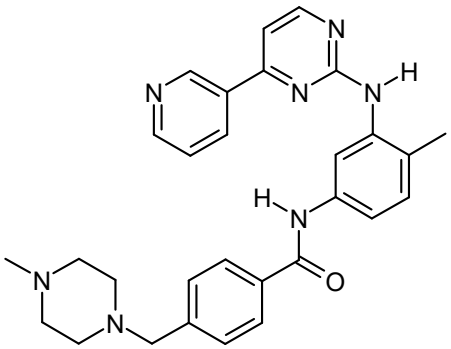
Hands-on exercises to the lecture „Modern Methods in Drug Discovery“ WS26/27

For this tutorial you need Oben Babel preferably in a LINUX environment as we won't make use of the GUI, but rather use command line instructions in a shell/terminal/console.

https://openbabel.org/docs/dev/Installation/install.html

1. Imatinib (show below) was the first small molecule inhibtor of the now large group of Tyrosine Kinase Receptor Inhibitors with the stem name "tinib".



The SMILES are given in the file `TyrosineKinaseInhibitors_tinib.smi` (available for download from the same site as the lecture slides and also from the MS-Teams). This is basically a text file containing SMILES and corresponding compound names.
Copy that file into your working directory.
To perform queries with SMILES/SMARTS we use the command `obgrep` of Open Babel that works similar as the UNIX command `grep`. Here are some examples:

```
./obgrep "[N;H1]C(=O)" TyrosineKinaseInhibitors_tinib.smi
```
print all molecules that contain a peptide linkage

```
./obgrep -c "C(=O)O" TyrosineKinaseInhibitors_tinib.smi
```
print only the number of matching molecules

```
./obgrep -v "C(=O)O" TyrosineKinaseInhibitors_tinib.smi
```
invert matching, print non-matching molecules

```
./obgrep -n "C(=O)O" TyrosineKinaseInhibitors_tinib.smi
```
print the names of the matching molecules, only

See also the SMILES/SMARTS slides of lecture 3 for more examples, patterns, and operators. Check your results by having a look at the structures of the compounds that can be found in PubChem (search for the respective compound name there).

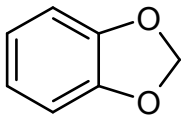
a) Which compounds contain chlorine? (search for Cl)

b) Which compounds do not contain fluorine? (use inverted matching for F)

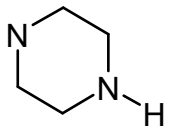
c) How many compounds do not contain any halogens (F, Cl, Br, I)? (use "," as logical OR operator)

d) How many compounds contain a 7-membered ring? (search for ring size of 7)

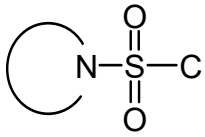
e) Which compounds contain this fragment?
(specify the left ring as being aromatic)



f) Which compounds contain this fragment?
(take care to specifiy the correct number of hydrogen atoms)

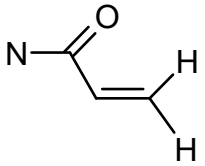


g) Which compounds contain this where nitrogen is part of a ring?



h) Which compounds contain an unbranched alkyl chain of three or more CH_2 units?
(search for ring size of 0)

i) Which compounds contain a reactive Michael acceptor group?
(take care to specify the correct number of hydrogen atoms)



j) What do following SMARTS mean? Draw the corresponding patterns. Look up those that contain these patterns.

[CX4][NH2]

[OX2;H0][CH3]

k) Construct a SMARTS string that matches as many as possible compounds using the shown fragment (e.g. use lower case letters for all atoms of the rings):

