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GEORG THIEME VERLAG · STUTTGART · NEW YORK

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ORGANO-FLUORINE COMPOUNDS

Editors

B. Baasner
BAYER AG, Leverkusen / Germany

H. Hagemann
BAYER AG, Leverkusen / Germany

J.C. Tatlow
Birmingham / Great Britain

Authors

A.Ya. Il'chenko
Kiev / Ukraine

J. Kvíčala
Prague / Czech Republic

R. Miethchen
Rostock / Germany

O. Paleta
Prague / Czech Republic

D. Peters
Rostock / Germany

J. Podlech
Stuttgart / Germany

J.P. Richmond
Heidelberg / Germany

M. Rieland
Hannover / Germany

St. Rüdiger
Rangsdorf / Germany

W. Rudolph
Hannover / Germany

J.T. Welch
Albany, NY / USA

2000

GEORG THIEME VERLAG · STUTTGART · NEW YORK

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Preface

Organo-fluorine compounds have become increasingly important in the last 50 years, as synthetic routes to them have been developed; very few occur naturally. Their chemical behavior covers the entire range from inertness to high reactivity and their physical properties show unique features. These characteristics have led to many specialist uses in various fields particularly as inert fluids, polymers (e.g., Teflon), elastomers, surfactants, surface treatment agents, and fire extinguishers. These properties are also very important in biological and medicinal applications (e. g., the pharmaceutical Prozac and the fluoroquinolone antibiotics) and agriculture (e.g., Trifluralin).

Houben-Weyl Vol. E 10 Organo-Fluorine Compounds is a critical survey of the academic and patent literature, organized in a systematic and structured way.

In Volume E 10a, an introduction section details the history of the subject (including the role played by F. Swarts), an outline of nomenclature, physical and physicochemical properties, elemental analysis, structure determination, toxicity, and applications of these extraordinarily interesting compounds. This is followed by Section A which details the diverse range of fluorinating agents used to make C–F bonds, covering everything from hydrogen fluoride to high valence oxidizing metal fluorides. In Volume E 10b described in detail in Section B are methods for the synthesis of fluorinated compounds from organo-fluorine precursors (the building block approach), while in Section C are outlined general reactions and reactivity of organo-fluorides. Those familiar with the Houben-Weyl series will know that in 1962 a volume (5/3) detailing methods for the preparation of organo-fluorine compounds, written in German, was first published and it is still cited as a source of information even today. Houben-Weyl Vol. E 10 Organo-Fluorine Compounds is written in the same tradition by leading experts in the field and will prove to be an invaluable tool for the student and researcher alike well into the next millennium.

Special thanks are due to all the authors who wrote their chapters with dedication and care and who have shown a lot of perserverance with this project. Moreover we are indebted to the editorial staff at Georg Thieme Verlag and all their technical coworkers for their support and help throughout each stage in the production of this volume.

Bernd Baasner
Leverkusen

Hermann Hagemann
Leverkusen

John Colin Tatlow
Birmingham

December 1998

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3. By Oxidation Reactions

O. Paleta

Oxidative reactions belong to the ten most important types of fundamental reactions in organic chemistry. Oxidations are frequently a convenient preparative method for obtaining synthetic intermediates as well as end products. During an oxidation reaction, a substrate is oxidized while an agent must be reduced. As an oxidation agent, a positively charged electrode (anode) can also be applied. A general view on oxidation, mostly applied in inorganic chemistry, defines the reaction in two ways: loss of electrons and increase in oxidation number. However, these definitions are not easy to apply in organic chemistry. In the case of oxidation numbers, several classes of compounds, formed from the same parent structure by reactions that are not classified as oxidations, can have the same oxidation number. As a simple example, substitution derivatives of methane can demonstrate the situation:

Approximate Oxidation Number of Carbon Atom	−4	−3	−3	−3	−3	−3	−3	−3
Compound	CH_4	MeF	MeCl	$MeNH_2$	$MeNO_2$	MeOH	MeSH	$MeSO_3H$

The original Lavoisier's definition of oxidation concerns reactions that involve a gain of oxygen and/or loss of hydrogen. In this section only reactions in which fluoro compounds are the substrates are discussed. Oxidations of fluorinated substrates are presented in the following order: aliphatic, alicyclic, aromatic, aryl–aliphatic, heterocyclic; the order for halogenated hydrocarbons: $C_xH_yF_z$, $C_xH_yF_zX_u$, C_xF_z, $C_xF_zX_u$, where X is a halogen other than fluorine.

The following types of reaction are usually included in discussions[1−3] on oxidation:

1. Reactions where the number of oxygen atoms in a parent molecule increases.
2. Reactions where the number of hydrogen atoms in a parent structure decreases, e.g. dehydrogenation.
3. Reactions where electrons are transferred to an oxidant or electrode, e.g. anodic oxidations.
4. Reactions where the skeleton of a parent molecule is cleaved by an oxidation agent: a typical example is the cleavage of a C=C bond. This type of reaction is described in Vol. E10a/Part 1, p 691ff.

This section includes oxidations of alkanes and cycloalkanes, alkenes and cycloalkenes, dienes, alkynes, aromatic fluorocarbons, alcohols, phenols, ethers, aldehydes, ketones and carbohydrates, carboxylic acids, nitrogen compounds, and organoelement compounds, such as boron, phosphorus, sulfur, selenium, and iodine compounds, and steroids.

3.1. Fluorinated Hydrocarbons

3.1.1. Aliphatic and Alicyclic

3.1.1.1. Alkanes and Cycloalkanes

Oxidations of highly fluorinated alkanes and cycloalkanes are rare due to the general resistance of these compounds to oxidation agents. Oxidation generally takes place at reactive centers, such as C−H and C−I bonds, that are susceptible to the radical attack of halogen atoms, oxygen, or dinitrogen tetroxide. The reactivity of the compounds can be considerably increased by irradiation of the mixture with UV light or passing the mixture through an electrical field of high voltage. Under such conditions, C−Cl bonds can also be attacked by the oxidizing agents. The products of the oxidation of alkanes are generally carboxylic acids or their halides.

Aldehydes, if formed, are obtained as minor products. The oxidation of higher alkanes is accompanied by C—C bond cleavage (oxidations of iodo compounds at the iodine atom are described in Section 3.4.3).

Alkanes with one or with isolated C—F bonds behave on oxidation almost as nonfluorinated substances. For example, oxidation of 2-fluorooctadecane by yeast of genera *Candida* (also *Torulopsis*) *gropengiesseri* gives a 9% yield of octadecanedioic acid and a 4.5% yield of hexadecanedioic acid.[4]

A series of halogenated ethanes **1** containing the trifluoromethyl group has been oxidized under various conditions.[5-7] When water is present in the reaction mixture, the acid **3** is usually formed during the reaction; when water is absent, the acid halide **2** formed can be hydrolyzed in a trap with water. Trifluoroacetaldehyde hydrate **4** is formed[6] as a minor product in addition to the acid when 2-chloro-1,1,1-trifluoroethane is treated with oxygen and chlorine under UV irradiation with subsequent reflux of the mixture with hydrogen peroxide.

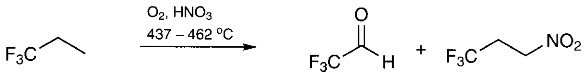
$$\underset{\mathbf{1}}{CF_3CHXY} \xrightarrow{\text{oxidizing agent}} \underset{\mathbf{2}}{CF_3COCl} + \underset{\mathbf{3}}{CF_3CO_2H} + \underset{\mathbf{4}}{CF_3CH(OH)_2}$$

X	Y	Conditions	Yield (%)			Ref
			2	**3**	**4**	
H	H	air, H_2O (vapor) 15000 V, 30 °C, 1 min		49		5
H	Cl	1. O_2, Cl_2, H_2O, hν, 2.5 h 2. 30% H_2O_2, reflux		28	16	6
Cl	Cl	O_2, H_2O, 250–360 °C	> 80[a]			7

[a] Minor products CF_3CCl_3 and $(CF_3CCl_2)_2$.

