Kirk-Othmer Encyclopedia of Chemical Technology.

FLUORINATED HIGHER CARBOXYLIC ACIDS

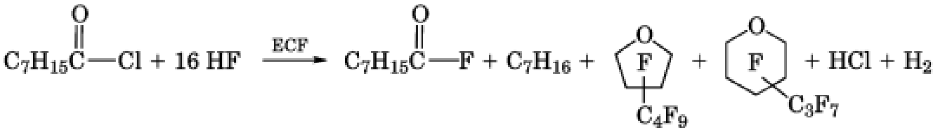
Perfluorinated carboxylic acids are corrosive liquids or solids. The acids are completely ionized in water. The acids are of commercial significance because of their unusual acid strength, chemical stability, high surface activity, and salt solubility characteristics. The perfluoroalkyl acids with six carbons or less are liquids; the higher analogues are solids (Table 1).

The higher members of the series decrease the surface tension of aqueous solutions well below the point possible with any type of hydrocarbon surfactant, although in practice because of their strong acid character and solubility characteristics, more commonly salts and other derivatives are employed. A 0.1% solution of $C_9F_{19}COOH$ has a surface tension of only 19 mN/m (dyn/cm) at 30°C (6).

0.0.1. Preparation

There are five methods for the preparation of long-chain perfluorinated carboxylic acids and derivatives: electrochemical fluorination, direct fluorination, telomerization of tetrafluoroethylene, oligomerization of hexafluoropropylene oxide, and photooxidation of tetrafluoroethylene and hexafluoropropylene.

Many of the perfluoroalkyl carboxylic acids were first prepared by the electrochemical fluorination (ECF) of the corresponding carboxylic acids (7). In ECF acid chlorides are converted to the corresponding perfluoroacid fluorides as shown in equation **1** for octanoyl chloride.



(1)

The principal by-products are cyclic perfluoroethers; the fluorine in the center of the ring denotes a perfluorinated ring structure. Octanoyl chloride gives only 10–15% of the perfluorooctanoyl fluoride (8), although the yield of fluorination can be improved by running under different cell conditions (9). As the chain length increases, formation of cyclic ethers and cleavage products becomes more prominent. In addition to cleavage and cyclization products, ECF results in isomerization of the carbon backbone in the product. The relative weight % of C_7F_{15} isomers in $C_7F_{15}COOH$ commercially produced by ECF is 78% linear, 9% internal branched, and 13% terminal (isopropyl) branched (4). Hydrolysis of the acid fluoride followed by removal of the fluoride ion and distillation yields the fluorinated acid.

Perfluorinated acid fluorides containing heteratoms are also accessible by ECF. Long-chain perfluorinated acid fluorides produced by ECF containing nitrogen (10–12), oxygen (13), and sulfur (14, 15) have been reported. The fluorinated mixed sulfonic acid–carboxylic acid precursors are also known. ECF of hydrocarbon sultones has led to formation of $FSO_2(CF_2)_nCOF$, where $n = 2, 3$ (16).

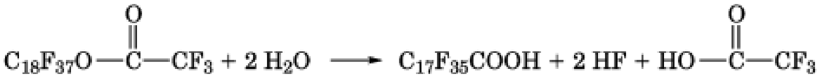
Direct fluorination involves the treatment of an appropriate hydrocarbon precursor dissolved in an inert liquid with fluorine gas to yield a perfluorinated precursor to a long-chain carboxylic acid. equations **2** and **3** illustrate the process for perfluorooctadecanoic acid (17).

Table 1. Properties of Perfluoroalkylcarboxylic Acids, $C_nF_{2n+1}COOH$[a]

Acid	CAS Registry Number	Bp, °C	Mp, °C	Density at 20°C, g/mL	Reference
perfluoropropanoic	[422-64-0]	96		1.561	1
perfluorobutanoic	[375-22-4]	120	−17.5	1.641	(1, 2)
perfluoropentanoic	[2706-90-3]	139		1.713	(1, 3)
perfluorohexanoic	[307-24-4]	157		1.762	(1, 3)
perfluorocyclohexane carboxylic[b]	[374-88-9]	168		1.789	(1, 2)
perfluoroheptanoic	[375-85-9]	175		1.792	(1, 2)
perfluorooctanoic	[335-67-1]	189	52–54	1.792	(1, 2, 4)
perfluorodecanoic	[335-76-2]	218			(1, 2)
perfluorotetradecanoic		270			(1, 5)

[a] Except where noted.
[b] Cyclo-$C_6F_{11}COOH$.


