Subject: Generating derivatives of parent structure
Posted by lutek14 on Sun, 05 Nov 2023 09:09:08 GMT
View Forum Message <> Reply to Message

Hello,

I appreciate the quality of the program, but require some assistance. I have an original structure and wish to generate derivatives by substituting specific locations by certain residues. Is this achievable? Alternatively, could you recommend any freely available software that can accomplish this task efficiently?

Thanks

Subject: Re: Generating derivatives of parent structure
Posted by nbehrnd on Sun, 05 Nov 2023 18:14:19 GMT
View Forum Message <> Reply to Message

Hello,

this taps into the generation of a combinatorial library you find below Chemistry -> enumerate combinatorial library. Either you find your reaction among the templates DW ships by default, or you create your own reaction pattern. Tab «reactants» allows you to use molecules already defined in a .dwar, or .sdf; or to let DW select ones which are commercially available (criteria are adjustable).

See chapter «chemical structures», section «combinatorial library» in DW's help or the online web page[1] for additional information. It however is time well invested to follow Isabelle Girault's video tutorial about the topic «RSC CICAG Open Source Tools for Chemistry Workshops:- Advanced DataWarrior»[2] recorded in 2021 around 47:18 min:s on youtube. (There is sequal «DataWarrior workshop by Isabelle Giraud»[3] by her to complement the insight about DW, too.)

Regards,

Norwid

[1] https://openmolecules.org/help/chemistry.html#VirtualLibrari es
[2] https://www.youtube.com/watch?v=mQCf9GakQW0
[3] https://www.youtube.com/watch?v=Is2hLqqSFvM

Subject: Re: Generating derivatives of parent structure
Posted by lutek14 on Sun, 05 Nov 2023 20:15:33 GMT
View Forum Message <> Reply to Message

Hello, thank you for your response.
However, I am not seeking reactions themselves, but just structures. For instance, I would like to create combinations with substituted hydrogen atoms on the aromatic ring, altered heterocycle, and various sized side chain .

Subject: Re: Generating derivatives of parent structure
Posted by nbehrnd on Sun, 05 Nov 2023 21:36:35 GMT
View Forum Message <> Reply to Message

The combinatorial library is generated within a .dwar file and eventually contains an array of the structures of the product, as well as as of the corresponding starting materials.

Departing from here, you can either

- edit this array to selectively copy & paste the column(s) of interest / remove columns not suitable, or
- export the .dwar file as such as a .sdf file which then contains only the structures of the products.

