Naturally Occurring Organofluorines

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† This chapter is dedicated to the memory of Professor Richard E. Stoiber, 1911–2001, a Dartmouth College colleague and volcanologist who first discovered organic fluorine compounds in volcanic gases.

Although 3700 naturally occurring organohalogens are now known to exist, only relatively few contain fluorine. The presence of several fluoroalkanes in volcanic and other geothermal emissions is well documented, although exactly how these compounds are produced remains a mystery. Also unknown is the impact that these natural fluoroalkanes have on the global atmospheric budget compared to their anthropogenic counterparts, since the concentrations of the natural compounds vary widely depending on the source. The remarkable ability of a few plants to sequester and convert fluoride into the highly toxic fluoroacetate and other fluorocarboxylic acids is well recognized, and the mechanisms for their formation are becoming understood.

Keywords. Organofluorine fluoroacetate, Fluoroacetic acid gifblaar fluorocitrate, Fluorinated fatty acids, Nucleocidin, 4-Fluorothreonine, Fluoroacetaldehyde, Fluorite, Hydrogen fluoride, Fluoroalkanes, Trifluoroacetic acid, Tetrafluoroethylene, Tetrafluoromethane

1
Introduction

After several decades of skepticism from scientists and outright ridicule from environmental activists, the fact that nature produces organohalogen compounds is now well established and can no longer be ignored. Several reviews of naturally occurring organohalogens have appeared [6, 9, 14–22, 34, 59, 82, 90, 97]. While only about a dozen organohalogen compounds were recognized

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in the mid-1950s, the number today has grown to about 3650 as of December 2001 [23]. As summarized below most of these organohalogens contain chlorine or bromine (or both halogens). A far lesser number contain iodine or fluorine:

- Organochlorines: 2150
- Organobromines: 1850
- Organoiodines: 95
- Organofluorines: 30

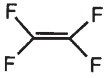
Two quite distinct sources of natural organohalogen compounds exist: biogenic and abiogenic. Biogenic organohalogens are produced by bacteria, fungi, lichen, marine plants and animals, terrestrial plants, several insects, and some higher animals including humans. Abiogenic organohalogens are formed in, or released during, geothermal processes such as volcanoes, biomass fires, and other geological processes.

Fluorine with a mean abundance of 950 ppm in the earth's crust is the 13th most abundant element and occurs mainly as fluorite (calcium fluoride) (45%), with the remainder in the minerals fluoroapatite, cryolite, and to a minor extent in topaz [30]. These inorganic fluorides are not readily converted into organic fluorine except in the circumstances discussed in Sect. 2. By comparison, chlorine with a mean abundance of 130 ppm in the earth's crust is the 26th most abundant element. For excellent previous reviews of naturally occurring organofluorine compounds, the reader is referred to reviews by Harper, O'Hagan and colleagues [32, 54, 65]. These articles are outstanding and treat natural organofluorine compounds in greater depth than in the present review.