$$C_{18}H_{37}O{-}C({=}O){-}CF_3 + 37\,F_2 \longrightarrow C_{18}F_{37}O{-}C({=}O){-}CF_3 + 37\,HF \qquad (2)$$


$$C_{18}F_{37}O{-}C({=}O){-}CF_3 + 2\,H_2O \longrightarrow C_{17}F_{35}COOH + 2\,HF + HO{-}C({=}O){-}CF_3 \qquad (3)$$

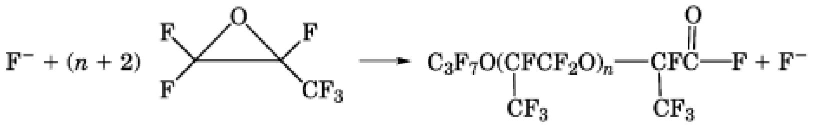
Unlike ECF, direct fluorination does not alter the carbon backbone; preparation of isomerically pure acids is possible (18). Both direct fluorination and ECF permit a great variety of structures to be made, but each method is better at certain types of structures than the other. Ether acids are produced in good yields, by direct fluorination (17), while ECF of ether-containing acids is fair to poor depending on the substrate. Despite much industrial interest, the costs and hazards of handling fluorine gas have prevented commercial application of this process.

Fluorinated carboxylic acids are also prepared by telomerization of tetrafluoroethylene, followed by oxidation (19–21).

$$C_2F_5I + n\,CF_2 \longrightarrow C_2F_5(CF_2CF_2)_nI \xrightarrow{SO_3} C_2F_5(CF_2CF_2)_{n-1}CF_2COOH \qquad (4)$$

This process yields a purely straight-chain acid of even carbon number. Typically, the value of n varies from two to six, and distillation yields the pure components. Du Pont pioneered the development of this technology. Allied has used hexafluoroacetone to produce telomer iodides containing the perfluoroisopropoxy end group, eg, $(CF_3)_2CFO(CF_2CF_2)_nI$ (22, 23). Dichromate oxidation (24) or ozonolysis (25) of $C_2F_5(CF_2CF_2)_nCH{=}CH_2$, derived from reaction of the telomer iodide shown in equation 4, gives the acid $C_2F_5(CF_2CF_2)_nCOOH$.

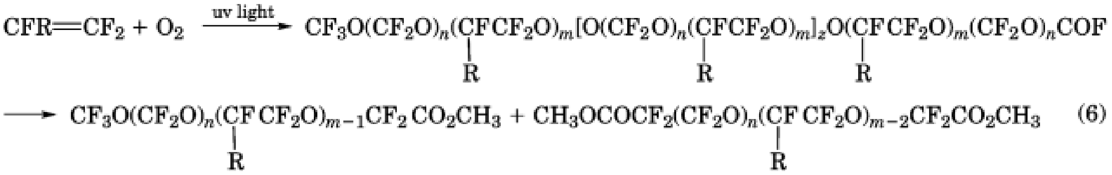
Fluoride ion-catalyzed oligomerization of fluorinated epoxides leads to long-chain ether-containing acids. equation **5** exemplifies this reaction for hexafluoropropylene oxide (HFPO). Tetrafluoroethylene oxide can undergo similar ring-opening reactions, but is seldom used because of its chemical instability. HFPO, however, is stable at room temperature in an anhydrous atmosphere, and in the absence of acid and base (26). Thermal decomposition occurs only at temperatures of 150°C or higher (27).



(5)

Hydrolysis of the acid fluoride, removal of fluoride ion, and distillation yield the perfluorinated acid. The value of n typically varies from one to six, depending on reaction conditions. Higher values of n are possible by employing more rigorous conditions. These acids are marketed by Du Pont under the trade name of Krytox acids. This process yields perfluoroether acids containing regular repeat units of perfluoroisopropoxy group and terminated by an alpha-branched carboxylate. The C_3F_7O end of the molecule can be varied by fluoride ion condensation of a perfluorinated acid fluoride with HFPO (26).

