Critical Review

Fluorinated Organics in the Biosphere

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The use of organofluorine compounds has increased throughout this century, and they are now ubiquitous environmental contaminants. Although generally viewed as recalcitrant because of their lack of chemical reactivity, many fluorinated organics are biologically active. Several questions surround their distribution, fate, and effects. Of particular interest is the fate of perfluoroalkyl substituents, such as the trifluoromethyl group. Most evidence to date suggest that such groups resist defluorination, yet they can confer significant biological activity. Certain volatile fluorinated compounds can be oxidized in the troposphere yielding nonvolatile compounds, such as trifluoroacetic acid. In addition, certain nonvolatile fluorinated compounds can be transformed in the biosphere to volatile compounds. Research is needed to assess the fate and effects of nonvolatile fluorinated organics, the fluorinated impurities present in commercial formulations, and the transformation products generated by biochemical processes and/or oxidation in the troposphere.

Introduction

Research investigating the environmental fate of halogenated compounds has largely focused on brominated and chlorinated organics. Fluorinated organics have received less attention because fewer are regulated, measurement of nonvolatile perfluorinated organics is more difficult, and they are perceived as more inert biologically and therefore less likely to have an impact on human health or the environment. Of course, the perception of "inertness" and its environmental significance are debatable: inert molecules tend to persist and accumulate, and they are more difficult to remediate. In addition, several fluorinated organics are subject to at least limited biotransformation under appropriate environmental conditions. Moreover, organofluorine molecules actually do exhibit significant biological effects, as inhibitors of enzymes, cell−cell communication, membrane transport, and processes for energy generation (*1*−*7*).

The chemistry of organofluorine molecules is unique because of the properties of fluorine. The fluorine atom has a van der Waals radius of 1.47 Å, a size more comparable to that of oxygen (1.52 Å) than to that of the other halogens (chlorine, 1.8 Å; bromine, 1.95 Å; iodine, 2.15 Å). Fluorine was once thought to be similar in size to hydrogen (1.2 Å), but it is now considered isosterically similar to a hydroxyl group (*8*). Compared to other halogens, fluorine is extremely electronegative having an electronegativity of 4.0 as compared to an electronegativity of 3.0 for chlorine and 2.8 for bromine (*9*). This high electronegativity confers a strong polarity to the carbon−fluorine bond. The carbon−fluorine bond also has one of the largest bond energies in nature. For monofluorinated alkanes, the carbon−fluorine bond is 25 kcal/mol stronger than that of the carbon-chlorine bond (*10, 11*). The strength of the carbon−fluorine bond contributes to the stability of fluorinated molecules. In fact, many fluorinated agrochemicals capable of enzyme inhibition are fluorine-stabilized analogues of the natural enzyme substrate. A dramatic illustration of the strength and stability of the C−F bond is monofluoroacetate, which can withstand boiling with 100% sulfuric acid without any defluorination (*12*). For many man-made fluorinated organics, such as the perfluorinated organics, stability is also probably related to the fact that their molecular structure is unlike anything currently known in nature.

Fluorine is the most abundant halogen in the earth's crust and ranks 13th in abundance among all elements (*13*). This may explain instances of natural organofluorine production. The best known of these natural organofluorine compounds is monofluoroacetate (MFA). MFA is produced by plants in the genus *Dichapetalum* as well as *Palicourea marcgravii*, *Acacia georginae*, *Gastrolobium grandiflorum*, and *Oxylobium* species (*14*). The West African plant *Dichapetalum toxicarium* also produces ω-fluorooleic acid, ω-fluoropalmitic acid, and possibly ω-fluorocaprate and ω-fluoromyristate (*15*). Certain fungi also produce fluorinated organics; *Streptomyces clavus* and *Streptomyces cattleya* produce the fluorine-containing antibiotic nucleocidin and 4-fluorothreonine, respectively (*14*−*16*). *S. cattleya* is also capable of producing monofluoroacetate (*16*). Finally, production of CFC-11, CFC-12, CFC-113, HCFC-21, HCFC-22, tetrafluoroethylene, and chlorotrifluoroethylene has been reported in volcanic gases and drill wells (*17, 18*). It is important to note that all of the known biologically produced fluorinated organics contain only one fluorine atom. This contrasts with many man-made fluorinated organics, which often contain many fluorine substituents and may even be fully fluorinated.

Because of their many useful properties, the number of man-made fluorinated organics has dramatically increased over the past few years. According to a report from Business Communications Company, Inc., sales of fluoropolymers (including surfactants, textile finishes, fluoroelastomers, and polymer resins) were expected to increase from $1.35 billion in 1994 to $1.76 billion by 1999 (*19*). Table 1 list several examples of aliphatic fluorinated compounds and their

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TABLE 1. Examples of Fluorinated Aliphatic Compounds and Their Applications

compound	molecular formula	application
	Volatile	
CFC-11	$CFCl_3$	refrigerant
CFC-12	CF_2Cl_3	refrigerant
HFC-134a	CF_3CH_2F	refrigerant
HCFC-22	CHF_2Cl	refrigerant
methoxyflurane	$CHCl_3CF_2OCH_3$	anaesthetic
Halothane	$CF_3CHClBr$	anaesthetic
perfluorotributylamine	$(C_4F_9)_3N$	foam blowing agent
	Nonvolatile	
carboxylic acid		
monofluoroacetic acid	CH_2FCO_2H	pesticide
trifluoroacetic acid	CF_3CO_2H	reagent
perfluorooctanoic acid	$C_7F_{15}CO_2H$	surfactant
sulfonic acid		
trifluoromethanesulfonic acid	CF_3SO_3H	catalyst/reagent
perfluorooctanesulfonic acid	$C_8F_{17}SO_3H$	surfactant
1*H*,1*H*,2*H*,2*H*-perfluorooctanesulfonic acid	$C_6F_{13}CH_2CH_2SO_3H$	surfactant
sulfonamide		
N-acetic-*N*-ethyl perfluorooctane sulfonamide	$C_8F_{17}SO_2N(CH_2COOH)(CH_2CH_3)$	surfactant
sulfluramid	$C_8F_{17}SO_2NH(CH_2CH_3)$	insecticide
miscellaneous		
polytetrafluoroethylene	$(-(CF_2CF_2)n-)$	Teflon
perfluoropolyether	$(-(CF(CF_3)CF_2O)n-)$	lubricant
Zonyl alcohol	$C_8F_{17}CH_2CH_2OH$	surfactant

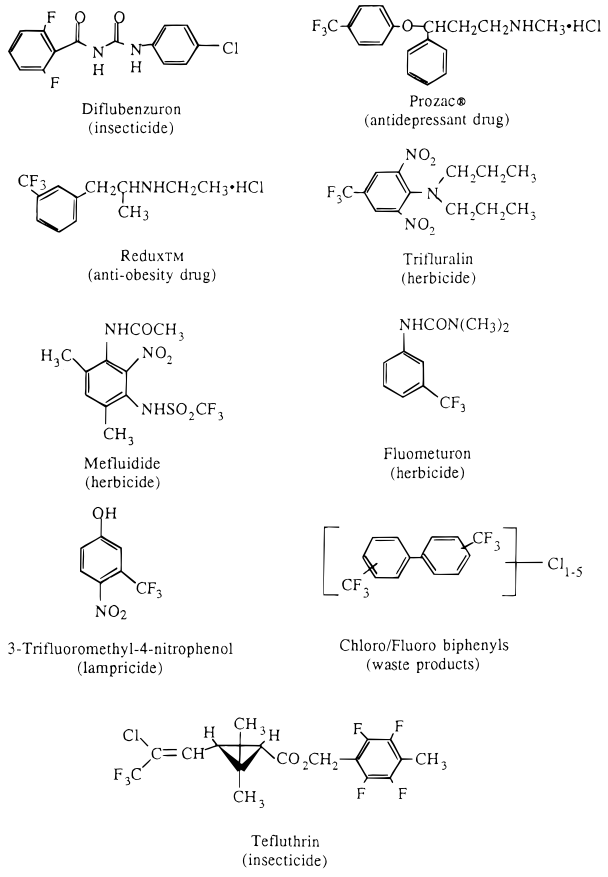


FIGURE 1. Examples of aromatic fluorinated compounds and their applications.

applications. Representative structures of some aromatic fluorinated compounds and their applications are illustrated in Figure 1. These or related compounds have been used in aerosol propellants, surfactants, refrigerants, plastics, anesthetics, pesticides, plant growth regulators, medicines, adhesives, fire retardants, and even blood substitutes (*2, 20*−*37*). Synthesis is accomplished using classical chemical or electrochemical processes, although production of novel fluorochemicals using microbial pathways is also possible (*38*).

