

Molecular modeling exercise with MacroModel (Maestro)

DOWNLOAD AND INSTALL

Schrodinger suite installation

Create a web account at <https://www.schrodinger.com/request-account>.

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Request Web Account

To help serve you better please provide the following information.

Required information

Please provide your contact information below.

Name Prefix*

First Name* Last Name*

Title

Organization (without abbreviations)*

Organization Type* Department

E-mail (Please provide your work or institutional email address)*

Password (8-15 Characters)*

Confirm Password*

Address (Line 1)

Address (Line 2)

Country* State/Province*

City* Postal Code

Telephone Fax

After you receive a confirmation email from schrodinger, click the link to validate your email. Then go to download and select the appropriate OS. Fill in with your credential when asked.

Download Releases




Please choose the version of the release you'd like to download:

Version: Release 2017-4





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Schrödinger Release 2017-4

The download bundle includes the following suites

-  SMALL-MOLECULE DRUG DISCOVERY SUITE
-  MATERIALS SCIENCE SUITE
-  BIOLOGICS SUITE

Please choose your OS:

-  Linux
-  Windows 64-bit
-  Windows 32-bit
-  Mac

[Click here](#) to view a list of supported platforms for Release 2017.4

Run the installer and then to copy the license file into the schrodinger suite folder. Next, you need to run the configuration tool to set the license path.

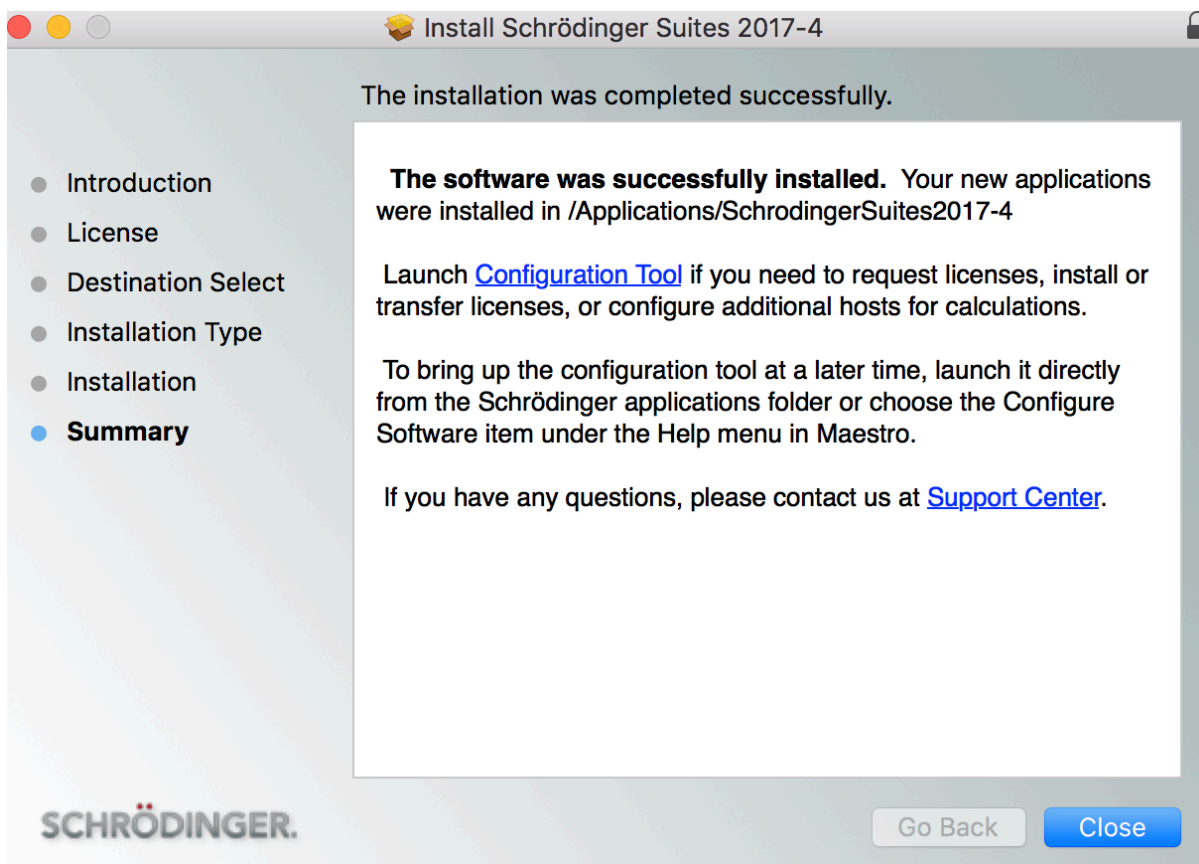
N.B. the license file is the schrodinger.lic that you find in the same folder you found these instructions.