Photooxidation of tetrafluoroethylene (TFE) and hexafluoropropylene (HFP) yield peroxides that can be decomposed to esters and ultimately long-chain ether-containing carboxylic acids. equation **6** shows a simplified version of what occurs during photooxidation and workup (TFE R = F, HFP R = CF_3) (28, 29).



$$\mathrm{CFR{=}CF_2 + O_2 \xrightarrow{\text{uv light}} CF_3O(CF_2O)_n(\underset{\substack{|\\ R}}{C}FCF_2O)_m[O(CF_2O)_n(\underset{\substack{|\\ R}}{C}FCF_2O)_m]_zO(\underset{\substack{|\\ R}}{C}FCF_2O)_m(CF_2O)_nCOF}$$

$$\mathrm{\longrightarrow CF_3O(CF_2O)_n(\underset{\substack{|\\ R}}{C}FCF_2O)_{m-1}CF_2CO_2CH_3 + CH_3OCOCF_2(CF_2O)_n(\underset{\substack{|\\ R}}{C}FCF_2O)_{m-2}CF_2CO_2CH_3} \qquad (6)$$

The acid is obtained by saponification of the ester. Photooxidation of TFE in practice yields mostly difunctional ether acids. Photooxidation of HFP yields mostly the monofunctional ether acid, but yields significant quantities of inert materials that are difficult to separate out. The segments ($CFRCF_2O$) and (CF_2O) are randomly arranged in the chain. The random arrangement of these units in the chain is thought to be responsible for the exceptional low temperature properties of polymers and other materials derived from this route (30). Molecular weight of the resulting materials is determined by process control parameters and subsequent distillation.

0.1. Derivatives

In general, the reactions of the perfluoro acids are similar to those of the hydrocarbon acids. Salts are formed with the ease expected of strong acids. The metal salts are all water soluble and much more soluble in organic solvents than the salts of the corresponding hydrocarbon acids. Esterification takes place readily with primary and secondary alcohols. Acid anhydrides can be prepared by distillation of the acids from phosphorus pentoxide. The amides are readily prepared by the ammonolysis of the acid halides, anhydrides, or esters and can be dehydrated to the corresponding nitriles (31).

The ammonium salts, $C_nF_{2n+1}COONH_4$, where n equals 7 and larger, are particularly useful as emulsifiers in the polymerization of fluorinated olefin monomers such as tetrafluoroethylene or vinylidene fluoride. Their surface activity, low rate of chain transfer, and the highly fluorochemical nature of micelles formed in aqueous media are unique features that give them broad utility in the emulsification and polymerization of fluorochemical monomers (32).

Amines of the formula $C_nF_{2n+1}CH_2NH_2$ can be prepared by the lithium aluminum hydride reduction of the corresponding amide, hydrogenolysis of the nitrile, or diborane reduction of the amide (33). The analogous alcohols, $C_nF_{2n+1}CH_2OH$, can be prepared by high pressure hydrogenation of an appropriate ester (ie, $C_nF_{2n+1}COOCH_3$) over a barium oxide stabilized chromite catalyst, lithium aluminum hydride reduction of the acid or esters, or sodium borohydride reduction of the esters (34, 35) or acid fluorides (36, 37). Acrylate esters

Table 2. Properties of Perfluoroalkanedicarboxylic Acids, $HOOC(CF_2)_nCOOH$

n	Acid	CAS Registry Number	Mp, °C	Bp, $^\circ C_{kPa}$[a]	Bp of ester,[b] $^\circ C_{kPa}$[a]	Reference
1	perfluoromalonic	[1514-85-5]	117		$58–58_{1.2}$	(35, 42)
2	perfluorosuccinic	[377-35-8]	115–116	150_2	173	35
3	perfluoroglutaric	[376-73-8]	78–88	$134_{0.4}$	$100_{4.5}$	5
4	perfluoroadipic	[336-08-3]	134		$108–110_4$	(35, 43, 44)
6	perfluorosuberic	[678-45-5]	154–158		$156–159_{3.6}$[c]	45
8	perfluorosebacic	[307-78-8]			$102–113_{0.005}$	44
12	perfluorotetradecanedioic		191			35

[a] To convert kPa to mm Hg, multiply by 7.5.
[b] Methyl ester unless otherwise noted.
[c] Ethyl ester.

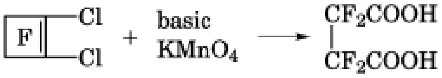
of the dihydroalcohols copolymerize with hydrocarbon acrylates and other monomers and have been found to impart resistance to a variety of organic liquids at elevated temperatures (38).

$$C_nF_{2n+1}CH_2OC(=O)C(R){=}CH_2$$

The surface energy of the homopolymers of these acrylates, 10.6 mN/m(dyn/cm), is among the lowest ever recorded (39), lower even than Teflon, 18.5 mN/m(dyn/cm) (40).