As 2-chloro-1,1,1-trifluoroethane (HCFC-133b) and 2,2-dichloro-1,1,1-trifluoroethane (HCFC-123b) are industrially produced CFC alternatives, the original academic oxidative reaction to produce them is now of technical importance:[7] a thermal oxidation method for 2,2-dichloro-1,1,1-trifluoroethane that is attractive from an industrial point of view has been developed[7] and high yields of trifluoroacetic acid were obtained in a continuous process; in addition, minor products were characterized. The acid is formed by continuous hydrolysis of the reaction mixture.[7]

The results of the oxidations of polyfluoropropanes and higher alkanes are strongly dependent both on the structure of the substrate and the oxidation agent. Shorter chain compounds formed by degradative oxidation are usually present in the reaction mixture as byproducts. Thus, 1,1,1-trifluoropropane can be converted by nitric acid and oxygen into a mixture of trifluoroacetaldehyde (**5**) and 1,1,1-trifluoro-3-nitropropane (**6**).[8]



5 20 - 24% **6** 16%

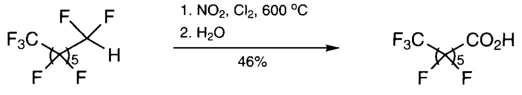
Trifluoroacetaldehyde (5) and 1,1,1-Trifluoro-3-nitropropane (6); Typical Procedure:[8]
1,1,1-Trifluoropropane (1342 g, 13.7 mol), HNO_3, and O_2 (molar ratio 9.9–11.9 : 1 : 0.1–0.15) were treated at atmospheric pressure in the gas phase at 437–462 °C for an exposure time of 1.7–2.0 s. Condensate collected at 0 °C in the first trap and, after an aliquot was titrated for nitric acid (NaOH), was immediately extracted with Et_2O. The condensate collected at − 80 °C in the second trap was distilled at atmospheric pressure to remove unreacted 1,1,1-trifluoropropane, then extracted with Et_2O. The ethereal extracts were combined, dried (Na_2SO_4), and fractionally distilled on a packed column (80 × 1.5 cm, helices). After

removal of the Et_2O, the following fractions were obtained: (1) 72.5 g, bp 101–103 °C; (2) 11.6 g, bp 128–134 °C.

Trifluoroacetaldehyde (**5**): Fraction 1 (a 20-g aliquot) was extracted with H_2O (20 mL) at rt; the remaining insoluble liquid (7.6 g) was combined with Fraction 2. The aqueous extract (12.5 g aliquot) was added dropwise to P_2O_5 (50 g) and a colorless gas was evolved which solidified in a condenser immersed in liquid N_2. Considerable decomposition of the mixture occurred during the dehydration. Redistillation of the condensate yielded the product as a colorless hygroscopic liquid; yield: 3 g; bp − 18.8 to − 17.5 °C/748 Torr.

1,1,1-Trifluoro-3-nitropropane (**6**): Rectification of Fraction 2, after removal of trifluoroacetaldehyde hydrate, yielded the product; bp 134–134.8 °C/748 Torr.

More selective is the oxidation of the difluoromethyl group in 1*H*-decafluoroheptane with a mixture of nitrogen dioxide and chlorine, which produces the corresponding perfluoroheptanoic acid (**7**) after hydrolysis of the initially formed perfluoroheptanoyl fluoride.[9] The difluoromethyl group in polychlorofluoroalkanes has also been selectively oxidized to a carboxylic group by a mixture of nitrogen dioxide and chlorine in high yields (Table 1).[10] It is surprising that the chlorofluorinated chain is not cleaved in the reaction.[10]



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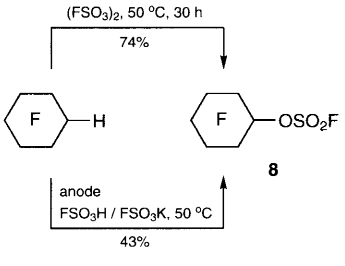
Perfluoroheptanoic Acid (7); Typical Procedure:[9]
A mixture of 1*H*-decafluoroheptane (24.7 g, 67 mmol), NO_2 (6.6 g), and Cl_2 (5.2 g) (molar ratio 1 : 2 : 1) was passed through the reactor (sloping 52 × 2.5 cm empty Ni pipe in a 33-cm electric tube furnace) at a wall temperature of 600 °C in 15 min with a contact time of 11 s. The product in the ice trap (17.8 g) was hydrolyzed in cold H_2O (100 mL), and concd H_2SO_4 (25 mL) was added which caused the separation of a lower phase containing the perfluoro acid. The aqueous phase was extracted with perfluoro inert $c\text{-}C_6F_{12}O$ (a cyclic ether), in which fluorocarbon acids are soluble. The lower layer was separated and the product was recovered from the perfluorinated solvent by distillation; yield: 11.1 g (46 %); bp 170–175 °C/740 Torr.

The terminal difluoromethyl group and monofluoromethylene groups in 1*H*-perfluoroalkanes and -cycloalkanes are oxidized at the C–H bond to perfluoroalkyl and perfluorocycloalkyl fluorosulfates by anodic oxidation in fluorosulfonic acid. Two modifications of the method are used: direct electrolysis of the acid[11,12] and oxidation by fluorosulfonyl peroxide generated electrolytically prior to the reaction,[12] e. g. formation of **8**.[12] The first method[11,12] gives better yields for primary C–H bonds, while the second method[12] is more successful in the oxidation of secondary and tertiary C–H bonds, which are generally less reactive than the primary bonds. (Table 1).



8

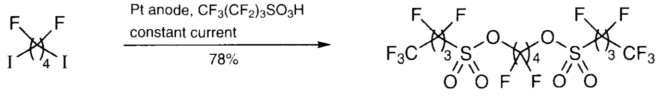
Perfluorocyclohexyl Fluorosulfate (8); Typical Procedures:[12]
*Reaction of 1*H*-Undecafluorocyclohexane with* $(FSO_3)_2$:
$(FSO_3)_2$ was prepared by electro-oxidation of FSO_3H at a Pt electrode in a divided cell and was distilled under a dynamic vacuum as it formed. 1*H*-Undecafluorocyclohexane (28.2 g, 0.1 mol) was distilled by vacuum transfer into a solution of $(FSO_3)_2$ (20 g, 0.1 mol) in FSO_3H (50 mL). Two aliquots (0.5 mL)

for references see p 82

were sealed in separate NMR tubes. One was used as a reference and the other used to study the NMR changes with increasing temperature from – 50 to 50 °C. The mixture and the reference tube were kept at 50 °C for 30 h until all the starting material had disappeared. The products were distilled from the mixture under reduced pressure (20 Torr) into a dry ice trap. The condensate was washed with ice water, separated, and dried ($MgSO_4$). Distillation in vacuo afforded the product; yield: 28 g (74%); bp 108 °C/1 Torr.

Direct Electrolysis:
A Kel F divided electrolytic cell (100 mL) with a porous PTFE membrane (3-mm thick, porosity 200–400 μm) and Pt electrodes was charged at – 25 °C with 1*H*-undecafluorocyclohexane (6.8 g, 24 mmol) and 0.2 M FSO_3K/FSO_3H (25 mL) containing $TfOCF_3$ (1 mL) (used as an inert solvent to dissolve the sublimed substrate from the condenser). The mixture was electrolyzed at a constant current of 100 mA at 50 °C while stirred, using a condenser cooled to –70 °C. After passage of 198 kC, the reaction was complete (electrical yield ca. 50%) and the product was distilled from the mixture in vacuo; yield: 3.86 g (43%).

The terminal difluoroiodomethyl (CF_2I) group in perfluoroheptyl iodide is selectively oxidized by nitrogen dioxide at high temperatures to give the fluorocarbonyl group;[9] the intermediate gives perfluoroheptanoic acid in 59% yield (Table 1). Selective formation of hexafluoro-4-iodobutanoic acid in 30–53% yield is observed on electrolysis of octafluoro-1,4-diiodobutane in dimethylformamide saturated with oxygen (Table 1).[14] Anodic oxidation of 1-iodo- or 1-iodo-1*H*,1*H*,2*H*,2*H*-perfluoroalkanes in perfluoroalkanesulfonic acids gives the corresponding perfluorosulfonic esters and fluorosulfates; this methodology enables the preparation of long-chain sulfonic esters.[13] With α,ω-diiodo-substituted perfluoroalkanes and fluorosulfonic or perfluorobutanesulfonic acids both the mono- and the diester can be obtained selectively, for examples see the formation of **9** and Table 1.[13]



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The summarized results of several oxidation reactions[9,15,16] for perhalogenated fluoroalkanes bearing at least one halogen atom other than fluorine in the terminal trihalomethyl group CFXY allows a generalized reactivity order for the groups to be deduced, this is as follows: $CF_3 << CF_2Cl << CFCl_2 << CFClBr \approx CF_2I < CFClI$.