2
Abiotic Production of Organic Fluorine Compounds

Despite the fact that fluorine, as fluoride salts and hydrogen fluoride, was well known to be abundant on earth, the existence of natural fluoroalkanes remained unknown until relatively recently. Harnisch and Eisenhauer estimate that 5×10^{21} g of calcium fluoride (fluorite) is present on earth [30]. For comparison the mass of the earth's crust is 2.4×10^{25} g. Interestingly, samples of the dark purple fluorite from Bavaria, called "Stinkspat" by local miners, when crushed exude the unmistakable smell of molecular fluorine! Chemists since the early 1800's such as Wöhler, Morissan, Becquerel, and Schönbein have made this observation [30]. This molecular fluorine may originate from calcium fluoride via decay of radioactive uranium and thorium which are also present in this mineral. Kranz was the first to propose this theory to account for the presence of fluoroalkanes in fluorites [46] (see below). Volcanoes are a major source of hydrogen fluoride along with a myriad of other gases. Both large, but infrequent, volcanic eruptions and passively degassing volcanoes are major sources of stratospheric and tropospheric hydrogen fluoride, respectively. An estimate of $0.06-6 \times 10^{12}$ g/year of volcanic hydrogen fluoride has been given [87]. For example, the volcanoes Hekla in 1970 [67], El Chichón in 1982 [98], Guatemala in 1978 [7], and Kilauea [66] all have produced and continue to produce large quantities of hydrogen fluoride in addition to hydrogen chloride. It is estimated that Kilauea on Hawaii, which has been continuously erupting since 1983, produces 180 tons of hydrogen fluoride daily. A new technique, "Passive Infrared Spectroscopy", has been developed for detecting gases in erupting volcanic gas plumes at a 17-km distance [47]. This study of the Popocatépetl volcano in Mexico over the period 1994–1997 has revealed that hydrogen fluoride is released to the extent of hundreds of tons per day. Hydrogen chloride is released on the order of thousands of tons per day. In contrast, sulfur tetrafluoride is only released to the extent of a few tons per day. It might be noted that Popocatépetl as of December 2000 was undergoing explosive eruptions. A related study of Mount Etna in 1997 revealed volcanic emission rates of 2.2 kg/s of hydrogen fluoride and 8.6 kg/s of hydrogen chloride, making Mount Etna the largest known point source of these two gases [10]. This latter study, which employed remote solar occultation spectroscopy, also summarized other volcanic eruptions and estimated the global emission rates of hydrogen fluoride from volcanoes and anthropogenic sources as 1.9 – 190 and 15.8 kg/s, respectively. Interestingly, hydrogen fluoride has recently been detected in interstellar space [60]. This exciting observation parallels the earlier discovery of hydrogen chloride, the only two halogen-containing molecules to be identified in interstellar space thus far.

Given the abundance of both hydrogen fluoride in volcanic gases and fluoride-containing minerals in the earth's crust, it perhaps should not be surprising that abiogenic fluoroalkanes are present in the environment. Stoiber et al. were the first to report in 1971 the presence of organofluorine compounds, including some CFCs, in the volcanic gases from the fumaroles of the Santiaguito volcano in Guatemala [83]. In addition to detecting methane, hydrogen fluoride, hydrogen chloride, and about 30 other organic compounds, these workers identified tetrafluoroethylene (**1**), hexafluoropropene (**2**), chlorodifluoromethane (**3**), chlorotrifluoroethylene (**4**), dichlorofluoromethane (**5**), trichlorofluoromethane (**6**), and 1,1,2-trichloro-1,2,2-trifluoroethane (**7**). The authors suggest that these compounds "probably resulted from reactions of hydrocarbons with hydrogen fluoride and hydrogen chloride, inorganic halides, or halide-containing minerals under high temperature conditions which prevailed at the source. The most likely sources of organic compounds are probably sediment or fossil soil layers beneath the volcano" [83]. Unfortunately, quantitative measurements were not carried out, but the organic compounds were separated and identified by gas chromatography-mass spectrometry.



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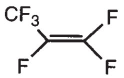

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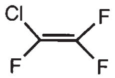
CHF_2Cl

3



4

$CHFCl_2$

5

$CFCl_3$

6

$CFCl_2CF_2Cl$

7

CF_2Cl_2

8

Me_2SiF_2

9

In extensive studies of the Kamchatka volcanoes on the Siberian peninsula, Isidorov and colleagues have also identified several organofluorines in these volcanic solfataric gases [36, 37, 39]. These workers reported **5**, **6**, dichlorodifluoromethane (**8**), and dimethyl difluorosilane (**9**). From one solfataric vent the concentration of these organofluorines exceeded background levels by 400 times. Isidorov estimates that 75% of the world's 2000 active volcanoes have the requisite mineral composition and geological configuration to produce organofluorine compounds such as **1**–**9**. He has proposed the set of reactions in Scheme 1 to account for the formation of fluoroalkanes [36, 37]. Methane, chloroform, and carbon tetrachloride are also present in these solfataric gases.

