyfluoroheterocycloallenes with 2,3-unsaturated alcohols. 5-Fluoro-2-phenyl-4-trifluoromethyl-1,3-oxazole **92**,[87] reacting exothermically in the presence of KOH with allyl type alcohols which involves the primary formation of the ethers **93**–**96**, proved to be a convenient model for the study of certain characteristics of the low-temperature [3,3]-sigmatropic rearrangement observed in these reactions and for the development of new approaches to the synthesis of trifluoromethyl substituted α-aminoacids.[81, 82, 84, 85]

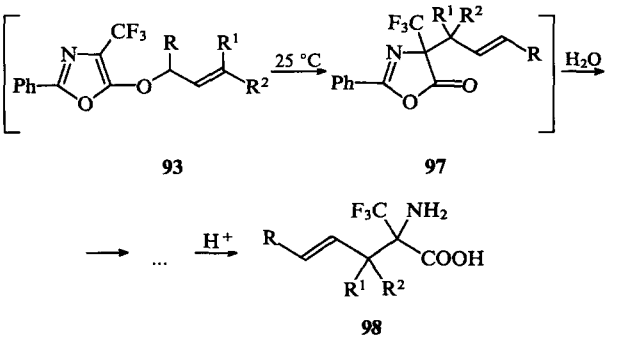


92 **93** **94** **95** **96**

5-Allyloxy-1,3-oxazoles, which do not have pronounced aromatic properties, are known[88] to enter more readily than allyl aryl ethers into the [3,3]-sigmatropic reaction (the oxazole–oxazolone rearrangement or the Steglich–Claisen rearrangement). The allyl group then migrate initially to the 4-position in the ring and then to the 2-position.

In contrast to the non-fluorinated analogues, 4-trifluoromethyl-1,3-oxazoles **93**–**95** undergo the spontaneous Steglich–Claisen rearrangement under the conditions of their synthesis even at 25 °C. The rearrangement is completed by the shift of the 'allyl' fragment of the molecule only to the 4-position.

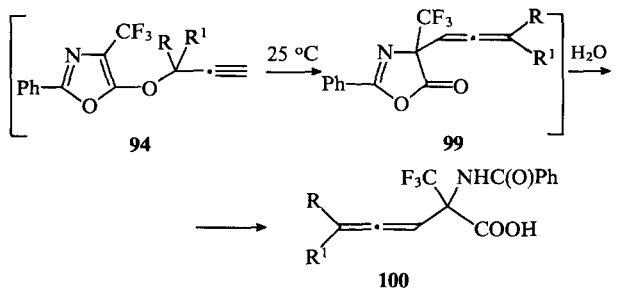
The conditions in the rearrangement of the allyl ethers **93** are almost independent of the numbers of substituents in the allyl group. The oxazolones **97** formed as a result of the rearrangement are hydrolysed without isolation (the reaction was followed by ^{19}F NMR spectroscopy) to give a satisfactory yield (up to 78%) of 2-alkenyl-3,3,3-trifluoroalanines **98**.[81]



93 **97** **98**

R, R^1, R^2 = H, Me, Et, Pr^n.

The propargyl ethers **94** isomerise just as smoothly to the oxazolones **99**, the hydrolysis of which leads to derivatives of 2-alkadienyl-3,3,3-trifluoroalanines **100** in yields up to 64%.[81]

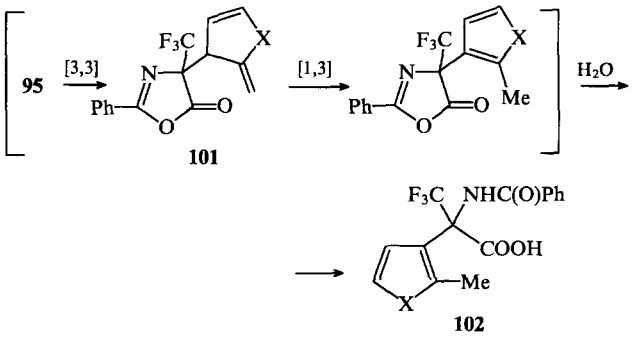


94 **99** **100**

R, R^1 = H, Me, Et.

The [3,3]-sigmatropic rearrangements of the furfuryl and thienyl ethers **95** are accompanied by a [1,3]-prototropic shift.[84]

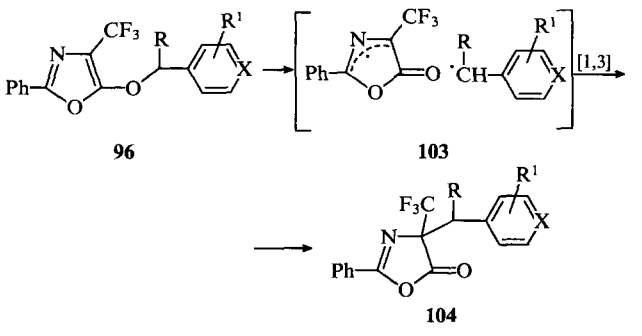
The high reactivity of the *exo*-methylene intermediates **101** is apparently the reason for the low-yield of the final products **102a** (47%) and **102b** (30%).



101 **102**

X = O(**a**), S(**b**).

The rearrangement of the benzyl ethers **96**, which is a key stage in a new method of synthesis of fluorine-containing derivatives of phenylalanine developed by Burger and coworkers,[82-85] constitutes a special case. In contrast to the oxazoles **93-95**, the benzyl derivatives **96** can be isolated in a free state although some of them are extremely thermolabile and isomerise to the corresponding oxazolones **104** at room temperature even in the crystalline state.[83, 84]

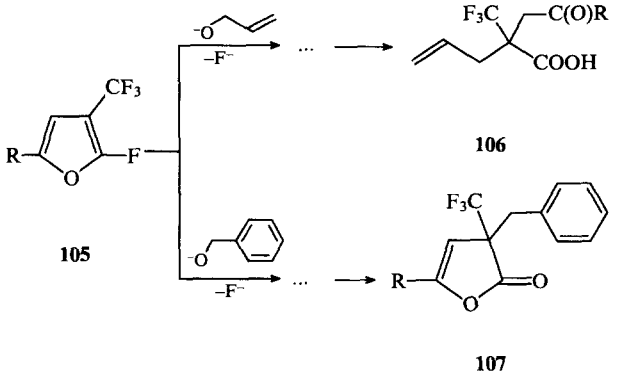


96 **103** **104**

X = CR^2, N; R = H, Me, COOH;
R^1 = H, OMe; R^2 = H, F, Cl, Br, NO_2, OMe, Ph.

The temperature range of this reaction is fairly wide (25 °C–120 °C). However, its main feature consists in the fact that, according to the authors,[84] it is not a concerted [3,3]-sigmatropic process and takes place as a result of the [1,3]-shift of the benzyl group, formed on thermal dissociation of the ethers **96** into the radical pair **103**. This mode of reaction has been demonstrated by the isolation of the mixed products in 'cross-experiments'.[84] The absence of the inversion of the benzyl fragment is also evidence in support of this mechanism.

The slight enhancement of the aromatic properties of the 'vinyl' component on replacement of the fluorine-containing oxazole fragment by the furan fragment apparently also exerts only a slight influence on the rearrangement conditions. The reactions of 2-fluoro-3-trifluoromethyl-5R-furans **105** with allyl and benzyl alcohols in the presence of HF acceptors leads either to the products of the low-temperature Claisen rearrangement (with subsequent ring opening), namely the ketoacids **106**, or to the products of the [1,3]-benzyl shift—the butenolides **107**.[86] The isolation of the intermediates in the nucleophilic substitution of the fluorine atom was not reported.

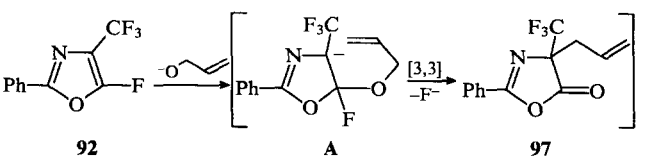


105 **106** **107**

One may postulate that the corresponding allyl and benzyl ethers obtained from 2-fluoro-3-trifluoromethylthiophene[86] can exhibit an increased thermal stability (which is characteristic of, for example, 5-benzyloxy- and 5-benzylthio-4-trifluoromethyl-1,3-thiazoles[87]) as a consequence of the much greater aromacity of the thiophene ring compared with the furan ring.

The [3,3]-sigmatropic rearrangements of derivatives of polyfluorinated cycloenols and heterocycloenols examined above made it possible to synthesise previously unavailable organofluorine compounds such as polyfluorocycloalkenones containing the allyl and 1,2-dienyl groups and CF_3-containing carboxylic 4-ketoacids, butenolides, and oxazolones. The last compounds proved to be promising precursors of a wide variety of trifluoromethylated α-aminoacids[81, 82, 84] (including derivatives of aspartic acid[89]), which were used in their turn for the modification of biologically active peptides.[85, 90]

The instances of the low-temperature Steglich–Claisen rearrangement in the reactions of the oxazole **92** with 2,3-unsaturated alcohols are of special theoretical interest. In our view, the spontaneous transformations of the intermediates are caused, in the first place, by the synchronous influence of the electron-accepting CF_3 group in the C(1) position and the electron-donating substituents (fluorine and oxygen) at the C(2) atom on the kinetic lability of the multiple bond of the oxazole **92**, as a result of which these reactions apparently occur via a carbanionic mechanism. The concerted effects of the substituents in the molecule of the oxazole **92** at the instant of attack by the alkoxide ion favour the stabilisation of the carbanionic intermediate **A** and the subsequent [3,3]-sigmatropic shift coupled with the elimination of the fluoride ion.



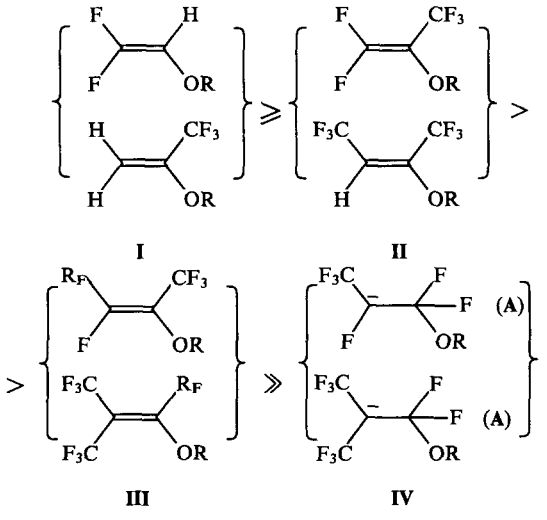
92 **A** **97**

IV. Rearrangements of polyfluorovinyl ethers

The allyl and propargyl ethers of acyclic polyfluoroenols enter into the Claisen rearrangement even more readily than the derivatives of polyfluorocycloenols, because in this case the fluorine atoms and the fluorine-containing substituents exert the maximum influence on the properties of the vinyl fragment.

According to Dolbier's data,[41, 91a] the conjugation of the geminal fluorine atoms with the sp^3 orbitals of carbon is thermodynamically more favourable (almost to the extent of 5 kcal mol^{-1}) than the conjugation with the sp^2 orbitals, which gives rise to, for example, the mild conditions in the rearrangement of allyl difluorovinyl ethers.[92] On the other hand, the trifluoromethyl group, which increases the thermodynamic stability of unsaturated compounds, the same time increases greatly the kinetic lability of the unsaturated bond.[91b] The combination of the effects of these substituents, which depends on their number and positions, leads to a sharp differentiation of polyfluorovinyl ethers (PFVE) in terms of their tendency to undergo the [3,3]-sigmatropic shift, which is manifested most clearly under the conditions of the rearrangement of these compounds.

In conformity with this finding, the PFVE can be divided into four groups (I–IV) in order of decreasing temperature and apparently in order of increasing rate of rearrangement of the compounds. The first two groups (I and II) contain relatively stable CFVE, which isomerise as a rule at 50–100 °C.



I II III IV

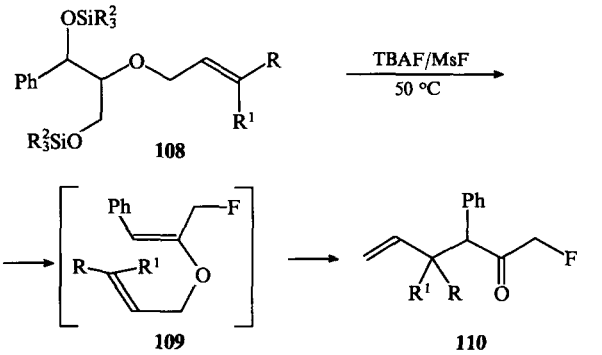
R_F = CF_3, C_2F_5; R = CH_2CH = CH_2.

As the CF_3 groups accumulate in the C(1) position, the rearrangement temperature falls to 20–40 °C (group III), whilst, following the appearance in the PFVE of the capacity to stabilise carbanionic states, the changes in the rate under the conditions of the reactions become dramatic: the fluorocarbanions A (group IV) undergo a spontaneous rearrangement in the instant of generation even on strong cooling.

1. Rearrangements of stable polyfluorovinyl ethers

The synthesis of stable PFVE has been determined only in recent years and for this reason there are few examples of rearrangements of compounds of this kind. The monofluoro- and difluoro-substituted vinyl ethers, capable of undergoing the Claisen rearrangement with formation of α-fluoroketones, are usually obtained by three methods.

In the first method, developed by Japanese workers[93, 94] and called 'fluoroolefin formation', the starting materials employed are alkyl allyl ethers, the alkyl fragment of which contains two readily removable groups (for example, trimethylsiloxy- or methanesulfonyloxy-groups), one of which is exchanged for fluorine. Thus treatment of alkenyl 2-phenyl-2,2'-bis(trimethylsiloxy)isopropyl ethers **108** with a mixture of tetrabutylammonium fluoride (TBAF) and methanesulfonyl fluoride (MsF) in tetrahydrofuran (THF) leads regiospecifically to alkenyl 1-fluoromethyl-2-phenylvinyl ethers **109** which are either transformed *in situ* in the fluoroolefin formation process (THF), 50 °C, 12–36 h) or are converted into monofluoromethyl ketones **110** under more severe conditions (toluene, refluxing, 2 h).[93]

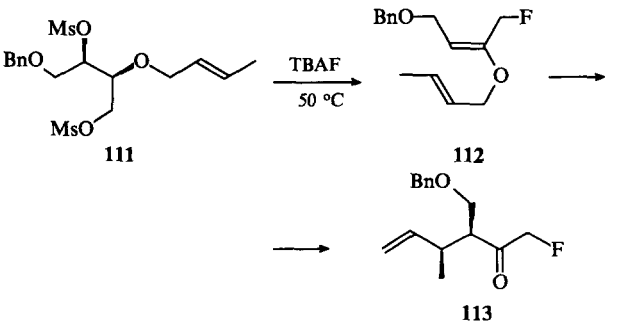


108 **109** **110**

R = R^1 = H (95%);
R = H, R^1 = Me (89%);
R = R^1 = Me (53%).

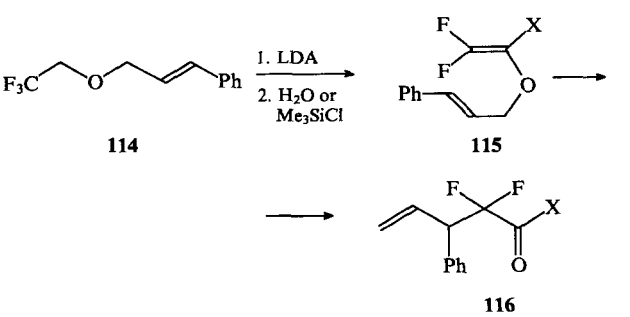
Benzyl 1-fluoromethyl-2-phenylvinyl ether synthesised in this way[93] proved to be a stable compound incapable of undergoing the Claisen rearrangement.

The monofluoromethyl ketone **113**, which is a key compound in the multistage stereospecific synthesis of (±)-fluorobotriodiplodin — a fluoride containing analogue of a natural micotoxin — was obtained by a procedure similar to that used for the ketones **110**.[94] The fluoroolefin formation reaction involving crotyl 2-2'-bis(methanesulfonyloxy)isobutyl ether **111** affords crotyl 1-fluoromethylvinyl ether **112** in 70% yield. Compound **112** rearranges in boiling xylene to compound **113** in 92% yield and with a high degree of stereoselectivity.



111 **112** **113**

The second method is based on the dehydrofluorination of allyl trifluoroethyl ethers, formed on alkenylation of 2,2,2-trifluoro-IR-ethanols.[92] For example, the trifluoroethyl ether **114**, synthesised by the reaction of sodium trifluoroethoxide with cinnamyl chloride, is readily (THF, −70 °C) dehydrofluorinated

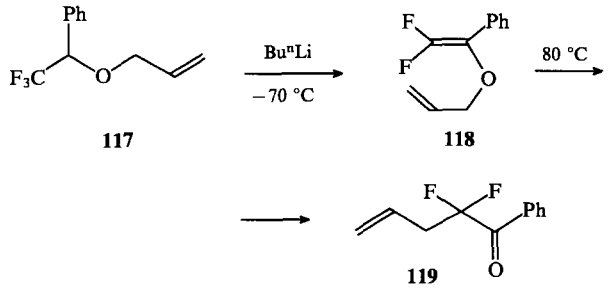


114 **115** **116**

X = H (**a**), AR (**b**).