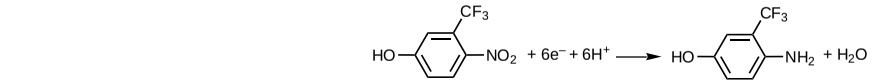
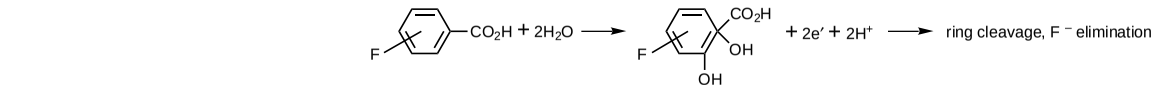
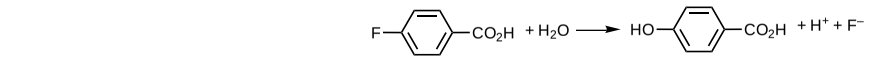
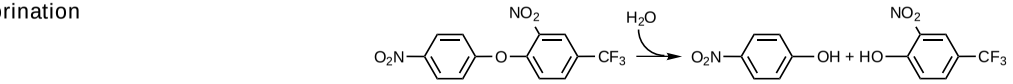
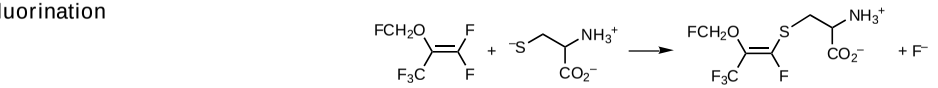
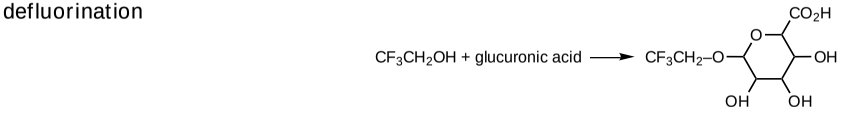
The environmental fate of fluorinated organics depends upon the structure of the molecule. Instances in which the carbon−fluorine bond is ruptured by direct attack are only known for a rarely observed reductive defluorination of tri-, di-, and monofluoroacetate (*39*), for hydrolytic defluorination of monofluorinated organics (*40, 41*), and for conjugation with cysteine (*42*). Reductive defluorination seems to require extreme and uncommon reducing conditions and so far has been observed only under methanogenic conditions that proved impossible to replicate (*43*). In addition, hydrolytic defluorination of carbon atoms with two or more fluorine substituents appears to be too slow to be of environmental significance (*44*). More often, transformation of highly fluorinated organics requires attack at functional groups or bonds attached to the fluorinated moiety. Attack on adjacent functional groups can be nucleophilic, oxidative, or reductive and can result in decarboxylation, desulfonation, deamination, and fluoride elimination (Table 2).

Broadly speaking, fluorinated organics can be classified as either volatile or nonvolatile. Volatile fluorinated organics consist primarily of partially or completely fluorinated alkanes, ethers, or amines. Fully halogenated fluorinated organics have very long lifetimes in the atmosphere and migrate to the stratosphere where they are destroyed by photolysis (*58*−*60*). By contrast, volatile fluorinated organics containing one or more hydrogen atoms are susceptible to oxidation by hydroxyl radicals in the troposphere, yielding fluoride, chloride, and partially oxidized organic species, the most significant of which is trifluoroacetic acid (TFA) (*61, 62*). TFA is also produced industrially, as are many other commercially important nonvolatile fluorinated organics.

Over the past 15 years, the number of fluorine-containing agricultural chemicals has grown from 4% to approximately 9% of all agrochemicals and has increased in number faster than non-fluorinated agrochemicals (*2*). These compounds are primarily used as herbicides (48%), insecticides (23%), and fungicides (18%) (*2*).

Given the widespread production and use of fluorinated organics, it is perhaps not surprising that organic fluorine has been detected in the blood of individuals from the general public as well as industrial workers (*63, 64*). For workers handling fluoroorganics, organic fluorine levels of 1.0−71 ppm

TABLE 2. Biological Transformation of Fluorinated Organics

presumed mechanism	example	environment or culture	ref
	Reduction		
direct defluorination	$CF_3CO_2H + 2e^- + H^+ \rightarrow CHF_2CO_2H + F^-$	anaerobic sediments	39
indirect defluorination	$CF_3CHBrCl + 2e^- + H^+ \rightarrow CF_2CHCl + F^- + Br^-$	mice and rats	45
no defluorination	$CFCl_3 + 2e^- + H^+ \rightarrow CFHCl_2 + Cl^-$	sulfate-reducing	46
		anaerobes and rats	47, 48
	Oxidation		
indirect defluorination	$CCl_2CF_2 + 4H_2O \rightarrow C_2O_4^{2-} + 2e^- + 8H^+ + 2F^- + 2Cl^-$	*P. putida* (dioxygenase)	49
	$C_8F_{17}C_2H_4OH + 5H_2O \rightarrow C_7F_{15}CO_2H + 12e^- + 14H^+ + 2F^- + 2CO_2$	adult male rats	50
		Pseudomonad (aerobic)	51
no defluorination	$CF_3CHBrCl + 2H_2O \rightarrow CF_3CO_2H + 2e^- + 4H^+ + Cl^- + Br^-$	mice	52
	$CFH_2COCO_2H + H_2O \rightarrow CFH_2CO_2H + 2e^- 2H^+ + CO_2$	cell-free extract of *D. cymosum* (plant)	53
	Nucleophilic		
direct hydrolytic defluorination	$CFH_2CO_2H + H_2O \rightarrow HOCH_2CO_2H + F^- + H^+$	Pseudomonad	54
		*Aureobacterium* (aerobic)	41
indirect defluorination decarboxylation, and hydrolysis	$CFH_2COCO_2H + H_2O \rightarrow CH_3CO_2H + F^- + H^+ + CO_2$	*E. coli* (pyruvate dehydrogenase)	55
hydrolysis, no defluorination		aerobic soils	56
conjugation with defluorination		rats	42
conjugation without defluorination		mice	57

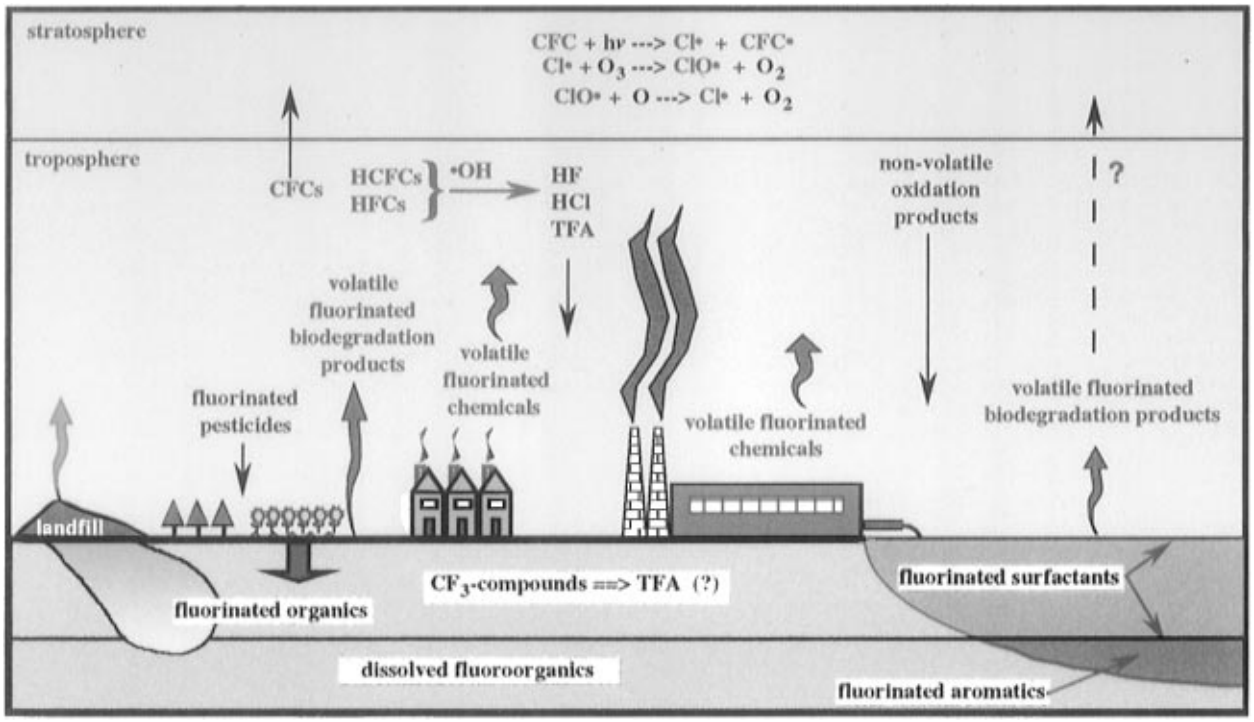


FIGURE 2. Biogeochemical cycling of fluorinated organic compounds.

TABLE 3. Fluorocarbon Production Worldwide

compd	molecular formula	estd atmos lifetime[a] (years)	total cumulative world production[b] (t × 10^3)	cumulative for years
HCFC-22	CHF_2Cl	6.7	3 600 ± 15	1970−1994
HFC-134a	CF_3CFH_2	14	86 ± 1	1990−1994
HCFC-141b	$CFCl_2CH_3$	7.1	139 ± 1	1990−1994
HCFC-142b	CF_2ClCH_3	17.8	193 ± 1	1981−1994
CFC-11	$CFCl_3$	60	8 580 ± 15	1931−1994
CFC-12	CF_2Cl_2	105	11 200 ± 20	1931−1994
CFC-113	$CF_2ClCFCl_2$	90	2 240 ± 9	1980−1994
CFC-114	CF_2ClCF_2Cl	185	185 ± 1	1980−1994
CFC-115	CF_3CF_2Cl	380	167 ± 1	1980−1994

[a] Refs 23 and 74. [b] Ref 75.

have been reported in their blood serum (*63*). Individuals who have not been exposed to industrial fluorochemicals had organic fluorine concentrations from 0.0 to 0.13 ppm. However, in another study of blood serum of 106 people, an average organic fluorine level of 25.7 ± 16.2 ppm was reported (*65*). Guy *et al.* suggest that there is widespread contamination of human tissues with organofluorine compounds derived from commercial sources such as perfluorooctanoic acid (*65*).

