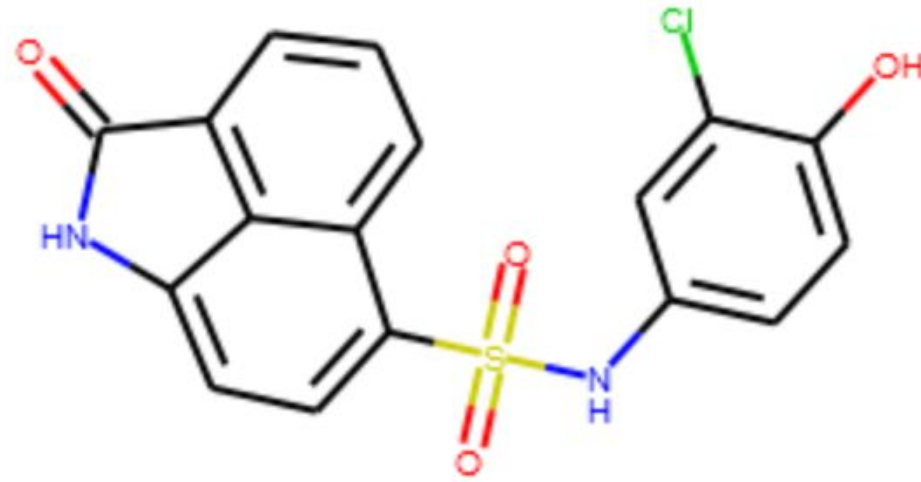


Трехмерное
представление молекул.
Фармакофоры.

Проблема трехмерного представления и выравнивания молекул

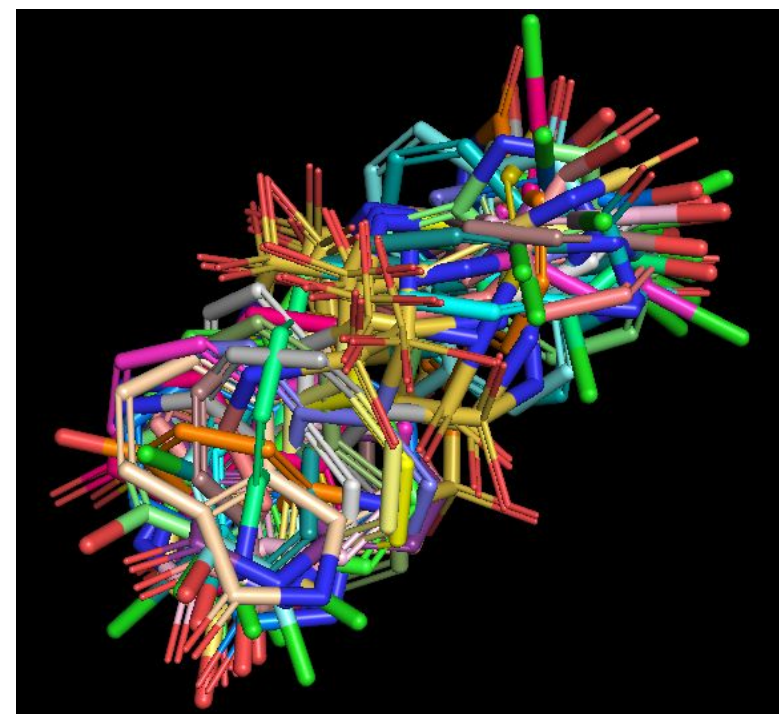
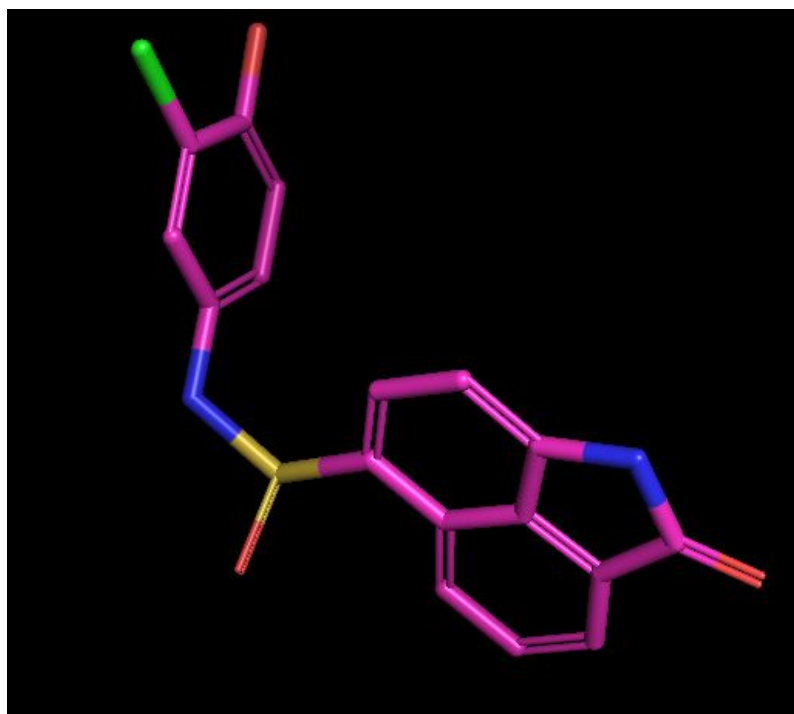
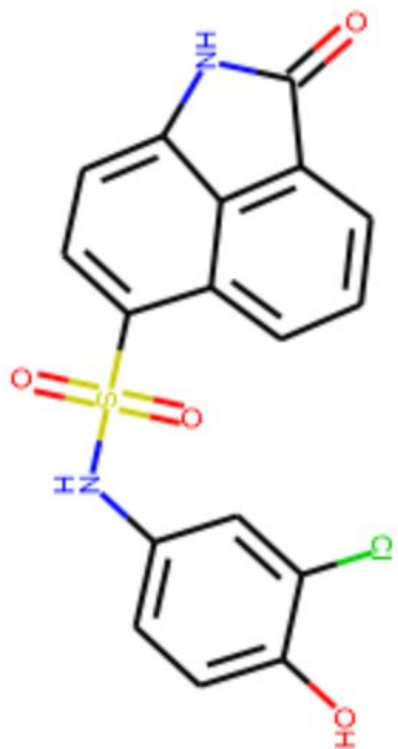
Проблема перехода 2D – 3D

