Fluorine Compounds, Organic

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1. Introduction

Organic fluorine compounds are characterized by their carbon–fluorine bond. Fluorine can replace any hydrogen atom in linear or cyclic organic molecules because the difference between the van der Waals radii for hydrogen (0.12 nm) and fluorine (0.14 nm) is small compared to that of other elements (e.g., chlorine 0.18 nm). Thus, as in hydrocarbon chemistry, organic fluorine chemistry deals with a great variety of species. When all valences of a carbon chain are satisfied by fluorine, the zig-zag-shaped carbon skeleton is twisted out of its plane in the form of a helix. This situation allows the electronegative fluorine substituents to envelop the carbon skeleton completely and shield it from chemical (especially nucleophilic) attack. Several other properties of the carbon–fluorine bond contribute to the fact that highly fluorinated alkanes are the most stable organic compounds. These include low polarizability and high bond energies, which increase with increasing substitution by fluorine (bond energies: C – F bond in CH₃F, 448 kJ/mol; C – H bond in CH₄, 417 kJ/mol; C – Cl bond in CH₃Cl, 326 kJ/mol; and C – F bond in CF₄, 486 kJ/mol).

The cumulative negative inductive effect of the fluorine in perfluoroalkyl groups may reverse the polarity of adjacent single bonds (e.g., in the pair HₑC < H and FₑC > I) or double bonds (e.g., CH₃C⁺H = C⁶⁺H₂ and CF₃–C⁵⁻H = C⁵⁺H₂). Fluorine substitution changes the reactivity of olefins and carbonyl compounds. Polyyfluorinated olefins possess an electron-deficient double bond, which reacts preferentially with nucleophiles. Carboxy groups are affected by the presence of an adjacent perfluoroalkyl radical. In carboxylic acids, the acidity is markedly increased. In other carbonyl compounds, the reactivity is increased without any fundamental change in the chemistry of the compound. Correspondingly, the basicity of amines is reduced by the introduction of fluorine.

Fluorine attached to the ring of aromatic compounds acts mainly as a para-directing substituent, whereas perfluoroalkyl groups behave as meta-directing substituents.

 Naturally, the influence of fluorine is greatest in highly fluorinated and perfluorinated compounds. The fact that these compounds have a high thermal stability and chemical resistance and are physiologically inert makes them suitable for many applications for which hydrocarbons are not. Properties that are exploited commercially include high thermal and chemical stability, low surface tension, and good dielectric properties, for example, in fluoropolymers, perfluorinated oils and inert fluids.

Individual fluorine atoms or perfluoroalkyl groups do not change the technical properties of a hydrocarbon fundamentally. However, this is not the case with physiological properties. A fluorine atom in a bioactive material may simulate a hydrogen atom, and although this does not prevent metabolic processes from occurring, the end products may be ineffective or toxic. Accordingly, such fluorine compounds are important in, for example, pesticides and pharmaceuticals.

A bibliography of the scientific literature of organofluorine chemistry was published in 1986 [16]; commercial applications of fluorine products are reviewed in [7], [17], and [18].

**Nomenclature.** Any organic fluorine compound can be named according to the rules of the International Union for Pure and Applied Chemistry (IUPAC) [19]. However, for highly fluorinated molecules with several carbon atoms, this nomenclature can be confusing. Therefore, the term “perfluoro” may be used when all hydrogen atoms bonded to the carbon skeleton have been replaced by fluorine. The designation of hydrogen atoms belonging to functional groups (e.g., CHO or COOH), of the functional groups themselves, and of other substituents is not affected [19]. Examples are given in Table 1.
In the case of highly fluorinated compounds with few hydrogen atoms (1 – 4), the perfluoro compound can be taken as the parent compound. The hydrogen atoms are named according to their number and position; the letter H or the prefix hydryl (hydro) are used for hydrogen. The symbol F was approved by the American Chemical Society as abbreviation for perfluoro [20].

**Historical Development.** The pioneering work in organofluorine chemistry dates from 1835 to 1940 [21]. Controlled production of organic fluorine compounds was started in 1892 by exchanging halogen for fluorine in hydrocarbons, using antimony(III) fluoride. The industrial phase began in 1929 in the United States with the discovery of the nonflammable, nontoxic refrigerants CCl₃F and CCl₂F₂ [22]. In Germany, commercial production of aromatic fluorine compounds started in 1930.

The first fluoropolymer, polychlorotrifluoroethylene, was synthesized in 1934 in Germany, followed by the discovery of polytetrafluoroethylene in 1938 in the United States. During World War II, thermally and chemically stable working materials for the separation of uranium isotopes were investigated by the United States Manhattan Project [23]. After World War II, numerous novel applications were discovered. The development of new organic fluorine compounds with novel applications continues undiminished.

### 2. Production Processes

The four principal methods for the preparation of organic fluorine compounds are as follows [1], [2], [24], [25]:

1. substitution of hydrogen in hydrocarbons using fluorine, high-valency metal or nonmetal fluorides, or electrochemical fluorination
2. halogen – fluorine exchange with hydrogen fluoride, hydrogen fluoride-base complexes, or metal fluorides
3. synthesis of higher molecular mass fluorine compounds from reactive fluorinated synthons
4. addition of fluorine, hydrogen fluoride, or reactive nonmetal fluorides to unsaturated bonds

Only a few of the many possibilities in each group have been developed commercially, with varying degrees of success.

2.1. Substitution of Hydrogen

**Fluorination with Elemental Fluorine** [26], [27]. The action of elemental fluorine on organic compounds normally leads to violent, mainly explosive, reactions. The substrate fragments into units with a varying degree of fluorination because the heats of formation of the C – F bond (ca. 460 kJ/mol) and the H – F bond (566 kJ/mol) are greater than the heat of formation of the C – C bond (ca. 348 kJ/mol).

Therefore, direct fluorinations must take place with strict control of the reaction and removal of the heat generated. This may be achieved by dilution of the fluorine with inert gases (e.g., N₂ or CO₂), dilution of the organic substrates with inert solvents [28], intensive mixing, and reduction of the temperature to as low as –150 °C.

Direct fluorination can also be carried out in the gas phase in a tubular reactor packed with silver- or gold-plated copper turnings [29]. Specialized methods are based on LaMar fluorination [26], aerosol fluorination [30], porous-tube fluorination [31], and jet fluorination [32]; high product selectivities are achieved at a laboratory scale.

### Table 1. Nomenclature of organic fluorine compounds

<table>
<thead>
<tr>
<th>Formula</th>
<th>CAS registry no.</th>
<th>IUPAC designation</th>
<th>Perfluoro designation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF₂CF₃</td>
<td>[76-16-4]</td>
<td>hexafluoroethane</td>
<td>perfluoroethane, F-ethane</td>
</tr>
<tr>
<td>CF₂CF₂CF₂CHO</td>
<td>[375-02-0]</td>
<td>Heptafluoro-n-butyraldehyde</td>
<td>Perfluoro-n-butyraldehyde, F-n-butyraldehyde</td>
</tr>
<tr>
<td>CF₂(CF₂)₇COOH</td>
<td>[335-67-1]</td>
<td>Pentadecafluoro-n-octanoic acid</td>
<td>Perfluoro-n-octanoic acid</td>
</tr>
<tr>
<td>CF₂(CF₂)₇CHF₂</td>
<td>[375-17-7]</td>
<td>1,1,1,2,2,3,3,4,4-Nonafluoro-n-butane</td>
<td>1H-Perfluoro-n-butane, 1-hydryl-F-n-butane</td>
</tr>
<tr>
<td>CF₂(CF₂)₉CH₂OH</td>
<td>[423-46-1]</td>
<td>2,2,3,3,4,4,5,5,6,6,6-Dekadecafluoro-n-hexanol</td>
<td>1,1,1,1,1-decylofluoro-n-hexanol</td>
</tr>
</tbody>
</table>

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scale. Commercial operation remains to be developed.

**Fluorination with Metal Fluorides** [33]. Metal fluorides that can transfer fluorine to organic substrates by changing the oxidative state of the metal, such as cobalt(III) fluoride (CoF₃) and silver(II) fluoride (AgF₂), serve as fluorinating agents in an oxidizing fluorination. The spent metal fluoride is regenerated with elemental fluorine.

\[
\text{CoF}_3 + \text{HF} \rightarrow \text{CoF}_2 + \text{HCl}
\]

Fluorination and regeneration can be cyclical, permitting a commercial operation.

**Electrochemical Fluorination.** The Simons process [34], [35] is used commercially for the production of perfluorinated compounds. Solutions of organic compounds (mainly carboxylic acids, sulfonic acids, and tertiary amines) are electrolyzed in anhydrous hydrogen fluoride in a single cell without intermediate formation of free fluorine. Fluorination takes place at a nickel anode by a free-radical mechanism at current densities of 10–20 mA/cm² [36]. Selectivity decreases sharply as the number of carbons increases.

Volatile, hydrogen-containing compounds (hydrocarbons and chlorohydrocarbons) can be electrofluorinated on porous graphite anodes in KF-containing hydrogen fluoride in a process developed by Phillips Petroleum [37], [38], [39] and now referred to as CAVE (Carbon Anode Vapor Phase Electrochemical Fluorination), in operation at 3 M [40]. The organic compound is introduced into the cell through the anode. In the pores of the anode, i.e., at the phase boundary, partial or complete exchange of the hydrogen, but not the chlorine, takes place. To date this process has been used only on a small scale.

### 2.2. Halogen – Fluorine Exchange

**Exchange of chlorine with hydrogen fluoride** is used in many commercial processes both for the production of chlorofluoroalkanes and for the side-chain fluorination of aromatic and N-heterocyclic compounds [41]. The method involves exchange of chlorine for fluorine in poly-halogenated compounds using hydrogen fluoride [42]:

\[
-\text{Cl} + \text{CF}_3 \text{H} + 2 \text{CoF}_3 \rightarrow -\text{CF}_3 -\text{F} + \text{HCl} + 2 \text{CoF}_2
\]

Whether the process takes place with or without a catalyst depends on the reactivity of the chlorine atoms to be exchanged. With compounds containing several chlorine atoms of differing reactivity, selective fluorination can be achieved by selecting suitable process conditions.

Fluorinations without a catalyst such as

\[
\text{CCl}_3\text{CH}_3 \rightarrow \text{CF}_3\text{CH}_3 \text{or } \text{CCl}_3\text{CHCl}_2 \rightarrow \text{CF}_3\text{CHCl}_2
\]

are carried out in liquid, anhydrous hydrogen fluoride at 100–150 °C in pressure vessels made of steel, alloy steels, or nickel. The process can be carried out by batch (e.g., autoclave) or continuous methods (autoclaves in series or a tubular reactor). In either case, the hydrogen chloride that is generated during fluorination is removed from the reactor to maintain the desired pressure.

Most liquid-phase fluorinations, e.g., of CCl₄, CHCl₃, CCl₃CCl₃, CCl₃CHCl₂, or CCl₃CH₂Cl, are carried out in the presence of a catalyst [43] to promote the exchange, which becomes increasingly difficult as fluorination progresses. The main catalysts used are antimony(III) and antimony(V) halides with low volatility. Addition of chlorine oxidizes the antimony to the pentavalent state.

In addition to the liquid-phase processes, many commercially important gas-phase fluorinations employ hydrogen fluoride [43]. The components in the gas phase are passed through a tubular reactor containing the catalyst. The composition of the product can be controlled within wide limits by varying temperature, pressure, residence time, catalyst, and the proportions of the reactants. Various metal fluorides are suitable catalysts, e.g., aluminum fluoride [44] or basic chromium fluoride [45].

For further processing of the mixture produced by gas- or liquid-phase fluorination, the following criteria should be satisfied [46]:

1. The hydrogen chloride generated should be separated in a pure form to permit further use.
2. Unreacted hydrogen fluoride should be recovered.
3. Acid residues, water, and other impurities must be removed from the product.

Usually, the hydrogen chloride is separated from the crude fluorination mixture by fractional distillation. The bulk of the hydrogen fluoride may then be separated from the residue. Further treatment includes washing to remove traces of acid, drying, and fractional distillation.

**Exchange of Chlorine with Nonoxidizing Metal Fluorides** [41]. Alkali fluorides, especially potassium fluoride, are often used to exchange chlorine in carboxylic acid chlorides, sulfonic acid chlorides, α-chlorocarboxylic acid derivatives (esters, amides, and nitriles), aliphatic monocloro compounds, or activated aromatic chloro compounds (Halex process) [47].

The dry, finely powdered metal fluoride is employed in a solvent-free process at 400 – 600 °C, e.g., with polychlorinated aromatic compounds, or, in most other cases, in the presence of a solvent. For slow reactions, polar, aprotic solvents are used.

**2.3. Synthesis from Fluorinated Synthons**

The variety of organic fluorine compounds can be greatly increased by the use of easily accessible, low molecular mass fluoroalkanes and olefins to synthesize higher molecular mass products. Halo- and alkoxy-olefins add to halogenated ethylenes to form halogenated fluoropropanes [48]. An industrially applied reaction is the addition of iodopentafluoroethane to tetrafluoroethylene yielding a homologous series of long-chain 1-iodoperfluoroalkanes (see Section 3.4). The pyrolysis of dichlorodifluoromethane is the industrial source of tetrafluoroethylene, hexafluoropropene, and the corresponding oligomers and polymers (see Sections 4.2 and 4.3). These examples illustrate the importance of this synthetic method, especially for the production of organic fluorine compounds containing more than two carbon atoms where the above-mentioned fluorination methods fail to give high yields of the desired products.

**2.4. Addition of Hydrogen Fluoride to Unsaturated Bonds**

Addition of hydrogen fluoride to alkenes and alkynes takes place below 0 °C with formation of mono- or difluoroalkanes; ethylene and acetylene are exceptions [24]. Ethyl fluoride is produced from ethylene and hydrogen fluoride at 90 °C; catalytic processes have been developed for the addition of hydrogen fluoride to acetylene to produce vinyl fluoride or 1,1-difluorooctane.

Unsymmetrical olefins obey Markovnikov’s rule. Chloroolefins can undergo chlorine – fluorine exchange after addition of hydrogen fluoride. Addition of hydrogen fluoride to the electron-deficient double bond of perfluoroolefins can be performed using trialkylamine trihydrofluorides at moderate temperatures [49].

**2.5. Miscellaneous Methods**

**Substitution of Amino Groups in Aromatic Compounds** [50]. Introduction of one or two fluorine atoms into aromatic rings is carried out commercially by diazotization of aromatic amines in anhydrous hydrogen fluoride with solid sodium nitrite and decomposition of the dissolved diazonium salt (see Section 11.1.2).

**Fluorination with Nonmetal Fluorides.** Reactions of nonmetal fluorides with certain substrates are predominantly restricted to laboratory operations. Sulfur tetrafluoride and the following compounds can be used for the controlled introduction of fluorine into organic compounds: dialkylaminosulfur(IV) fluorides (R₂NSF₃) [51–53], fluoroalkylamines (e.g., 2-chloro-1,1,2-trifluoroethylamine or 1,1,2,3,3,3-hexafluoropropylamine), tetra-n-butylammonium fluoride, trialkylamine trishydrofluorides, nitrosyl fluoride, perchloryl fluoride, fluoroxylfluoroalkanes (e.g., CF₃OF) [54], xenon difluoride [55], or CH₃COOF [56]. They are of commercial value for the fluorination of complex organic compounds such as pharmaceuticals.

**2.6. Purification and Analysis**

Impurities are usually removed from organic fluorine compounds by fractional distillation,
fractional crystallization, or chromatographic methods. This does not apply to fluoropolymers and high-boiling perfluorinated oils, which require special measures, i.e., the use of extremely pure starting materials.

Quantitative determination of fluorine is possible in most cases by combustion and subsequent analysis of the hydrogen fluoride generated. Wet chemical methods are used to determine fluoride ions [57].

Because of the high volatility of organic fluorine compounds, purity can be readily determined by gas chromatography. \(^{19}\text{F}\)-Nuclear magnetic resonance spectroscopy is a valuable tool for determining the structure of organic fluorine compounds. Structure determinations, even of mixtures, are often easier using this method than with \(^1\text{H}\)-NMR spectra due to the larger chemical shifts of \(^{19}\text{F}\)-NMR spectra. The \(^{19}\text{F}\) signals can be integrated and used for quantitative analysis [58].

3. Fluorinated Alkanes

The hydrogen atoms of alkanes may be partially or totally replaced by fluorine. Partially fluorinated alkanes are hydrofluorocarbons (HFCs); fully fluorinated alkanes (perfluoroalkanes) are perfluorocarbons (PFCs). In chlorofluorocarbons (CFCs) and hydrochlorofluorocarbons (HCFCs), the alkane hydrogens are replaced by both chlorine and fluorine.

A special nomenclature [59] has been introduced to identify smaller chain length fluoroalkanes (up to four carbon atoms) used in refrigerants. It consists of a three-digit number combined with various letters. The first figure of the three-digit number indicates the number of carbon atoms minus one (for methane derivatives, the figure 0 is omitted); the second figure indicates the number of the hydrogen atoms plus one; and the third figure indicates the number of fluorine atoms. All other bonds are saturated with chlorine. The letter R before the code number is an abbreviation for refrigerant; the letter C indicates a cyclic compound. The complete number is called the refrigerant number. The American Society of Heating, Refrigerating, and Air Conditioning Engineers (Atlanta, Georgia) ASHRAE Standard 34 – 78 describes the method of coding. The abbreviation F is sometimes used and stands for fluorohydrocarbon.

This system does not allow isomerisms to be expressed for ethane derivatives; for such cases, a letter (a, b, . . . etc.) is added to isomers as their asymmetry increases, e.g.,

\[
\text{CF}_2\text{Cl} \rightarrow \text{CCl}_3\text{F} = \text{CFC 113 (R 113)} \\
\text{CF}_3 \rightarrow \text{CCl}_3 = \text{CFC 113 a (R 113 a)}
\]

The compound with the highest degree of symmetry is not given a letter.

A special isomer in the series of propane derivatives is designated by adding two letters to the numbers derived from the standard rules [60]. The first letter attached to the number refers to the central carbon atom, coding the total atomic mass of the two substituents attached (a = CCl₂, b = CFC₁, c = CF₂, d = CHCl, e = CHF, f = CH₂). The second appended letter is derived from the symmetry rule applied to the two terminal carbon atoms combined to an imaginary ethane unit. This unit is then treated like an ethane derivative with the difference that the letter a is given to the most symmetric combination. Examples for the codes of the isomeric propane derivatives C₃HCl₂F₅ are:

\[
\begin{align*}
\text{CF}_3\text{–CF}_2\text{–CHCl}_2 & \quad \text{HCFC 225 ca} \\
\text{CF}_2\text{Cl–CF}_2\text{–CHFCl} & \quad \text{HCFC 225 cb} \\
\text{CF}_3\text{–CHCl–CF}_2\text{Cl} & \quad \text{HCFC 225 da} \\
\text{CF}_3\text{–CHF–CFCl}_2 & \quad \text{HCFC 225 eb}.
\end{align*}
\]

Codes for the butane derivatives contain three letters appended to the numeral (e.g., CF₃–CH₂–CF₂–CH₃ is coded as HFC 365 mfc [61]).

3.1. Fluoroalkanes and Perfluoroalkanes

Properties. Monofluoroalkanes are attacked by bases and sometimes by heat; however, chemical resistance increases with increasing fluorine substitution, especially multiple substitution at the same carbon atom.

Perfluoroalkanes have distinct properties [62], [63]. Their physical properties differ from those of the corresponding hydrocarbons: densities and viscosities are higher, whereas surface tensions, refractive indices, and dielectric constants are lower. At room temperature perfluoroalkanes are attacked only by sodium in liquid ammonia. At 400 – 500 °C, they are degraded.
Another synthetic pathway is the exchange of chlorine (or bromine) for fluorine using hydrogen fluoride. Mono- and difluoroalkanes can be produced by addition of hydrogen fluoride to olefins or alkynes (e.g., CF$_2$H–CH$_3$, HFC 152 a). Another synthetic pathway is the exchange of chlorine (or bromine) for fluorine using hydrogen fluoride or metal fluorides such as antimony fluoride. Mono- and difluoroalkanes can be obtained by adding hydrogen fluoride to perfluoroalkanes (e.g., CF$_3$–CHF–CF$_3$, HFC 227 ea) or by decarboxylation of perfluoroalkoxycarboxylates in the presence of proton donors. The novel commercially interesting hydrofluorocarbons are produced by processes, that have been developed for the production of chlorofluorocarbons and hydrofluorocarbons and optimized during the last decades (see Section 3.2).