Table 1. Oxidation of Alkanes and Cycloalkanes

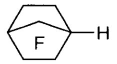
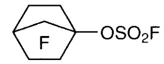
Substrate	Reagent, Solvent	Conditions	Products	Yield (%)	Ref
$F_2CCl(CF_2)_4CHF_2$	1. NO_2, Cl_2 2. H_2O	600 °C	$F_2CCl(CF_2)_4COF$ + $F_2CCl(CF_2)_4CO_2H$	72	9
$F_2CClCClF(CF_2)_nCHF_2$	1. N_2O_4 ($4.5\ L\cdot h^{-1}$) Cl_2 ($7.5\ L\cdot h^{-1}$) 2. H_2O	500 °C	$F_2CClCClF(CF_2)_nCO_2H$ n = 1 n = 2 n = 3	 75 84.5 76	10
$(CF_3)_2CHF$	anode, $FSO_3H/$ FSO_3K $(FSO_3)_2$	50 °C 60 °C, 3 h	$(CF_3)_2CFOSO_2F$	43 98	12 12
	anode, $FSO_3H/$ FSO_3K $(FSO_3)_2$	80 °C 60 °C, 15 h		6 70	12 12
$CF_3(CF_2)_5CF_2I$	1. NO_2 2. H_2O	550 °C	$CF_3(CF_2)_5CO_2H$	59	9
$ICF_2(CF_2)_2CF_2I$	O_2, Pt anode	MF	$ICF_2(CF_2)_2CO_2H$	30–53	14
CF_3CF_2I	Pt anode (constant current)	$CF_3CF_2SO_3H$	$CF_3CF_2OSO_2CF_2CF_3$	65	13

Table 1. (cont.)

Substrate	Reagent, Solvent	Conditions	Products	Yield (%)	Ref
$CF_3(CF_2)_3I$	Pt anode (constant current)	$CF_3(CF_2)_3SO_3H$	$CF_3(CF_2)_3OSO_2(CF_2)_3CF_3$	88	13
$CF_3(CF_2)_5I$		FSO_3H	$CF_3(CF_2)_5OSO_2F$	85	13
		CF_3SO_3H	$CF_3(CF_2)_5OSO_2CF_3$	92	13
		$CF_3(CF_2)_3SO_3H$	$CF_3(CF_2)_5OSO_2(CF_2)_3CF_3$	81	13
$CF_3(CF_2)_{11}I$		$CF_3(CF_2)_3SO_3H$	$CF_3(CF_2)_{11}OSO_2(CF_3)_3CF_3$	86	13
$CF_3(CF_2)_5CH_2CH_2I$		CF_3SO_3H	$CF_3(CF_2)_5CH_2CH_2OSO_2CF_3$	98	13
$I(CF_2)_4I$		FSO_3H	$FSO_2O(CF_2)_4I$	68	13
			$FSO_2O(CF_2)_4OSO_2F$	70	13
		$CF_3(CF_2)_3SO_3H$	$CF_3(CF_2)_3SO_2O(CF_2)_4OSO_2(CF_2)_3CF_3$	78	13

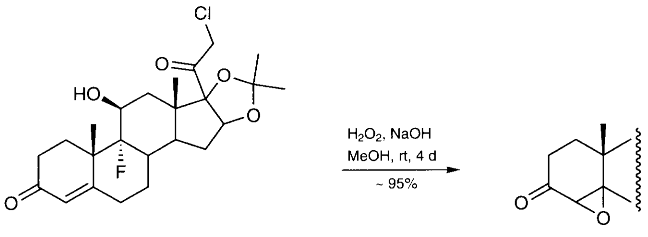
3.1.1.2. Alkenes and Cycloalkenes

This section concerns oxidation reactions of the C = C bond. This includes unsaturated compounds containing other characteristic groups (e.g., hydroxy, carbonyl, carbonitrile, or organoelement groups), or aromatic or heterocyclic aromatic rings in which only the C = C bond is oxidized. The reactions of substrates are generally arranged in such a manner that the section starts with less fluorinated and simple (e.g., short chain) structures followed by compounds bearing other halogens and/or other substituents and functional groups. Two general types of oxidation reactions are observed for fluoroalkenes: oxidation of the C = C bond without carbon chain cleavage and oxidative cleavage of the C = C bond. The second type is not included in this section as it is discussed in Vol. E10b/Part 1, p 691ff. Most frequent are oxidations of alkenes that can be converted into a series of compounds such as epoxides, halohydrins and their esters, ozonides (1,2,4-trioxolanes), α-hydroxy ketones, α-hydroxy ketone fluorosulfonates, α-diketones, and carboxylic acids and their derivatives.

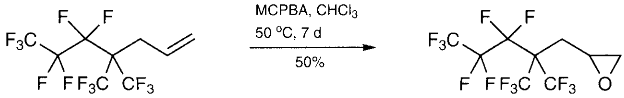
Epoxidation

Oxiranes (epoxides) are important intermediates in syntheses and for industrial processes, which produce useful compounds of high practical importance,[17,18] e.g. inert fluids, elastomers, and ionomer membranes. The epoxidation reaction of highly fluorinated C = C bonds are occasionally, especially in acidic media, accompanied by rearrangement of the primary epoxides (see Section 5.3.3.2.) and, in the case of stronger oxidants, by C = C bond cleavage (*vide infra*, see also Vol. E10b/Part 1, p 691 ff).

The presence of a 9α-fluorine in a 11β-hydroxy-Δ^4-3-oxo steroid **10** results in completely stereospecific alkaline epoxidation with hydrogen peroxide to give **11** in a much slower reaction (4 d vs 4 h) than that of the nonfluorinated analog.[19] The nonfluorinated C = C bond in 3-perfluoroalkylated prop-1-ene **12** is epoxidized, with difficulty, in 7 days by 3-chloroperoxybenzoic acid to give **13**.[20]

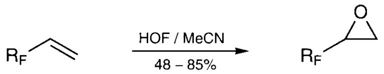


10 **11**



12 **13**

The epoxidation of perfluoroalkyl-substituted ethenes requires a more efficient reagent than a peroxy compound. Such a reagent is the hypofluorous acid/acetonitrile complex prepared in situ from elemental fluorine.[21] This is probably the best oxygen-transfer reagent that can generally epoxidize alkenes quickly and efficiently. The epoxidation is fully stereospecific, and the configuration of the starting alkene or diene is fully retained in the resulting oxirane. 1-(Perfluoroalkyl)ethenes react with this reagent at room temperature over 2–3 hours affording moderate yields of **14**, while alkenes containing a strongly electron-deficient C=C bond or electron-poor, sterically hindered alkenes, e.g. 1,2-bis(perfluorobutyl)ethene and 1-(perfluoroalkan-2-yl)ethene, are practically inert.[21] Epoxidation of a mixture of 3-(perfluoroalkyl)prop-1-enes at 0 °C is complete after 10 minutes in 80% yield, while the trifluorovinyl group in partially fluorinated dienes is not affected by this reagent. A terminal 1,13-diene with an interstitial deca(difluoromethylene) chain is converted to the corresponding diepoxide with a very large excess of hypofluorous acid/acetonitrile complex by the repeated procedure.[21]



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R_F	Conditions	Yield (%)
$(CF_2)_3CF_3$	0–20 °C, 3 h	63
$(CF_2)_5CF_3$	0–20 °C, 2 h	48
$(CH_2)_2CF=CF_2$	0 °C, 2 min	60
$(CH_2)_4CF=CF_2$	−40 °C, 2 min	50
$(CH_2)_6CF=CF_2$	−10 °C, 10 min	55

2-(Perfluoroalkyl)oxiranes 14; General Procedure:[21]

Caution! Molecular F_2 is a very toxic and corrosive gas; the reactions should be carried out in an efficient fume hood and the handler should be familiar with the correct precautions. A reaction apparatus for working with elemental F_2 is recommended.[22]

HOF/MeCN; General Procedure:

Mixtures of 10–15% F_2 diluted with N_2 were used. This mixture was passed at a rate of about 400 mL·min^{-1} through a cold (−10 °C) and vigorously stirred mixture of MeCN (400 mL) and H_2O (40 mL). The level of the oxidizing power was monitored by reacting aliquots with an acidic solution of KI. The liberated I_2 was titrated with standard aq $Na_2S_2O_3$. A concentration of oxidizing agent HOF/MeCN of more than 1 mol·L^{-1} can be generated.

General Epoxidation Procedure with HOF/MeCN:

The alkene (5–20 g) was dissolved in CH_2Cl_2 (~50 mL), cooled to 0 °C, and added in one portion to the reaction vessel in which the oxidizing agent had been prepared. Except for reactions with the more reactive alkenes, the cooling bath was removed and the reaction was stopped after 3 h by neutralization with solid $NaHCO_3$ or sat. aq $NaHCO_3$. Reactions can be left for longer periods, but most of the reagent decomposes after 3–4 h. The mixture was then poured into H_2O (1.5 L), extracted with $CFCl_3$, and washed with aq $NaHCO_3$ and H_2O until neutral. The organic layer was dried ($MgSO_4$), and the solvent was removed by distillation. The residue containing the crude product was usually distilled at either atmospheric or reduced pressure.

2-(Perfluorobutyl)oxirane [14, $R_F = (CF_2)_3CF_3$]:

1*H*,1*H*,2*H*-Nonafluorohex-1-ene (15 g, 6 mmol) dissolved in CH_2Cl_2 (30 mL) was added to the oxidizing solution (250 mmol). The reaction was left until no more oxidizing reagent could be detected and worked up as described above. The crude product was distilled to give the epoxide; yield: 10 g (63 %); bp 81–83 °C.