0.2. Perfluorodicarboxylic Acids

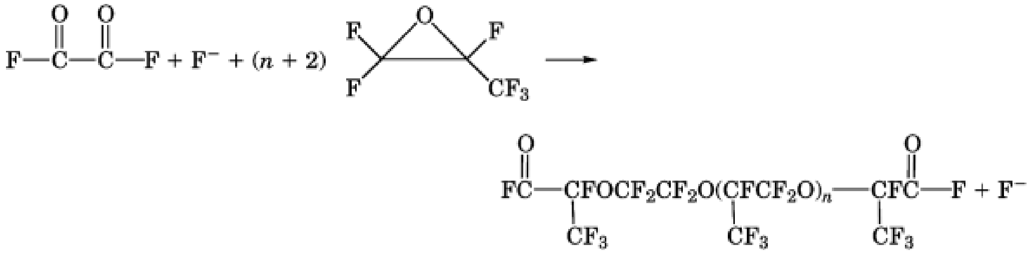
The lowest members of the series of perfluoroalkanedicarboxylic acids have been prepared and are stable compounds. They have been synthesized by oxidation of the appropriate chlorofluoroolefin as well as by electrochemical fluorination and direct fluorination. Perfluoromalonic acid is an oxidation product of $CH_2{=}CHCF_2CH{=}CH_2$ (21). Perfluorosuccinic acid has been produced by oxidation of the appropriate olefin (see eq. **7**) (5) or by electrochemical fluorination of succinyl chloride or butyrolactone (41) and subsequent hydrolysis.



(7)

Table 2 lists some typical properties of perfluoroalkanedicarboxylic acids and their esters along with references to their synthesis.

Fluorinated ether-containing dicarboxylic acidshave been prepared by direct fluorination of the corresponding hydrocarbon (17), photooxidation of tetrafluoroethylene, or by fluoride ion-catalyzed reaction of a diacid fluoride such as oxalyl or tetrafluorosuccinyl fluorides with hexafluoropropylene oxide (46, 47). equation **8** shows the reaction of oxalyl fluoride with HFPO. A difunctional ether-containing acid fluoride derived from HFPO contains regular repeat units of perfluoroisopropoxy group and is terminated by two alpha-branched carboxylates.


(8)

Fluorinated diacids offer a convenient method for introducing a perfluoro moiety into organic molecules. They are of potential interest in the preparation of polyamides and other fluorinated polymers. A detailed description of the perfluorocarboxylic acids and their derivatives has been published (1), and a review article on polyfluorinated linear bifunctional compounds has appeared (35).

Derivatives similar to those mentioned for the monofunctional fluorinated carboxylic acids have been prepared: tetrahydrodiols, tetrahydrodiamines, diamides, and diesters.

0.2.1. Toxicology and Safety

Because of their strong acidity, the perfluorinated carboxylic acids themselves are corrosive to the skin and eyes. Protective clothing, ie, gloves and face shield/safety glasses, should be employed when handling them (48, 49). Although perfluorooctanoic acid has been found to be corrosive to the eyes and severely irritating to the skin on contact, it is only slightly toxic on oral contact. The acute LD_{50} (rat) of perfluorooctanoic acid was found to be slightly less than 1000 mg per kg of body weight. However, in feeding studies the test animals suffered erosion of the gastric mucous membrane because of corrosivity of the acid (50). Perfluorodecanoic acid has been assessed for its genotoxic activity. It was found to test negative in the Ames test, Chinese hamster ovary gene mutation assay, sister chromatid exchange assay, chromosomal aberration assay, and *in vivo/in vitro* unscheduled DNA synthesis. Chromosomal aberrations were observed only when the S-9 fraction was incubated with perfluorodecanoic acid in the S-phase DNA synthesis assay (51).

The salts of the perfluorinated acids are not corrosive, so one is in a better position to discuss toxicity not related to corrosivity. The toxicity of the salts varies depending on the exact structure. The ammonium salt of perfluorooctanoic acid is nonirritating to the skin and moderately irritating to the eyes. Its oral toxicity is rated at moderate; the LD_{50} is 540 mg per kg of body weight (52). There has been some concern in the past that ammonium perfluorooctanoate was teratogenic. More recent results indicate that it is neither embryotoxic nor teratogenic (52, 53). It was not found to be mutagenic in either the Ames assay or one employing *Saccharomyces cerevisiae* D4 yeast (52). It also did not cause cell transformation in a mammalian cell transformation assay (53). Although ammonium perfluorooctanoate was fed to albino rats for two years, no compound-induced carcinogenicity was found in the study. There were statistically significant compound-related benign testicular tumors (52, 53). Prolonged or repeated exposure can cause liver damage which results in jaundice or tenderness of the upper abdomen (53). The dust from the ammonium salts of the perfluorinated acids is irritating to breathe and should only be handled in a well-ventilated area or preferably a hood.

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