Higher temperatures and higher hydrogen fluoride:substrate ratios are necessary to achieve complete replacement of all chlorine atoms in the starting chlorocompounds by fluorine. Both liquid-phase halogen exchange in the presence of catalysts such as antimony(V) or tin(IV) chlorofluorides and vapor phase reactions using solid-phase catalysts based on chromium are employed. Preferred starting materials are chloroform for HFC 23 [45], [65], dichloromethane for HFC 32 [66] and 1,1,1-trichloroethane for HFC 143 a [67]. The conversion of tetrachloroethylene to HFC 125 [68] and trichloroethylene to HFC 134 a [69] involves initial HF-addition across the double bond followed by a series of chlorine–fluorine exchange reactions. Vapor-phase hydrogenolysis of chlorofluorocarbons and hydrochlorofluoro-
carbons is also proposed for the production of hydrofluorocarbons [70], [71].

Perfluoroalkanes can be produced by a variety of routes. Indirect fluorination of hydrocarbons with cobalt(III) fluoride or silver(II) fluoride is carried out in a steel or nickel tube with stirring. The hydrocarbon vapors are passed at 150 – 450 °C over the fluorinating agent, which is regenerated in a fluorine stream [72], [73]. This process is suitable for the production of perfluoroalkanes containing up to 20 carbon atoms. It affords better process control and yields than the direct gas-phase fluorination using dilute fluorine and a metal catalyst, especially for longer-chain compounds [74].

Fluoroalkanes and perfluoroalkanes can also be produced electrochemically by the Phillips process. A summary of their properties is given in Tables 3 and 4.

**Table 3. Physical properties of hydrofluorocarbons**

<table>
<thead>
<tr>
<th>Property</th>
<th>CH₂F₂</th>
<th>CHF₃</th>
<th>CHF₂CH₃</th>
<th>CF₃CH₃</th>
<th>CF₃CH₂F</th>
<th>CF₃CHF₂</th>
<th>CF₃CH₂CHF₂</th>
<th>CF₃CHF₂CF₃</th>
<th>CF₃CH₂CF₂CH₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical temperature, °C</td>
<td>78.2</td>
<td>26.3</td>
<td>113.3</td>
<td>73.6</td>
<td>101.1</td>
<td>66.3</td>
<td>154.1</td>
<td>101.8</td>
<td>187.7</td>
</tr>
<tr>
<td>Critical pressure, MPa</td>
<td>5.80</td>
<td>4.87</td>
<td>4.52</td>
<td>3.83</td>
<td>4.06</td>
<td>3.63</td>
<td>3.57</td>
<td>2.93</td>
<td>2.75</td>
</tr>
<tr>
<td>Critical density, g/cm³</td>
<td>0.927</td>
<td>0.365</td>
<td>0.434</td>
<td>0.515</td>
<td>0.517</td>
<td>0.582</td>
<td></td>
<td></td>
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<tr>
<td>Heat of evaporation at bp, kJ/kg</td>
<td></td>
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<tr>
<td>Surface tension, N/cm</td>
<td>6.93  ×</td>
<td>9.94 ×</td>
<td>4.60 ×</td>
<td>8.02 ×</td>
<td>3.70 ×</td>
<td>10⁻⁵</td>
<td>10⁻⁵</td>
<td>10⁻⁵</td>
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<tr>
<td>Vapor pressure (kPa) at</td>
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<tr>
<td>– 120 °C</td>
<td>5.9</td>
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<tr>
<td>– 100 °C</td>
<td>31.5</td>
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<td>– 80 °C</td>
<td>113.9</td>
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<td>– 60 °C</td>
<td>314.0</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>– 40 °C</td>
<td>177.3</td>
<td>712.0</td>
<td>141.7</td>
<td>52.0</td>
<td>148.4</td>
<td>32.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– 20 °C</td>
<td>405.8</td>
<td>1403.0</td>
<td>120.7</td>
<td>316.4</td>
<td>134.0</td>
<td>337.6</td>
<td>19.7</td>
<td>86.7</td>
<td>6.3</td>
</tr>
<tr>
<td>0 °C</td>
<td>813.4</td>
<td>2504.3</td>
<td>264.2</td>
<td>620.2</td>
<td>293.0</td>
<td>670.6</td>
<td>53.6</td>
<td>196.2</td>
<td>18.8</td>
</tr>
<tr>
<td>20 °C</td>
<td>1474.6</td>
<td>4184.3</td>
<td>513.4</td>
<td>1104.3</td>
<td>572.0</td>
<td>1204.6</td>
<td>123.8</td>
<td>390.2</td>
<td>46.7</td>
</tr>
<tr>
<td>40 °C</td>
<td>2477.4</td>
<td>909.7</td>
<td>1831.5</td>
<td>1017.0</td>
<td>2008.1</td>
<td>251.8</td>
<td>702.9</td>
<td>100.9</td>
<td></td>
</tr>
<tr>
<td>60 °C</td>
<td>3933.4</td>
<td>1501.0</td>
<td>2884.7</td>
<td>1681.0</td>
<td>463.5</td>
<td>1174.7</td>
<td>194.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80 °C</td>
<td>2344.1</td>
<td>2631.0</td>
<td>788.8</td>
<td>1857.2</td>
<td>344.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100 °C</td>
<td>3511.4</td>
<td>3970.0</td>
<td>1261.0</td>
<td>2824.6</td>
<td>567.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>120 °C</td>
<td>1920.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>140 °C</td>
<td>1300.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower ignition limit (25 °C), vol %</td>
<td>12.7</td>
<td>none</td>
<td>3.1</td>
<td>7.1</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>5.5</td>
</tr>
<tr>
<td>Atmospheric lifetime, a</td>
<td>0.15</td>
<td>8.4</td>
<td>0.03</td>
<td>1.0</td>
<td>0.29</td>
<td>0.67</td>
<td>0.69</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HGWP = Halogen Global Warming Potential

**Table 4. Boiling points, melting points, and densities of liquid perfluorocarbons**

<table>
<thead>
<tr>
<th>Compound (also mixtures)</th>
<th>CAS registry no.</th>
<th>Molecular formula</th>
<th>M₀</th>
<th>Commercial designation</th>
<th>bp, °C</th>
<th>pour point, °C</th>
<th>d³</th>
<th>g/cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>F-pentanes</td>
<td>[678-26-2]</td>
<td>C₅F₁₀</td>
<td>288</td>
<td>PP150</td>
<td>29</td>
<td>– 120</td>
<td>1.604</td>
<td></td>
</tr>
<tr>
<td>F-methylcyclopentanes</td>
<td></td>
<td>C₁₀F₁₂</td>
<td>388</td>
<td>PP1C</td>
<td>48</td>
<td>– 70</td>
<td>1.707</td>
<td></td>
</tr>
<tr>
<td>F-hexanes</td>
<td>[355-42-0]</td>
<td>C₆F₁₄</td>
<td>338</td>
<td>PP1</td>
<td>57</td>
<td>– 90</td>
<td>1.682</td>
<td></td>
</tr>
<tr>
<td>F-methylcyclohexanes</td>
<td></td>
<td>C₁₂F₁₈</td>
<td>350</td>
<td>PP2</td>
<td>76</td>
<td>– 30</td>
<td>1.778</td>
<td></td>
</tr>
<tr>
<td>F-decalin (cis/trans)</td>
<td>[306-94-5]</td>
<td>C₁₀F₁₈</td>
<td>462</td>
<td>PP5</td>
<td>142</td>
<td>– 8</td>
<td>1.917</td>
<td></td>
</tr>
<tr>
<td>F-perhydrofluorene</td>
<td></td>
<td>C₁₁F₂₀</td>
<td>574</td>
<td>PP10</td>
<td>194</td>
<td>– 40</td>
<td>1.984</td>
<td></td>
</tr>
<tr>
<td>F-perhydrofluoranthene</td>
<td></td>
<td>C₁₄F₂₆</td>
<td>686</td>
<td>PP24</td>
<td>244</td>
<td>0</td>
<td>2.052</td>
<td></td>
</tr>
<tr>
<td>F-cyclohexymethyldecalin</td>
<td></td>
<td>C₁₇F₃₀</td>
<td>774</td>
<td>PP25</td>
<td>260</td>
<td>– 10</td>
<td>2.049</td>
<td></td>
</tr>
</tbody>
</table>

a Flutec notation (BNFL Fluorochemicals)
b F = perfluoro
Petroleum process or the electrochemical fluorination of alcohols, amines, carboxylic acids, and nitriles by the Simons process (see Section 2.1).

Tetrafluoromethane (carbon tetrafluoride, CF₄) can be produced by reaction of CCl₂F₂ or CCl₃F and hydrogen fluoride in the gas phase [75] or by direct fluorination of carbon [76].

Hexafluoroethane (PFC 116) is often obtained as a byproduct in the production of CFC 115. Octafluoropropane (PFC 218) can be produced by direct, electrochemical, or CoF₃-fluorination [79] of commercially available hexafluoropropene (see Section 4.3). Octafluorocyclobutane is obtained by dimerization of tetrafluoroethylene [80] or by passing 1,2-dichloro-1,1,2,2-tetrafluoroethane, CClF₂CClF₂, over a nickel catalyst at 590 °C [81].

Uses. Hydrofluorocarbons have been gaining increasing commercial interest as substitutes for chlorofluoro- and hydrochlorofluorocarbons since governmental regulations banned the worldwide production and consumption of CFCs by 1996 and introduced a specific timetable for the phase out of HCFCs [82]. In contrast to CFCs hydrofluorocarbons have no adverse effect on the ozone layer and only a low contribution to global warming (see below). The latter effect could be further minimized by avoiding leakages in refrigeration and air-conditioning equipment and by refrigerant recycling.

In all applications involving considerable emissions to the atmosphere, e.g., as propellants in aerosols (except medicinal aerosols), in open cell foams, or in extruded foams CFCs will be replaced by nonhalogenated compounds in the future.

Due to the presence of hydrogen in the molecule, the stability of HFCs is reduced. In the atmosphere they are degraded below the stratospheric level, leading to zero ozone depletion potentials (ODP = 0) and to reduced halogen global warming potentials (HGWP). However, depending on the structure of the HFCs this reduced stability can entail an increased flammability and thus make safe handling more difficult.

Therefore, alternatives to the CFCs need to retain the attractive properties of CFCs like low toxicity, nonflammability, good thermodynamic properties, and accessibility via economically and ecologically viable manufacturing processes, but avoid any adverse effect to the environment.

In refrigeration and air-conditioning systems CFC 12 is replaced by HFC 134a, HCFC 22 by the azeotropic mixtures HFC 507 (HFC 125/HFC 143 a : 1) or HFC 410 (HFC 32/HFC 125 : 1 : 1) and CFC 13 by HFC 23. HFC 134a and HFC 227 ea can be used as propellants in medicinal aerosols instead of CFC 114. HFC 245 fa and HFC 365 mfc are proposed as blowing agents for foams in replacing CFC 11, CFC 113 and HCFC 141 b [83]. Until now no HFC candidate for replacement of CFC 11 and CFC 113 as solvents, degreasing agents, or cleaning agents for textiles or metal surfaces has been identified. In the period 1990 – 1995 159.5 x 10³ t of HFC 134a have been produced [84].

Gaseous perfluorocarbons (PFC 14, PFC 116, PFC 218) are used in plasma etching processes in the microelectronic industry [85] and as gaseous dielectrics. Liquid perfluorocarbons [64] serve as heat-transfer media in transformers and in capacitors, as lubricants and hydraulic fluids, or in vapor-phase soldering [86] and vapor-phase sterilization [64].

Perfluoroalkanes, e.g., perfluorodecalin [306-94-5], are used in the production of blood substitutes [87].

<table>
<thead>
<tr>
<th>Property</th>
<th>PP50</th>
<th>PP1C</th>
<th>PP1</th>
<th>PP2</th>
<th>PP5/6</th>
<th>PP10</th>
<th>PP11</th>
<th>PP24</th>
<th>PP25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical temperature, °C</td>
<td>148.7</td>
<td>180.8</td>
<td>177.9</td>
<td>212.8</td>
<td>292.0</td>
<td>357.2</td>
<td>377</td>
<td>388.7</td>
<td>400.4</td>
</tr>
<tr>
<td>Critical pressure, MPa</td>
<td>2.05</td>
<td>2.26</td>
<td>1.83</td>
<td>2.02</td>
<td>1.75</td>
<td>1.62</td>
<td>1.46</td>
<td>1.51</td>
<td>1.13</td>
</tr>
<tr>
<td>Critical volume, L/kg</td>
<td>1.626</td>
<td>1.567</td>
<td>1.582</td>
<td>1.522</td>
<td>1.521</td>
<td>1.59</td>
<td>1.58</td>
<td>1.606</td>
<td>1.574</td>
</tr>
<tr>
<td>Heat of evaporation at bp, kJ/kg</td>
<td>90.8</td>
<td>75.8</td>
<td>85.5</td>
<td>85.9</td>
<td>78.7</td>
<td>71</td>
<td>68</td>
<td>65.8</td>
<td>67.9</td>
</tr>
<tr>
<td>Specific heat, kJ/kg·K⁻¹</td>
<td>1.05</td>
<td>0.878</td>
<td>1.09</td>
<td>0.963</td>
<td>1.05</td>
<td>0.92</td>
<td>1.07</td>
<td>0.93</td>
<td>0.957</td>
</tr>
<tr>
<td>Refractive index, n²</td>
<td>1.283</td>
<td>1.265</td>
<td>1.2509</td>
<td>1.2781</td>
<td>1.3130</td>
<td>1.3289</td>
<td>1.3348</td>
<td>1.3462</td>
<td>1.3376</td>
</tr>
<tr>
<td>Surface tension, N/cm²</td>
<td>9.4 x 10⁻³</td>
<td>12.6 x 10⁻³</td>
<td>11.1 x 10⁻⁵</td>
<td>15.4 x 10⁻⁵</td>
<td>17.6 x 10⁻⁵</td>
<td>19.7 x 10⁻⁵</td>
<td>19 x 10⁻⁵</td>
<td>22.2 x 10⁻⁵</td>
<td></td>
</tr>
<tr>
<td>Viscosity (dynamic), nPa·s</td>
<td>0.465</td>
<td>1.049</td>
<td>0.656</td>
<td>1.561</td>
<td>5.10</td>
<td>9.58</td>
<td>28.4</td>
<td>31.5</td>
<td>114.5</td>
</tr>
<tr>
<td>Vapor pressure (kPa) at 25 °C</td>
<td>8.62</td>
<td>3.68</td>
<td>2.94</td>
<td>1.41</td>
<td>0.09</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
Trade Names. Hydrofluorocarbons substituting chlorofluorocarbons and hydrochlorofluorocarbons are marketed worldwide under protected trade names. The individual product is characterized by the HFC code number following the trade name. Some worldwide applied trade names are:

- **France**: Rhône-Poulenc Isceon, Elf Atochem Forane
- **Germany**: Hoechst Reclin, Solvay Solkane
- **United Kingdom**: ICI Klea
- **Italy**: Montefluos Algogrene
- **Japan**: Asahi Glass Asahiflon, Daikin Daiflon
- **United States**: Allied Signal Genetron, DuPont Suva, Great Lakes Chemical FM, 3 M 3M Brand

Perfluorocarbons are offered under trade names such as Freon C-51–12; Perfluorokerosene FCX-329, FCX-330; Perfluorolube oil FCX-512, FCX-412 (DuPont); Flutec PP-1, PP-2, PP-3, PP-9, etc. (BNFL Fluorochemicals), Multi fluor Inert Fluids (Air Products and Chemicals).

### 3.2. Chlorofluoroalkanes

For more than 50 years chlorofluorocarbons and hydrochlorofluorocarbons have been the most important organic fluorine compounds commercially. The five products listed in Table 6 have been by far the most important of these with regard to the field of applications and to the amount produced [84].

The results of the investigation on postulated atmospheric changes caused by CFCs [89], [90] verified the adverse impact on the stratospheric ozone layer and the significant contributions to global warming due to the long atmospheric lifetimes of the CFCs. In 1987, a United Nations agreement, called the Montreal Protocol – revised in 1992 during the Copenhagen Intergovernmental Conference – set the deadline for the phase out of CFCs in developed countries. Since 1996 production and consumption of CFCs are prohibited, except as intermediates in the production of fluorine chemicals, especially fluoropolymers. For HCFCs with reduced atmospheric stabilities a timetable has been introduced for their phase out. HCFCs are allowed to be used as drop-in alternatives for CFCs until suitable HFC substitutes (see Section 3.1) will have been developed, but no longer than until 2015 to 2030 [82].

High molecular mass chlorofluorocarbons, a small but significant class of CFCs will not be affected by the ban.

**Properties.** Chlorofluoroalkanes are characterized by high chemical and thermal stabilities, which increase with their fluorine content. Low flammability (or nonflammability) and low toxicity are additional commercial advantages. Most of these compounds have a pleasant, weak odor; some are mild anesthetics [91].

Boiling points, freezing points, and densities of formerly commercially important chlorofluoroalkanes are shown in Table 7; other physical properties are listed in Table 8. Physical properties of some high molecular mass CFCs produced from chlorotrifluoroethylene are given in Table 9.

**Production.** Commercial production of chlorofluoroalkanes employs halogen exchange, with hydrogen fluoride in the liquid phase in the presence of a catalyst. The production scheme for dichlorodifluoromethane shown in Figure 1 is

---

### Table 6. Economically most important organic fluorine compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>Total production through 1995, 10^6 t</th>
<th>Maximum annual production (year), 10^3 t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichlorofluoromethane (R 11, CFC 11)</td>
<td>8.62</td>
<td>382 (1987)</td>
</tr>
<tr>
<td>Dichlorodifluoromethane (R 12, CFC 12)</td>
<td>11.28</td>
<td>425 (1987)</td>
</tr>
<tr>
<td>Chlorodifluoromethane (R 22, HCFC 22)</td>
<td>3.85</td>
<td>243 (1995)</td>
</tr>
<tr>
<td>1,2,2-Trichloro-1,1,2-trifluoroethane (R 113, CFC 113)</td>
<td>2.97</td>
<td>251 (1989)</td>
</tr>
<tr>
<td>1,2-Dichloro-1,1,2,2-tetrafluoroethane (R 114, CFC 114)</td>
<td>0.51</td>
<td>19 (1986)</td>
</tr>
</tbody>
</table>
to 100 and 20 kg of chlorine, and the mixture is heated
tetrachloride, 220 kg of antimony(III) chloride,
500 kg of hydrogen fluoride, 1540 kg of carbon
seals are made from aluminum or copper. The
stainless steel (V2A) serves as the reactor. The

A steam-heated steel autoclave (a) lined with
stainless steel (V2A) serves as the reactor. The
seals are made from aluminum or copper. The
autoclave (capacity 2 – 5 m³) is filled with
500 kg of hydrogen fluoride, 1540 kg of carbon
tetrachloride, 220 kg of antimony(III) chloride,
and 20 kg of chlorine, and the mixture is heated
to 100 °C. After ca. 2 h and an increase in
pressure to ca. 3 MPa, the fluorination products
with lower boiling points are removed together
with the hydrogen chloride that is generated and
some hydrogen fluoride; higher-boiling products in
the exit gases are condensed and recycled. The
low-boiling fraction is first washed with water in
a tower (e) lined with poly(vinyl chloride) and
packed with graphite; it is then washed with caustic
in a tower (f) filled with porcelain pack-
ing. After being washed to neutrality, the product
is dried in a tower (i) containing concentrated sulfuric
acid, compressed to a liquid, and fed into
an intermediate storage tank (m). Each batch
takes ca. 24 h to process. The antimony catalyst
remains in the reactor and is regenerated before
each subsequent batch by adding a small amount
of chlorine to convert it to the catalytically active
Sb(V) form.

The crude product is fractionally distilled
under pressure (0.6 – 0.8 MPa). The lower-
boiling fraction contains some chlorotrifluoro-
methane and most of the dichlorodifluorometh-
ane (yield 90 % based on carbon tetrachloride,
80 % based on hydrogen fluoride). The higher-
boiling fraction consists of trichlorofluoromethane
(5 – 10 % based on carbon tetrachloride), which
can be recycled. The distilled product is passed
through a caustic filter (s). Steel bottles, pressure
vessels, tank cars, and tank trucks are used for
transport.

More recently developed exchange processes
are carried out continuously in the gas phase at
100 – 400 °C, using catalysts based on chromium
[45], aluminum [44], or iron [94]. Starting
materials, which include carbon tetrachloride,
chloroform, tetrachloroethylene, and trichloro-
ethylene, are passed over the catalyst with excess
hydrogen fluoride and, where necessary, chlorine.
Further processing follows the same principles as in the liquid-phase process.

In the Montedison chlorofluorination process,
reaction of C₁₋ and C₂₋ hydrocarbons with chlo-
rine and hydrogen fluoride takes place in a single
step in a fluidized-bed reactor. A suitable catalyst
is a combination of aluminum chloride and other metals [95–97]:

\[
\text{CH}_4 + 4 \text{Cl}_2 + 2 \text{HF} \xrightarrow{\text{Cat}} \text{CICl}_2 + 6 \text{HCl}
\]

Commercial production of chlorofluoroalkanes is also possible by the electrochemical...
fluorination process developed by Phillips Petroleum (see Section 2.1).

