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Organofluorine chemistry

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The fascination of organofluorine chemistry stems from the fact that, apart from a few exceptions, molecules containing carbon–fluorine bonds do not occur in nature and so the field is entirely ‘man-made’.

Many fluoro-organic molecules are encountered by the general public on a daily basis, but this is probably not widely recognized even by the scientific community. For example, the chlorofluorocarbon (CFC) refrigerants, now being replaced by the ozone-friendly hydrofluorocarbons (HFC), are present in everybody’s kitchens. Anaesthesia has been revolutionized by fluorinated anaesthetics, and many pharmaceuticals, including the well-known antidepressant Prozac[®], owe their enhanced biological activity to the presence of fluorine atoms in their structures. Fluoropolymers have found widespread use in applications ranging from non-stick coatings on cookware (Teflon[®], Du Pont), waterproof clothing (Goretex[®], W. L. Gore), and as high-performance lubricants. In fact, supersonic flight and space travel would probably not have been possible without the use of perfluorinated materials that can withstand such harsh operating environments. Fluorinated materials prepared many years ago continue to find new applications: for instance, perfluorocarbon fluids, originally prepared in the 1930s, are being developed as imaging agents for the diagnosis of heart disease and as oxygen-carrying ‘blood substitutes’.

Given the success of organofluorine chemistry in such a wide variety of applications, the future of the subject is very bright. This essay outlines some of the fascination of studying the chemistry of fluoro-organic molecules, gives a brief overview of how organofluorine chemistry has helped shape some of the remarkable developments of the 20th century, and provides a personal view of the role of fluorine chemistry in the initial stages of the new millennium.

Keywords: organic chemistry; organofluorine;
elemental fluorine; selective fluorination

1. Introduction

Organic molecules containing fluorine atoms are used on a daily basis by everybody in the developed world. Many of the astonishing scientific developments of the past 50 years have been made possible by organofluorine compounds, although this is probably not widely recognized even by the scientific community, and, in fact, it is unusual for even a university chemistry degree course to include any organofluorine chemistry on its syllabus.

Naturally occurring molecules largely consist of carbon, hydrogen, nitrogen and oxygen atoms, and all molecules containing carbon frameworks possess many carbon

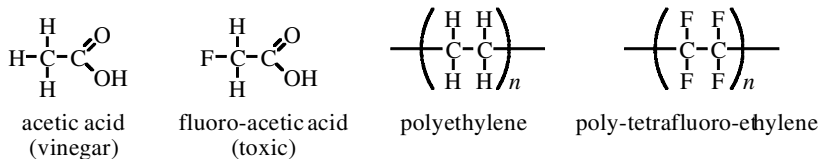


Figure 1. Fluorinated analogues of some hydrocarbon systems.

atoms that are attached to hydrogen atoms. Of the countless naturally occurring molecules, only a handful of systems have carbon atoms that are attached to fluorine atoms, and most of these are metabolites in tropical plants found in the Southern Hemisphere (Harper & O'Hagan 1994). The existence of molecules containing carbon-fluorine bonds is due almost entirely to human efforts in the 20th century because nature, after billions of years, has never found a generally effective method of introducing fluorine atoms into organic systems, even though she has had plenty of raw material with which to experiment (fluorine is the 13th most abundant element in the Earth's crust).

Fluorine is not significantly different in size to hydrogen, and, in principle, it is possible to take any of nature's molecules and replace either one hydrogen atom with fluorine, to give a selectively fluorinated derivative, or all the hydrogen atoms by fluorine, to create a fully fluorinated (perfluorinated) system.

The introduction of one or more fluorine atoms into a naturally occurring molecule can have a profound effect on its physical, chemical and biological properties. For example, the replacement of one hydrogen in acetic acid (used as vinegar to flavour food) by fluorine gives highly poisonous fluoro-acetic acid (figure 1), which is present in gifblaar (*Dichapetalum cymosum*), a plant that has caused many livestock fatalities on the South African veld. In another example, the fully fluorinated (perfluorinated) polymer, polytetrafluoroethylene (figure 1) is far more thermally and chemically resistant than the non-fluorinated compound polyethylene.

There is the possibility of creating an infinite number of new organic systems that contain fluorine atoms, with each new molecule having its own distinct properties and chemical reactivity. Organofluorine chemistry, therefore, provides a potentially vast extension to organic chemistry.

2. Why fluorine?

Why do fluorine atoms give rise to molecules with such different properties to analogous non-fluorinated molecules? There are two main reasons (Chambers 1973) as follows.

