

Is organofluorine sustainable?

Life cycle consideration of the manufacture and use of organofluorine compounds

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Résumé	Considérations sur le cycle de vie de production et d'utilisation des dérivés organiques fluorés Les composés organiques dérivés du fluor font partie intégrante de notre société. Cependant, de nombreuses inquiétudes concernant leur toxicité ainsi que leur persistance dans l'environnement ont amené à reconsidérer l'usage d'entre eux. Les risques et bénéfices liés à ces composés tout à fait uniques sont analysés dans cet article et le cycle de vie des principaux types de dérivés organiques fluorés y sont étudiés afin d'analyser les principales sources d'inquiétudes.
Mots-clés	Composés organofluorés, fluoro-aromatiques, composés perfluorés, synthèse, cycle de vie, toxicité, environnement, développement durable.
Abstract	Organofluorine compounds have become integrated into the infrastructure of modern society. However, concerns over toxicity and persistence in the environment are causing reassessment of the use of many industrial organofluorine products. A risk-benefit analysis of these unique compounds and life-cycle studies of the major types of organofluorine compounds are conducted in this article in order to identify and address the real issues of concern.
Keywords	Organofluorine compounds, manufacturing, fluoro-aromatics, perfluorinated compounds, sustainability, life cycle, environment.

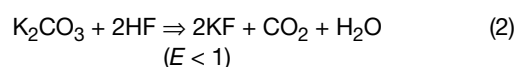
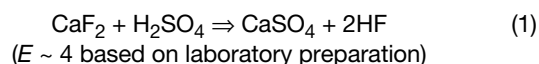
Organofluorine compounds – from selectively fluorinated aromatics in electronics and pharmaceuticals to perfluorinated compounds in textiles and coatings – have become integrated into the infrastructure of modern society [1]. However, concerns over toxicity and persistence in the environment are causing a careful reassessment of the use of many industrial organofluorine products [2]. Increasingly demanding legislation will threaten the continued use of many of these through enforced authorisation and restrictions, while pressure from environmental action groups and non-governmental organisations will encourage users to seek less controversial alternatives [3]. It is vital that we seek a more rational risk-benefit analysis of these unique compounds and look at the full life-cycles of the major types of organofluorine compounds so that we can identify and seek to address the real issues of concern.

The simplest form of a life-cycle for a chemical involves feedstocks, production, use and fate. Transportation is not included here but with increasing fuel costs and concerns over CO₂ emissions, it is clearly important when the total environmental footprint is to be calculated. The first stage for manufacture of any organofluorine chemical will involve the extraction of calcium fluoride and its conversion to hydrogen fluoride. Subsequent processes to produce the required fluorinating agent will depend on the particular product. Pre-processing to produce the organic substrate must also be considered and in some cases may be very resource-intensive and wasteful (*figure 1*).

We need not be concerned about the long-term availability of HF: there are known world reserves of fluorspar

circa 400 × 10⁶ tonnes, with an annual world production of *circa* 5 × 10⁶ tonnes in 2003 [4]. Any future shortfalls in fluorspar as a precursor for HF are likely to be met from fluorosilicic acid by-product in phosphoric acid production. Similarly, the other major chemicals used *en route* to the principle fluorinating agents (F₂, HF, KF and other metal fluorides) may be considered as sustainable. Furthermore, their price is not expected to increase at a particularly fast rate in the foreseeable future although the market distortions resulting from regional industrial growth in Asia are unpredictable.

A number of chemical metrics are now in place to help assess the efficiency and environmental impact of chemical processes [5]. One of the most popular of these is the *E-factor*, the mass ratio of by-products to desired product. The pre-processing steps for converting the mineral into useful fluorinating agents are energy-intensive and wasteful with poor mass efficiency (equation 1). Extending this pre-processing to the preparation of KF, a commonly used fluorinating agent for facile nucleophilic substitutions, only slightly increases the *E-factor* (equation 2).