High molecular mass chlorofluoroalkanes are produced by fluorination with chlorine trifluoride \[ \text{CF}_3\text{Cl} \] \[98\], \[99\].

Other important processes for production of high molecular mass CFCs are based on the telomerization of chlorotrifluoroethylene (see Section 4.8) with carbon tetrachloride \[ \text{CCl}_4 \] [100] or CFC 113 [101] as telogens. Stabilization and end-group fluorination are achieved using cobalt trifluoride as fluorinating agent [102], [103].

**Specifications.** Chlorofluoroalkanes (and also the alternative HCFCs and HFCs) produced on an industrial scale are subject to stringent standards. Impurities must not exceed the following limits (vol %):

<table>
<thead>
<tr>
<th>Component</th>
<th>Limit (vol %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acids</td>
<td>0</td>
</tr>
<tr>
<td>Moisture</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Higher-boiling fractions</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Other gases</td>
<td>2</td>
</tr>
</tbody>
</table>

**Uses.** Up to the ban in the USA in 1978 chlorofluoroalkanes had been used mainly as aerosol propellants and as spraying and foam blowing agents (R 11, R 12, R 114). Further important applications up to 1996 had been in the area of refrigerants, where R 11, R 12, R 13, R 22, R 113, R 114, R 115, and the chlorine-free compounds R 23 and RC 318 were preferred. Of the drop-in alternatives to CFCs HCFC 22 is the most important compound, used as refrigerant (annual production in 1995 \(243 \times 10^3\) t [84]), followed by HCFC 141 b \((113 \times 10^3\) t in 1995 [84]) and HCFC 142 b \((38 \times 10^3\) t in 1995 [84]) used as blowing agents for closed cell foams. For HFCs as alternatives see Section 3.1.

Chlorofluoroalkanes, especially R 11 and R 113, were also employed as solvents and degreasing and cleaning agents for textiles; HCFC 22, CFC 113, and HCFC 142 b will be important intermediates for the production of fluoroolefins also in the future.

Higher molecular mass perchlorofluoroalkanes are used as oils, greases, and waxes, as lubricants, hydraulic fluids, damping oils, heat-transfer media, impregnating agents, and plasticizers. Oligomers of chlorotrifluoroethylene have achieved special importance in this area [104].

**Trade Names.** Chlorofluoroalkanes were sold worldwide under protected trade names; the refrigerant numbers describing the chemical composition (see Table 7) are included to specify individual compounds. Some of the trade names that were applied worldwide are:
Trade names of higher molecular mass chlorofluoroalkanes include Florubes (ICI), Fluorolube oils, Fluorolube greases (Hooker Industrial Chemicals Division), Halocarbon oils, greases, and waxes (Halocarbon Products), Kel-F oils, greases, and waxes (3M), and Voltalef (Atochem).

### 3.3. Bromofluoroalkanes

Bromofluoro compounds of practical importance are found mainly in the methane and ethane series.

In the refrigerant (R) numbering system for bromofluoroalkanes, the corresponding chlorofluoroalkanes are taken as the basic structures (see also Section 3); the substitution of chlorine by bromine is expressed by the addition of B1, B2, etc. For example, bromotrifluoromethane is denoted as R 13B1 and 1,2-dibromotrifluoromethane as R 114B2. In fire-fighting applications the Halon numbering system is used, specifying the number of carbon, fluorine, chlorine, and bromine atoms in the molecules when reading from left to right (e.g., Halon 1301 denotes CF3Br; Halon 1211 is CF2ClBr; and Halon 2402 denotes CF2BrCF2Br).

Bromofluorocarbons (BFCs) and hydrobromofluorocarbons (HBFCs) are involved in the depletion of stratospheric ozone and global warming like the CFCs and HCFCs; however the contributions of the bromine-containing compounds are distinctly higher. Therefore, the 1992 Copenhagen meeting agreed to phase out the production of BFCs and HBFCs by 1994, with the exception of Halon for some essential fire-fighting applications. HFC 125 and HCFC 123 (DuPont) or HFC 227 ea (Great Lakes) are announced as alternatives though they are significantly less efficient as fire extinguishing agents than the BFC Halons.

**Properties.** Fully halogenated compounds with a high fluorine content have excellent thermal stability; they are nonflammable and some (e.g., CF3Br) are physiologically inert [92]. At high temperature, thermal cleavage of the C – Br bond into radicals occurs, which is responsible for the utility of some of these compounds in extinguishing fires (→ Fire Extinguishing Agents) [105]. Their chemical stability is slightly lower than that of the corresponding chlorofluoroalkanes. However, as with the chlorofluoroalkanes, stability increases with the fluorine : bromine ratio. Some compounds have a marked anesthetic effect [91]. Physical properties are listed in Table 10.

**Production.** Bromofluoromethanes are obtained by bromination of a stream of the appropriate fluoromethane [106] or chlorofluoromethane [107] at 300 – 600 °C. Ethane derivatives can also be obtained by thermal bromination [108] or by addition of bromine or hydrogen bromide [109] to fluoroolefins. In some cases hydrogen bromide can be used to exchange a chlorine atom in a chlorofluoroalkane for a bromine atom [110]. Iodine – bromine exchange in a fluoroiodoalkane can be effected with bromine [111].

**Uses.** The lower-boiling compounds CBrF3 (R 13B1; Halon 1301) and CBrClF2 (R 12B1; Halon 1211) had been used as fire extinguishing agents. Producers were Atochem, ICI, and Solvay in Europe, DuPont and Great Lakes in the USA and Asahi Glass, Daikin, and Nippon Halon in Japan. The total worldwide Halon production was estimated to be $25 \times 10^3$ t in 1986.
Perfluoro-1-bromo-n-octane [423-55-2] is physiologically inert and is useful as an X-ray contrast agent, especially for lung examinations [112]. With its low surface tension it penetrates small spaces and evenly wets healthy lung tissue.

2-Bromo-2-chloro-1,1,1-trifluoroethane [151-67-7], also known as halothane, has been used worldwide since 1956 as an effective, nonflammable inhalation anesthetic (Anesthetics, General). It is commonly produced by the ICI process:

\[ \text{CF}_2\text{ClCH}_3 + \text{Br}_2 \rightarrow \text{CF}_2\text{ClCHBrCl} \]

or the Hoechst process [43, pp. 208 – 210]:

\[ \text{CF}_2\text{CClIF} + \text{HBr} \xrightarrow{h\nu} \text{CFBr}_2\text{CCIF} \xrightarrow{\text{Cat.}} \text{CF}_2\text{CHBrCl} \]

As alternatives for halothane a series of fluorinated ethers (containing in addition hydrogen and chlorine atoms or exclusively hydrogen atoms) have been developed, that retain or even surmount the desirable properties of halothane as inhalation anesthetic [113]. However, also these compounds have an adverse effect on the ozone layer.

**Trade Names.** Fluothane (ICI), Halothane “HOECHST” (Hoechst).

### 3.4. Iodofluoroalkanes

Iodofluoroalkanes have become important intermediates in the commercial production of compounds containing a perfluorinated moiety.

**Properties.** In contrast to chloro- and bromofluoroalkanes, iodofluoroalkanes readily undergo chemical reactions [24, Chap. 6], reacting preferentially by homolytic cleavage of the C–I bond.

The radical intermediates \( \text{C}_n\text{F}_{2n+1}^+ \) and \( \text{I}^+ \) can add to double bonds; thus, reaction with ethylene yields \( 1\text{H},1\text{H},2\text{H},2\text{H}-1\)-iodoperfluoroalkanes, which are commercially important intermediates [114]:

\[ \text{C}_n\text{F}_{2n+1}^+\text{I} + \text{CH}_2 = \text{CH}_2 \rightarrow \text{C}_n\text{F}_{2n+1}\text{CH}_2\text{CH}_2\text{I} \]

Control of the reaction between iodofluoroalkanes and fluoroolefins, especially tetrafluoroethylene, can result in oligomerization (telomerization) of the olefin [115]:

\[ \text{CF}_3\text{I} + n \text{CF}_2 = \text{CF}_2 \rightarrow \text{CF}_3(\text{CF}_2\text{CF}_2)_n\text{I} \]

This reaction is employed commercially and is initiated by free radicals, UV irradiation, or heat [116].

Iodofluoroalkanes also form organometallic compounds, some of which are useful intermediates, e.g., for Grignard reactions [117].

Iodoperfluoroalkanes cannot be used as alkylating agents and their applications are therefore limited. However, derivatives of the FITS-type reagent are alkylating agents [118]:

\[ \text{C}_n\text{H}_2\text{I}+\text{OSO}_3^-\text{CF}_3 \rightarrow \text{FITS reagent (perfluoroalkyl)phenyliodonium triflate} \]

Physical constants of some iodofluoroalkanes are shown in Table 11.
Production. Iodofluoroalkanes can be produced by heating the silver salts of the perfluorocarboxylic acids with iodine [119] or the corresponding sodium salts with iodine in dimethylformamide [120]. Of commercial importance is the production of pentafluoroiodoethane (CF₃CF₂I) by reaction of tetrafluoroethylene with a mixture of iodine pentafluoride and iodine [121]:

\[
5 \text{CF}_2 = \text{CF}_2 + \text{IF}_5 + 2 \text{I}_2 \rightarrow 5 \text{CF}_2\text{CF}_3I
\]

Heptafluoro-2-iodopropane (CF₃CFICF₃) is obtained similarly from hexafluoropropene.

The higher homologues CₙFₙ+₁I (n = 4 – 12) are produced commercially by reaction of the lower members with tetrafluoroethylene (telomerization).

α,ω-Diiodoperfluoroalkanes are obtained from tetrafluoroethylene and iodine [122]:

\[
\text{I}_2 + \text{CF}_2 = \text{CF}_2 \rightarrow \text{ICF}_3\text{CF}_2\text{I} \rightarrow \text{I}(\text{CF}_2\text{CF}_3)\text{I}
\]

Uses. 1-Iodoperfluoroalkanes and 1H,1H,2H,2H-1-iodoperfluoroalkanes are intermediates in the production of surfactants and textile finishes [123]. Perfluorocarboxylic acids, especially perfluoroacetic acid, are obtained from perfluorooctanoic acids [124], and perfluorinated dicarboxylic acids are obtained from α,ω-diiodoperfluoroalkanes [125].

4. Fluorinated Olefins

The commercial importance of fluoro- and chlorofluoroolefins lies in the production of fluorinated plastics and inert fluids.

Properties. The chemical behavior of fluoroolefins [126] is governed by the number of vinylic fluorine atoms. In contrast to their hydrocarbon analogues, fluoroolefins are attacked by electrophiles only with difficulty [127], which increases with the degree of fluorination. However, fluoroolefins react readily with nucleophiles [128], [129], because as the number of vinylic fluorine atoms increases, the π-electron system of the double bond is destabilized. Thermodynamic calculations have shown that the strength of the C – C π-bond in tetrafluoroethylene

\[
\text{CF}_2 = \text{CF}_2 \rightarrow \text{CF}_2 = \text{CF}_2
\]

is only ca. 160 kJ/mol as opposed to 241 kJ/mol in ethylene [130]. In unsymmetrically substituted fluoroolefins, the nucleophile attacks the carbon atom that is made strongly positive by the neighboring fluorine atoms and is shielded only weakly (sp² hybridization). The reactivity of fluoroolefins toward nucleophiles increases as follows:

\[
\text{CF}_2 = \text{CF}_2 < \text{CF}_2 = \text{CF} = \text{CF}_3 < \text{CF}_2 = \text{C}(\text{CF}_3)_2
\]

Fluoroolefins are slightly to highly toxic and must be handled with care. The toxicity of fluorinated olefins is apparently proportional to their reactivity toward nucleophiles [131]. Perfluoroisobutene, \( \text{CF}_2 = \text{C}(\text{CF}_3)_2 \) [382-21-8], for example, is far more toxic than its lower homologues.

Physical properties of commercial fluoro- and chlorofluoroolefins are given in Table 12.

Fluoroolefins also differ from hydrogen-containing olefins in their marked tendency to undergo cycloaddition [132].
Production. Fluoroolefins are produced by dehalogenation of chlorofluoro-, bromofluoro-, or iodofluoroalkanes with zinc and alcohol, by dehydrohalogenation of hydrogen-containing haloalkanes with alcoholic alkali, or by heating. Other common methods include addition of hydrogen halides to alkynes, decarboxylation of fluorocarboxylic acid salts, and pyrolysis of fluorohydrocarbons [133–135].

4.2. Tetrafluoroethylene

Properties. Tetrafluoroethylene (TFE), perfluoroethylene, 

\[
\text{CF}_2=\text{CF}_2,
\]

a colorless, odorless gas, is flammable in oxygen, producing tetrafluoromethane and carbon dioxide. For physical properties, see Table 12. At low temperature in the presence of oxygen, explosive peroxides are formed [136], [137]. Tetrafluoroethylene must be handled with great care since, even in the absence of oxygen, it can decompose explosively into carbon and tetrafluoromethane under pressure above

\[\frac{276}{20} \text{ kJ/mol at 298 K}.\]

If the polymerization to polytetrafluoroethylene (PTFE) \(\Delta H = -172 \text{ kJ/mol at 298 K}\) is uncontrolled, a more strongly exothermic decomposition reaction can occur. Polymerization inhibitors include dipentene [138-86-3], \(\alpha\)-pinene [80-56-8], which are added to liquid tetrafluoroethylene during purification and storage (at \(-30^\circ\) C) [138]. In the United States, the transportation of liquid TFE containing stabilizers is permitted.

In the gas phase at ca. 300 – 500 °C, tetrafluoroethylene dimerizes to perfluorocyclobutane [139]. Above 600 °C, hexafluoropropylene (see Section 4.3) and the highly toxic perfluoroisobutene are formed [139].

Production. Many commercial processes for the production of tetrafluoroethylene are known, e.g., reaction of tetrafluoromethane in an electric arc [140], dechlorination of \(\text{CF}_2\text{Cl}_2\) with a metal [141], and thermal decomposition of trifluoroacetic acid [142]:

\[2\text{CF}_3\text{COOH} \rightarrow \text{CF}_2=\text{CF}_2 + 2\text{HF} + 2\text{CO}_2\]

The two principal commercial methods are pyrolysis of trifluoromethane [143]:

\[2\text{CHF}_3 \xrightarrow{700–800^\circ\text{C}} \text{CF}_2=\text{CF}_2 + 2\text{HF}\]

and pyrolysis of chlorodifluoromethane [144]:

\[2\text{CHCl}_3 \xrightarrow{600–800^\circ\text{C}} \text{CF}_2=\text{CF}_2 + 2\text{HCl}\]

In the second method (Fig. 2), the chlorodifluoromethane gas is passed at atmospheric or reduced pressure through a heated platinum, silver, or carbon tubular reactor (a). The 28% conversion obtained under these conditions is low (yield, 83%), but can be increased to ca. 65% with the same yield by adding steam [145]. In modification of this method, chlorodifluoromethane is treated with superheated steam at ca. 700 °C, which results in a conversion rate of 60 – 80% and a selectivity of 84 – 93% [146]. The pyrolysis gas is washed with water (b) to cool it and to remove HCl. After being washed with caustic soda (c) and dried with concentrated sulfuric acid (d), the crude product can be stored

\[\text{Table 12. Physical properties of fluoroolefins and chlorofluoroolefins}\]

<table>
<thead>
<tr>
<th>Property</th>
<th>Tetrafluoro-</th>
<th>Hexafluoro-</th>
<th>1,1-Difluoro-</th>
<th>Fluoro-</th>
<th>Chlorotri-</th>
<th>3,3,3-Tri-</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ethylene</td>
<td>propene</td>
<td>ethylene</td>
<td>ethylene</td>
<td>fluoroethylene</td>
<td>fluoro- prop-1-ene</td>
</tr>
<tr>
<td></td>
<td>[116-14-3]</td>
<td>[116-15-4]</td>
<td>[75-38-7]</td>
<td>[75-02-5]</td>
<td>[359-29-5]</td>
<td>[677-21-4]</td>
</tr>
<tr>
<td>(M_r)</td>
<td>100.02</td>
<td>150.02</td>
<td>64.03</td>
<td>46.04</td>
<td>116.47</td>
<td>96.05</td>
</tr>
<tr>
<td>(bp), °C</td>
<td>75.6</td>
<td>29.4</td>
<td>82</td>
<td>72.2</td>
<td>28.36</td>
<td>27</td>
</tr>
<tr>
<td>(mp), °C</td>
<td>142.5</td>
<td>156.2</td>
<td>144</td>
<td>160.5</td>
<td>158.2</td>
<td></td>
</tr>
<tr>
<td>(d_0), g/cm³</td>
<td>1.519 (76.3)</td>
<td>1.292 (29.4)</td>
<td>0.617 (23.6)</td>
<td>0.775 (30)</td>
<td>1.51 (40)</td>
<td></td>
</tr>
<tr>
<td>Critical pressure, MPa</td>
<td>33.3</td>
<td>86.2</td>
<td>30.1</td>
<td>54.7</td>
<td>105.8</td>
<td>107</td>
</tr>
<tr>
<td>Critical density, g/cm³</td>
<td>0.58</td>
<td>2.75</td>
<td>4.29</td>
<td>5.43</td>
<td>3.93</td>
<td>4.14</td>
</tr>
<tr>
<td>Heat of evaporation, J/mol (t, °C)</td>
<td>16 821 (75.6)</td>
<td>20 100 (29)</td>
<td>13 189 (40)</td>
<td>13 494 (20)</td>
<td>20 893 (28.4)</td>
<td></td>
</tr>
</tbody>
</table>
in liquid or gaseous form (e). It is a complex mixture from which tetrafluoroethylene is separated by distillation in the presence of dipentene or a similar stabilizer to prevent polymerization. An overhead fraction containing inert gases and trifluoromethane is obtained in a low-boiling fractionation column (f) before isolating pure TFE (column g).

The higher-boiling fractions are processed (i) to recover unreacted CHCl₂F and to isolate hexafluoropropene, a byproduct. Extractants such as methanol are added because of the formation of azeotropes during distillation [147]. Methanol also reacts with the toxic perfluoroisobutene, (CF₃)₂C=CF₂, to give an addition product.

Uses. Currently, tetrafluoroethylene is the most important fluoroolefin; it is used mainly for the production of fluoropolymers (→ Fluoropolymers, Organic). It reacts with perfluoronitrosopropylene to produce so-called nitroso rubbers [148]. Tetrafluoroethylene is also used in the production of low molecular mass compounds and intermediates, e.g., for the manufacture of iodoperfluoroalkanes (see Section 3.4).

Polytetrafluoroethylene [9002-84-0], (PTFE) is a homopolymer sold under the trade names Algoflon (Montefluos), Fluon (ICI), Halon (Al.lied Chemical), Hostaflon TFE (Hoechst), Teflon TFE (DuPont), Fluon (Asahi Glass), and Polytetrafluoroethylene (Daikin). Copolymers with fluorinated or fluorine-free olefins or vinyl ethers are also commercially available.

4.3. Hexafluoropropene

Properties. Hexafluoropropene (HFP), CF₃CF=CF₂, a colorless, odorless gas, is non-flammable in air at room temperature. For physical properties, see Table 12. It exhibits no special tendency toward radical homopolymerization [149], but like other fluoroolefins, it reacts readily with nucleophiles [128], [129].

Liquid hexafluoropropene has unlimited storage life under pressure at room temperature in steel containers, even without stabilizers. In many countries the liquid can be transported in steel cylinders or tank cars. Hexafluoropropene is toxic (LC₅₀ 3000 ppm) and can decompose thermally to form highly toxic perfluoroisobutene.
**Production.** Hexafluoropropene is produced commercially by temperature-controlled pyrolysis of chlorodifluoromethane (cf. production of tetrafluoroethylene, see Section 4.2) [150]. Hexafluoropropene can also be obtained from tetrafluoroethylene by heating at normal or reduced pressure, preferably in the presence of an inert gas (e.g., CO₂) or water vapor [151]:

\[
3 \text{CF}_2=\text{CF}_2 \xrightarrow{700-900{\degree}C} 2 \text{CF}_2=\text{CF}_2
\]

**Uses.** An important application of hexafluoropropene is the production of copolymers, e.g., with tetrafluoroethylene or 1,1-difluoroethylene (→ Fluoropolymers, Organic, Section 2.3., → Fluoropolymers, Organic, Section 3.2.). The versatile epoxide, hexafluoropropylene oxide [428-59-1] (see Section 6.1.2), can be obtained from hexafluoropropene by oxidation.

### 4.4. 1,1-Difluoroethylene

Vinylidene fluoride (VDF) CH₂=CF₂, is a commercially important, partially fluorinated olefin. It is a colorless, flammable gas that undergoes homopolymerization and copolymerization. For physical properties, see Table 12.

