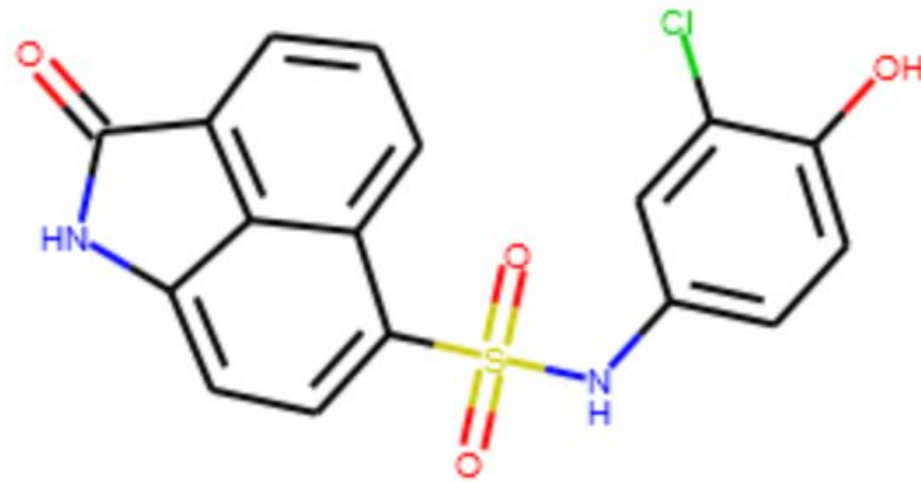


Трехмерное  
представление молекул.  
Фармакофоры.

# Проблема трехмерного представления и выравнивания молекул

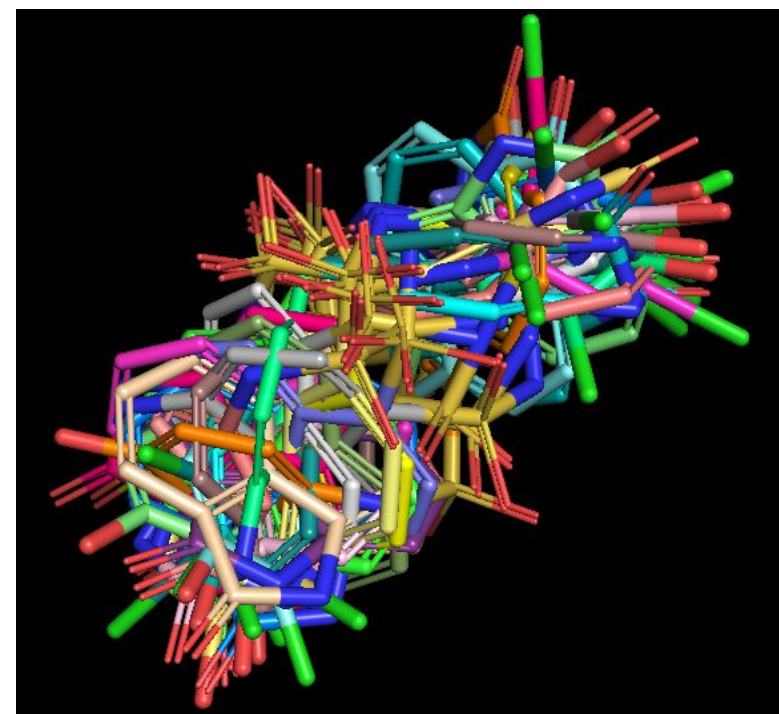
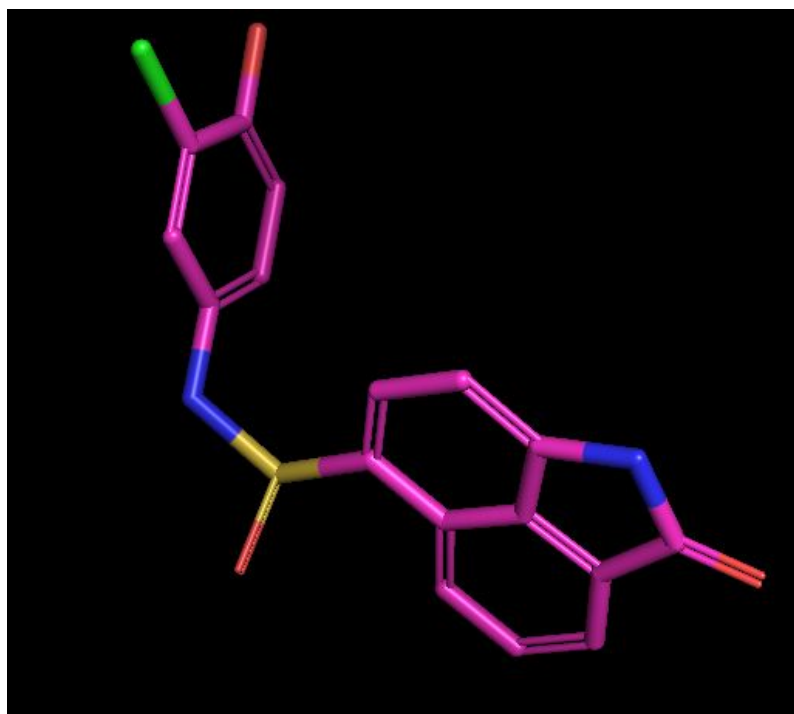
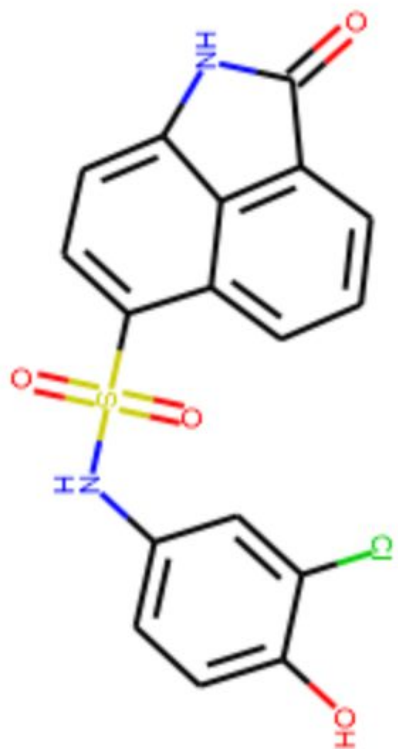
# Проблема перехода 2D – 3D