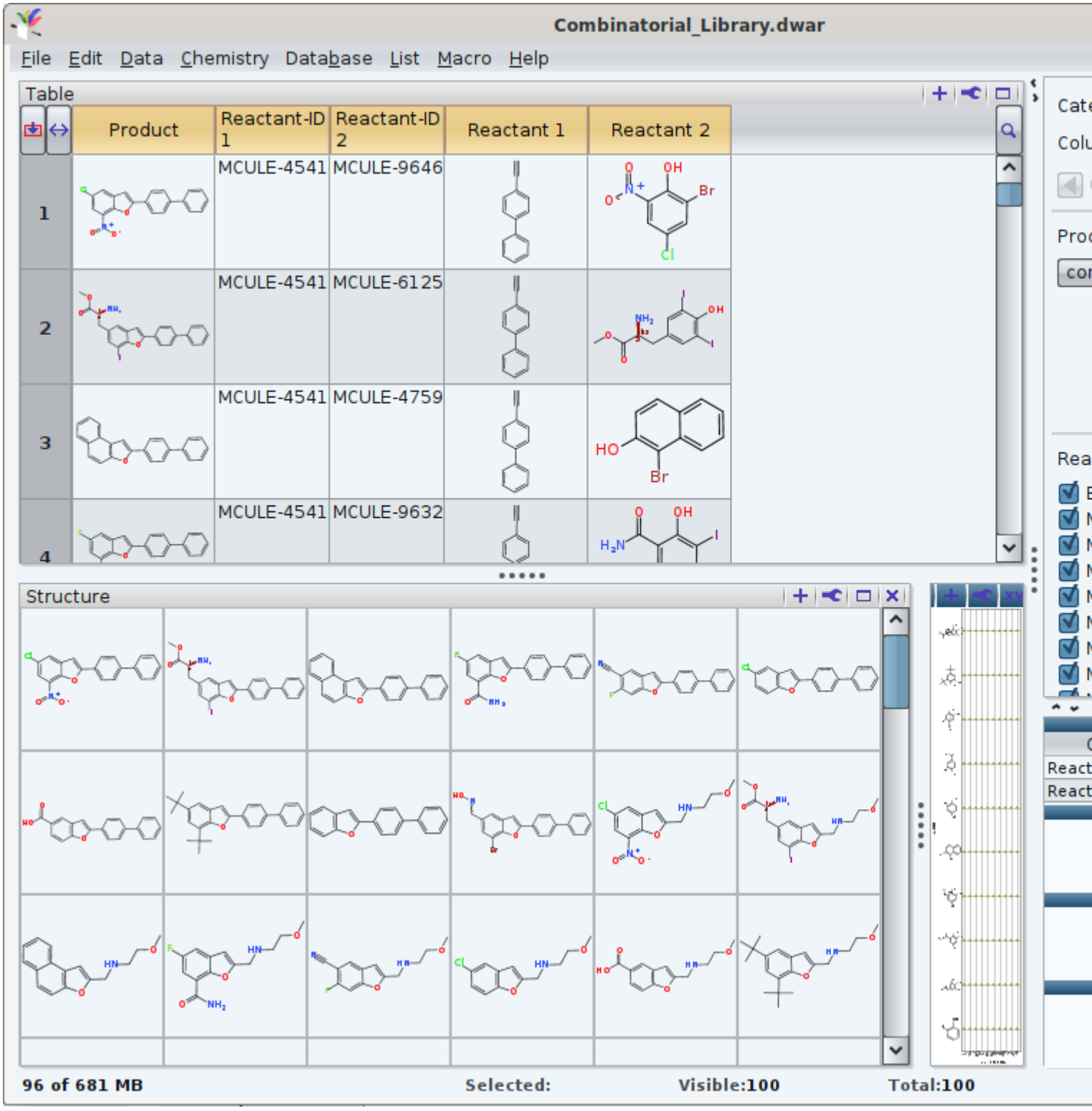
See the .dwar and .png attached for a small 10 by 10 library to yield benzophenones as illustration. This approach DW provides is intuitive, the implementation to recur on compounds only known «in house» or commercially available delivers the results quickly.