A vinyl group attached to pentafluorobenzene is also readily oxidized to the corresponding epoxide by hypofluorous acid in aqueous acetonitrile in high yield.[21] The oxidizing agent made from fluorine[21] is fully capable of epoxidizing the somewhat more electron-deficient 2,2,2-trifluoroethyl methacrylate, which is converted into the epoxide in 85% yield[23] without the need for drastic conditions (temperature, reaction time or pH), however a reaction time of 30 minutes is required (Table 2).

Table 2. Epoxidation of Fluoroalkenes

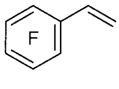
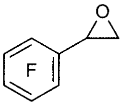
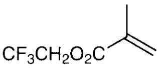
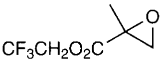
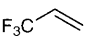
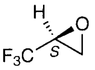
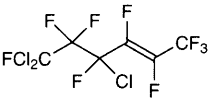
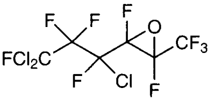
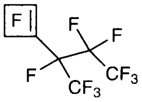
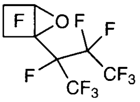
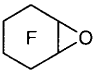
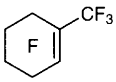
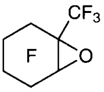
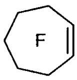
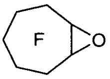
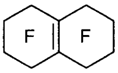
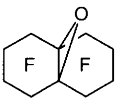
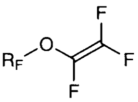
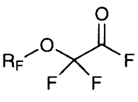
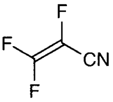
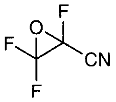
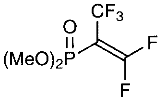
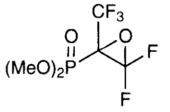
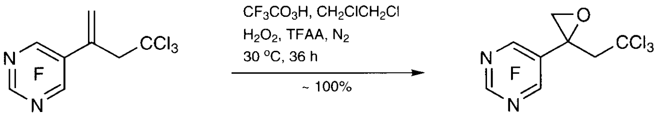
Substrate	Reagent, Solvent	Conditions	Products	Yield (%)	Ref
	HOF/MeCN, H_2O, CH_2Cl_2	0 °C, 5 min		85	21
	$F_2/H_2O/MeCN$, CH_2Cl_2	0 °C, 30 min		85	23
	air, *Nocardia corallina*	rt		58	24
	NaOCl, MeCN, PTC	12–15 °C, 2 h		80	70
	NaOCl, MeCN, H_2O	18–25 °C, 0.5–5 h		89	62
	NaOCl, MeCN, H_2O NaOCl, MeCN, H_2O	20 °C, 1 h 15–20 °C, 2 h		92 89	71 72
	NaOCl, MeCN, H_2O	rt, 20 min; 50 °C, 2 h		93	73
	NaOCl, MeCN, H_2O	15 °C, 1 h		86	74
	NaOCl, MeCN, H_2O	− 10 °C, 2 h		94	75
	O_2, SbF_5	rt		41[a]	76

Table 2. (cont.)

Substrate	Reagent, Solvent	Conditions	Products	Yield (%)	Ref
	O_2, $CF_2ClCFCl_2$	110°C, 50 atm		48	77
	MCPBA	− 5 to 20°C, 3.5 h		60	78

[a] $R_F = CF_2CF(CF_3)O(CF_2)_2CF_3$.

Optically active 2-(trifluoromethyl)oxirane, an intermediate for drugs and agrochemicals, is prepared by biochemical oxidation of 3,3,3-trifluoropropene with air (Table 2).[24] A vinyl group attached to a trifluoropyrimidine ring, as shown in **15**, is oxidized by trifluoroperacetic acid in a nonbuffered system in almost quantitative yield to the epoxy derivative **16**.[25] The same reaction with the trichloropyrimidine ring analog gives a quantitative yield of the epoxide. The unexpected stability of the epoxide **16** in the acid media enables ready isolation.



1,1,1-Trichloro-3,4-epoxy-3-(2,4,6-trifluoropyrimidin-5-yl)butane (16); Typical Procedure:[25]

To a three-necked flask (250 mL) containing 1,2-dichloroethane (100 mL) and 70% H_2O_2 (0.2 g, 4 mmol), TFAA (10 mL, 14.9 g, 70 mmol) was slowly added with cooling. After 30 min, 4,4,4-trichloro-2-(2,4,6-trifluoropyrimidin-5-yl)but-1-ene (**15**; 0.83 g, 3 mmol) in 1,2-dichloroethane (20 mL) was added dropwise. The reaction was continued for 36 h at 30°C under N_2 to complete conversion. Sat. $NaHSO_3$ was then added and the layers were separated. The organic layer was washed with sat. brine, H_2O, and dried. After removing the solvent, the product **16** was obtained in near analytical purity in almost quantitative yield.

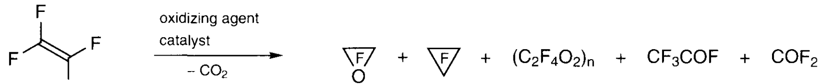
Due to their industrial applications, tetrafluorooxirane and perfluoro(2-methyloxirane) are the most frequently mentioned epoxides in the literature, and a number of methods have been developed for their synthesis. Although the epoxidation of perfluoroalkenes with hydrogen peroxide in alkaline media appears to be the most general method for the synthesis of perfluorinated epoxides, it cannot be used in the preparation of tetrafluorooxirane due to the hydrolytic decomposition of the alkene.

Highly fluorinated ethenes react readily with oxygen to yield epoxides, polymeric peroxides, perfluorocyclopropane, and, by rearrangement, fluorinated acetyl halides; carbonyl fluoride and carbon dioxide are undesired byproducts, the amount of which is dependent on the method used.

Most of the reported methods for the synthesis of tetrafluorooxirane utilize the reaction of tetrafluoroethene with molecular oxygen, generally in the presence of a free-radical source. Several variations of this method have been used. Energetic oxidation by oxygen gives only carbon dioxide and carbon tetrafluoride.[26] Heating or irradiation of the mixture of oxygen and tetrafluoroethene with γ- and X-rays results in a complex mixture of products,[27,28] but up to 70% yield of tetrafluorooxirane is isolated when heating at 120°C is applied.[29] Liquid-phase oxidation with oxygen gives complex polymers.[30] Initiation of the oxidation with UV light in the presence of a small amount of bromine leads to conversions of up to 35% and yields of 43–56% of the tetrafluorooxirane.[31]

The reaction in the gas phase and in perfluorinated liquids gives a mixture of products including a rubber-like explosive polymer.[32] Catalytic amounts of ozone as an initiator were found to significantly increase the oxidation of tetrafluoroethene and higher perfluoroalkenes. Thus, the oxidation with ozone-containing oxygen can be carried out without the formation of explosive products;[33] the total conversion of tetrafluoroethene is 41% with a net epoxide yield of 46%. Ozonization of tetrafluoroethene gave, in addition to traces of the ozonide, mainly tetrafluorooxirane and carbonyl fluoride.[33] A mixture of products is also formed in the photochemically induced oxidation of tetrafluoroethene in the gas phase.[34] When the ozone-initiated oxidation of tetrafluoroethene with oxygen is carried out at 100°C, a 71% yield of carbonyl fluoride is obtained (Table 3).[35]

Table 3. Reaction of Tetrafluoroethene with an Oxidizing Agent and Catalyst



17 18 19 20 21

Reagent	Conditions	Conversion (%)	Yield (%)					Ref
			17	**18**	**19**	**20**	**21**	
O_2	100°C, 14 h		15	42			42	28
O_2	hν, 24 h		40	7			47	
O_2	X-ray, 1.5 h		37	4.5			47	
O_2	γ-ray, 2 h		30	6			47.5	
O_2	120°C		70					29
O_2, C_6F_6	15°C, 5 d		24		1.5 g		23	32
O_2	hν, rt, 7 h		52	11	14		48	34
O_2, O_3	100°C	57				[a]	71	35
O_2/air	C_8F_{18}, hν, 100°C							36
	$CFBr_3$	62	74					
	$C(NO_2)_4$	29	71					
	$CHF_2(CF_2)_3CH_2ONO_2$	32	75					
	$EtONO_2$	21	76					
O_2, $CF_3N_2CF_3$	hν, rt, 4 h		~ 29				[b]	38
$KMnO_4$, HF	− 70, 3 h; then to rt		~ 38			8		39
CrO_3, HF	− 70, 3 h; then to rt					15.5		40

[a] Small amount. [b] Yield of **21** and CO_2 not calculated.

