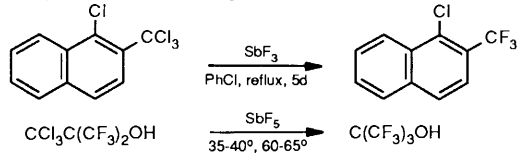
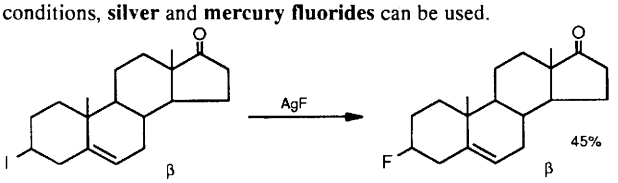
# Reagents for Fluorination

*Aldrich offers the world's largest range of fluorine-containing products. In addition, we offer many reagents for introducing fluorine into molecules, most of which can be handled safely and easily in standard laboratory glassware. There are four general classes of fluorination reactions, and Aldrich offers reagents suitable for use in each class.*[1]

**1. Halogen exchange** is perhaps the best known method for introduction of fluorine into organic compounds. Pioneering work by Swarts using **antimony fluorides** made the early preparation of benzotrifluorides and fluoroalkanes possible. These compounds are more



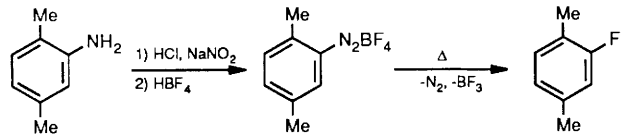

commonly prepared now using large-scale batch or continuous processes employing **HF**. In small-scale reactions needing much milder conditions, **silver** and **mercury fluorides** can be used.




**Potassium fluoride** offers a readily available source of fluoride ion and is used extensively in so-called 'Halex' reactions to produce good yields of highly fluorinated products. The desire to obtain better yields under milder conditions has resulted in the development of a number of new reagents such as **TBAF, KF/CaF$_2$** and **TAS-F**.[2]

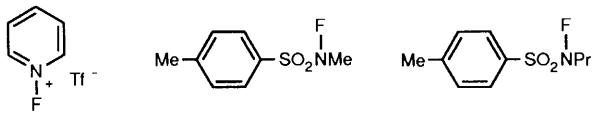
A new and easy-to-handle source of nucleophilic fluoride ion is **triethylamine trihydrofluoride** ($Et_3N{\cdot}3HF$). The versatility of this reagent has been demonstrated in halofluorination reactions of alkenes,[3] quantitative opening of epoxides to fluoroalcohols[4] and the fluoride substitution of activated alcohols.

**2. Balz-Schiemann** reactions are the classical method for introducing fluorine to an aryl nucleus. An arylamine is converted to a diazonium tetrafluoroborate and then decomposed thermally to the aryl fluoride. Improved yields have been reported in some cases using arenediazonium hexafluoroantimonate or hexafluorophosphate intermediates or by photolytic decomposition of the tetrafluoroborate salt.




**3. Sulfur tetrafluoride and analogs** have been used extensively for the conversion of oxygen-containing functional groups to fluorinated substituents. **Sulfur tetrafluoride** itself presents handling and toxicity problems and replacements are continually being sought. Perhaps the best known is **diethylaminosulfur trifluoride** (DAST)[2] which can be used to convert -CHO to -CHF$_2$ and -CH$_2$OH to -CH$_2$F. Recently, **morpholinosulfur trifluoride**[5] has been reported as a safer alternative to DAST. Other aminosulfur trifluorides are also available.


**4. Electrophilic fluorinating agents** have been developed as alternatives to elemental fluorine for the selective introduction of fluorine into biologically active molecules. ***N*-Fluoropyridinium triflates** and ***N*-fluorosulfonamides** offer varying fluorination strength by altering the substitution on the molecule.




**References:**


1) For a more detailed discussion, see Hewitt, C.D.; Silvester, M.J. *Aldrichim. Acta* **1988,** *21*(1), 3.
2) For references, see *Aldrichim. Acta* **1988,** *21*(1), 27.
3) Alvernhe, G.; Laurent, A.; Haufe, G. *Synthesis* **1987,** *6,* 562.
4) *Idem J. Fluorine Chem.* **1986,** *34,* 147.
5) For references, see *Aldrichim. Acta* **1988,** *21*(4), 109.