Regards,

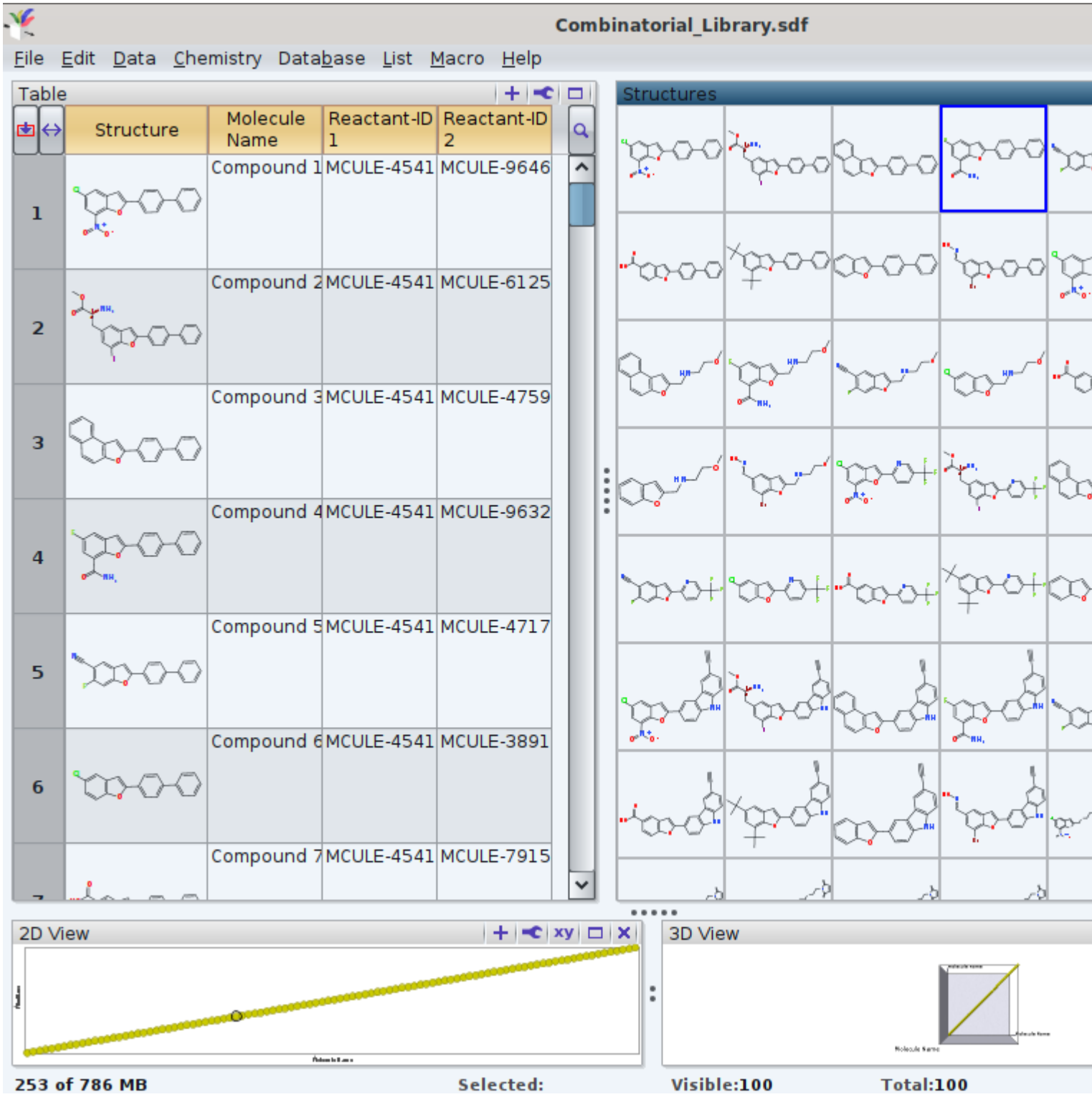
Norwid

File Attachments

1) Combinatorial_Library_dwar_file.png, downloaded 367 times



2) Combinatorial_Library.dwar, downloaded 468 times
3) Combinatorial_Library_exported_sdf_file.png, downloaded 375 times



4) Combinatorial_Library.sdf, downloaded 452 times

Subject: Re: Generating derivatives of parent structure
Posted by thomas on Fri, 08 Dec 2023 23:42:10 GMT
View Forum Message <> Reply to Message

You could also use the "Build Evolutionary Library..." functionality. This creates new molecules from a starting generation by random small modifications. You can also define parts of the molecule that shall not be modifed by just selecting it. I tried that with your molecule and selected all but 4 ring positions. This causes random modifications at all selected atoms, which includes ring cleavages.