A general overview of processes influencing the distribution and cycling of fluorinated organics is provided in Figure 2. In the following sections, we elaborate on the general scheme illustrated in Figure 2, with sections on volatile and nonvolatile fluorinated organics, and we provide a critical review of the fate and the effect of these compounds in the biosphere.

Fate and Effects of Volatile Fluorinated Organics

Chlorofluorocarbons. Volatile fluorinated organics include the chlorofluorocarbons (CFCs), the hydrochlorofluorocarbons (HCFCs), the hydrofluorocarbons (HFCs), halothane and similar anesthetics, fluorinated ethers, and fluorinated amines. Chemical formulas, atmospheric lifetime estimates, and production values for some of the CFCs, HCFCs, and HFCs are provided in Table 3. CFCs have long been used as refrigerants and aerosols in industrial processes and domestic products. In 1974, CFCs were implicated as agents of depletion of stratospheric ozone by Molina and Rowland (*59*) and more recently as contributors to global warming (*66*). As a result, worldwide production of the CFCs is being phased out under the terms of the Montreal Protocol and its amendments. Nevertheless, CFCs continue to be released into the environment due to past production and continued use. For all practical purposes, the sole sink for CFCs is stratospheric oxidation. In aerobic aquatic environments, CFCs are recalcitrant, but they are transformed in anaerobic soils and sediments as well as anaerobic aquatic environments (Table 2) (*46*, *67*−*73*). The expected anaerobic degradation products are HCFCs and HFCs. However, this sink for CFCs is negligible as compared with stratospheric transformation.

Hydrochlorofluorocarbons (HCFCs) and Hydrofluorocarbons (HFCs). The phase out of CFC production and use inspired a major research effort to assess the environmental fate of CFC alternatives. Much of this effort was funded by AFEAS (Alternative Fluorocarbon Environmental Acceptability Study), a consortium of companies engaged in fluorocarbon manufacturing. The HCFC and HFC alternatives are one- and two-carbon aliphatics, similar in structure and physical properties to the CFCs, but containing one or more hydrogen atoms. The presence of hydrogen makes HCFCs and HFCs susceptible to tropospheric oxidation and therefore less likely to enter the stratosphere. In the troposphere, HCFCs and HFCs are oxidized by hydroxyl radicals, yielding HF, CO_2,

TABLE 4. Trifluoromethyl-Substituted Compounds and Their Applications

compd	application	compd	application	compd	application
HCFC 123	fluorocarbon	fluazinam	fungicide	flazasulfuron	herbicide
HCFC 124	fluorocarbon	flusulfamide	fungicide	fluazifop	herbicide
HFC 134a	fluorocarbon	flutolanil	fungicide	fluchloralin	herbicide
HFC 143a	fluorocarbon	furconazole	fungicide	flumetralin	herbicide
fluroxene	anaesthetic	furconazole-*cis*	fungicide	fluometuron	herbicide
halothane	anaesthetic	triflumizole	fungicide	fluoroglycofen	herbicide
methoxyflurane	anaesthetic	bromethalin	rodenticide	flurazole	herbicide
isoflurane	anaesthetic	flocoumafen	rodenticide	fluridone	herbicide
sevoflurane	anaesthetic	flupropadine	rodenticide	flurochloridane	herbicide
desflurane	anaesthetic	trifluoromethylnitrophenol	lampricide	flurprimidol	herbicide
bendroflumethiazide	antihypertensive	acrinathrin	insecticide	flurtamone	herbicide
dexfenfluramine	obesity	bifenthrin	insecticide	fluxofenim	herbicide
fenfluramine	anorectic	chlorfluazuron	insecticide	fomesafen	herbicide
fluoxetine	antidepressant	cyhalothrin	insecticide	furyloxyfen	herbicide
fluphenazine	antipsychotic	flucofuron	insecticide	haloxyfop	herbicide
flutamide	cancer	flufenoxuron	insecticide	lactofen	herbicide
fluvoxamine	obsessive compulsive disorder	π-fluvalinate	insecticide	mefluidide	herbicide
halofantrine	antimalaria	hydramethylnon	insecticide	nipyraclofen	herbicide
mefloquine hydrochloride	antimalaria	tefluthrin	insecticide	norflurazon	herbicide
nilutamide	cancer	triflumuron	insecticide	oxyfluorfen	herbicide
tolrestat	diabetes	acifluorifen	herbicide	perfluidone	herbicide
trifluoroethanol	reagent	benfluralin	herbicide	prodiamine	herbicide
trifluoroacetate	reagent	diflufenican	herbicide	profluralin	herbicide
trifluoromethane sulfonic acid	reagent	dinitramine	herbicide	thiazafluron	herbicide
trifluoroethane sulfonic acid	reagent	dithiopyr	herbicide	trifluralin	herbicide
trifluorobenzoate	reagent	ethalfluralin	herbicide	various dyes	textile colors

HCl (in the case of HCFCs), and in some cases trifluoroacetic acid (TFA) (*58, 62, 74, 76*). Rainfall is believed to be the primary mechanism for removal of TFA from the atmosphere (*61, 74, 77, 78*). In general, tropospheric oxidation is expected to be the most significant sink for the HCFCs and the HFCs.

A minor sink for HCFCs and HFCs is biochemical reduction or oxidation in aquatic systems. Lesage *et al.* (*70*) reported reductive transformation of HCFC-123a ($CHClFCF_2Cl$) to chlorotrifluoroethane under methanogenic conditions. Oremland *et al.* (*79*) have also reported reductive dechlorination of HCFC-123 (CF_3CHCl_2) to chlorotrifluoroethane under anaerobic conditions and degradation of HCFC-21 ($CHFCl_2$) under both aerobic and anaerobic conditions. Oxidative transformations mediated by monooxygenases are known, but these reactions proceed slowly as compared to the oxidation of chlorinated analogues, and they are not likely to influence the global HFC/HCFC balance (*80*−*82*). Chang and Criddle (*82*) reported oxidation of HCFC-22 (CHF_2Cl), with indirect evidence of product toxicity for HCFC-22 transformation and production of TFA from HFC-134a. Thus, if certain HCFC and HFC emissions are treated biochemically using monooxygenase-mediated systems, TFA is a likely transformation product (*80, 82, 83*).

Fluorinated Anesthetics. Several volatile compounds containing a trifluoromethyl group have been used or are currently being used as anesthetics (Table 4). Examples include fluroxene, halothane, sevoflurane, desflurane, and isoflurane. Of these, halothane is the most widely used; fluroxene is no longer used, and sevoflurane was only recently approved for use. TFA is a metabolite of nearly all of the trifluoromethyl-substituted anesthetics. Fluroxene ($CF_3CH_2OCHCH_2$) is metabolized to trifluoroethanol, which is further oxidized to TFA (*57, 84*). Oxidative metabolism of halothane yields TFA (*85*), while reduction yields 1,1-difluoro-2-chloroethylene and 1,1,1- trifluoro-2-chloroethane (Table 2) (*45, 86*). Desflurane ($CF_3CHFOCHF_2$) is also oxidized to TFA with release of fluoride (*87*). Sevoflurane ($(CF_3)_2CHOCFH_2$) undergoes base-catalyzed dehydrofluorination, in anesthesia machines, to produce the nephrotoxin FDVE ($CF_2C(CF_3)OCFH_2$). FDVE may also be present as a trace contaminant in sevoflurane. FDVE is biotransformed in rats to 3,3,3-trifluoro-2-(fluoromethoxy)propanoic acid and fluoride through a cysteine (glutathione) conjugate (Table 2) (*42*).

Anesthetics can be biotransformed by multiple pathways. Methoxyflurane ($CH_3OCF_2CHCl_2$), an anesthetic used in veterinary applications, is metabolized by two different pathways (*88*). The first is *O*-demethylation with release of fluoride to form dichloroacetic acid. The second is hydroxylation at the β-carbon with release of chloride and the formation of methoxydifluoroacetic acid.

Fate and Effects of Nonvolatile Fluorinated Organics

Trifluoromethyl-Substituted Organics. Table 4 lists some of the trifluoromethyl-substituted compounds produced and used today. Most of the fluorinated organics used in agricultural applications are trifluoromethyl-substituted aromatics (54.5%) (*2*). While several of these agrochemicals are reported to "dissipate" in soils, mineralization has not been demonstrated in most cases. The only reports of ring cleavage of trifluoromethyl-substituted aromatics were co-metabolism of 3- and 4-trifluoromethylbenzoates (*89*−*91*), yielding the common dead-end metabolite 7,7,7-trifluoro-2-hydroxy-6-oxohepta-2,4-dienoic acid (7-TFHOD). We were unable to identify fate studies that provide conclusive evidence as to the fate of the trifluoromethyl group. The following paragraphs summarize information on some of the better studied trifluoromethyl-substituted aromatics.

