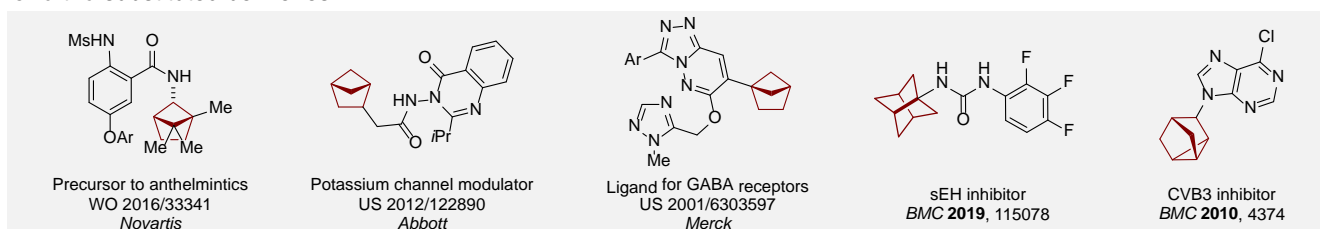


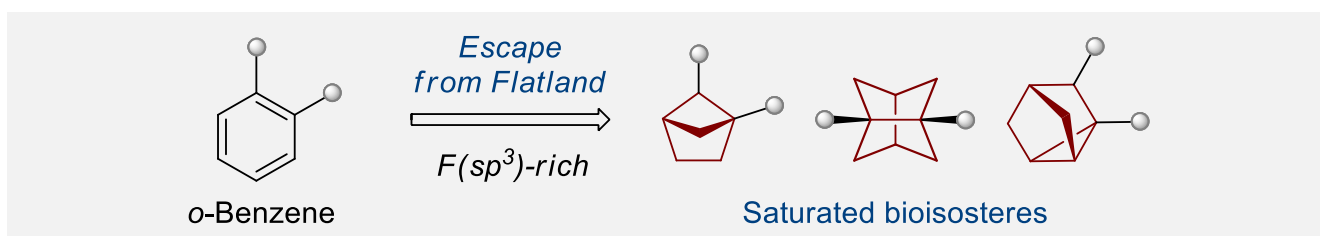
Saturated Bioisosteres for *ortho*-substituted Benzenes

Introduction

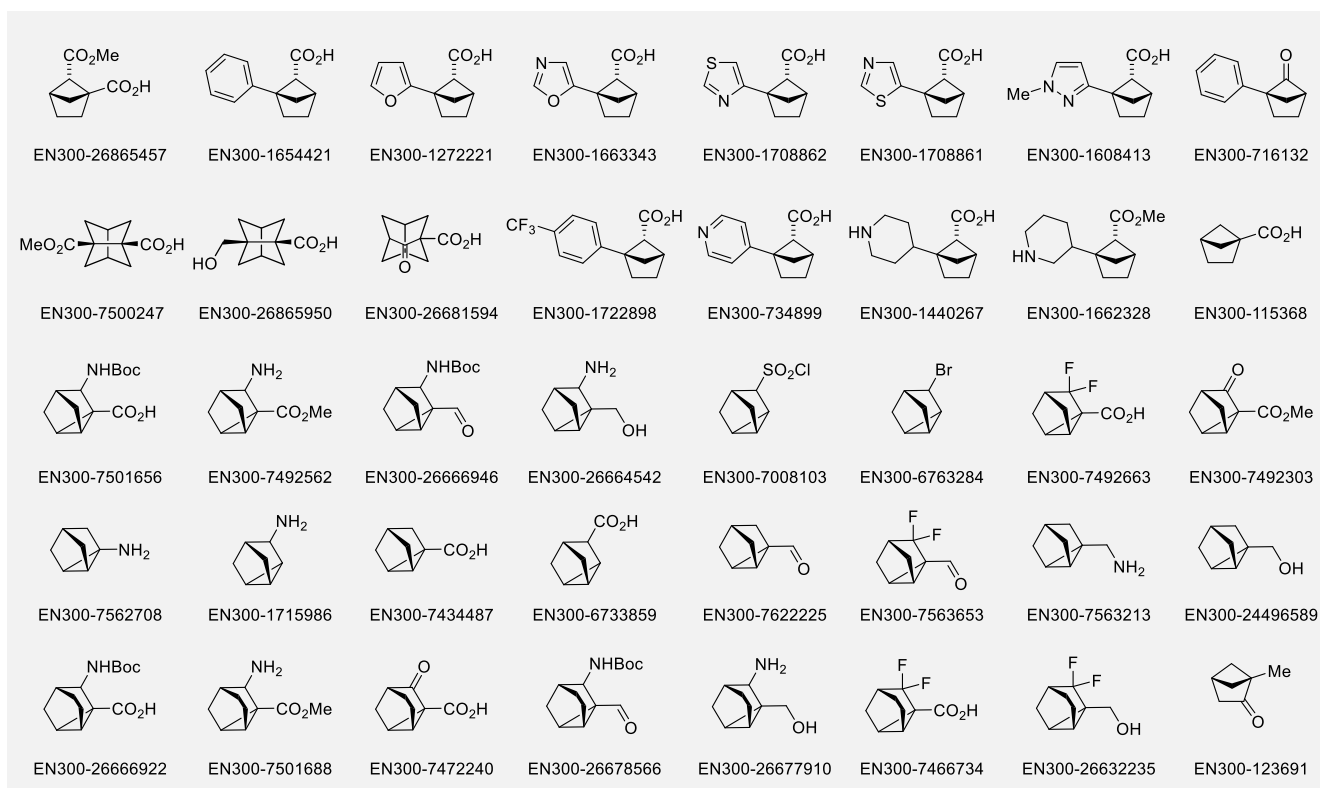
The fragment of benzene is the most popular ring in bioactive compounds.¹ In fact, more than 500 drugs and agrochemicals are benzene-containing molecules.² In 2012, chemists at Pfizer replaced the substituted phenyl fragment in a γ -secretase inhibitor *Avagacestat* with the bicyclo[1.1.1]pentyl skeleton.³ The obtained analogue showed higher activity, solubility and metabolic stability. Since then, bicyclo[1.1.1]pentanes, bicyclo[2.2.2]octanes and cubanes are used in medicinal chemistry as saturated bioisosteres for *para*-substituted benzenes.^{4,5} Therefore, here we have designed and synthesized saturated mimetics for *ortho*-substituted benzenes.



Design



We offer



References

1. R. D. Taylor et al. *J. Med. Chem.* **2014**, *57*, 5845.
2. P. Mykhailiuk *Org. Biomol. Chem.* **2019**, 2839.

3. A. F. Stepan et al. *J. Med. Chem.* **2012**, *55*, 3414.
4. P. K. Mykhailiuk et al. *ANIE* **2006**, *45*, 5659.

5. A. Denisenko et al. *ANIE* **2020**, just accepted
(doi.org/10.1002/anie.202004183)