O=C1Nc2ccc(S(=O)(=O)Nc3ccc(O)c(Cl)c3)c3ccccc1c23



?

Виной всему - Rotatable bonds



Implement in RDKit !!

Решение – минимизация энергии молекулы

Молекула стремится пребывать в состоянии с наименьшей энергией.

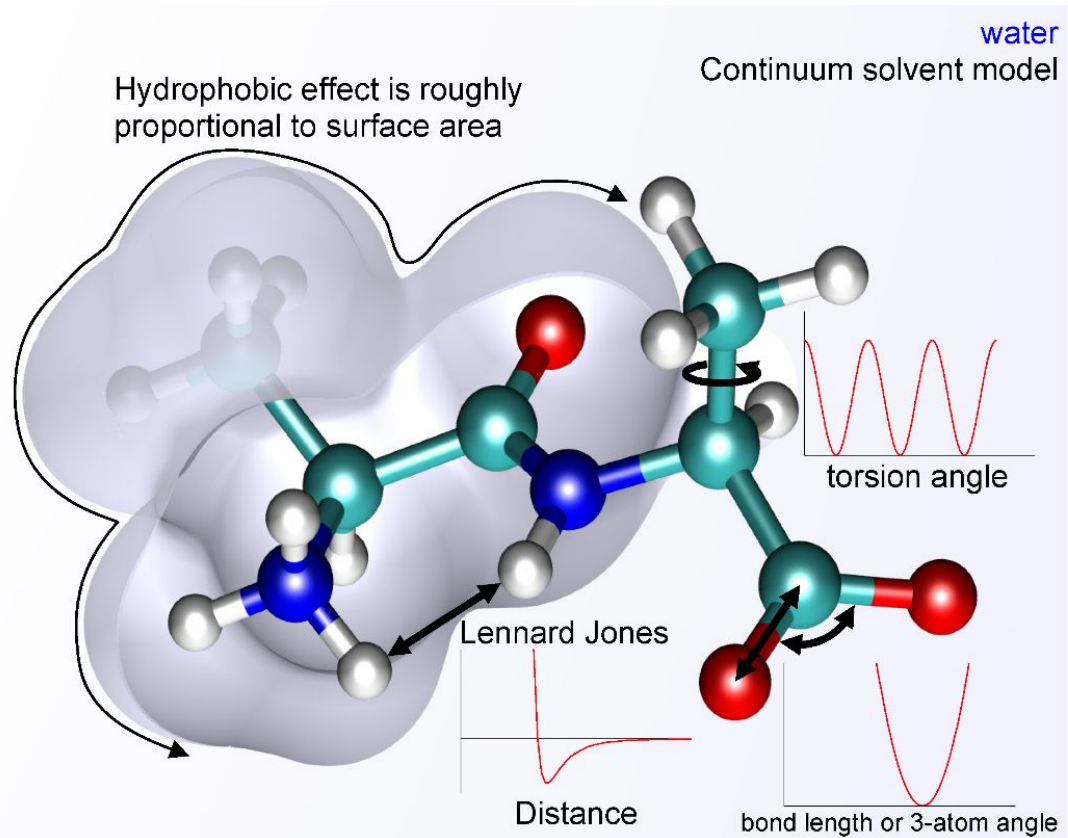
Как найти значение энергии молекулы?