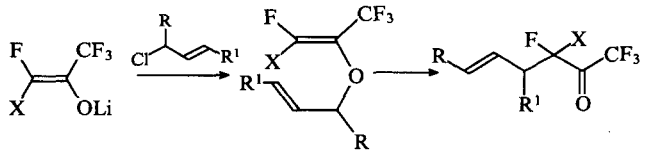
by lithium diisopropylamide (LDA). The resulting cinnamyl 2,2-di-fluorovinyl ethers **115** fully isomerise to the 2,2-difluoro-substituted aldehyde **116a** or the ketone **116b** on refluxing in CCl_4 (80 °C, 1 h).[92] It is remarkable that the cinnamyl vinyl ether rearranges only at 200 °C.[95]

Butyllithium is also a convenient dehydrofluorinating agent in these reactions. Treatment of allyl 1-phenyltrifluoroethyl ether **117** with this reagent affords the ether **118**, which is converted on subsequent heating into the difluoroketone **119** in 41% yield.[92]



117 **118** **119**

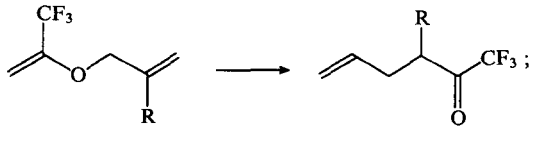
The third method of synthesis of stable PFVE is extremely promising and is applicable only in organofluorine synthesis. It consists in the *O*-alkenylation of the lithium salts of stable polyfluorophenols such as the enol of pentafluoroacetone and its analogues **120**. The alkenyl 2-fluoro-1-trifluoromethylvinyl ethers **121** obtained in this way undergo the Claisen rearrangement at 40–65 °C with formation of trifluoromethyl ketones **122**.[96]



120 **121** **122**

X = F, Bu, Ph .

Evidently the CF_3 group in the C(2) position does not prevent the [3,3]-sigmatropic shift. The influence of the trifluoromethyl group at the C(2) atom on the rate of the Claisen rearrangement has been studied in greater detail by Gajewski et al.[35] They established that allyl 1-trifluoromethylvinyl ether **123a** is converted into the trifluoromethyl ketone **124a** in cyclohexane (61–98.5 °C, $\tau_{1/2}$ = 7.5 h) 73 times faster than the non-fluorinated analogue in a similar reaction.



123 **124**

R = H(**a**), Ar(**b**).

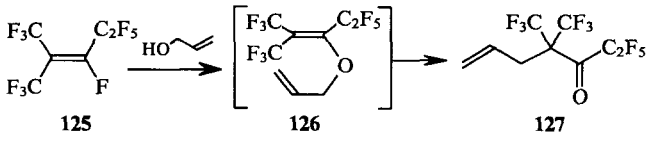
On the other hand, a similar effect is not observed in the Cope rearrangement of *cis*-2-trifluoromethylocta-1,5-diene. According to the authors,[35] the acceleration of the rearrangement of the ether **123a** is associated with the destabilisation of the ground state of the molecule under the influence of the CF_3 group and with the increase in the polarity of the transition state. Indeed the rate of the rearrangement of the ether **123a** in a polar solvent (DMSO, 80 °C, $\tau_{1/2} \simeq 2.4$ h) is higher almost by a factor of 3.[35]

For comparison, one may note that the methoxycarbonyl group in the C(2) position accelerates the Claisen rearrangement by a factor of 79,[97] while the CN group in the same position causes an acceleration by a factor of 111,[33] the gain in the free energy of activation for the C(2)-substituted substrate amounting to 2.0–2.5 kcal mol^{-1}.[35]

2. Rearrangements in the reactions of internal polyfluoroalkenes

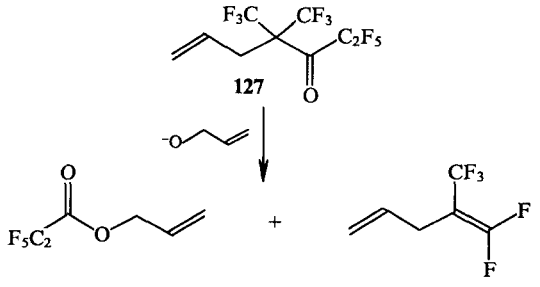
The interaction of 2,3-unsaturated alcohols with internal polyfluoroalkenes (PFA) and fluorinated alkynes and cumulenes leads to the ethers of poly(fluoroalkyl)enols, which isomerise more readily than monofluoro-, difluoro-, and monotrifluoromethyl-substituted vinyl ethers.

Thus the ether **126**, formed in a mixture with other products by the reaction of perfluoro-2-methylpent-2-ene **125** with allyl alcohol in the presence of NEt_3, rearranges to the ketone **127** already under the conditions of the synthesis (Et_2O, 20 °C, 2 h).[98]



125 **126** **127**

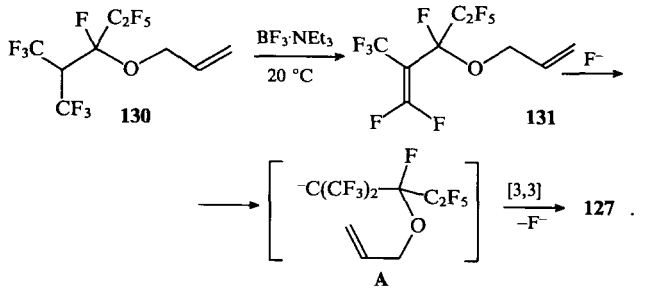
The half-conversion time for the ether **126** at 36 °C, established by ^{19}F NMR, is ~1 h. As the ketone **127** accumulates, it undergoes a partial 'haloform' cleavage under these conditions by the allylate anion to allyl perfluoropropionate **128** (yield 28%) and pentafluoropentadiene **129**.[98]



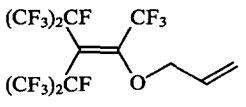
128 **129**

In a polar medium, the rate of conversion of the pentene **125** into the propionate **128** increases, so that, when the reaction of the pentene **125** with allyl alcohol is carried out in acetonitrile (NEt_3, 60 °C),[99] the propionate **128** is formed in 65% yield, while the ketone **127** is not isolated at all.

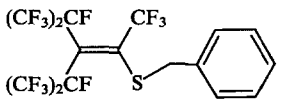
It is essential to emphasise that, under the conditions of the above study,[98] the rearrangement of the ether **126** takes place in the presence of fluoride ions, so that the smooth formation of the ketone **127** can be explained also by a carbanionic reaction mechanism. The latter probably operates in the reaction with the fluoride ion of the stable allyl pentafluoroalkenyl ether **130** — one of the products of the reaction of the pentene **125** with allyl alcohol.[98] However, one cannot rule out the possibility that the formation of the ketone **127** as a side product (yield 25%) in this reaction is altogether independent of the synthesis of the ether **131** and takes place in a reaction competing with the formation of the latter in the instant of the deprotonation of the initial adduct via the mechanism **130** → **A** → **127**.



The stability of tris(polyfluoroalkyl)vinyl ethers depends significantly on the steric effects of the fluoroalkyl groups and their position. For example, the allyl ether **132**[100] and the sulfide **133**,[101] substituted in the C(1) position by the bulky $(CF_3)_2CF$ groups, do not undergo the Claisen rearrangement.

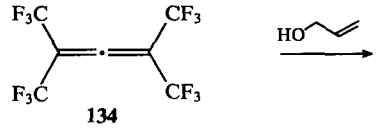


132

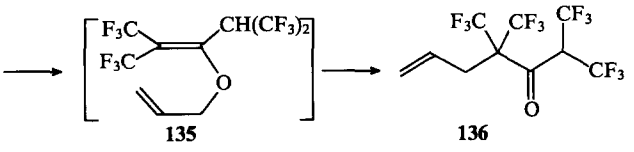


133

The steric effects of the substituents at the C(2) atom exert a much smaller influence on the tendency towards their rearrangement. Allyl 1-(α-*H*-hexafluoroisopropyl)-2,2-bis(trifluoromethyl)-vinyl ether **135**, obtained by the addition of allyl alcohol to tetrakis(trifluoromethyl)allene **134**, isomerises slowly to the ketone **136** even at 36 °C. At 65–72 °C, the ether **135** is fully converted after 1.5 h into the ketone **136**, the yield of which reaches 71%.[102]

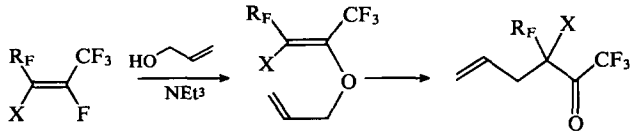


134



135 **136**

Vicinal bis(perfluoroalkyl)-substituted vinyl ethers proved to be, like the ethers **126** and **135**, thermodynamically unstable. The allyl ethers **138a** and **138b**, obtained from 2-chloroheptafluoro-but-2-ene **137a** and perfluoropent-2-ene **137b** can be isolated only by vacuum fractionation at 30–35 °C.[79] At 36 °C, they are slowly transformed into the ketones **139a** and **139b** with half conversion periods of 24 h (**a**) and 72 h (**b**).[79]

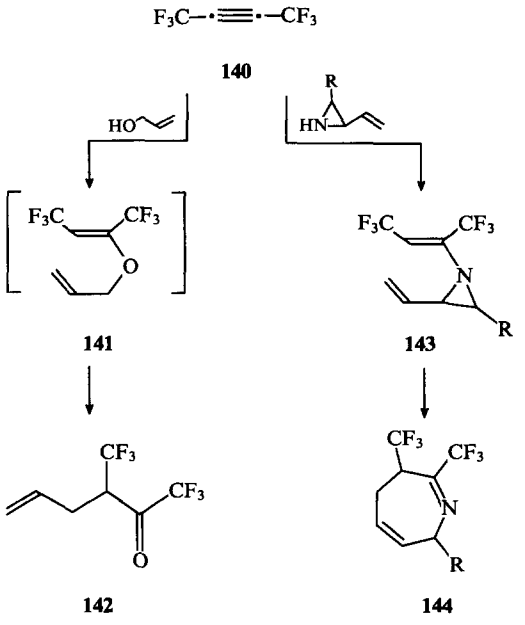


137 **138** **139**

$R_F = CF_3$, X = Cl(**a**) ;
$R_F = C_2F_5$, X = F(**b**) .

The mild conditions in the rearrangement of ethers **138** are appreciably influenced apparently by the halogen atom in the C(1) position, because allyl 1,2-bis(trifluoromethyl)vinyl ether **141**, formed in the reaction of perfluorobut-2-yne **140** with allyl alcohol (catalysed by NaOH), rearranges to the ketone **142** (yield 74%) on heating to 89 °C.[36]

The low-temperature Claisen amino-rearrangement is observed in the reaction of perfluorobutyne **140** with 2-vinyl-aziridines.[103] The adducts **143** isomerise at room temperature or on slight heating (50 °C) to CF_3-containing azepines **144**, which are rare products of the [3,3]-sigmatropic rearrangement, by virtue of the involvement of the aziridine ring in the latter.



140 **141** **142** **143** **144**

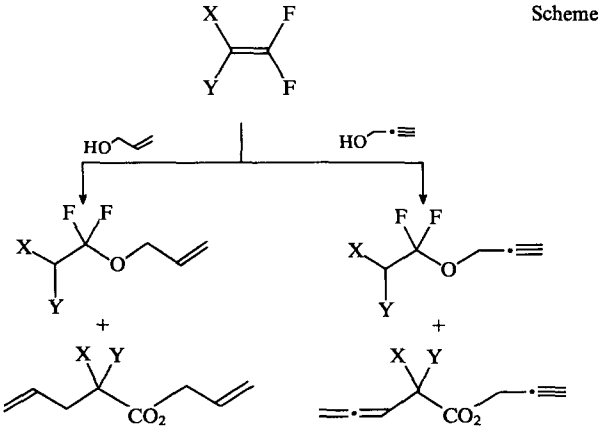
R = H, CH = CH_2.

3. Rearrangements in the reactions of terminal polyfluoroalkenes

The interaction of terminal PFA with unsaturated alcohols proceeds via intermediate fluorocarbanions and leads to either adducts of the initial reactants or to alkyl polyfluorovinyl ethers†.[104, 105a, 106] The latter pathway operates as a rule in the presence of favourable conditions for the transformation of the carbanionic intermediates via the elimination of the fluoride ion, for example, in the reactions of PFA with alkoxides in protophilic or aprotic solvents.

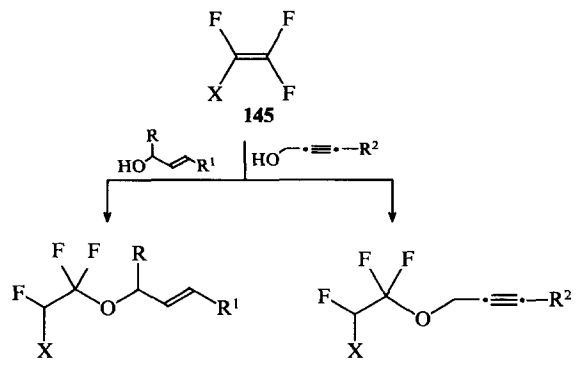
Accordingly, in the reactions of terminal PFA with 2,3-unsaturated alcohols one might have expected the generation in the first stage of the fluorocarbanions **A** (see p. 562, group IV) with the subsequent formation of allyl(propargyl) polyfluorovinyl ethers capable of undergoing the non-catalysed thermal Claisen rearrangement. However, in none of the reactions investigated was it possible to isolate the corresponding PFVE. The products of these reactions were found to be exclusively the adducts of the initial compounds and the rearrangement products — derivatives of fluorine-containing alk-4-ene(alka-3,4-diene)carboxylic acids (Scheme 1), the proportions of which depend on the structure of the PFA and the conditions of its interaction with the alcohol.

Scheme 1



† The products of the substitution of the allylic fluorine atom are sometimes formed.[104, 106]

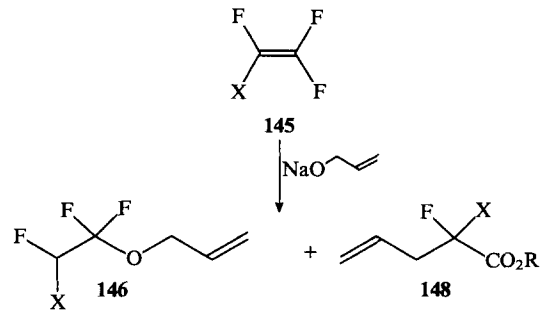
The tetrafluoroethylene **145a** and chlorotrifluoroethylene **145b** interact with allyl[107-112] and propargyl[113-116] alcohols‡ in the presence of KOH,[107, 108, 115, 116] catalytic amounts of metallic sodium,[110-113] or ion exchange resin[114] or at a low§ pressure[108] with formation of only adducts — allyl 2-*H*-polyfluoroethyl ether **146** and propargyl 2-*H*-polyfluoroethyl ether **147**.



145 **146** **147**

X = F(**a**), Cl(**b**); R = H, Me; R^1 = H, Me, Ph; R^2 = H, Cl, Br, I.

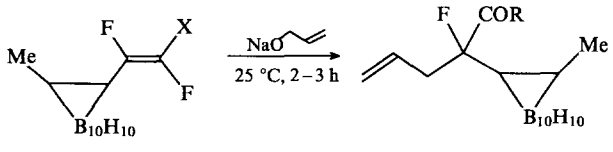
In the reactions of the polyflurorethylenes **145** with sodium allylate,[110, 117] which take place particularly readily (0 °C) in THF,[110] the products of the rearrangement — derivatives of 2-fluoropent-4-enoic acid **148** (yield 16%-34%) — were obtained together with the ethers **146** (yield 22%-25%).



145 **146** **148**

X = F(**a**), R = H; X = Cl(**b**), R = $CH_2CH=CH_2$.

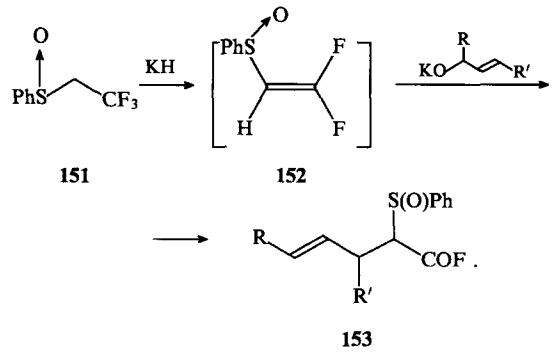
Fluoroethylenes with functional group-substituents interact unambiguously with allylates. Thus the reaction of 1-methyl-2-polyfluoroalkenyl-*o*-carbaboranes **149** with sodium allylate results in the formation of only the rearrangement products **150** in 40% (**a**) and 44% (**b**) yields.[118]



149 **150**

X = Cl, R = $OCH_2CH=CH_2$(**a**); X = R = CF_3 (**b**).