**Production.** Currently, three basic methods are used for the commercial production of vinylidene fluoride:

1. Dechlorination of 1,2-dichloro-1,1-difluoroethane [1649-08-7], R 132 b in the gas phase and on a metal catalyst [142], [152]:

\[
\text{CH}_2\text{CICCl}_2 \xrightarrow{500{\degree}C, \text{Ni}} \text{CH}_2=\text{CF}_2 + \text{Cl}_2
\]

2. Dehydrochlorination of 1-chloro-1,1-difluoroethane [75-68-2], R 142 b [144], [153]:

\[
\text{CH}_2\text{CICH}_2 \xrightarrow{700-900{\degree}C} \text{CH}_2=\text{CF}_2 + \text{HCl}
\]

In the presence of steam the temperature can be reduced to 500 – 650 °C [154].

3. Dehydrofluorination of 1,1,1-trifluoroethane [420-46-2], R 143 a [155]:

\[
\text{CH}_3\text{CF}_3 \xrightarrow{1100-1300{\degree}C} \text{CH}_2=\text{CF}_2 + \text{HF}
\]

Vinylidene fluoride is transported as a liquid in steel cylinders without stabilizers.

**Uses.** 1,1-Difluoroethylene is the starting material for the commercially important homopolymer poly(vinylidene fluoride) [24937-79-9], (PVDF) (→ Fluoropolymers, Organic, Section 2.8.).

The copolymer with hexafluoropropene [116-15-4] is marketed as Viton (DuPont) and Fluorel (3M).

### 4.5. Monofluoroethylene, Monofluoroethylene

Vinyl fluoride (VF), CH₂=CHF, is a colorless, highly flammable gas; up to 0.2 % of polymerization inhibitors are added for stabilization during transport and storage. For physical properties, see Table 12.

**Production.** In the past, vinyl fluoride was produced by dehydrofluorination of 1,1-difluoroethane [75-37-6], obtained in two steps by addition of hydrogen fluoride to acetylene [24, p. 59 – 66], [156]:

\[
\text{CH}≡\text{CH} + 2 \text{HF} \xrightarrow{\text{Cat.}} \text{CH}_2\text{CHF}_2 \xrightarrow{\text{Cat.}} \text{CH}_2=\text{CHF} + \text{HF}
\]

However, with mercury catalysts, vinyl fluoride can be produced directly from acetylene and hydrogen fluoride [24, p. 59 – 66], [157]:

\[
\text{CH}≡\text{CH} + \text{HF} \xrightarrow{\text{Hg Cat.}} \text{CH}_2=\text{CHF}
\]

The dehydrochlorination of 1-chloro-1-fluoroethane [1615-75-4], CHClFCH₃, and 1-chloro-2-fluoroethane [762-50-5], CH₂FCH₂Cl, are also utilized commercially [158].

**Uses.** The main use of monofluoroethylene is in the production of poly(vinyl fluoride) [24981-14-4] (PVF) (→ Fluoropolymers, Organic,
Section 2.8., → Fluoropolymers, Organic, Section 2.9.).

**Trade Names (PVF).** Tedlar (DuPont), Dalbon (Diamond Shamrock, USA). Worldwide annual production (1988): $1.6 \times 10^3$ t

### 4.6. 3,3,3-Trifluoropropene

3,3,3-Trifluoropropene, CF$_3$CH=CH$_2$ (TFP), is produced almost exclusively by fluorination and dehalogenation of 1,1,1,3-tetrachloropropane [1070-78-6] (TCP), CCl$_3$CH$_2$CH$_2$Cl. With sodium fluoride at 400 – 475 °C, trifluoropropene is obtained in a single step, involving chlorine – fluorine exchange and dehydrochlorination [159]. Using hydrogen fluoride and oxygen, the reaction can be carried out at 300 °C over a chromium fluoride catalyst [160]. Liquid-phase fluorination of 1,1,1,3-tetrachloropropane with hydrogen fluoride in the presence of an antimony catalyst yields 1,1,1-trifluoro-3-chloropropane, CF$_3$CH$_2$CH$_2$Cl, which gives 3,3,3-trifluoropropene when treated with a base [161]. The conversion is effected in a single operation with a mixture of hydrogen fluoride and a tertiary amine [162].

\[
\text{CCl}_3\text{CH}_2\text{Cl} \rightarrow \text{CF}_3\text{CH}_2\text{CH}_2\text{Cl} \rightarrow \text{CF}_3\text{CH}=	ext{CH}_2
\]

A multistep synthesis starts from vinylidene fluoride (CF$_2$==CH$_2$) [163].

**Uses.** The main use of trifluoropropene is in the production of fluorine-containing silicones used in hydraulic fluids [159], [164].

### 4.7. 3,3,3-Trifluoro-2-(trifluoromethyl)-prop-1-ene

3,3,3-Trifluoro-1-(trifluoromethyl)prop-1-ene [382-10-5], hexafluoroisobutene, (HFIB), (CF$_3$)$_2$C==CH$_2$, is a colorless, toxic gas (4-h LC$_{50}$ 1700 ppm) with a bp of 14.1 °C at 101.3 kPa. A number of processes for its production have been described; the most important use hexafluoroacetone [165] or perfluoroisobutene [166] as the starting material.

\[
\text{(CF}_3\text{)}_2\text{O} + \text{CH}_2\text{==C}=\text{O} \rightarrow \text{(CF}_3\text{)}_2\text{C}==\text{O}
\]

\[
\text{H}_2\text{C}==\text{C}=\text{O}
\]

\[
\text{(CF}_3\text{)}_2\text{C}==\text{CH}_2 + \text{CO}_2
\]

\[
\text{(CF}_3\text{)}_2\text{C}==\text{CH}_2 + \text{CH}_2\text{OH} \rightarrow \text{(CF}_3\text{)}_2\text{CHCF}_2\text{OCH}_3
\]

Several steps \[
\text{(CF}_3\text{)}_2\text{C}==\text{CH}_2
\]

Acetic anhydride can be used with hexafluoroacetone instead of ketene. The multistep reaction takes place in a single operation in a copper reactor above 300 °C [167]. Presumably, processes based on the highly toxic perfluoroisobutene are designed to remove it as a harmful byproduct of tetrafluoroethylene or hexafluoropropene production.

Hexafluoroisobutene is used for the production of fluoropolymers. The trade name of the copolymer [34149-71-8] with vinylidene fluoride is CM-X (Ausimont) [168].

### 4.8. Chlorofluoroolefins

Among the numerous known chlorofluoroolefins [134], [134], 1,1-dichloro-2,2-difluoroethylene [79-35-6] has some importance as a starting material in the production of methoxyfluorane [76-38-0], an inhalation anesthetic. However, chlorotrifluoroethylene is the most important member of this class.

**Chlorotrifluoroethylene** [359-29-5] (CTFE), CF$_2$==CFCl, a colorless, flammable gas, is less reactive than tetrafluoroethylene. For physical properties, see Table 12. Although chlorotrifluoroethylene is more stable than tetrafluoroethylene, stabilizers such as tributylamine are used during transportation and storage in steel cylinders [169]. Chlorotrifluoroethylene is toxic.

**Production.** Chlorotrifluoroethylene is produced commercially by dechlorination of 1,1,2-trichloro-1,2,2-trifluorothane [76-13-1], (R 113) with zinc in methanol [170]:

\[
\text{CCIF}_2\text{CClF} + \text{Zn} + \text{CH}_2\text{OH} \rightarrow \text{CF}_2\text{==CCIF} + \text{ZnCl}_2
\]

An alternative route is dechlorination in the gas phase, e.g., on an aluminum fluoride – nickel phosphate catalyst; this catalyst is highly stable [171].
Uses. Chlorotrifluoroethylene is a starting material for homopolymers and copolymers (PCTFE) (→ Fluoropolymers, Organic, Section 2.6., → Fluoropolymers, Organic, Section 2.7.). In addition, chlorotrifluoroethylene is an intermediate in the production of the inhalation anesthetic halothane. (2-Chloro-1,1,2-trifluoroethyl)-diethylamine [357-83-5], ClFHCCF₂N(C₂H₅)₂ (an addition product of chlorotrifluoroethylene with diethylamine), is used as a fluorinating agent to replace hydroxyl groups in steroids and carbohydrates with fluorine [54], [172]. Another use of chlorotrifluoroethylene is in telomerization with carbon tetrachloride or chloroform. The products are stabilized with fluorine or CoF₃ and are used as inert fluids, hydraulic fluids, or lubricants [104], [173].


5. Fluorinated Alcohols [174]

Primary and secondary alcohols that have fluorine and hydroxyl groups on the same carbon atom are unstable, and readily lose hydrogen fluoride to form carbonyl compounds. Primary and secondary perfluoroalkoxides, however, can be prepared in polar solvents under aprotic conditions from carbonyl compounds and a source of ionic fluoride [175]; typical counterions are alkali-metal, tetraalkylammonium, or tris(dialkylamino)sulphonium cations. The perfluoroalkoxides are moderately nucleophilic and are used in situ to prepare compounds containing perfluoroalkoxy groups (see Section 6.3). Tris(dialkylamino)sulphonium perfluoroalkoxides are unusually stable and, in some cases, have been isolated as crystalline solids [176]. Tertiary perfluoro alcohols, e.g., perfluoro-tert-butanol (1,1,1,3,3,3-hexafluoro-2-trifluoromethyl-2-propanol) [2378-02-1] [177] and alcohols containing CH₂ groups between the fluorinated segment and the OH group are also stable. Fluorinated alcohols are more acidic than their nonfluorinated analogues because fluorine is highly electronegative (see Table 13) [178].

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>R = H</th>
<th>R = F</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR₃CH₂OH</td>
<td>15.9</td>
<td>12.8</td>
</tr>
<tr>
<td>(CR₃)$_2$CHOH</td>
<td>17.1</td>
<td>9.3</td>
</tr>
<tr>
<td>(CR₃)$_3$COH</td>
<td>19.2</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Table 13. pKₐ values of alcohols [178]

Long-Chain Fluoroalcohols. The unique hydro- and oleophobic properties of long perfluoroalkyl chains lead to many applications of long-chain fluoroalcohols and their derivatives as surfactants, antisolvents, and surface-treatment agents [187]. Structures can be represented by,

\[ X-(CF₃)₃(CH₂)ₙOH \]

where X is typically F, H, or CH₃, n is 6 – 12, and m is 1 or 2. The most important compounds are the 1H,1H-perfluoroalcohols (X = F, m = 1), prepared by reduction of the corresponding perfluorinated carboxylic acids [188], and the 1H,1H,2H,2H-perfluoroalcohols (X = F, m = 2); the latter are prepared by treatment of the corresponding 1-iodo-1H,1H,2H,2H-perfluorokanes with oleum [189]. Alcohols of the formula H(CF₂)nCH₂OH, where n is an even
number, are prepared by telomerization of tetrafluoroethylene with methanol [190].

For use as soil-repellent finishes, the long-chain fluoroalcohols are converted into derivatives to adjust the hydrophobicity, solubility in aqueous and organic solutions, surface retention, and stability for each specific application. These derivatives include esters, phosphates, carboxylates, and polyoxyethylenes. Polymeric alcohols are prepared by esterification with (meth)acryloyl chloride, followed by polymerization.

**Trade Names.** Teflon, Zepel, and Zonyl (DuPont), Scotchgard (3M), and Oleophobal (Chemische Fabrik Pfersee, Ciba-Geigy).

### 6. Fluorinated Ethers [191]

#### 6.1. Perfluoroethers

Perfluorinated ethers are less basic than their hydrogen-containing analogues [192]. The saturated aliphatic and cycloaliphatic perfluoroethers are noncombustible, and, with the exception of the perfluorinated epoxides, display high chemical and thermal stability. Other properties of the stable ethers, such as a large difference between the melting and boiling points at ambient pressure, and a low pour point, surface tension, and dielectric constant, are the basis of applications such as dielectric and heat-exchange fluids in, for example, high power transformers. Higher molecular mass perfluoroethers are used as lubricants and hydraulic fluids in extreme service conditions, i.e., at high temperature and/or in a corrosive environment.

##### 6.1.1. Low Molecular Mass Perfluoroethers

The low molecular mass perfluoroethers are usually prepared by electrochemical fluorination of aliphatic ethers, alcohols, or carboxylic acids [193]. Typical empirical formulas are $\text{C}_n\text{F}_{2n+2}\text{O}$, $\text{C}_n\text{F}_{2n+4}\text{O}$, and $\text{C}_n\text{F}_{2n+6}\text{O}$; these ethers often consist of isomer mixtures. Compound PC-75 [11072-16-5] (3M), mostly perfluorobutyltetrahydrofurans, is a useful solvent that has been explored as an oxygen-transport agent in artificial blood [194]. Perfluorinated ethers can also be prepared from partially fluorinated or nonfluorinated ethers by fluorination with cobalt fluoride or elemental fluorine under carefully controlled conditions [195].

**Trade Names.** Fluorinert liquids (3M) and Galden fluorinated fluids (Montedison).

#### 6.1.2. Perfluorinated Epoxides

In contrast to other perfluorinated cyclic ethers, ring strain in perfluorinated epoxides results in high reactivity, making them versatile precursors to other fluorinated compounds [196]. The most important is hexafluoropropylene oxide [428-59-1] (HFPO), trifluoro(trifluoromethyl)oxirane [197]. It is prepared from hexafluoropropene by reaction with elemental oxygen [198], by electrochemical oxidation [199], or by reaction with hypochlorites [200] or hydrogen peroxide [201] in alkaline media.

Hexafluoropropylene oxide ($bp = 27.4 \degreeC$) is stable at room temperature, but decomposes above 150 $\degreeC$ to form trifluoroacetyl fluoride and difluorocarbene [202]. In the presence of strong Brønsted or Lewis acids, such as alumina or aluminum chloride, HFPO undergoes catalytic rearrangement to hexafluoroacetone, constituting a convenient synthesis of this compound [203]. Most significantly, HFPO reacts readily with nucleophiles. Attack usually occurs at the central carbon atom [204], resulting in formation of an acid fluoride by loss of a fluoride ion from the intermediate perfluoroalkoxide, which can react further with HFPO to form higher oligomers. Acid fluorides are precursors to the commercially important perfluorovinyl ethers and higher molecular mass perfluoroethers.

\[
\begin{align*}
\text{CF}_2\text{CF} = \text{CF}_2 + X \rightarrow \text{XCFCF}_2\text{OF}^- \rightarrow \text{XCFCOF} \\
\rightarrow \text{HFPO} \\
\text{X} = (\text{CFCF}_2\text{OF}) = (\text{CFCOF}) \\
\end{align*}
\]

where $X =$ nucleophile, e.g., fluoride ion.

Both tetrafluoroethylene oxide [694-17-7] (TFEO), also called tetrafluorooxirane [205], and epoxides of longer chain-length perfluoroolefins [206] are known; however, the former is unstable at room temperature and rearranges to form
trifluoroacetyl fluoride, whereas the latter are prepared from inaccessible perfluoroolefins. Only HFPO has achieved commercial significance because it is used for the synthesis of hexafluoroacetone (see Hexafluoroacetone), high molecular mass perfluoroethers, Section 6.1.3, and fluorinated vinyl ethers (Section 6.2).

6.1.3. High Molecular Mass Perfluoroethers

High molecular mass perfluorinated ethers are prepared by fluoride-catalyzed oligomerization of HFPO [207]. The resulting terminal acid fluoride group is removed by hydrolysis and decarboxylative fluorination with elemental fluorine. Chemically inert ethers are produced which have the formula,

\[
\text{CF}_3\text{CF}_2\text{O}[(\text{CFCF}_2)_n\text{CF}_2\text{CF}_3]_n
\]

These ethers are obtained in various molecular mass and viscosity ranges by controlling oligomerization conditions or by partial distillation of the oligomeric mixture. In an alternative method [208], perfluorinated olefins (e.g., tetrafluoroethylene or hexafluoropropene) react photochemically with oxygen to form oligomeric perfluoroethers with terminal acid fluoride groups and peroxide bonds [209]. These end groups and the unstable peroxide linkages are eliminated by fluorination. Perfluoroethers with molecular masses of ca. 500 – 6000 are used as inert fluids, lubricants, and hydraulic fluids in applications that require resistance to high temperature or strongly corrosive environments.

Trade Names. Krytox (DuPont), Aflunox (SCM Specialty Chemicals), and Fomblin (Montedison).

6.2. Perfluorovinyl Ethers

Perfluorovinyl ethers are comonomers used in the preparation of melt-processable fluoropolymers, fluorinated elastomers, and perfluropolymers containing functional groups [210] (→ Fluoropolymers, Organic, Section 3.3.). The ethers are synthesized by reaction of a fluorinated alkoxide generated in situ, or of other nucleophiles with HFPO. The resulting acid fluorides are converted to acid salts, which lose carbon dioxide and metal fluoride when heated in an aprotic environment. For example, HFPO is treated with cesium trifluoromethoxide (from cesium fluoride and carbonyl fluoride). Hydrolysis and decarboxylation of the resulting acid fluoride gives perfluoro(methyl vinyl ether) [1187-93-5].

\[
\begin{align*}
\text{CF}_3\text{O} + \text{CsF} & \rightarrow \text{CF}_3\text{OCs} \\
\text{CF}_3\text{OCFCOF} & \xrightarrow{\text{heat}} \text{CF}_3\text{OFCF} = \text{CF}_3
\end{align*}
\]

This compound is a comonomer with tetrafluoroethylene in a perfluorinated elastomer [211].

Perfluoro(propyl vinyl ether) [1623-05-8], \(\text{CF}_3\text{CF}_2\text{OCF} = \text{CF}_3\), prepared from the dimer of HFPO [212], is copolymerized with tetrafluoroethylene to a melt-processable perfluoroplastic. Perfluorovinyl ethers containing specific functional groups and usually two or more moles of hexafluoropropylene oxide are prepared in a similar fashion. These compounds have the structure \(\text{RO(C}_3\text{F}_6\text{O}) = \text{CF}_3\); they are used as functional groups in perfluoroelastomers which can undergo a crosslinking reaction, i.e., cure-site monomers (\(\text{R} = \text{CF}_2\text{CF}_2\text{CN}\) or pentafluorophenyl) [213] and as monomers that provide the ionic groups in perfluorinated ion-exchange resins (\(\text{R} = \text{CF}_2\text{CF}_2\text{SO}_2\text{F}, \text{CF}_2\text{CF}_2\text{CF}_2\text{CO}_2\text{CH}_3, \text{or CF}_2\text{CF}_2\text{CO}_2\text{CH}_3\)) [214]. Synthesis of the sulfonyl fluoride-substituted vinyl ether is illustrative. Reaction of tetrafluoroethylene with sulfur trioxide gives a sultone, which rearranges to fluorosulfonyldifluoroacetyl fluoride. The anion formed after addition of fluoride ion to this acid fluoride gives a 2 : 1 adduct with HFPO [215]. Pyrolysis of the sodium salt over sodium carbonate gives the functional monomer [216].
Perfluorovinyl ethers can also be prepared by deiodofluorination of iodine-containing ethers, \( XR CF_2OCF_2CF_2I \), where \( X \) is hydrogen, halogen, \( CO_2R \), \( CONR_2 \), \( SO_2F \), or \( PO(OR)_2 \) (\( R = \) alkyl) and \( R_f \) is a perfluoroalkyl group. Initially, an organometallic derivative of the iodide is formed by reaction with metals, such as \( Mg, Cu, Zn, Sn \), or \( Sb \). Heating in the absence of a proton source affords the vinyl ethers [217].

### 6.3. Partially Fluorinated Ethers

Partially fluorinated ethers are synthesized by several methods. Fluoroalkyl alkyl or fluoroalkyl aryl ethers are prepared from alkoxides or phenoxides and fluoroolefins [218]; for example, 1,1,2,2-tetrafluoro-1-methoxyethane \([425-88-7]\) is prepared from tetrafluoroethylene and sodium methoxide – methanol. Higher perfluoroolefins can also be employed [219]. The methyl ethers are valuable intermediates, which can be converted to acid fluorides with sulfur trioxide [220] or other Lewis acids [221]. Primary and secondary perfluorinated alkoxides (see Chap. 5) are not sufficiently nucleophilic to react with fluorinated or nonfluorinated olefins. However, they react with a variety of olefins in the presence of halogen to give ethers [222], e.g.,

\[
\begin{align*}
(CF_3)_2CFO^- + CH_2=CF_2 + I^- & \longrightarrow (CF_3)_2CFOCF_2CH_2I + Cl^- \\
2CF_3CH_2OH + HC=CH & \longrightarrow CH_3CH(OCH_2CF_3)_2 \\
& \longrightarrow CH_2=CHOCH_2CF_3
\end{align*}
\]

The flammability behavior of the compound is not significantly better than that of nonfluorinated anesthetics, and it behaves as a mutagen in the Ames test [226]; therefore, the compound is not currently produced commercially.

