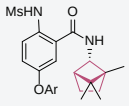
Saturated Bioisosteres of *ortho-/meta-*substituted Benzenes

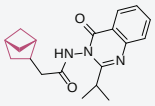
A. Denisenko, P. Garbuz, P. Mykhailiuk, A. Tolmachev

Introduction and Aim

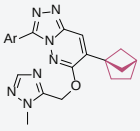
The fragment of benzene comprises of the structure of more than 500 FDA-approved drugs.[1] In 2012, *Stepan* and coworkers showed that bicyclo[1.1.1]pentane skeleton could act as a saturated "*nonclassical phenyl ring bioisostere*".[2-6] Adding one carbon atom gives the closest homologue – bicyclo[2.1.1]hexane. The lack of the practical synthetic approaches restricts the common use of bicyclo[2.1.1]hexanes in chemistry. Herein we have designed and synthesized a library of saturated mimics of the *ortho*- and *meta*-benzene ring for drug design.



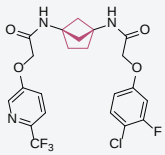
Precursor to anthelmintics
WO 2016/33341
Novartis



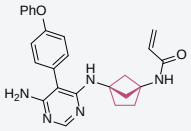
Potassium channel modulators
US 2012/122890
Abbott



Ligand for GABA receptors
US 2001/6303597
Merck

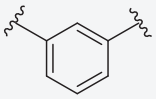


Modulator of the integrated stress pathway
WO 2017/193034
Calico



Inhibitor of Bruton's tyrosine kinase
WO 2012/170976
Merck

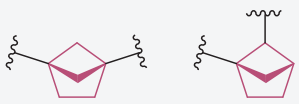
Design



meta-substituted Benzene

Escape from Flatland

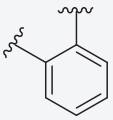
$F(sp^3)$-*rich*
>100 drugs



Mimics for *ortho-/meta*-substituted Benzenes

Escape from Flatland

$F(sp^3)$-*rich*
>100 drugs

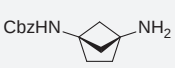


ortho-substituted Benzene

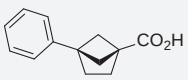
We offer more than 20 *ortho-/meta*-substituted benzene mimics in our stock:

EN300-115368

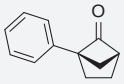
EN300-70833



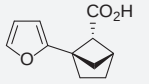
EN300-64076



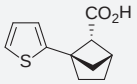
EN300-1472308



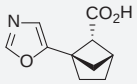
EN300-716132



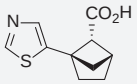
EN300-1272221



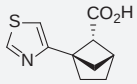
EN300-1272220



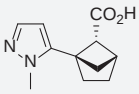
EN300-1663343



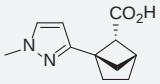
EN300-1708861



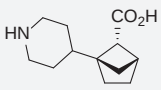
EN300-1708862



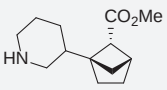
EN300-1608412



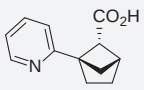
EN300-1608413



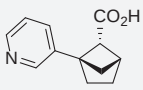
EN300-763031



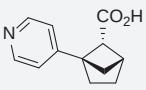
EN300-1654406



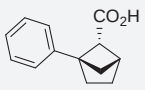
EN300-1272222



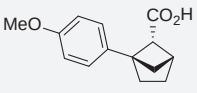
EN300-1272223



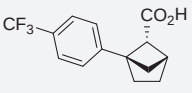
EN300-651294



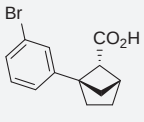
EN300-396330



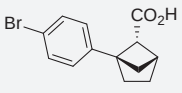
EN300-1572743



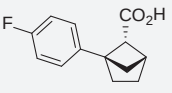
EN300-1702676



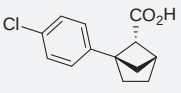
EN300-2010063



EN300-6472668



EN300-1572747



EN300-6479063

Contact

Pavel Mykhailiuk, Dr. Sci., PhD
Pavel.Mykhailiuk@gmail.com
Enamine Ltd, www.enamine.net
78 Chervonotkatska St, 02660 Kyiv, Ukraine

References

1. R. D. Taylor et al. *J. Med. Chem.* **2014**, 57, 5845.
2. A. F. Stepan et al. *J. Med. Chem.* **2012**, 55, 3414.
3. Y. L. Goh et al. *J. Am. Chem. Soc.* **2016**, 138, 1698.
4. P. K. Mykhailiuk et al. *ANIE* **2006**, 45, 5659.
5. S. O. Kokhan et al. *ANIE* **2016**, 55, 14788.
6. S. O. Kokhan et al. *Eur. J. Org. Chem.* **2017**, 43, 6455.