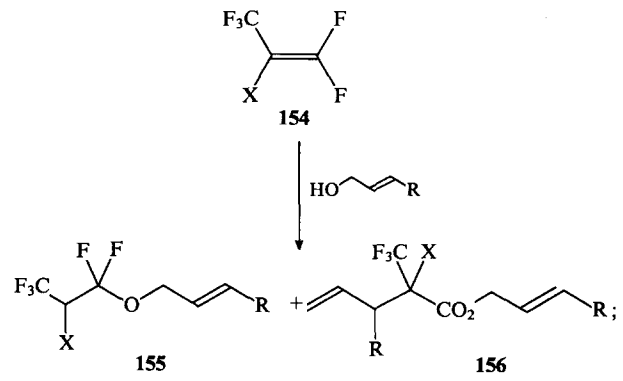
The reaction of allylates with *gem*-difluorovinyl phenyl sulfoxide **152**, generated *in situ* from trifluoroethyl phenyl sulfoxide **151** with the aid of potassium hydride, under mild



151 **152** **153**

conditions (THF, 0-5 °C, 0.5-2.0 h) also leads exclusively to the rearrangement products — the acid fluorides 153.[199]

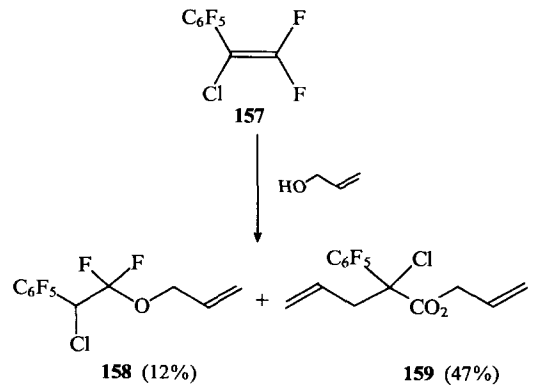
The terminal PFA **154**, which are more electrophilic than the perfluoroethylene **145a**, interact with 2,3-unsaturated alcohols to form a mixture of adducts and rearrangement products. In the reaction of hexafluoropropene **154a** with allyl alcohol (catalysed by KOH, 20-30 °C¶), allyl 2-fluoro-2-trifluoromethylpent-4-enoate **156a** was isolated in 5% yield together with allyl 2-*H*-hexafluoropropyl ether **155a**.[120]



154 **155** **156**

X = F, R = H(**a**); X = CF_3, R = H, Me(**b**), X = SMe, R = H(**c**).

α-Chloroperfluorostyrene **157** reacts under similar conditions (KOH, 20-45 °C, 0.5-1.0 h) with allyl alcohol to form preferentially the rearrangement product — allyl 2-chloro-2-pentafluorophenylpent-4-enoate **159**.[121] The adduct — allyl β-chloro-β-*H*-heptafluorophenylethyl ether **158** — is formed in an insignificant amount.



157 **158** (12%) **159** (47%)

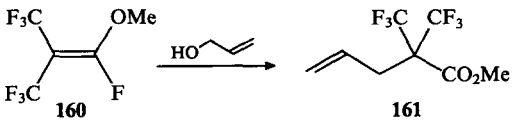
In the reaction of the perfluoroisobutene **154b** with allyl alcohol (0-50 °C)[36] even in the absence of bases, the yield of the rearrangement product — allyl 2,2-bis(trifluoromethyl)pent-4-

‡ The reaction of propargyl alcohols with *gem*-bromochlorodifluoroethylene, formed under the conditions of phase transfer catalysis from $CF_3CHBrCl$, has been investigated.[116]

§ The reaction of compound **145a** with allyl alcohol at a pressure of 500 atm affords a product of the cyclodimerisation of the initial

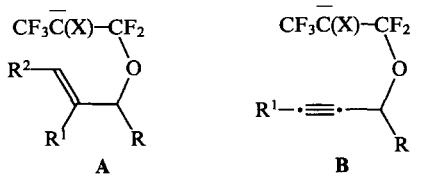
¶ In the absence of bases, the polyfluoroalkenes **154a** and **157** do not interact with allyl alcohol.

enoate **156b** (R = H)† — reaches 15%. 1-Methoxy heptafluoroisobutene **160** reacts with allyl alcohol just as smoothly in the presence of KOH, being converted into methyl 2,2-bis(trifluoromethyl)pent-4-enoate **161** in 39% yield.[36]



160 **161**

In the examples examined above, the yield of the rearrangement products is correlated with the ability of the internal PFA to generate stable fluorocarbanions‡, which are transformed into PFVE after the elimination of the fluoride ion. However, these intermediates could not be detected in the reaction medium by ^{19}F NMR even at −30 °C.[120] It was therefore natural to suppose[37, 120, 123] that the precursors of the rearrangement products in these reactions are the fluorocarbanions **A** or **B**, which at the instant of formation undergo, at a high rate, a spontaneous [3,3]-sigmatropic rearrangement coupled with the elimination of the fluoride ion.

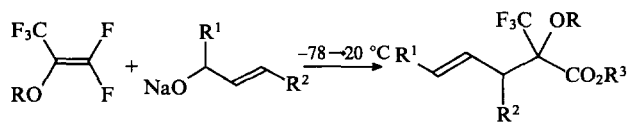


A **B**

The probability of the [3,3]-sigmatropic shift is determined by the structural features of the fluorocarbanions and their lifetime necessary for the formation of the transition state of type **A***.

Indeed in protophilic solvents [DMF, DMSO, hexamethylphosphoramide (HMPA)], which tend to stabilise carbanionic intermediates, and in the presence of 'mild' HF acceptors, for example potassium fluoride, the reactions of the perfluoroisobutene **154b** with allyl and crotyl alcohols proceed unusually easily (−30 to −10 °C), the formation of the rearrangement products **156b** being the main pathway§ (yield up to 70%).[37, 120, 123] Under similar conditions (KF/DMF, 5–20 °C), in the interaction of allyl alcohol with hexafluoropropene **154a**[120, 123] and 2-methylthiopentafluoropropene **154c**[124] the rearrangement products **156a** and **156c** were obtained in 15% and 32% yields respectively.

Another approach to the stabilisation of the intermediate fluorocarbanions is associated with the use of powerful nucleophiles such as alkoxides. Derivatives of 2-alkoxy-2-trifluoromethylalk-4-enoic acids **163** were obtained in this way from 2-alkoxy-pentafluoropropenes **162** in a yield up to 66%.[125, 126]



162 **163**

R = CH_2OMe,  ; R^1, R^2 = H, Me, Ph;

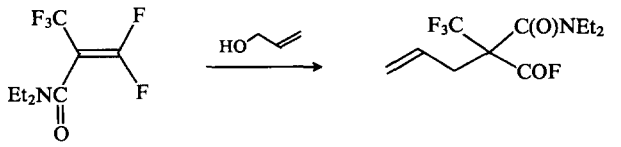
R^3 = H, $CH(R^1)CH = CHR^2$.

† It was believed previously[122] that the side product in this reaction is not the pentenoate **156b** but *O,O*-diallylbis(trifluoromethyl)ketenal.

‡ For the influence of fluorine atoms and CF_3 and CO_2R groups on the stability of the fluorocarbanions, see Refs 106 and 127a, b.

§ The corresponding adducts **115** and a fairly large amount of $(CF_3)_2CHX$ — the adducts of HF and the initial PFA — are also formed in these reactions.

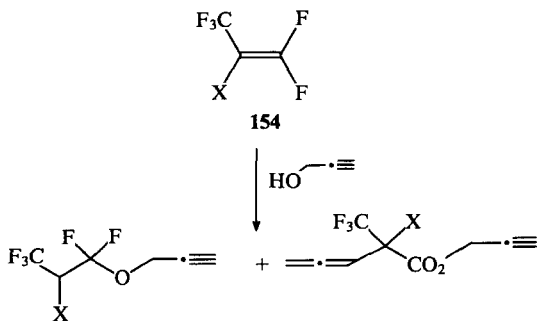
Under the conditions of effective intermolecular stabilisation of the carbanionic states, there is no need to use protophilic solvents, HF acceptors, or alkoxides. In the absence of any kind of reagents, the reaction of perfluoromethacrylic acid diethylamide **164**, the amide group of which stabilises the adjoining carbanionic centre,[127a] with allyl alcohol leads chemospecifically to the rearrangement product — the acid fluoride **165** (yield up to 90%).[128] The excess of the amide **164** serves as the HF acceptor in this reaction.



164 **165**

Terminal PFA reacts similarly with acetylenic alcohols.[120, 123, 129]

In a protophilic medium (KF/DMF), the reactions of perfluoroalkenes **154a** and **154b** with propargyl alcohol take place at −10 to 0 °C, while the [3,3]-sigmatropic shift in the intermediate **B** is accompanied by the acetylene–allyne rearrangement, which makes it possible to obtain CF_3-substituted penta-3,4-dienoates **167** in yields of 13% (**a**) and 59% (**b**) together with 2-*H*-polyfluoroalkyl propargyl ethers **166**.[120, 123]

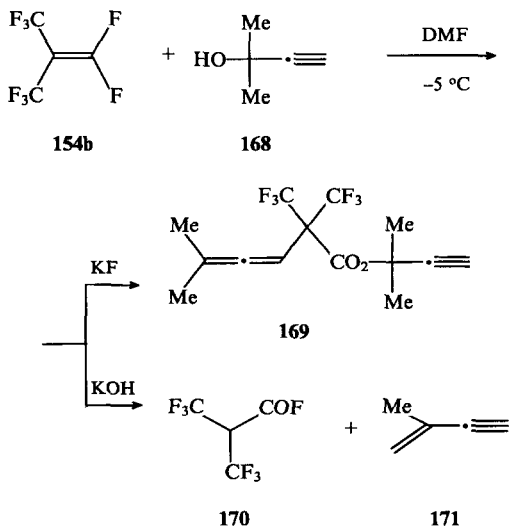


154

166 **167**

X = F (**a**), CF_3(**b**).

In a number of instances, the influence of the nature of the base employed on the mode of the reactions of PFA with homologues of propargyl alcohol has been noted. The reaction of the perfluoroisobutene **154b** with 1,1-dimethylprop-2-yn-1-ol **168**



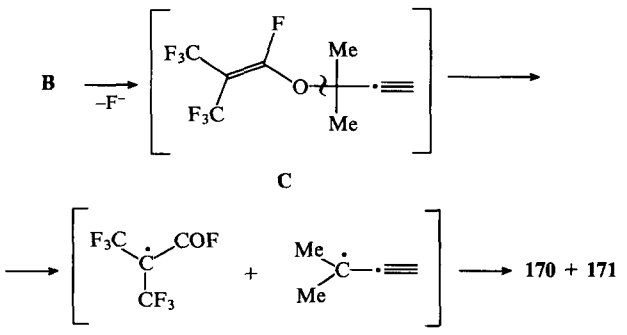
154b **168**

169

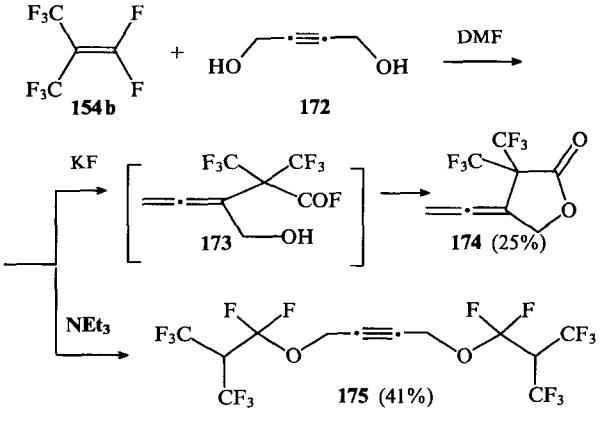
170 **171**

under optimum conditions (KF/DMF) leads to the rearrangement product **169** (yield 48%), while the reaction catalysed by KOH affords a mixture of the acid fluoride **170** and isopropenylacetylene **171**.[129]

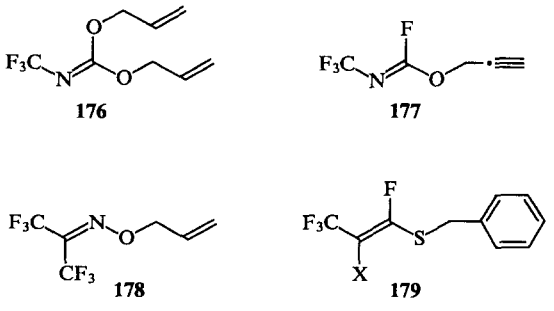
Apparently in the presence of a strong base the elimination of the fluoride ion from the intermediate **B** is faster that its rearrangement and the resulting polyfluorovinyl ether **C** undergoes homolytic decomposition owing to the steric hindrance to the [3,3]-sigmatropic shift.



Two pathways operate also in the reaction of the perfluoroisobutene **154b** with but-2-yne-1,4-diol **172**.[129] In the presence of an excess of KF, the main product is 2,2-bis(trifluoromethyl)-3-vinylidene-4-butanolide **174**, formed on lactonisation of the intermediate **173** in the rearrangement, but, when this reaction was catalysed by triethylamine, only the adduct **175** was obtained.



It is noteworthy that, in the reactions of a terminal azaalkene such as perfluoro-2-azapropene with allyl and propargyl alcohols, the products of the [3,3]-sigmatropic rearrangement are not formed at all and allyl polyfluoro-2-azapropenyl ether **176** and propargyl polyfluoro-2-azapropenyl ether **177** do not isomerise even at 150 °C.[130] The *O*-allyl ether of hexafluoroacetone oxime **178** is just as stable.[130]



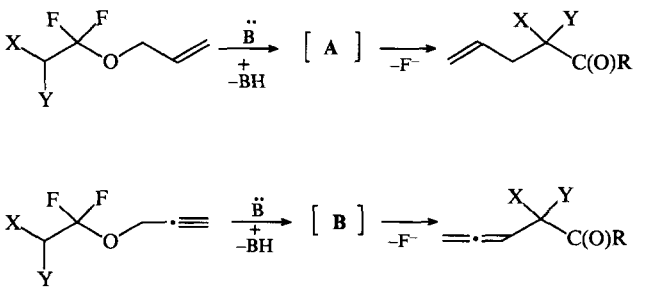
X= CF_3, $C(O)NMe_2$.

The benzyl sulfides **179**, obtained in the reactions of toluene-α-thiol with perfluoroisobutene[131] and perfluoromethacrylic acid dimethylamide,[132] also proved to be thermodynamically stable.

4. Rearrangements on deprotonation of 2-*H*-polyfluoroalkyl ethers

Another preparative method of synthesis of alkyl polyfluorovinyl ethers is based on the dehydrofluorination of the products of the addition of alcohols to terminal PFA, for example, to perfluoroisobutene.[133] On the other hand, the dehydrofluorination of the adducts of 2,3-unsaturated alcohols and terminal PFA—allyl(propargyl)2-*H*-polyfluoroalkyl ethers—leads not to the expected polyfluoroenols but to the rearrangement products—derivatives of fluorine-containing alk-4-enoic and alka-3,4-dienoic acids. The fluorocarbanions **A** or **B**, generated at the instant of the deprotonation of the initial CH acids, are probably the direct precursors of the rearrangement products in this case too (Scheme 2).

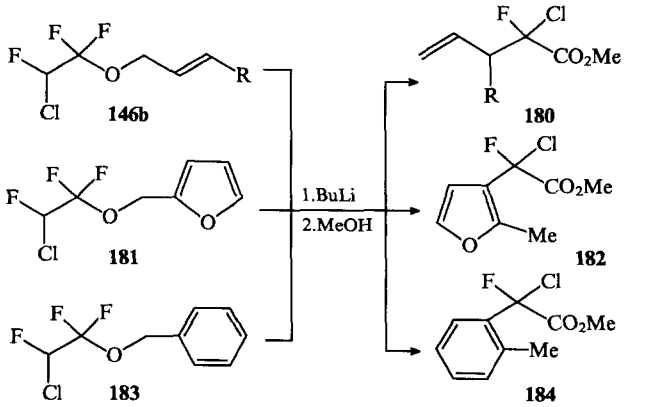
Scheme 2



R = F, OH, OMe.

This method of synthesis of unsaturated carboxylic fluoroacids and their derivatives was first used by Normant and coworkers[110, 111] in relation to the initial 2-*H*-chlorotrifluoroethyl ethers. The use of butyllithium as the deprotonating agent made it possible to obtain from the adducts of chlorotrifluoroethylene with allyl, crotyl, cinnamyl (compound **146b**; R = H, Me, Ph), furfuryl (compound **181**), and benzyl (compound **183**) alcohols at negative temperatures the corresponding products **180**, **182**, and **184** of the [3,3]-sigmatropic rearrangement in satisfactory yields.