2-Chloro-1-(difluoromethoxy)-1,1,2-trifluoroethane \([13838-16-9]\) [trade name: Ethrane (Anaquest)], which is nonflammable, is prepared by successive chlorination and fluorination of the hydrocarbon ether [227]. 1-Chloro-1-(difluoromethoxy)-2,2,2-trifluoroethane \([26675-46-7]\) [trade name: Forane (Anaquest)] is prepared in a similar fashion [228]. Other possible anesthetics include 2,2-dichloro-1,1-difluoro-1-methoxyethane \([76-38-0]\) [229] and 1,1,1,3,3,3-hexafluoro-2-(fluoromethoxy)propane \([28523-86-6]\) [230].

### 7. Fluorinated Ketones and Aldehydes

The carbonyl groups in partially or perfluorinated ketones and aldehydes are electron deficient owing to the inductive effect of the highly electronegative fluorine atom. Compared with their hydrocarbon counterparts, fluorinated ketones and aldehydes are, consequently, much more reactive toward nucleophilic reagents. Stable addition compounds with water, alcohols, and amines are commonly formed. By contrast, fluorinated ketones and aldehydes are relatively unreactive toward electrophilic reagents. An extreme case is hexafluoroacetone, which is not protonated by the \( FSO_3H - SbF_5 \) superacid [231].

A wide variety of fluoroalkyl ketones and aldehydes has been synthesized, often by special methods that are unique to polyfluorinated compounds [232]. Of the many known examples, a few fluorinated acetones, aldehydes, and 1,3-diketones are of practical importance.

#### 7.1. Fluoro- and Chlorofluorooacetones

Several fluoro- and chlorofluorooacetones (propa- none) are listed in Table 14. Hexafluoroacetone...
and, to a lesser extent, chloropentafluoroacetone and \textit{sym}-dichlorotetrafluoroacetone are commercially important. Hexafluoroacetone is manufactured by DuPont in the United States and by Hoechst in the Federal Republic of Germany. The two chlorofluoroacetones were made in pilot-plant quantities by Allied in the 1960s [233], but their production has been discontinued.

**Hexafluoroacetone**, 1,1,1,3,3,3-hexafluoro-2-propanone, is made industrially by the vapor-phase reaction of hexachloroacetone with hydrogen fluoride in the presence of a chromium catalyst [234], [235]. The rearrangement of hexafluoropropylene oxide induced by Lewis acids [203] is an attractive new route that avoids the highly toxic \textit{sym}-dichlorotetrafluoro- and chloropentafluoroacetones. A convenient laboratory synthesis uses hexafluoropropylene as a starting material [236]:

\[
2 \text{CF}_3\text{CF} = \text{CF}_2 + \frac{1}{2} \text{Sb} \xrightarrow{\text{KF}} \text{dimethylformamide} \xrightarrow{\text{KCl}} 2 \text{CF}_3\text{COCF}_3
\]

Hexafluoroacetone is used mainly for the manufacture of the solvent hexafluoro-2-propanol and high-performance fluoropolymers. For the properties, chemistry, and uses of hexafluoroacetone, see → Acetone.

**Chloropentafluoroacetone**, 1-chloro-1,1,3,3,3-pentafluoro-2-propanone [trade name: 5FK (Allied)] and \textit{sym}-dichlorotetrafluoroacetone, 1,3-dichloro-1,1,3,3-tetrafluoro-2-propanone (4FK, Allied) can be made by the incomplete exchange of chlorine in hexachloroacetone, using hydrogen fluoride and a \textit{Cr}^{3+} or \textit{Cr}^{5+} catalyst [234], [235], [237]. Their properties and chemical reactivities are similar to those of hexafluoroacetone [238]. Like hexafluoroacetone, chloropentafluoroacetone and \textit{sym}-dichlorotetrafluoroacetone form stable, acidic hydrates and hemiacetals, e.g., \textit{CClF}_2\text{COCF}_3/C\text{H}_2\text{O}\xrightarrow{\text{34202-28-3}, \text{bp} \ 105 \ ^\circ\text{C}} \text{CClF}_2\text{COCClF}_2/C\text{H}_2\text{O}\xrightarrow{\text{34202-29-4}, \text{bp} \ 106 \ ^\circ\text{C}}. \text{The hydrates are powerful solvents for acetal resins and various polar polymers [239], [240]. These chlorofluoroacetones and some of their derivatives possess herbicidal or fungicidal activity [241–243] and are useful intermediates for synthesizing repellants for textile fibers [244], [245], specialty polycarbonates [246], [247], and inhalation anesthetics [248].}

**Table 14. Molecular masses and boiling points of fluoro- and chlorofluoropropanones**

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS registry no.</th>
<th>Formula</th>
<th>( M_r )</th>
<th>( \text{bp, } ^\circ\text{C} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1,1-Trifluoro-2-propanone</td>
<td>[421-50-1]</td>
<td>( \text{CF}_3\text{COCH}_3 )</td>
<td>112.05</td>
<td>21.5 – 22.5</td>
</tr>
<tr>
<td>1,1,3,3-Tetrafluoro-2-propanone</td>
<td>[360-52-1]</td>
<td>( \text{CHF}_2\text{COCHF}_2 )</td>
<td>130.05</td>
<td>58</td>
</tr>
<tr>
<td>1,1,1,3,3,3-Hexafluoro-2-propanone</td>
<td>[684-16-2]</td>
<td>( \text{CF}_3\text{COCF}_3 )</td>
<td>166.03</td>
<td>– 27.4</td>
</tr>
<tr>
<td>1-Chloro-1,1,3,3,3-pentafluoro-2-propanone</td>
<td>[79-55-8]</td>
<td>( \text{CCIF}_2\text{COCF}_3 )</td>
<td>182.48</td>
<td>7.8</td>
</tr>
<tr>
<td>1,3-Dichloro-1,1,3,3-tetrafluoro-2-propanone</td>
<td>[127-21-9]</td>
<td>( \text{CCIF}_2\text{COCCIF}_2 )</td>
<td>198.93</td>
<td>45.2</td>
</tr>
<tr>
<td>1,1,3-Trichloro-1,3,3-trifluoro-2-propanone</td>
<td>[79-52-7]</td>
<td>( \text{CCIF}_3\text{COCCIF}_2 )</td>
<td>215.38</td>
<td>84.5</td>
</tr>
<tr>
<td>1,1,3,3-Tetrachloro-1,3-difluoro-2-propanone</td>
<td>[79-51-6]</td>
<td>( \text{CCl}_3\text{COCCl}_2\text{F} )</td>
<td>231.83</td>
<td>123.9</td>
</tr>
<tr>
<td>1,1,1,3-Pentachloro-3-fluoro-2-propanone</td>
<td>[2378-08-7]</td>
<td>( \text{CCl}_4\text{COCl}_2\text{F} )</td>
<td>248.28</td>
<td>163.7</td>
</tr>
<tr>
<td>1,1,1,3,3,3-Hexachloro-2-propanone</td>
<td>[116-16-5]</td>
<td>( \text{CCl}_6\text{COCl}_3 )</td>
<td>264.73</td>
<td>203.6</td>
</tr>
</tbody>
</table>

1,1,1-Trifluoro-2-propanone can be prepared in quantitative yield by the acid hydrolysis of ethyl trifluoroacetate, the ethyl ester of 4,4,4-trifluoro-3-oxobutanoic acid [372-31-6], which is made by the alkali-promoted condensation of ethyl trifluoroacetate with ethyl acetate [249]. 1,1,1-Trifluoro-2-propanone is easily made in the laboratory by the reaction of trifluoroacetic acid with methylmagnesium iodide [250]. Its aryl hydrazone derivatives show nematocidal and acaricidal activity [251].

1,1,3,3-Tetrafluoro-2-propanone is made by the acid hydrolysis of the ethyl ester of 2,2,4,4-tetrafluoro-3-oxobutanoic acid, \( \text{CHF}_2\text{COCF}_2\text{CO}_2\text{C}_2\text{H}_5 \) [249]. The ketone is used as an intermediate in the synthesis of inhalation anesthetics [252], [253].
7.2. Perhaloacetaldehydes

Perchlorofluoroacetaldehydes. Some physical properties of the perchlorofluoroacetaldehydes are shown in Table 15. Their chemical reactivities are similar to those of the perchlorofluoroacetones.

Chlorodifluoroacetaldehyde and dichlorofluoroacetaldehyde can be prepared by the lithium aluminum hydride reduction of the corresponding methyl chlorofluoroacetates [254], [255].

Trifluoroacetaldehyde (fluoral) and some of its derivatives have found practical importance as monomers and intermediates for biologically active compounds.

Properties. Trifluoroacetaldehyde is a colorless gas at ambient temperature and pressure. Like hexafluoroacetone, it reacts with water to form a stable, solid hydrate – 1,1-dihydroxy-2,2,2-trifluoroethane [421-53-4], CF₃CH(OH)₂, mp 69 – 70 °C. It reacts in a manner similar to hexafluoroacetone with alcohols to give stable hemiacetals: 2,2,2-trifluoro-1-methoxyethanol [431-46-9], CF₃CH(OH)OCH₃, bp 96 – 96.5 °C (101.3 kPa); and 2,2,2-trifluoro-1-ethoxyethanol [433-27-2], CF₃CH(OH)OC₂H₅, bp 104 – 105 °C (99.3 kPa). Unlike hexafluoroacetone, it readily homopolymerizes upon cationic, anionic, or free-radical initiation [254], [255].

Production. Several laboratory syntheses of trifluoroacetaldehyde have been developed, including reduction of trifluoroacetic acid and its alkyl esters, trifluoroacetic anhydride, and trifluoroacetyl chloride [256]. Trifluoroacetaldehyde can be manufactured on a large scale by the reaction of trichloroacetaldehyde (chloral) with hydrogen fluoride in the presence of chromium catalysts [235]. The product is a CF₃CHO · HF complex, bp 38 °C (133.3 kPa), which requires treatment with a hydrogen fluoride acceptor (e.g., sodium fluoride) to give free trifluoroacetaldehyde. Hydrolysis of the inhalation anesthetic Halothane, CF₃CHBrCl, by a mixture of 65 % oleum, mercuric oxide, and silver oxide also produces trifluoroacetaldehyde in high yield [257].

Trifluoroacetaldehyde is commercially available as its hydrate or methyl and ethyl hemiacetals, which liberate the pure aldehyde in polyphosphoric acid at 150 – 180 °C. A Hoechst process for the manufacture of its hemiacetals involves treating the product from the gas-phase fluorination of chloral with tetraalkoxyl silanes, or with alcohols and silicon tetrachloride. This process avoids the need to isolate or handle free trifluoroacetaldehyde [258], [259].

<table>
<thead>
<tr>
<th>Name</th>
<th>Formula</th>
<th>CAS registry no.</th>
<th>bp, °C (101.3 kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trichloroacetaldehyde</td>
<td>CCl₃CHO</td>
<td>[75-87-6]</td>
<td>97.8</td>
</tr>
<tr>
<td>Dichlorofluoroacetaldehyde</td>
<td>CCl₂FCHO</td>
<td>[63034-44-6]</td>
<td>56</td>
</tr>
<tr>
<td>Chlorodifluoroacetaldehyde</td>
<td>CClF₂CHO</td>
<td>[811-96-1]</td>
<td>17.8</td>
</tr>
<tr>
<td>Trifluoroacetaldehyde</td>
<td>CF₃CHO</td>
<td>[75-90-1]</td>
<td>– 18 to – 19°</td>
</tr>
</tbody>
</table>

*At 99.7 kPa

Uses of Perhaloacetaldehydes. Certain oximes [260] and hydrazones [251] of trifluoroacetaldehyde have insecticidal or acaricidal activity. Its hemiacetal, 2,2,2-trifluoro-1-methoxyethanol, has been used as a starting material for the preparation of fluorocether inhalation anesthetics [261] (see Section 6.3), including isoflurane, CF₃CHClOCHF₂ [262], and its isomer CF₃CHFOCHCIF [263], [264].

The stereoregularity of perchlorofluoroacetaldehyde polymerizations has been an area of active research, although no commercial uses of the polymers have yet appeared.

Trifluoroacetaldehyde can be homopolymerized to give insoluble crystalline, or soluble, amorphous, polyoxyethylene polymers depending upon the polymerization conditions [254], [255]. This is in contrast with trichloroacetaldehyde which can only be polymerized to a crystalline, apparently isotactic polymer. Copolymers of perhaloacetaldehydes have been prepared [254], [255].
7.3. Fluorinated 1,3-Diketones

Fluorinated 1,3-diketones in which the two carbonyl groups are separated by a methylene or methine group form complexes with a wide variety of metal ions. This property is the basis of their utility in chromatographic analysis of metals, laser technology, NMR spectroscopy, and hydrometallurgical separations. The properties, preparation, and uses of fluorinated 1,3-diketones and their metal complexes have been extensively reviewed [265–267].

Properties and Production. Some physical properties of the industrially important fluorinated 1,3-diketones are shown in Table 16. These compounds are considerably more acidic than their nonfluorinated analogues, i.e., 1,3-pentanedione \([\text{CH}_3\text{COCH}_2\text{COCH}_3]\) \((pK_a = 8.9)\), \(\text{CF}_3\text{COCH}_2\text{COCH}_3\) \((pK_a = 6.7)\), and \(\text{CF}_3\text{COCH}_2\text{COCF}_3\) \((pK_a = 4.6)\) [267]. Fluorinated 1,3-diketones have a high enolic content, typically 92 – 100%, in comparison with ca. 80% for 1,3-pentanedione. Their enolic protons can be readily replaced by metals or metal salts to form 1,3-diketonates of the type

Fluorinated 1,3-diketones form hydrates with water and hemiketals with shorter alcohols. They are usually obtained by a Claisen condensation of

### Table 16. Molecular masses and boiling points of fluorinated 1,3-diketones

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS registry no.</th>
<th>Formula</th>
<th>(M_r)</th>
<th>(bp, ^\circ\text{C} (\text{kPa}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,1,1-Trifluoro-2,4-pentanedione</td>
<td>[367-57-7]</td>
<td>(\text{CF}_3\text{COCH}_2\text{COCH}_3)</td>
<td>154.09</td>
<td>105 – 107 (101.3)</td>
</tr>
<tr>
<td>1,1,1,5,5,5-Hexafluoro-2,4-pentanedione</td>
<td>[1352-22-1]</td>
<td>(\text{CF}_3\text{COCH}_2\text{COCF}_3)</td>
<td>208.06</td>
<td>70 – 71 (101.3)</td>
</tr>
<tr>
<td>1,1,1-Trifluoro-5,5-dimethyl-2,4-hexanedione</td>
<td>[22767-90-4]</td>
<td>(\text{CF}_3\text{COCH}_2\text{COC(CH}_3)_2)</td>
<td>196.17</td>
<td>138 – 141 (101.3)</td>
</tr>
<tr>
<td>1,1,1,2,2,3,3-Heptafluoro-7,7-dimethyl-4,6-octanedione</td>
<td>[17587-22-3]</td>
<td>(\text{CF}_3\text{CF}_2\text{CF}_2\text{COCH}_2\text{COC(CH}_3)_3)</td>
<td>296.19</td>
<td>46 – 47 (0.67)</td>
</tr>
<tr>
<td>4,4,4-Trifluoro-1-phenyl-1,3-butanedione</td>
<td>[326-06-7]</td>
<td></td>
<td>216.16</td>
<td>224 (101.3)(^a)</td>
</tr>
<tr>
<td>4,4,4-Trifluoro-1-(2-thienyl)-1,3-butanedione</td>
<td>[326-91-0]</td>
<td></td>
<td>222.18</td>
<td>96 – 98 (1.07)(^b)</td>
</tr>
<tr>
<td>3-(Trifluoroacetyl)camphor, 1,7,7-trimethyl-3-(trifluoroacetyl)-bicyclo[2.2.1]heptan-2-one</td>
<td>[51800-98-7]</td>
<td></td>
<td>248.25</td>
<td>100 – 101 (2.13)</td>
</tr>
<tr>
<td>3-(Heptafluorobutaryl)camphor, 3-(2,2,3,3,4,4,4-heptafluoro-1-oxo-butyl)-bicyclo[2.2.1]heptan-2-one</td>
<td>[51800-99-8]</td>
<td></td>
<td>348.26</td>
<td>60 – 70 (0.03)</td>
</tr>
</tbody>
</table>

\(^a\)mp 38 – 40 \(^\circ\text{C}\).  
\(^b\)mp 42 – 43 \(^\circ\text{C}\).
a fluorinated carboxylic acid ester with a ketone, using a strong base such as a sodium alkoxide or sodium hydride.

**Uses.** The 1,3-diketones RCOCH₂COR' (R = CF₃, n-C₃F₇ and R' = t-C₄H₉, C₆F₃) that form volatile, thermally and hydrolytically stable complexes are useful for liquid or gas chromatographic analysis of metals. These diketones, especially 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanenedione are widely used for the extraction of metal ions from aqueous solutions at variable pH [268]. 4,4,4-Trifluoromethyl-1-(2-thienyl)-1,3-butanedione is especially suited for the analysis of uranium and other radioactive elements. The *tetrakis*-chelates of 4,4,4-trifluoro-1-phenyl-1,3-butanedione with rare-earth elements are potential laser materials.

The paramagnetic lanthanide complexes of heptafluoro-7,7-dimethyl-4,6-octanenedione have gained considerable importance as NMR shift reagents for simplifying the interpretation of complex NMR spectra [269]; the europium complex is the most widely used.

\[
\begin{align*}
(CH₂)₃C_\text{C-O} & \quad \text{M} = \text{Ag; } n = 1 \\
HC_\text{C-O} & \quad \text{M} = \text{Dy, Eu, Gd, Ho, Pr, Yb; } n = 3
\end{align*}
\]

The chiral-shift reagents derived from 3-heptafluorobutyryl-(-)- or -(−)-camphor and 3-trifluoroacetyl-(-)- or -(−)-camphor are very useful for the NMR assay of enantiomeric purity in solution [269].

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{R = CF₃, n-C₃F₇} \\
\text{R} & \quad \text{M = Eu, Pr, Yb}
\end{align*}
\]

**8. Fluorinated Carboxylic Acids and Fluorinated Alkanesulfonic Acids**

**8.1. Fluorinated Carboxylic Acids**

**8.1.1. Fluorinated Acetic Acids**

Fluorination increases the strength of acetic acid as seen in the pKₐ values of monofluoroacetic acid (2.66), difluoroacetic acid (1.24), and trifluoroacetic acid (0.23) compared to the pKₐ of 4.74 for acetic acid [270].

**Production.** Trifluoroacetic acid has been prepared by the electrochemical fluorination of acetyl chloride or acetic anhydride in anhydrous hydrogen fluoride using the Simons process (Section 2.1) followed by hydrolysis of the resulting trifluoroacetyl fluoride. The yield is excellent (> 90%) [271], [272]. The Phillips Petroleum electrochemical process (Section 2.1) employs acetyl fluoride as feed to produce trifluoroacetyl fluoride along with mono and difluoroacetyl fluoride [273]. Sulfur trioxide treatment of CF₃CCl₃, obtained by isomerization of Freon 113, CF₂ClCFCl₂, yields CF₃COCl [274]. The acid is purified by hydrolysis of the acyl halide with alkali, followed by acidification and distillation.

**Uses.** Most uses of fluorinated acetic acids are confined to trifluoroacetic acid, its anhydride, and its derivative, 1,1,1-trifluoroethanol. Monofluoroacetic acid derivatives (salts, esters, amides, and alcohols) are toxic because they are metabolized to fluorocitric acid which inhibits respiration (see Section 13.5) [275]. ω-Fluoro acids of the formula F(CH₂)ₙCOOH, where n is an odd number, are extremely toxic, because of degradation in vivo to monofluoroacetic acid and finally to fluorocitric acid [275]. Sodium monofluoroacetate has been used as a rodenticide, but is now banned.

**8.1.2. Long-Chain Perfluorocarboxylic Acids**

**Properties.** The boiling points and densities of straight-chain perfluorocarboxylic acids are shown in Table 17.

**Production.** Long-chain perfluorocarboxylic acids are prepared by the Simons electrochemical fluorination (see Section 2.1.) of the corresponding acyl halide:

\[
\text{C}_\text{H}_{2n+1}-\text{COF} + (2n + 1) \text{HF} \rightarrow \text{C}_\text{F}_{2n+1}-\text{COF} + (2n + 1)\text{H}_2
\]

The acids are obtained by hydrolysis of the perfluoroacetyl fluoride, followed by distillation. Some carbon – carbon bond scission occurs to
form lower homologous acids along with inert fluorocarbons and cyclic ethers. The acid yield decreases with increasing chain length; for example, perfluorobutyric acid yields are ca. 36 % compared to ca. 20 % for the industrially important perfluorooctanoic acid [271], [272]. Trifluoroacetic acid is also prepared by the Phillips electrochemical method, employing a KF \cdot HF molten salt electrolyte [273]. Acids with higher boiling points are not easily or efficiently prepared by the Phillips process.