Example - Mac

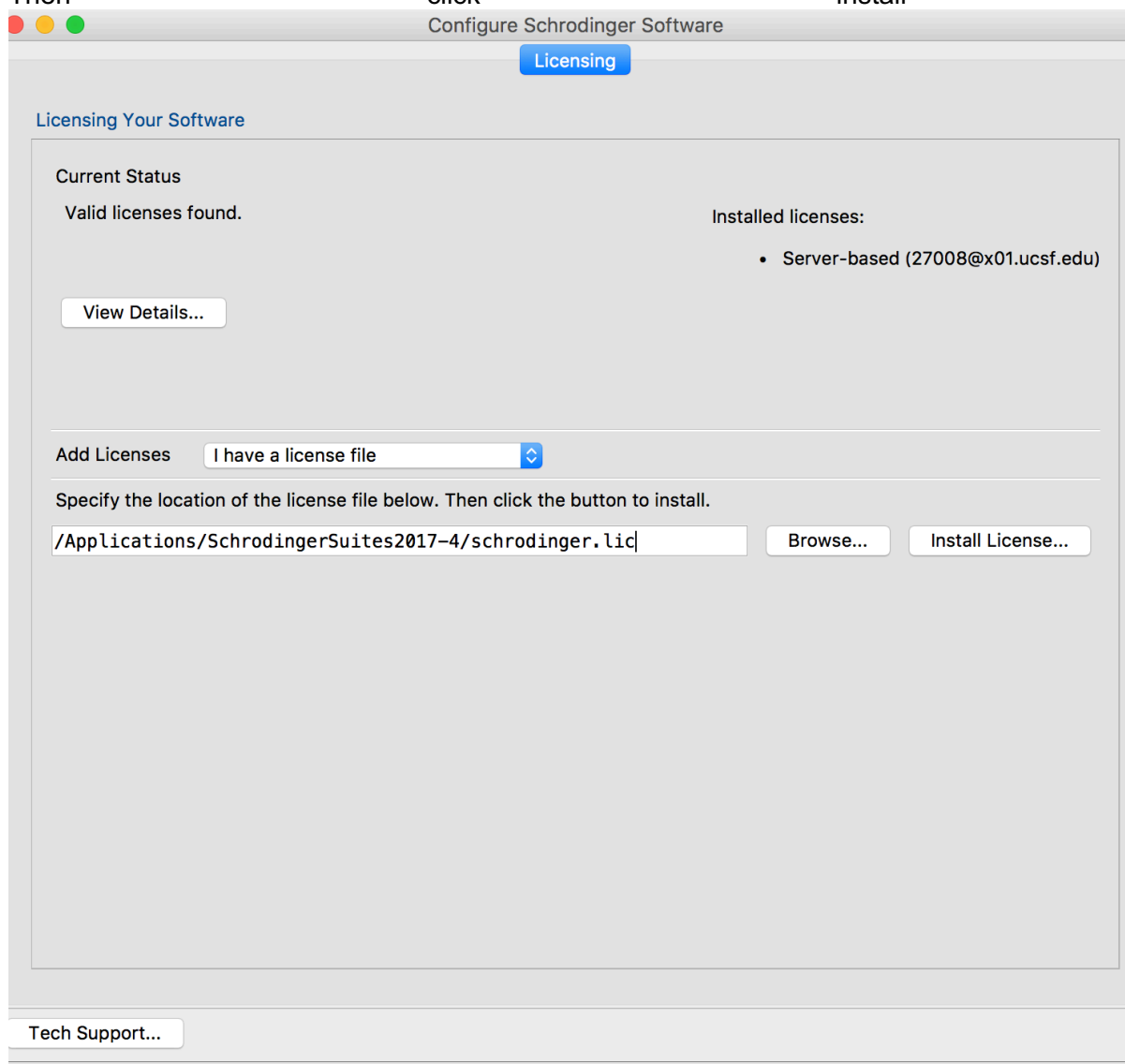
If you download for mac, run the Schrodinger_Suites*.pkg installer and click continue in the Window below.