- (1) Fluorine is the most electronegative element, which means that a fluorine atom can attract the negatively charged electrons present in a chemical bond towards itself, a property that can completely change the electronic environment and, therefore, affect the chemical reactivity of an organic molecule. For example, in hydrocarbon systems such as benzene, the presence of negatively charged electrons on the aromatic ring makes the molecule reactive towards positively charged reagents called electrophiles (E^+ , figure 2). In contrast, electronegative fluorine atoms 'suck' the electrons out of the hexafluorobenzene ring, making the carbon atoms slightly positively charged and, therefore, reactive towards

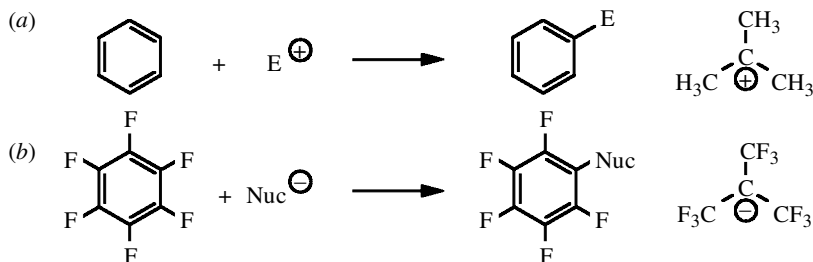


Figure 2. Fluorocarbon chemistry can ‘mirror’ hydrocarbon chemistry. (a) Naturally occurring hydrocarbon systems. (b) ‘Man-made’ fluorocarbon systems.

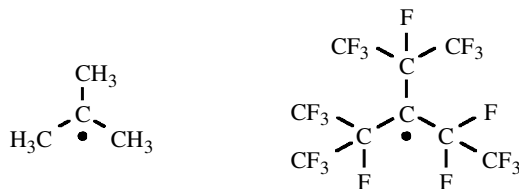


Figure 3. The perfluorinated radical is much more stable than the hydrocarbon radical.

negatively charged reagents (nucleophiles, Nuc^-). Similarly, positively charged hydrocarbon systems (Olah *et al.* 1985) (carbocations) are ‘mirrored’ by the existence of negatively charged fluorocarbon derivatives (Bayliff & Chambers 1988) (see also figure 2, carbanions).

- (2) A fluorine atom possesses three pairs of negatively charged electrons in its outer electronic shell that are not involved in bonding with any other atoms. This ‘cloud’ of non-bonding electrons surrounding each fluorine atom can, in highly fluorinated systems such as PTFE, be regarded as a ‘protective sheath’ that shields the carbon backbone of each molecule from chemical attack, providing many highly fluorinated systems with very high thermal and chemical stability.

The increased stability conferred upon molecules by the presence of fluorine atoms allows a number of unusual systems to be synthesized and studied that would otherwise be extremely reactive or unstable. Hydrocarbon radicals are highly reactive transient species due to the presence of a free unpaired electron on a carbon atom and have lifetimes that can only be measured in milliseconds (Fossey *et al.* 1995). In contrast, some fully fluorinated radicals (figure 3) are stable (Scherer *et al.* 1985) even when heated for several hours!

Pyridine derivatives, protected by several perfluoroalkyl groups, can be transformed by ultraviolet light into the Dewar and prismane valence bond isomers (figure 4; see also Chambers & Middleton (1977)), all of which can be isolated and stored unchanged over long periods of time, unlike the non-fluorine-containing analogues.

These few examples illustrate how different the chemistry and properties of fluorinated molecules can be compared with analogous hydrocarbon systems, and, quite frequently, the chemistry of some fluorocarbon systems is so unexpected that it places quite a strenuous test on our theories and understanding of organic chemistry. As Professor D. Seebach notes, ‘... a few personal experiences [in organofluorine chemistry] would suggest that one should be prepared for anything with even the simplest

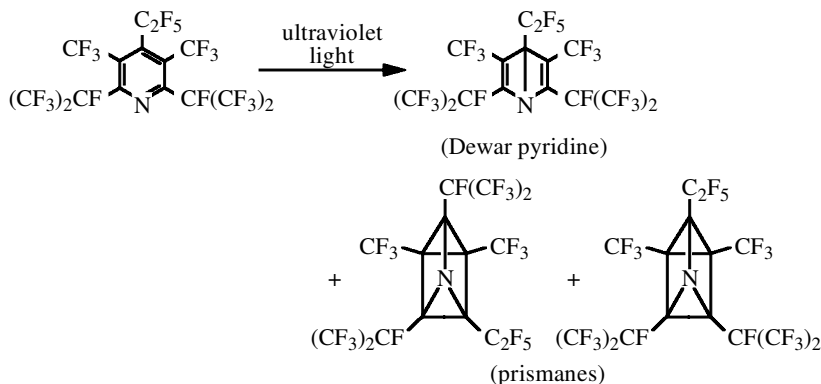


Figure 4. Unusually stable valence isomers of fluorinated pyridine derivatives.

reactions—a thrilling prospect' (Seebach 1990). This is the continuing fascination of organofluorine chemistry.

3. Organofluorine chemistry, the 20th century

The future of any scientific subject, and its impact upon the general public, must have its roots in the achievements of the past, and in order to try to predict future directions in organofluorine chemistry as we enter the new millennium, we must first consider current knowledge (Banks *et al.* 1986).