2,2,3,3-Tetrafluorooxirane (17); Typical Procedures:

By Auto-oxidation:[32]

A mixture of tetrafluoroethene (2.45 g, 24.5 mmol), O_2 (24.5 mmol) and O_3 (0.03 mmol) was condensed in a Pyrex tube (33 mL) with a long capillary neck containing hexafluorobenzene (8.3 g). After 5 d reaction in the dark at 15°C, the ampule was opened and the volatile products were analyzed and separated by GC [He as carrier gas, −9°C, bis(2-ethylhexyl) sebacate on kieselguhr]; yields: **17** (0.67 g, 24%), **21** (0.38 g, 23%). A highly viscous residue that contained **19** (1.5 g) was diluted with hexafluorobenzene and treated with a slight excess of 57% HI (1 part) and glacial HOAc (10 parts), usually at rt. The whole apparatus was swept with He and the CO_2 evolved during the reduction was absorbed by standard $Ba(OH)_2$.

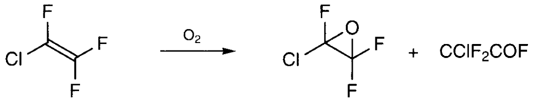
In the Presence of Bis(trifluoromethyl)diazene:[38]

A 12.5-L evacuated flask connected to a pressure meter was charged with tetrafluoroethene, oxygen and bis(trifluoromethyl)diazene (vol. ratio 45:45:10). The mixture was then irradiated from outside with a medium-pressure Hg lamp for 3.5–4 h until the pressure decreased to 190 Torr. Volatile products were passed through two traps cooled with dry ice/acetone mixture and liquid N_2, respectively. The N_2-cooled trap contained a mixture of **21** and CO_2. The condensate in the first trap (9.1 g) was separated by low-temperature fractional distillation on a packed column to give pure **17**; yield: 6 g (ca. 29%); bp –57°C.

Photochemically induced epoxidation of tetrafluoroethene by oxygen with improved yields (71–76%, conversion 21–62%) is achieved in the presence of radical generators such as tribromofluoromethane, 1,2-dibromotetrafluoroethane, ethyl nitrite or 1*H*,1*H*,5*H*-octafluoropentyl nitrite.[36] The oxidation of tetrafluoroethene with oxygen can also be catalyzed with bis(trifluoromethyl)diazene; an undistillable viscous oil with peroxide composition is formed initially which can be quantitatively converted into carbonyl fluoride when heated.[37,38]

Tetrafluoroethene is found to react with potassium permanganate in hydrogen fluoride to give the corresponding epoxide (Table 3).[39] It has been suggested[39] that the first step of the oxidation is an electrophilic attack on the C=C bond by the acid fluoride of permanganic acid formed in situ. The reaction with chromium(VI) oxide in anhydrous hydrogen fluoride gives trifluoroacetyl fluoride[40] (Table 3) that most probably results from a rearrangement of the initial oxidation product, the epoxide.[40]

Chlorotrifluoroethene (**22**) is oxidized by oxygen to chlorodifluoroacetyl fluoride (**24**), which is probably formed by rearrangement of the initially formed unstable chlorotrifluorooxirane (**23**).[41] The epoxide **23** can be prepared at low temperatures,[42] while under irradiation of the reaction mixture with UV light the yield of the epoxide is low and the formation of the acid fluoride is preferred.[43,44] Similar results are obtained for 1,1-dichloro-2,2-difluoroethene (**25a**).[44]

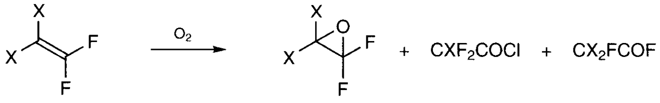


22 **23** **24**

Conditions	Yield (%)		Ref
	23	**24**	
–80°C, 10 h	25		41
7–21 atm, 25–50°C		43	41
hν, 5 d		36	43
hν, reflux	60[a]	40[a]	44

[a] Relative ratio of the products.

1,1-Dibromo-2,2-difluoroethene (**25b**) gives on oxidation with oxygen a mixture of both possible haloacetyl halides.[45]

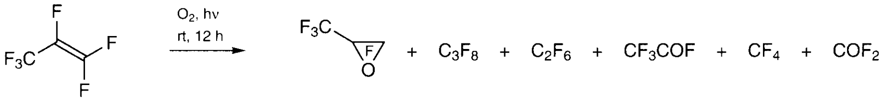


25 **26** **27** **28**

Substrate		Conditions	Yield (%)			Ref
25	X		**26**	**27**	**28**	
a	Cl	hν, reflux, 10 h	40[a]	50[a]	10[a]	45
b	Br	hν, 10 h		40	50	45

[a] Relative yield of the products.

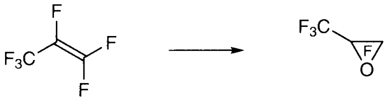
Hexafluoropropene (**29**) can be oxidized in a similar way as tetrafluoroethene, but it can also be oxidized by different methods. Gas-phase oxidations generally lead to mixtures of products. A mixture of products is obtained in the photoinitiated oxidation of **29** with oxygen in both the liquid and gaseous state; in addition to low conversions into perfluoro(2-methyloxirane) (**30**) and other volatile compounds, a clear viscous polymer is obtained as the major product.[46] The oxidation at low temperatures gives the epoxide as the dominant product,[47] but the conversion is only 24 %. Epoxide **30** is obtained in moderate yield, among other products, when a mixture of hexafluoropropene and oxygen difluoride is irradiated with UV light.[48] Without irradiation, the mixture does not react at room temperature.[48]



29 **30** 34% 36% 2% 12% 13% 3%

A more recent oxidation of hexafluoropropene (**29**) with oxygen over silica gel gives epoxide **30** in 79 % yield.[49] Among oxidations of **29** in solution, a highly selective continuous electrochemical method for the industrial production of **30** has been reported.[50] This process is carried out in aqueous acetic acid/nitric acid/hydrogen fluoride on a lead(IV) oxide anode.

Another successful epoxidation of hexafluoropropene (**29**) is based on using alkaline hydrogen peroxide at low temperatures,[51,52] with 25–32 % isolated yields. Methanol is generally added to the mixture to allow the reaction to be carried out without freezing and to partly dissolve the alkene.[52]



29 **30**

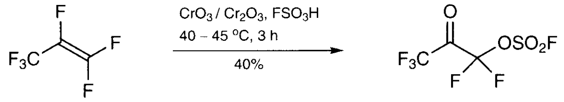
Reagent	Conditions	Yield (%)	Ref
O_2	hν, 11 atm, 38 °C	74[a]	47
O_2, silica gel	200 °C, 4.5 h	79	49
PbO_2 anode, HOAc, HNO_3, HF	1 atm, 30–40 °C	65–75	50
CrO_3, HF	autoclave, 20 °C, 3 d	–[b]	40
alkaline H_2O_2		25–32	51, 52

[a] Conversion 24 %.

[b] Hexafluoroacetone 24 %, trifluoroacetyl fluoride 23 %.

Hexafluoropropene (**29**) has been found to react in an interesting manner with potassium permanganate in hydrogen fluoride to give the corresponding epoxide **30**.[39,56] In contrast to this oxidation, the reaction of hexafluoropropene (**29**) with chromium(VI) oxide in anhydrous hydrogen fluoride gives hexafluoroacetone that results most probably from rearrangement of the initial oxidation product, the epoxide **30**.[56]

Hexafluoropropene (**29**) is also converted into epoxide **30** in 55 % yield by bubbling through a solution of chromium(VI) oxide in fluorosulfonic acid;[54] good yield of **30** is obtained owing to the unreactivity of the acid toward the epoxide at ambient temperature.[54] An analogous reaction with a mixture of chromium(VI) oxide and chromium(III) oxide in fluorosulfonic acid gives pentafluoroacetonyl fluorosulfate (**31**).[54]



29 **31**

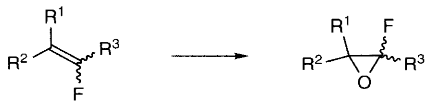
Perfluoro(2-methyloxirane) (30); Typical Procedures:
By Hydrogen Peroxide Oxidation:[51-53]
A 3-L four-necked flask, fitted with a dry ice/EtOH cooled reflux condenser and a delivery tube, was charged with 85% KOH (160 g, 2.44 mol), H_2O (150 mL), and MeOH (750 mL). The solution was cooled to -50 °C while 30% H_2O_2 (525 mL) was added and then hexafluoropropene (135 g, 0.9 mol) was introduced. The reaction was continued for 1.5 h at -50 to -40 °C. The temperature was then slowly raised to rt. The volatile products were passed through H_2O, then over granular $CaCl_2$, and were condensed at -78 °C in a cylinder. The crude epoxide (40 g, ca. 25% yield) contained 3–4% CO_2 and 1–2% hexafluoropropene. Passing the crude epoxide through a Br_2 soln, H_2O, and over granular $MgSO_4$ or redistillation gave[55] almost 100% pure product; bp -28 °C.