$$\begin{aligned}
CO + 3H_2 &\longrightarrow CH_4 + H_2O \\
CO_2 + 4H_2 &\longrightarrow CH_4 + 2H_2O \\
2CH_4 + 6HCl &\longrightarrow 2CHCl_3 + 3H_2 \\
CHCl_3 + HCl &\longrightarrow CCl_4 + H_2 \\
CHCl_3 + HF &\longrightarrow CHFCl_2 + HCl \\
2CCl_4 + 3HF &\longrightarrow CFCl_3 + CF_2Cl_2 + 3HCl
\end{aligned}$$

Scheme 1

These organofluorines have also been discovered in the gases from hydrothermal vents and thermal springs in the Kamchatka, Ashkhabad, and Tskhaltubo regions of the former Soviet Union [38, 40]. These organofluorines and numerous organochlorines, organobromines, and other organic compounds are released when certain rocks, shales, and minerals are crushed and processed in mining operations [6, 37, 40, 41]. In addition to **6** and **8**, the new naturally occurring trifluoromethane (**10**) [40] and polyfluorinated propane **11** [6] were identified in these investigations. In his study of carbonaceous black shales from Central Asia, Buslaeva concludes that these haloalkanes could arise from the interaction of alkanes "with halogens in the rocks at the temperatures and pressures characteristic for geological processes" [6]. Isidorov suggests that the world's mining industry, which processes hundreds of millions of tons of ore for the production of potassium salts alone, is a significant source of atmospheric halocarbons including 10–15 kilotons of chloroform and 0.1–0.15 kilotons of trichlorofluoromethane (**6**) and carbon tetrachloride [4].

CHF_3

10

$CF_3CF_2CF_2H$

11

CF_3CO_2H

12

It has been suggested that trifluoroacetic acid (**12**) has an as yet unidentified natural source since the concentration of this compound in rainwater is higher than the levels predicted from the degradation of anthropogenic compounds [43]. Trifluoroacetate is discussed in Chap. 5 by Scott Mabury.

Three recent studies of the composition of volcanic emissions have verified the earlier work of Stoiber and Isidorov. Thus, Wahrenberger et al. have identified both isomers of tetrachlorodifluoroethane, 1,2-difluoro-1,1,2,2-tetrachloroethane (**13**) and 1,1-difluoro-1,2,2,2-tetrachloroethane (**14**) from the Italy volcano Vulcano [94]. Another study by this same group has identified nine halocarbons from Vulcano and Kudriavy (Kuriles, Russia) including 1-chloro-1,1-difluoroethane (**15**), which is "HCFC-142b" [95]. The flux of **15** from these volcanoes is at least three orders of magnitude above tropospheric background concentrations.

CCl_2FCCl_2F

13

CCl_3CClF_2

14

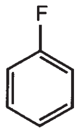
CF_2ClCH_3

15

Jordan et al. have examined the fumarole and lava gas samples from four volcanoes (Kuju, Satsuma Iwojima, Mount Etna, and Vulcano) [44]. They identified more than 300 organic compounds, including 135 that contain halogen. Of these, five are fluorinated: trichlorofluoromethane (**6**), a trifluoropropene (**16**), fluorobenzene (**17**), a tetrafluorobenzene (**18**), and a chlorofluorobenzene (**19**). In the cases of **16**, **18**, and **19** the exact structures were not determined. The authors conclude that volcanic CFC **6** contributes a negligible amount compared with the anthropogenic sources of this compound.