Let us consider the organic stream of the pre-processing stage in the organofluorine life-cycle (*figure 1*): long-term sustainability could be under threat due to diminishing

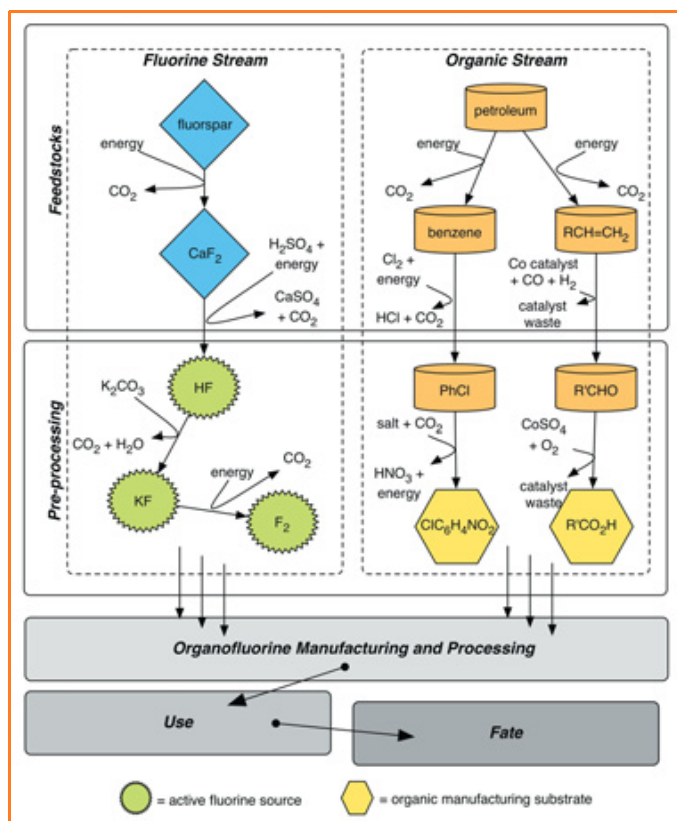
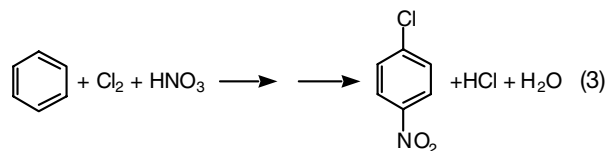


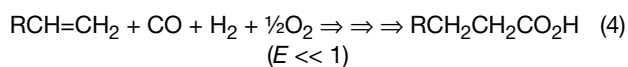
Figure 1 - Critical factors in the life cycle of organofluorine chemical products.

petroleum reserves and the increasing costs of petrochemicals in a highly competitive market. The high premium for organofluorine compounds compared to most other uses for these raw materials will help offset this. The processes which convert the petrochemical feedstocks into substrates for fluorination may be hazardous, wasteful and energy-consuming, and are liable to resource limitations. For example, conversion of benzene into 4-chloronitrobenzene (equation 3) does not have an especially large E -factor, yet this hides the hazards of handling chlorine and strong mineral acids, and the potentially explosive aromatic nitration process, for which it is more difficult to develop a system of metrics.



($E \sim 3$, based on laboratory preparation)

In contrast, the conversion of an alkene to a carboxylic acid is an efficient, catalytic, low-waste process as reflected in the low E -factor (equation 4).



In the second stage of the life-cycle, the intermediate organic substrate is reacted with the fluorinating agent as shown with typical examples in figure 2 (nucleophilic aromatic fluorination, i.e. "halex", and electrochemical perfluorination).