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.

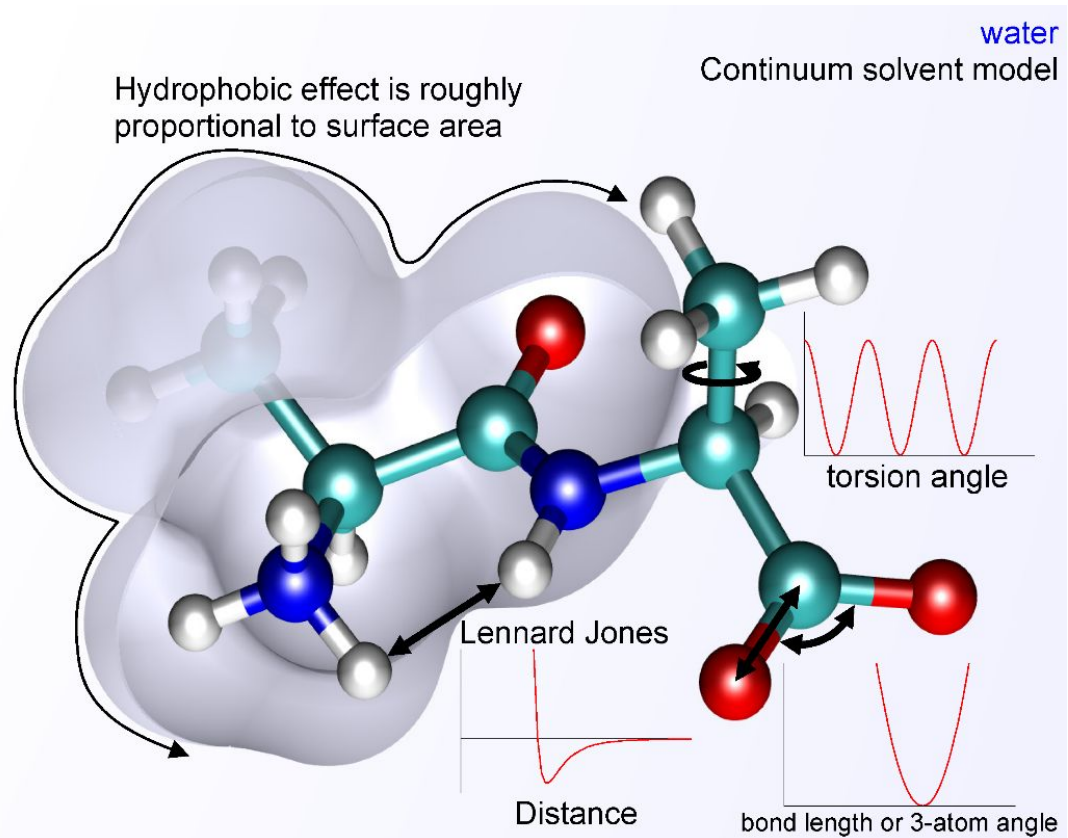
Как найти значение энергии молекулы?