The low-temperature preparative syntheses of derivatives of 2,2-difluoropent-4-enoic acid were subsequently developed on the basis of Normant's method.[112, 134]

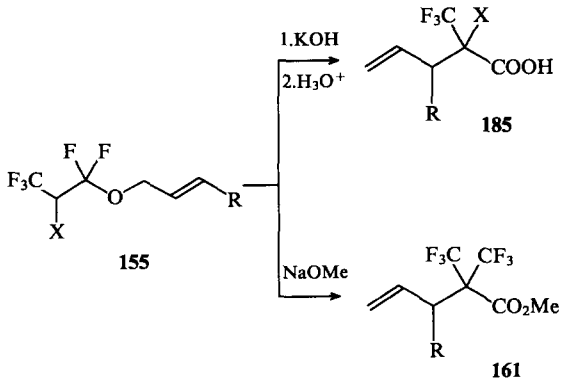


R = H, Me, Ph.

According to Normant and coworkers,[110, 111] the products of the rearrangement in the reactions described above are formed from the intermediate PFVE. However, it is difficult to explain from this standpoint the very high rate of the Claisen rearrangement of the above intermediates even at −70 °C,[111, 134] whereas cinnamyl 2,2-difluorovinyl ether **115a** is extremely stable.[92]

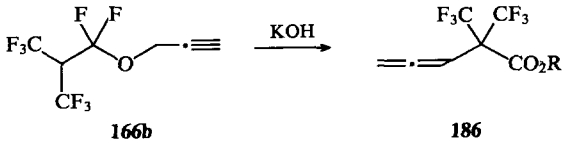
Even stronger CH acids, for example the 2-*H*-hexafluoropropyl ether **155a**, the 2-*H*-octafluoroisobutyl ether **155b**, and 2-methylthio-2-*H*-pentafluoropropyl ether **155c** are depronated by potassium hydroxide, being converted into 2-trifluoromethylpent-4-enoic acids **185** in yields of 32% (**a**), 60%–78% (**b**), and 67% (**c**).[123, 124, 135]

Methyl 2,2-bis(trifluoromethyl)pent-4-enoates **161** have been synthesised from the ether **155b** with the use of sodium methoxide or Claisen's alkali (a solution of KOH in dry methanol) as the deprotonating agents.[120]



X = F, R = H (**a**) (DMSO, 60–65 °C);
X = CF_3, R = H, Me (**b**) (Et_2O, 30–35 °C);
X = SMe, R = H (**c**) (THF, 60–65 °C).

The propargyl ether **166b** is converted into 2,2-bis(trifluoromethyl)pent-3,4-dieonoic acid **186** (R = H) on reaction with KOH in diethyl ether (35 °C, 2 h),[136] whilst in methanol the reaction affords the ethyl ester of the acid **186** (R = Me).[120]

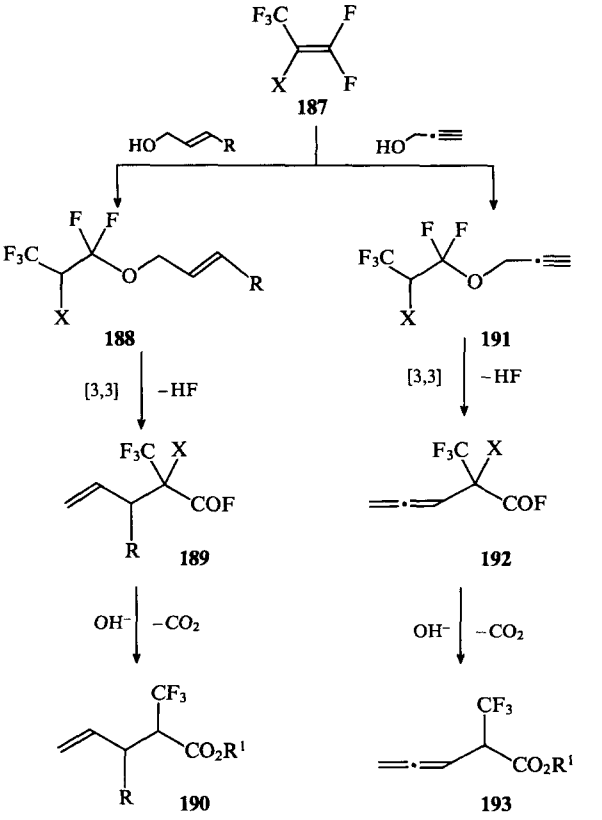


R = H (54%), Me (51%).

Allyl 2-*X*–2-*H*-pentafluoropropyl ether **188** and propargyl 2-*X*–2-*H*-pentafluoropropyl ether **191**, obtained by the addition of 2,3-unsaturated alcohols to highly electrophilic PFA with functional-group substituents in the 2-position, namely methyl perfluoromethacrylate **187a**, perfluoromethacryloyl fluoride **187b**, and 2-fluorosulfonylpentafluoropropene **187c**, are particularly readily deprotonated. Being strong CH acids, the adducts **188** and **191** interact smoothly with a weak base such as the complex $BF_3 \cdot NEt_3$. Depending on the strength of the initial CH acid, the deprotonation begins at 25–30 °C (**c**),[137, 138] 40–45 °C (**b**),[138] or 70–80 °C (**a**).[123, 128] The subsequent [3,3]-sigmatropic rearrangements of the fluorocarbanions **A** or **B** take place almost instantaneously and with evolution of much heat, leading to the selective formation of the acid fluorides **189** and **192** in 85%–90% at 65%–85% yields respectively.

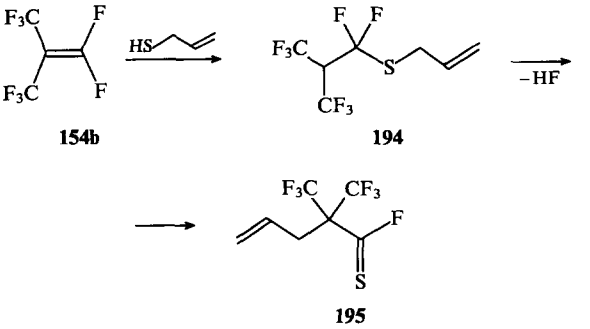
On alkaline hydrolysis, the acid fluorides **189a,b** and **192a,b** are readily decarboylated, being transformed into the 2-trifluoromethylpent-4-enoic acid **190** (R = R^1 = H) and 2-trifluoromethylpenta-3,4-dienoic acid **193** (R^1 = H) or their methyl esters.[139] The latter can be obtained under the conditions of phase transfer catalysis directly from 2-methoxycarbonyl-2-*H*-pentafluoropropyl ethers, namely from compound **191a**,[139] by-passing the stage involving the isolation of the corresponding acid fluorides.

The thio- and amino-[3,3]-sigmatropic rearrangements proceed with greater difficulty on deprotonation of the adducts of perfluoroisobutene with propene-3-thiol [allyl mercaptan] **194**



X = CO_2Me (**a**), COF (**b**), SO_2F (**c**); R = H, Ph; R^1 = H, Me.

and allylamine **196**¶. The sulfide **194** is converted into 2,2-bis(trifluoromethyl)pent-4-enethioyl fluoride **195** in 70% yield only on heating with the complex $BF_3 \cdot NEt_3$ to 100–110 °C.[140]

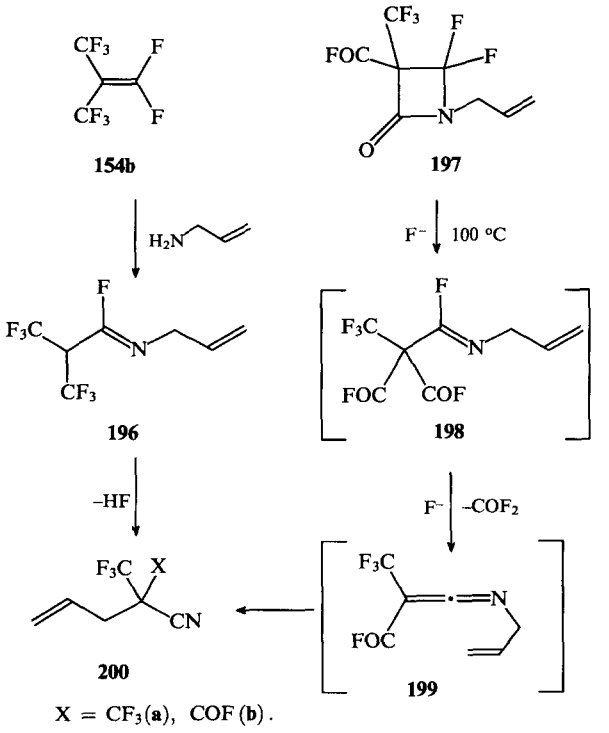


The thermolysis of the imidoyl fluoride **196** at 120 °C leads to the nitrile of 2,2-bis(trifluoromethyl)pent-4-enoic acid **200a** (yield 53%) in the absence of deprotonating agents.[141]

It is of interest that the reaction of the β-lactam **197** with caesium fluoride also involves the formation of the nitrile of 2-trifluoromethylpent-4-enoic acid **200b** in a low yield.[142] According to the authors, the ketene imine **199** — the product of the opening of the lactam ring and of the 'haloform' cleavage of the intermediate imidoyl fluoride **198** by the fluoride ion — is a precursor of compound **200b**.

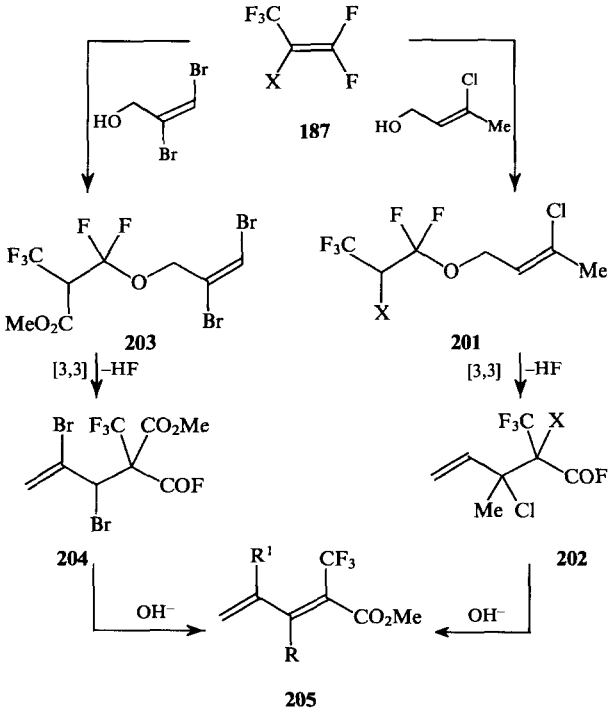
The deprotonation of 2-*H*-polyfluoroalkyl ethers proved to be a convenient method of synthesis of not only derivatives of fluorine-containing alk-4-ene- and alka-3,4-diene-carboxylic acids

¶ The rearrangement products are formed in extremely insignificant amounts in the reactions of perfluoroisobutene **154b** with propene-3-thiol and allylamine.[120]



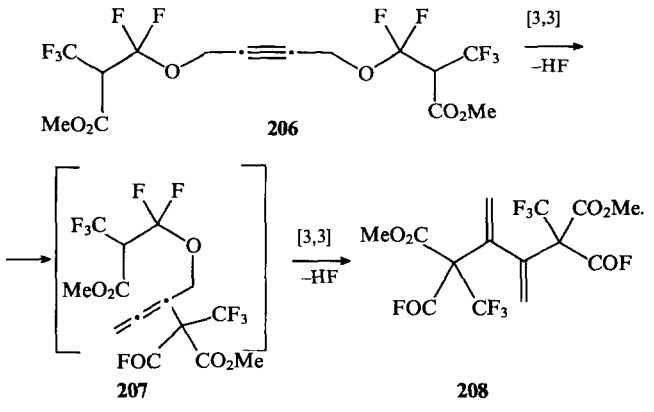
but also of the corresponding dienoates.[143, 144] Furthermore, the possibility of using this method for the synthesis of new[145] or the modification of the already available fluorinated heterocycles[146] has been demonstrated in individual instances. In all cases, the use of $BF_3 \cdot NEt_3$ as the deprotonating agent is most effective.

The adducts **201** and **203**, obtained by the addition of 3-chloro(bromo)allyl alcohols to the perfluoromethacrylates **187a,b** on heating with $BF_3 \cdot NEt_3$ to 85–110 °C, are converted into the acid fluorides **202** and **204** containing an allylic halogen atom.

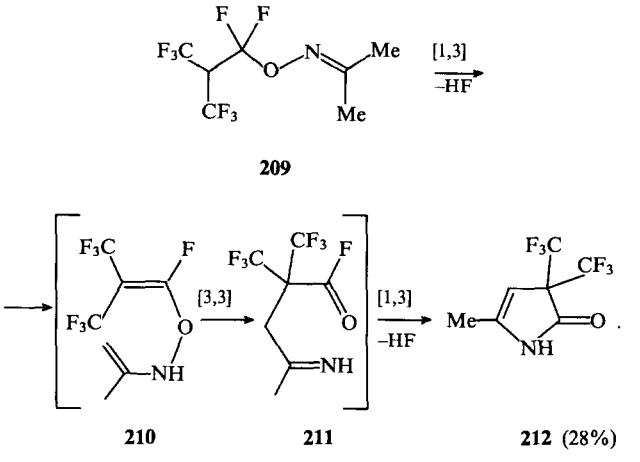


The formation of a vicinal (in relation to this atom) CH acid centre during the mild hydrolysis of the acid fluorides **202** and **204** is therefore accompanied by dehydrohalogenation with formation of methyl 2-trifluoromethylpenta-2,4-dienoates **205**† in yields up to 80%.[143]

When the 2:1 adduct of methyl perfluoromethacrylate and butynediol **206** is heated (85 °C) with the complex $BF_3 \cdot NEt_3$, the difluoride of 3,4-dimethylenehexane-1,6-dioic acid **208**—the product of the sequential [3,3]-sigmatropic reaction—is formed in 34% yield.[144] The relatively high selectivity of this reaction is achieved despite the significant steric hindrance to the [3,3]-sigmatropic shifts, especially in the deprotonation of the intermediate **207**.



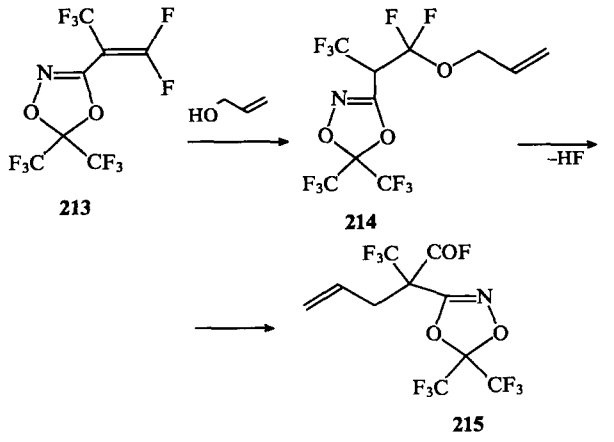
Sequential shifts in the intermediate structures occur also in the reaction of acetone *O*-(2-*H*-perfluoroisobutyl)oxime **209** with bases (KOH or $BF_3 \cdot NEt_3$). According to Zeifman et al.,[145] the dehydrofluorination of compound **209** is accompanied by a [1,3]-prototropic shift in the oxime part of the molecule with formation of the enamine **210**, which undergoes at 20 °C the Cope 3-oxa-4-aza-rearrangement to the imino-substituted acid fluoride **211**. The latter cyclises under the reaction conditions to the pyrrolinone **212**.[145]



The mild deprotonation conditions and the high rate of rearrangement, characteristic of strong fluorine-containing CH acids, have been used successfully for the modification of the pentafluoroisopropenyl-substituted 1,4,2-dioxazoline **213**.[146] The allyl ether **214** obtained from it is readily transformed on treatment with $BF_3 \cdot NEt_3$ into the acid fluoride **215**. There is no doubt that this method may prove to be extremely promising for the modification of other 2-heteroarylpentafluoropropenes.

