3D Shape Diverse Fragment Library

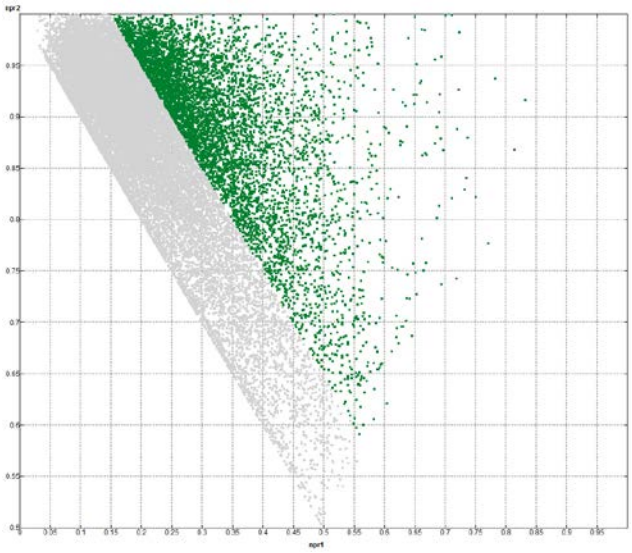
1,200 compounds

Unique 3D diversity among shaped molecules

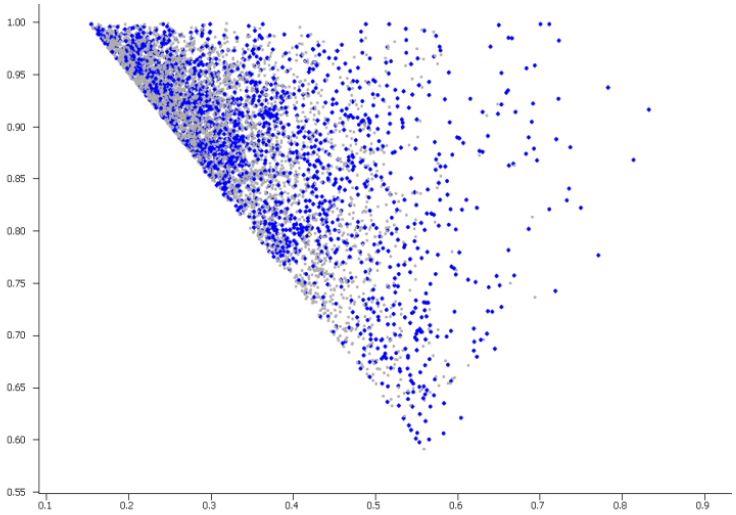
Enamine has been working on synthesis of new sp^3-rich heterocycles and expanding of spirocyclic chemistry already over 16 years. Our own research in this area enabled synthesis of large variety of 3D shaped molecules that are well represented in stock screening collection. Synthesis of derivatized series of aliphatic and sterically hindered cores, often exclusive only for Enamine, led to a number of readily available analogs that is a crucial point in fragment hit optimization and follow-up stage.

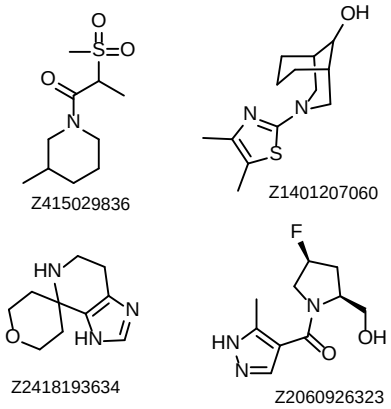
- R Ro3 compliant dataset was refined with strict MedChem filters (FAF-Drugs3) and Fsp^3 cut off 0.35.
- 3D-dimensionality criteria: NPR1 ≥ 0.15; NPR2 ≥ 1.15 - value of npr1 (PMI plot 1).
- K-mean clustering of preselected 8,000 3D fragments has been carried out using NPR1/2 values. Only centroid molecules were included in the library, PMI plot 2.

Parameter	Range
MW	120 … 300
Heavy atoms	8 … 19
ClogP	-1.5 … 3
HBD	0 … 3
HBA	0 … 3
RotBonds	0 … 3
TPSA,	≤ 80 Å^2
Aromatic rings	≤ 2
N+O count	1 … 9
Chiral centers	≤ 2
S count	≤ 1
Cl, Br, CN, amide, synfonamide	≤ 1



PMI plot 1: green dots correspond to **8,000** compounds indicated as **3D Fragments Set** from Enamine in-stock Ro3 compliant molecules (grey dots).





PMI plot 2: distribution of molecules in the library (centroids, blue spots) among of 8,000 of 3D-shaped initial set.