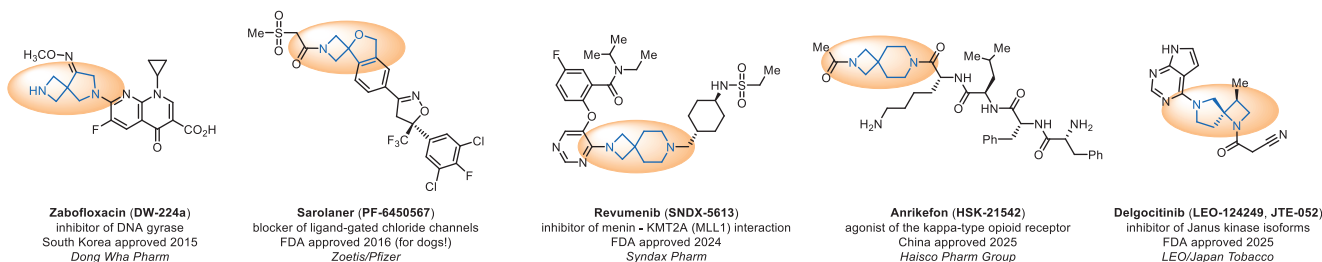


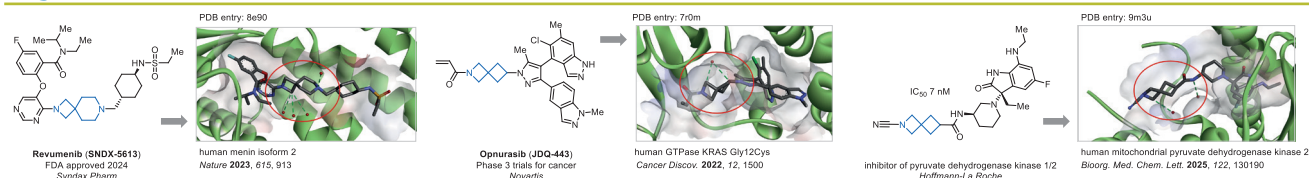
Magic Methyl for Spirocyclic Scaffolds

Introduction

Recent medicinal chemistry projects frequently use spirocyclic linkers to enhance molecular three-dimensionality and reduce metabolic susceptibility. A notable example is the family of spirocyclic azetidines, found in 5 approved drugs and 19 clinical trial candidates. However, crystal structure analyses often reveal crystallographic water in binding sites, suggesting a room for small substituents like methyl groups.^{1,2} To date, Deglocitinib, a Janus kinase inhibitor FDA-approved in 2025 for chronic hand eczema,³ is the only drug exemplifying the "magic methyl" concept⁴ in spiroazetidines. With *Enamine* now supplying a battery of methylated and other substituted derivatives, we anticipate more structures adopting this design.

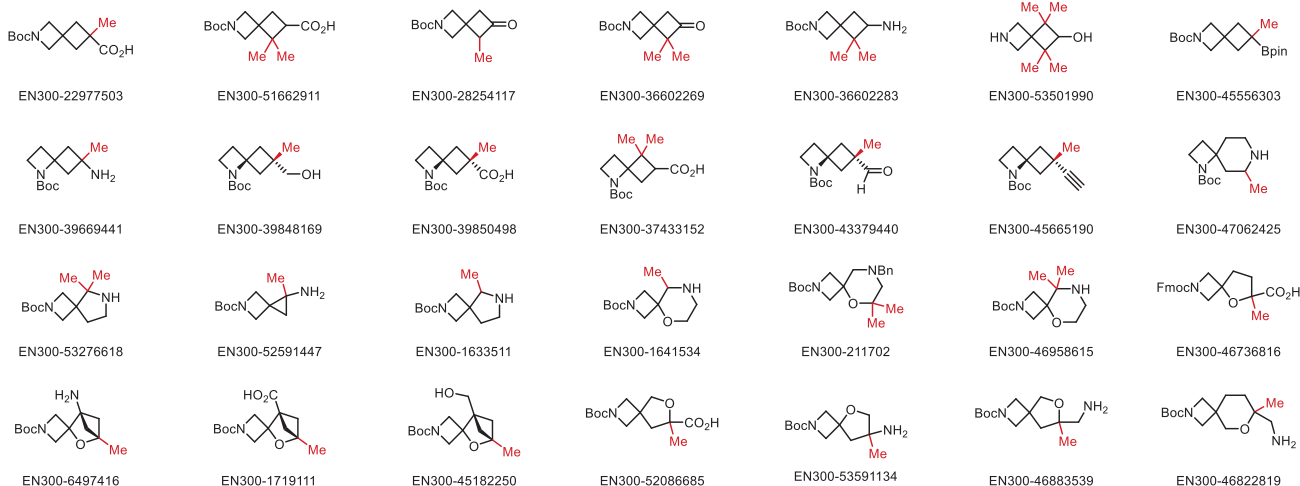


Crystal structures

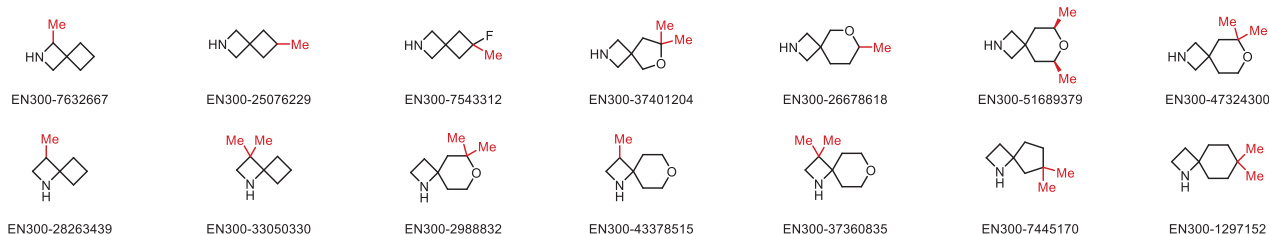


We offer: over 100 methyl spiroazetidines from stock on 5-10 gram scale.

linkers



stoppers



References

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2. H. Xu et al. *Bioorg. Med. Chem. Lett.* **2025**, 122, 130190.

3. S. Noji et al. *J. Med. Chem.* **2020**, 63, 7163.
4. P. Pinheiro et al. *Pharmaceuticals* **2023**, 16, 1157.



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