In the 1920s, the Belgian chemist Frederic Swarts began his seminal studies on halogen exchange reactions, which involved the replacement of chlorine atoms in organic molecules by fluorine using hydrogen fluoride gas as the fluorinating reagent. His work prompted American scientists (Midgley & Henne 1930) to prepare the first chlorofluorocarbons (CFCs), which were immediately developed as safe non-flammable refrigerants, as alternatives to liquid ammonia and sulphur dioxide, which were being used up to that time. CFC refrigerants were used globally in everyone's kitchens and automobile air-conditioning systems until the deleterious impact of the CFCs on the ozone layer became fully apparent (Rowland 1996) in the mid-1980s, and the use of such materials for refrigeration was banned in developed countries under the terms of the Montreal protocol. Since refrigeration is now an essential part of modern life (indeed, in Paul Theroux's (1982) novel *The mosquito coast*, the chief protagonist invents a refrigeration system because he argues that 'Ice is civilisation'), the global chemical industry responded to both social and environmental requirements in a very short time. A new range of hydrofluorocarbons (HFCs) is now available as 'drop-in' replacements to the harmful CFCs; it is perhaps worth emphasizing here that it is the chlorine atoms, not the fluorine, that are the root cause of the ozone depletion problem!

Towards the end of the Thirties, Dr R. J. Plunkett, a scientist at the Du Pont company, found that the contents of a cylinder containing tetrafluoroethylene, prepared from one of the newly available CFCs, had solidified, and after sawing the cylinder in half, he obtained the first samples of solid polytetrafluoroethylene (PTFE). Shortly afterwards, Professor W. T. Miller (Cornell) prepared polytrifluorochloroethylene (Kel-F[®], 3M Co.), and, after the tremendous chemical and thermal stability of both materials had been recognized, these polymers became crucial in the successful fabri-



Figure 5. Babu Chiri Sherpa, a Nepalese mountaineer, who spent a record 21 h on the summit of Everest in May 1999, wearing Goretex[®] protective clothing. (Photograph: Popperfoto Ltd.)

cation of the first atomic weapons (the US Manhattan project). The separation of the fissionable uranium-235 isotope by gaseous diffusion of uranium hexafluoride (UF_6) through a permeable membrane to provide a U-235 enriched sample of uranium was made possible by the new fluorocarbon polymers, which could withstand the highly corrosive materials, such as elemental fluorine, required by the enrichment process. After the crucial role played by fluorocarbon materials in the Manhattan project was published (Goldwhite 1986), a number of groups around the world took up the challenge of exploring the chemistry of fluorinated molecules and the field developed rapidly.

PTFE is now used by humankind for many applications, such as waterproof clothing (figure 5), gaskets, artificial veins, and as non-stick coatings for kitchenware (e.g. Teflon[®]-coated frying pans). Indeed, the roof of the Millennium Dome (figure 6), perhaps the most visible symbol of the millennium celebrations in the UK, is fabricated from panels containing PTFE. Many other perfluorinated polymers continue to find new uses; for instance, in the aerospace industry, and, in fact, supersonic



Figure 6. The Millennium Dome, Greenwich, London. (Photograph: Popperfoto Ltd.)

flight and space travel would probably have not been possible without the use of perfluorinated materials that could withstand such demanding operating conditions. For example, perfluoropolyethers are used as lubricants on orbiting spacecraft because such materials are chemically inert to liquid propellants and remain as fluids over a wide temperature range (from $-90\text{ }^{\circ}\text{C}$ to $+250\text{ }^{\circ}\text{C}$), essential for lubrication of spacecraft that must cope with the high temperatures of take-off and the extreme cold of a space orbit. Consequently, the US Space Shuttle (figure 7) and the international space station presently under construction make full use of a variety of highly fluorinated materials. However, the failure of a fluorocarbon O-ring seal on the solid rocket booster of the space shuttle was found to be responsible for the explosion that led to the destruction of the Challenger spacecraft and the tragic loss of seven US astronauts in 1986. The unusual cold ($29\text{ }^{\circ}\text{F}$) of the morning of the launch caused the crucial O-ring seals to become brittle and fail, a property that was illustrated by Professor Richard Feynman, using a glass of ice-water, before the presidential commission investigating the cause of the disaster (Feynman 1993).

Perfluorinated materials, or materials coated with a thin fluorocarbon layer, possess the additional property of having a very low surface energy. This means that water or oil, placed on a fabric surface that has been covered by fluorine atoms, does not soak into the fabric (figure 8) but remains as droplets on the surface, which can be easily removed by wiping. Now, many carpets and items of upholstered furniture are protected by fluorocarbon surfaces (e.g. Scotchgard[®] treatment, 3M Co.). Similarly, fluorocarbon-based paint is weatherproof and is used for coating many external surfaces (figure 9).

Much smaller fully fluorinated molecules, such as perfluorobutane, were also first prepared as part of the Manhattan project and, even now, new uses for such compounds are being developed. Nycomed Amersham estimates that a perfluorocarbon fluid used as an ultrasound contrast imaging agent for visualizing heart disease (fig-