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

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

# Force Fields

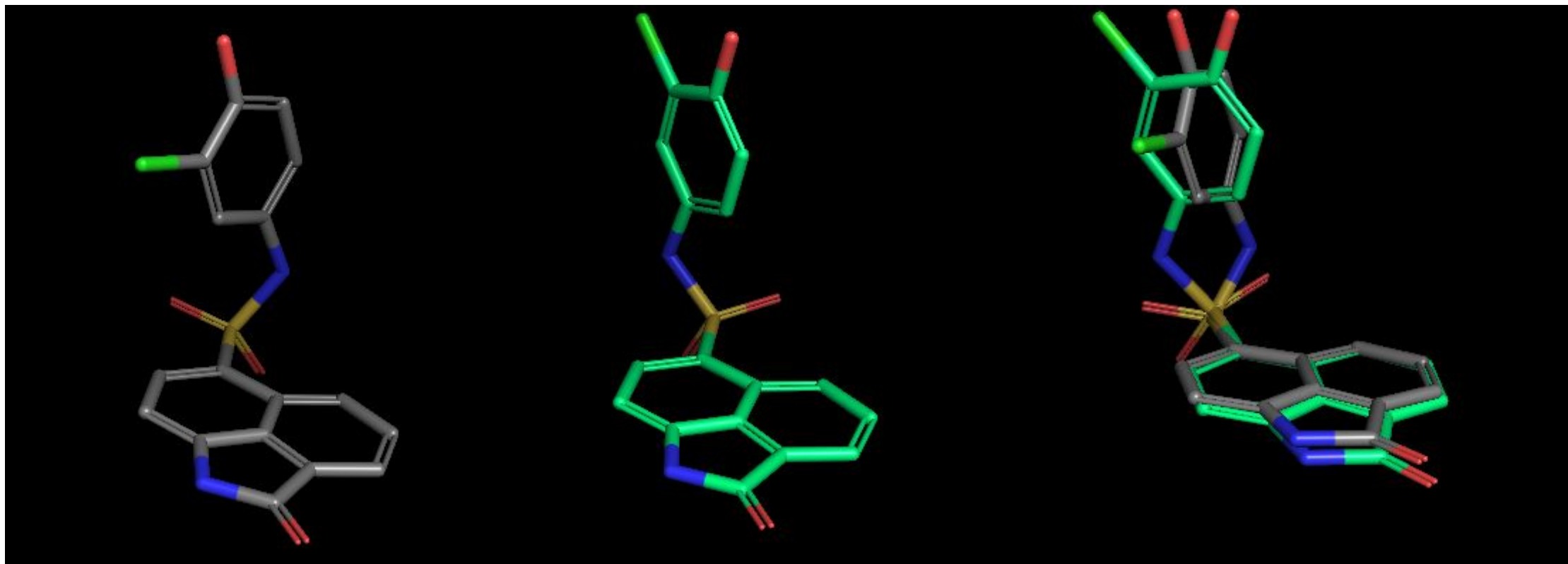
$$E_{\text{total}} = E_{\text{bonded}} + E_{\text{nonbonded}}$$



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

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

# MMFF optimization



46,95

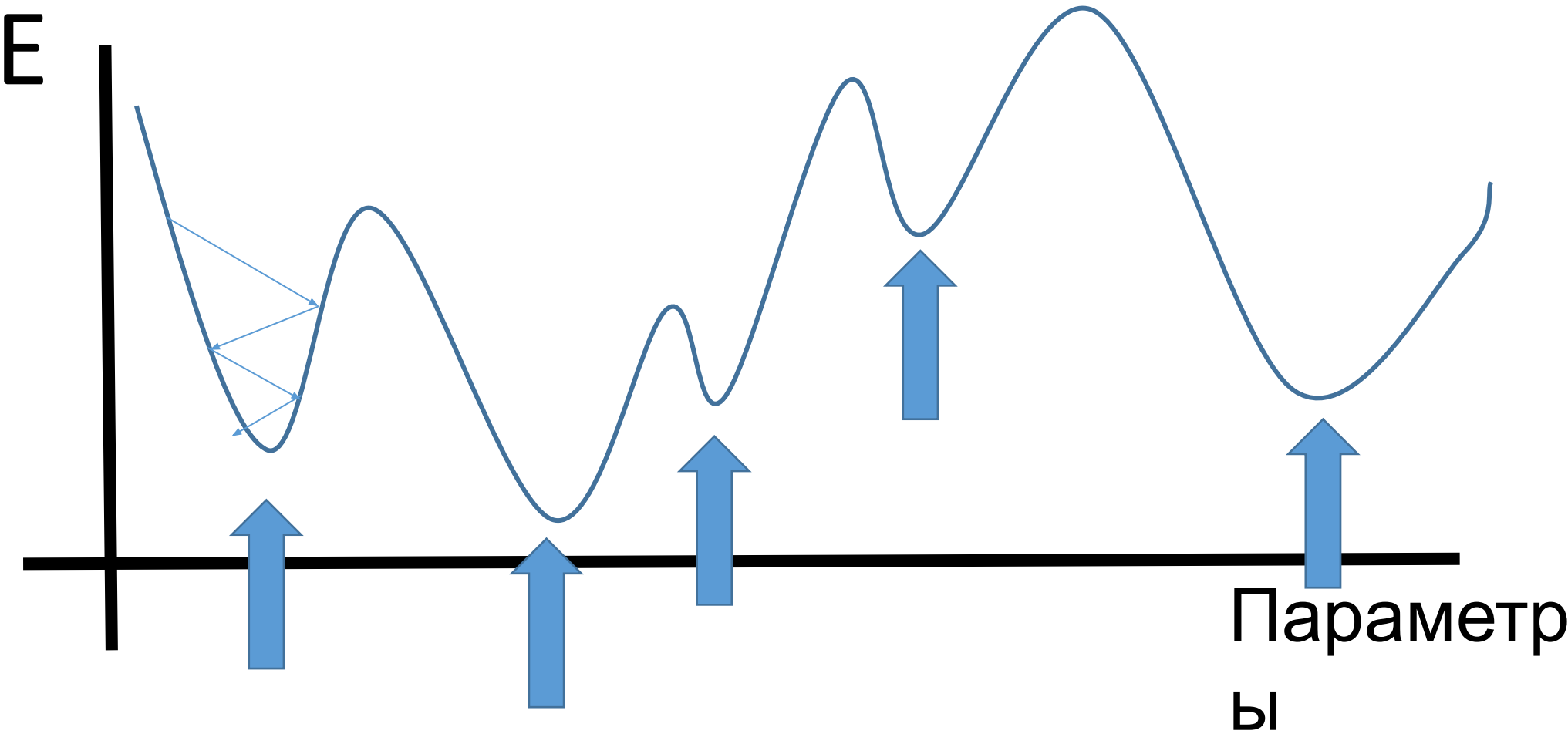
48,27

наложени

Implement in RDKit !!