By Permanganate Oxidation:[39]
A flask equipped with dry ice cooled reflux condenser was charged with $KMnO_4$ (45 g) and HF (150 g) and cooled to -70 °C. Hexafluoropropene (37 g, 0.25 mol) was added to the mixture at -70 °C for 3 h while stirring. The temperature was then slowly increased to rt and the evolving gas was collected in a dry ice trap. Fractional distillation of the condensate gave pure product; yield: 12 g (29%); bp -30 to -29 °C.

By Chromium(VI) Oxide Oxidation:[54]
A three-necked flask fitted with a thermometer and a stirrer was charged with CrO_3 (28 g, 0.28 mol) and HSO_3F (100 mL). Hexafluoropropene (25 g, 0.17 mol) was added to the mixture at -70 °C for 4.5 h while stirring. The temperature was then slowly increased to rt and the evolving gas was collected in a dry ice trap. According to IR spectra, the condensate was almost pure product; yield: 15.4 g (55%).

Alkaline hydrogen peroxide oxidation[52] has been extended to higher perfluorinated alk-1-enes, perfluorinated cycloalkenes and certain alkenes with internal C=C bonds.[52,57] A convenient reagent for the preparation of perfluoroalkene epoxides is sodium hypochlorite in a mixture with aqueous acetonitrile or another aprotic solvent. Several *cis*- and *trans*-perfluoroalkenes are oxidized to **32** with retention of configuration (Table 4).[58-63]

Table 4. Epoxidation of Fluorinated Alkenes



32

R^1	R^2	R^3	Oxidizing Agent, Conditions[a]	Yield (%)	Ref
CF$_3$	CF$_3$	F	A	32	52
CF$_3$	F	CF$_2$H	B	70	58, 63
CF$_3$	F	(*E*)-CF$_3$	C	80	58
CF$_3$	F	CF$_3$	D	90.5	61
CF$_3$	CF$_3$	CF$_2$CF$_3$	D	94	59
CF$_2$CF$_2$H	F	F	E	34.5	57
CF$_2$CF$_3$	F	CF$_3$	C	72	58
CF$_2$CF$_3$	F	CF$_3$	D	91.5	61
CF$_2$CF$_3$	F	(*E*)-CF$_2$CF$_3$	D	84.5	60

Table 4. (cont.)

R^1	R^2	R^3	Oxidizing Agent, Conditions[a]	Yield (%)	Ref
CF_2CF_3	CF_3	CF_3	F	66	62
$(CF_2)_2CF_2H$	F	F	E	60	57
$(CF_2)_2CF_3$	F	CF_3	C	94	58
$(CF_2)_2CF_3$	F	CF_3	D	94	61
$(CF_2)_2CF_3$	F	CF_2CF_3	D	91	61
$CH(CF_3)_2$	F	CF_3	D	92	61
$CF(CF_3)_2$	F	(*E*)-CF_3	G	89	59
$(CF_2)_3CF_2H$	F	F	E	82	57
$(CF_2)_4CF_3$	F	CF_3	D	95	61
$C(CF_3)(CF_2CF_3)_2$	CF_3	(*E*)-CF_3	F	94	62
$C(CF_3)(CF_2CF_3)_2$	$CF(CF_3)CF_2CF_3$	F	F	89	62
$(CF_2)_5CF_2H$	F	F	A	51	52

[a] A: 30% H_2O_2, NaOH, −20 to −50 °C, 2–4 h; B: NaOCl, MeCN, −10 to 0 °C, 5 h; C: NaOCl, diglyme, rt, 1.5 h; D: NaOCl, MeCN, 20 °C, 1 h; E: 60% H_2O_2, KOH, MeOH, −20 °C, 10 h; F: NaOCl, MeCN, 18–25 °C, 0.5–5 h; G: NaOCl, MeCN, 20 °C, several h.

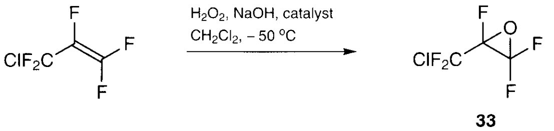
4*H*-1,2-Epoxyheptafluorobutane (32, $R^1 = CF_2CF_2H$; $R^2 = R^3 = F$); Typical Procedure:[57]
4*H*-Heptafluorobut-1-ene (91 g, 0.5 mol) was slowly introduced into a flask (equipped with a low-temperature reflux condenser) that contained a vigorously stirred mixture of 60% H_2O_2 (140 mL) and MeOH cooled to −20 °C. To this mixture, a solution of KOH (75 g) in MeOH (200 mL) was added during 4 h at −20 °C and the reaction was continued under these conditions for 6 h. The lower organic layer was separated, washed with ice water, dried ($MgSO_4$), and distilled. Dry Br_2 was added to the distillate and the mixture was externally irradiated with UV light. The volatile mixture was then passed through sat. $Na_2S_2O_3$ and dried (P_2O_5). Fractional distillation on a column gave the product; yield: 32 g (34.5%); bp 21–22 °C.

1*H*-(*E,Z*)-2,3-Epoxyheptafluorobutane (32, $R^1 = CF_3$; $R^2 = F$; $R^3 = CF_2H$); Typical Procedure:[58,63]
Preparation of NaOCl soln:[58] Cl_2 was introduced into 25% NaOH at −20 to −10 °C until the pH was 10–11.

A flask equipped with a low-temperature reflux condenser was charged with 1*H*-heptafluorobut-2-ene [20 g, 0.11 mol; ratio (*E*/*Z*) 48:52] and MeCN (30 mL). To the vigorously stirred mixture, NaOCl soln (70 mL) was added at −10 to 0 °C and the reaction was continued under these conditions for 5 h. The lower organic layer was separated, washed with H_2O, and dried ($MgSO_4$). The crude product was brominated with dropwise addition of Br_2 and external irradiation with UV light to separate any unreacted starting alkene. The product was obtained by fractional distillation on a packed column (metal spirals); yield: 15.2 g (70%); (*E*/*Z*) 46:54; bp 22–23 °C.

(*E*)-Perfluoro(2,3-epoxy-4-ethyl-3,4-dimethylhexane) [32, $R^1 = C(CF_3)(CF_2CF_3)_2$; $R^2 = CF_3$; $R^3 =$ (*E*)-CF_3]; Typical Procedure:[62]
(*E*)-Perfluoro(4-ethyl-3,4-dimethylhex-2-ene) (40 g, 80 mmol) was carefully added to a vigorously stirred mixture of 12% NaOCl (100 mL) and MeCN (120 mL) and the reaction was maintained for 5 h at 18 °C. There was some evolution of heat. After the reaction, the fluorocarbon layer was separated, washed with H_2O, and dried (P_2O_5). Distillation gave the product; yield: 39 g (94%); bp 147–148 °C.

The conversion of 3-chloropentafluoropropene to 2-(chlorodifluoromethyl)-2,3,3-trifluorooxirane (**33**) can be carried out[64] by heating the mixture of the alkene and oxygen in 1,1,2-trichlorotrifluoroethane (CFC-113) in an autoclave.[64] The oxidation with hydrogen peroxide in alkaline solution is negatively influenced by the high nucleophilic reactivity of allylic chlorine.[65,66] The reaction is performed at very low temperatures that favor the attack of the hydroperoxy anion in competition with the hydroxy anion. Acceptable yields of 31–38% are obtained in the presence of a phase-transfer catalyst.[66]



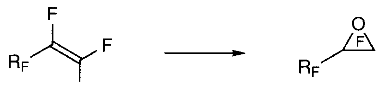
33

Conditions	Conversion (%)	Yield (%)
36% H_2O_2, Bu_4NBr	17	8
45% H_2O_2, Bu_4NBr	48	4
60% H_2O_2, Bu_4NBr	35	31
60% H_2O_2, $Me_3[Me(CH_2)_{15}]NBr$	72	38

2-(Chlorodifluoromethyl)-2,3,3-trifluorooxirane (33); Typical Procedure:[66]

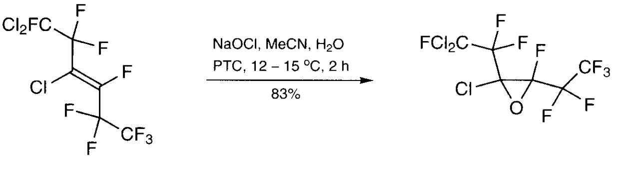
A flask equipped with an efficient mechanical stirrer, a low-temperature stillhead and addition funnel was charged with MeOH (270 mL), CH_2Cl_2 (90 mL), 30% H_2O_2 (450 mL), and $Me_3[Me(CH_2)_{15}]NBr$ (9 g). The flask was cooled to −55 °C and 3-chloropentafluoroprop-1-ene (90 g, 0.5451 mol) was condensed into the mixture while intensively stirring. A solution of KOH (72 g) in MeOH (200 mL) was slowly added to the mixture over 5 h, the reaction was continued for 0.5 h and warmed slowly (1 h) to rt. The gas evolved was condensed in a dry ice trap. The contents of the trap (92.8 g) were fractionally distilled (Vigreux column) to yield a fraction at 4–6 °C (59.2 g) consisting of **33** and unreacted fluoropropene. This mixture was passed through a solution of Br_2 (60 g) in $CF_2ClCFCl_2$ (CFC-113, 100 mL) under irradiation with a lamp and finally aq Na_2SO_3. The purified product **33** was dried by passing through a tube with $CaCl_2$; yield: 45.5 g (46%).