Once the installation is done, click the **Configuration Tool** link in the window below to run the configuration tool to set the license path.



Scroll down the window to select “I have a license file” and specify the path of the license file by clicking Browse. Then click install License



If you are not within the UCSF network you will need to have the VPN on, because the license server is on x01.ucsf.edu.

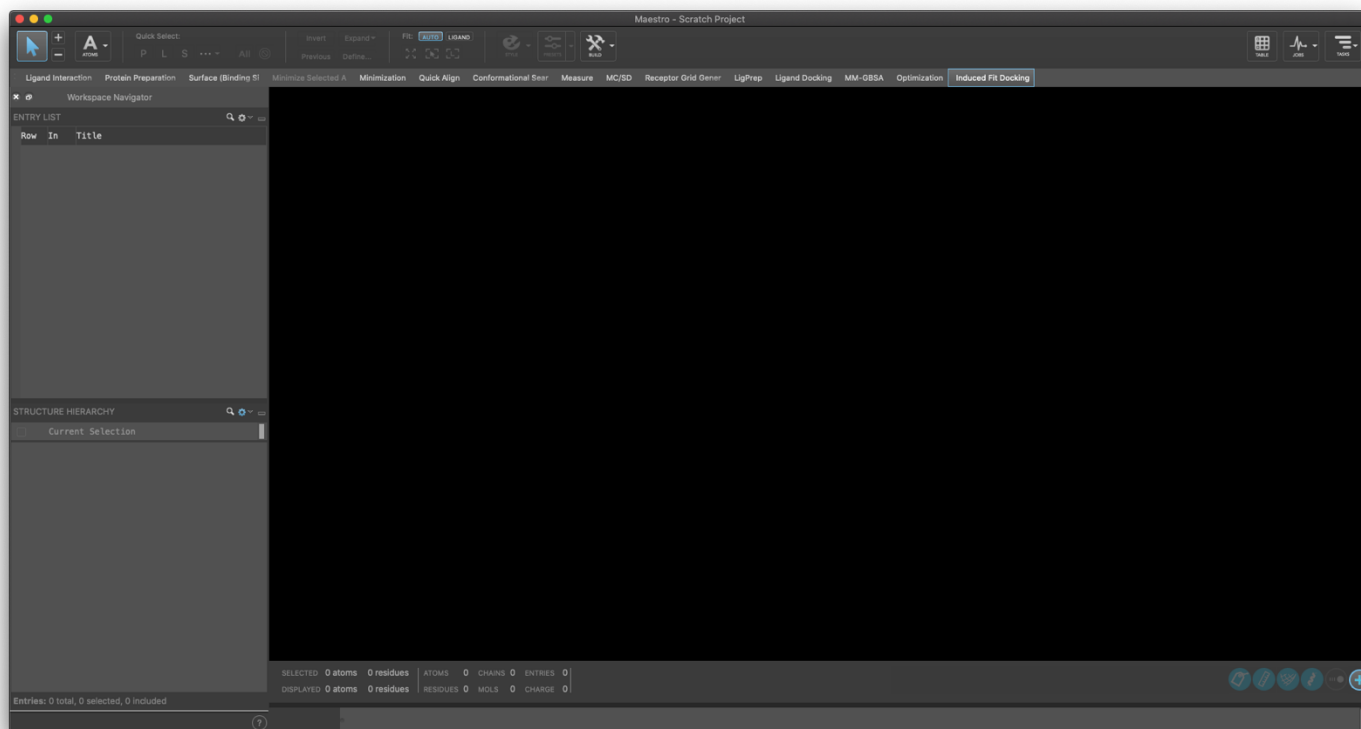
If MAC OS, you need to start Maestro with the following terminal command;

```
export SCHRODINGER=/opt/schrodinger/suites2019-1/  
$SCHRODINGER/maestro -console &
```

