CNS Library

Library of novel small molecules with high CNS MPO scores

47 040 compounds

To enable the discovery of new CNS actives we employed versatile approaches, bearing in mind molecular properties preferable for BBB permeability. The resulting final selection of 47,040 compounds from the initial 2.6 M screening collection possess the most preferable CNS-like properties and structural features, maintaining high level of *Novelty* and *Diversity* .
In order, to facilitate and speed up Hit finding we created **pre-plated library**, comprising 45,440 high quality compounds, ready for immediate shipping. Using our CNS Library you receive multiple benefits with a much time saving in the next stages of **hit follow-up**:

- **Analogs and hit samples resupply from dry stock of over 2.6 M compounds.**
- **Straightforward & low-cost synthesis of follow-up libraries through our REAL Database technology**
- **Medicinal chemistry support enhanced with on-site broad ADME/T panel**

You have also an option to screen the librray directly at Enamine. In this case we will be happy to offer you discount on library cost depending on the collaboration scope.

Most popular library formats available for immediate supply

Item	Catalog No.	No of compounds	No of plates	Amount	Plates and format
1	**CNS-45-Y-0**	45 440	142	Any suitable for 1 assay	384-well plates, 320 cpds per plate, first two and last two columns empty
2	**CNS-45-Y-10**	45 440	142	10 µL of 10mM DMSO stock solutions	384-well plates, 320 cpds per plate, first two and last two columns empty
3	**CNS-45-Y-50**	45 440	142	50 µL of 10mM DMSO solutions	384-well plates, 320 cpds per plate, first two and last two columns empty

Library Design

Overcoming the difficulty of delivering therapeutic agents to specific CNS sites is one of a major challenge for treatment of the majority of CNS disorders. The criteria for selection of CNS-active molecules which are able to penetrate blood-brain barrier (BBB) were low polar surface area (TPSA < 70 Å^2 (median value 48 Å^2), *cf.* 45 Å^2 for the marketed CNS drugs), low degree of possible hydrogen bond formation (total number of hydrogen bond acceptors and donors are less than 8) and low ClogP values, the everage is 1.63. Further selection was driven by evaluation of CNS MPO desirability scores for each candidate compound. The algorithm included parameters for selection included:

CNS MPO ≥ 4 (ClogP, ClogD, MW, TPSA, HBD, and pKa for most basic center)

MW ≤ 350 (median value 283, *cf.* 305 for the marketed CNS drugs),

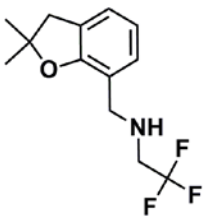
ClogP ≤ 3.0 (mean value 1.63, *cf.* 2.8 for the marketed CNS drugs),

Amide groups ≤ 1, **Hbond Donor** ≤ 2, QProp **CNS** value > 0.

Parameter	Range	Parameter	Range
MW	170 ... 350	RotBonds	≤ 4
ClogP	**-0.5 ... 3.0**	**Aromatic rings**	**1 ... 3**
TPSA	**≤ 70 Å^2**	Fsp^3	0.15 ... 0.8
Hbond Donor	≤ 2	QPPCaco-2	> 500
Amide groups	≤ 1	Basic N	≤ 2
Total H-bonding	< 8	QPlogBB	-1.0 – 0.8
Carboxylic acids	≤ 1	**CNS**	**> 0**
CNS MPO	**≥ 4**	pKa_bs	-1,5 ... 8,0
QPlogKhsa	-1.2 – 0.92	No quaternary Nitrogen	

Key features

Modern CNS drug discovery notions suggest that conformational constraints and rigidity of the molecules are important structural features of CNS-active compounds. Our selection of CNS compounds was enriched with recently synthesized molecules having sp^3-rich saturated ring cores of various architectures including spirocyclic (1,341 compounds, 14.5%), bridged and fused scaffolds (4,106 compounds, 44.5%).



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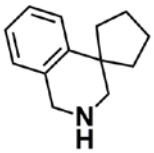

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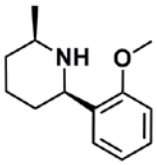

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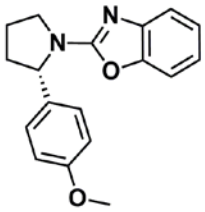

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Novelty

Compounds included into CNS focused Library were selected from all three screening collections - HTS, Advanced and Premium. Preference was given to the compounds synthesized within the last 4 years, based on innovative scaffolds and with use of advanced building blocks to enhance the novelty value of the library.