The oxidation of 1,1,2,3-tetrachlorodifluoroprop-1-ene with oxygen and a small amount of chlorine under UV light irradiation is claimed to give a mixture of the corresponding epoxide and propanoyl chloride.[67] In contrast, the oxidation of 2,3-dichlorohexafluorobut-2-ene by oxygen under similar conditions yields mainly[68] or exclusively[69] trifluoroacetyl chloride, while the product of intermediate epoxide rearrangement, 3,3-dichlorohexafluorobutan-2-one is isolated in low yield.[68] Epoxides **34** of polychlorofluoroalkenes with a terminal trifluorovinyl group are obtained by alkaline oxidation with hydrogen peroxide.[57,70] Even chlorofluoroalkene **35** with an internal chlorinated C=C bond is transformed to the epoxide **36** in high yield by sodium hypochlorite.[70] It is interesting that the oxidation is performed above 0 °C.



34

R_F	Reagent	Conditions	Yield (%)	Ref
CF_2CF_2Cl	60% H_2O_2, KOH	MeOH, −20 °C, 10 h	65	57
CF_2CCl_3	60% H_2O_2, KOH	MeOH, −20 °C, 10 h	44	57
$(CF_2)_2CF_2Cl$	60% H_2O_2, KOH	MeOH, −20 °C, 10 h	82	57
$CF_2CFClCF_2CFCl_2$	30% H_2O_2, KOH	MeOH, < 8 °C, 2 h	66	70
$CF_2CF_2CCl_3$	30% H_2O_2, KOH	MeOH, −20 °C, 10 h	60	57



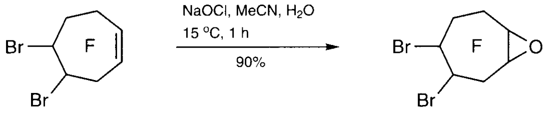
35 36

PTC = $(C_8H_{17})_3NMeCl$

trans-1,1,3-Trichloro-3,4-epoxynonafluorohexane (36); Typical Procedure:[70]

(_E_)-1,1,3-Trichlorononafluorohex-3-ene (**35**; 7 g, 20 mmol) was added dropwise to a solution of 14% NaOCl (32 mL) in MeCN (4 mL) in the presence of one drop of $(C_8H_{17})_3NMeCl$ at 8°C over 15 min while stirring. The mixture was allowed to react at 12–16°C for 2 h and then ice water (100 mL) was poured in. The bottom layer was separated and distilled to give a fraction of crude product at 125–130°C; yield: 6.1 g (83%); crude **36** was purified by semipreparative GC (dinonyl phthalate, 100°C).

Cyclic perfluoroalkenes are oxidized to the corresponding epoxides by methods analogous to those used for acyclic perfluoroalkanes. A general method is the oxidation by sodium hypochlorite in aqueous acetonitrile at 0–20°C that gives high yields of the corresponding epoxides. This chemical behavior is observed for perfluoro(1-alkylcyclobutene)[62] (89% yield), perfluorocyclohexene[71,72] (89–92%), perfluoro(1-methylcyclohexene)[73] (91% yield), and perfluorocycloheptene[74] (84% yield). Even 4,5-dibromodecafluorocycloheptene is selectively converted into the epoxide **37** in high yield[74] (90%). The reactions of perhalogenated cycloheptenes proceed more readily than those with comparable fluorocyclohexenes. Presumably, the greater flexibility of the cycloheptane ring, as compared with the cyclohexane ring, allows the epoxide system to be formed with less eclipsing of fluorine substituents.[74]



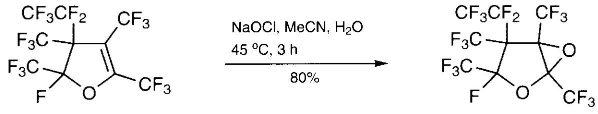
37

1,2-Dibromo-4,5-epoxydecafluorocycloheptane (37); Typical Procedure:[73,74]

4,5-Dibromodecafluorocycloheptene (10 g, 22 mmol) was added over 15 min to a vigorously stirred mixture of NaOCl (60 mL, 12% available Cl) and MeCN (25 mL). The mixture was then stirred at 15°C for 1 h. H_2O (100 mL) was added and the lower layer was separated, washed with aq $NaHSO_3$ and H_2O, dried ($MgSO_4$), and distilled to give the product; yield: 9.3 g (90%); bp 86°C/10 Torr; mp 26°C.

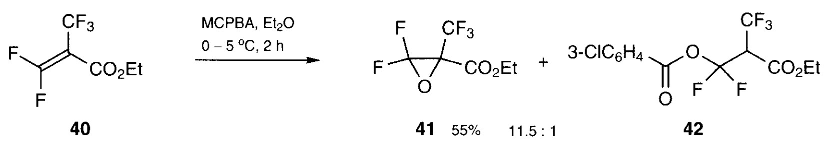
Perfluorobicyclo[4.4.0]dec-1(6)-ene is readily converted into the corresponding epoxide by the same methodology as perfluorinated cycloalkenes[75] using sodium hypochlorite.

A series of functionalized alkenes has been subjected to selective epoxidation reactions. Oxidation of perfluorinated vinyl polyethers by bubbling oxygen through the liquid that contains a catalytic amount of a Lewis acid, e.g. antimony(V) fluoride, results in the formation of acid fluorides together with a smaller amount of C=C bond cleavage.[76] Perfluorinated pentaalkyl-2,3-dihydrofuran **38**, an example of an unsaturated cyclic ether that is quite stable owing to perfluoroalkylation, is epoxidized by hypochlorite to the product **39** at 45°C.[62]



38 **39**

Trifluoroacrylonitrile can be epoxidized by oxygen with 1,1,2-trichlorotrifluoroethane (CFC-113) as a solvent under pressure at elevated temperatures in moderate yield (Table 2).[77] Substituted peroxybenzoic acids are used for the epoxidation of trifluorovinyl alkenes with attached functionalities such as ester, amide or dimethoxyphosphoryl groups (Table 2).[78] Functional derivatives of perfluoro-2-methylprop-2-enoic acid are oxidized to the corresponding epoxy compounds in this reaction.[78] In the case of ethyl ester **40**, the epoxide **41** is contaminated with the adduct of 3-chloroperoxybenzoic acid to the C=C bond, compound **42**, that is formed even at low temperatures.[78]

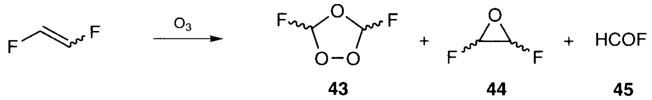


Ethyl 2,3-Epoxy-3,3-difluoro-2-(trifluoromethyl)propanoate (41); Typical Procedure:[78]

Ethyl 3,3-difluoro-2-(trifluoromethyl)prop-2-enoate (**40**; 9.8 g, 51 mmol) was added dropwise during 20 min to a vigorously stirred solution of 85% MCPBA (9.9 g) in anhyd Et_2O (9.8 g) at 0–5 °C. The reaction was continued for 2 h, the precipitate was filtered off, and all volatile products were distilled in vacuo (ca. 20 °C/1 Torr) and condensed in a dry ice trap. Et_2O was then removed from the distillate to give a crude product mixture of **41** and **42** [6.5 g, ratio (**41**/**42**) 11.5 : 1]. Product **41** was obtained by distillation; yield: 6 g (55%); bp 97–98 °C (admixture of **42**, 6% rel.).

