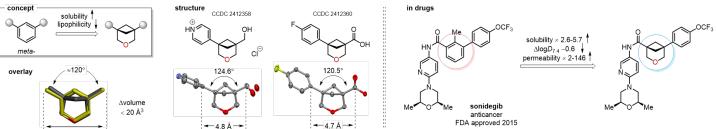
meta-Benzene Isosteres with Improved Solubility

Introduction

In recent research, benzene-based aromatics have been highly disfavored in favor of aliphatic isosteric alternatives that help improve the bioavailability of organic molecules.^{1,2} In 2025, two groups from *Janssen*³ and *Enamine*⁴ reported independently innovative aromatic isosteres based on the structures of 3-oxabicyclo[3.1.1]heptane. The bicyclic molecular skeleton is highly resembling to the geometric features of the *meta*-substituted benzene ring, while the oxygen atom helps improve water solubility, lower lipophilicity, and increase permeability of drugs.^{3,4} The innovative skeleton has appeared in several patents since 2022, and this number will grow. Explore *Enamine*'s collection of *circa* 90 new building blocks containing the 3-oxabicyclo[3.1.1]heptane core skeleton.

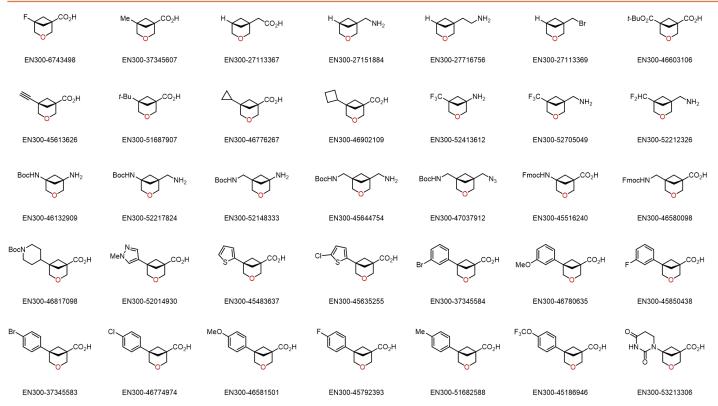


Concept



Org. Lett. 2025, 27, 3291 (Janssen) and Angew. Chem. Int. Ed. 2025, 64, e202505519 (Enamine)

We offer: over 50 3-oxabicyclo[3.1.1]heptanes from stock on 5-10 gram scale.



References

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- 3. J. Morvan et al. Org. Lett. 2025, 27, 3291.
- 4. D. Dibchak and P. Mykhailiuk. *Angew. Chem. Int. Ed.* **2025**, 64, e202505519.