Perfluorocarboxylic acids are also prepared by nonelectrochemical methods. Treatment of perfluoroalkyl iodides (RfI) with sulfur trioxide [276] or chlorosulfonic acid [277] gives the carboxylic acid in good yield. Another method employs fuming sulfuric acid (oleum) [278]. Another process involves the preparation of perfluorotetrahydroalkyl iodides, RfCH2CH2I, obtained by the free-radical addition of ethylene to perfluoroalkyl iodides, followed by dehydroiodination and oxidation by dichromate [279] or ozonolysis [280]:

\[
\begin{align*}
C_6F_{14}I + CH_2=CH_2 & \rightarrow C_6F_{14}CH_2CH_2I \\
C_6F_{14}CH=CH_2 & \rightarrow C_6F_{14}COOH
\end{align*}
\]

This process produces carboxylic acids having one more carbon atom than the starting perfluoroalkyl iodide, in contrast to the electrochemical and oleum routes, which produce acids containing the same number of carbon atoms as the original acyl halide or telomeric iodide. In all processes utilizing fluorinated iodine-containing telomers, it is important to find uses for the telomers and to recover the expensive iodine.

Polyfluoroalkoxyacyl fluorides of the type

\[
R_n\text{CF}_3\text{O}([\text{CF}_2\text{CF}_2\text{O}]_m\text{CF}_2\text{O})\text{CF}_3\text{COF}
\]

are prepared by the addition of perfluoroacetyl fluorides and hexafluoropropylene oxide catalyzed by alkali-metal fluorides [281]. Acids, salts, or esters are obtained by hydrolysis, neutralization, or esterification, respectively.

Addition reactions of perfluorodiacyl fluorides with hexafluoropropylene oxide [282] give ether-containing diacyl fluorides, such as

\[
\text{CF}_3\text{CO}_2\text{CF}_3 + \text{CF}_3\text{O}([\text{CF}_2\text{CF}_2\text{O}]_m\text{CF}_2\text{O})\text{CF}_3\text{COF} \rightarrow \text{CH}_3\text{CO}_2\text{CF}_3\text{O}([\text{CF}_2\text{CF}_2\text{O}]_m\text{CF}_2\text{O})\text{CF}_3\text{COF}
\]

where \(n\) is usually 2 – 4, and at least two units are derived from hexafluoropropylene oxide (i.e., \(m \geq 2\)) [282]. The addition reaction may occur at one or both acyl groups of the starting diacyl fluoride. Selectivity can be maintained by esterifying one of the acyl fluoride groups. Thus, CH3OCO(CF2)2COF, prepared by addition of methanol to perfluoro-\(\gamma\)-butyrolactone or perfluorosuccinyl fluoride, reacts with hexafluoropropylene oxide to give ester acyl fluorides of the formula

\[
\text{CF}_3\text{CO}_2\text{CF}_3\text{O}([\text{CF}_2\text{CF}_2\text{O}]_m\text{CF}_2\text{O})\text{CF}_3\text{COF}
\]

[283], [284]. The acyl halides are converted to acids or salts by hydrolysis or neutralization, respectively.

Uses. Long-chain perfluoroalkanecarboxylic acids and their salts are surface-active chemicals (surfactants), which greatly reduce the surface

<table>
<thead>
<tr>
<th>Acid</th>
<th>CAS registry no.</th>
<th>Formula</th>
<th>bp, °C (kPa)</th>
<th>(d^2_{20}), g/cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfluoroacetic</td>
<td>[76-85-1]</td>
<td>CF3CO2H</td>
<td>72.4</td>
<td>1.489</td>
</tr>
<tr>
<td>Perfluoropropanonic</td>
<td>[422-64-0]</td>
<td>C2F5CO2H</td>
<td>96</td>
<td>1.561</td>
</tr>
<tr>
<td>Perfluorobutyric</td>
<td>[375-22-4]</td>
<td>C3F7CO2H</td>
<td>120</td>
<td>1.651</td>
</tr>
<tr>
<td>Perfluorovaleric</td>
<td>[2706-90-3]</td>
<td>C4F9CO2H</td>
<td>130</td>
<td>1.762</td>
</tr>
<tr>
<td>Perfluorobutyric</td>
<td>[275-47-7]</td>
<td>C6F13CO2H</td>
<td>189</td>
<td></td>
</tr>
<tr>
<td>Perfluorovaleric</td>
<td>[275-47-7]</td>
<td>C7F15CO2H</td>
<td>189</td>
<td></td>
</tr>
<tr>
<td>Perfluoropropionic</td>
<td>[275-47-7]</td>
<td>C10F21CO2H</td>
<td>245</td>
<td></td>
</tr>
</tbody>
</table>

Table 17. Boiling points and densities of perfluorocarboxylic acids
tension (surface energy) of water, aqueous solutions, and organic liquids even at low concentrations. These acids (C<sub>6</sub>–C<sub>12</sub>) and derivatives are used as wetting, dispersing, emulsifying, and foaming agents.

Ammonium perfluorooctanoate (FC-143, 3M) is used as an emulsifier in the polymerization of fluorinated monomers, especially tetrafluoroethylene. It has exceptional chemical stability and lowers the surface tension of water to ca. 3 μN · m at 0.5 wt %. In contrast with hydrocarbon emulsifiers, ammonium perfluorooctanoate does not interfere with the emulsion polymerization of tetrafluoroethylene.

**Trade Names.** Fluorad FC-26, 126, 143 (3M), Fluorowet CP (Hoechst), RM 350, 370 (Rimar), and Surflon S-111P (Asahi Glass).

### 8.1.3. Fluorinated Dicarboxylic Acids

**Properties.** The boiling points and densities of perfluorodicarboxylic acids are shown in Table 18.

**Production.** α,ω-Perfluoroalkanedicarboxylic acids are prepared by the electrochemical method, followed by hydrolysis, acidification, and extraction. Other methods include the oxidation of the appropriate chlorofluoroolefin or perfluoroolefin. Perfluoroglutaric acid is prepared from hexachlorocyclopentadiene by halogen exchange, followed by oxidation and acidification [285]. Perfluoroadipic acid is prepared by an analogous method from hexachlorobenzene [286]. The cyclic anhydrides from perfluorosuccinic and perfluoroglutaric acid are prepared by dehydration of the acids with phosphorus pentoxide. They are used to prepare the corresponding alcohols by reduction.

### 8.1.4. Tetrafluoroethylene – Perfluorovinyl Ether Copolymers with Carboxylic Acid Groups

Ion-exchange membranes, used in fuel cells and chloralkali production, are copolymers of tetrafluoroethylene and perfluorovinyl ethers that contain esters or other acid precursor groups [287]. These membranes have excellent thermal and chemical resistance to hot concentrated alkali (up to 40 %).

**Production.** The vinyl ethers are prepared by the reaction of hexafluoropropylene oxide and methyl-3-fluorocarbonyl perfluoropropionate [285], followed by pyrolysis to give:

\[
\text{CF}_3\text{CFO(CF}_{2}\text{CFO)}(\text{CF}_2)\text{COOCH}_3
\]

Copolymerization with tetrafluoroethylene followed by saponification produces a polymer with terminal carboxylic acid groups.

**Trade Names.** Flemion (Asahi Glass), Naflon (DuPont), Neosepta (Tokuyama Soda), and Aciplex (Asahi Chemical).

### 8.2. Fluorinated Alkanesulfonic Acids

#### 8.2.1. Perfluoroalkanesulfonic Acids

**Properties.** The first member of the series, trifluoromethanesulfonic acid, was reported in 1954 [288]. Perfluoroalkanesulfonic acids are among the strongest acids known. Conductivity measurements in acetic acid show that the acid strength of trifluoromethanesulfonic acid is comparable to that of fluorosulfonic and perchloric acids [289]. Boiling points are listed in Table 19. Because of their ability to lower surface energy,
the longer-chain perfluoroalkanesulfonic acids and sulfonyl fluoride derivatives have found utility as surface-active agents and water repellents and for antisoiling treatment of textiles and fabrics.

**Production.** Perfluoroalkanesulfonyl fluorides are usually made by the Simons electrochemical fluorination process (see Section 2.1), in which a hydrocarbon sulfonyl fluoride is electrolyzed in anhydrous hydrogen fluoride at nickel electrodes:

\[
\text{C}_n\text{H}_{2n+1}\text{SO}_2\text{F} + (2n + 1)\text{HF} \rightarrow \text{C}_n\text{F}_{2n+1}\text{SO}_2\text{F} + (2n + 1)\text{H}_2
\]

The electrochemical yield is excellent for the first member of the series and decreases progressively with the increasing length of the carbon chain; the yield for octanesulfonyl fluoride is ca. 40% [271], [290]. Alkaline hydrolysis of perfluoroalkanesulfonyl fluorides gives the corresponding salts, which when acidified and distilled from concentrated sulfuric acid yield the anhydrous sulfonic acids [288].

A nonelectrochemical method for the preparation of trifluoromethanesulfonic acid derivatives is shown below:

\[
\text{CF}_3\text{SO}_2\text{F} + \text{RCH}_2\text{NH}_2 \rightarrow \text{CF}_3\text{SO}_2\text{NH}-(\text{CH}_3)_2\text{NCH}_3
\]

Perfluoroalkanesulfonamide alcohols are also used as mold-release agents. Esterification with phosphoric acid gives phosphate ester salts of the type

\[
[R,\text{SO}_2\text{N(C}_3\text{H}_{2l+1})_m\text{PO(OH)}_n]_k
\]

which are useful oil repellents for paper products [296].

**Trade Names.** Paper Treatment FC-807, 808 (3M), Textile Treatment Dic-Guard (Dainippon Ink), and Scotchgard (3M).

### 8.2.2. Fluorinated Alkanedisulfonic Acids

a,ω-Perfluoroalkanesulfonyl fluorides are prepared by the electrochemical fluorination of perfluoroalkanesulfonyl fluorides [292], [293]. The higher homologues exhibit good surfactant properties; the derivatives of perfluorohexanesulfonyl fluoride are employed in fire extinguishing formulations. Useful derivatives containing the sulfonamido group can be prepared by reaction of the sulfonyl fluoride with a diamine, followed by quaternization with alkylating agents such as methyl iodide to give a cationic surfactant. As an example, reaction of perfluorohexanesulfonyl fluoride with 3-dimethylaminopropylamine gives

\[
\text{C}_6\text{F}_{13}\text{SO}_2\text{NH}-(\text{CH}_3)_2\text{NCH}_3\cdot\text{H}_2\text{O}
\]

The properties related to the low surface energy of the perfluorooctanesulfonyl fluoride, \(\text{C}_8\text{F}_{17}\text{SO}_2\text{F}\), are utilized in many derivatives. These derivatives include alcohols and their acrylate and methacrylate esters; they are used as comonomers in polymers that impart oil-, water-, and soil-repellent properties to porous substrates such as paper and textiles [294], [295]. A typical reaction sequence for the synthesis of a perfluoroalkanesulfonamide acrylate monomer is shown below:

\[
\text{C}_6\text{F}_{13}\text{SO}_2\text{F} + \text{RCH}_2\text{NH}_2 \rightarrow \text{C}_6\text{F}_{13}\text{SO}_2\text{NH}-(\text{CH}_3)_2\text{NCH}_3
\]

\[
\text{C}_6\text{F}_{13}\text{SO}_2\text{N}-(\text{CH}_3)_2\text{NCH}_3\cdot\text{H}_2\text{O} \rightarrow \text{C}_6\text{F}_{13}\text{SO}_2\text{N}-(\text{CH}_3)_2\text{NCH}_3\cdot\text{H}_2\text{O}
\]

### Table 19. Boiling points of perfluoroalkanesulfonic acids

<table>
<thead>
<tr>
<th>Acid Formula</th>
<th>CAS registry no.</th>
<th>bp, °C (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF₃SO₂H</td>
<td>[149-13-6]</td>
<td>60 (0.4)</td>
</tr>
<tr>
<td>C₂F₅SO₂H</td>
<td>[354-88-1]</td>
<td>81 (0.29)</td>
</tr>
<tr>
<td>n-C₄F₉SO₂H</td>
<td>[59933-66-3]</td>
<td>76 – 84 (0.13)</td>
</tr>
<tr>
<td>n-C₅F₁₁SO₂H</td>
<td>[3872-25-1]</td>
<td>110 (0.67)*</td>
</tr>
<tr>
<td>n-C₆F₁₃SO₂H</td>
<td>[355-46-4]</td>
<td>95 (0.46)</td>
</tr>
<tr>
<td>n-C₈F₁₇SO₂H</td>
<td>[1763-23-1]</td>
<td>133 (0.8)</td>
</tr>
</tbody>
</table>

* n-C₅F₁₁SO₂H · H₂O
hydrocarbon disulfonyl fluorides. The corresponding acids are prepared by alkaline hydrolysis of the fluoride and acidification, or by aqueous permanganate oxidation of the disulfone, \( \text{CH}_3\text{SO}_2(\text{CF}_2\text{CF}_2)_n\text{SO}_2\text{CH}_3 \) [297]. Distillation of the acids from phosphorus pentoxide yields the cyclic anhydrides [298].

8.2.3. Tetrafluoroethylene – Perfluorovinyl Ether Copolymers with Sulfonic Acid Groups

Ion-exchange membranes are prepared by the copolymerization of tetrafluoroethylene with perfluorovinyl ethers containing sulfonyl halide groups, followed by hydrolysis to yield sulfonic acids. These membranes have excellent chemical and thermal properties similar to those of ion-exchange membranes with terminal carboxylic acid groups (see Section 8.1.4) [299–301].

**Production.** These ethers are prepared by the condensation of hexafluoropropylene oxide with fluorosulfonylfluoroacetyl fluoride, \( \text{FSO}_2\text{CF}_2\text{COF} \), which is prepared from \( \text{C}_2\text{F}_4 \) and \( \text{SO}_3 \), followed by isomerization [302], [303]. Condensation of hexafluoropropylene oxide with \( \gamma \)-fluorosulfonylperfluoroalkyl carbonyl fluorides, \( \text{FSO}_2(\text{CF}_2)_n\text{COF} \) (prepared by electrochemical fluorination of the respective aliphatic sulfone) [304], [305]) gives perfluoroether fluorosulfonyl acyl fluorides, e.g., [306]

\[
\begin{align*}
\text{CF}_3 & \quad \text{CF}_3 \\
\text{FCOC(OF}_2\text{CFO)}_n(\text{CF}_2)_n\text{SO}_2\text{F} \\
\text{CF}_3 & = \text{CFO(OF}_2\text{CFO)}_n(\text{CF}_2)_n\text{SO}_2\text{F}
\end{align*}
\]

Subsequent conversion to the vinyl ether followed by copolymerization with tetrafluoroethylene gives polymers with fluorosulfonyl side chains, which are hydrolyzed to sulfonate group side-chains [307].

9. Fluorinated Tertiary Amines

**Physical Properties.** Relative to their molecular mass, perfluoroalkyl-tert-amines, like the perfluoroethers, have low boiling points and low freezing or pour points, as shown in Table 20. Low polarity and weak intermolecular forces are responsible for other unusually low values for properties such as viscosity, solubility, heat of vaporization, refractive index, dielectric constant, and surface tension [308]. Some perfluorobis(dialkylaminoalkyl) ethers have even lower pour points and liquid ranges as broad as 250 °C. These ethers exhibit increased internal flexibility through the combined effect of the nitrogen and oxygen atoms [311].

**Chemical Properties.** Perfluorinated tert-amines are chemically inert and thermally stable [308], [312]. The electron-withdrawing nature of the perfluoroalkyl substituents deprives the nitrogen atom of its basic character and reactivity. Fluorinated tert-amines do not form salts or complexes with strong acids and are not attacked by most oxidizing or reducing agents. With aluminum chloride they form chlorinated imines [313]. Because of their nonpolar nature, fluorinated tert-amines are poor solvents and are immiscible with water and alcohols [308]. Gases such as oxygen, nitrogen, and carbon dioxide have unusually high solubility in perfluorinated tert-amines. For example, perfluorotributylamine dissolves 40 vol % of oxygen at ambient conditions and has been used in artificial blood as an effective oxygen-transport medium [313].

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS registry no.</th>
<th>Formula</th>
<th>( M_w )</th>
<th>bp, °C</th>
<th>Pour point, °C</th>
<th>( d_4^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfluorotrimethylamine</td>
<td>[432-03-1]</td>
<td>N(CF_3)_3</td>
<td>221</td>
<td>–11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfluorotriethylamine</td>
<td>[359-70-6]</td>
<td>N(C_2F_5)_3</td>
<td>371</td>
<td>69</td>
<td></td>
<td>1.74</td>
</tr>
<tr>
<td>Perfluorotripropylamine</td>
<td>[338-83-0]</td>
<td>N(C_3F_7)_3</td>
<td>521</td>
<td>130</td>
<td>–52</td>
<td>1.82</td>
</tr>
<tr>
<td>Perfluorotributylamine</td>
<td>[311-89-7]</td>
<td>N(C_4F_9)_3</td>
<td>671</td>
<td>178</td>
<td>–50</td>
<td>1.88</td>
</tr>
<tr>
<td>Perfluorotriamylamine</td>
<td>[338-84-1]</td>
<td>N(C_5F_11)_3</td>
<td>821</td>
<td>215</td>
<td>–25</td>
<td>1.93</td>
</tr>
<tr>
<td>Perfluorotrihexylamine</td>
<td>[432-08-6]</td>
<td>N(C_6F_13)_3</td>
<td>971</td>
<td>256</td>
<td>33</td>
<td>1.90**</td>
</tr>
</tbody>
</table>

*Freezing point.
** \( d_4^2 \)
**Production.** Electrochemical fluorination via the Simons process (see Section 2.1) is the preferred route to fluorinated tertiary alkylamines. The hydrogen atoms are completely replaced by fluorine atoms. Perfluorotributylamine, for example, is synthesized as follows:

\[
(C_8H_{18})_3N + 27 \text{HF} \rightarrow (C_F_3)_{18}N + 27 \text{H}_2
\]

The crude product contains a significant amount of perfluorinated isomers and cleavage products because of molecular rearrangement during electrolysis; it is purified by fractional distillation and treatment with base.

**Uses.** The combination of unusual physical and chemical properties, excellent dielectric properties, nonflammability, and lack of toxicity make the perfluorinated tert-amines useful for many fluid applications that involve direct contact with sensitive materials [308], [313]. The electronic industry relies heavily on these fluids in reliability testing of electronic components, as direct-contact coolants for integrated circuits, and as heating media in vapor-phase reflow soldering. Perfluorinated tributylamine, triamyamine, and trihexylamine are the main constituents of Fluorinert electronic liquids FC-43, FC-70, and FC-71 (3M).

Information on the preparation and utility of other nitrogen-containing fluoroaliphatic compounds can be found in the general references [1–15].

10. Aromatic Compounds with Fluorinated Side-Chains

The first aromatic compound with a fluorinated side-chain, benzotrifluoride [98-08-8], trifluoromethylbenzene, was synthesized in 1898 [314]. The perfluoroalkyl substituents of aromatic compounds are meta-directing; this influence can, of course, be overcome by a stronger ortho- or para-directing substituent. These compounds are usually prepared from iodoperfluoroalkanes and halogenated aromatic compounds in the presence of a copper catalyst [315–317]. Except for the benzotrifluorides, aromatic compounds with fluorinated side-chains have only scientific interest [318]. Aromatic compounds with one or two trifluoromethyl substituents on the benzene ring gained commercial importance in the early 1930s for two reasons: 1) the recognition of the advantageous properties of aromatic dyes with CF₃ substituents, and 2) the development of an economical production process [4]. Since then, their importance in the production of dyes, pharmaceuticals, and pesticides has increased.

10.1. Properties

The physical properties of benzotrifluorides are shown in Table 21.

If no other substituents are present in the benzene ring, the trifluoromethyl group is thermally stable up to 350 °C and resistant to bases up to 130 °C. It is inert toward reducing agents [319], [320] and inhibits oxidation of the benzene ring. However, in the presence of aluminum chloride the trifluoromethyl group undergoes chlorolysis to produce a trichloromethyl group [321], and acid hydrolysis forms a carboxy group [322]. Substituents such as amino or hydroxyl groups destabilize the trifluoromethyl group [323].