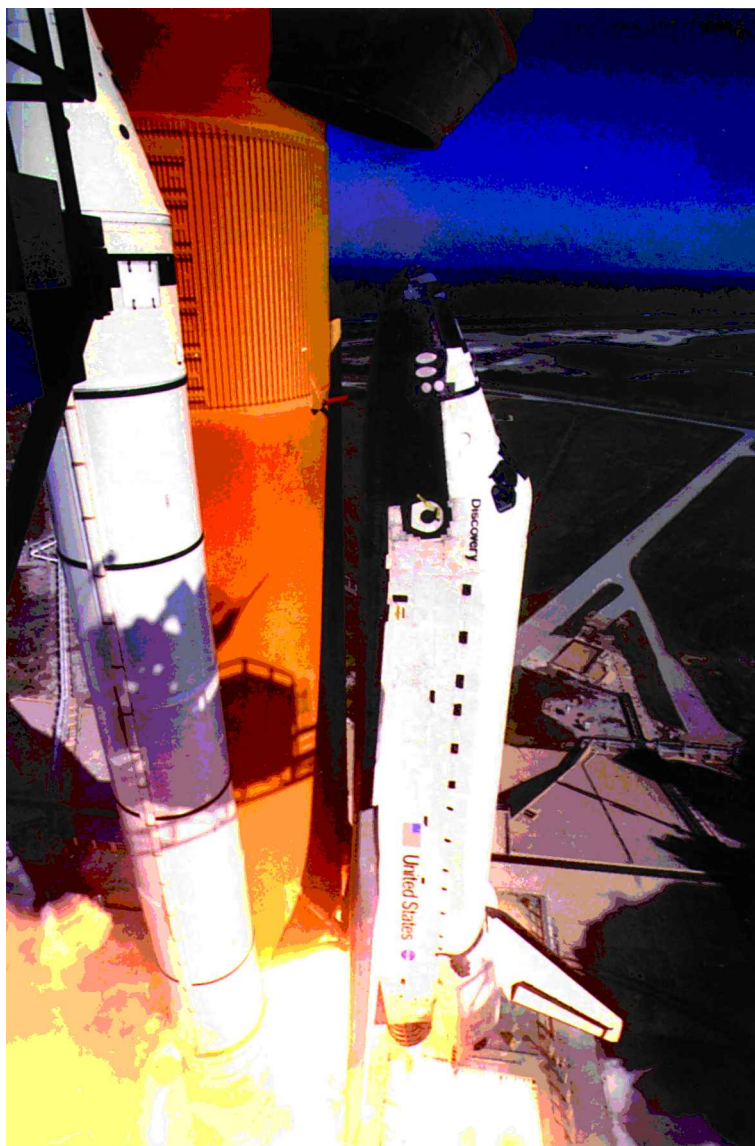


Figure 7. The Space Shuttle. Fluorocarbon materials are used in many aeronautical applications such as gaskets and lubricants. (Photograph: Popperfoto Ltd.)

ure 10) and liver damage (Carmichael 1998) will be worth £ 1000 million in sales by 2005. A particularly interesting property of perfluorocarbon (PFC) fluids is that they readily absorb large quantities of oxygen (Clark & Gollan 1966), and this idea was adopted by the director James Cameron in his film *The Abyss*, in which deep-sea divers were shown to be 'breathing' such oxygenated liquids. This is not completely science fiction because the use of PFCs for filling the deflated lungs of premature babies has recently been cleared by the FDA.

Anaesthesia, and, consequently, medical surgery, has also been revolutionized by organofluorine chemistry, and the anaesthetics of the past, ether and chloroform,

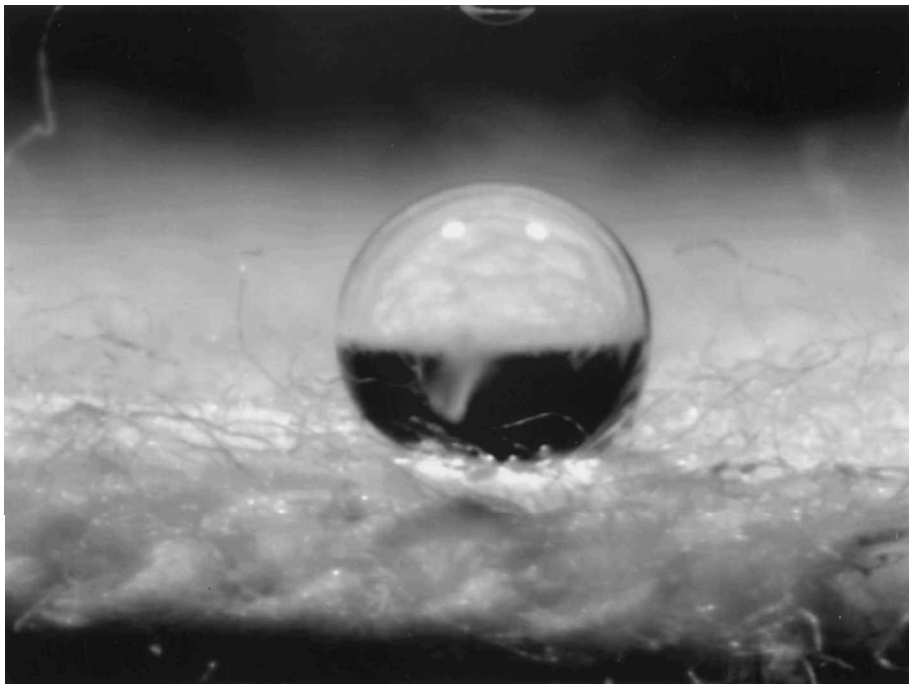


Figure 8. A droplet of oil on a textile treated with a ‘super repellent’ fluorocarbon surface prepared by plasma polymerization. (Photograph: Professor J. P. S. Badyal, University of Durham, UK.)

