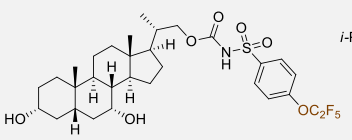
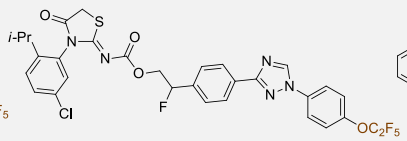
Fluoroalkyl ethers for Drug Design

Introduction

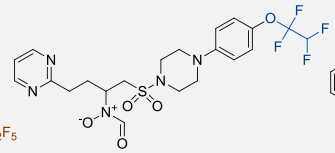
More than 20% of all modern pharmaceuticals and up to 30% of agrochemicals contain at least one fluorine atom. As a typical fluoroalkoxy group, trifluoromethoxy (-OCF_3) is prevalent in bioactive compounds. Compared to the well-studied -OCF_3 group, its bulkier analogue, pentafluoroethoxy (-OC_2F_5) group, has been much less explored. In fact, -OC_2F_5 and -OCF_3 groups have similar electronic properties, lipophilicity and metabolic stability.[1-4] In this context, *Enamine* offers a library of various fluoroalkyl-substituted ethers for drug design.



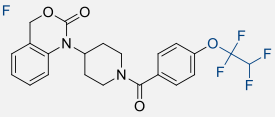
FXR modulator
WO 2018/152171 A1
Enanta Pharm.



Crop protection
WO 2020/139566 A1
Dow AgroSciences

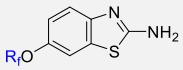


Metalloproteinase inhibitor
WO 2005/000822 A1
AstraZeneca



Oxytocin receptor antaginist
US 5726172, 1998, A
Merck & Co.

Case studies



Riluzole (R_f = CF_3)
(treatment of neurological diseases)

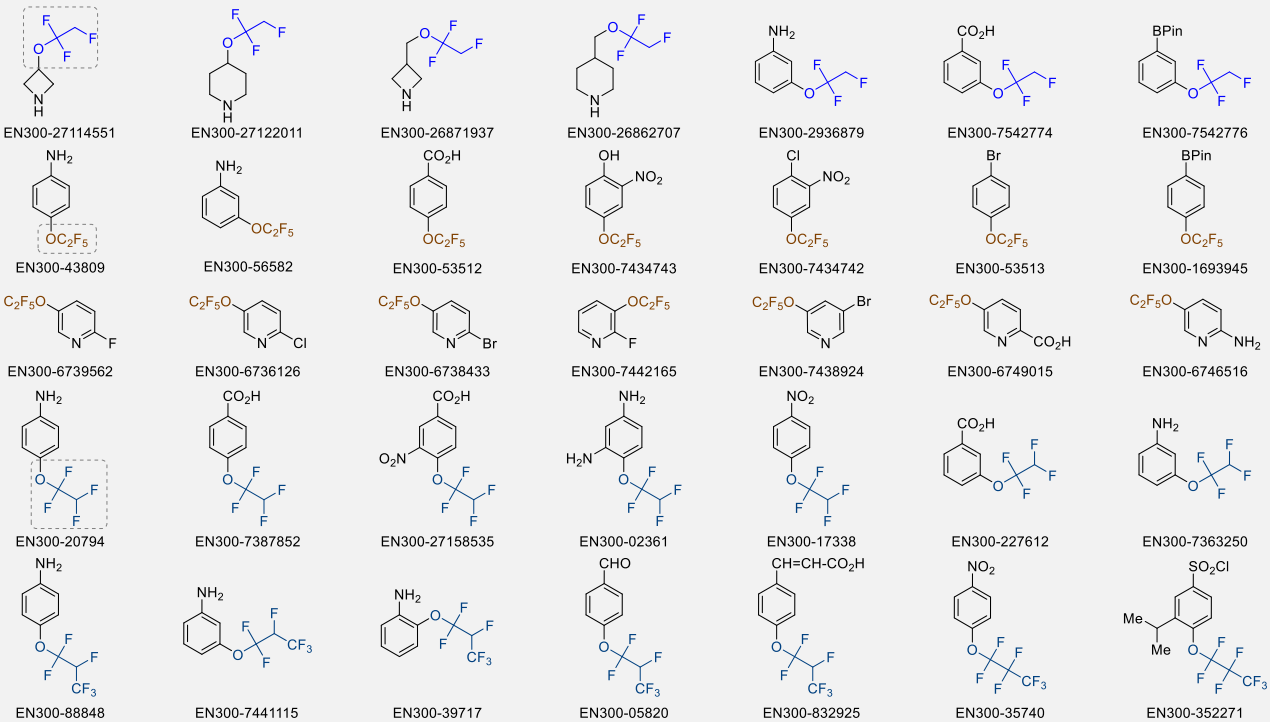
R_f	CF_3	CF_2H	CH_2CF_3	CF_2CF_3	CF_2CF_2H
ED_{50}	3.2	7.5	6.5	2.5	8.5

"Antiglutamate" activities of 6-fluoroalkoxy-2-benzothiazolamines.[3]

Properties

- ↑ lipophilicity;
- ↑ electron-withdrawing ability;
- ↑ chemical and thermal stability;
- ↑ metabolic stability.

We offer: more than 50 of fluoroalkyl ethers from stock on a 5-10 g scale.



References

1. T. Besset et al. *Org. Chem. Front.* **2016**, *3*, 1004.
2. M.-L. Fu et al. *J. Org. Chem.* **2017**, *82*, *7*, 3702.
3. P. Jimonet et al. *J. Med. Chem.* **1999**, *42*, *15*, 2828.
4. A. Granados et al. *J. Org. Chem.* **2020**, *85*, *16*, 10378.