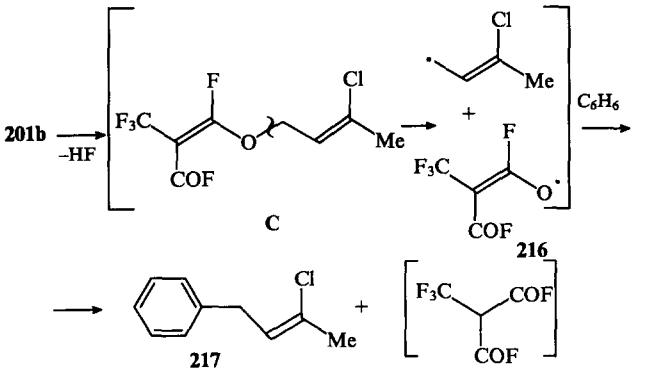
In a number of instances, the interaction of 2-*H*-polyfluoroalkyl ethers with bases is complicated by radical reactions. When 3-chlorocrotyl 2-fluorocarbonyl-2-*H*-pentafluoropropyl

† Derivatives of 2,4-dienecarboxylic acids have also been obtained in other studies[111, 119, 147, 148, 167, 169] as a result of the [3,3]-sigmatropic[111, 119, 147, 167, 169] or [2,3]-sigmatropic[148] rearrangements.



213 214 215

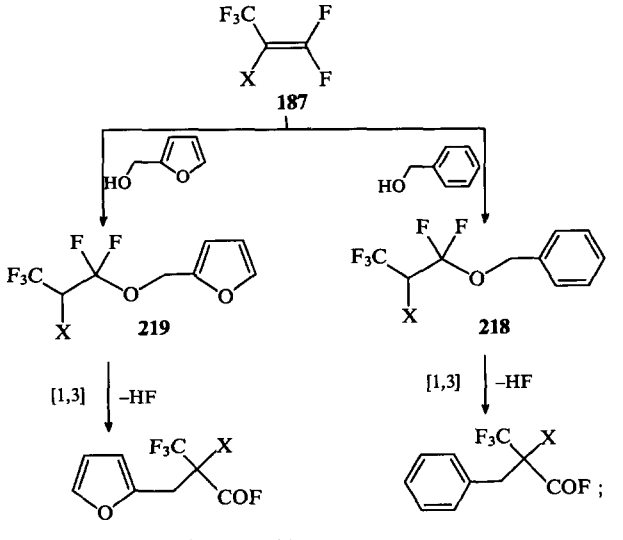
ether **201b** is heated with $BF_3 \cdot NEt_3$ in benzene, 3-chlorocrotylbenzene **217** is formed together with the rearrangement products **202b**.[143] Apparently, owing to the steric effect of the substituents at the double bond of the allyl group, stabilisation of the intermediate fluorocarbanion **A** is achieved in this instance not only via a [3,3]-sigmatropic shift but also via the elimination of a fluoride ion with subsequent homolytic cleavage of the tetrafluoropropenyl ether **C** to give the radical pair **216**.[143]



C **216** **217**

It must be emphasised that, on deprotonation of the ether **201a**, a similar reaction is not observed, evidently as a consequence of the greater stability of the corresponding carbanion.

The free radical reactions apparently occur also on dehydrofluorination of the very unstable adducts **218** and **219** formed in the reactions of the perfluoromethacrylates **187a,b** with benzyl and furfuryl alcohols.[37] [1,3] Shifts of benzyl (furfuryl) radical

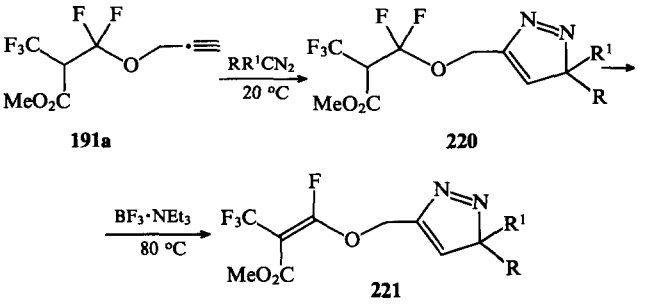


187 **219** **218**

X = CO_2Me (**a**), COF (**b**).

occur in these reactions, similar to those observed by Burger et al.[84] for benzyl ethers **96**.

On the other hand, the dehydrofluorination of the adduct **220**, obtained in the reaction of the propargyl ether **191a** with bis(trifluoromethyl)diazomethane or ethyl diazoacetate, afford the very stable 3'-pyrazolylmethyl tetrafluoropropenyl ethers **221**, the structure of which does not change even on heating to 150 °C.[149]



191a **220**

221

R = R^1 = CF_3; R = H, R^1 = CO_2Et.

On the whole, it is essential to emphasise that the high rate and chemoselectivity, satisfactory yields, and the simplicity of the apparatus provide grounds for the claim that the deprotonation of the corresponding 2-*H*-polyfluoroalkyl ethers is the most convenient and most suitable for technological synthesis of a wide variety of aliphatic fluoro-products of the [3,3]-sigmatropic rearrangement —in the first place fluorine-containing alk-4-ene; and alka-3,4-dienecarboxylic acids and their derivatives. The choice of the deprotonating agent and of the conditions in the rearrangement are determined by the CH acid properties of the initial adducts.

The unsaturated carboxylic fluoroacids and their derivatives, which have become available as a result of the use of this method, are promising synthons for the synthesis of a large number of analogues of biologically active natural products of practical value, for example fluorine-containing 4-butanolides.[111, 136, 139, 150]

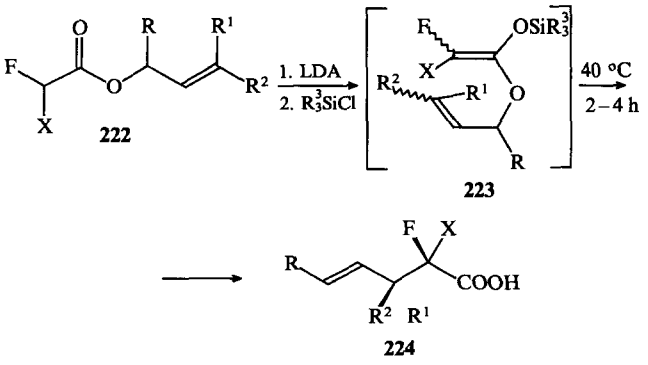
V. Rearrangements of polyfluorocarboxylic acid esters

The [3,3]-sigmatropic rearrangement of the alkenyl esters of 2-*H*-carboxylic acids, known as the Ireland–Claisen rearrangement,[151] usually occurs under mild conditions after the transformation of the alkenyl carboxylates under the influence of organolithium reagents into the corresponding lithium enolates or *O'*-alkenyl-*O*-trialkylsilylketenals. This method, characterised by an exceptionally high diastereoselectivity, is believed to be one of the best for the synthesis of alk-4-enecarboxylic acids.[152] In recent years, the Ireland–Claisen rearrangement has been successfully extended also to the allyl esters of 2-*H*-fluorocarboxylic acids as a result of the efforts of Welch and coworkers.[153–155]

The allyl esters of fluoroacetic acid **222a** and 1-fluoropropionic acid **222b** are stereoselectively deprotonated in THF (−100 to −78 °C) by lithium amides (the best of which is lithium diisopropylamide) with formation of 2-fluoropent-4-enoic acids **224**‡ in 15%–97% yield.[153, 154] The use of silylating agents as enolate traps in the second stage made it possible to establish that the (*E*)-form of the intermediate fluoroketenals **223** participates in the rearrangement.[153, 154]

The presence of fluorine atoms in the molecules of the fluoroketenals **223** apparently facilitates somewhat, and accelerates, their rearrangement. This is indicated by the half-reaction time ($\tau_{1/2}$ = 40 min at 40 °C) measured for compound **223a** (R = R^1 = H, R^2 = Me) and also by the fact that the ketenals **223** can be isolated in a free state,[153] in contrast to the non fluorinated analogues.[152]

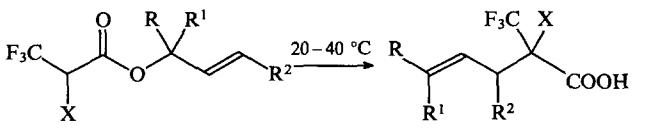
‡ 2-Fluoro-4-butanolides have also been obtained by converting the acids **224** into lactones.[153–155]



X = H(a), Me(b); R, R¹, R² = H, Me.

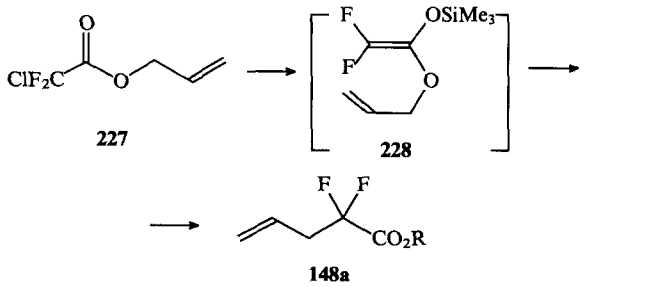
Equimolar mixtures of triethylamine and trialkylsilyl triflates (R_3SiOTf) are more convenient reagents for the generation of silylated fluoroketenals. In this case, the reactions do not require ultralow temperatures. The suitability of the Ireland–Claisen rearrangement for the synthesis in a satisfactory yield of not only the 2-monofluoro-substituted unsaturated acids[96, 155] but also of the polyfluorinated acids of this kind[96, 156, 157] must be regarded as its advantage.

Nakai and coworkers[156, 157] found that 2-trifluoromethylalk-4-ene carboxylic acid **226a** and 2-fluoro-2-trifluoromethylalk-4-enecarboxylic acid **226b** are formed smoothly when alkenyl polyfluoropropionates **225** are treated with a mixture of NEt_3 and Me_3SiOTf in methylene chloride with subsequent refluxing of the reaction solution for 5–12 h (**a**) or its stirring (at 20 °C) for 36 h (**b**).



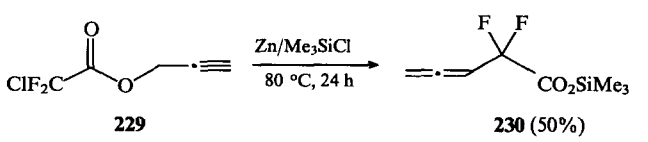
X = H (**a**), F (**b**); R, R¹, R² = H, Me.

Allyl chlorodifluoroacetate **227** undergoes the [3,3]-sigmatropic rearrangement only under the conditions of the Reformatskii reaction. When a mixture of compound **227**, freshly activated zinc, and chlorotrimethylsilane is heated in acetonitrile (100 °C, 20 h), derivatives of 2,2-difluoropent-4-enoic acid **148a** are formed after the rearrangement of the intermediate ketenal **228** and the appropriate treatment.[158]

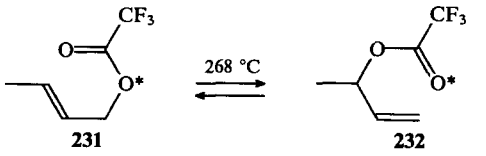


R = H (78 %), Et (60 %), $SiMe_3$ (95 %).

Other 2,2-difluoroalk-4-enecarboxylic acids, including some extremely difficult to obtain, are also formed under these conditions form the corresponding esters of chlorodifluoroacetic acid. In addition, the ester of 2,2-difluoropenta-3,4-dienoic acid **230** was obtained from propargyl chlorodifluoroacetate **229**.[158]

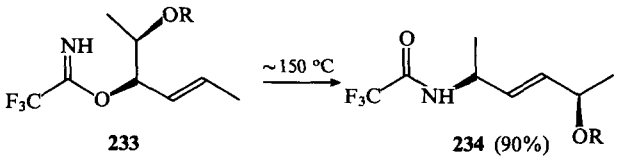


The allyl esters of trifluoroacetic acid are incapable of entering into a similar reaction. However, it has been shown with the oxygen-labelled crotyl trifluoroacetate **231**[159] that, when the latter compound is heated in the gas phase, a reversible [3,3]-sigmatropic rearrangement of this compound to the 1-methylallyl ester **232** takes place.

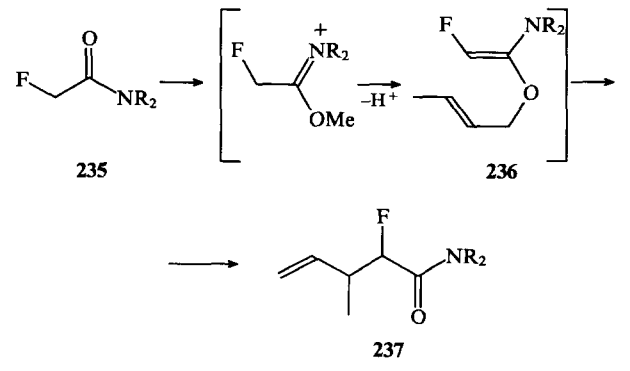


On the other hand, the trifluoroacetic acid iminoester **233** undergoes smoothly and stereoselectively the Cope 1-aza-3-oxa-rearrangement, on heating in xylene (20 h), to *N*-alkenyltrifluoroacetamide **234**, which is a precursor of an optically active polyoxamic acid.[160]

The analogous iminoester of trichloroacetic acid isomerises after more prolonged refluxing in xylene (48 h), but the yield of the final trichloroacetamide does not exceed 40%.[160]



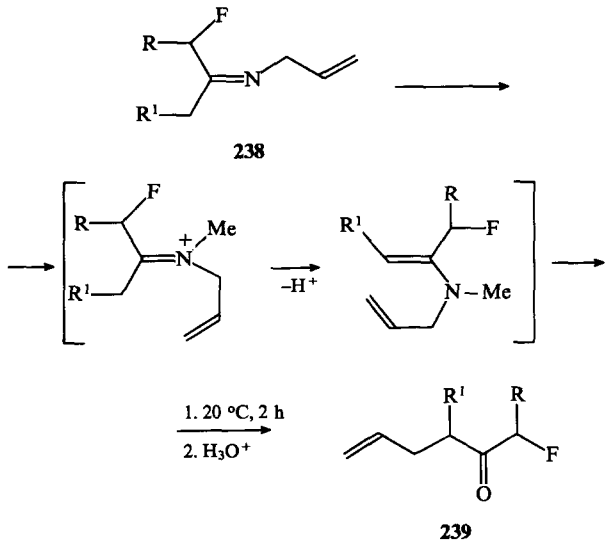
The optically active amides of monofluoro-substituted alk-4-enecarboxylic acids are obtained under milder conditions via intermediate aminoketenals, for example, compound **236**.[161a] The fluoroacetamides **235** are alkylated in the first stage with methyl triflate (MeOTf) or dimethyl sulfate, after which the product is treated with the lithium salt of the geometrically pure crotyl alcohol. The products of the rearrangement (the amides **237**) are isolated in 23%–78% yield (depending on the configuration of crotyl alcohol) after stirring the reaction solution (THF or methylene chloride, at 225 °C) for at least 14 h.



R = Me, $-(CH_2)_4-$, Pr^i.

The optically active *N*-(2′-fluoro-3′-methylpent-4′-enoyl)-2,5-dimethylpyrrolidine was obtained in the same way (at 20 °C, 24 h) in 61% yield.[161b]

The Claisen amino-rearrangement (the Cope 3-aza-rearrangement) of the α-halogenated and non-halogenated ketimines proceeds via a similar mechanism with participation of the quaternised nitrogen atom.[162] Successive treatment of *N*-fluoroalkylideneallylamines **238** with alkylating (MeOTf) and deprotonating [solution of 1,8-bis(dimethylamino)naphthalene in MeCN] agents under mild conditions leads to the monofluoroketones **239**.



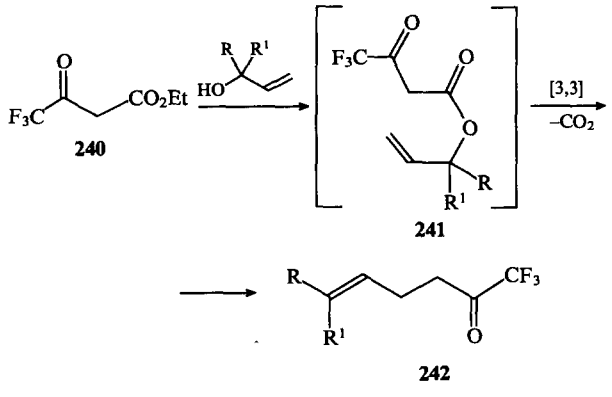
238

239

R = Me, R^1 = H (54%); R, R^1 = $-(CH_2)_3-$ (31%).

The high regioselectivity of these reactions[162] permits their use as a convenient method of synthesis of α-halogenated 4,5-unsaturated ketones.

Camps and coworkers[163, 164] investigated in relation to several examples the behaviour of the esters of fluorine-containing acids in the base-catalysed Carroll rearrangement. Ethyl 4,4,4-trifluoroacetoacetate **240** was used as the starting compound in this rearrangement. The transesterification of the acetate **240** with 1-substituted allyl alcohols is carried out in the presence of catalytic amounts of sodium acetate (150 °C, 15 h). The allyl ethers **241**, generated as a result of this reaction, undergo *in situ* a [3,3]-sigmatropic shift, coupled with decarboxylation and formation of CF_3-substituted 4,5-unsaturated ketones **242**.[163]



240

241

242

R = R^1 = Me (80%); R = Me, R^1 = $(CH_2)_2CH$ = CMe_2 (84%).

