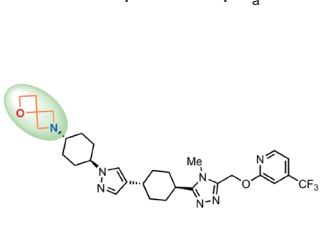
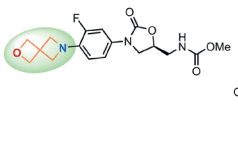
Spiro Morpholines

Introduction

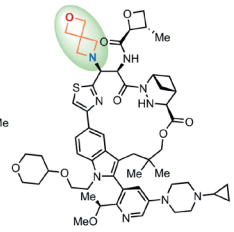
The morpholine fragment is one of the most common amine moieties in drug design, valued for excellent solubility and permeability features.[1] However, it also introduces metabolic liabilities, such as CYP-mediated oxidation, dealkylation, and ring opening.[2] Its closest spirocyclic analogues, oxaazaspiro[3.3]heptanes (spiro morpholines), have recently shown strong potential in drug development, with several candidates currently in clinical trials.[3,4] *Enamine* offers one of the most advanced and diverse collections of spiro morpholines, including isomeric structures and substitutions. The isomers enable variations in molecular dipole and pK_a while retaining a molecular volume nearly identical to that of morpholine.



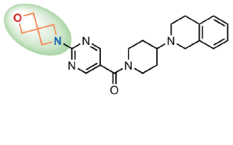
IMU-856
inhibitor of histone deacetylase enzyme SIRT6
Phase 1/1b clinical trials
Immunic/Daiichi Sankyo



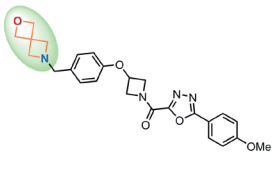
TBI-223
oxazolidinone antibiotic for tuberculosis
Phase 2 trials ongoing
Global Alliance/IMM



RMC-5127
inhibitor of KRAS Gly12Val
Phase 1 trials ongoing
Revolution Medicines

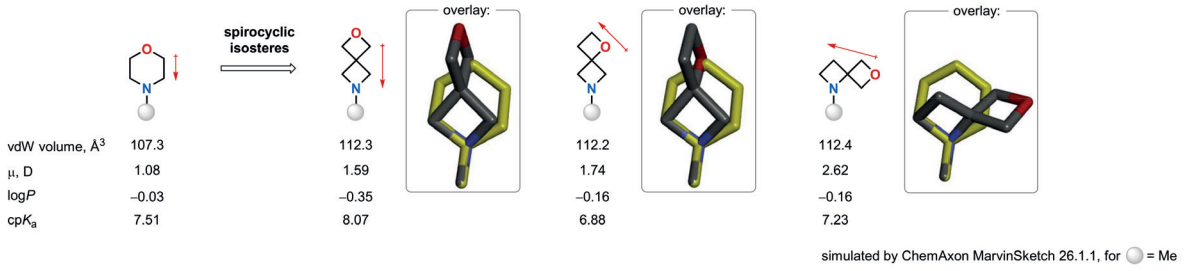


Fadaltran (BAY-1193397)
antagonist of α_{2C}-adrenoreceptor
Phase 2 trials for diabetic foot
Bayer



AZD-1979
antagonist of melanin-concentrating hormone receptor 1
Phase 1 trials
AstraZeneca

Concept



vdW volume, Å^3	107.3		112.3		112.2	
μ, D	1.08		1.59		1.74	
log*P*	–0.03		–0.35		–0.16	
cpK_a	7.51		8.07		6.88	
					112.4	
					2.62	
					–0.16	
					7.23	

simulated by ChemAxon MarvinSketch 26.1.1, for ○ = Me

We offer: over 25 oxaazaspiro[3.3]heptanes from stock on gram scale.

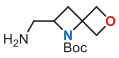
EN300-37313478

EN300-46966900

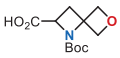
EN300-52232245

EN300-52149500

EN300-7547702



EN300-53541503



EN300-52035875

EN300-190273

EN300-52803953

EN300-27780144

EN300-39681130

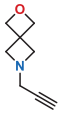
EN300-19060922

EN300-55072732

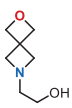
EN300-53822328

EN300-52454016

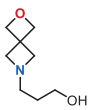
EN300-23004595



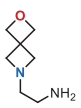
EN300-3439123



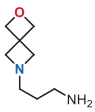
EN300-265093



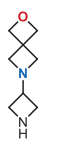
EN300-265106



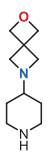
EN300-1587825



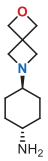
EN300-3150878



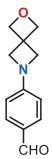
EN300-3160163



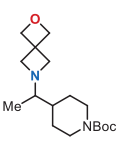
EN300-3160169



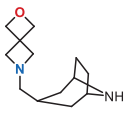
EN300-52760374



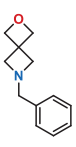
EN300-726058



EN300-37336268



EN300-37294218



EN300-6482490

References

1. J. Shearer et al. *J. Med. Chem.* **2022**, *65*, 8699.
2. A. Kourounakis et al. *Med. Chem. Res.* **2020**, *40*, 709.
3. A. Johansson et al. *J. Med. Chem.* **2016**, *59*, 2497.
4. A. Lombardi et al. *Antimicrob. Agents Chemother.* **2025**, *69*, e01542-24.