Selective fluorination of an aromatic substrate can be accomplished by a number of routes, principally halogen exchange (halex, as shown here in the examples), Balz-Schiemann and direct fluorination. A fourth route based on oxidative fluorination using CuF_2 is also worth considering and has been described as "environmentally friendly", although a full and comparative consideration of resources and process including energy is required [6]. A superficial analysis of the four routes is shown in table 1. Despite the inherent atom efficiency advantages of direct fluorination, health and safety issues take precedent, although these are more difficult to quantify. Thus the halex route has traditionally been the method of choice, despite its need for a multi-stage substrate activation process (indicated in the organic stream in figure 1) and the slow, energy-demanding and high waste fluorination step (figure 2a). Halex technology in particular is accessible to many chemical manufacturing facilities and, with an open global market, low labour costs in emerging nations, and variable degrees of regulatory control, this will continue to be an attractive option for manufacturing molecules with such high added value. Safer direct fluorination methods such as the use of intensive processing (for example *microreactors* which work with very small reaction volumes [7]) should be taken up by specialised industries that can handle highly reactive reagents such as F_2 . This will require construction of new plant, but we can expect return on this investment as the costs of waste disposal and energy continue to escalate.

Perfluorination can be accomplished by electrochemical fluorination (ECF) processes. The advantage of this technology from a lifecycle consideration is the use of HF, the closest useful fluorinating agent to the raw material (figure 1). The most obvious process advantage is that the reaction is one step although fluorination of the functional (carboxyl) group may require a final hydrolysis (to yield an acid) or other process to give the desired product. There are, however, process restrictions, with a limited choice of anode materials (normally nickel alloys) and there are major safety concerns over the use of highly corrosive and toxic anhydrous HF as well as risks associated with the formation of by-products such as the explosive OF_2 (from fluorination of any water present). The two major flaws from an environmental impact consideration are:

(i) low reaction yields with by-products from degradation, rearrangement and other reactions catalysed by the highly acidic medium;

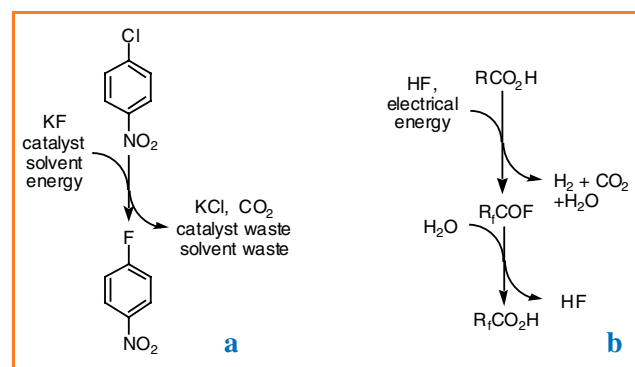
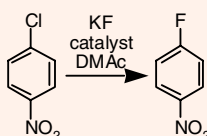
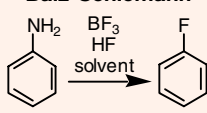
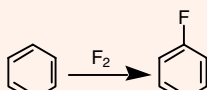
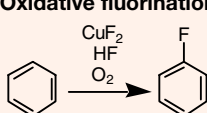


Figure 2 - Critical factors in the second stage of the life-cycles for representative organofluorine chemicals (R_f = perfluorinated alkyl group).

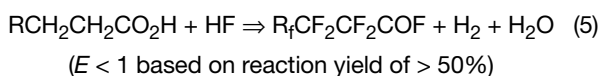
a: halex reaction; b: electrochemical perfluorination.

Table 1 - Evaluation of four common methods for manufacturing fluoroaromatics.

Route	Pre-processing (organics)	Atom efficiency	Waste	Health and safety	Energy	Other costs	Complexity
Halex 	Considerable: 2 stage route from hydrocarbon	low-moderate	salt solvent catalyst	medium	high	moderate	three steps from resource
Balz-Schiemann 	Considerable: 2 stage route from hydrocarbon	low-moderate	salt lost solvent	high (unstable intermediate)	medium	moderate-high	four steps from resource
Direct fluorination 	none, except where substituents are required	high	acid (neutralised to form salt)	high	medium (cooling)	high (F ₂ resistant reactor)	one/two steps from resource
Oxidative fluorination 	none, except where substituents are required	high (if Cu is catalytic)	acid (neutralised to form salt)	medium	high	moderate-high (HF resistant reactor)	one/two steps from resource

(ii) high energy requirements of electrochemical synthesis.