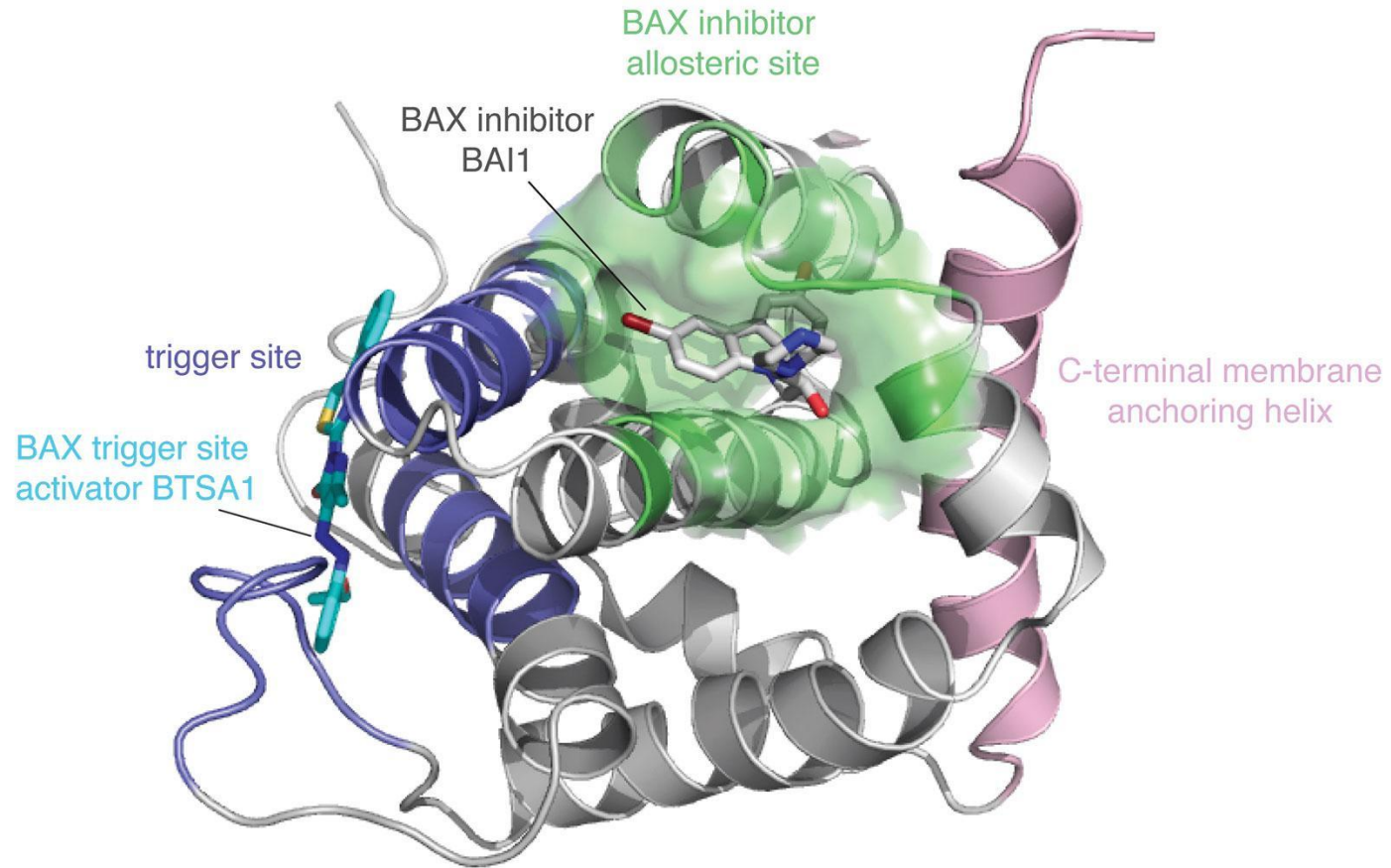
e

# Проблема локального минимума

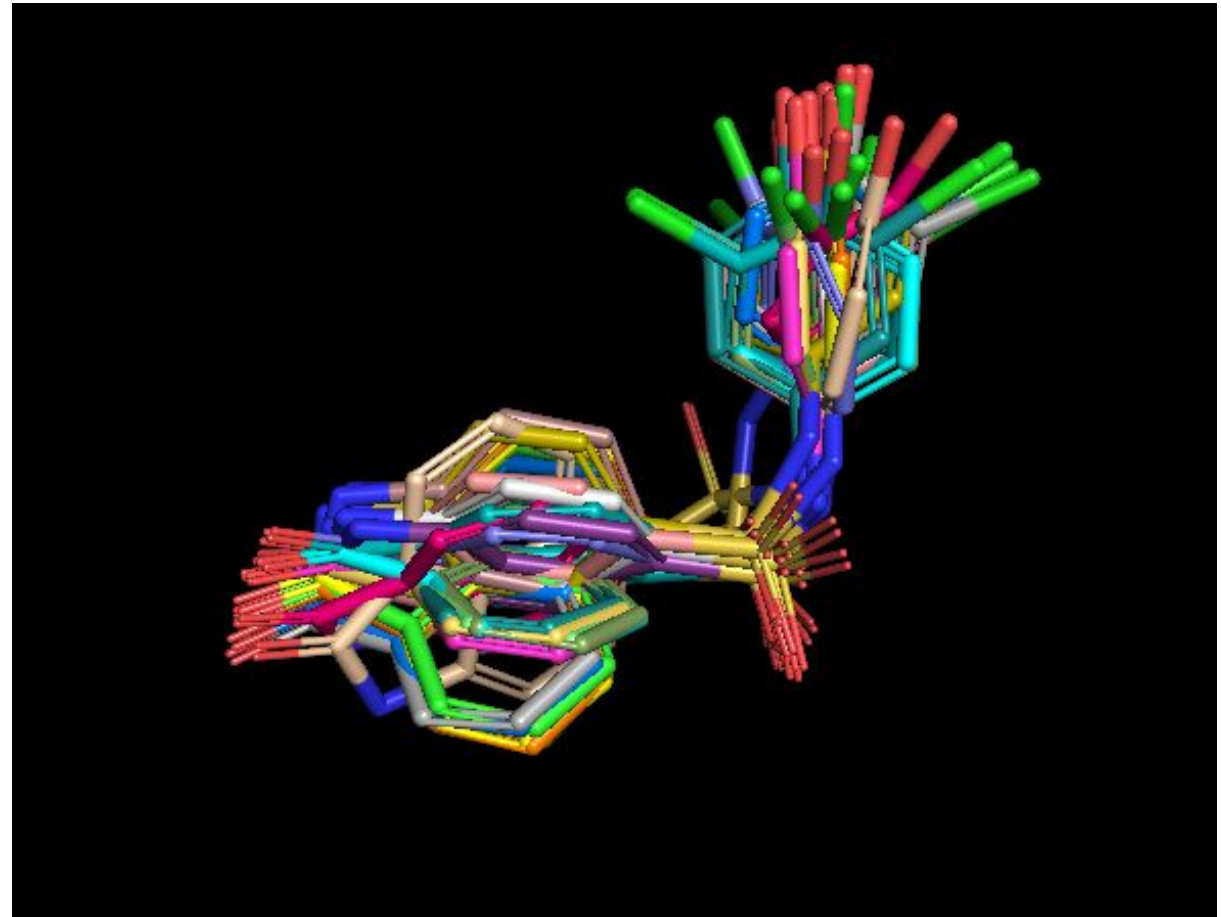