Trifluralin (1,1,1-trifluoro-2,6-dinitro-*N*,*N*-dipropyl-*p*-toluidine) is the most commonly used pre-emergent herbicide in the United States. According to the Agricultural Chemical Usage—1995 Field Crop Summary (*92*), approximately 6600 t of trifluralin was used on corn, cotton, soybean, and wheat crops in 1995. It should be noted that these are only application values for a limited number of crops and do not reflect the total amount of trifluralin used in the United States. In addition, global application values must be much higher.

Figure 3 illustrates the complex degradation pattern of trifluralin. Transformation proceeds by hydroxylation, N-dealkylation, nitro group reduction, conjugation, and cyclization, yielding a complex array of transformation products (*93*−*96*). Degradation of the trifluoromethyl group or ring cleavage has not been reported. Trifluralin had little effect on rumen microbe populations, as determined by volatile fatty acid production and endogenous gas evolution (*96*). However, the biological effects of trifluralin degradation products have not been well characterized.

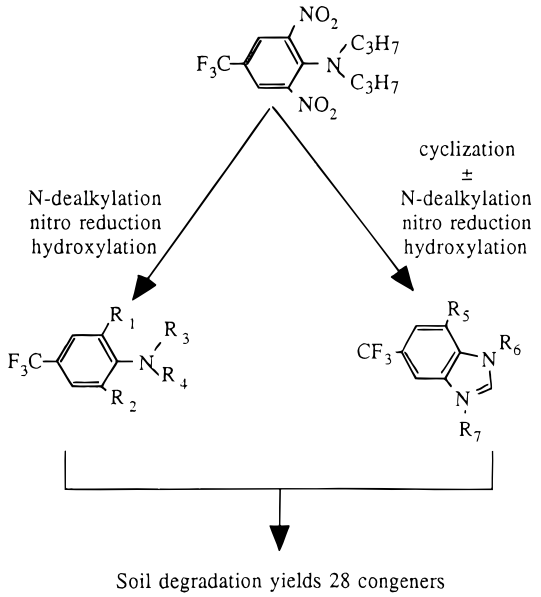


FIGURE 3. Pathways for transformation of trifluralin (*93*–*96*).

The pre-emergent herbicides norflurazon and fluridone, both trifluoromethyl-containing aromatics, inhibit carotenoid biosynthesis (*2*). This inhibition causes overoxidation of chlorophyll and subsequently the loss of the ability to photosynthesize. Flurprimidol, a fluorine-containing plant growth regulator, interferes with gibberellin (plant growth hormone) biosynthesis (*2*). Fluotrimazole and the structurally similar flutriafol are fungicides that weaken the cell membrane by blocking the carbon-1,4 α-demethylation step in ergosterol biosynthesis (*97*).

Several trifluoromethyl-substituted aromatics have been detected in sediments and in fish from the Niagara River and Lake Ontario (*26*). Various trifluoromethyl-substituted polychlorinated biphenyls, dichloro(trifluoromethyl)benzophenone, and dichloro(trifluoromethyl)difluorodiphenylmethane were found (Figure 1). These compounds originated at a dump site containing 55 000 t of halogenated waste, of which 10% was from the production of 4-chloro(trifluoromethyl)benzene (*26*). Dichloro(trifluoromethyl)difluorodiphenylmethane was present in fish at concentrations as high as 0.85 mg/g and in sediments from a creek near the dump site at concentrations as high as 35 mg/g. The trifluoromethyl-substituted PCBs are believed to bioaccumulate and partition into the sediment more effectively than non-fluorine-containing PCBs based on octanol/water partition coefficients (log K_{ow} from 6.8 to 9.0) (*26*).

The lampricide, 3-trifluoromethyl-4-nitrophenol (TFM), has been used since 1958 to combat the sea lamprey problem in the Great Lakes basin. It is placed in rivers and streams known to contain lamprey larvae. From 1991 through 1995, the 5-year average use of TFM was 41 t/year (active ingredient) (*98*). Nitro reduction of TFM has been observed under anaerobic conditions and in rats; however, no further degradation was observed (Table 2) (*47, 48*). Carey and Fox (*99*) observed defluorination of TFM by photolysis, but reported that only 15% degraded, based on the assumption that complete defluorination would yield 3 mol of fluoride. This assumption has not been adequately verified. Of interest is the recent report of a suite of trifluoromethyl-substituted impurities in technical grade TFM formulations (*100*). Impurities include trifluoromethyl-substituted phenols, diphenyl ethers, and dibenzo-*p*-dioxins. One or more of these impurities was responsible for inducing mixed-function oxygenase (MFO) activity in a class of detoxification enzymes, while pure TFM was not (*100*). Most likely these impurities originate during the industrial synthesis of TFM. It is likely that other technical grade fluorinated chemicals are also contaminated with impurities that may have toxicological properties unlike that of the main ingredient.

Fluorinated Aromatics. In 1994, the estimated world market for fluoroaromatics was 10 000 t (*101*). In general, these compounds are attacked oxidatively in aerobic environments, yielding transformation products that may or may not defluorinate. In some cases, these products are toxic.

Diflubenzuron (1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)-urea), a urea-based larvicide, inhibits chitin synthesis and the molting process in a broad spectrum of insects. Four fungal isolates (*Fusarium* sp., *Penicillium* sp., *Rhodotoruia* sp., and *Cephalosporium* sp.) are capable of degrading diflubenzuron (*102*). The proposed pathway for this transformation is through 4-chlorophenylurea and 2,6-difluorobenzoic acid. Although 4-chlorophenylurea is completely metabolized, 2,6-difluorobenzoic acid is persistent and lethal to soil microbes (*102*). Several investigators have shown that diflubenzuron affects non-target aquatic organisms (*103*).

Several bacterial isolates defluorinate fluorobenzoic acids (*41, 51, 91, 104*–*107*). The general pathway for degradation of fluorobenzoic acids is attack by a 1,2- dioxygenase followed by decarboxylation to yield toxic fluorocatechols; however, Oltmanns *et al.* (*41*) have demonstrated hydrolytic defluorination to yield hydroxybenzoic acid and fluoride (Table 2). Some of these fluorocatechols are subject to ring cleavage followed by defluorination.

Fluorinated Sulfonamides and Sulfonates. The perfluorinated sulfonamides and sulfonates are found in pesticides and surfactants. Perfluorinated surfactants are distinctly different from their hydrocarbon counterparts: whereas hydrocarbon chains are oleophilic and hydrophobic, perfluorinated chains are both oleophobic and hydrophobic. In addition, the perfluorinated alkyl chain is more "rigid" due to fluorine atoms on the molecule (*108*). This rigidness almost certainly interferes with molecule/enzyme interactions, protecting fluorocarbon molecules from biological attack. Solubilizing side moieties such as carboxylic acids, sulfonic acids, phosphates, and quaternary ammonium groups can change the solubility of perfluorinated surfactants (*21, 27*). In general, perfluorinated molecules resist defluorination and are only attacked at non-fluorinated side chains.

Sulfluramid (*N*-ethylperfluorooctanesulfonamide), a perfluorinated insecticide used to control cockroaches and ants, is deethylated to perfluorooctanesulfonamide in rats, dogs, and rabbit renal mitochondria (*4, 109*–*111*). Perfluorooctanesulfonamide has not been shown to undergo further transformation, but it is probably converted to the highly recalcitrant perfluorooctanesulfonic acid (PFOSA; $C_8F_{17}SO_3H$). Schnellman *et al.* (*4*) demonstrated that perfluorooctanesulfonamide and sulfluramid are potent uncouplers of oxidative phosphorylation in rabbit renal mitochondria. They also reported that the metabolite perfluorooctanesulfonamide was three times more potent than sulfluramid at uncoupling oxidative phosphorylation. Other fluorinated sulfonamides have demonstrated delayed action toxicity in red imported fire ants (*36*). This delayed action toxicity allows the insecticide to be applied in baits that are taken back to the colony by foraging members that distribute it throughout the ant colony.

Perfluorinated sulfonic acids are used as industrial surfactants and as catalysts depending on their chain length. Trifluoromethanesulfonic acid (triflic acid; CF_3SO_3H) is an excellent oligomerization/polymerization catalyst. Triflic acid is one of the strongest acids known, has great thermal stability, does not release fluoride in the presence of strong nucleophiles, and resists both oxidation and reduction (*33*). PFOSA also has excellent chemical and thermal stability. PFOSA is important commercially as a surfactant and as a precursor of other fluorinated surfactants (*112*).

PFOSA and triflic acid are resistant to biological attack. However, a surfactant similar to PFOSA, 1*H*,1*H*,2*H*,2*H*-perfluorooctanesulfonic acid (H-PFOSA; $C_6F_{13}C_2H_4SO_3H$), was partially degraded by a Pseudomonad under aerobic and sulfur-limiting conditions yielding 1−2 mol of fluoride/mol of H-PFOSA (*113*). The degradation of H-PFOSA produced several volatile fluorinated compounds that have not yet been identified. 2,2,2-Trifluoroethanesulfonic acid (TES; $CF_3CH_2SO_3H$) was also partially degraded with equimolar release of fluoride (*113*). Another fluorinated sulfonate, difluoromethanesulfonate (DFMS; CHF_2SO_3Na), was completely degraded by this Pseudomonad yielding stoichiometric amounts of fluoride (*113*). Transformation of DFMS, TES, and H-PFOSA was subsequently observed with *Bacillus subtilis* and *Escherichia coli* (*113*). However, *E. coli* was not capable of utilizing H-PFOSA. Evidence of H-PFOSA degradation was also observed in soil incubations. This and other work suggest that the transformation of fluorinated sulfonates requires the presence of hydrogen on the fluorinated alkyl chain.