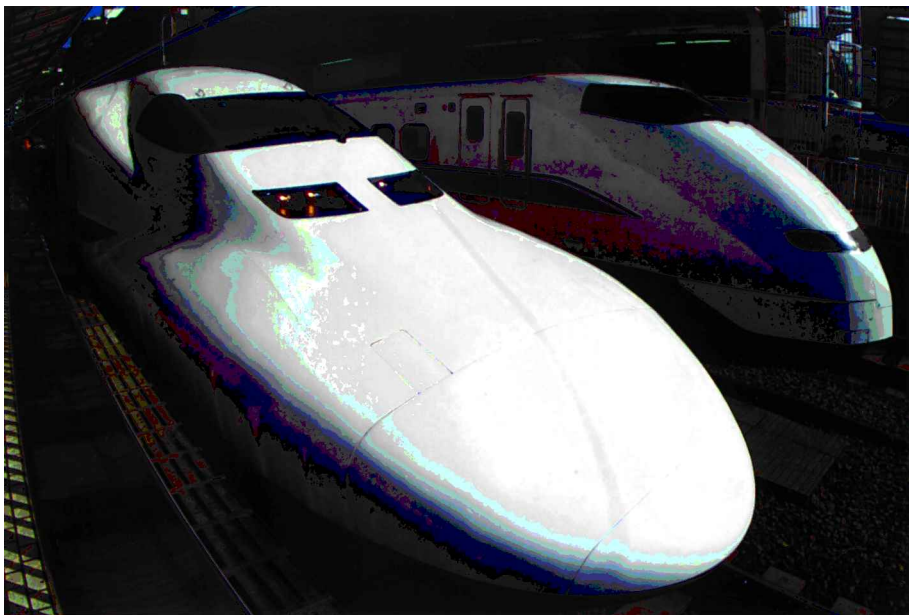


Figure 9. The Japanese Shinkansen ‘bullet trains’ are decorated and weatherproofed with fluorocarbon paint. (Photograph: Popperfoto Ltd.)

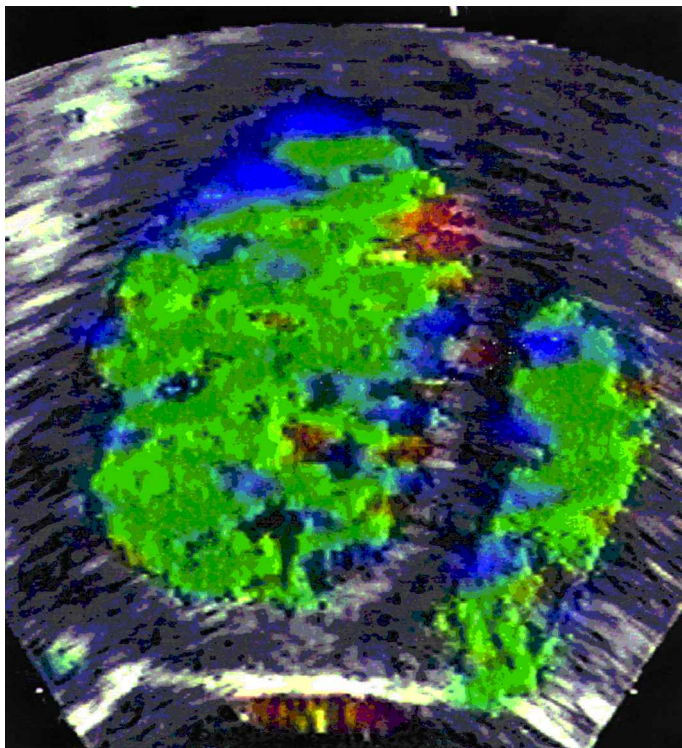


Figure 10. Heart imaging using perfluorocarbon image contrast agents. Perfluorocarbon microbubbles (green) contrast with the heart wall (grey) and make evaluation of this dog's heart easier. (Photograph: Dr A. K. Fahlvik, Nycomed Amersham.)

have now been replaced by safer, more easily handled alternatives such as halothane ($\text{CF}_3\text{-CHClBr}$).

So far, we have focused on applications of molecules that have had most, or all, of their hydrogen atoms replaced by fluorine, but even when a single fluorine atom is introduced into a naturally occurring system, useful effects can be found. Fried & Sabo (1954) prepared the first singly fluorinated steroids, which proved to be considerably more biologically active than the parent steroids. Since this early finding, many pharmaceuticals that owe their bioactivity to the presence of fluorine atoms in their structures have been developed, and particularly successful fluorinated drugs have been marketed as antibiotic, antifungal, anticancer and antiviral agents. For example, Prozac[®] (Eli Lilly), the controversial antidepressant drug, owes its ability to easily traverse the blood-brain barrier, and, therefore, deliver its effect to the brain, to the presence of a trifluoromethyl group (CF_3) (figure 11). The widespread use of fluorinated drugs is indicated by the fact that Prozac[®] and Cipro[®] were among the worldwide top 20 bestselling drugs of 1993.