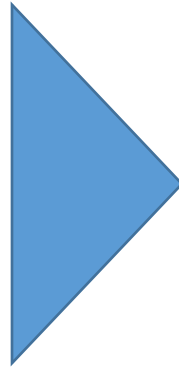
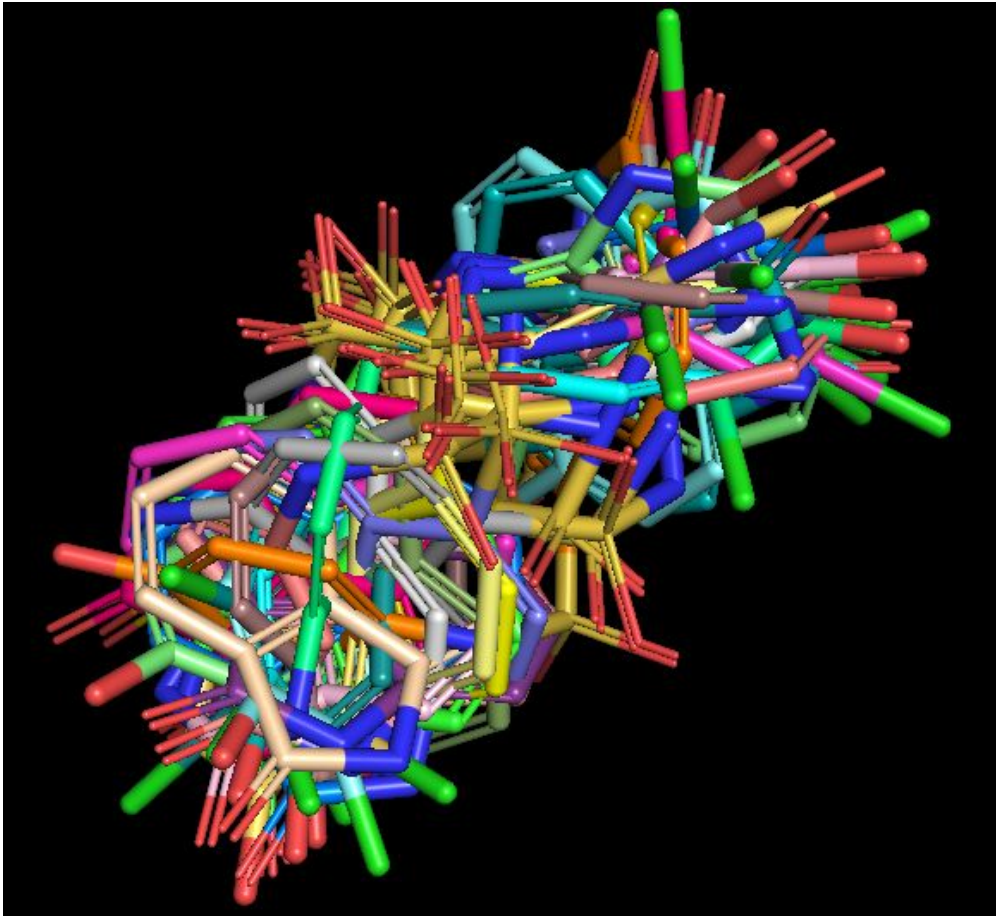