Ozonization

The reaction of fluorinated alkenes with ozone generally affords two types of products depending on the presence of fluorine atoms and perfluoroalkyl groups at the C=C bond. Traditionally, ozonization is used as a gentle method for C=C bond cleavage.[3,79] On the other hand, the presence of perfluoroalkyl groups at the C=C bond stabilizes otherwise unstable ozonides (1,2,4-trioxolanes) to such a level that they can be characterized at ambient temperatures (*vide infra*). Ozonides are generally obtained by the reaction of fluoroalkenes with ozone. Thus, ozonide (3-fluoro-1,2,4-trioxolane) has been identified by mass spectra at low temperature (−95 °C) following ozonization of fluoroethene.[80] It is interesting, that the same ozonide is formed by the ozonolysis of a mixture of (*Z*)-1,2-difluoroethene with ethene thus verifying an intermolecular recombination process in the ozonide formation from molozonide.[80] A number of products have been identified on ozonolysis of fluoroethene at low temperatures. The major volatile products are formyl fluoride and the ozonide (3-fluoro-1,2,4-trioxolane) (Table 5).[81] Small amounts of both cross ozonides (i.e., 3,5-difluoro-1,2,4-trioxolane and 1,2,4-trioxolane) have also been observed.[81] The oxidation of (*Z*)- and (*E*)-1,2-difluoroethene by ozone leads to a mixture of the corresponding epoxides and ozonides together with formyl fluoride. The composition of the mixture from reactions at −78 °C depends on the solvent used.[82,83] Two interesting results are observed: the reaction of (*Z*)- and (*E*)-1,2-difluoroethene in chloromethane gives *cis*-2,3-difluorooxirane (*cis*-**44**) and a *cis*/*trans* ozonide **43** ratio of 10 : 90 is determined for the ozonolysis of both alkene isomers.[82] Similar results are obtained when the ozonolysis is carried out in perhalogenated chlorofluoromethanes and 1,1,2-trichlorotrifluoroethane.[83] The previously unknown compounds, fluorinated cyclopropanes, are detected in the ozonolysis of 1,2-difluoroethene.[83,84]



Alkene	Conditions	Yields (%)				
		43	[Ratio (*cis*/*trans*)]	*cis*-**44**	*trans*-**44**	**45**
Z	CF_3Cl, −95 °C	16	[5:95]	12	0.4	30
E		6	[6:94]	0.5	10	33
Z	$CF_2ClCFCl_2$, 0 °C	6	[8:92]	5		45
E		3	[12:88]	0.3	0.5	50
E	CF_2Cl_2, −78 °C	13	[7:93]	0.4	7	–[a]

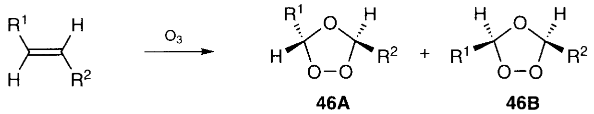
[a] Not determined.

3,5-Difluoro-1,2,4-trioxolane (43) and 2,3-Difluorooxirane (44); Typical Procedure:[83]
1,2-Difluoroethene (0.19 g, 3 mmol) was dissolved in CF_3Cl (2 mL) at − 95 °C. The alkene was ozonized to 100% completion using flow rates of 0.10–0.15 mL of $O_3 \cdot min^{-1}$. Immediately after the completion of ozonolysis, the volatile material in the reactor was allowed to warm and was trap-to-trap distilled through − 140 and − 196 °C traps. The contents of the − 196 °C trap were examined by gas-phase IR spectroscopy and contained only CF_3Cl and a small amount of unreacted ozone, SiF_4 and HCOF.

The contents of the − 140 °C trap were purified further by another trap-to-trap distillation through traps cooled to − 95, − 116, and − 196 °C. The contents of the − 95 °C trap were found to be *cis*-2,3-difluorooxirane (*cis*-**44**), *cis*- and *trans*-3,5-difluoro-1,2,4-trioxolane (**43**), and small amounts of *cis,cis*-1,2,3-trifluorocyclopropane and HCO_2H. As previously mentioned the *cis,cis*-cyclopropane is formed only on ozonolysis of the *Z*-alkene. The − 116 °C trap contained *trans*-2,3-difluorooxirane (*trans*-**44**), *cis,trans*-1,2,3-trifluorocyclopropane, and small amounts of the *cis*-epoxide. The − 196 °C trap contained mostly HCOF and small amounts of SiF_4. The contents of each trap were further purified by preparative GC (17 ft × 0.25 in. Teflon column packed with 10% Halocarbon oil on 40–60 mesh Chromosorb T at 22 °C).

Each reaction left a liquid residue at the bottom of the reaction flask. This material was likely peroxidic in nature because of its slow reaction with aq KI.

In studies of the reactions of 1,1-difluoroethene, trifluoroethene, and perfluoroethene, the mechanism of ozonide, epoxide, and cyclopropane formation have been studied.[84] Unusually stable ozonides **46A** and **B** are prepared by treating mono- and bis(fluoroalkyl)ethenes with ozone[85] at room temperature or on heating the substrate to which ozone is introduced. The rates are approximately 10^{10} slower than that for the nonfluorinated analogs. Mono-perfluoroalkylated ethene seems to react several times more rapidly than the bis-perfluoroalkylated ethene.[85]



R^1	R^2	Conditions	Yield (%)	
			46A	**46B**
$(CF_2)_3CF_3$	$(CF_2)_3CF_3$	20 °C, 6 h	70	30
$(CF_2)_5CF_3$	$(CF_2)_5CF_3$	100 °C, 10 h	75	25
$(CF_2)_7CF_3$	H	60 °C, 1 h	100	

Partially fluorinated cyclobutene gives at 0 °C an ozonide that is stable in dichloromethane solution at room temperature.[86] It is decomposed by acid hydrogen peroxide yielding fluorinated butanedioic acid.[86] Bubbling ozone into a pentane solution of hexakis(trifluoromethyl)benzvalene gives a pale-yellow ozonide which is stable at room temperature (Table 5).[87]

Table 5. Ozonolysis of Fluoroalkenes

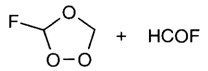
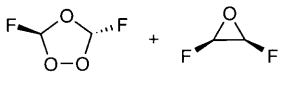
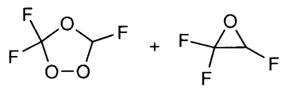
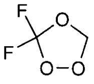
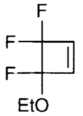
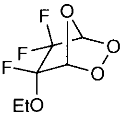
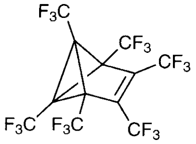
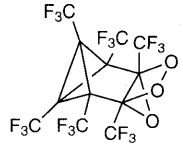
Substrate	Reagent, Solvent	Conditions	Products	Yield (%)	Ref
$FHC=CH_2$	O_3, MeCl O_3, neat	− 95 °C − 126 °C		33 + 40 45 + 33	81 81
(E/Z)-FHC=CHF	O_3, $CHMe_3$	− 78 °C		major + minor	82
$F_2C=CHF$	O_3, $CF_2ClCFCl_2$ O_3, CF_2Cl_2 O_3, CF_3Cl	0 °C − 78 °C − 95 °C		10 + 13[a] 7 + 7[b] 5 + 6[c]	84 84 84

Table 5. (cont.)

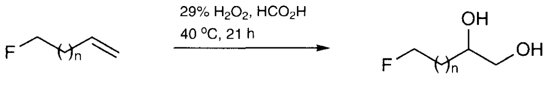
Substrate	Reagent, Solvent	Conditions	Products	Yield (%)	Ref
$F_2C=CH_2$	O_3, $CF_2ClCFCl_2$	0 °C		22	84
$F_2C=CF_2$	O_3, $CF_2ClCFCl_2$	0 °C	 + COF_2	8 + 16	81
	O_3, O_2, CH_2Cl_2	0 °C, 8 h		~ 100	86
	O_3, cyclopentane	− 20 to − 10 °C		~ 100	87

[a] In addition HCOF and COF_2 were formed.
[b] In addition HCOF (25%) and COF_2 (30%) were formed.
[c] In addition HCOF (20%) and COF_2 (25%) were formed.

Dihydroxylation

Dihydroxylation, the addition of two hydroxy groups across a C = C bond, converts fluorinated alkenes into different products depending on the presence or absence of a fluorine atom at the hydroxylated carbon. Partially fluorinated alkenes with vicinal hydrogen atoms attached to the C = C bond can be hydroxylated to vicinal diols. When the reaction is performed with a sufficiently strong oxidizing agent, the initially formed diols are oxidized to vicinal diketones as the end products.

The dihydroxylation of terminal ω-fluoroalkenes is accomplished by a mixture of hydrogen peroxide and formic acid. The first step is obviously the formation of an epoxide followed by ring opening.[88] The reactivity of the C = C bond is very probably not affected by the distant C – F bond.[88]



47 n = 2 30%
n = 8 75%

11-Fluoroundecane-1,2-diol (47, n = 8); Typical Procedure:[88]

To a well-stirred mixture of 11-fluoroundec-1-ene (10 g, 58 mmol) and HCO_2H (30 mL) at rt was added 29% H_2O_2 (7 g, 60 mmol). The mixture was stirred and heated at 40 °C for 21 h. The excess HCO_2H was removed under reduced pressure at 40 °C, and the residue was refluxed for 1 h with 3 M NaOH (50 mL). A large excess of hot H_2O was added, and the crude glycol layer was separated. This was washed with hot H_2O, extracted with Et_2O, and the extract was washed with cold H_2O. Removal of Et_2O gave the crude product that was used for subsequent oxidation without further purification; yield: 9 g (75%); mp 42–43 °C (after 2 d in a vacuum desiccator).