The characteristic reaction of benzotrifluorides is electrophilic substitution of the benzene ring; chlorination and nitration are commercially important. Chlorination of benzotrifluoride at 65 °C with FeCl₃ as a catalyst yields 83%
3-chlorobenzotrifluoride [98-15-7] [324]; chlorination of 4-chlorobenzotrifluoride gives 3,4-dichlorobenzotrifluoride [328-84-7]. Nitration of benzotrifluoride results in a 6:3:91 mixture of 2-nitro- [384-22-5], 4-nitro- [402-54-0], and 3-nitrobenzotrifluoride [98-46-4] [325]. Other commercially important nitrations are the conversion of 2-chlorobenzotrifluoride [88-16-4] to 2-chloro-5-nitrobenzotrifluoride [777-37-7] and the conversion of 4-chlorobenzotrifluoride to yield 99% 4-chloro-3-nitrobenzotrifluoride [121-17-5] or 4-chloro-3,5-dinitrobenzotrifluoride [393-75-9] [326]. These derivatives are reduced to amines or are further processed.

10.2. Production

Benzotrifluorides are prepared on a laboratory scale by the reaction of aromatic compounds with iodotrifluoromethane [315]; by the reaction of aromatic carboxylic acids and their derivatives with sulfur tetrafluoride [51–53]; or by chlorine – fluorine exchange in trichloromethyl aromatic compounds with metal fluorides [327].

In the commercial process, known since 1931, chlorine is exchanged for fluorine with use of anhydrous hydrogen fluoride in the presence or absence of catalyst [328]:

\[
\text{CCl}_3 + 3\text{HF} \rightarrow \text{CF}_3 + 3\text{HCl}
\]

This reaction can be carried out as a batch process in autoclaves or continuously in a series of autoclaves [329] (Fig. 3) or tubular reactors [330]. Typical conditions for the production of benzotrifluoride are a temperature of 80 – 110 °C, pressure of 1.2 – 1.4 MPa, and a molar ratio of HF: benzotrifloride of 4 : 1. A yield of 70% is obtained within 3 – 4 h [331]. In continuous processing, a yield of over 90% is obtained in a nickel flow tube with a residence time of 1 h at 90 – 130 °C and at 3 – 5 MPa [332]. Yields are increased by using additives such as hexamethylenetetraamine [333] or by employing chlorine – fluorine exchange in the gas phase in the presence of a transition metal – aluminum oxide catalyst [334]. Corrosion is reduced by lowering the reaction temperature (< 60 °C) and adding iron or iron compounds [335], [336].

This method is used to produce benzotrifluoride, 2-chlorobenzotrifluoride, 4-chlorobenzotrifluoride, 2,4-dichlorobenzotrifluoride, 1,3-bis(trifluoromethyl)benzene, 1,4-bis(trifluoromethyl)benzene, 3-(trifluoromethyl)benzoyl fluoride, and 4-(trifluoromethyl)benzoyl fluoride [368-94-5] from the corresponding trichloromethyl compounds.

Figure 3. Production of benzotrifluorides in a series of autoclaves [329].
  a) Reactor; b) Pressure distillation column; c) Separator; d) Product distillation column; e) Product storage tank
The trifluoromethyl group can also be introduced into aromatic compounds by the Friedel–Crafts reaction with carbon tetrachloride in the presence of hydrogen fluoride [337].

\[
\begin{array}{c}
\text{CF}_3 \\
\text{R} = \text{alkyl, aryl, halogen}
\end{array}
\]

10.3. Uses

Benzotrifluoride and 4-chlorobenzotrifluoride are key intermediates for the synthesis of dyes, pharmaceuticals, and pesticides.

Dyes. Trifluoromethyl aromatic compounds were first used in dyes [4] and are still important intermediates for azo, anthraquinone, and triphenylmethane dyes. The strongly electronegative trifluoromethyl group improves color clarity and fastness to light and washing; it also shifts light absorption to the visible and ultraviolet ranges.

Some of these dye intermediates [338] for the production of anthraquinone and azo dyes (Naphtol AS, Hoechst AG) and azo pigments are still used, especially for polyesters and polyamides. These compounds include 2-aminobenzotrifluoride [88-17-5] for C.I. Pigment Yellow 154 [63661-02-9]; 3-amino-4-chlorobenzotrifluoride [121-50-6] for C.I. Pigment Orange 60 [68399-99-5]; 3-(trifluoromethyl)benzoyl fluoride for Indanthren Blue CLB [6492-78-0] (BASF) as well as 2-amino-5-chlorobenzotrifluoride [445-03-4], 3,5-bis(trifluoromethyl)aniline [328-74-5], and 3-amino-4-ethylsulfonylbenzotrifluoride [382-85-4].

Pharmaceuticals. The trifluoromethyl substituent is highly lipophlic; it increases the lipid solubility of pharmaceuticals and thus accelerates their absorption and transport in a living organism [339], [340]. In some cases, introduction of the CF$_3$ group also increases drug effectiveness and reduces undesirable side effects; therefore, benzotrifluorides are used in the synthesis of many pharmaceuticals [341]. These include the analgesics flufenamic acid [530-78-9] and niflumic acid [4394-00-7], the antidepressant fluoxetine [54910-89-3], the muscle relaxant flumetramide [7125-73-7], the appetite depressants fenfluramine [458-24-2] and fludorex [15221-81-5], and the tranquilizers triflupromazine [146-54-3] and fluphenazine [69-23-8]. Bendroflumethiazide [73-48-3] is an effective diuretic and antihypertensive agent.

Pesticides. Benzotrifluorides are also important in the production of pesticides [342]. The key intermediate, 4-chloro-3,5-dinitrobenzotrifluoride [393-75-9], is obtained by dinitration of 4-chlorobenzotrifluoride. Reaction with secondary amines gives trifluralin [1582-09-8], profluralin [26399-36-0], and benfluralin [1861-40-7]. 4-Chlorobenzotrifluoride and 3,4-dichlorobenzotrifluoride are intermediates for herbicides with a diphenyl ether structure – fluorodifen [15457-05-3] and acifluorfen [50594-66-6] and the insecticide fluvalinate [69409-94-5]. 3-Aminobenzotrifluoride [98-16-8] is obtained from benzotrifluoride by nitration and hydrogenation. It is used to make the selective herbicide flometuron [2164-17-2] or is used as a component of the herbicide norflurazon [27314-13-2].

11. Ring-Fluorinated Aromatic, Heterocyclic, and Polycyclic Compounds

The compounds discussed in this chapter contain one or more fluorine atoms that are directly attached to aromatic, heterocyclic, or polycyclic rings. Unlike chlorination and bromination, fluorination with elemental fluorine is rarely employed for their production because its violence produces many side reactions (ring-opening, coupling, polymerization, and charring). Therefore, indirect methods are used, distributing the reaction enthalpy over several controllable steps [318].

Diazonium salts are suitable for introducing up to three fluorine atoms per ring. Chlorine–fluorine exchange (halogen exchange, Halex process) with alkali – metal fluorides is suitable in cases where activating substituents are present.

Ring-fluorinated aromatic, heterocyclic, and polycyclic compounds are predominantly used as intermediates for pharmaceuticals, pesticides, dyes and other products. The exceptional
properties of fluorinated cyclic compounds (bioactivity spectrum, effectiveness, and solubility) justify the higher production costs compared to those of fluorine-free compounds.

11.1. Mono- and Difluoroaromatic Compounds

Research on ring-substituted aromatic fluorine compounds began in 1870. The fluorine atom attached to the benzene ring is strongly electronegative; it preferentially directs new substituents into the para position and rarely, if ever, into the ortho position [343]. Important aspects, especially for biological applications, are (1) the influence of the strongly electronegative fluorine substituent on adjacent groups, (2) its participation in the resonance system of the aromatic compound by returning electron density, and (3) the simulation of hydrogen or hydroxy substituents that is due to the similarity in space requirements and has led to the synthesis of a series of monofluoro aromatic enzyme inhibitors. The varying lability of the carbon – fluorine bond in mono- and difluoro aromatic compounds has been exploited to prepare indicators and analytical reagents, especially for biogenic and metabolic studies.

11.1.1. Properties

Replacement of aromatic hydrogen by fluorine has only a minor effect on boiling points. Density increases, whereas refractive index and surface tension decrease. Physical constants are shown in Table 22.

The reactivity of fluorine in benzene derivatives depends on the nature of the other ring substituents. Nucleophilic substitution occurs only where activating groups (e.g. nitro) are present in the ortho or para position. In other cases, e.g., with 1-bromo-4-fluorobenzene [460-00-4], the carbon – fluorine bond is stronger; hydrolysis gives 4-fluorophenol [371-41-5] [344], [345].

11.1.2. Production

Among the published processes for the production of mono- or difluoroaromatic compounds, ring fluorination with dilute fluorine or fluorinating agents such as xenon difluoride [346–349] does not follow a clear course (i.e., without side reactions) and has no commercial value. Fluorobenzene itself can be prepared by pyrolysis of chlorodifluoromethane or chlorotrifluoroethylene in the presence of cyclopentadiene at 300 – 800 °C [350] and by anodic fluorination of benzene with tetraethylammonium fluoride in acetonitrile [351]. Promising methods are the decarboxylation of benzoyl fluorides in the presence of tris(triphenylphosphine)rhodium(I) chloride in boiling xylene [352] and the thermal decarboxylation of aryl fluoroformates [353].

**Diazotization.** Aromatic compounds containing one or two fluorine substituents are produced commercially by diazotization of aromatic amines and decomposition of the resulting diazonium fluorides [318], [354]. In one process, aromatic amines are diazotized with dry sodium nitrite in anhydrous hydrogen fluoride at 0 – 20 °C [355] (see Fig.4).

### Table 22. Physical properties of ring-fluorinated aromatic compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS registry number</th>
<th>Empirical formula</th>
<th>( M_r )</th>
<th>( bp, ^\circ C ) (101.3 kPa)</th>
<th>( d_4^0 (\theta, ^\circ C) )</th>
<th>( n_0^0 (\theta, ^\circ C) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorobenzene</td>
<td>[462-06-6]</td>
<td>C(_6)H(_5)F</td>
<td>96.1</td>
<td>84.7</td>
<td>1.083 (25)</td>
<td>1.4629 (25)</td>
</tr>
<tr>
<td>2-Fluorotoluene</td>
<td>[95-52-5]</td>
<td>C(_7)H(_7)F</td>
<td>110.13</td>
<td>113 – 114</td>
<td>1.003 (21)</td>
<td>1.4727 (20)</td>
</tr>
<tr>
<td>3-Fluorotoluene</td>
<td>[352-70-5]</td>
<td>C(_7)H(_7)F</td>
<td>110.13</td>
<td>115</td>
<td>0.991 (25)</td>
<td>1.4691 (20)</td>
</tr>
<tr>
<td>4-Fluorotoluene</td>
<td>[352-32-9]</td>
<td>C(_7)H(_7)F</td>
<td>110.13</td>
<td>116</td>
<td>0.991 (25)</td>
<td>1.4688 (20)</td>
</tr>
<tr>
<td>4,4'-Difluorodiphenylmethane</td>
<td>[457-68-1]</td>
<td>C(<em>{13})H(</em>{10})F(_2)</td>
<td>204.22</td>
<td>263.5°</td>
<td>1.145 (20)</td>
<td>1.5362 (20)</td>
</tr>
<tr>
<td>1,3-Difluorobenzene</td>
<td>[372-18-9]</td>
<td>C(_6)H(_4)F(_2)</td>
<td>114.09</td>
<td>82 – 83</td>
<td>1.1572 (20)</td>
<td>1.4440 (20)</td>
</tr>
<tr>
<td>1,4-Difluorobenzene</td>
<td>[540-36-3]</td>
<td>C(_6)H(_4)F(_2)</td>
<td>114.09</td>
<td>88 – 89</td>
<td>1.176 (20)</td>
<td>1.4421 (20)</td>
</tr>
</tbody>
</table>

*At 100.5 kPa*
The temperature is increased to 30 – 120 °C, and the formed diazonium fluorides decompose to form fluoroaromatic compounds. A yield of over 90% of mono- and difluorinated compounds is obtainable. Yields of ca. 81% are reported for batch operations on a 1-t scale.

In a continuous process the three exothermic steps are controlled by separation; i.e., hydrofluorination of the aromatic amine, diazotization, and thermal decomposition [356]. This permits safe operation on a large scale. Diazotization with nitrosyl chloride [357] and nitrosyl fluoride – HF complexes [358] is also possible. Problems associated with these processes are hydrogen fluoride recovery and waste gas treatment.

In another method (Balz – Schiemann reaction), water-insoluble diazonium fluoroborates are prepared by diazotization of aromatic amines with sodium nitrite in the presence of 40% fluoroboric acid or sodium or ammonium tetrafluoroborate in HCl [327], [359]. After filtration the diazonium salts are dried and thermolyzed [360] (Fig. 5):

This thermal decomposition must be strictly controlled, especially when nitro substituents are present, to avoid an explosion. Diazonium tetrafluoroborates usually decompose at a higher temperature than the corresponding diazonium fluorides. The Balz – Schiemann process has rarely been used on a large scale because of the difficulties in handling diazonium tetrafluoroborates. However, it is convenient as a laboratory process because it does not require specialized apparatus. A plant of several 100 t/a has been reported [361].

A large number of fluoroaromatic compounds have been produced by using the two diazotization routes described [327], [362]. Those of commercial interest include fluorobenzene from aniline; 2-, 3-, and 4-fluorotoluene from the appropriate toluidines; 4,4'-difluorodiphenylmethane from 4,4'-diaminodiphenylmethane; 1,3-difluorobenzene from m-phenylenediamine; and 1,4-difluorobenzene from p-phenylenediamine.

The reaction sequence of nitration, reduction, diazotization, and thermal decomposition can be...
repeated to introduce up to four fluorine atoms into the benzene ring.

**Chlorine – Fluorine Exchange.** Of similar commercial importance to diazotization is the replacement of activated chlorine atoms with the aid of alkali-metal fluorides [318], [354]. The usual activating groups are ortho and para nitro, cyano, and trifluoromethyl groups [363]. Aprotic – polar solvents are preferred, such as dimethylformamide, dimethylacetamide, dimethyl sulfoxide, N-methyl-2-pyrrolidone, and tetrahydrothiophene-1,1-dioxide (sulfolane).

Phase-transfer catalysts are sometimes used [364]. The effectiveness of the fluoride source decreases in the order $\text{CsF} > \text{KF} > \text{NaF} > \text{LiF}$.

In commercial batch or semicontinuous operations, the *Halex process* (Fig. 6), potassium fluoride and the activated chloroaromatic compound...
are thoroughly mixed (1:1) with a large volume of an aprotic solvent (dimethyl sulfoxide or sulfolane) and are heated to 150 – 250 °C [363], [365]. The reaction is 90% complete within 48 h. Removal of KCl and distillation of the product present no difficulty, but efficient solvent recovery is important to reduce costs.

Cost is also reduced by regenerating the potassium fluoride by treating the KCl with HF [366]. The Halex process has the clear advantage of readily accessible raw materials, simplicity of a single-step procedure, and structural specificity. Certain products are accessible in no other way.

The following commercially important intermediates are obtained by the Halex process: 1-fluoro-2-nitrobenzene [1493-27-2] and 1-fluoro-4-nitrobenzene [350-46-9] from the corresponding chloronitrobenzenes; 1-chloro-2-fluoro-5-nitrobenzene [350-30-1] from 1,2-dichloro-4-nitrobenzene; 1-chloro-4-fluoro-3-nitrobenzene [345-18-6] from 1,4-dichloro-2-nitrobenzene; 1-fluoro-2,4-dinitrobenzene [70-34-8] from 1-chloro-2,4-dinitrobenzene; 5-fluoro-2-nitrobenzotrifluoride [393-09-9] from 5-chloro-2-nitrobenzotrifluoride [118-83-2]; 1,3-difluoro-4-nitrobenzene [446-35-5] from 1,3-dichloro-4-nitrobenzene; and 2,6-difluorobenzonitrile [1897-52-5] from 2,6-dichlorobenzonitrile. These intermediates are mostly used for substituted anilines and compounds with carbonyl and carboxy functions.

11.1.3. Uses

Fluorobenzene, difluorobenzenes, and their derivatives are used widely in the synthesis of pharmaceuticals and pesticides, and as fine chemicals. Fluoroaromatics have played a special role in the development of drugs that act on the central nervous system [367]. The increase in lipid solubility due to fluorine atoms facilitates the absorption and transport of drugs through the blood – brain barrier into the central nervous system.

Fluorobenzene derivatives are used in neuroleptics such as haloperidol [52-86-8], tranquillizers such as fluspiridene [1841-19-6], sedatives such as flurazepam [17617-23-1], and antidepressants such as fluvoxamine [54739-18-3].

Pesticidal [342] and fungicidal fluorobenzene derivatives [368] include the insecticide difluorobenzuron [35367-38-5] (made from 2,6-difluorobenzonitrile), the herbicides flamprop [58677-63-3] and fluoronitrofen [13738-63-1], and the fungicides nuarimal [63284-71-9] and flurimid [41205-21-4].

4,4′-Difluorobenzophenone [345-92-6], a starting material for aromatic polycondensates, is produced by oxidation of 4,4′-difluorodiphenylmethane, which is obtained by diazotization of the corresponding diamine. 4,4′-Difluorobenzophenone undergoes polycondensation with hydroquinone, yielding a polyetherether ketone (PEEK) resin, a thermoplastic. 4-Fluoroniline [371-40-4], 4-fluorobenzaldehyde [459-57-4], and 4-fluorobenzoic acid [456-22-4] are intermediates for liquid crystal polymers [369].

Aromatic compounds with reactive fluorine substituents are used for the characterization of amino acids (Sanger’s reagent, 1-fluoro-2,4-dinitrobenzene [70-34-8]), the immobilization of enzymes (4-fluoro-3-nitrophenylazide [28166-06-5]), and peptide cross-linkage (1,5-difluoro-2,4-dinitrobenzene [327-92-4]).

Aromatic fluorine compounds have been developed for medical applications, such as 19F-magnetic resonance imaging (MRI) and in 18F positron emission tomography (PET) [370].

11.2. Highly Fluorinated Aromatic Compounds

Compounds in which an aromatic ring is substituted by three to five fluorine atoms have little commercial importance. 1,2,4-Trifluorobenzene [367-23-7], bp 88 °C, and 1,3,5-trifluorobenzene [372-38-3], bp 75.5 °C, are produced by the Balz – Schiemann reaction (see Section 11.1.2) from 2,4-difluoroaniline [367-25-9] and 3,5-difluoroaniline [372-39-4], respectively. 1,3,5-Tricyano-2,4,6-trifluorobenzene [3638-97-9], mp 148 – 150 °C, is used as an intermediate for pesticides; it is obtained by chlorine – fluoride exchange from 1,3,5-tricyano-2,4,6-trichlorobenzene [371].

1,2,3,5-Tetrafluorobenzene [2367-82-0], bp 83 °C, is obtained by the Balz – Schiemann reaction from 2,3,5-trifluoroaniline [363-80-4], and 1,2,4,5-tetrafluorobenzene [327-54-8], bp 90 °C, from 2,4,5-trifluoroaniline [57491-45-9]. 1,2,3,4-Tetrafluorobenzene [551-62-2], bp 95 °C, pentafluorobenzene [363-72-4], bp
85 °C, and hexafluorobenzene are produced by the CoF₃ method (see Section 11.3). The Halex process (Section 11.1.2) is used commercially to produce 1,4-dicyano-2,3,5,6-tetrafluorobenzene [1835-49-0], mp 197 – 199 °C, from the corresponding tetrachloro derivative [372]. This compound is used as a monomer for thermostable polymers.

11.3. Perhaloaromatic Compounds

Hexafluorobenzene [392-56-3], bp 80.3 °C, has been thoroughly investigated [373]. Nucleophilic substitution produces pentafluoroaromatic compounds such as bromopentafluorobenzene [344-04-7], bp 135.6 °C, pentafluorophenol [771-56-2], bp 117 – 118 °C, pentafluorobenzaldehyde [653-37-2], bp 164 – 166 °C, pentafluorobenzoic acid [602-94-8], bp 220 °C.

Production. Hexafluorobenzene was first produced in 1955 by pyrolysis of tribromofluoromethane [353-54-8] in a platinum tube at 640 °C under atmospheric pressure [374],

\[
C_6Br_6 \rightarrow C_6F_6 + 9 Br_2
\]

Of greater commercial interest is the pyrolysis of an equimolar mixture of dichlorofluoromethane [75-43-40] and chlorofluoromethane [593-70-4] at 600 – 800 °C [375],

\[
3\text{CHCl}_2\text{F} + 3\text{CH}_2\text{ClF} \rightarrow C_6\text{F}_6 + 9 \text{HCl}
\]

For many years a commercial multistep process employed CoF₃ as the fluorinating agent [376]. For example, at 150 °C benzene gives a mixture of cyclohexanes containing 8 – 11 fluorine atoms.

\[
\begin{align*}
C_6\text{H}_6 + \text{CoF}_3 & \rightarrow C_6\text{H}_{12-n}\text{F}_n + \text{CoF}_2 \\
& + \text{MOH} \\
& \rightarrow C_6\text{H}_{11-n}\text{F}_{n-1} + C_6\text{H}_{10-n}\text{F}_{n-2} \\
& \text{Fe or FeF}_4
\end{align*}
\]

\(n = 8 – 11\), \(M = \text{alkali metal}\)

The CoF₂ formed in this reaction is fluorinated to CoF₃ with elemental fluorine, and reused. The organic products are heated with an alkali-metal hydroxide to form a mixture of polyfluorocyclohexenes and polyfluorocyclohexadienes. These products are aromatized by passage over iron or iron compounds at 400 – 600 °C to give hexafluorobenzene, pentafluorobenzene, and tetrafluorobenzenes. Octafluorotoluene [434-64-0] and the three perfluoroxylenes are also obtained by this method.