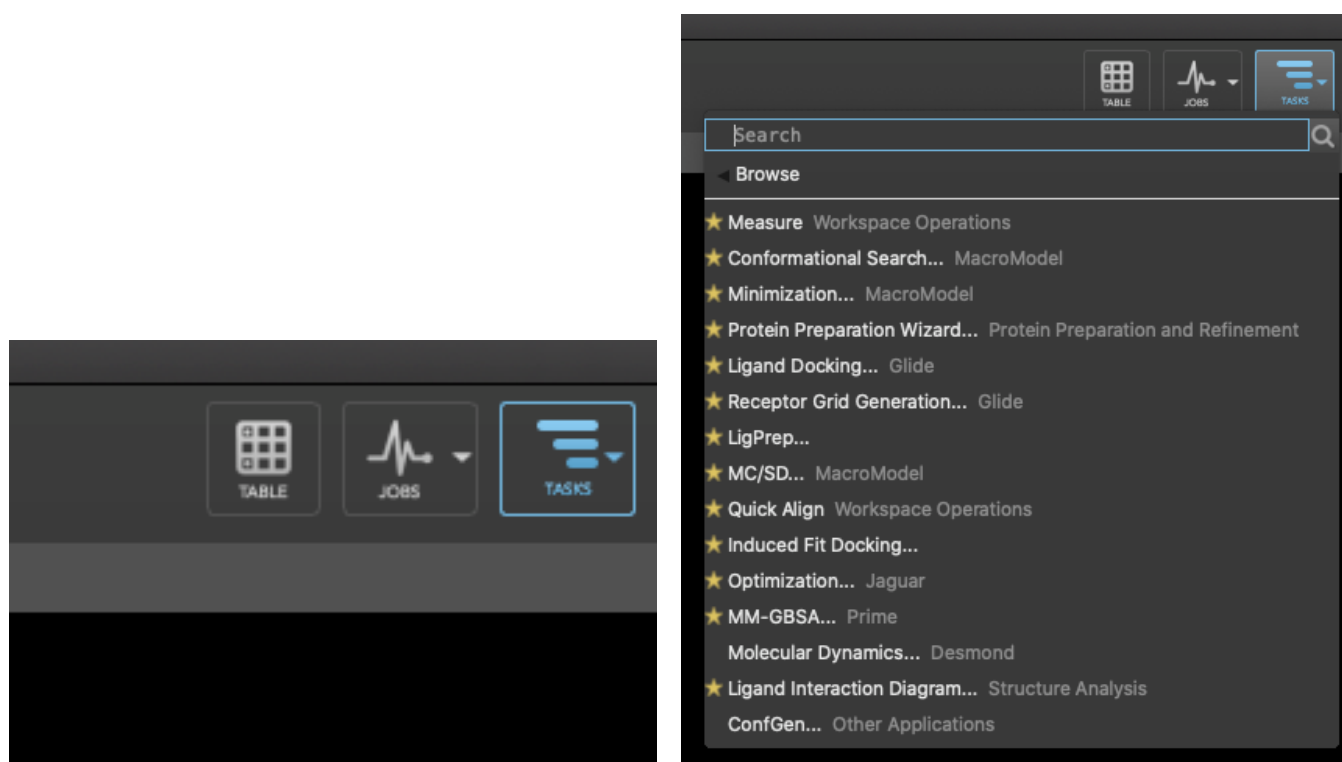
EXERCISE – Drawing and minimizing strychnine

From Yang “I am following Prof. James Nowick’s chem203 spectroscopy class for the following MacroModel workshop.”