It has been noted[163] that the presence of the CF_3 group in the acetate **240** is responsible for the less severe reaction conditions compared with those which obtain in the Carroll rearrangement of ethyl acetoacetate.[165]

Although this method is not distinguished by a high stereoselectivity, it makes it possible to obtain in satisfactory yields certain compounds of practical value, for example geranyltrifluoroacetone,[164] which is a trifluoro-analogue of juvenile hormone.

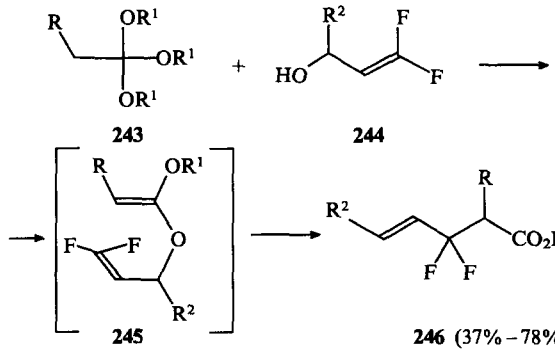
VI. Rearrangements of polyfluoroallyl ethers

Fluorine-containing 2,3-unsaturated alcohols are precursors of polyfluoroallyl vinyl ethers which undergo *in situ* [3,3]-sigmatropic transformations, involving Johnson–Claisen, Claisen, and Ireland–Claisen rearrangements. Preparative syntheses of fluorinated allyl and propargyl alcohols began to be actively developed only during the last decade and one can therefore postulate that there are good prospects for the development of methods of synthesis of unsaturated compounds based on the rearrangements of the corresponding polyfluoroallyl ethers.

The initial components in the Johnson–Claisen rearrangement[166] are trialkyl orthoacetates and allyl alcohols. The high stereoselectivity of the rearrangement requires the use of geometrically pure alcohols, whilst its fairly severe conditions (110 °C–150 °C, the presence of an acid catalyst generating the vinyl component) permit the involvement of highly substituted unsaturated alcohols in these reactions.

Among fluorinated alcohols, only the most readily available 3,3-difluoroallyl and trifluoromethylated allyl and propargyl alcohols have been made to undergo the Johnson–Claisen rearrangement.

The 3,3-difluoroallyl alcohols **244** react with the orthoesters **243** in boiling toluene in the presence of catalytic amounts of propionic acid. The resulting difluoroallyl vinyl ethers **245** isomerise under the reaction conditions (115 °C, 5 h) to the esters of 4,5-dialkyl-3,3-difluoroalk-4-enecarboxylic acids **246**.[167] Under the influence of alkali, the esters **246** are readily dehydrofluorinated, being converted into alkyl 3-fluoro-5R^2-penta-2,4-dienoates.[167]



243

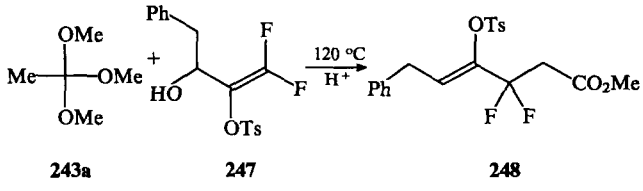
244

245

246 (37%–78%)

R = H (**a**), Me (**b**); R^1 = Me, Et; R^2 = H, CH_2CH_2Ph, C_5H_{11}.

The analogous reaction of the orthoester **243a** (R^1 = Me) with 1-benzyl-3,3-difluoro-2-tosyloxyallyl alcohol **247** is smoothly completed after 1.5 h by the formation of the ester **248** in 84% yield.[92]

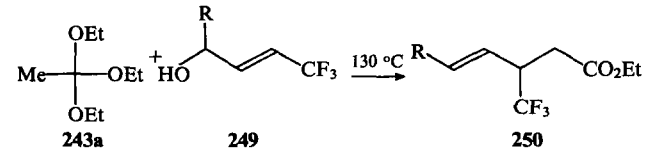


243a

247

248

Trifluoromethyl-substituted unsaturated alcohols undergo the Johnson–Claisen rearrangements under virtually the same conditions. Japanese workers have shown[147, 168, 169] that these reactions constitute a convenient method for the stereoselective synthesis of the esters of 3- and 4-CF_3-substituted unsaturated acids. Thus, ethyl 3-trifluoromethyl-5R-pent-4-enoates **250** have been obtained by heating 1-alkyl-3-trifluoromethylallyl alcohols **249** in a large excess of the orthoester **243a** (R^1 = Et) in the presence of a catalyst (EtCOOH).[147]



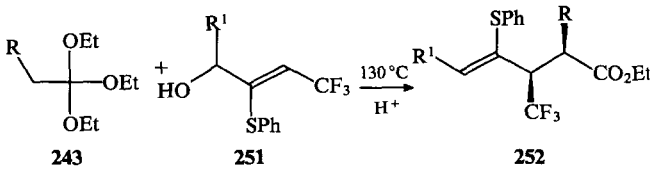
243a

249

250

R = CH_2CH_2Ph (71%), CH_2OCH_2Ph (45%), n-C_6H_{13} (81%).

The reactions of 2-phenylthio-3-trifluoromethylallyl alcohols **251** with the orthoesters **243** lead stereoselectively to the esters of 4-phenylthio-3-trifluoromethylalk-4-ene carboxylic acids **252** in 55%–87% yield.[168]

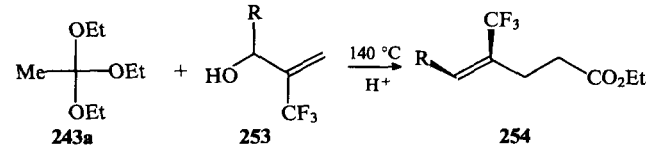


243 **251** **252**

R = H, Me; R¹ = Me, Et, Pr^i, Ph.

The presence of the phenylthio-group at the double bond in the alcohol **251** does not exert a significant influence on the conditions of the rearrangement.

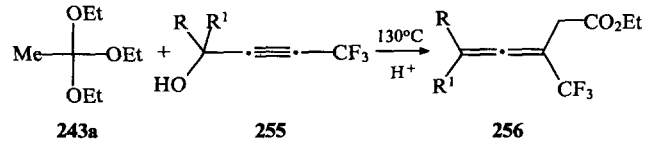
2-Trifluoromethylallyl alcohols **253** react with the orthoester **243a** under somewhat more severe conditions. The esters of 4-trifluoromethylalk-4-enecarboxylic acid **254** are formed stereoselectively as the final products in this instance.[169]



243a **253** **254**

R = CH_2CH_2Ph (86%), CH_2OCH_2Ph (73%).

Trifluoromethyl-substituted acetylenic alcohols also enter into a reaction of a similar type. Interaction of 1-R-3-trifluoromethylpropargyl alcohols **255** with the orthoester **243a** leads to derivatives of 3-trifluoromethylpenta-3,-4-dienoic acid **256** in 32%–55% yields.[147]

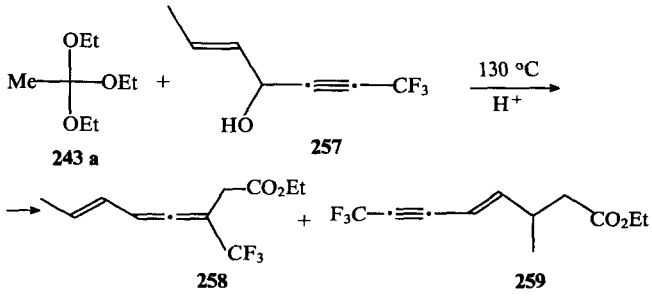


243a **255** **256**

R = CH_2CH_2Ph, CH_2OCH_2Ph, *n*-C_6H_{13}, R¹ = H; R = R¹ = $-(CH_2)_5-$.

The base-catalysed isomerisation of compound **256** affords 3-trifluoromethyl-5-R-penta-2,4-dienoate (R = CH_2OCH_2Ph).[147]

It is of interest that allyl and propargyl alcohols exhibit the same tendency to undergo the Johnson–Claisen rearrangement. The use of 1-propenyl-3-trifluoromethylpropargyl alcohol **257** in this reaction leads to a mixture of the esters of 3-trifluoromethylocta-3,4,6-trienoic acid **258** and 7-trifluoromethylhept-4-en-6-ynoic acid **259** in proportions of 1 : 1.[147]



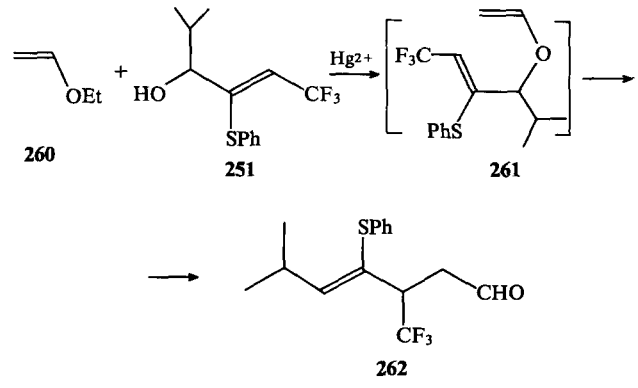
243 a **257**

258 **259**

At the same time, an attempt to involve 1-(4′-methoxyphenyl-2′,3′,6′-trimethyl)-3-trifluoromethylpropargyl alcohol in the Johnson–Claisen rearrangement was unsuccessful,[170] apparently owing to the powerful steric effect of the bulky substituent in the 1-position.

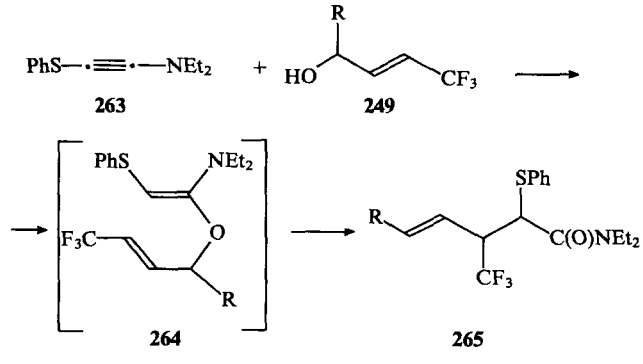
The ability of polyfluoroallyl ethers to enter into the Claisen and Ireland–Claisen rearrangements has also been investigated.

The thermal condensation (150 °C) of ethyl vinyl ether **260** and 3-trifluoromethylallyl alcohol **251** (R = Pr^i) catalysed by mercury acetate affords 3-trifluoromethylheptenal **262** in 50% yield.[168] At temperatures below 150 °C, the Claisen rearrangement of the initial 3-trifluoromethyl vinyl ether **261** does not occur.



260 **251** **261** **262**

Another method of generation of the intermediate Claisen substrate is involved in the reaction of phenylthioalkynamine **263** with trifluoromethylallyl alcohol **249**.[147] The adduct **264** of these reactants isomerises on refluxing in toluene to the amide **265**, which is subsequently oxidised to 3-trifluoromethylalk-2,4-dienoate. The use of (*Z*)-**249** instead of (*E*)-**249** lowers the yield of the amide **265** from 62% to 35%.

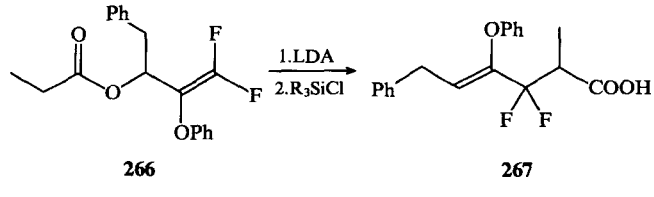


263 **249** **264** **265**

R = CH_2OCH_2Ph.

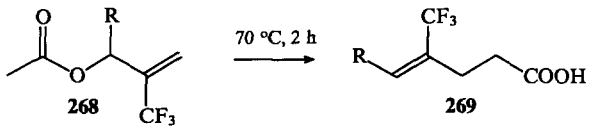
The polyfluoroallyl esters of carboxylic acids undergo the Ireland–Claisen rearrangement under standard conditions, although unsuccessful attempts to involve certain difluoroallyl carboxylates in this reaction have been noted.[167]

The difluoroallyl propionate **266** is readily transformed into 3,3-difluoro-2-methylalk-4-enecarboxylic acid **267** in 57% yield on successive treatment with lithium diisopropylamide and trialkylchlorosilane.[92]



266 **267**

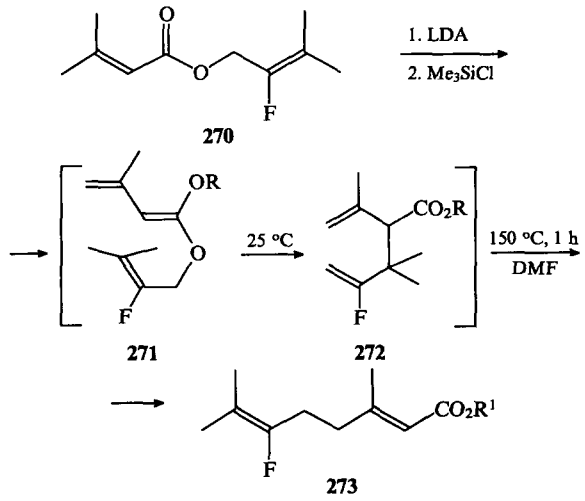
On treatment with lithium isopropylcyclohexylamide and *tert*-butylchlorodimethylsilane in hexamethylphosphoramide, 2-trifluoromethylallyl acetates **268** are similarly converted into 4-trifluoromethylalk-4-enecarboxylic acid **269** (in yields up to 86%).[169]



268 269

R = CH_2CH_2Ph, CH_2OCH_2Ph.

The tandem Ireland–Claisen/Cope rearrangement used by Camps et al.[171] is a key stage in the multistage synthesis of the monofluoro-analogues of one of the juvenile hormones from 2-fluoroallyl acrylate **270**.



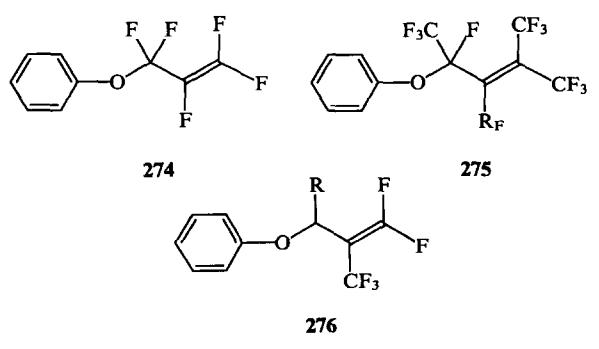
270 271 272 273

R = $SiMe_3$; R^1 = H, Me.

When these reactions are carried out in one stage without the isolation of the intermediates **271** and **272**, it is possible to obtain the ester of 6-fluoro-3,7-dimethyl-octa-2,6-dienoic acid **273** in 78% yield.[171]

Overall, one may note that the fluorine atoms and the trifluoromethyl group apparently do not exert a significant influence on the conditions and rate of the [3,3]-sigmatropic rearrangements of polyfluoroallyl ethers. This has been confirmed by the calculations of Gajewski et al.,[35] who determined the activation parameters for the Claisen rearrangement of 1-trifluoromethylallyl vinyl ether. According to the authors' data,[35] the CF_3 group at the C(4) atom does not have an appreciable influence on the rate of the rearrangement, in contrast to, for example, the CN group, which ensures a gain in activation free energy of 3.5 kcal mol^{-1} in this position.[33]

The thermodynamic stability of phenyl polyfluoroallyl ethers is evidently also close to that of the fluorine-free allyl ethers of phenols. Indeed, perfluoroallyl phenyl ether **274**[172] and phenyl polyfluoroalkenyl ethers **275**[100] and **276**[173] have fairly high thermal stabilities and do not isomerise after prolonged storage or on heating under the reaction conditions.



274 275

276

R_F = $CF(CF_3)_2$, R = $CF_2(CH_2CF_2)_nF$.

The absence of positive effects by the fluorine atoms on the CF_3 group in the [3,3]-sigmatropic rearrangements of polyfluoroallyl vinyl ethers in no way reduces the preparative value of these compounds. They make it possible to synthesise highly stereoselectively, and in a satisfactory yield, 3- and 4-fluoro(trifluoromethyl)-substituted unsaturated acids and their derivatives which are otherwise difficult to obtain.

VII. Conclusion

Whereas only two studies[35, 44] devoted to the Claisen rearrangement were mentioned in Hudlicky's fundamental monograph[105b] in 1976, towards the end of the 1980s the continuous growth in the number of studies on the [3,3]-sigmatropic rearrangements of organofluorine compounds already made it possible to recognise these reactions as one of the important methods of synthesis of fluorine-containing synthons.[174] Analysis of the data presented in this review permits an assessment at a deeper level of the applied and theoretical importance of the [3,3]-sigmatropic rearrangements of compounds of the organofluorine series.

