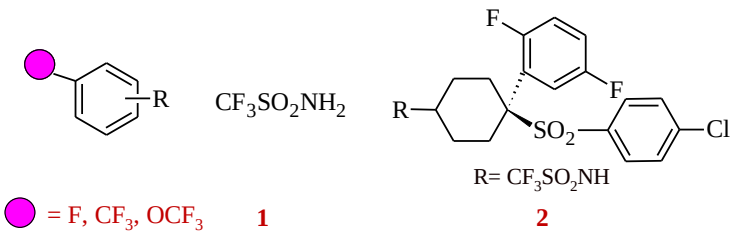
Fluorinated Drugs

The utility of fluorinated alkyl, aryl, and heterocyclic compounds as efficient electrophiles in numerous reactions has become an actively developing field in pharmaceutical research due to unique physical and chemical properties associated with fluorine atom. The fluorinated substituents can influence the pharmacodynamics and pharmacokinetic properties of therapeutically active compounds.



Fluorinated substituents

It is sufficient to mention that the introduction of fluorine into a bioactive compounds can influence the molecular conformation; tailor pK_a values; facilitate cell membrane penetration; and increase the metabolic stability of compounds. The biological activity of fluorinated substituents to a great extent is due to both their strong electron-withdrawing effect and their lipophilicity than their analogues as shown in the Table.

Atom/group	Pauling Electronegativity	Hydrophobicity π
H	2.1	0.00
F	4.0	0.14
CH_3	2.3	0.56
CF_3	3.5	0.88

From the clinical point of view, the incorporation of fluorine into bioactive compounds has been considered as potent drugs. For instant, lipophilicity of trifluoromethanesulfonamides **1** (triflamide) facilitate the transfer of protons from the mitochondrial inner-membrane space into the mitochondrial matrix. The triflamide derivative **2** were shown to be highly potent compounds that strongly lower the level of Alzheimer's amyloid-β peptides in brains and cerebrospinal fluid.

Thus, the growing interest of using fluorinated substituents in drug design presents challenging synthetic strategies that allow more facile access to a wide range of fluorinated compounds.

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