# Проблема лиганд-рецепторного взаимодействия

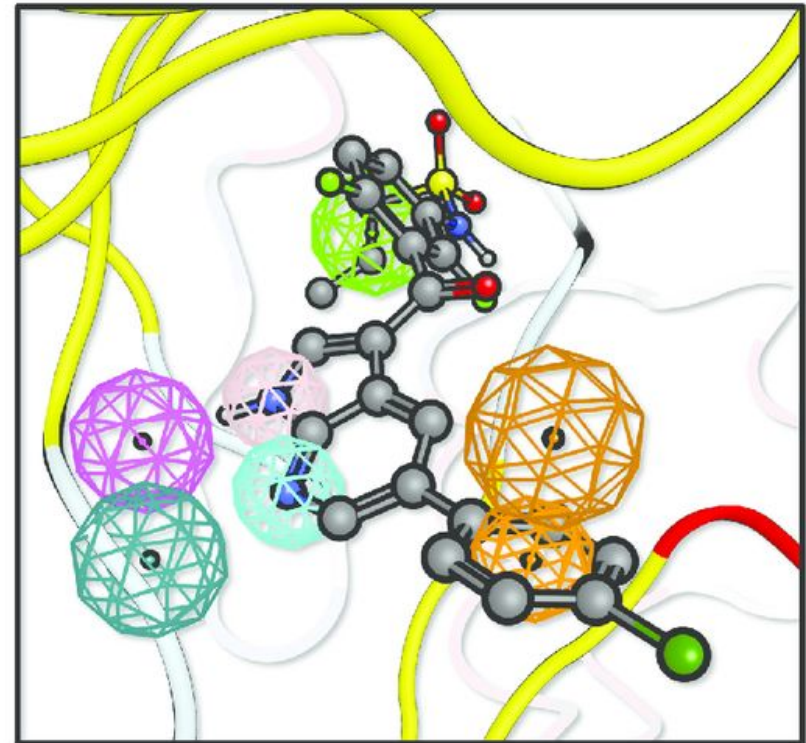
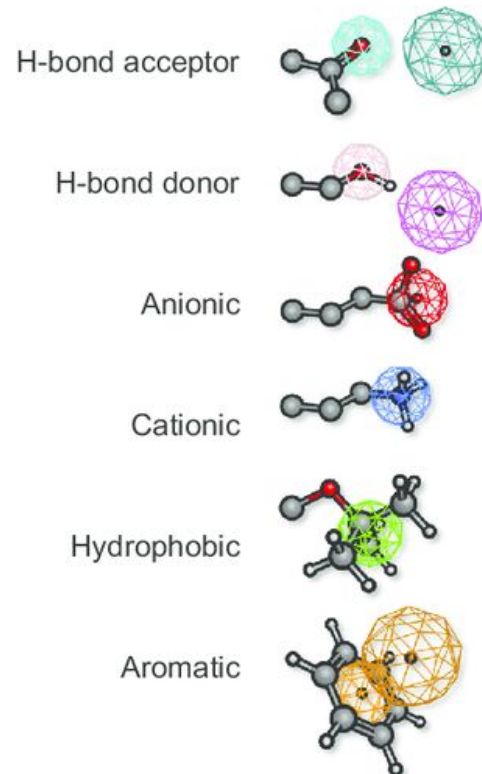