Although PFOSA is resistant to metabolism, it is not biologically inactive. For example, PFOSA was shown to inhibit gap junction intercellular communication (GJIC) in rat liver epithelial cells cultured in vitro (*7*). In addition, Gadelhak (*6*) showed that PFOSA was an uncoupler of phosphorylation in rat liver mitochondria. Although PFOSA alone was not as potent of an uncoupler as perfluorooctanesulfonamide, when PFOSA was ion-paired with various monoamines, polyamines, and phospholipids, the effect of uncoupling was in some instances as high as that of perfluorooctanesulfonamide (*6*).

Fluorinated Alcohols. While some of the perfluorinated organics undergo limited biotransformation, none undergo extensive defluorination. Another example of a highly fluorinated molecule that has shown some limited defluorination is 1*H*,1*H*,2*H*,2*H*-perfluorodecanol. 1*H*,1*H*,2*H*,2*H*-Perfluorodecanol was metabolized first to 2*H*,2*H*-perfluorodecanoic acid and then to perfluorooctanoic acid (PFOA) in adult male rats (*50*). Hagen *et al.* (*50*) suggest that the overall reaction is oxidation of 1*H*,1*H*,2*H*,2*H*-perfluorodecanol with the production of PFOA and release of 2 mol of fluoride (Table 2). PFOA is metabolically stable in rats (*114*) and has been found in the blood serum of humans (*50*). The pesticide 1,3-difluoro-2-propanol is defluorinated to the toxic metabolite erythrofluorocitrate in rats, by a mixed-function liver oxidase (*28*). Trifluoroethanol has been used for several years in synthetic chemistry as a solvent and fluorinating agent. Trifluoroethanol and its glucuronic acid conjugate are found as toxic metabolite of the anesthetic fluroxene in mice (Table 2) (*57, 84*).

Fluorinated Carboxylic Acids. Fluorinated carboxylic acids can undergo hydrolytic defluorination, reductive defluorination, and decarboxylation. To date, however, significant defluorination has only been observed for hydrolytic attack of monofluorinated carboxylic acids. Compounds with more than one fluorine per carbon atoms are generally recalcitrant.

Monofluoroacetate (MFA) is one of the most toxic substances known, based on a lethal dose (LD_{50}) of 0.7−2.1 mg/kg for man (*115*). Its toxicity is due to "lethal synthesis" of fluorocitrate, which inhibits the aconitase enzyme of the citric acid cycle (*3*) although recent investigations implicate fluorocitrate as a "suicide" substrate instead of a competitive inhibitor (*1*). Given that certain plants can produce MFA, it is not surprising that several microorganisms can metabolize MFA. Pseudomonads and other bacteria as well as some fungi have been shown to grow with MFA and monofluoroacetamide (rat poison) as a carbon source aerobically (*40, 53, 105, 116−121*). The first step in degradation of MFA is a hydrolytic attack of the carbon−fluorine bond yielding glycolic acid (Table 2) (*40*). Many of the same organisms are also capable of growth on and defluorination of MFA under denitrifying conditions (*113*). Gregg *et al.* (*122*) demonstrated defluorination of MFA by genetically modified rumen bacteria *Butyrivibrio fibrisolvens*. This was accomplished by transferring the plasmid responsible for MFA defluorination from *Moraxella* sp. strain B into *B. fibrisolvens*. We know of only one other report of anaerobic MFA degradation. Visscher *et al.* (*39*) reported reductive dehalogenation of MFA to acetate, under methanogenic conditions, but this transformation was not reproducible in subsequent investigations (*43*). MFA has been shown to inhibit methanogenesis in anaerobic digestor sludge, rumen fluid, and freshwater mud (*44*).

Other fluorinated carboxylic acids of industrial significance include PFOA, perfluorodecanoic acid (PFDA), and TFA. No evidence of PFOA or PFDA transformation has been reported. Although, PFOA and PFDA are not metabolized, they have been found to inhibit GJIC in rat liver epithelial cells and human kidney epithelial cells at concentrations of 100 and 250 μM, respectively (*5*). The inhibition of GJIC has been implicated in tumor promotion during carcinogenesis (*123−125*), teratogenesis (*126*), and reproductive dysfunction (*127−129*).

A few examples of decarboxylation are known (Table 2). Meyer and O'Hagan have demonstrated decarboxylation of 3-fluoropyruvate to MFA by cell-free extracts of *D. cymosum* (*53*). In addition, Chauhan *et al.* (*130*) have demonstrated decarboxylation of TFA by *Azoarcus tolulyticus* TOL-4. An intensive international effort is currently underway to explore the fate and effects of TFA, and some results of this effort are summarized in the next section.

A Case History—Trifluoroacetic Acid

Three of the CFC alternatives (HCFC-123, HCFC-124, and HFC-134a) are expected to yield TFA as an atmospheric degradation product (Figure 2) (*61, 62, 74, 131*). A 1994 estimate of TFA levels in rainwater predicted 0.16 μg/L TFA in rainwater by the year 2010 (*132*). This estimate was based on 100% conversion of HCFC-123 and HCFC-124 and 20% conversion of HFC-134a. Because of local usage patterns, it is possible that TFA levels in urban areas could reach levels as high as 2−20 μg/L (*78*). However, recent estimates of HFC-134a conversion to TFA indicate only 7−20% conversion to TFA, so earlier estimates of rainwater concentrations are probably conservative (*133*). Even more significant, recent measurements of current TFA concentrations give levels of 0.1 μg/L in rainwater, 0.14 μg/L in surface waters, and 50 pg/m^3 in air (*134*). These data indicate that current average TFA levels in rainwater are already at the level previously predicted for the year 2010. These concentrations are higher than the level that would result from tropospheric degradation of man-made fluorinated organics, such as halothane and HFC-134a, at current production levels. An as yet unidentified source of TFA seems likely. The only known natural source of HCFCs is volcanoes (*17, 18*), but none of the HCFCs emitted by volcanoes are known to be transformed to TFA.

TFA is concentrated in plant leaves, and it has the potential to accumulate in ecosystems such as saline lakes, vernal and temporary rain pools, closed basin lakes, playa lakes, and aestival ponds and certain prairie lakes that exhibit high evaporative potential (*61, 77*). Environmental factors such as climate, geology, topography, biota, and time all affect evapoconcentration. The reported high levels of TFA in the Dead Sea (6.4 μg/L) (*134*) tend to confirm the potential significance of evapoconcentration.

TFA adsorbs weakly to most soils; therefore, soils are not expected to be a permanent sink for TFA. However, adsorption is favored in low pH soils that are enriched with iron and aluminum oxides (*135*). Photooxidation of TFA−iron complexes by near-UV radiation in clouds and the ocean was dismissed because of the low concentrations of iron in these environments (*136*). Sinks for TFA would include groundwater due to leaching from soils and vegetation due to

bioaccumulation (*136*). TFA can be degraded by the enzyme acetyl-CoA synthetase, but rates are low even with high concentrations of enzyme and substrate (>10 mM) (*44*). As a result, this pathway is unlikely in the environment where TFA is at nanomolar levels (*44*). Hydrolysis of TFA is also an unlikely mechanism for degradation due to the extreme stability of the carbon−fluorine bond and the shielding effect of three fluorine atoms on the carbon atom.

Even small quantities of TFA in solution can influence the pH of unbuffered solutions because TFA behaves like a strong inorganic acid at environmental pH (*136*). Bioaccumulation in animals is thought to be unlikely due to a low octanol/water partition coefficient ($\log K_{ow} = -4.21$) (*136*), but TFA can accumulate in plants through root uptake. Estimates of the concentration factor give approximately 10−32 times the soil concentration in plant leaves with virtually no degradation in the plant (*136, 137*). Vascular plants seem to be affected by TFA when bioaccumulation through roots to leaves occurs; however, little toxicity was shown for seed germination (*137*).

Toxicological tests have been performed on five species of algae. Three species (freshwater diatom *Navicula*, marine diatom, *Skeletonema*, and freshwater blue-green *Anabaena*) showed no toxic effects from TFA concentrations up to 1000 mg/L. The freshwater green alga *Chlorella* sp. also showed no toxicity up to 1200 mg/L. However, a second freshwater green alga, *Selenastrum capricornutum*, exhibited toxicity at concentrations as low as 360 μg/L (*137*). Bott and Standley (*138*) reported that TFA did not significantly affect the metabolism of acetate by microbial communities at environmentally expected concentrations. However, Visscher *et al.* reported inhibitory effects on methanogenic activity at TFA concentrations ≥1 μM (*39*). TFA appears to be nonmutagenic in bacteria (*139*).

The LD_{50} of TFA is reported to be between 200 and 400 mg/kg (oral exposure to rats), and sodium TFA is only slightly toxic when administered intraperitoneally to mice with no deaths at doses up to 5000 mg/kg (*57*). In addition, TFA does not interfere with the homeostasis of rat liver epithelial cell by inhibiting GJIC (*7*). As mentioned previously, TFA is a metabolite of the anesthetic halothane; however, it is unlikely that TFA is responsible for the hepatotoxicity that can result from inhalation of halothane (*140*). On the other hand, TFA is reported to have long retention time in the amniotic fluid of mice exposed to halothane or intravenous TFA (*52*), and this has prompted calls for studies to evaluate the possibility of fetal toxicity (*141*). It has been suggested that conjugation of the trifluoroacetyl moiety to hepatocytes may induce a immunological response resulting in halothane hepatitis (*142*).