1. Quantum mechanics
2. Semi-empirical
3. Force-field

$$H(t) |\psi(t)\rangle = i\hbar \frac{d}{dt} |\psi(t)\rangle$$

Force Fields

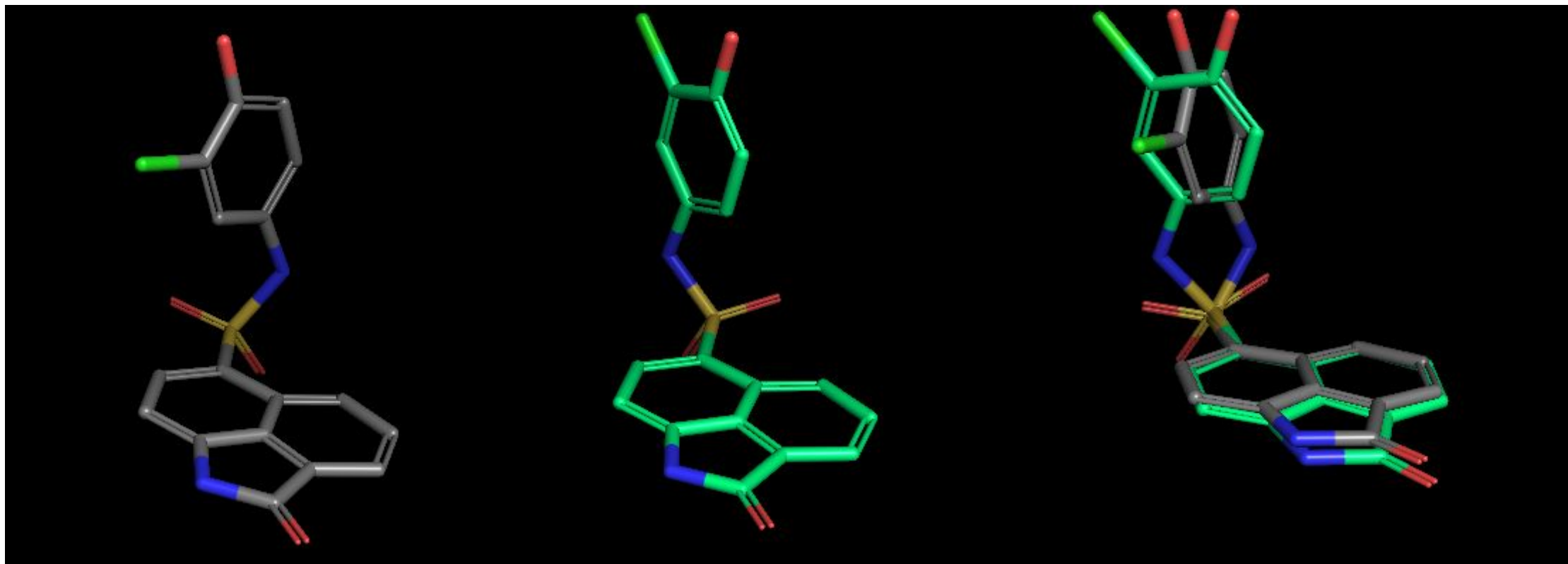
$$E_{\text{total}} = E_{\text{bonded}} + E_{\text{nonbonded}}$$