$C_3H_3F_3$

16



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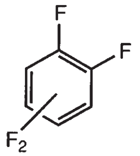

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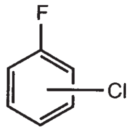


19

CF_4

20

Tetrafluoroethylene (**1**), which was previously identified in the Santiaguito volcanic gases and which is the anthropogenic precursor to the commercial polymer Teflon, has been discovered in natural fluorites along with tetrafluoromethane (**20**) [29, 30]. Sulfur hexafluoride is also present in these minerals. Tetrafluoromethane has a large anthropogenic source from the production of aluminum (15,000 tons/year) [84], but the authors estimate that approximately half of the current atmospheric burden of tetrafluoromethane has accumulated from natural sources since the lifetime of this compound is thought to be 50,000 years! Natural gas also contains significant traces of tetrafluoromethane that probably result from weak radiogenic sources in the lithosphere. This observed cold degassing from the Earth's crust is estimated to be 0.1–10 tons/year, which is negligible compared with current anthropogenic emissions [29]. Earlier Kranz suggested that these fluorite-containing organofluorines arise from reactions of molecular fluorine with encased organic material [46]. The formation of fluorine might occur as a result of the alpha radiation from the decay of uranium and thorium present in the fluorites [29, 46]. Harnisch and Eisenhauer have examined the gases from several volcanoes (Mauna Loa, Iilewa, Mount Erebus, Mount Etna, Vulcano, Mount Kuju, and Satsuma Iwojima) and find that they are not significant sources of either tetrafluoromethane or sulfur hexafluoride [30].

Although studies of biomass burning in North America and Canada have revealed the presence of high amounts of dichlorodifluoromethane (**8**) and other CFCs, the authors conclude that these compounds are solely anthropogenic [5, 33], since "dichlorodifluoromethane cannot be produced by fires" [33]. Hoekstra has recently disputed this conclusion on two grounds [35]. To quote Hoekstra, "The calculated global emission rate [from biomass burning] equals about half of the estimated total annual emission of dichlorodifluoromethane and the deposition of dichlorodifluoromethane will be evenly distributed around the globe because of its very long lifetime, while the area which is annually burned is relatively small" [35]. In other words, significantly more dichlorodifluoromethane is present in these forest fires than could be accounted for from the revolatization of preexisting dichlorodifluoromethane in the fuel.

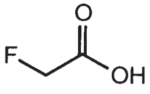
Both bromotrifluoromethane and bromochlorodifluoromethane have been identified in the atmosphere [68], but no natural source has been identified for these two compounds and they are presumed to be of anthropogenic origin.

Although the concentration of fluoride in seawater is only 1.4 ppm, the sponge *Halichondria moorei* contains potassium fluorosilicate (K_2SiF_6) to the extent of up to 11.5% (dry weight) [12]. Whereas this animal is able to sequester and concentrate fluoride, another sponge species from the same taxonomic order and in a nearby location contains no fluoride or fluorosilicate. Interestingly, potassium fluorosilicate is a potent inflammatory agent [12].

3
Biogenically Produced Organic Fluorine Compounds

3.1
Range of Structures

Nearly all of the known biogenic organofluorine compounds are fluorinated carboxylic acids. Fluoroacetic acid (**21**) (hereafter fluoroacetate, which is the form at physiological pH values) was the first such compound to be isolated and characterized nearly 60 years ago (see below), although methyl fluoroacetate (**22**) was synthesized in 1896 [85, 86]. Fluoroacetate itself was also first prepared in 1896 [79, 85].



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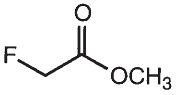
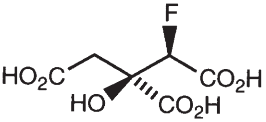