Few reports of biodegradation of TFA are available. Visscher *et al.* (*39*) reported instances of reductive defluorination of TFA under methanogenic and sulfate-reducing conditions. TFA was sequentially defluorinated to difluoroacetic acid (DFA), MFA, and acetic acid, which was cleaved to yield methane. Under aerobic conditions, they also reported production of fluoroform (CHF_3) (*39*). These results were not subsequently reproducible, leading to a general conclusion that TFA is widely recalcitrant to biodegradation (*43*). Chauhan *et al.* (*130*) demonstrated that *A. tolulyticus* TOL-4 is capable of decarboxylating TFA. Cells were grown under denitrifying conditions with toluene as the carbon source and then incubated aerobically without nitrate. No fluoride or volatile fluorinated products were detected. The trifluoromethyl moiety was recovered in the non-ether-extractable fraction of the aqueous phase. As emphasized elsewhere in this review, the fate of the trifluoromethyl substituent is also unclear for other trifluoromethyl-substituted compounds. Photolysis of the trifluoromethyl moiety has been reported for trifluoromethylbenzoate and 3-trifluoromethyl-4-nitrophenol (*99, 143*). Taylor *et al.* (*143*) observed equimolar concentrations of fluoride from trifluoromethylbenzoate. Carey and Fox (*99*) observed defluorination of 3-trifluoromethyl-4-nitrophenol by photolysis, but only 15% degraded assuming complete defluorination. In both cases, partial defluorination of the trifluoromethyl moiety appears likely. Of particular interest is the fate of these trifluoromethyl groups, their photodegradation products, and the role of photolysis as a sink. In the absence of photolysis, it seems plausible that the trifluoromethyl group remains intact during biotransformation of trifluoromethyl-substituted aromatics, possibly contributing to the TFA load on the environment. Figure 4 illustrates a proposed pathway for oxidative degradation of trifluoromethyl-substituted aromatic compounds that would yield TFA. This pathway is a generalization of one proposed by Engesser *et al.* (*90*).

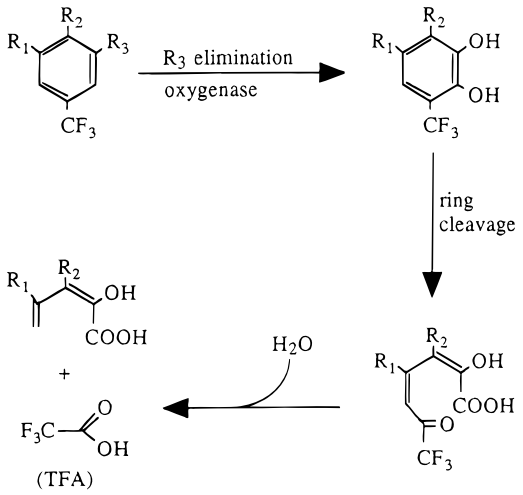


FIGURE 4. Proposed oxidative reaction sequence yielding TFA from trifluoromethyl-substituted aromatics.

Biogeochemical Cycling of Organofluorine Compounds

The products of partial transformations of organofluorine compounds are of interest with regard to their lifetimes in the environment and their effects on the biosphere directly or indirectly. Nonvolatile fluorinated compounds, such as sulfluramid and 1*H*,1*H*,2*H*,2*H*-perfluorooctanesulfonic acid, can be transformed in the biosphere to volatile fluorinated forms (*111, 113*), while volatile compounds can be transformed in the atmosphere to nonvolatile forms, such as TFA (*61, 62, 74, 131*). These observations raise the prospect of possible biogeochemical cycling of fluorinated compounds (Figure 2). The high concentration of TFA currently measured in rainwater is suggestive of as yet unknown sources of trifluoromethyl groups in the atmosphere. One potential source of trifluoromethyl groups in the biosphere is the trifluoromethyl-substituted aromatics. Clearly, there is a real possibility of biochemical conversion to TFA (Figure 4). To date, however, there is little evidence that these compounds can be degraded to volatile products that would enter the troposphere. Combustion of materials containing fluorinated organics might generate such volatile products. Biogeochemical cycling of fluorinated compounds is just now being discovered, and future research will no doubt illuminate these issues.

Summary

Organofluorine molecules are unique with regard to their physical, chemical, and biological properties, and as a result, they do not fit with the usual paradigm of chemicals of environmental concern. This paper has emphasized a number of key areas where major uncertainties exist concerning the distribution, fate, and biological behavior of organofluorine compounds in the environment. Because fluorinated organics are increasingly used in a multitude of

commercial and domestic products, it is reasonable to expect that they will be widely distributed in the biosphere. Unfortunately, production and usage rates for most of the these compounds are considered proprietary information by manufacturers and are generally not disclosed to the public (*144*). Disclosure of these values as well as research targeted at determining the environmental distribution of these compounds is needed. The stability that makes fluorinated compounds desirable for commercial use also makes them potentially significant environmental contaminants due to their persistence. Although there have been instances of partial defluorination of perfluoroalkyl chains, the ultimate fate and effect of perfluorinated substituents is unknown. Of concern is the fact that such substituents confer both chemical inactivity (recalcitrant) and biological activity. Further research is needed to evaluate the toxicological effects of these compounds, their transformation products, and impurities found in commercial formulations of fluorinated organics. Research is also needed to understand sorption and biochemical processes whereby these compounds might enter food chains or be altered to more toxic forms.

