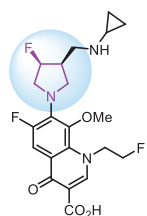


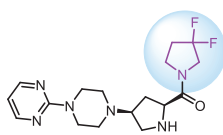
Enhancing Permeability with Fluoropyrrolidines

Introduction

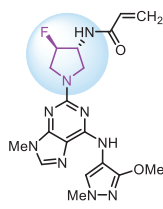
Pyrrolidine ring is the third most common heterocycle in the newly approved drug structures.¹ However, the basicity of the nitrogen atom poses serious problems when protonation prevents passive permeability. Fluorination lowers the pK_a to near or below physiological values, thus creating an optimal balance of the activity and permeability.² The electronic effect of fluorine also enhances the dynamics of the amide and related conjugated structures.³ Finally, fluorination helps block major metabolic sites thus creating better bioavailable molecules.⁴ Explore our rich collection of fluorinated pyrrolidine building blocks.



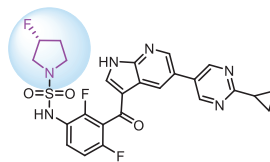
Lascufloxacin
against Gram+ bacteria
approved as antibiotic
Kyorin



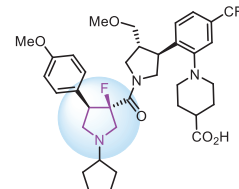
Gosogliptin
dipeptidyl peptidase-4 inhibitor
approved against diabetes
Pfizer



Mavelertinib
mutant epidermal growth factor receptor inhibitor
Phase 1-2 trials against lung cancer
Pfizer

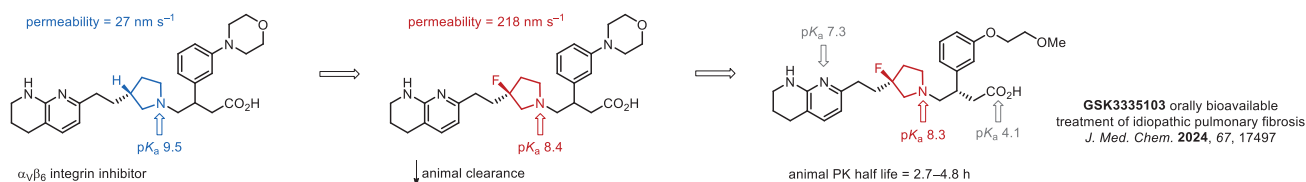


Plexorafenib (Plx8394)
serine/threonine-protein kinase B-raf inhibitor
Phase 1-2 trials against advanced cancers
Pfexikon

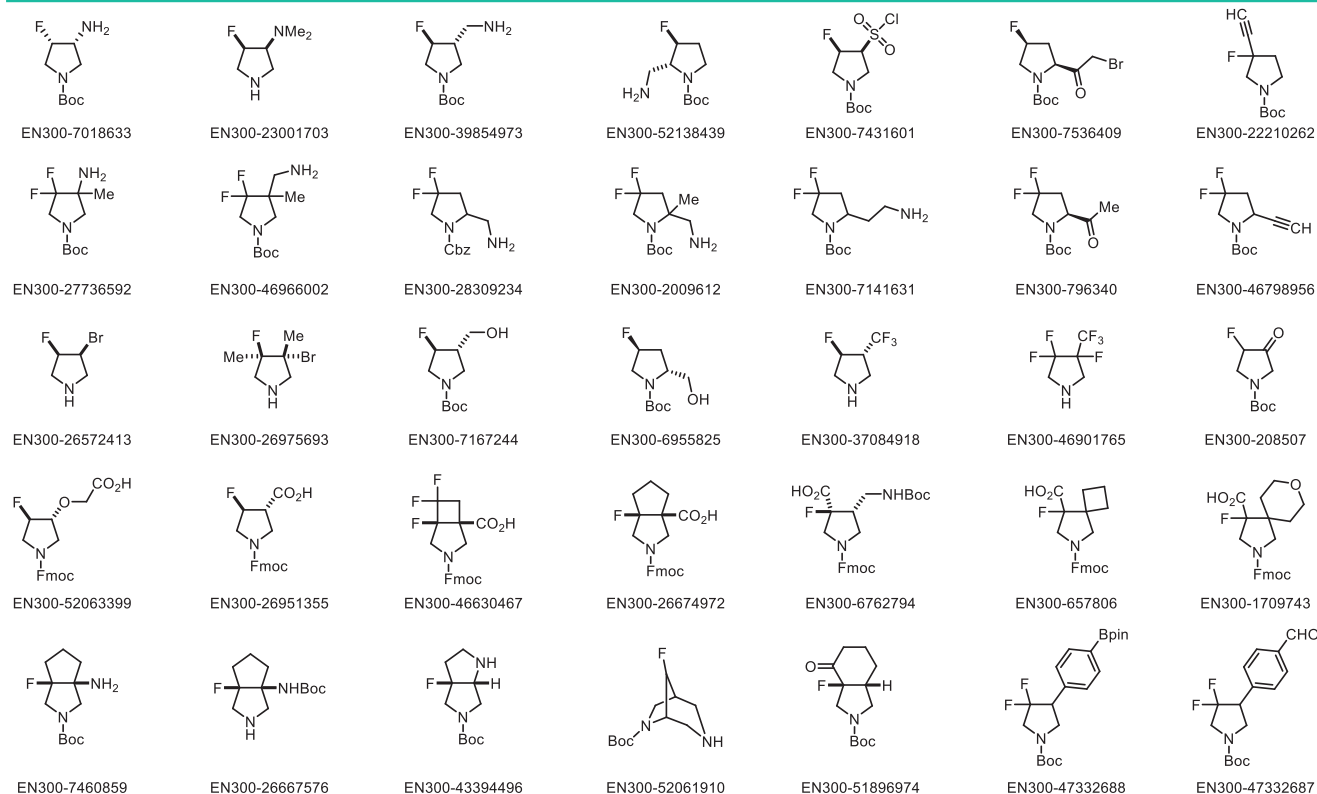


Dersimelagon (MT-7117)
agonist of melanocortin 1 receptor
FDA orphan designation
Mitsubishi Tanabe Pharma

Case study



We offer: over 100 fluoropyrrolidines from stock on 5-10 gram scale.



References

1. C. Marshall et al. *J. Med. Chem.* **2024**, *67*, 11622.
2. P. Procopiou et al. *J. Med. Chem.* **2024**, *67*, 17497

3. L. Brewitz and C. Schofield. *J. Med. Chem.* **2024**, *67*, 11656.
4. Z. Chen et al. *J. Med. Chem.* **2024**, *67*, 18606.



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