

Fluorine, the most electronegative of all the elements, forms very strong covalent (see table 1) or ionic bonds to most other elements. The strength of the carbon-fluorine bond and the small size of the fluorine atom (van der Waals radius: 1.35 Å; hydrogen: 1.20 Å) give rise to a range of valuable chemical, physical and biological properties in organic molecules with one or more fluorine atoms attached to carbon. A rapid growth of interest in fluoro-organics has occurred in many areas of application, including polymers and materials, specialty solvents, performance fluids, medicinal agents, agrochemicals and in numerous reagents and intermediates for chemical synthesis.

**Table 1: Typical covalent bond energies<sup>1</sup>**

BOND	BOND ENERGY	
	kcal mol <sup>-1</sup>	kJ mol <sup>-1</sup>
F-F	38	159
Cl-Cl	58	242
H-F	136	566
H-Cl	103	431
C-H	98	411
C-F	116	484
C-Cl	81	338
Si-F	139	582
Si-Cl	91	381
P-F	117	490
P-Cl	76	319

Because of the reactivity and hazards of elemental fluorine and hydrogen fluoride, the task of introducing fluorine into organic molecules has presented a particular challenge to synthetic chemists and has led to the development of specialized fluorination technologies and reagents. This article gives a brief outline of fluorination methods, highlighting specific reagents available from Alfa Aesar. Further details and literature references can be found under specific products in the main section of the Catalogue and in numerous texts and reviews on fluorination and organofluorine chemistry.<sup>2-14</sup>

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## Electrophilic fluorination

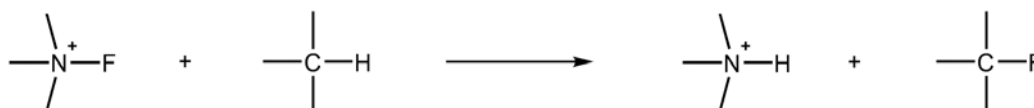
Elemental fluorine is one of the most chemically reactive substances known, due to the relative weakness of the F-F bond and the great strength of its bonds to most other elements, including hydrogen, carbon and silicon, illustrated in Table 1.

Fluorine can behave both as a fluorinating agent and a powerful oxidant. It reacts readily with almost every other element and attacks many common materials, often with near-explosive violence. In organic molecules, C-H bonds tend to be attacked indiscriminately by both free-radical and ionic mechanisms. Elemental fluorine has been successfully harnessed, notably by Chambers' group,<sup>14</sup> using strongly acidic, polar media to promote selective heterolytic fluorination and suppress the non-selective free-radical mode of reaction. Other well-established techniques for moderating the reactivity of fluorine involve the use of inert diluents and very low temperatures. However, many alternative electrophilic fluorination reagents have been introduced with the objective of providing selectivity and ease of handling.

## N-Fluoro reagents

A variety of N-fluorinated amines, quaternary salts, amides and sulfonamides have been proposed as reagents for selective electrophilic fluorination under mild conditions (scheme 1). These are usually stable, easily-handled solids, and provide a range of fluorinating power from mild to moderate, depending on the structure of the reagent and the nature of the substrate. Another advantage is that, since free hydrogen fluoride is not a major by-product in fluorination reactions with this type of reagent, conventional glass equipment is often suitable.

## Scheme 1



The chemistry of N-F fluorinating agents has been reviewed.<sup>15</sup>

**L17003** 1-Chloromethyl-4-fluoro-1, 4-diazoniabicyclo [2.2.2]octanebis(tetrafluoroborate) [F-TEDA-BF<sub>4</sub>]

**L13955** N-Fluorobenzenesulfonimide [Accufluor® NFSi]

**L17628** 1-Fluoro-4-hydroxy-1,4- diazoniabicyclo [2.2.2] octane bis(tetrafluoroborate) [Accufluor® NFTh]

**L13231** N-Fluoropyridinium pyridine heptafluoro-diborate [Accufluor® NFPy]

**L14324** N-Fluoropyridinium trifluoromethane sulfonate

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# Fluorinating Agents in Organic Chemistry

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## Other electrophilic reagents

Xenon fluorides, especially the difluoride, can be used in the selective fluorination of substrates including arenes, alkenes and active methylenes, and also in the fluoro-decarboxylation of carboxylic acids (scheme 2), providing a useful alternative to the Hunsdiecker reaction.<sup>16</sup>

## Scheme 2



The use of cobalt(III) fluoride [or cobalt(II) fluoride/ fluorine] is a well-established method for the fluorination of hydrocarbons, ethers, etc., but requires high temperatures and specialised equipment. Silver(II) fluoride has found some limited use in the fluorination of aromatics. Several highly reactive species can be generated from elemental fluorine, including trifluoromethyl hypofluorite, acetyl hypofluorite (explosive), and cesium fluoroxy-sulfate (unstable, shock-sensitive), prepared from cesium sulfate (product A16767) and fluorine.

**13074** Cobalt(II) fluoride  
**11490** Cobalt(III) fluoride

**11610** Silver(II) fluoride  
**39739** Xenon difluoride

## Electrochemical fluorination

This technique was introduced by J. H. Simons in the 1940's, using anhydrous HF as solvent, with or without an ionic fluoride as supporting electrolyte, and is now an established industrial route to perfluorinated molecules. More recent studies have investigated the selective fluorination of a variety of aliphatic and aromatic substrates, for which acetonitrile has become the preferred solvent, with the addition of a supporting electrolyte such as HF-pyridine or triethylamine trihydrofluoride.<sup>17</sup>

**L17117** Hydrogen fluoride pyridine complex  
**A13031** Potassium hydrogen fluoride

**L14417** Triethylamine trihydrofluoride  
**A10211** Tetraethylammonium tetrafluoroborate

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