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Literature Cited

(1) Clarke, D. D. *Neurochem. Res.* **1991**, *16*, 1055.
(2) Cartwright, D. In *Organofluorine chemistry: Principles and commercial applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum Press: New York, 1994; pp 237−257.
(3) Peters, R. In *Carbon-fluorine compounds: Chemistry, biochemistry, and biological activities* (*A Ciba Foundation Symposium*); Associated Scientific Publishers: Amsterdam, 1972; pp 55−76.
(4) Schnellmann, R. G.; Randall, O. M. *Biochim. Biophys. Acta* **1990**, *1016*, 344.
(5) Deocampo, N. D.; Upham, B. L.; Trosko, J. E. *Fundam. Appl. Toxicol.* (*Suppl.*) **1996**, *30*, 1065.
(6) Gadelhak, G. G. Ph.D. Dissertation, Michigan State University, 1992.
(7) Upham, B. L. Michigan State University, E. Lansing, personal communication, 1996.
(8) Smart, B. E. In *Organofluorine Chemistry: Principles and Commercial Applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum Press: New York, 1994; pp 57−88.
(9) Pauling, L. *The nature of the chemical bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960.
(10) Smart, B. E. In *Molecular Structure and Energetics*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: Deerfield, FL, 1986; Vol. 3.
(11) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493.
(12) Saunders, B. C. In *Carbon-fluorine compounds; chemistry, biochemistry and biological activities* (*A Ciba Foundation Symposium*); Elliott, K., Birch, J., Eds.; Associated Scientific Publishers: Amsterdam, 1972; pp 9−32.
(13) Paul, E. A.; Huang, P. M. *Handbook of Environmental Chemistry*; Springer Verlag: Berlin, 1980.
(14) Harper, D. B.; O'Hagen, D. *Nat. Prod. Rep.* **1994**, *11*, 123.
(15) Suida, J. F.; DeBernardis, J. F. *Lloydia* **1973**, *36*, 107.
(16) Tamura, T.; Wada, M.; Esaki, N.; Soda, K. *J. Bacteriol.* **1995**, *177*, 2265.
(17) Isidorov, V. A. *Organic Chemistry of the Earth's Atmosphere*; Springer-Verlag: Berlin, 1990.
(18) Gribble, G. W. *Environ. Sci. Technol.* **1994**, *28*, 310.
(19) Business Communications Company Inc. *RC-193 Performance fluorine chemicals and polymers: Future prospects*; Business Communications Company, Inc.: Norwalk, CT, 1995.
(20) Carey, J. H.; Fox, M. E.; Schleen, L. P. *J. Great Lakes Res.* **1988**, *14*, 338.
(21) Allison, M. C. In *Industrial Applications of Surfactants* (*Special Publication 59*); Royal Society of Chemistry: London, 1987; pp 333−342.
(22) Banitt, E. H.; Coyne, W. E.; McGurran, K. T.; Robertson, J. E. *J. Med. Chem.* **1974**, *17*, 116.
(23) Elliot, A. J. In *Organofluorine chemistry: Principles and commercial applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum Press: New York, 1994; pp 145−157.
(24) Fielding, H. C. In *Organofluorine chemicals and their industrial applications*; Banks, R. E., Ed.; Ellis Horwood Ltd.: Chichester, 1979; pp 214−232.
(25) Filler, R. In *Organofluorine compounds in medicinal chemistry and biomedical applications*; Filler, R., Kobayashi, Y., Yagupolskii, L. M., Eds.; Elsevier: Amsterdam, 1993; pp 1−23.
(26) Jaffe, R.; Hites, R. A. *Environ. Sci. Technol.* **1985**, *19*, 736.
(27) Kissa, E. *Fluorinated surfactants: synthesis, properties, and applications*; Marcel Dekker, Inc: New York, 1994.
(28) Mead, R. J.; Feldwick, M. G.; Bunn, J. T. *Wildl. Res.* **1991**, *18*, 27.
(29) Moore, G. G. I.; Harrington, J. K. *J. Med. Chem.* **1975**, *18*, 386.
(30) Moore, G. G. I. *J. Org. Chem.* **1979**, *14*, 1708.
(31) Moore, G. G. I.; Lappi, L. R.; Bauchhuber, J. E.; Conway, A. C. *106th National Meeting of the American Chemical Society*; MEDI Abstracts: Chicago, IL, 1970.
(32) Rao, N. S.; Baker, B. E. In *Organofluorine chemistry: Principles and commercial applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum Press: New York, 1994; pp 321−336.
(33) Stang, P. J.; White, M. R. *Aldrichim. Acta* **1983**, *16*, 15.
(34) Trepka, R. D.; Harrington, J. K.; Robertson, J. E.; Waddington, J. T. *J. Agric. Food Chem.* **1970**, *18*, 1176.
(35) Trepka, R. D.; Harrington, J. K.; McConville, J. W.; McGurran, K. T.; Mendel, A.; Pauly, D. R.; Robertson, J. E.; Waddington, J. T. *J. Agric. Food Chem.* **1974**, *22*, 1111.
(36) Vander Meer, R. K.; Lofgren, C. S.; Williams, D. F. *J. Econ. Entomol.* **1985**, *78*, 1190.
(37) Yamanouchi, K.; Heldebrandt, C. *Chemtech* **1992**, *22*, 354.
(38) Ribbons, D. W.; Cass, A. E. G.; Rossiter, J. T.; Widdowson, D. A.; Williams, S. R.; Baker, P. B.; Martin, R. E. *J. Fluor. Chem.* **1987**, *37*, 299.
(39) Visscher, P. T.; Culbertson, C. W.; Oremland, R. S. *Nature* **1994**, *369*, 729.
(40) Goldman, P. *J. Biol. Chem.* **1965**, *240*, 3434.
(41) Oltmanns, R. H.; Muller, R.; Otto, M. K.; Lingens, F. *Appl. Environ. Microbiol.* **1989**, *55*, 2499.
(42) Spracklin, D. K.; Kharasch, E. D. *Chem. Res. Toxicol.* **1996**, *9*, 696.
(43) Oremland, R. S.; Matheson, L. J.; Guidetti, J. R.; Schaefer, J. K.; Visscher, P. T. *Summary of research results on bacterial degradation of trifluoroacetate* (*TFA*), *November, 1994−May, 1995*; Open File Report 95-OF 95-0422; USGS: Denver, CO, 1995.
(44) Emptage, M. *Proceedings of the 1994 AFEAS Workshop on the environmental fate of trifluoroacetic acid*; AFEAS Administrative Organization, SPA-AFEAS, Inc.: Miami Beach, FL, 1994.
(45) Gorsky, B. H.; Cascorbi, H. F. *Anesthesiology* **1979**, *50*, 123.
(46) Sonier, D. N.; Duran, N. L.; Smith, G. B. *Appl. Environ. Microbiol.* **1994**, *60*, 4567.
(47) Lech, J. J. *Toxicol. Appl. Pharmacol.* **1971**, *20*, 216.
(48) Bothwell, M. L.; Beeton, A. M.; Lech, J. J. *J. Fish. Res. Board Can.* **1973**, *30*, 1841.
(49) Wackett, L. P.; Sadowsky, M. J.; Newman, L. M.; Hur, H.-G.; Li, S. *Lett. Nature* **1994**, *368*, 627.
(50) Hagen, D. F.; Belisle, J.; Johnson, J. D.; Venkateswarlu, P. *Anal. Biochem.* **1981**, *118*, 336.
(51) Schreiber, A.; Hellwig, M.; Dorn, E.; Reineke, W.; Knackmuss, H. *Appl. Environ. Microbiol.* **1980**, *39*, 58.
(52) Ghantous, H.; Parnerud, I.; Danielsson, B. R. G.; Dencker, L. *Acta Pharmacol. Toxicol.* **1986**, *59*, 370.
(53) Meyer, J. J. M.; O'Hagan, D. *Phytochemistry* **1992**, *31*, 2699.
(54) Horiuchi, N. *Seikagaku* **1962**, *34*, 92.
(55) Leung, L. S.; Frey, P. A. *Biochem. Biophys. Res. Commun.* **1978**, *81*, 274.
(56) Tewfik, M. S.; Hamdi, Y. A. *Soil Biol. Biochem.* **1975**, *7*, 79.
(57) Blake, D. A.; Cascorbi, H. F.; Rozman, R. S.; Meyer, F. J. *Toxicol. Appl. Pharmacol.* **1969**, *15*, 83.
(58) W. M. O. *Global Ozone Research and Monitoring Project; Scientific Assessment of Stratospheric Ozone: 1989, Vol. I & II*; Report 20; World Meteorological Organization: Geneva, Switzerland, 1989.
(59) Molina, M. J.; Rowland, F. S. *Nature* **1974**, *249*, 810.
(60) Rowland, F. S.; Molina, M. J. *Rev. Geophys. Space Phys.* **1975**, *13*, 1.
(61) Tromp, T. K.; Ko, M. K. W.; Rodriguez, J. M.; Sze, N. D. *Nature* **1995**, *376*, 327.
(62) Wallington, T. J.; Hurley, M. D.; Ball, J. C.; Kaiser, E. W. *Environ. Sci. Technol.* **1992**, *26*, 1318.
(63) Belisle, J. *Science* **1981**, *212*, 1509.
(64) Gilliland, F. D.; Mandel, J. S. *Am. J. Ind. Med.* **1996**, *29*, 560.
(65) Guy, W. S.; Taves, D. R.; Brey, W. S. In *Biochemistry Involving Carbon-Fluorine Bonds*; Filler, R., Ed.; American Chemical Society: Washington, DC, 1976; Vol. 28.