$$E_{\text{bonded}} = E_{\text{bond}} + E_{\text{angle}} + E_{\text{dihedral}}$$

$$E_{\text{nonbonded}} = E_{\text{electrostatic}} + E_{\text{van der Waals}}$$

MMFF optimization



46,95

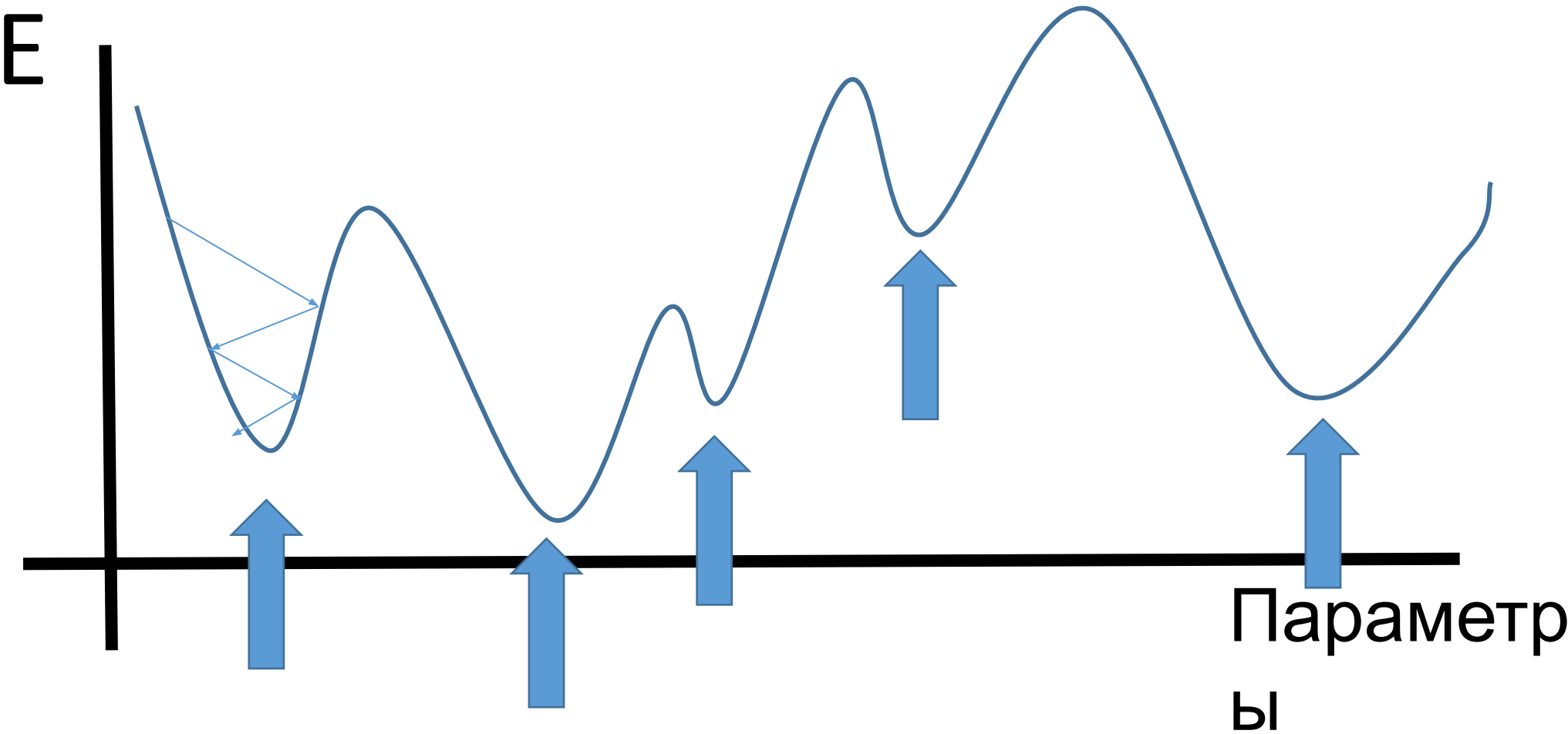
48,27

наложени

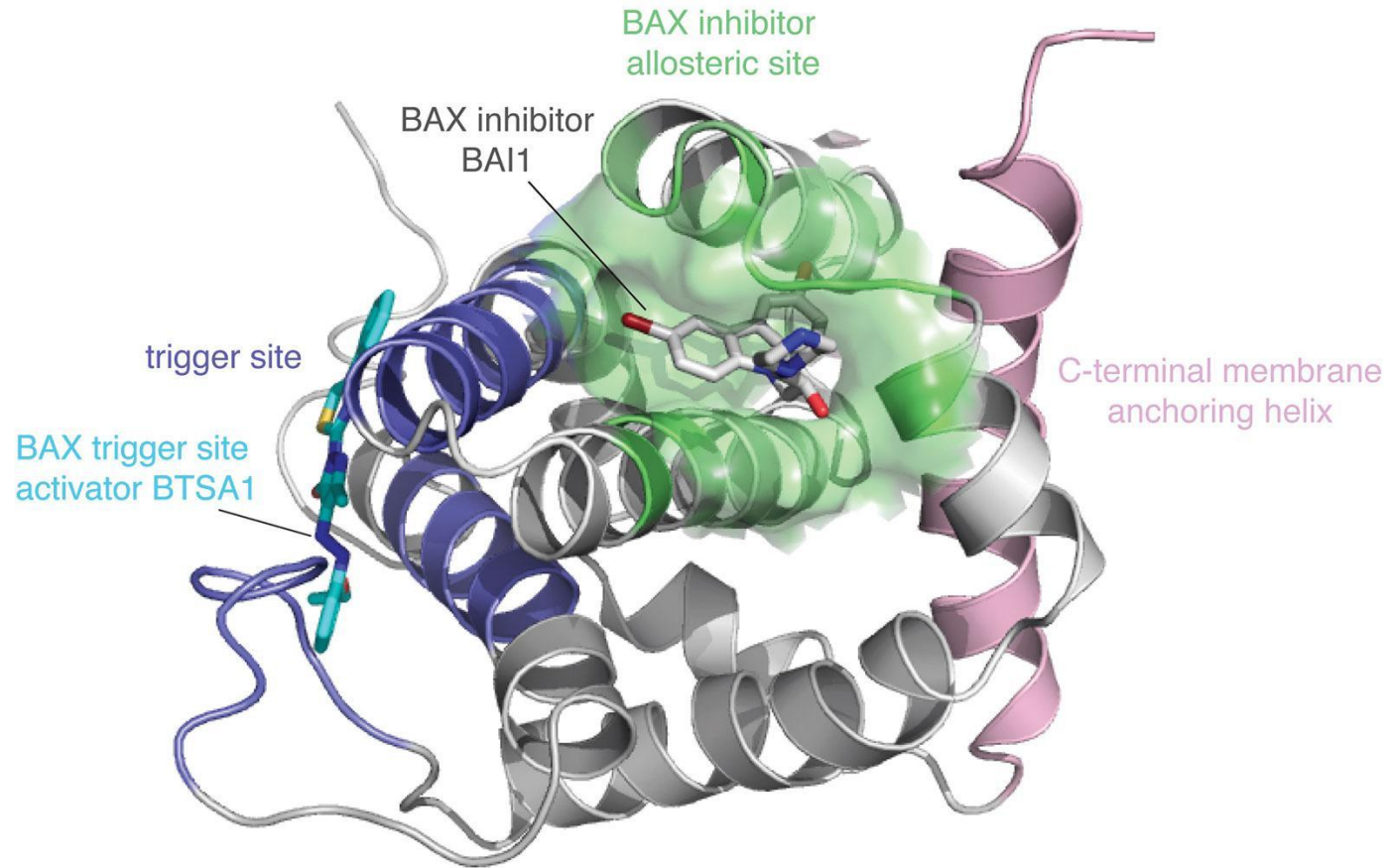
Implement in RDKit !!

