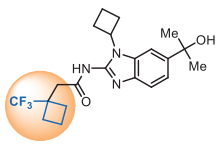
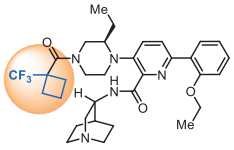
CF_3-Cyclobutane for Enhanced Metabolic Stability

Introduction

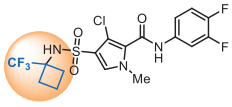
Achieving resistance to metabolic clearance is a key objective in optimizing the structures of orally available drugs. In pursuit of this goal, replacing *tert*-butyl groups[1,2] aromatic moieties,[3] and several other hydrophobic functional groups[4] with a 1-trifluoromethyl-cyclobutyl group has shown promising results, maintaining bioactivity while reducing metabolic degradation. Recently, scientists at Enamine developed a practical synthetic approach to prepare dozens of building blocks featuring the 1-trifluoromethyl-cyclobutyl group, facilitating future construction of bioactive compounds.[2]



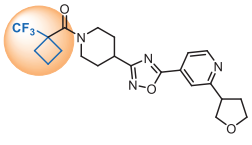
Kv7 potassium channel activator
WO 2024/054811
Biohaven Ther



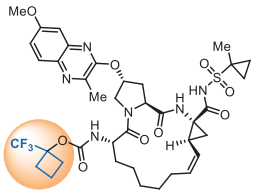
melanocortin type 2 receptor antagonists
WO 2024/211343
Crinetics Pharm



capsid assembly modulator, against HBV
WO 2021/178612
Janssen

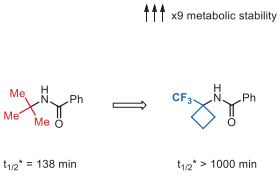


SCD1 and SCD5 inhibitors
WO 2019/209948
Yumanity Ther

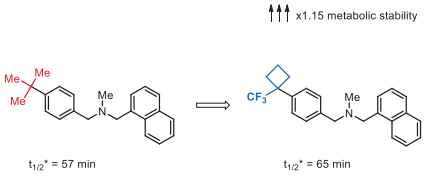


HCV NS3/4A protease inhibitor
WO 2020/247736
University of Massachusetts

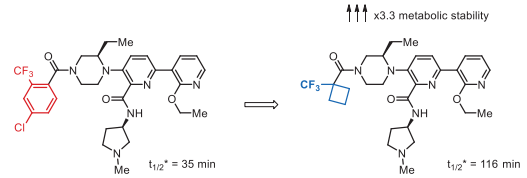
Key advantage



JACS Au **2024**, *4*, 4507



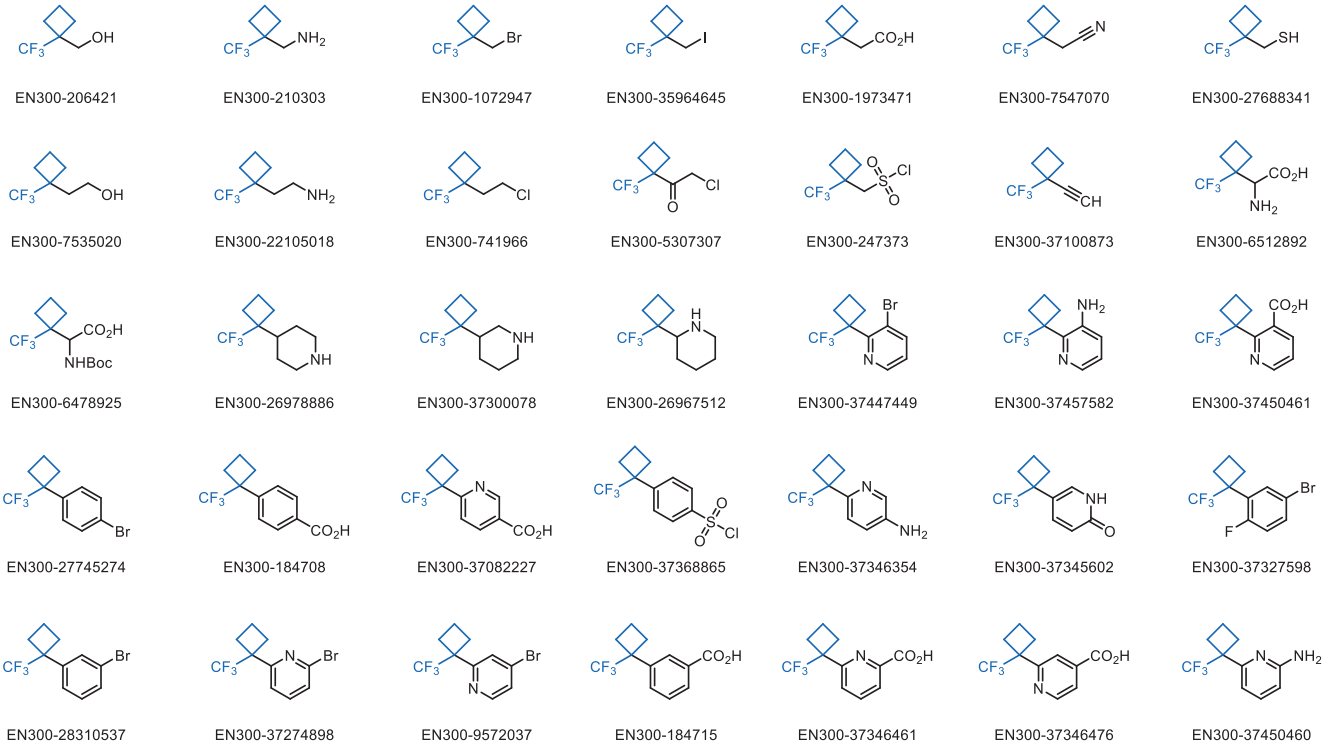
JACS Au **2024**, *4*, 4507



ACS Med. Chem. Lett. **2024**, *15*, 478

* in human liver microsomes

We offer: over 50 1-trifluoromethylcyclobutanes from stock on 5-10 gram scale.



References

1. D. Rao et al. *J. Med. Chem.* **2021**, *64*, 11972.
2. V. Ahunovych et al. *JACS Au* **2024**, *4*, 4507.
3. S. Kim et al. *ACS Med. Chem. Lett.* **2024**, *15*, 478.
4. J. Mowat et al. *J. Med. Chem.* **2024**, *67*, 17429