In the first place, one should note their undoubted applied value. At the present time, this method is used to synthesise many organofluorine compounds of different classes. They include perfluorinated aromatic or heteroaromatic fragments of pyrans, furans, thiophens, and pyrroles condensed with a benzene ring, polyfluorinated 4,5-unsaturated ketones, derivatives of alk-4-ene, alka-3,4-diene-, and alka-2,4-diene-carboxylic acids, alkenylmalonic and carboxylic 4-ketoacids, furans, thiophens oxazolones, 4-butanolides, and compounds of other types. At the same time, the [3,3]-sigmatropic rearrangements have been used successfully in the preparative syntheses of fluorine-containing[81, 82, 84, 89] and non-fluorinated[160] α-aminoacids and fluorine- and trifluoromethyl-modified micotoxins,[94] phospholipids,[112] nucleosides,[155] juvenile hormones,[164, 171] and new medicinal[53, 157] and pesticidal[77, 157] preparations.

In addition, the considerable potential possibilities of the [3,3]-sigmatropic rearrangements as a universal method for the formation of the C–C bond can probably find applications in the solution of certain problems in the industrial chemistry of fluorine of current interest. For example, in the large-scale manufacture of hexafluoropropene, they can be used for the selective removal of a highly toxic impurity, namely perfluoroisobutene, from the main product with the simultaneous synthesis of the products of the rearrangement of the impurity. The same rearrangements can be used for the ecologically clean assimilation of the existing industrial manufacture of ozone-damaging Khladons (Freons), which are capable of being transformed into polyhaloalkenes under certain conditions.[175]

Theoretical studies on the [3,3]-sigmatropic rearrangements of organofluorine compounds have also proved extremely fruitful. By virtue of the unique effect of the fluorine atoms and the fluoroalkyl groups on the electronic system of the double bond of the 'vinyl' fragment in the series of 2,3-unsaturated ethers of polyfluoroalkenols and polyfluorocycloalkenols, compounds with a broad spectrum of reactivities were obtained (ranging from compounds thermodynamically stable at 150 °C to compounds which isomerise spontaneously under the conditions of their synthesis even on intense cooling). It has been shown that the probability and conditions of the rearrangement are determined primarily by the level of the population of the π-orbital of the vinyl bond, its capacity for polarisation from the C(2) to the C(1) atom, and the steric effect of the bulky fluorine-containing substituents in the C(1) position. The necessary preconditions for the prediction of the behaviour of the corresponding ethers of polyfluoroalkenols (polyfluorocycloalkenols) in the [3,3]-sigmatropic rearrangement and for the control of this process were thus created.

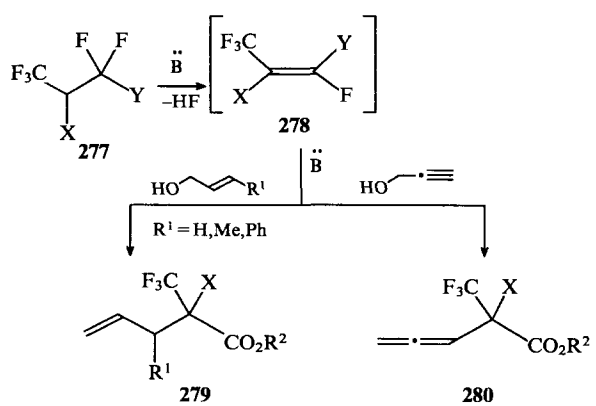
The phenomenon of the low-temperature anionic Claisen and Cope rearrangements, widely discussed in recent years,[9, 13, 28-32] has been manifested particularly clearly in the study of the [3,3]-sigmatropic rearrangements of fluorocarbanions.[37] The general features of an anionotropic [3,3]-sigmatropic process, the driving force of which is the highly effective symmetry-allowed charge-controlled pπ interactions, are characteristic of these rearrangements. However, instances of the easiest sigmatropic shifts have been noted precisely in the reactions of certain polyfluoroalkenes (perfluoroisobutene, perfluoromethacrylic acid diethylamide) with 2,3-unsaturated alcohols even in the absence of basic reagents.

The results in the study of the [3,3]-sigmatropic rearrangements of fluorine-containing compounds obtained hitherto indicate the appearance of a new modern method of organofluorine synthesis which reflects the unusual character of the fluorine chemistry as a whole. These results constitute a good practical and theoretical basis for further still more vigorous development of this field of chemistry.

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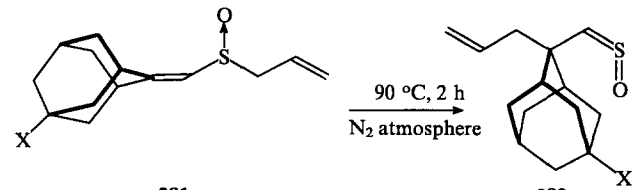
The studies published during the brief period of the preparation of the present review for the press confirm the steady interest of investigators in the problem considered. In one of the latest monographs devoted to fluorine chemistry, a review by Welch et al.[176] was published in which the Claisen rearrangements of the acetals of fluoroacetamides (fluorine-containing aminoketenals) are considered as an effective instrument for asymmetric synthesis.

A new convenient method of synthesis of derivatives of 2-trifluoromethyl-substituted unsaturated acids has been developed recently.[177] The fluorinated CH acids **277** interact in the presence of bases (B̈) with allyl and propargyl alcohols to form the products of the [3,3]-sigmatropic rearrangement — the esters of 2-trifluoromethylpent-4-enoic acid **279** and 2-trifluoromethylpenta-3,4-dienoic acid **280**. The reaction conditions and yields of the final products **279** and **280** are determined by the strength of the CH acids **277**, from which the polyfluoroalkenes **278** are generated initially. The latter undergo further reactions *in situ*. The new method[177] makes it possible to obtain in one stage the derivatives of unsaturated fluorocarboxylic acids, by-passing the laborious syntheses of polyfluroalkenes and their adducts with 2,3-unsaturated alcohols.



X = CF_3, CO_2R; Y = F, OR;
R = Me, Et; R^2 = R, CH_2CH = CHR^1, $CH_2C{\equiv}CH$.

American investigators[178] studied the thio-[3,3]-sigmatropic rearrangement of the unsubstituted and 5-fluoro-substituted adamantylidenemethyl allyl sulfoxides **281**, which leads to a mixture of the stereoisomeric sulfines **282** [the stable (*Z*)-form is illustrated]. The introduction of a fluorine atom in the 5-position does not alter the reaction conditions, but increases the number of diastereoisomers formed from 2 to 4.

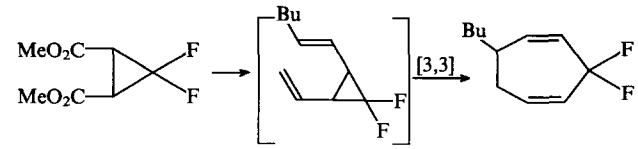


281 **282**

X = H, F.

It was established[178] that the steric and electronic effects of the substituents in compound **281** influence equally the stereochemistry of the process, in contrast to the Cope oxy-rearrangement,[43] investigated by the same workers, in which the influence of the steric factor predominated.

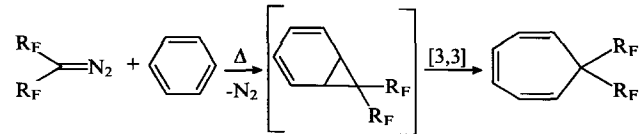
One of the few examples of the practical use of the Cope rearrangement has been described in a study[179] devoted to the preparative synthesis of fluorinated analogues of cycloheptadiene pheromones present in brown seaweed. The di(methoxycarbonyl)-substituted *gem*-difluorocyclopropane **283** was used as the synthon for the synthesis of the *trans*-dialkenyl-substituted *gem*-difluorocyclopropane **284**. The extreme instability of the cyclopropane **284**, which rearranges spontaneously at room temperature to 3,3-difluorocyclohepta-1,4-diene **285**, was unexpected.



283 **284** **285**

The kinetic parameters of the isomerisation of compound **284** to **285**, determined by the authors,[179] made it possible to discover the marked influence of the geminal fluorine atoms, weakening the opposite bond of the cyclopropane ring and leading to milder reaction conditions.

It is essential to note that a similar rearrangement had been observed earlier in relation to *gem*-perfluoroalkylnorcaradienes **287**. Krespan and coworkers[180] showed that the pyrolysis of the perflurodiazoalkanes **286** in an excess of benzene (150 °C–200 °C, 8 h) affords 7,7-bis(perfluoroalkyl)cyclohepta-1,3,5-trienes **288** as the main products in yields of 62% (**a**) and only 22% (**b**). Compounds **288** are formed as a result of the Cope rearrangement of the intermediate norcaradienes **287**.



286 **287** **288**

R_F = CF_3 (**a**), C_2F_5 (**b**).

The cycloheptatriene **288a** is formed as a side product in 11% yield on photolysis of bis(trifluoromethyl)diazomethane **286a** (benzene, 40 h).[180]

The preparative value of the Cope rearrangement of substrates of the type of compounds **284** and **287** increases sharply if this process is considered as a convenient approach to the synthesis of tropylidene structures containing fluorine and fluoroalkyl substituents, which are otherwise difficult to obtain.

References

1. L Claisen *Ber. Dtsch. Chem. Ges.* **45** 3157 (1912)
2. D S Tarbell *Org. React. (N.Y.)* **2** 1 (1944)
3. S J Rhoads, in *Molecular Rearrangements* Vol. 1 (Ed. P de Mayo) (New York: Interscience, 1963) p. 660
4. A Jefferson, F Scheinmann *Quart. Rev.* **22** 391 (1968)
5. A C Cope, E M Hardy *J. Am. Chem. Soc.* **62** 441 (1940)
6. S J Rhoads, N R Raulins *Org. React.* **22** 1 (1975)
7. T Hayashi *J. Synth. Org. Chem. Jpn.* **34** 396 (1976)
8. G B Bennett *Synthesis* 589 (1977)
9. R P Lutz *Chem. Rev.* **84** 205 (1984)
10. L E Overman *Angew. Chem., Int. Ed. Engl.* **23** 579 (1984)
11. A W Murray *Org. React. Mech.* 429 (1988); 457 (1989)
12. Ch J Moody *Adv. Heterocycl. Chem.* **42** 203 (1987)
13. F E Ziegler *Chem. Rev.* **88** 1423 (1988)
14. L E Overman *Acc. Chem. Res.* **13** (7) 218 (1980)
15. L Morin, J Lebaud, D Paquer, R Chaussin, B Daniel *Phosphorus Sulfur* **7** 69 (1979)
16. A V Anisimov, E A Viktorova *Khim. Geterotsikl. Soedin.* 435 (1980); A V Anisimov, E A Viktorova, T A Danilova *Molekulyarnye Peregruppirovki Seraorganicheskikh Soedinenii* (Molecular Rearrangements of Organosulfur Compounds) (Moscow: Izd. Moskov. Gos. Univ., 1989) p. 53
17. N M Przheval'skii, I I Grandberg *Usp. Khim.* **56** 814 (1987) [*Russ. Chem. Rev.* **56** 477 (1987)]
18. S Blechert *Synthesis* 71 (1989)
19. R B Woodward, R W Hoffmann *Angew. Chem., Int. Ed. Engl.* **8** 781 (1969)
20. T Nakai, K Mikami, N Sayo *J. Synth. Org. Chem. Jpn.* **41** 100 (1983)
21. R K Hill, in *Asymmetric Synthesis* Vol. 3 (Ed. J D Morrison) (Orlando: Academic Press, 1984) p. 503
22. F E Ziegler *Acc. Chem. Res.* **10** (6) 227 (1977)
23. P A Barlett *Tetrahedron* **36** 3 (1980)
24. T Nakai *Kagaku to Seibutsu* **23** 471 (1985); *Chem. Abstr.* **104** 19 192b (1986)
25. T Kametani, H Kasai, E Sato, T Suzuki *Proc. Indian Acad. Sci. Chem. Sci.* **100** (2–3) 91 (1988); *Chem. Abstr.* **110** 24 118k (1989)
26. T Suzuki, E Sato, K Unno *Akita Igaku* **15** 759 (1988); *Chem. Abstr.* **112** 56 391b (1990)
27. T I Temnikova, S N Semenova *Molekulyarnye Peregruppirovki v Organicheskoi Khimii* (Molecular Rearrangements in Organic Chemistry) (Leningrad: Khimiya, 1983) p. 36
28. D A Evans, A M Golob *J. Am. Chem. Soc.* **97** 4765 (1975)
29. S E Denmark, M A Harmata *J. Am. Chem. Soc.* **104** 4972 (1982)
30. S E Denmark, M A Harmata *J. Org. Chem.* **48** 3369 (1983)
31. G Buchi, D E Vogel *J. Org. Chem.* **50** 4664 (1985)
32. S E Denmark, M A Harmata, K S White *J. Am. Chem. Soc.* **111** 8878 (1989)
33. C J Burrows, B K Carpenter *J. Am. Chem. Soc.* **103** 6983 (1981)
34. M J S Dewar, E F Healy *J. Am. Chem. Soc.* **106** 7127 (1984)
35. J J Gajewski, K R Gee, J Jurayj *J. Org. Chem.* **55** 1813 (1990)
36. C G Krespan *Tetrahedron* **23** 4243 (1967)
37. V G Andreev, A F Kolomiets, A V Fokin *J. Fluorine Chem.* **56** 259 (1992)
38. S T Purrington, S C Weeks *J. Fluorine Chem.* **56** 165 (1992)
39. J F M Oth, R Merenyi, H Rottele, G Schroder *Tetrahedron Lett.* **9** 3941 (1968)
40. Y Kobayashi, A Ando, K Kawada, I Kumadaki *J. Am. Chem. Soc.* **103** 3958 (1981)
41. W R Dolbier, K S Medinger *Tetrahedron* **38** 2411 (1982)
42. W R Dolbier, A C Alty, O Phanstiel *J. Am. Chem. Soc.* **109** 3046 (1987)
43. M-h Lin, W J le Noble *J. Org. Chem.* **54** 997 (1989); M-h Lin, W H Watson, R P Kashyap, W J le Noble *J. Org. Chem.* **55** 3597 (1990)
44. G M Brooke *Tetrahedron Lett.* **12** 2377 (1971)
45. G M Brooke, D H Hall, H M M Shearer *J. Chem. Soc., Perkin Trans. 1* 780 (1978)
46. G M Brooke *J. Chem. Soc., Perkin Trans. 1* 233 (1974)
47. G M Brooke *J. Chem. Soc., Perkin Trans. 1* 1463 (1976)
48. G M Brooke, D H Hall *J. Fluorine Chem.* **20** 163 (1982)
49. G M Brooke *J. Fluorine Chem.* **22** 483 (1983)
50. G M Brooke, R S Matthews, N S Robson *J. Fluorine Chem.* **16** 461 (1980)
51. G M Brooke, R S Matthews, N S Robson *J. Chem. Soc., Perkin Trans. 1* 102 (1980)
52. G M Brooke, I M Eggleston, F A Hale *J. Fluorine Chem.* **38** 421 (1988)
53. G M Brooke, J A K J Ferguson *J. Chem. Soc., Perkin Trans.1* 515 (1986)
54. C K Ingold *Structure and Mechanism in Organic Chemistry* (Translated into Russian) (Moscow: Mir, 1973) p. 711
55. B Iddon, H Suschitzky, J A Taylor *J. Chem. Soc., Perkin Trans. 1* 2756 (1979)
56. G M Brooke, D I Wallis *J. Chem. Soc., Perkin Trans. 1* 1417 (1981)
57. G M Brooke, J R Cooperwaite, J A K J Ferguson, A G Morpeth *J. Fluorine Chem.* **29** 113 (1985)
58. G M Brooke, J R Cooperwaite, A G Morpeth *J. Chem. Soc., Perkin Trans. 1* 2637 (1985)
59. G M Brooke, D I Wallis *J. Fluorine Chem.* **20** 173 (1982)
60. G M Brooke *J. Chem. Soc., Perkin Trans. 1* 107 (1982)
61. (a) G M Brooke, R S Matthews, M E Harman, M B Hursthouse *J. Fluorine Chem.* **53** 339 (1991); (b) W S Trahanovsky, S L Emeis, A S Lee *J. Org. Chem.* **41** 4043 (1976); (c) R F C Brown, F W Eastwood *J. Org. Chem.* **46** 4588 (1981)
62. V N Kovtonyuk, L S Kobrina, G G Yakobson *Zh. Org. Khim.* **15** 1447 (1979)
63. G M Brooke, D I Wallis *J. Chem. Soc., Perkin Trans. 1* 1659 (1981)
64. G M Brooke, J R Cooperwaite *J. Chem. Soc., Perkin Trans. 1* 2643 (1985)
65. T D Petrova, V P Mamaev, G G Yakobson *Izv. Akad. Nauk SSSR, Ser. Khim.* 679 (1969)
66. G M Brooke *J. Chem. Soc., Perkin Trans. 1* 821 (1983)
67. F D Benke, G M Brooke *J. Fluorine Chem.* **26** 77 (1984)
68. (a) D L Ladd, D Gaitanopoulos, J Weinstock *Synth. Commun.* **15** 61 (1985); (b) M T Clark, D D Miller *Tetrahedron Lett.* **26** 4299 (1985)
69. K Maruyama, N Nagai, Y Naruta *J. Org. Chem.* **51** 5083 (1986)
70. M A Patrick, S K Sethi, S E Unger, S Mirsadegni, A A Ribeiro, D R Thakker *J. Org. Chem.* **56** 888 (1991)
71. E T McBee, E Rapkin *J. Am. Chem. Soc.* **73** 2375 (1951)
72. (a) J M Bruce, Y Roshan-Ali *J. Chem. Soc., Perkin Trans. 1* 2677 (1981); (b) T Hayashi, M Goto *Nippon Kagaku Kaishi* 1512 (1977)
73. J Borgulya, R Madeja, P Fahrni, H-J Hansen, H Schmid, R Barner *Helv. Chim. Acta* **56** 14 (1973)
74. A G Mustafin, R R Gatulin, Z N Saraeva, Z Kh Valitova, I B Abdrakhmanov, G A Tolstikov, in *Tezisy Dokladov VI Vsesoyuznoi Konferentsii po Khimii Ftororganicheskikh Soedinenii, Novosibirsk, 1990* (Abstracts of Reports at the VIth All-Union Conference on the Chemistry of Organofluorine Compounds, Novosibirsk, 1990) p. 76
75. R P Ruh US P. 2 613 228 (1952); *Chem. Abstr.* **47** 8 774i (1953)
76. R A Bekker, V Ya Popkova, I L Knunyants *Zh. Org. Khim.* **13** 2104 (1977)
77. S Gelfand US P. 3 655 765 (1972); *Chem. Abstr.* **77** 34 040t (1972)
78. V F Snegirev, K N Makarov *Izv. Akad. Nauk SSSR, Ser. Khim.* 1331 (1986)
79. V F Snegirev, Candidate's Thesis in Chemical Sciences, Institute of Organoelement Compounds, USSR Academy of Sciences, Moscow, 1989, p. 66
80. R A Bekker, V Ya Popkova, I L Knunyants *Izv. Akad. Nauk SSSR, Ser. Khim.* 2347 (1982)
81. K Burger, K Geith, K Gaa *Angew. Chem., Int. Ed. Engl.* **27** 848 (1988)
82. K Burger, K Gaa, K Geith, in *Abstracts of the IX European Symposium on Fluorine Chemistry, Leicester, UK*; *J. Fluorine Chem.* **45** 126 (1989)
83. Ch Schierlinger, K Gaa, K Geith, N Sewald, K Burger, in *Abstracts of the IX European Symposium on Fluorine Chemistry, Leicester, UK; J. Fluorine Chem.* **45** 146 (1989)
84. K Burger, K Gaa, K Geith, Ch Schierlinger *Synthesis* 850 (1989)
85. K Burger, K Gaa, E Hoss *J. Fluorine Chem.* **47** 89 (1990)
86. B Helmreich, O Jendrewski, K Burger, in *Abstracts of the X European Symposium on Fluorine Chemistry, Padua, Italy*; *J. Fluorine Chem.* **58** 380 (1992)
87. K Burger, R Ottlinger, H Goth, J Firl *Chem. Ber.* **115** 2494 (1982)