22

Fluoroacetate was first isolated by Marais from the South African plant "gifblaar", *Dichapetalum cymosum*, in 1943 [48, 49]. This plant was long recognized as being highly toxic to cattle and sheep in South Africa [13, 32, 54, 65]. For example, less than an ounce of the leaves of this plant will kill a sheep and one half a leaf was fatal to an ox [80]. Several other *Dichapetalum* species contain fluoroacetate, including *D. stuhlmanii* [25, 64], *D. toxicarium* [92], *D. heudelotii* [93], *D. michelsonii* [93], *D. guineense* [93], *D. venenatum* [93], *D. braunii* [64, 93], *D. macrocarpum* [93], *D. ruhlandii* [93], *D. barteri* [62], and *D. edule* [64]. Although plants in general contain only 0.1–10 ppm fluoride, *D. toxicarium* can sequester fluoride up to levels of 450 ppm in young leaves from an initial soil concentration of only 1–10 ppm [92]. The Tanzanian *D. braunii* can attain fluoroacetate levels of 7200 ppm in young leaves and 8000 ppm in the seeds [64]. Several analytical methods have been developed to assay plants and other biological materials for fluoroacetate. For example, ^{19}F Nuclear Magnetic Resonance Spectroscopy (NMR) can detect fluoroacetate at levels of 4 ppm in plants [3], and High Pressure Liquid Chromatography (HPLC) can detect this compound at levels down to 0.1 ppm [55].

Several other tropical and semitropical countries have plants containing fluoroacetate. The Australian *Acacia georginae*, widespread in Northwest Queensland and the Northern Territory covering 28,000 square miles, has caused serious sheep and cattle losses due to the presence of natural fluoroacetate [2, 58, 63]. The highly toxic Brazilian *Palicourea marcgravii*, known as "rat weed", contains fluoroacetate [8], as does the Australian *Gastrolobium grandiflorum*, which killed 2000 sheep in a single episode [50]. A few other fluoroacetate-containing plants are *Oxylobium parviforum* [24, 25], *Spondianthus preussii* [45], and *Cyamopsis tetragonolobus*, known as "Guar Gum" [91]. The latter plant is used medicinally in Finland following extraction of the fluoroacetate that is present in the gum at levels of 0.07–1.4 ppm [91]. Interestingly, none of these plants grows in high fluoride soil and there does not appear to be a strong correlation between soil fluoride and plant fluoroacetate [24, 25]. For a more extensive discussion of fluoroacetate in plants, the reader is directed to the Harper and O'Hagan review [32].

As we will see in the section on biosynthesis, the actual toxic metabolite may be, at least in part, fluorocitrate (**23**). Fluorocitrate is also present in commercial tea leaves (<30 ppm) and oatmeal (<62 ppm) [4, 75]. The latter also contains some fluoroacetate. These levels of fluorocitrate are apparently below toxic levels. The natural stereoisomer of fluorocitrate, and the only one to be toxic of the four stereoisomers, has the 2R,3R configuration as shown.



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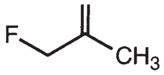

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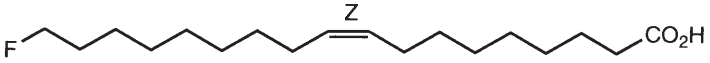
In their studies with *Acacia georginae*, Peters and Shorthouse observed fluoroacetone (**24**) in the volatiles from this plant [73, 74, 76]. However, O'Hagan and Harper have questioned this result and have suggested that this volatile organofluorine may in fact be fluoroacetaldehyde [65]. The alleged fluoroacetone was isolated as the 2,4-dinitrophenylhydrazone derivative. The melting points of these two 2,4-dinitrophenylhydrazones are sufficiently different to make a distinction possible. Interestingly, several of the other possible monohalo acetones and acetaldehydes have been isolated from red algae [18].

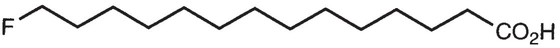
Seeds of the Sierra Leone shrub *Dichapetalum toxicarium*, also known as ratsbane, contain several fluorinated fatty acids. These have been characterized as 18-fluorooleic acid (**25**) [69–72], 16-fluoropalmitic acid (**26**) [96], 10-fluorocapric acid (**27**) [96], 14-fluoromyristic acid (**28**) [96], and *threo*-18-fluoro-9,10-dihydroxystearic acid (**29**) [31]. As we will see later, these even-numbered carbon chain fluorinated fatty acids are equally toxic as fluoroacetate, since they are metabolized by β-oxidation to fluoroacetate in accord with the theory of fatty acid oxidation.