Many agrochemicals are used regularly for plant protection as herbicides, insecticides and fungicides. Some well-known brand-name fluorinated agrochemicals, all manufactured and used in large tonnages, are shown in figure 11. The number of fluorinated agrochemicals in general use continues to grow, and, indeed, of all the plant protection products (herbicides, pesticides, fertilizers, etc.) currently undergo-

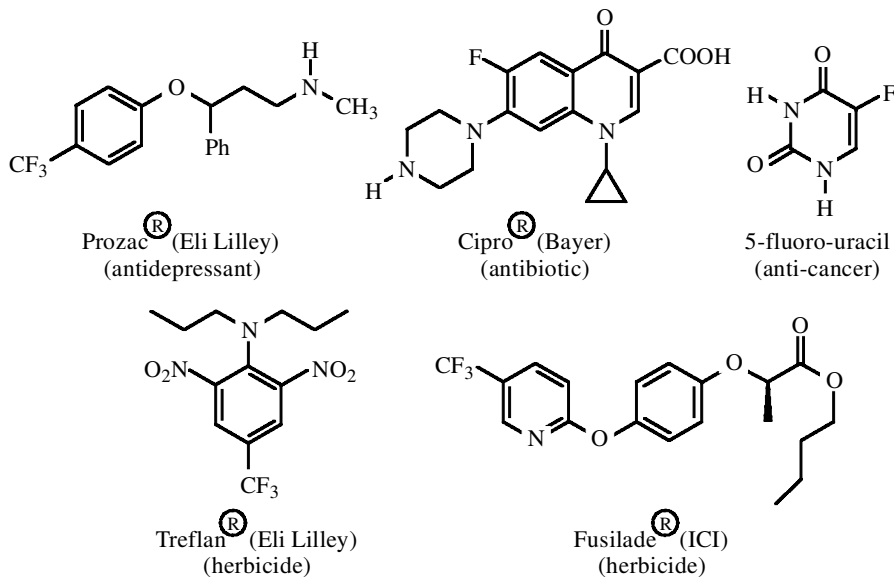


Figure 11. Pharmaceuticals and agrochemicals that have fluorine atoms in their structure.

ing field trials, nearly half of the molecules contain fluorine atoms. Thus, biologically active molecules containing fluorine atoms will undoubtedly play an increasing role, worldwide, in health-care and agriculture in the new millennium.

In total, the combined value of all commercially available products that contain fluorine atoms, of which only a fraction of applications (Banks *et al.* 1994) are outlined above, was estimated by Rozen (1992) to be in the region of \$50 billion per year in sales, a figure that has undoubtedly grown and continues to increase.

We have discussed the importance of fluorinated compounds to the general public, but, of course, the invention of chemical reactions and synthetic methodology, the study of chemical processes, and the development of fundamental understanding of the chemistry of fluorinated systems had to be established before any practical, commercial applications arose. Thus, the role of academia, interacting closely with industry, is extremely important and will undoubtedly continue.

4. Approaches to the synthesis of organofluorine compounds, current research on direct-fluorination processes

As we have seen, organofluorine chemistry is a subject that cuts across the whole of the chemical and pharmaceutical arenas, and, consequently, there is a great deal of ongoing research in this field involving groups across the world. As an example of current research work in organofluorine chemistry, we will focus, in this section, on our recent work concerning direct-fluorination methodology, although, of course, it is not intended to suggest that this is the only important research challenge, far from it!

Before we can explore and exploit the chemistry of organofluorine molecules, we must first synthesize them. However, as nature has found, this is not a trivial task, and much current research is focused upon the development of convenient, safe, efficient and economic methods for the introduction of fluorine atoms



Figure 12. Modern fluorine generation. The fluorine cell room used in the manufacture of per-fluorocarbon gases and fluids, F2 Chemicals Ltd, Preston, UK. (Photograph: M. Atherton, F2 Chemicals Ltd.)

into organic species. The author's current research, in collaboration with Professor Richard Chambers at the University of Durham, UK, has focused upon developing the use of the element itself, fluorine gas (F_2) to accomplish this task.

In 1886, the French chemist Henri Moissan isolated the first sample of pure elemental fluorine (F_2) by electrolysis, and this process is essentially still in use today. In the UK alone, BNFL produces *ca.* 1500 t of fluorine per annum (figure 12) for the synthesis of UF_6 for the uranium-235 enrichment process, which is essential to the nuclear electricity generation industry. Moissan quickly discovered that fluorine is a tremendously reactive, toxic and corrosive gas, and his initial studies of reactions between fluorine and various organic molecules, such as methane, resulted in explosions. Quite understandably, it was nearly 30 years before other chemists got involved in research using fluorine gas, and even now the image of fluorine being violently reactive still generally prevails.

The problem with direct-fluorination reactions is that a large amount of heat is generated upon transforming a carbon–hydrogen bond in an organic molecule into a carbon–fluorine bond, and this can lead to the uncontrolled reactions or explosions witnessed by Moissan. Fluorine has now been ‘tamed’, to some extent, by dilution in an inert gas such as nitrogen, using low temperatures and appropriate solvents, and a growing number of effective direct-fluorination processes have been reported (Hutchinson & Sandford 1997). The Durham group recently found that direct-fluorination reactions could be efficiently carried out in acidic media such as formic acid. The preparation of fluorinated 1,3-dicarbonyl compounds (Chambers *et al.* 1996) by direct-fluorination technology (figure 13) first carried out at Durham in 1993, has been scaled up to a manufacturing process by F2 Chemicals Ltd (BNFL) to supply customers in the pharmaceutical industry.

