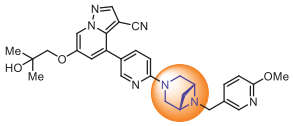
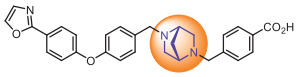
Bridged Piperazines for Drug Discovery

Introduction

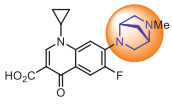
Bridging has demonstrated exceptional success in optimizing piperazine linkers across a range of drugs and lead molecules.[1] These structural motifs effectively constrain molecular conformation variability, achieving this with only a minimal increase in molecular volume and weight.[2,3] Interestingly, recent studies reveal that bridging can, somewhat counterintuitively, reduce a compound's lipophilicity even as molecular weight increases.[4] Try Enamine's collection of bridged piperazine molecular scaffolds!



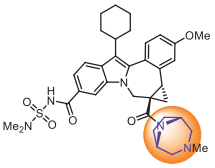
Selpercatinib
RET kinase inhibitor
FDA approved 2020 as anticancer
Eli Lilly



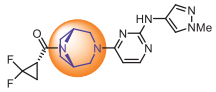
Acebilustat (CTX-4430)
inhibitor of leukotriene A_4 hydrolase
Phase 2 trials against inflammations
Schering and *Estrellita*



Danofloxacin
fluoroquinolone antibiotic
approved in 2002 for the use in cattle
Pfizer

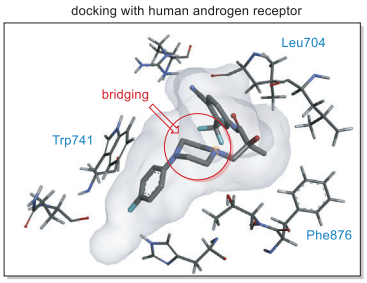


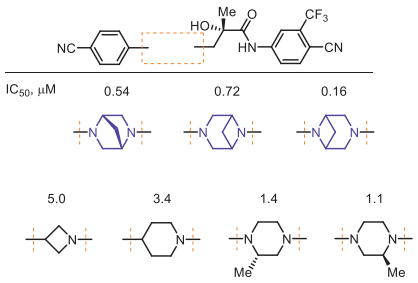
Beclabuvir (BMS-791325)
allosteric inhibitor of NS5B polymerase
Phase 4 trials against HCV
Bristol-Myers Squibb



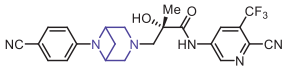
Brepocitinib (PF-06700841)
dual Janus and and tyrosine 2 kinase inhibitor
Phase 3 trials against panuveitis
Pfizer

Case study





selective topical androgen receptor antagonist



IC_{50} 135 nM

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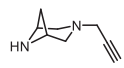
We offer: over 100 bridged piperazines from stock on 5-10 gram scale.



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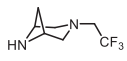

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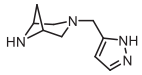

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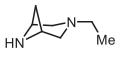

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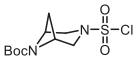

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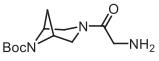

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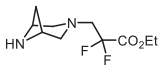

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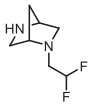

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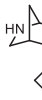

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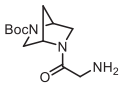

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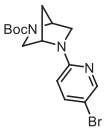

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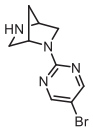

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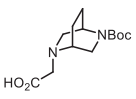

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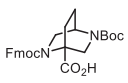

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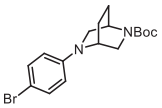

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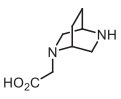

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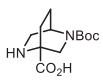

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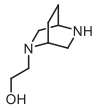

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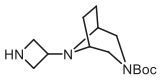

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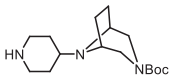

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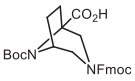

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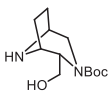

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References

1. N. Meanwell and O. Loiseleur. *J. Agric. Food Chem.* **2022**, *70*, 10971.
2. X. Wang et al. *J. Med. Chem.* **2025**, *68*, 13990.
3. Z. Bian et al. *J Med. Chem.* **2025**, *68*, 14357.
4. S. Degorce et al. *J. Med. Chem.* **2018**, *61*, 8934.