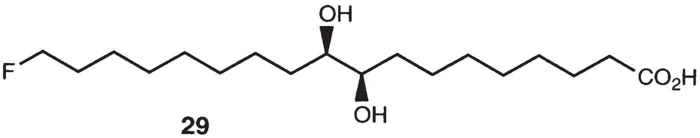
25 (18-fluorooleic acid)

26 (16-fluoropalmitic acid)

27 (10-fluorodecanoic acid)



28 (14-fluoromyristic acid)



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A more recent examination of the seed oil from *D. toxicarium* by Hamilton and Harper has uncovered six additional novel 16-fluorinated fatty acids [27]. These are 16-fluoropalmitoleic acid (**30**), 18-fluorostearic acid (**31**), 18-fluorolinoleic acid (**32**), 20-fluoroarachidic acid (**33**), 20-fluoroeicosenoic acid (**34**), and 18-fluoro-9,10-epoxystearic acid (**35**). The latter compound is strongly suspected of being present but not yet confirmed. The major fluoro fatty acids in the seed oil of *D. toxicarium* are 18-fluorooleic acid (**25**) (75%) and 16-fluoropalmitic acid (**26**) (15%). This study did not find 10-fluorodecanoic acid (**27**) or 14-fluoromyristic acid (**28**), in contrast to the earlier work by Ward and co-workers [96].

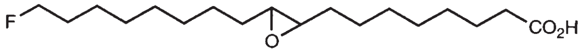
30 (16-fluoropalmitoleic acid)

31 (18-fluorostearic acid)

32 (18-fluorolinoleic acid)

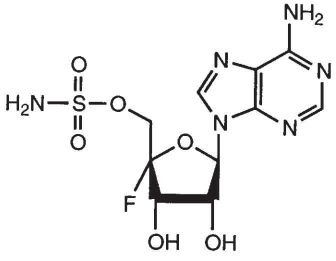
33 (20-fluoroarachidic acid)

34 (20-fluoroeicosenoic acid)



35 (18-fluoro-9,10-epoxystearic acid)

Although terrestrial plants provide most of the known natural organofluorines (see above), *Streptomyces* bacteria have furnished a few such compounds. The antibiotic nucleocidin (**36**) was isolated in 1957 from cultures of *Streptomyces calvus* [89], and its correct structure was finally determined in 1968 [56, 81]. Total synthesis confirmed the structure beyond all doubt [42]. This novel fluorinated nucleoside appears to be naturally derived as fluoride salts were not added to the culture medium. Unfortunately, recent attempts to re-isolate nucleocidin have been unsuccessful [51]. An excellent discussion of the discovery and structure elucidation of nucleocidin is given by Harper and O'Hagan D [32].



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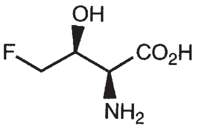

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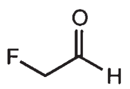

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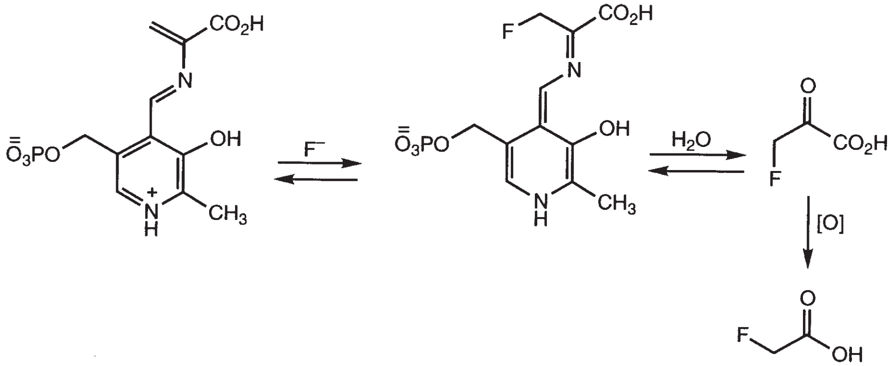
Not only does *Streptomyces cattleya* produce fluoroacetate but also the novel amino acid 4-fluorothreonine (**37**) [78]. This bacterium produces the antibiotic thienamycin. The structure of **37** as the 2S,3S isomer has been confirmed by total synthesis [1]. As will be discussed in the section on biosynthesis, Harper and co-workers have presented strong evidence that fluoroacetaldehyde (**38**) is the intermediate biosynthetic precursor of both fluoroacetate and 4-fluorothreonine in *S. cattleya* [57].