The chemistry of fluoro-dicarbonyl molecules has not been explored, even though

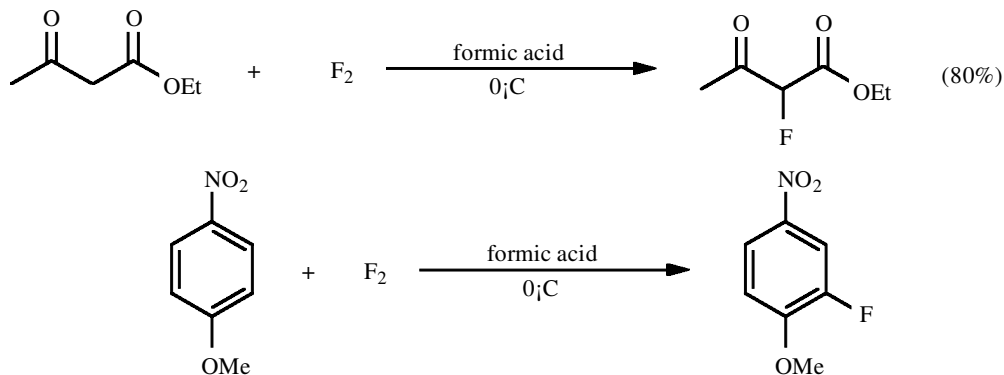


Figure 13. Recent successful reactions using fluorine gas.

chemists would expect such derivatives to be extremely versatile ‘building blocks’, because a realistic large-scale preparative route to this class of compounds has not been available previously. The exploration of the chemistry of these systems awaits (Hutchinson *et al.* 1998).

As recently as 1992, most advanced organic chemistry textbooks offered the view that, for example, ‘direct fluorination of aromatic rings with F₂ is not feasible at room temperature because of the extreme reactivity of F₂... at low temperatures, the reaction is not of preparative significance’ (March 1992). However, the Durham group found that direct-fluorination reactions of many aromatic systems (figure 13) could also be effectively carried out in acidic media (Hutchinson *et al.* 1998). Controlled selective fluorination of diverse systems such as heterocycles and carbohydrate derivatives is now possible using techniques developed recently (Hutchinson *et al.* 1998).

The potential for using fluorine gas as a reagent is only just beginning to be recognized, and, apart from the process described above, only one selectively fluorinated molecule, 5-fluoro-uracil (an anticancer drug) is currently manufactured using fluorine. The development of new, potentially high-tonnage uses, of fluorine gas is particularly timely because new plasma procedures recently announced by BNFL (Bailey *et al.* 1997) allow for the recovery of fluorine gas and uranium metal from ‘spent’ uranium hexafluoride. The nuclear arms race and nuclear electricity industry have generated tens of thousands of tons of uranium hexafluoride, which is presently stored in containers in, for example, the deserts of the western US. This situation cannot continue indefinitely, and useful redeployment of the fluorine ‘trapped’ in uranium hexafluoride will clearly be beneficial on environmental grounds alone, providing, of course, that new uses for the regenerated fluorine can be found.

5. Organofluorine chemistry in the new millennium

The successful exploration of the chemistry of organic compounds containing fluorine and the wide variety of applications found for such materials, e.g. in pharmaceuticals and as materials used in space flight, suggests that the future of the subject is very bright.

One of the major driving forces for chemistry at present is the continued need for humankind to develop new pharmaceuticals, either for the treatment of previously

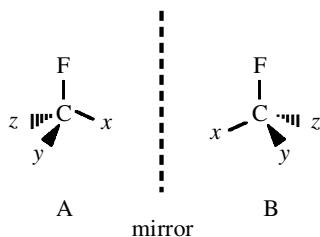


Figure 14. A and B are mirror images (enantiomers). Enantiomers A and B may have considerably different chemical properties and physiological effects.

incurable illnesses, such as cancer or Aids, or to provide more effective medicines than are currently available. It is of great concern that nature has developed antibodies capable of resisting the many effective antibiotics that have been in general use over the past 50 years (Niccolai *et al.* 1997), and, at present, only one antibiotic, vancomycin, is still effective against all forms of bacteria. If this situation changes, health treatments could revert to the conditions of the days before the general use of penicillin, where bacterial infection (pneumonia, tuberculosis, etc.) often proved fatal. Humankind must continue to find either new naturally occurring medicines (e.g. Taxol[®], isolated from the bark of the Pacific yew tree, is very active against cancer), or develop non-natural biologically active molecules. The preparation of organic molecules that are rendered biologically active by the presence of at least one fluorine atom continues to offer one route towards addressing this issue, and, indeed, the fluoro-quinolone antibacterial agents (e.g. Cipro[®], figure 12) show the potential of this approach. The number of fluorine-containing pharmaceuticals and agricultural chemicals in general use will undoubtedly grow.