Maestro start screen looks like this;



On the right top, click tasks then search for the following programs and make them your favorite by clicking stars (minimization MacroModel; Conformational Search MacroModel; Protein Preparation Wizard; Receptor Grid Generation; Ligand Docking Glide; LigPrep).

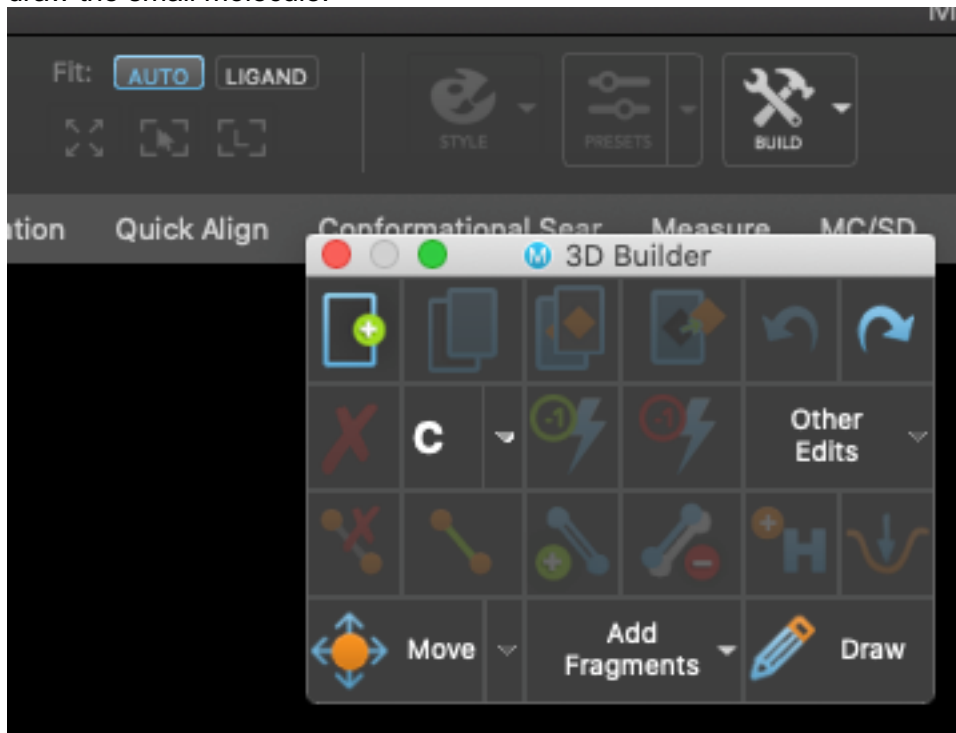


The favorite programs will now show up on the top tab as shown below;

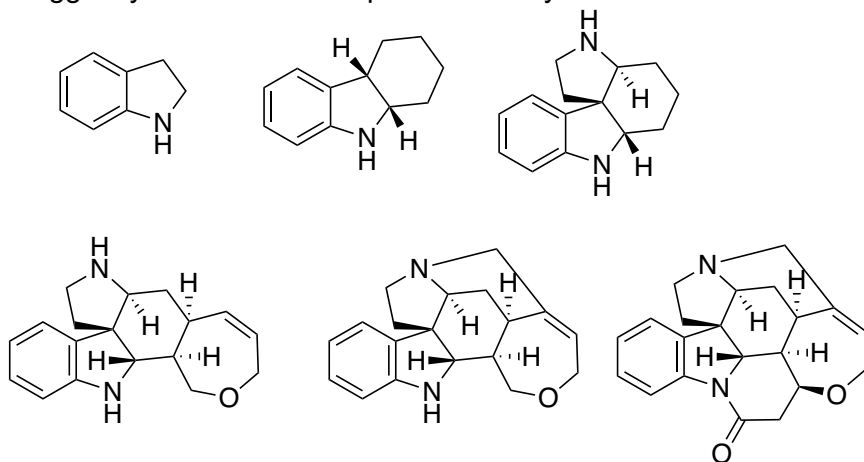


We are now start going to build strychnine for this exercise.