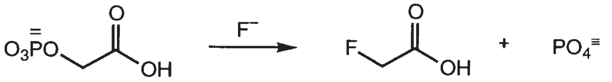
3.2
Biogenesis

Several biosyntheses have been proposed for the formation of fluoroacetate and the other natural fluorocarboxylic acids. These are discussed in detail by Harper and O'Hagan [32]. The first of these involves the well-known pyridoxal phosphate mechanism as proposed by Mead and Segal [52]. Although attempts thus far to support this mechanism have been unsuccessful [53], Harper and O'Hagan point out that these negative results do not necessarily invalidate this pathway (Eq. 1) [32].



(eqn. 1)

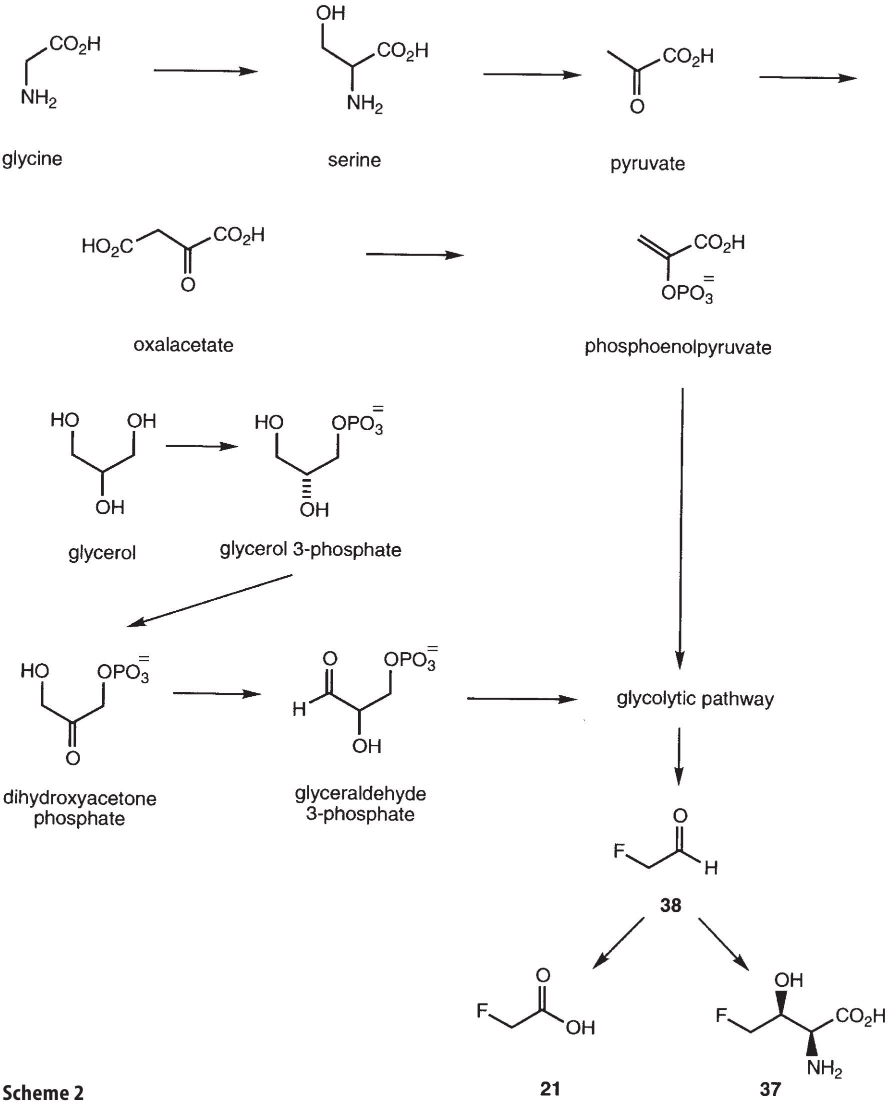
A second possible pathway involves fluoride displacing phosphate from phosphoglycolate in an S_N2 reaction (Eq. 2). Such nucleophilic displacement reactions involving α-substituted carbonyl substrates are much faster than those involving simple alkyl substrates [84]. For example, α-chloroacetophenone is a powerful lachrymator ("MACE") as are the haloacetones, except fluoroacetone. Thus far, evidence to support this mechanism has been negative [11].