e

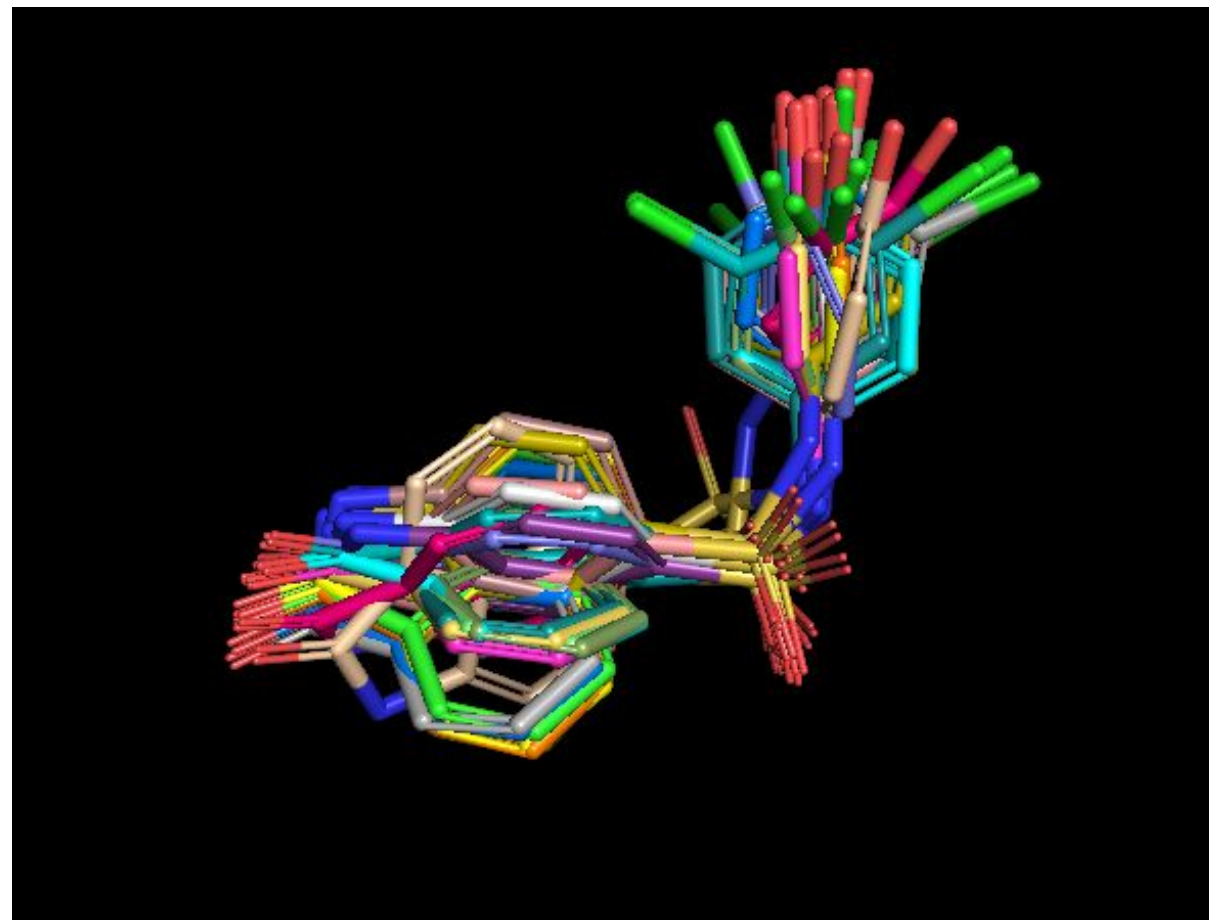
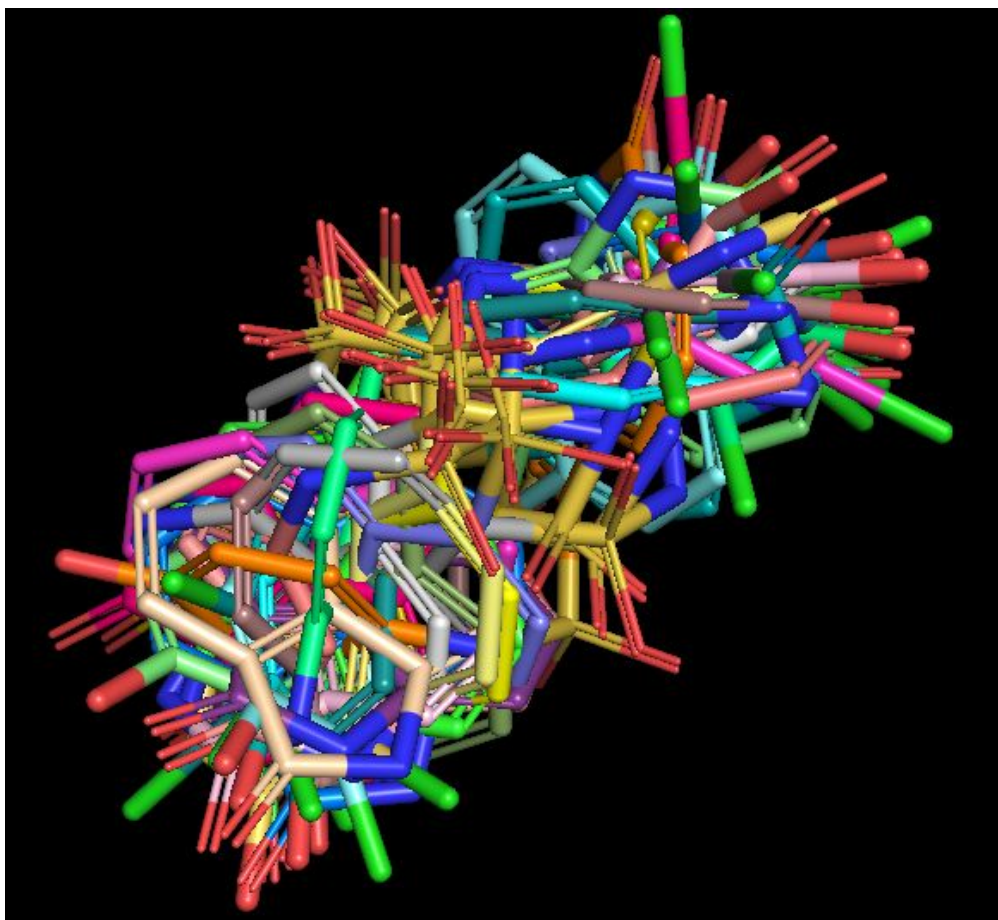
Проблема локального минимума



