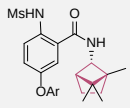
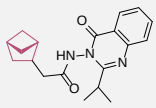
Saturated Bioisosteres of *ortho-/meta*-substituted Benzenes

Introduction

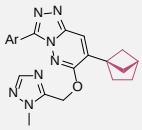
The fragment of benzene comprises to the structure of more than 500 FDA-approved drugs.[1] In 2012, *Stepan* and coworkers showed that bicyclo[1.1.1]pentane skeleton could act as a saturated "*nonclassical phenyl ring bioisostere*".[2-6] Adding one carbon atom gives the closest homologue – bicyclo[2.1.1]hexane. 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
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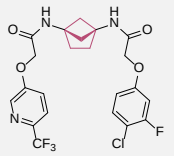
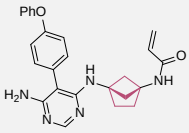


Modulator of the integrated stress pathway
WO 2017/193034
Calico



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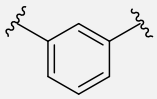
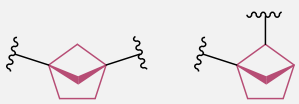
Design



meta-substituted Benzene

Escape from Flatland

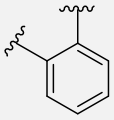
$F(sp^3)$-*rich*
>100 drugs



Mimics for *ortho-/meta*-substituted Benzenes

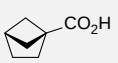
Escape from Flatland

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



ortho-substituted Benzene

We offer



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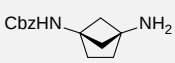

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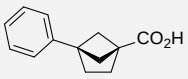

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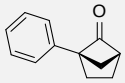

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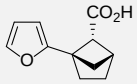

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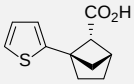

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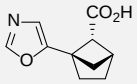

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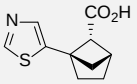

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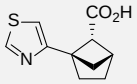

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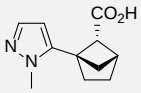

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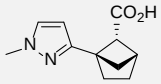

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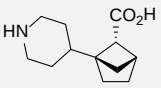

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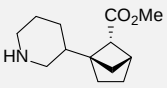

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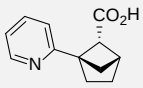

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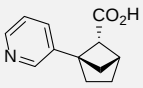

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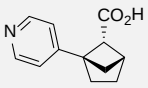

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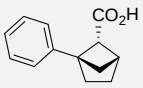

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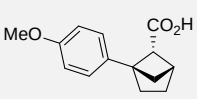

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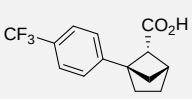

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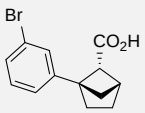

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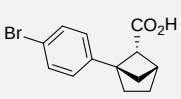

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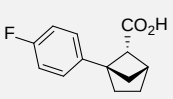

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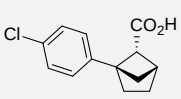

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References

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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.
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6. S. O. Kokhan et al. *Eur. J. Org. Chem.* **2017**, *43*, 6455.