88. N Engel, B Kubel, W Steglich *Angew. Chem., Int. Ed. Engl.* **16** 394 (1977)
89. K Burger, K Gaa, K Geith *J. Fluorine Chem.* **41** 429 (1988)
90. K Mutze, W Hollweck, K Burger, in *Abstracts of the X European Symposium on Fluorine Chemistry, Padua, Italy*; *J. Fluorine Chem.* **58** 381 (1992)
91. (a) W R Dolbier *Acc. Chem. Res.* **14** (7) 195 (1981); (b) A Greenberg, J F Liebman, D Van Vechten *Tetrahedron* **36** 1161 (1980)
92. B W Metcalf, E T Jarvi, J P Burkhart *Tetrahedron Lett.* **26** 2861 (1985)
93. M Shimizu, Y Nakahara, S Kanemoto, H Yoshioka *Tetrahedron Lett.* **28** 1677 (1987)
94. Y Nakahara, M Shimizu, H Yoshioka *Tetrahedron Lett.* **29** 2325 (1988)
95. P Cresson *Bull. Soc. Chim. Fr.* 2618 (1964)
96. T Nakai, C-P Qian, M Kobayashi, T Hirasa, in *Abstracts of the XIII International Symposium on Fluorine Chemistry, Bochum, FRG*; *J. Fluorine Chem.* **54** 68 (1991)
97. J J Gajewski, J Jurayj, D R Kimbrough, M E Gande, B Ganem, B K Carpenter *J. Am. Chem. Soc.* **109** 1170 (1987)
98. V F Snegirev, K N Makarov *Izv. Akad. Nauk SSSR, Ser. Khim.* 106 (1986)
99. Y Katsuhara, M Ozawa, T Komatsu *Jpn. Kokai Tokkyo Koho* 78-144 525 (1978); *Chem. Abstr.* **90** 186 400s (1979)
100. K N Makarov, L L Gervits, Yu A Cheburkov, I L Knunyants, V P Sass *J. Fluorine Chem.* **10** 323 (1977)
101. V Ya Popkova, V F Snegirev, M Yu Antipin, Yu T Struchkov *Izv. Akad. Nauk SSSR, Ser. Khim.* 1123 (1989)
102. I L Knunyants, E G Abduganiev, S T Kocharyan, M V Urushadze, V A Lifshits, Yu E Aronov, E M Rokhlin *Izv. Akad. Nauk SSSR, Ser. Khim.* 110 (1971)
103. E L Stogryn, S J Brois *J. Am. Chem. Soc.* **89** 605 (1967)
104. O Paleta *Chem. Listy* **64** 31; 366 (1970)
105. (a) M Hudlicky *Chemistry of Organic Fluorine Compounds* (2nd Ed.) (Chichester: Ellis Horwood, 1976) p. 281; (b) p. 514
106. Yu V Zeifman, E G Ter-Gabrielyan, N B Gambaryan, I L Knunyants *Usp. Khim.* **53** 431 (1984) [*Russ. Chem. Rev.* **53** 256 (1984)]
107. J T Barr, K E Rapp, R L Pruett, C T Bahner, J D Gibson, R H Lafferty *J. Am. Chem. Soc.* **72** 4480 (1950)
108. A D Petrov, V A Ponomarenko, G V Odabashyan *Dokl. Akad. Nauk SSSR* **121** 307 (1958)
109. D R Baer *J. Org. Chem.* **23** 1560 (1958)
110. J F Normant, O Reboul, R Sauvetre, J Villieras *C.R. Acad. Sci. Ser. C* **274** 1954 (1972)
111. J F Normant, O Reboul, R Sauvetre, H Deshayes, D Masure, J Villieras *Bull. Soc. Chim. Fr.* 2072 (1974)
112. W Yuan, R J Berman, M H Gelb *J. Am. Chem. Soc.* **109** 8071 (1987)
113. D C England, L R Melby, M A Dietrich, R V Lindsey *J. Am. Chem. Soc.* **82** 5116 (1960)
114. Ch T Pumpelly, J J Pedjac, E R Larsen B. P. 1 208 010 (1970)
115. K von Werner *J. Fluorine Chem.* **20** 215 (1982)
116. O A Radchenko, A Ya Il'chenko, in *Abstracts of the X European Symposium on Fluorine Chemistry, Padua, Italy*; *J. Fluorine Chem.* **58** 154 (1992)
117. A T Monakhova, E L Zaitseva, A P Simonov, A Ya Yakubovich *Zh. Org. Khim.* **5** 1937 (1969)
118. L I Zakharkin, V N Lebedev *Zh. Obshch. Khim.* **41** 817 (1971)
119. T Nakai, K Tanaka, K Ogasawara, N Ishikawa *Chem. Lett.* 1289 (1981)
120. V G Andreev, Candidate's Thesis in Chemical Sciences, VAKhZ, Moscow, 1980
121. V G Andreev, A F Kolomiets, K V Dvornikova, V E Platonov *Izv. Akad. Nauk SSSR, Ser. Khim.* 1925 (1992)
122. R J Koshar, T C Simmons, F W Hoffman *J. Am. Chem. Soc.* **79** 1741 (1957)
123. V G Andreev, A F Kolomiets, G A Sokol'skii *Dokl. Akad. Nauk SSSR* **250** 1386 (1980)
124. V G Andreev, A Yu Sizov, A F Kolomiets, A V Fokin, in *Abstracts of the XIII International Symposium on Fluorine Chemistry, Bochum, FRG*; *J. Fluorine Chem.* **54** 263 (1991)
125. T Kubota, Y Kondoh, Y Suda, A Tanaka, S Katoh, T Ohyama, T Tanaka *Chem. Express* **2** 619 (1987)
126. T Kubota, Y Kondoh, T Ohyama, T Tanaka *Nippon Kagaku Kaishi* 1576 (1989)
127. (a) I L Knunyants, E M Rokhlin *Sov. Sci. Rev. B., Chem. Rev.* **5** 97 (1984); (b) A E Bayliff, M R Bryce, R D Chambers, R S Matthews *J. Chem. Soc., Chem. Commun.* 1018 (1985)
128. V G Andreev, A F Kolomiets, G A Sokol'skii *Zh. Org. Khim.* **15** 2417 (1979)
129. V G Andreev, Yu I Sorochkin, A F Kolomiets, G A Sokol'skii *Zh. Vses. Khim. O-va im. D I Mendeleeva* **24** 663 (1979)
130. V G Andreev, A F Kolomiets, G A Sokol'skii *Izv. Akad. Nauk SSSR, Ser. Khim.* 1643 (1990)
131. R A Bekker, V Ya Popkova, I L Knunyants *Izv. Akad. Nauk SSSR, Ser. Khim.* 1692 (1980)
132. U Utebaev, E M Rokhlin, E P Lur'e *Izv. Akad. Nauk SSSR, Ser. Khim.* 142 (1976)
133. I L Knunyants, L S German, B L Dyatkin *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* 1353 (1956)
134. M Kolb, F Gerhart, J-P Francois *Synthesis* 469 (1988)
135. V G Andreev, A F Kolomiets, G A Sokol'skii *Zh. Vses. Khim. O-va im. D I Mendeleeva* **25** 106 (1980)
136. V G Andreev, Yu I Sorochkin, A F Kolomiets, G A Sokol'skii *Zh. Org. Khim.* **15** 1999 (1979)
137. V G Andreev, A F Kolomiets, G A Sokol'skii *Izv. Akad. Nauk SSSR, Ser. Khim.* 2391 (1989)
138. V G Andreev, A F Kolomiets, A F Eleev, G A Sokol'skii *Izv. Akad. Nauk SSSR, Ser. Khim.* 1672 (1990)
139. V G Andreev, A F Kolomiets, A V Fokin *Izv. Akad. Nauk SSSR, Ser. Khim.* 2805 (1991)
140. V G Andreev, A F Kolomiets, G A Sokol'skii *Zh. Org. Khim.* **15** 2419 (1979)
141. V G Andreev, A F Kolomiets, G A Sokol'skii *Zh. Org. Khim.* **15** 2000 (1979)
142. D C England, C G Krespan *J. Fluorine Chem.* **3** 91 (1973/74)
143. V G Andreev, A F Kolomiets, A V Fokin *Dokl. Akad. Nauk SSSR* **323** 490 (1992)
144. V G Andreev, A F Kolomiets, G A Sokol'skii *Zh. Org. Khim.* **16** 1773 (1980)
145. Yu V Zeifman, G S Kaitmazova, E M Rokhlin, M B Gambaryan *Izv. Akad. Nauk SSSR, Ser. Khim.* 204 (1989)
146. N V Vasil'ev, A F Kolomiets, G A Sokol'skii, in *Tezisy Dokladov IV Vsesoyuznoi Konferentsii po Khimii Ftororganicheskikh Soedinenii, Tashkent, 1982* (Abstracts of Reports at the IVth All-Union Conference on the Chemistry of Organofluorine Compounds, Tashkent, 1982) p. 185
147. Y Hanzawa, K Kawagoe, A Yamada, Y Kobayashi *Tetrahedron Lett.* **26** 219 (1985)
148. G Shi, Y Xu, M Xu *Tetrahedron* **47** 1629 (1991)
149. V G Andreev, V V Linev, A F Kolomiets, A V Fokin, in *Abstracts of the X European Symposium on Fluorine Chemistry, Padua, Italy*; *J. Fluorine Chem.* **58** 344 (1992)
150. V G Andreev, A F Kolomiets, G A Sokol'skii *Izv. Akad. Nauk SSSR, Ser. Khim.* 516 (1991)
151. R E Ireland, R H Mueller, A K Willard *J. Am. Chem. Soc.* **98** 2868 (1976)
152. D Barton, W D Ollis, (Eds) *Comprehensive Organic Chemistry* (Oxford: Pergamon Press, 1979) Vol. 2
153. J T Welch, J S Samartino *J. Org. Chem.* **50** 3663 (1985)
154. J T Welch, J S Plummer, T-S Chou *J. Org. Chem.* **56** 353 (1991)
155. K Araki, J S Plummer, F Gyenes, J O'Toole, J T Welch, in *Abstracts of the XIII International Symposium on Fluorine Chemistry, Bochum, FRG*; *J. Fluorine Chem.* **54** 198 (1991)
156. T Yokozawa, T Nakai, N Ishikawa *Tetrahedron Lett.* **25** 3991 (1984)
157. T Nakai, O Takahashi, Eur. P. 350 334 (1990); *Chem. Abstr.* **113** 39 950m (1990)
158. H Greuter, R W Lang, A J Romann *Tetrahedron Lett.* **29** 3291 (1988).
159. E S Lewis, J T Hill *J. Am. Chem. Soc.* **91** 7458 (1969)
160. I Savage, E J Thomas *J. Chem. Soc., Chem. Commun.* 717 (1989)
161. (a) J T Welch, S Eswarakrishnan *J. Org. Chem.* **50** 5909 (1985); (b) T Yamazaki, J T Welch, J S Plummer, R H Gimi *Tetrahedron Lett.* **32** 4267 (1991)
162. J T Welch, B De Corte, N De Kimpe *J. Org. Chem.* **55** 4981 (1990)
163. F Camps, J Coll, A Messeguer, A Roca *Tetrahedron Lett.* 791 (1976)

164. F Camps, R Canela, J Coll, A Messeguer, A Roca *Tetrahedron* **34** 2179 (1978)
165. M F Carroll *J. Chem. Soc. Pt II* 1266 (1940)
166. W S Johnson, L Werthemann, W R Bartlett, T J Brocksom, T-t Li, D J Faulkner, M R Petersen *J. Am. Chem. Soc.* **92** 741 (1970)
167. T Taguchi, T Morikawa, O Kitagawa, T Mishima, Y Kobayashi *Chem. Pharm. Bull.* **33** 5137 (1985)
168. T Yamazaki, N Ishikawa *Bull. Soc. Chim. Fr.* 937 (1986)
169. Y Hanzawa, K Kawagoe, K Nobuyuki, Y Kobayashi *Chem. Pharm. Bull.* **34** 3953 (1986)
170. B A Pawson, K K Chan, J DeNoble, R-J Han, V Piermattie, A C Speciman, S Srisethnil, P W Trown, O Bohoslawec, L J Machlin, E Gabriel *J. Med. Chem.* **22** 1059 (1979)
171. F Camps, A Messeguer, F-J Sanchez *Tetrahedron* **44** 5161 (1988)
172. I L Knunyants, B L Dyatkin *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* 648 (1958)
173. G C Apsey, R D Chambers, M J Salisbury, G Moggi *J. Fluorine Chem.* **40** 261 (1988)
174. K Tanaka, in *Compounds of Fluorine, Synthesis and Applications* (Ed. N. Isikawa; Translated into Russian from Japanese) (Moscow: Mir, 1990) p. 265
175. *Promyshlennye Ftororganicheskie Produkty* (Industrial Organofluorine Products) Handbook (Leningrad: Khimiya, 1990) p. 464
176. J T Welch, T Yamazaki, R H Gimi, in *Synthetic Fluorine Chemistry* (Eds G A Olah, R D Chambers, G K S Prakash) (New York: Wiley, 1992) p. 329
177. V G Andreev, A F Kolomiets, in *Abstracts of International Symposium 'Fluorinated Monomers and Polymers' Prague, 1993* (Programme Booklet)
178. A Mukherjee, E M Schulman, W J le Noble *J. Org. Chem.* **57** 3120 (1992)
179. P Erbes, W Boland *Helv. Chim. Acta* **75** 766 (1992)
180. D M Gale, W J Middleton, C G Krespan *J. Am. Chem. Soc.* **88** 3617 (1966)