Проблема лиганд-рецепторного взаимодействия

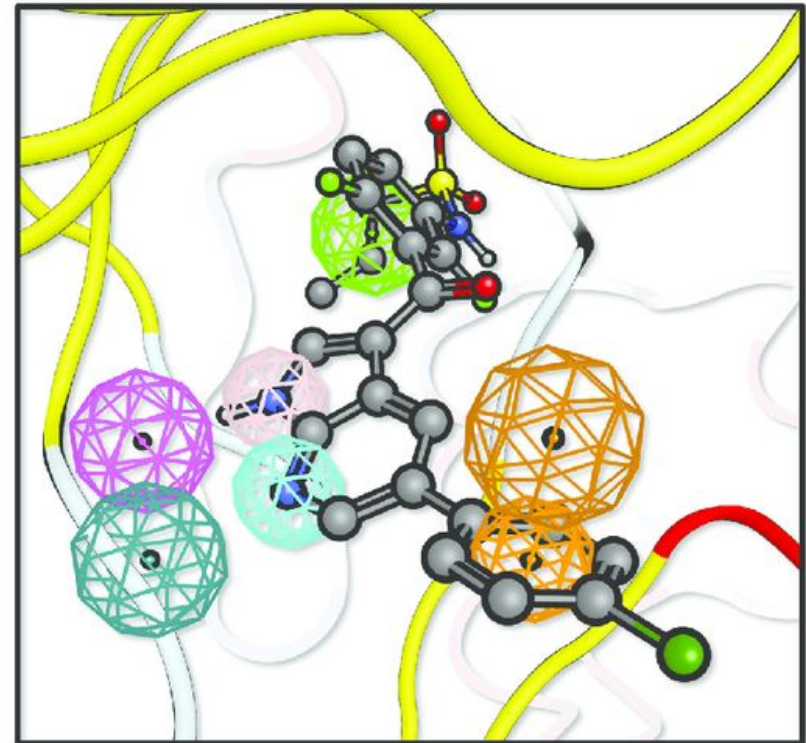
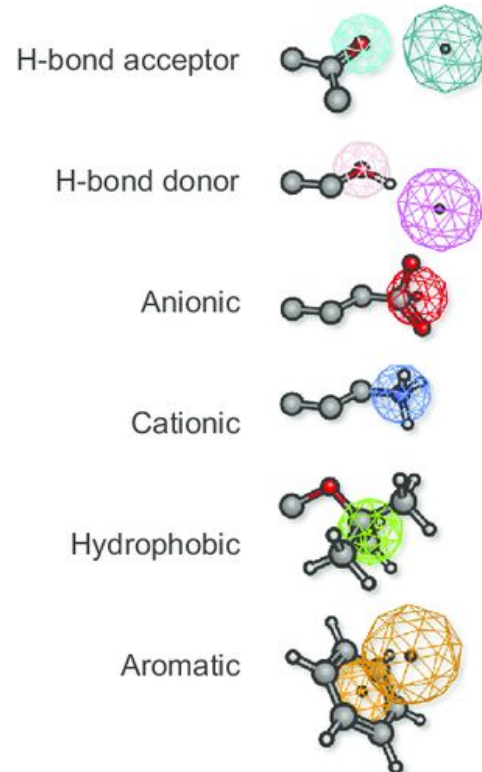


Выравнивание и наложение молекул



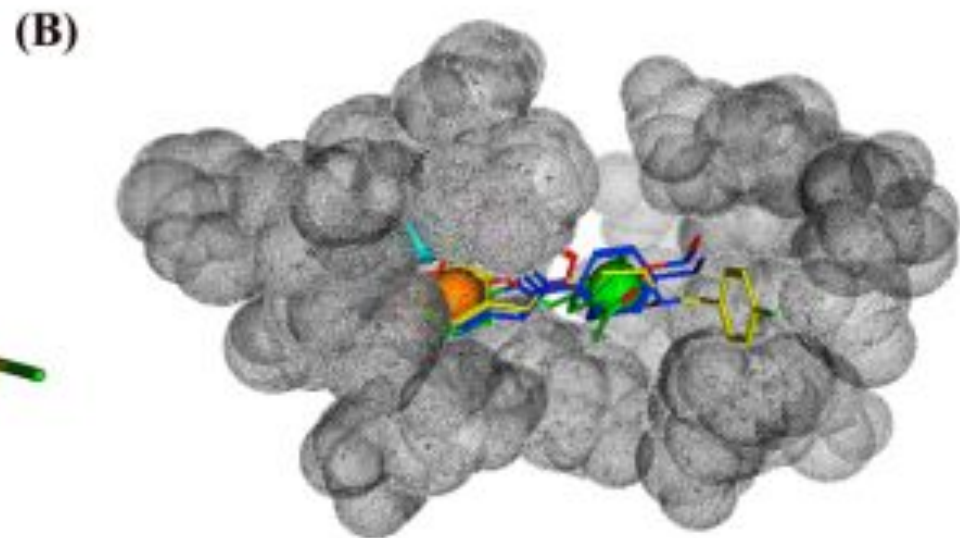
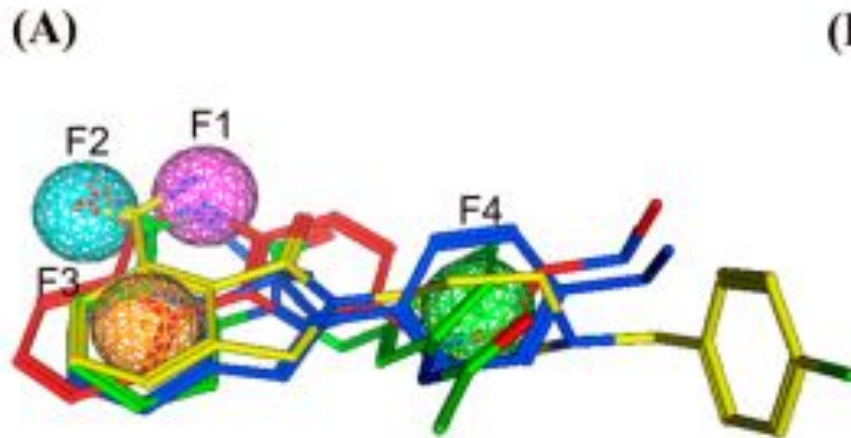
Фармакофор