Effective methodology for the preparation of new selectively fluorinated 'building blocks' and fluorinated natural-product analogues must continue to evolve to provide a large diversity of fluorocarbon structures essential in drug-discovery programmes, although recent work concerning direct-fluorination processes, described above, and the availability of other fluorinating reagents, has gone some way towards addressing this important issue. Of immediate concern, however, is the lack of methodology for synthesizing selectively fluorinated chiral molecules, where a fluorine atom is attached to a stereogenic carbon centre. Chiral molecules contain a carbon atom (stereogenic centre) attached to four different groups, and in these situations two possible molecular orientations arise, where A has a 'mirror image' B (an enantiomer), which, although structurally the same, in the way a right and a left hand are, can actually have extremely different properties (figure 14).

The tragic case of the use of the hydrocarbon derivative phthalidomide in the 1960s, where both enantiomers of the phthalidomide drug were administered to pregnant women, unfortunately showed that one enantiomer gave the desired effect of lowering the patients blood pressure, but the other enantiomer led to deformation of the foetus. Indeed, to register a new pharmaceutical with the FDA in the US at present, each mirror image of the drug molecule must be isolated and screened for biological activity.

Consequently, before selectively fluorinated molecules can be exploited fully in the drug-discovery arena, methods for synthesizing not only carbon-fluorine bonds in organic systems (which is hard enough!) but the selective synthesis of one enantiomer

of the derived fluorinated molecule, rather than a mixture of two mirror images, is urgently required.

Once the preparation of chiral selectively fluorinated molecules has been mastered, the application of such 'building blocks' to the preparation of many structurally diverse systems using the developing techniques of combinatorial chemistry as part of drug-discovery programmes, will undoubtedly arise. Combinatorial chemistry (Gordon & Kerwin 1998) could, as an example, involve taking a fluorinated 'building block' and reacting this with ten different substrates in the same reaction vessel, to yield a mixture of ten initial fluorine-containing products. This mixture of initial products would then be reacted with a further ten different substrates and after this second series of reactions a mixture of a total of 100 different selectively fluorinated final products would be obtained, in two easy steps, all of which could be tested for biological activity. In principle, by increasing the number of reactions and the number of substrates in each step, millions of selectively fluorinated molecules could be synthesized by these types of process, increasing the chance of discovering a lead compound in the search for the next fluorine-containing 'blockbuster' drug.

Systems containing many fluorine atoms will also continue to play an important role in tomorrow's society. The possibility that chemically inert perfluorocarbons could act as artificial blood substitutes (Ritter 1998) (both PFCs and blood dissolve oxygen) remains an important long-term goal, especially since public blood supplies are diminishing and have the added possibility of HIV infection.

The potential for the synthesis of new highly fluorinated polymeric systems, both in the bulk and at surfaces, is also considerable and of widespread utility. The widely criticized chlorofluorocarbons (CFCs) and related hydrochlorofluorocarbons (HCFCs) have been used as feedstocks for the synthesis of a number of 'downstream' commercial products; for example, CF_2HCl (refrigerant) is the precursor of a number of important polymers, such as the highly versatile PTFE. The more environmentally friendly hydrofluorocarbons (HFCs), the replacements for CFCs, could also yield similarly valuable and useful downstream high-performance materials in the years to come.

Direct fluorination of a wide range of hydrocarbon polymers could also provide routes to the fabrication of important new materials. For example, the perfluorinated analogue of polypropylene could be made readily available by harnessing developing techniques in direct fluorination, because continuous flow processes, being developed by the Durham group, could potentially be used for the perfluorination of a wide range of systems including high-molecular-weight polymers.

6. Conclusions

Molecules containing fluorine touch on everybody's lives in the developed world on a daily basis and the new millennium will see an even greater number of fluorinated materials in everyday use, providing that methods of synthesizing these fascinating systems and their fundamental chemistry continues to be developed. The prediction of Professor Simons (1950), made 50 years ago, that he would one day travel in an aircraft consisting of plastics, lubricants, etc., fabricated from fluorine-containing systems, has only partly been borne out but, after the considerable developments of recent years, can now be replaced by a much more general vision. In the new millennium, man could be travelling home in cars powered by engines lubricated by

fluorocarbon greases and fabricated from fluorocarbon polymers to houses coated by weatherproof fluorinated paints. On entering the home, furnished with carpets with fluorinated surfaces that never need cleaning, fluorocarbon kitchenware is used to prepare food that was grown with the aid of fluorinated agricultural agents. Illnesses are detected by fluorocarbon imaging agents and treated using fluorinated drugs in operations carried out under fluorocarbon gas anaesthetics.

Nature has never learned how to use the element called fluorine, but humankind has, and will continue to do so, to great benefit, provided, of course, that fundamental research into the synthesis and chemistry of these fascinating molecules continues to thrive.

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Born in Manchester, Graham Sandford studied at Durham University, where he obtained a BSc in chemistry in 1988 and his PhD in 1991 under the direction of Professor R. D. Chambers. After spending 1992 in the laboratories of Professor G. A. Olah (1994 Nobel Laureate) at the University of Southern California, he returned to Durham as a BNFL Postdoctoral Research Fellow, and subsequently took up his present position as a Royal Society University Research Fellow in 1996. Aged 33, he has published 25 research papers and several patents in the area of organofluorine chemistry. Scientific interests include all aspects of organofluorine chemistry (especially selective fluorination methods, heterocyclic, free radical and carbanion chemistry). Recreations include cycling, mountain walking and travel.