(66) Fisher, D. A.; Hales, C. H.; Wang, W. C.; Ko, M. K. W.; Sze, N. D. *Nature* **1990**, *344*, 513.
(67) Semprini, L.; Hopkins, G. D.; Roberts, P. V.; McCarty, P. L. *EOS, Trans. Am. Geophys. Union* **1990**, *71*, 1324.
(68) Denovan, B. A.; Strand, S. E. *Chemosphere* **1992**, *24*, 935.
(69) Lovely, D. R.; Woodward, J. C. *EOS, Trans. Am. Geophys. Union* **1990**, *71*, 1236.
(70) Lesage, S.; Brown, S.; Hosler, K. R. *Chemosphere* **1992**, *24*, 1225.
(71) Hur, H.-G.; Sadowsky, M. J.; Wackett, L. P. *Appl. Environ. Microbiol.* **1994**, *60*, 4148.
(72) Lovely, D. R.; Woodward, J. C. *Environ. Sci. Technol.* **1992**, *26*, 925.
(73) Krone, U. E.; Thauer, R. K. *FEMS Microbiol. Lett.* **1992**, *90*, 201.
(74) Wallington, T. J.; Schneider, W. F.; Wornsnop, D. R.; Nielsen, O. J.; Sehested, J.; Debruyn, W. J.; Shorter, J. A. *Environ. Sci. Technol.* **1994**, *28*, 320.
(75) AFEAS. *Production, sales, and atmospheric release of fluorocarbons through 1994*; Alternative Fluorocarbons Environmental Acceptability Study (AFEAS): 1996.
(76) Franklin, J. *Chemosphere* **1993**, *27*, 1565.
(77) Tromp, T. K.; Rodriguez, J. M.; Ko, M. K. W.; Heisey, C. W.; Sze, N. D. *Proceedings of the 1994 AFEAS Workshop on the environmental fate of trifluoroacetic acid*; AFEAS Administrative Organization, SPA-AFEAS, Inc.: Miami Beach, FL, 1994.
(78) Schwarzbach, S. E. *Nature* **1995**, *376*, 297.
(79) Oremland, R. S.; Lonergan, D. J.; Culbertson, C. W.; Lovely, D. R. *Appl. Environ. Microbiol.* **1996**, *62*, 1818.
(80) Olson, M. J.; Reidy, C. A.; Johnson, J. T.; Pederson, T. C. *Drug Metab. Dispos.* **1990**, *18*, 992.
(81) DeFlaun, M. F.; Ensley, B. D.; Steffan, R. J. *Biotechnology* **1992**, *10*, 1576.
(82) Chang, W. K.; Criddle, C. S. *Biodegradation* **1995**, *6*, 1.
(83) Ma, T. G.; Ling, Y. H.; McClure, G. D.; Tseng, M. T. *J. Toxicol. Environ. Health* **1990**, *31*, 147.
(84) Blake, D. A.; Rozman, R. S.; Cascorbi, H. F.; Krantz, J. C. *Biochem. Pharmacol.* **1967**, *16*, 1237.
(85) Van Dyke, R. A. *Environ. Health Perspect.* **1977**, *21*, 121.
(86) Mukai, S.; Morio, M.; Fuujii, K.; Hanaki, C. *Anesthesiology* **1977**, *47*, 248.
(87) Sutton, T. S.; Kolbin, D. D.; Gruenke, L. D. *Anesth. Analg.* **1991**, *73*, 180.
(88) Mazze, R.; Hitt, B. *Drug Metab. Dispos.* **1978**, *6*, 680.
(89) Engesser, K. H.; Cain, R. B.; Knackmuss, H. *Arch. Microbiol.* **1988**, *149*, 188.
(90) Engesser, K. H.; Cain, R. B.; Knackmuss, H. *Arch. Microbiol.* **1988**, *149*, 198.
(91) Engesser, K. H.; Rubio, M. A.; Knackmuss, H. *Appl. Microbiol. Biotechnol.* **1990**, *32*, 600.
(92) NASS/ERS. *Agricultural Chemical Usage—1995 Field Crop Summaries*; Report Ag Ch 1 (96); USDA: Washington, DC, 1996.
(93) Golab, T.; Occolowitz, J. L. *Biomed. Mass Spectrom.* **1979**, *6*, 1.
(94) Erkog, F. U.; Menzer, R. E. *J. Agric. Food. Chem.* **1985**, *33*, 1061.
(95) Probst, G. W.; Golab, T.; Herberg, R. J.; Holzer, F. J.; Parka, S. J.; van der Schans, C.; Tepe, J. B. *J. Agric. Food. Chem.* **1966**, *15*, 592.
(96) Williams, P. P.; Feil, V. J. *J. Agric. Food. Chem.* **1971**, *19*, 1198.
(97) Worthington, P. A. In *Synthesis and Chemistry of Agrochemicals*; Baker, D. R., Fenyes, J. G., Moberg, W. K., Cross, B., Eds.; ACS Symposium Series 355; American Chemical Society: Washington, DC, 1987; pp 302−315.
(98) Great Lakes Fishery Commission, Ann Arbor, MI, personal communication, 1996.
(99) Carey, J. H.; Fox, M. E. *J. Great Lakes Res.* **1981**, *7*, 234.
(100) Hewitt, L. M.; Munkittrick, K. R.; Scott, I. M.; Carey, J. H.; Solomon, K. R.; Servos, M. R. *Environ. Toxicol. Chem.* **1996**, *15*, 894.
(101) Du Boisson, R. A. In *Organofluorine chemistry: Principles and commercial applications*; Banks, R. E., Smart, B. E., Tatlow, J. C., Eds.; Plenum Press: New York, 1994; pp 579−593.
(102) Seuferer, S. L.; Braymer, H. D.; Dunn, J. J. *Pestic. Biochem. Physiol.* **1979**, *10*, 174.
(103) Wilson, J. E. H.; Cunningham, P. A.; Evans, D. W.; Costlow, J. D. In *Environmental toxicology and risk assessment*; Hughes, J. S., Biddinger, G. R., Mones, E., Eds.; American Society for Testing and Materials: Philadelphia, 1995; Vol. 3.
(104) Engesser, K. H.; Auling, G.; Busse, J.; Knackmuss, H. *Arch. Microbiol.* **1990**, *153*, 193.
(105) Goldman, P. *Degradation of synthetic organic molecules in the biosphere*; National Academy of Sciences: Washington, DC, 1971; pp 147−165.
(106) Schlomann, M.; Fischer, P.; Schmidt, E.; Knackmuss, H. *J. Bacteriol.* **1990**, *172*, 5119.
(107) Schennen, U.; Braun, K.; Knackmuss, H. *J. Bacteriol.* **1985**, *161*, 321.
(108) Guo, W.; Brown, T. A.; Fung, B. M. *J. Phys. Chem.* **1991**, *95*, 1829.
(109) Grossman, M. R.; Mispagel, M. E.; Bowen, J. M. *J. Agric. Food. Chem.* **1992**, *40*, 2505.
(110) Manning, R. O.; Bruckner, J. V.; Mispagel, M. E.; Bowen, J. M. *Drug Metab. Dispos.* **1991**, *19*, 205.
(111) Arrendale, R. F.; Stewart, J. T.; Manning, R.; Vitayavirasuk, B. *J. Agric. Food. Chem.* **1989**, *37*, 1130.
(112) Abe, T.; Nagase, S. In *Preparation, properties, and industrial applications of organofluorine compounds*; Banks, R. E., Ed.; John Wiley & Sons: New York, 1982; pp 19−44.
(113) Key, B. D. Ph.D. Dissertation, Michigan State University, 1996.
(114) Ophaug, R. H.; Singer, L. *Proc. Soc. Exp. Biol. Med.* **1980**, *163*, 19.
(115) Atzert, S. P. *A review of sodium monofluoroacetate (compound 1080) its properties, toxicology, and use in predator and rodent control*; Special Science Report on Wildlife 146; U.S. Fish and Wildlife Service: Washington, DC, 1971.
(116) Goldman, P.; Milne, G. W. A. *J. Biol. Chem.* **1966**, *241*, 5557.
(117) Goldman, P.; Milne, G. W. A.; Keister, D. B. *J. Biol. Chem.* **1968**, *243*, 428.
(118) Kelly, M. *Nature* **1965**, *208*, 809.
(119) Meyer, J. J. M.; Grobbelaar, N.; Steyn, P. L. *Appl. Environ. Microbiol.* **1990**, *56*, 2152.
(120) Tonomura, K.; Futai, F.; Tanabe, O.; Yamaoka, T. *Agric. Biol. Chem.* **1965**, *29*, 124.
(121) Walker, J. R. L.; Lien, B. C. *Soil Biol. Biochem.* **1981**, *13*, 231.
(122) Gregg, K.; Cooper, C. L.; Schafer, D. J.; Sharpe, H.; Beard, C. E.; Allen, G.; Xu, J. *Bio/Technology* **1994**, *12*, 1361.
(123) Trosko, J. E.; Jone, C.; Chang, C. C. *Mol. Toxicol.* **1987**, *1*, 83.
(124) Holder, J. W.; Elmore, E.; Barrett, J. C. *Cancer Res.* **1993**, *53*, 3475.
(125) Yamasaki, H.; Naus, C. C. G. *Carcinogenesis* **1996**, *17*, 1199.
(126) Trosko, J. E.; Chang, C.; Netzloff, M. *Teratog. Carcinog. Mutagen.* **1982**, *2*, 31.
(127) Trosko, J. E.; Chang, C.; Madhukar, B. V. *Risk Anal.* **1994**, *14*, 303.
(128) Ye, Y.; Bombick, D.; Hirst, K.; Zhang, G.; Chang, C.; Trosko, J. E.; Akera, T. *Fundam. Appl. Toxicol.* **1990**, *14*, 817.
(129) Bergoffen, J.; Scherer, S. S.; Wnag, S.; Oronzi Scott, M.; Bone, L. J.; Paul, D. L.; Chen, K.; Lensch, M. W.; Chance, P. F.; Fischbeck, K. H. *Science* **1993**, *262*, 2039.
(130) Chauhan, S.; Tiedje, J. M.; Criddle, C. S. Manuscript in preparation.
(131) Edney, E. O.; Gay, B. W.; Driscoll, D. J. *J. Atmos. Chem.* **1991**, *12*, 105.
(132) Kotamarthi, V. R. *EOS, Trans. Am. Geophys. Union* **1994**, *75*, 137.
(133) Wallington, T. J.; Hurley, M. D.; Fracheboud, J. M.; Orlando, J. J.; Tyndall, G. S.; Sehested, J.; Mogelberg, T. E.; Nielson, O. J. *J. Phys. Chem.* **1996**, *100*, 18116.
(134) Frank, H.; Klein, A.; Renschen, D. *Nature* **1996**, *382*, 34.
(135) Driscoll, C. T. *Proceedings of the 1994 AFEAS Workshop on the environmental fate of trifluoroacetic acid*; AFEAS Administrative Organization, SPA-AFEAS, Inc.: Miami Beach, FL, 1994.
(136) Calamari, D. *Proceedings of the 1994 AFEAS Workshop on the environmental fate of trifluoroacetic acid*; AFEAS Administrative Organization, SPA-AFEAS, Inc.: Miami Beach, FL, 1994.
(137) Thompson, R. S. *Proceedings of the 1994 AFEAS Workshop on the environmental fate of trifluoroacetic acid*; AFEAS Administrative Organization, SPA-AFEAS, Inc.: Miami Beach, FL, 1994.
(138) Bott, T. L.; Standley, L. J. *Proceedings of the 1994 AFEAS Workshop on the environmental fate of trifluoroacetic acid*; AFEAS Administrative Organization, SPA-AFEAS, Inc.: Miami Beach, FL, 1994.
(139) Blake, D. A.; DiBlasi, M. C.; Gorden, G. B. *Fundam. Appl. Toxicol.* **1981**, *1*, 415.
(140) Stock, J. G.; Strunin, L. *Anesthesiology* **1985**, *63*, 424.
(141) Ball, J. C.; Wallington, T. J. *J. Air Waste Manage.* **1993**, *43*, 1260.
(142) Kenna, J. G.; Martin, J. L.; Satoh, H.; Pohl, L. R. *Drug Metab. Dispos.* **1990**, *18*, 788.
(143) Taylor, B. F.; Amador, J. A.; Levinson, H. S. *FEMS Microbiol. Lett.* **1993**, *110*, 213.
(144) Flynn, R. M. In *Kirk-Othmer Encyclopedia of Chemical Technology*, 4th ed.; Kroschwitz, J. I., Howe-Grant, M., Eds.; John Wiley & Sons: New York, 1994; Vol. 11, pp 525−534.

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