- это набор пространственных и электронных признаков, необходимых для обеспечения оптимальных супрамолекулярных взаимодействий с определённой биологической мишенью.
- Доноры водорода
- Акцепторы водорода
- Ароматические циклы
- Гидрофобные участки



Моделирование фармакофора

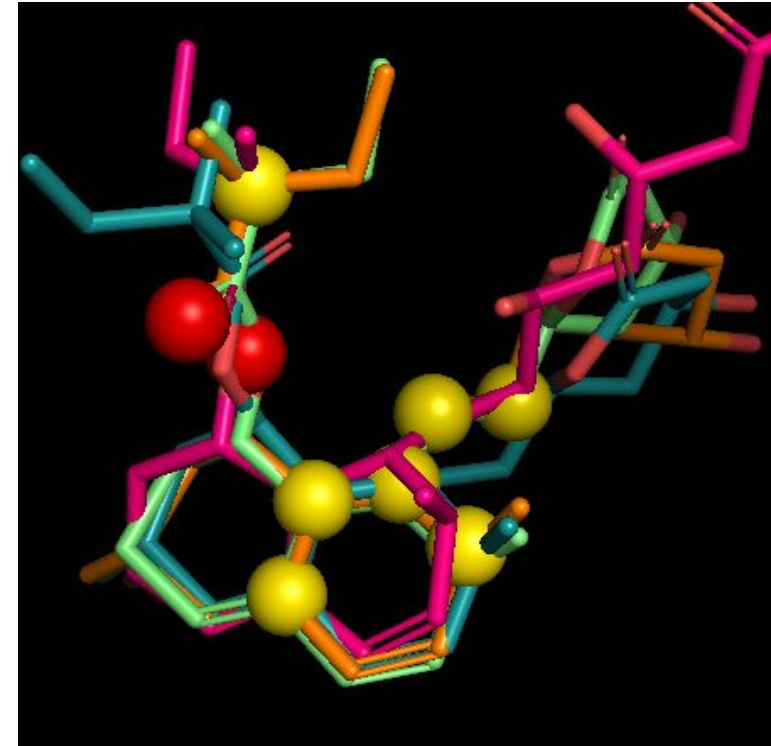
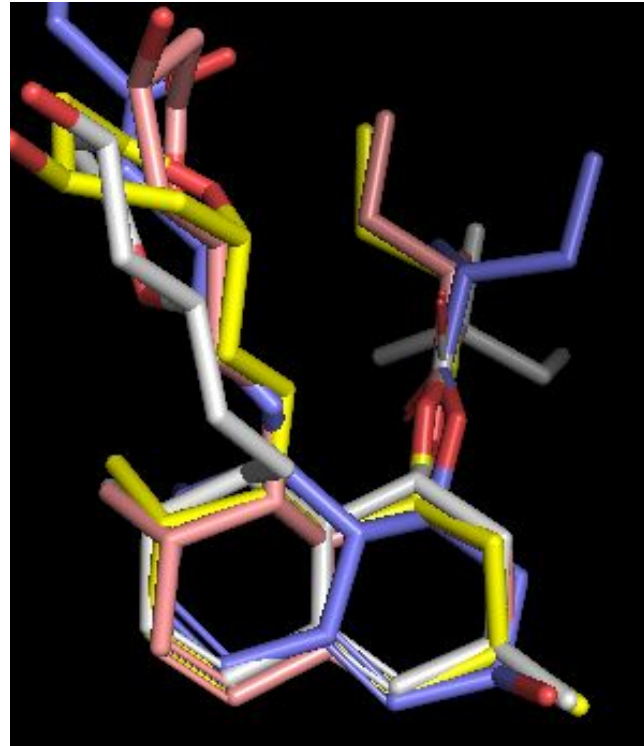
- Ligand-based
- Structure-based



Ligand-based

Этапы

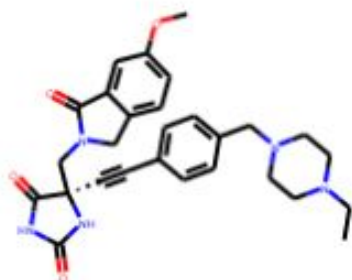
1. Выравнивание и наложение молекул
2. Выявление общих фармакофорных центров



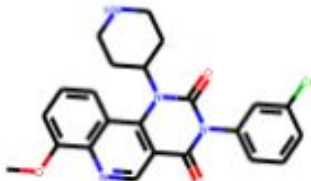
```
In [18]: print("Centroid molecules from first 5 clusters:")
# Draw molecules
Draw.MolsToGridImage(
    [compounds[clusters[i][0]][0] for i in range(5)],
    legends=[compounds[clusters[i][0]][1] for i in range(5)],
    molsPerRow=5,
)
```

Centroid molecules from first 5 clusters:

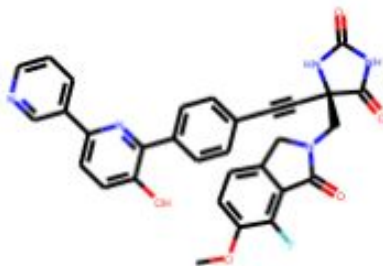
Out[18]:



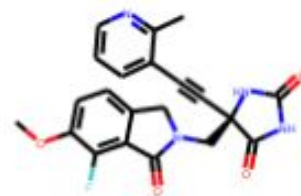
CHEMBI 1287881



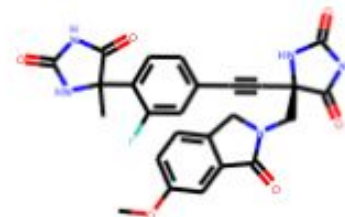
CHEMBI 3947142



CHEMBL3640366



CHEMBL3642535



CHEMBL3642544

```
In [29]: mols = [compounds[clusters[i][0]][0] for i in range(5)]
mols = [AllChem.AddHs(m) for m in mols]
[AllChem.EmbedMolecule(m) for m in mols]
mols = [AllChem.RemoveHs(m) for m in mols]
w = AllChem.SDWriter('my_mols.sdf')
for m in mols:
    w.write(m)
w.close()
```

<http://www.cheminfo.org/Chemistry/Cheminformatics/FormatConverter/index.html>

The screenshot displays the Cheminformatics Format Converter interface, which is used for converting chemical data between different formats. It is divided into three main sections: INPUT, Options, and OUTPUT.

INPUT: This section shows the chemical data being processed. It includes a table with columns for atom indices (1-25), atom types (C, N), and their 3D coordinates (x, y, z). The data is labeled as 'RDKit 3D' and 'V2000'.

Atom	Type	X	Y	Z
1	C	9.9913	2.8773	-0.9083
2	C	9.2335	1.9426	0.0111
3	N	7.9063	1.7796	-0.5573
4	C	7.9888	1.0358	-1.8064
5	C	6.9941	-0.1323	-1.7952
6	N	7.3990	-1.0263	-0.7283
7	C	6.6064	-2.2378	-0.7030
8	C	5.1530	-1.9158	-0.4908
9	C	4.1975	-2.9004	-0.4129
10	C	2.8540	-2.5932	-0.2141
11	C	2.4312	-1.2890	-0.0882
12	C	1.0425	-0.9312	0.1179
13	C	-0.1064	-0.6119	0.2797
14	C	-1.5203	-0.1926	0.4620
15	C	-2.3454	-1.3489	-0.0728
16	N	-3.7418	-0.9553	0.0866
17	C	-4.5760	-1.1921	1.2350
18	C	-5.9089	-0.5848	0.9219
19	C	-7.0464	-0.5368	1.7063
20	C	-8.1885	0.0866	1.2024
21	C	-8.1500	0.6392	-0.0697

Options: This section contains configuration settings for the conversion process. It includes dropdown menus for 'Input format*' (set to 'sdf -- MDL MOL format') and 'Output format*' (set to 'mol2 -- Sybyl Mol2 format'). There are also checkboxes for 'Generate coordinates' and 'Add / Delete hydrogens', and a text input field for 'pH to add hydrogens'.

OUTPUT: This section shows the resulting chemical data in the selected output format. It includes a header '@<TRIPOS>MOLECULE' and a list of atoms with their types and coordinates, labeled as '@<TRIPOS>ATOM'.

Atom	Type	X	Y	Z
1	C	9.9913	2.8773	-0.9083
2	C	9.2335	1.9426	0.0111
3	N	7.9063	1.7796	-0.5573
4	C	7.9888	1.0358	-1.8064
5	C	6.9941	-0.1323	-1.7952
6	N	7.3990	-1.0263	-0.7283
7	C	6.6064	-2.2378	-0.7030
8	C	5.1530	-1.9158	-0.4908
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12	C	1.0425	-0.9312	0.1179
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15	C	-2.3454	-1.3489	-0.0728
16	N	-3.7418	-0.9553	0.0866
17	C	-4.5760	-1.1921	1.2350
18	C	-5.9089	-0.5848	0.9219
19	C	-7.0464	-0.5368	1.7063

PharmaGist

Webserver

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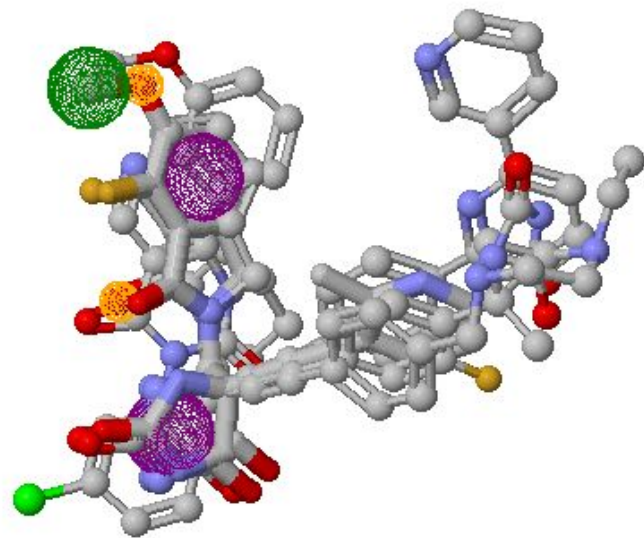
[Upload Input Molecules in Mol2 Format](#) (e.g. [input examples](#))

[No. of Output Pharmacophores:](#) ▼

[E-Mail Address:](#)

[Advanced Options:](#)

[\[Show\]](#)[\[Hide\]](#)



Results

Name	RMSD	Mass	RBnds
No query specified.			

Pharmacophore Filters Viewer

Submit Query

Pharmacophore Class	x	y	z	Radius	Enabled	
> HydrogenAcceptor	-0.06	13.16	-5.01	0.50	<input checked="" type="checkbox"/>	▼
> HydrogenAcceptor	0.36	10.23	-0.48	0.50	<input checked="" type="checkbox"/>	▼
> Aromatic	0.20	10.55	1.10	1.10	<input checked="" type="checkbox"/>	▼

Add Feature Load Features... Load Receptor... Clear ▼

Load Session... Save Session...

Save Results...

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