If the reaction efficiency is improved, then the actual atom efficiency is very good since H₂ and water are the only by-products (equation 5):



High energy consumption and health and safety issues remain as major concerns but given the above properties and effects the product can achieve, these may be considered worthwhile even in the light of more rigorous environmental assessment.

The final stages in the organofluorine chemical life-cycle, use and fate, have been the subject of considerable recent attention and ever-stricter chemicals legislation including REACH will continue to place highly functional synthetic chemicals such as organofluorine compounds under the spotlights [8].

Selectively functional compounds that contain small numbers of fluorine atoms are physiologically active and indeed, many of the products on the market are sold for use in pharmaceutical and agrochemical applications. A remarkable number of the new products in these sectors are partially fluorinated, and fluoroaromatics are particularly abundant here. Some compounds are extremely toxic, notably those containing the -CH₂F group such as monofluoroacetates which have been extensively used to control rodents and vertebrate pests. While some uses may be questionable when health hazards are considered alongside life-cycle analysis, medicinal applications seem secure for the foreseeable future. The substitution of less active substances with modern fluorine-containing drugs has generally led to a marked reduction in dosage which itself is likely to be beneficial in terms of resource, risk, transport, packaging and fate, although other factors must be taken into consideration. Lightly fluorinated molecules can be

expected to break down in the environment, releasing fluoride and forming less active organic compounds [9].

Ironically, it is the physiologically inert, less active, highly and perfluorinated chemicals that are proving to be less sustainable in use. The long-term stability and inertness of perfluorinated compounds gave them their special value, yet now these same properties are endangering their continued use. This has led to a number of bans, restrictions and phase-outs. The global warming potential of perfluorocarbons is extremely high – 10,000 times that of CO₂ – and it is believed they can persist in the atmosphere from 2,000-50,000 years [10]. This has resulted in considerable restrictions in use, for example through a voluntary agreement by the semiconductor industry in the USA [11]. Heavily fluorinated chemicals including perfluorocarboxylic acids, sulfonates and amides have been found to be highly persistent in the environment and in many cases to be bioaccumulative and toxic. There is an enormous volume of literature reporting for example, the detection of such substances in humans, mammals and other species [12]. Indeed, it has been suggested that the most notorious of these, perfluorooctane sulfonate (PFOS), is one of the most “apocryphal examples of 20th Century experimentation” [13]. 3M surprised the world in 2000 when they announced their elimination of PFOS-related products despite the buoyant growth in the market for the “Scotchguard” products as, in subsequent assessment, the US Environmental Protection Agency expressed concern over the combined persistence, bioaccumulation and toxicity of these chemicals [14]. It seems unlikely that perfluorinated and highly fluorinated chemicals will survive the enormous negative publicity and enforced restrictions, and future applications are likely to be very specialized.

The remarkable and complex effect of fluorination has led to an unparalleled diversity of molecular properties – from the highly active to the highly inert. In these environmentally

conscious days, the choice of molecule for any application must be based on sustainability and environmental impact as well as performance and cost. Apart from the general concern over the long-term availability of some petrochemical feedstocks, there are few obvious concerns over the sustainability of organofluorine compounds. The environmental impact of the manufacturing processes is sometimes high, yet could be improved by investment in new manufacturing plant. The critical issues for organofluorine compounds are very much use and fate related. For lightly-fluorinated compounds, high activity coupled with relatively facile degradation pathways may be expected to give a favourable risk-benefit balance: the large effect for low dose (be it in pharmaceuticals, agrochemicals, or electronic materials) and acceptable environmental impact is a desirable combination of factors for future growth. In contrast, highly fluorinated compounds offer excellent properties and product durability but only at what appears to be an unacceptably high environmental cost, making their future viability seem much less secure.

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