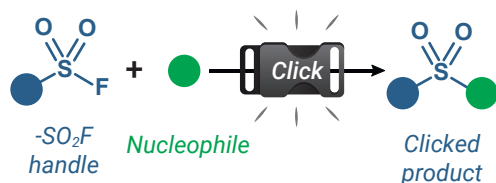


Sulfur-Fluorine Exchange: the second revolution of Click Chemistry

SuFEx is a family of click connective reactions based on the unique properties of the S^{VI}-F bond to forge new linkages with nucleophiles under mild conditions.



SuFEx handles	
 Aryl Fluorosulfate 17,970 fragments	 Sulfamoyl fluoride 56,573 fragments

Through a collaboration between OTAVACHemicals and Melius Organics, we introduce a new **SuFEx handle fragment library featuring 74,543 feasible fluorosulfate and sulfamoyl fluoride fragments**. Not only is this collection available for virtual screening, but these fragments can also be delivered physically, ensuring a seamless transition from computational exploration to tangible experimentation. With all starting materials in stock, we guarantee swift preparation and delivery—typically within just three weeks—empowering your discovery pipeline with speed and reliability.

Applications in Medicinal Chemistry and Chemical Biology

Aryl fluorosulfates and sulfamoyl fluorides are pivotal in medicinal chemistry as they can react with amino acids such as **lysine**, **tyrosine**, and **histidine** to form new covalent bonds.

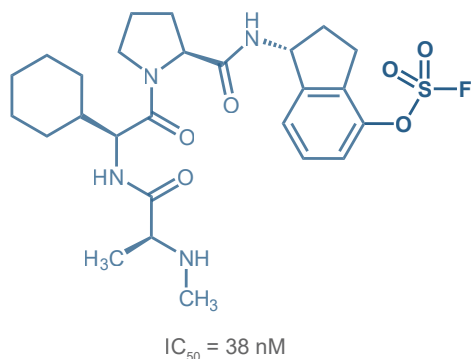
This makes these fragments suitable for **covalent warheads inhibitors, enzyme profiling, protein crosslinking and peptide conjugation**.

Biochemical features

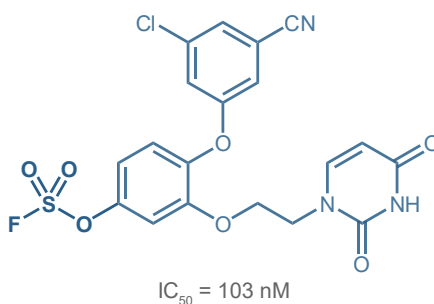
- “Masked electrophiles” activated in H-bonding environments
- High modification yields
- Water-stable
- Good stability in blood plasma, microsomes, and hepatocytes
- Not hampering cell permeability
- Fluoride leaving group safe up to mM

Covalent inhibitors

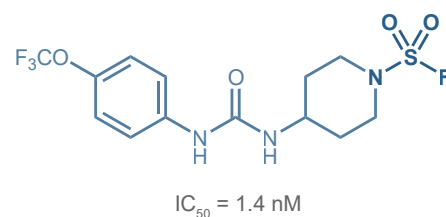
Covalent drug discovery is at the vanguard of current medicinal chemistry and chemical biology. While traditionally focused on targeting cysteine, the absence of this amino acid in many protein binding sites is driving exciting advancements in sulfur (VI) fluoride exchange (SuFEx) chemistry to expand the druggable proteome.



Pan-Inhibitor of Apoptosis Protein (IAP)
J. Med. Chem. 2019, 62, 9188



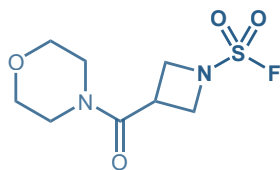
Wild-Type HIV-1 Reverse Transcriptase Inhibitor
ACS Med. Chem. Lett. 2021, 12, 249



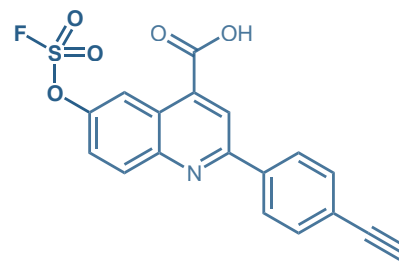
Inhibitor against human sEH
 WO 2015/188060
 Scripps Research Institute

Enzyme profiling and proteomics

Fluorosulfates and sulfamoyl fluorides are **ideal probes for protein labeling**, offering chemoselectivity and biocompatibility to study diverse biological processes. These probes are applied in mapping protein-ligand interactions to discover novel drug targets, investigating protein-protein interactions, and advancing therapeutic strategies.



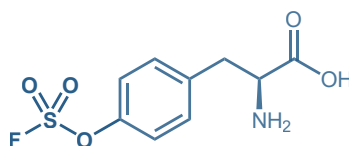
Probe to detect PIKK Kinases
ACS Chem. Biol. 2023, 18, 285



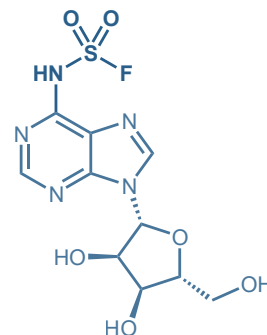
"Inverse Drug Discovery probe"
J. Am. Chem. Soc. 2018, 140, 200

Protein crosslinking and peptide conjugation

SuFEx hubs also find applications in **synthetic biology and bioconjugation**. For example, modified SO₂F-tyrosine has been used for in vivo protein crosslinking, while sulfamoyl fluoride-derived nucleosides have been employed to modify peptides.



Latent bioreactive unnatural amino acid
J. Med. Chem. 2018, 140, 4995



Adenosine derivate for peptide conjugation
Org. Lett. 2022, 24, 4977

Applications in Synthetic Chemistry

Fluorosulfates and **sulfamoyl fluorides** are versatile functional groups with significant applications in organic synthesis. Their "click chemistry" nature ensures **high-yielding reactions with minimal purification**, making them reliable tools in synthetic strategies.

These electrophilic functionalities can be activated under specific reaction conditions. Compared to their chlorinated analogs, fluorosulfates and sulfamoyl fluorides offer superior resistance to reduction, exceptional thermodynamic stability, and exclusive reactivity at the sulfur atom. Furthermore, they enable robust, high-yielding reactions that are even compatible with aqueous media, making them particularly **well-suited for late-stage functionalization due to their broad functional group tolerance**.

Additionally, their ability to react with a diverse range of nucleophiles (O-, N-, and C-based) provides access to an expansive and varied chemical space.