(eqn. 2)

Other pathways that have been proposed are the generation of fluorophosphate as a fluoride carrier and fluorodecarboxylation of malonic acid by a fluoroperoxidase enzyme. The reader is referred to the review by Harper and O'Hagan for further discussion of these proposed pathways [32]. The research groups of Harper et al. [26, 28, 57, 61, 77] and Tamura et al. [88] have independently studied the biosynthesis of fluoroacetate and 4-fluorothreonine by *Streptomyces cattleya.* This research follows earlier biosynthetic work by Sanada et al. on the same organism [78]. The two most recent papers by Harper et al. summarize the current state of knowledge regarding the biosynthesis of these fluorinated metabolites [28, 57]. Thus, glucose, glycerol, serine, β-hydroxypyruvate, and glycine are all incorporated into fluoroacetate and 4-fluorothreonine to various degrees. The most recent evidence indicates that fluoroacetaldehyde (**38**) is converted to both fluoroacetate and 4-fluorothreonine in *Streptomyces cattleya* [57]. Additional evidence with deuterated glycerols indicates that a common fluorinating enzyme for both of these compounds is present in this organism [28, 61]. Based on these results, a plausible biosynthetic pathway is illustrated in Scheme 2 [65], although it may not be the exclusive one.

The longer chain carboxylic acids **25**–**35** are presumably biosynthesized from fluoroacetic acid via fluoroacetyl CoA and malonyl CoA by the usual fatty acid biosynthesis pathway [32]. Interestingly, these long-chain fluorinated fatty acids



Scheme 2

are equally toxic as fluoroacetic acid since they appear to be degraded to the latter by the fatty acid degradation pathway [13]. The toxicity of fluoroacetic acid is discussed in detail by others [13, 32, 54, 65].

4
Unresolved Issues and Future Developments

While there is no disputing the presence of organic fluorine compounds in volcanic and hydrothermal emissions, the factors that determine the concentrations of these chemicals and the mechanisms of their formation remain largely not understood. Are these compounds formed in reactions between a carbon source and hydrogen fluoride or a fluoride mineral such as fluorite? What is the source of carbon? What is the source of chlorine in the chlorofluorocarbons? Lightning induced forest and brush fires rage regularly across our planet. Is biomass burning a significant source of organic fluorine compounds? What are the natural sources and quantities of tetrafluoromethane? How significant are the reactions shown in Scheme 1 for the formation of the chlorofluoroalkanes? What are the natural sources of trifluoroacetate? These and other questions regarding naturally occurring abiotic organic fluorine compounds remain unanswered. The presence of fluoroacetate, the most toxic low molecular weight natural compound known in numerous plants, is extraordinary. Although much is known about the biogenesis of fluoroacetate and the other natural fluorinated carboxylic acids, the full story has yet to be told. Why are some animals relatively impervious to the toxicity of fluoroacetate? What is the mechanism of toxicity? Can the fluorine-containing antibiotic nucleocidin be reisolated? Will other organic fluorine natural products be discovered along with the growing number of other naturally occurring organohalogen compounds?

5
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