The disadvantages of this process are the technological difficulties and the low utilization of fluorine, of which a large part is converted to hydrogen fluoride and alkali-metal fluorides. As a consequence, aromatic fluorine compounds containing other halogens are currently produced by the Halex method (Section 11.1.2). Reaction of hexachlorobenzene [365] with potassium fluoride at 450 °C and 1.03 MPa gives a yield of 21 % hexafluorobenzene together with chloropentafluorobenzene [344-07-0] (20 %), 1,3-dichloro-2,4,5,6-tetrafluorobenzene [1198-61-4] (14 %), and 1,3,5-trichloro-2,4,6-trifluorobenzene [319-88-0] (12 %).

\[
\text{C}_6\text{Cl}_6 + \text{KF} \rightarrow \text{C}_6\text{F}_6, \text{C}_6\text{ClF}_5, \text{C}_6\text{Cl}_2\text{F}_4, \text{C}_6\text{Cl}_3\text{F}_3,
\]

The yield of hexafluorobenzene can be increased by recycling the other products for further reaction with potassium fluoride. A yield of 42 % hexafluorobenzene is obtained from chloropentafluorobenzene with the more reactive, but more expensive, cesium fluoride [377].

Hexachlorobenzene reacts with KF in aprotic solvents such as dimethylformamide, dimethyl sulfoxide, N-methyl-2-pyrrolidone, and sulfolane to give not hexafluorobenzene, but the above-mentioned mixed products. The reaction temperature is 150 – 250 °C and the residence time 5 – 36 h. Detailed discussions of the process are given in [363], [365].

Uses. Hexafluorobenzene has been investigated as an inhalation anesthetic in veterinary medicine [378] and as a working fluid in Rankine-cycle engines for temperatures above 350 °C [379]. Derivatives such as pentafluorobenzaldehyde or pentafluorophenyl dimethylsilyl ether are used in the chromatographic analysis of steroids [380] and catecholamines [381], and as intermediates for the production of liquid...
crystal polymers [382]. Pentafluorophenoxy perfluorovinyl ethers are cross-linking comonomers for perfluorinated elastomers [383].

11.4. Fluorinated Heterocyclic and Polycyclic Compounds

Fluorinated pyridines, pyrimidines, and triazines are heterocycles with commercial importance. Only some representative polycyclic fluorine compounds are discussed as examples.

11.4.1. Ring-Fluorinated Pyridines

Introduction of fluorine into the pyridine ring reduces the basicity of the latter [384]. 2-Fluoropyridine [372-48-5], bp 126 °C (100.4 kPa), has a labile fluorine substituent. It is produced in 74% yield by reaction of 2-chloropyridine with potassium bifluoride at 315 °C in 4 h [385]. 3-Fluoropyridine [372-47-4], bp 105 – 107 °C (100.3 kPa), is produced in 50% yield from 3-aminopyridine using the Balz – Schiemann process (see Diazotization). 4-Fluoropyridine [694-52-0], bp 108 °C (100 kPa) is produced in 54% yield by diazotization of 4-aminopyridine in anhydrous hydrogen fluoride [386].

2,4-Difluoropyridine [34941-90-7], bp 104 – 105 °C, is obtained by the Halex process (see Chlorine – Fluorine Exchange) from 2,4-dichloropyridine with potassium bifluoride at 315 °C in 4 h [385]. 3-Fluoropyridine [372-47-4], bp 105 – 107 °C (100.3 kPa), is produced in 50% yield from 3-aminopyridine using the Balz – Schiemann process (see Diazotization). 4-Fluoropyridine [694-52-0], bp 108 °C (100 kPa) is produced in 54% yield by diazotization of 4-aminopyridine in anhydrous hydrogen fluoride [386].

2,4-Difluoropyridine [34941-90-7], bp 104 – 105 °C, is obtained by the Halex process (see Chlorine – Fluorine Exchange) from 2,4-dichloropyridine and potassium fluoride in sulfone [387]. 2,6-Difluoropyridine [1513-65-1], bp 124.5 °C (99.1 kPa), is obtained by the reaction of 2,6-dichloropyridine with potassium fluoride in the absence of solvent. The yield is 80% after 18 h at 400 °C [388].

For pentafluoropyridine [700-16-3], bp 83 °C, the preferred method is the reaction of pentachloropyridine with KF at 480 – 500 °C; the yield is 83% [389]. Nucleophilic substitution reactions have been thoroughly investigated [390].

Uses. Fluoropyridines are intermediates for pesticides. For example, 2-fluoro-4-hydroxypyridine [22282-69-5] is a precursor of 2-fluoro-3,5-dihalo-4-hydroxypyridine herbicides [391]; 2-fluoro-6-hydroxypyridine [55758-32-2] is used for insecticides and nematocides [392] and various derivatives of fluorinated pentahalogenpyridine herbicides [393]. Pentafluoropyridine in mixtures with hexafluorobenzene is used as the working fluid in Rankine-cycle engines up to 382 °C [379].

11.4.2. Trifluoromethylpyridines

2-Trifluoromethyl- [368-48-9], 3-trifluoromethyl- [3796-23-4], and 4-trifluoromethylpyridine [3796-24-5] can be obtained by the reaction of picolinic, nicotinic, or isonicotinic acid, respectively, with sulfur tetrafluoride [394]. Commercial processes use side-chain chlorination of the methylpyridines followed by chlorine – fluorine exchange with antimony chlorofluorides or anhydrous hydrogen fluoride [395]. 2-Chloro-5-trifluoromethylpyridine, bp 190 °C, is produced commercially from 2-chloro-5-trichloromethylpyridine and hydrogen fluoride at 180 – 200 °C and at a pressure of 3 – 4.5 MPa. It is an intermediate for the synthesis of the selective herbicide fluazifop [69335-91-7], [396].

11.4.3. Fluoropyrimidines

Certain fluoropyrimidines have gained commercial importance [397]. 5-Fluoropyrimidines are employed in cancer chemotherapy; their biochemistry and pharmacology have been intensively studied [398]. 5-Fluorouracil [51-21-8] is obtained in a 80 – 92% yield by the fluorination of 2,4-dihydroxyxypyrimidine with fluorine or trifluromethyl hypofluorite [399], [400]. 5-Chloro-2,4,6-trifluoropyrimidine [697-83-6], bp 114.5 °C (100 kPa), is produced commercially from 2,4,5,6-tetrachloropyrimidine by chlorine – fluorine exchange, using sodium fluoride at 300 °C [401] or anhydrous hydrogen fluoride in the liquid phase [402] or gas phase [403].

The 5-chloro-2,4-difluoropyrimidinyl radical acts as the reactive group in reactive dyes [397] for cellulose and cotton fibers such as Levafix EA (Bayer) and Drimaren K (Sandoz) and for wool, e.g., Verofix (Bayer) and Drimalene (Sandoz).

11.4.4. Fluorotriazines

2,4,6-Trifluoro-1,3,5-triazine [675-14-9], bp 72.4 °C (101.7 kPa), is produced commercially
from 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride) with either anhydrous hydrogen fluoride [404] or sodium fluoride in sulfolane [405]. It is used to manufacture reactive dyes by reaction between one or two fluorine substituents with amino groups of chromophores; the remaining fluorine binds to the fiber [406]. The reactive intermediates can be synthesized e.g., from the corresponding 6-substituted 2,4-dichlorotriazines and an alkali-metal fluoride or by reaction of cyanuric fluoride with anilines or phenols in organic solvents [406], [407]. Like the pyrimidine reactive dyes, the fluorotriazines are used on cellulose, polyesters, polyamides, and wool [397]. See also → Reactive Dyes.

11.4.5. Polycyclic Fluoroaromatic Compounds

Polycyclic fluoroaromatic compounds are used as intermediates for the production of pharmaceuticals.

4-Fluoro- [324-74-3] and 4,4'-difluorobiphenyl [398-23-2] are obtained by diazotization from the corresponding amines in yields of up to 80% [408]. Other biphenyl derivatives are prepared from fluorobenzenes. The analgesic diflunisal [22494-42-4] is produced from 2,4-difluoroaniline [367-25-9] by diazotization and coupling with salicylic acid. The anti-inflammatory drugs flurbiprofen [5104-49-4] and fluprofen [17692-38-5] are prepared from 2-fluoroaniline [75-54-9].

The anti-inflammatory drug sulindac [38194-50-2] is a monofluorinated indole-3-acetic acid.

12. Economic Aspects

The compounds discussed in Chapters 10 and 11 are not produced in large quantities and often command high prices. 4-Chlorobenzotrifluoride, 3,4-dichlorobenzotrifluoride, 3-trifluoromethylphenyl isocyanate, and benzotrifluoride are produced in the United States by Occidental Chemical, in Western Europe by Hoechst, Rhône-Poulenc, MitEni and Dow-Elanco, and in Japan by Daikin. The worldwide production capacity is ca. 35 000 – 40 000 t/a.

Heterocyclic fluorine compounds have economic importance in the production of reactive dyes. The main producers in Western Europe are Bayer AG, Ciba-Geigy, ICI, and Sandoz.

Fluorobenzene and its derivatives are produced in Western Europe by AlliedSignal – Riedel-de-Haën (production capacity 1600 t/a), Zeneca (2000 – 2500 t/a), Rhône-Poulenc (1000 t/a), MitEni (1000 t/a) in Europe, DuPont (1400 t/a), Mallinckrodt (1200 t/a) in the USA and Asahi Glass (1000 t/a) in Japan. Fluoronitrobenzenes and fluoroanilines are produced by the Halex process by Hoechst, MitEni, Rhône-Poulenc, Asahi Glass, and others. The total capacity for fluoroaromatic intermediates is estimated to be several thousand tons per year.

13. Toxicology and Occupational Health

With few exceptions, organic fluorine compounds are physiologically inert and display insignificant toxicity. This is a consequence of the chemical stability of the carbon – fluorine bond and the increased stability of hydrogen and halogen bonds attached to a fluorinated carbon atom. Low toxicity is an important factor in many applications of these compounds.

The difference in toxicity between a chloro or bromo compound and the corresponding fluoro compound is often striking. Thus, carbon tetrachloride [56-23-5] is a powerful liver and kidney toxin and a weak carcinogen, as reflected in its TLV of 5 ppm. However, the product obtained by replacing one chlorine atom with fluorine, trichlorofluoromethane [75-69-4], has no adverse effects on the liver, kidney, or other organs, and no carcinogenic effects on animals exposed to high concentrations for a lifetime; the TLV is 1000 ppm. Another example is the chemical warfare agent mustard gas, S(CH2CH2Cl)2 [505-60-2], which is a strong alkylating agent and notorious vesicant. The fluoro analog, bis(2-fluoroethyl) sulfide [373-25-1], is chemically and physiologically inert, with no vesicant properties [409].

The few highly toxic organofluorine compounds usually have easily replaceable fluorine atoms. Examples are diisopropyl fluorophosphate [55-91-4], a potent cholinesterase inhibitor, and perfluoroisobutylene [382-21-8], which causes pulmonary edema at low concentrations. Sodium fluoroacetate [62-74-8], a potent roden-
ticide, is an exception; it does not liberate fluo-
rine, but interferes with metabolism by mimick-
ing acetic acid.

13.1. Fluorinated Alkanes

Fluoroalkanes [410], [411]. Perfluoroalk-
anes have very low toxicity. Thus, rats exposed
to an 80:20 mixture of perfluorocyclobutane
[115-25-3] and oxygen for 4 h survived with no
ill effects. Likewise, no ill effects were seen in
four species of animals exposed to a 10% con-
centration in air 6 h/d for 90 d. Partially fluori-
nated alkanes have similarly low toxicity, as
shown by similar experiments with difluoro-
methane [75-10-5] and 1,1-difluoroethane [75-
37-6].

Chlorofluoroalkanes are more toxic than
the corresponding fluoroalkanes; nevertheless,
most chlorofluoroalkanes have low toxicity
[410–412]. High concentrations (10 – 50% in
air) of many of them, like lower concentrations of
many hydrocarbon and chlorohydrocarbon sol-
vents, can cause cardiac sensitization, i.e., sen-
sitization of the heart to the body’s adrenalin.
This can lead to cardiac arrhythmia (heartbeat
irregularity) and sometimes cardiac arrest.
Deaths have been caused by “aerosol sniffing”.
The toxicity of dichlorodifluoromethane [75-
71-8] has been thoroughly investigated. Rats
survived a 6-h exposure to an 80% mixture with
oxygen. Five species of animals continuously
exposed to 810 ppm for 90 d showed no effects
except for slight liver damage in guinea pigs.
Rats and dogs showed no significant health ef-
effects when fed a diet containing 0.3% for 2 years.
Teratogenic and reproductive tests in rats were
also negative. Repeated exposure caused little or
no irritation to rat skin or the rabbit eye. In a
screening test, dogs injected with adrenalin
showed cardiac sensitization on exposure to
50 000 ppm in air, but not to 25 000. On the
basis of animal data and human experience, a
TLV of 1000 ppm has been selected to provide an
ample margin of safety against cardiac sensiti-
zation and other injury [413]. The MAK is also
1000 ppm [414].

Compared to dichlorodifluoromethane, tri-
chlorofluoromethane [75-69-4] and 1,1,2-tri-
chloro-1,2,2-trifluoroethane [76-13-1] are slight-
ly more toxic, whereas 1,2-dichloro-1,1,2,2-tet-
rafluoroethane [76-14-2] is slightly less toxic.
However, for all three a TLV of 1000 ppm is
judged to provide an adequate margin of safety.
On the other hand, 1,1,2-tetrachloro-2,2-di-
fluoroethane [76-11-9] and 1,1,2,2-tetrachloro-
1,2-difluoroethane [76-12-0] cause liver and lung
damage to rats subjected to repeated exposure at
1000 ppm; therefore, a TLV of 500 ppm is re-
commended for these compounds. These data
indicate that the toxicity of chlorofluorocarbons
tends to increase with the chlorine : fluorine ratio
and the number of carbon atoms.

Although the toxicity of most chlorofluor-
oolkanes bearing hydrogen (chlorofluorohydro-
carbons) is also low, it tends to be higher than that
of the closely related chlorofluorocarbons. The
difference is usually slight, as in the case of 2-
chloro-1,1,2-tetrafluoroethane [2837-89-0],
which is a slightly stronger cardiac sensitizer
than 1,2-dichloro-1,1,2,2-tetrafluoroethane, but
is otherwise similar to it in toxic properties.
Chlorodifluormethane [75-45-6] is similar in
toxicity to dichlorodifluoromethane in most re-
spects, and has the same TLV of 1000 ppm. At
50 000 ppm it has a weak carcinogenic effect in
male rats, but not at lower concentrations or in
mice or female rats; therefore, this is considered
of no practical significance [415].

The toxicity of dichlorodifluormethane [75-
43-4] is more like that of chloroform than of
dichlorodifluoromethane or chlorotrifluoro-
methane [75-72-9], especially with respect to
injury on repeated exposure; its TLV, 10 ppm,
is low for a chlorofluoroalkane.

Bromofluoroalkanes, some of which are
fire extinguishing agents and anesthetics, are
more toxic than the corresponding chlorofluoro-
alkanes, but generally are low in toxicity com-
pared to other fire extinguishing agents and
anesthetics [409], [413]. Trifluorobromomethane
[75-63-8] produced no adverse effects
on dogs and rats exposed to 23 000 ppm 6 h/d,
5 d/week, for 18 weeks; its TLV is 1000 ppm
[413].

13.2. Fluorinated Olefins

Most fluorinated olefins have halogen atoms of
low reactivity and a correspondingly low-to-
moderate toxicity [409], [412]. The toxicities of the five most common members of the class, typical in these respects, are shown in Table 23.

In perfluoroisobutylene and 2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene [303-04-8], halogens are readily displaced by nucleophilic reactants; thus, these two compounds exhibit high acute toxicity. Perfluoroisobutene, with a LC50 of 0.5 ppm, acts much like phosgene in causing death by pulmonary edema. However, perfluoroisobutene is ca. 10 times as toxic as phosgene, so exposure to it must be carefully avoided. Pyrolysis of tetrafluoroethylene or its polymers above 400 °C is one of its sources.

### 13.3. Fluorinated Alcohols

2-Fluoroethanol [371-62-0] has a high acute toxicity (LD50 10 mg/kg), a consequence of its ready biological oxidation to fluoroacetic acid (see Section 13.6). Thus, contact with the skin and inhalation of vapors must be avoided. The di- and trifluoroethanols ([359-13-7] and [75-89-8], respectively) have relatively low acute toxicity, similar to the corresponding acetic acids [412]. The acute toxicity of 1,1,1,3,3,3-hexafluoro-2-propanol [920-66-1] is also low, but the substance is a strong skin and eye irritant.

### 13.4. Fluorinated Ketones

In 90-d inhalation studies in animals, hexafluoroacetone [684-16-2] caused severe damage to kidneys and other organs at 12 ppm, moderate damage at 1 ppm, and no damage at 0.1 ppm. Repeated skin exposure led to testicular damage in rats. These data and plant experience led to selection of a TLV of 0.1 ppm, with a warning against skin exposure [413]. Studies of hexafluoroacetone and three fully halogenated chlorofluoroketones indicated moderate acute toxicity [416].

### 13.5. Fluorinated Carboxylic Acids

Fluoroacetic acid [144-49-0] is highly toxic to mammals; its sodium salt is an effective, but indiscriminate, rodenticide; in rats the LD50 of the salt is only 1.7 mg/kg [413]. In contrast, difluoroacetic acid [381-73-7] and perfluoroalkanoic acids have low acute toxicity.

The unusually high toxicity of fluoroacetic acid compared to the more highly fluorinated acids is due to its unique ability to interfere with the citric acid cycle, the oxidation pathway used for energy production from amino acids, fatty acids, and carbohydrates. Fluoroacetic acid enters the cycle at the same site as acetic acid and is converted to fluoroacetic acid analogously to the conversion of acetic acid to citric acid. The fluorocitric acid inhibits aconitase, a key enzyme for the breakdown of citric acid, with the result that the citric acid concentration soon rises to lethal levels [417]. Substances that yield fluoroacetic acid on biochemical oxidation, such as straight-chain, even-numbered, ω-fluoro alcohols or alkanoic acids, are also very toxic.

### 13.6. Other Classes

Simple perfluoroethers, and the oily oligomers of hexafluoropropylene oxide with modified end groups, have the low toxicity expected from their chemical inertness. Hexafluoropropylene oxide itself, a reactive substance, is moderately toxic to rats (4-h LC50, 3700 ppm) [418]. Several partially fluorinated ethers are used as anesthetics, e.g., Enflurane [13838-16-9], F₄CHOCH₂CHFCl, and Methoxyflurane [76-38-0], CH₃OCF₂CHCl₂. Their toxicity is low compared to that of most anesthetics (→ Anesthetics, General).

Perfluorinated tertiary aliphatic amines are inert both chemically and biologically. This is illustrated by perfluorotripropylamine [338-83-0]; in emulsion with perfluorodecalin [306-94-5], it has shown promise as a blood substitute in clinical trials [419].

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**Table 23. Toxicities of fluorinated olefins**

<table>
<thead>
<tr>
<th>Compound</th>
<th>CAS registry no.</th>
<th>Lethal conc., ppm</th>
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<tr>
<td>Vinyl fluoride</td>
<td>[75-02-5]</td>
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<td>[116-14-3]</td>
<td>40 000 (LC50)</td>
</tr>
<tr>
<td>Hexafluoropropene</td>
<td>[116-15-4]</td>
<td>3 000 (LC50)</td>
</tr>
<tr>
<td>Chlorotrifluoroethylene</td>
<td>[79-38-9]</td>
<td>1 000 (LC50)</td>
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* Inhalation by rats, 4-h exposure.
** Approximate lethal concentration.

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* Inhalation by rats, 4-h exposure.
** Approximate lethal concentration.
Fluorine substituents usually have little effect on the toxicity of aromatic compounds, whether monocyclic, polycyclic or heterocyclic [416].

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**Further Reading**