# Выравнивание и наложение молекул



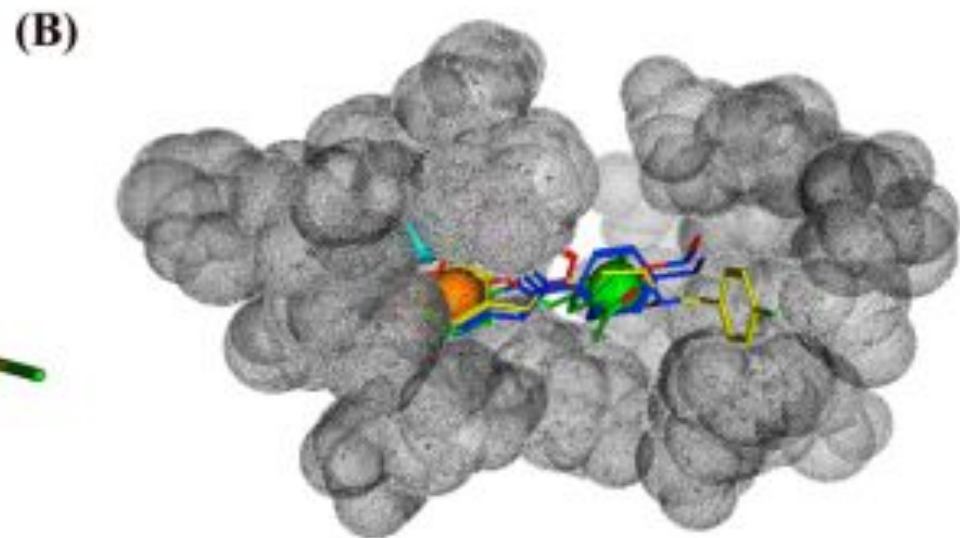
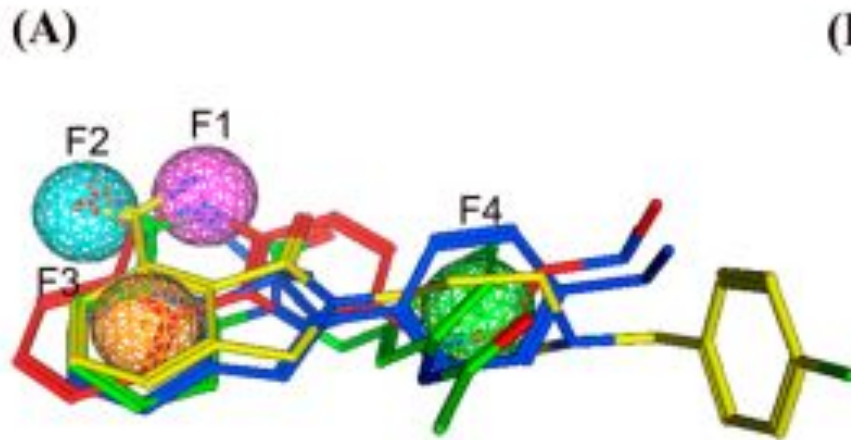
# Фармакофор

- 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

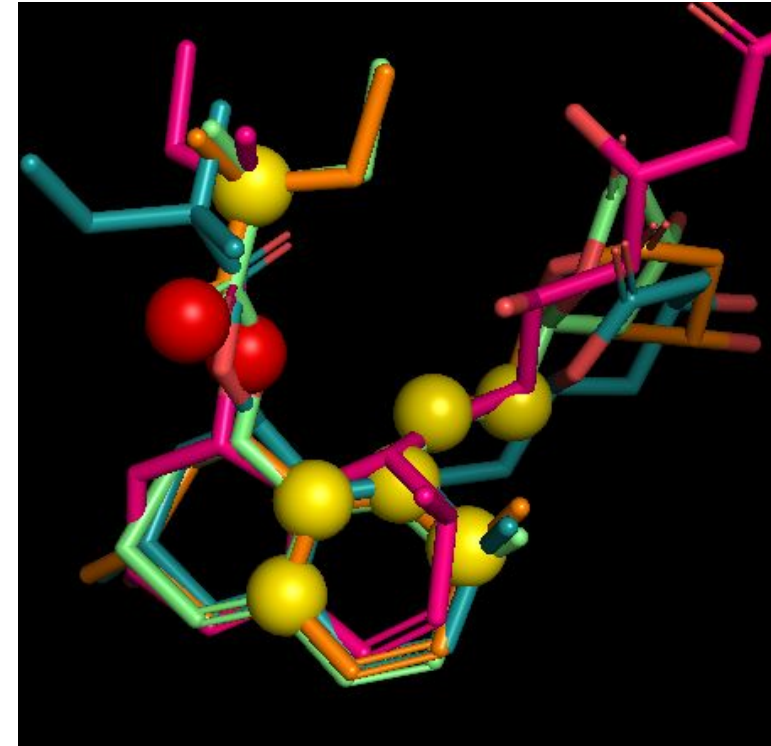
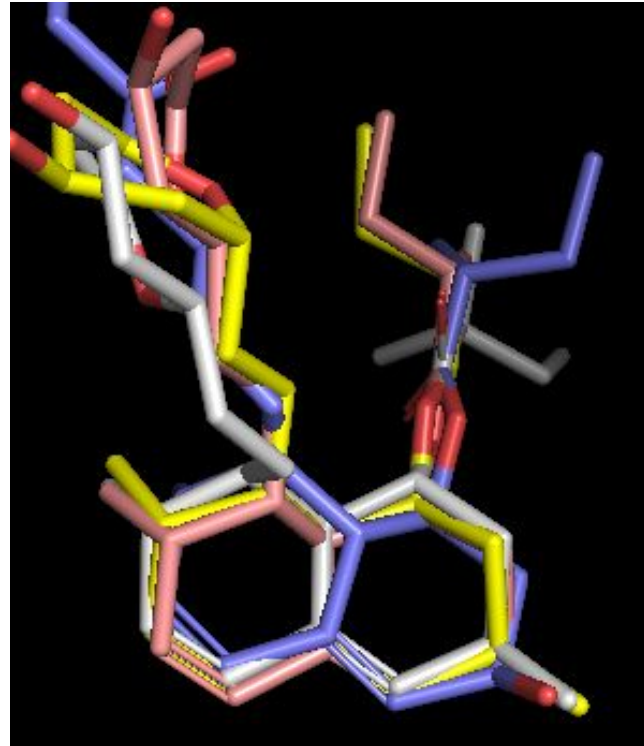
- Ligand-based
- Structure-based