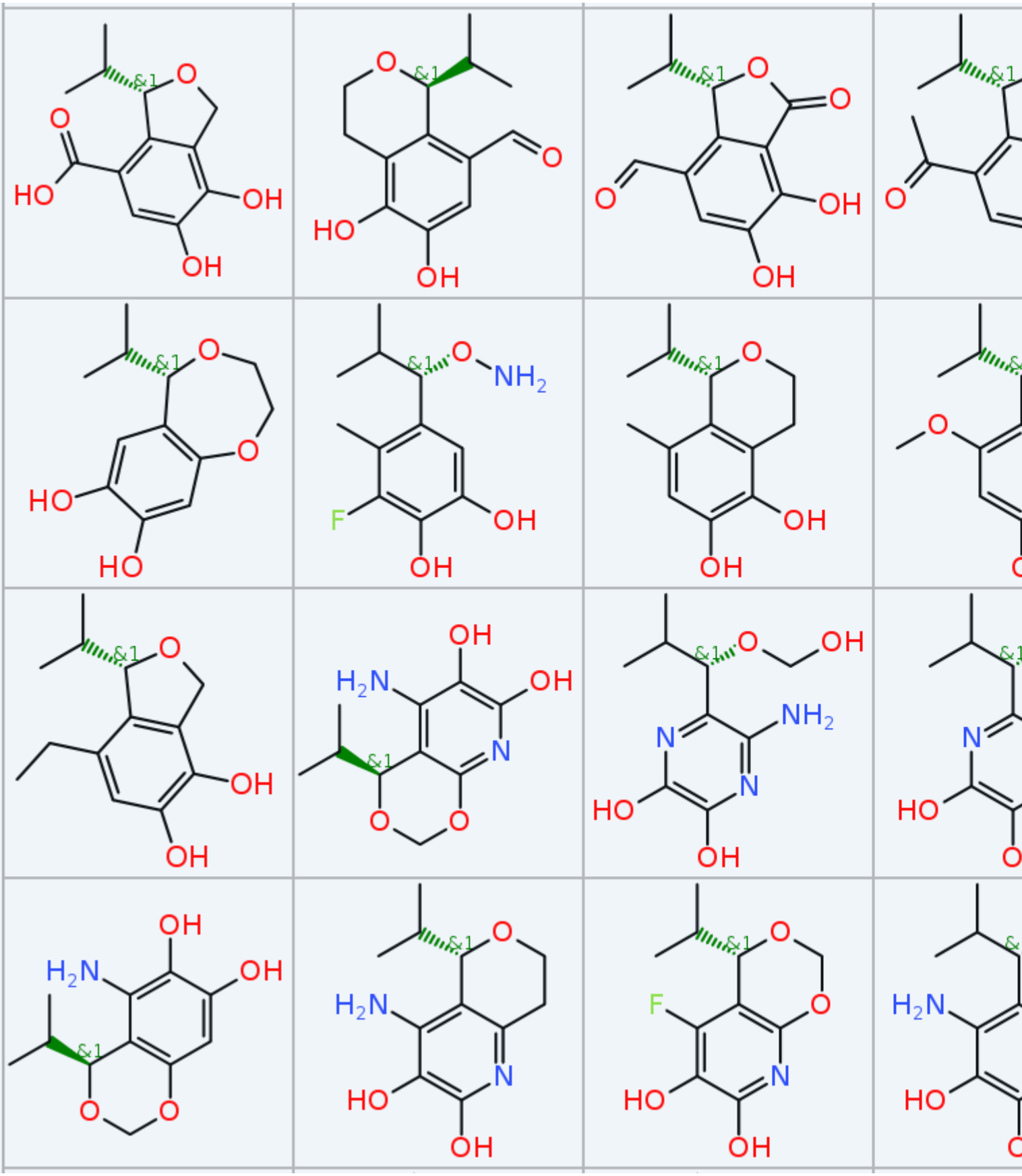
Then you are supposed to add fitness criteria, which are used to value the quality of created structures. Those structures, that match your criteria best will be kept and form at the same time the parent generation for the next round of random changes. I just defined a simple criterion: the molecular weight shall be not higher than 240. Otherwise I just use default options for everything else. The settings look like this:

In less than one second DataWarrior created 267 different molecules in 15 generations that all contain the selected (red) part of your defined starting structure, with lots of variations regarding substitution, ring size, partially open ring structures and molecular weights always below 240. The picture shows a small subset.

Of course, you can be more specific with fitness criteria, e.g. use chemical similarities, pharmacophore similaries or even a docking score...

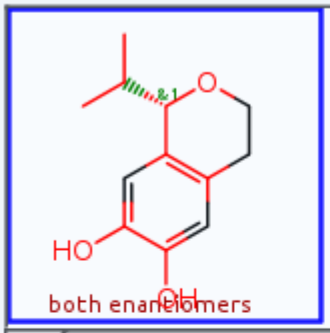
File Attachments

1) temp2.png, downloaded 675 times



2) temp1.png, downloaded 722 times

Root generation compounds: Default



(Select sub-structures to protect

automatic Cycle

128 Compounds per cycle

8 Compounds survive a cycle

Fitness Criteria

Prefer 'Molecular weight' >= and <= 240