# Ligand-based

## Этапы

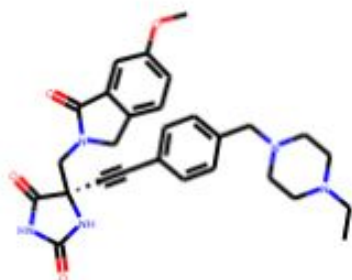
1. Выравнивание и наложение молекул
2. Выявление общих фармакофорных центров



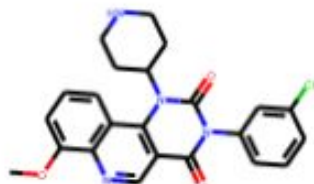
```
In [18]: print("Centroid molecules from first 5 clusters:")
# Draw molecules
Draw.MolsToGridImage(
    [compounds[clusters[i][0]][0] for i in range(5)],
    legends=[compounds[clusters[i][0]][1] for i in range(5)],
    molsPerRow=5,
)
```

Centroid molecules from first 5 clusters:

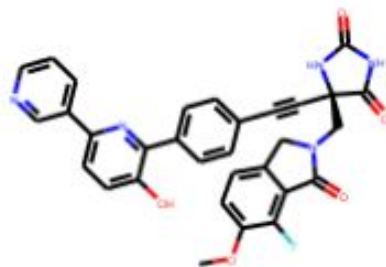
Out[18]:



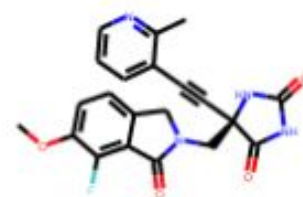
CHEMBI 1287881



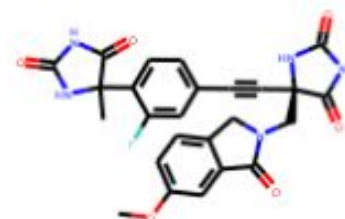
CHEMBI 3947142



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 presented in a grid format, with the first few rows showing the molecule's basic information and the subsequent rows showing the coordinates for each atom.

**Options:** This section contains several configuration options for the conversion process:

- Input format\*:** A dropdown menu set to "sdf -- MDL MOL format".
- Output format\*:** A dropdown menu set to "mol2 -- Sybyl Mol2 format".
- Generate coordinates:** A dropdown menu set to "3D". Below it, a note reads: "Allows to generate 2D or 3D coordinates".
- Add / Delete hydrogens:** A dropdown menu set to "Add".
- pH to add hydrogens:** A text input field with a value of "7.0". Below it, a note reads: "Specify a pH at which the molecule should be protonated".

**OUTPUT:** This section shows the resulting chemical data after conversion. It includes a table with columns for atom indices (1-26), atom types (C, N), and their 3D coordinates (x, y, z). The data is presented in a grid format, with the first few rows showing the molecule's basic information and the subsequent rows showing the coordinates for each atom.

**Convert:** A button located at the bottom center of the interface, used to execute the conversion process.

# PharmaGist

## Webserver

[\[About\]](#) [\[WebServer\]](#) [\[Download\]](#) [\[FAQ\]](#) [\[Help / Getting Started\]](#) Contact: [duhovka@gmail.com](mailto:duhovka@gmail.com) [ppdock@tau.ac.il](mailto:ppdock@tau.ac.il)

---

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

[No. of Output Pharmacophores:](#)  ▼

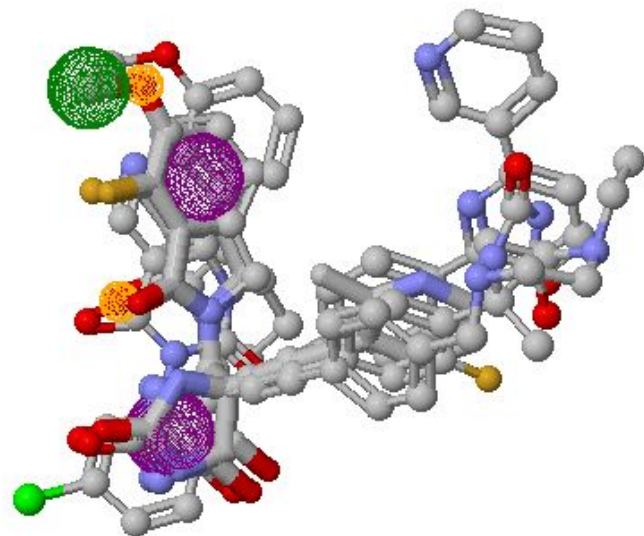
[E-Mail Address:](#)

---

[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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