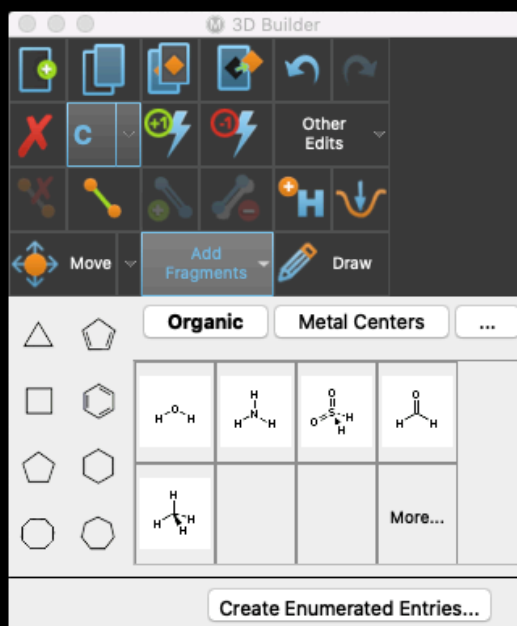
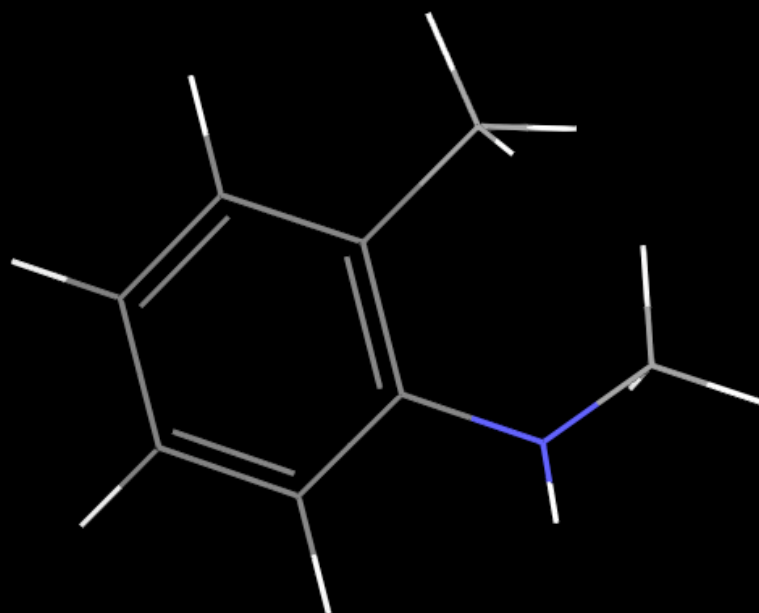
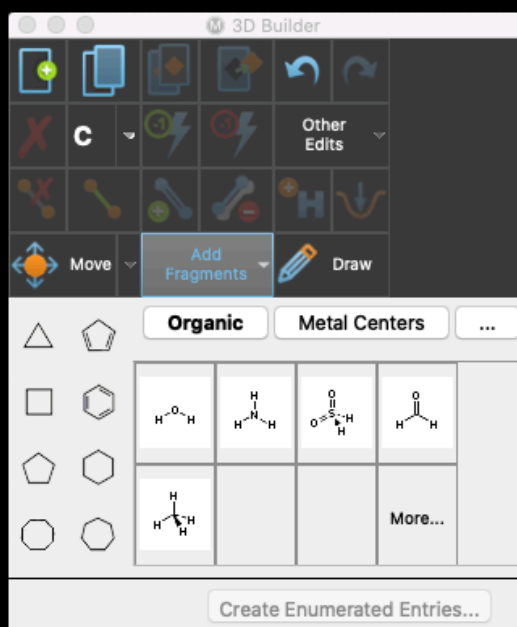
Click Build from the top tab and the 3D Builder tab should appear. Just like one would be drawing on PyMOL, draw the small molecule.

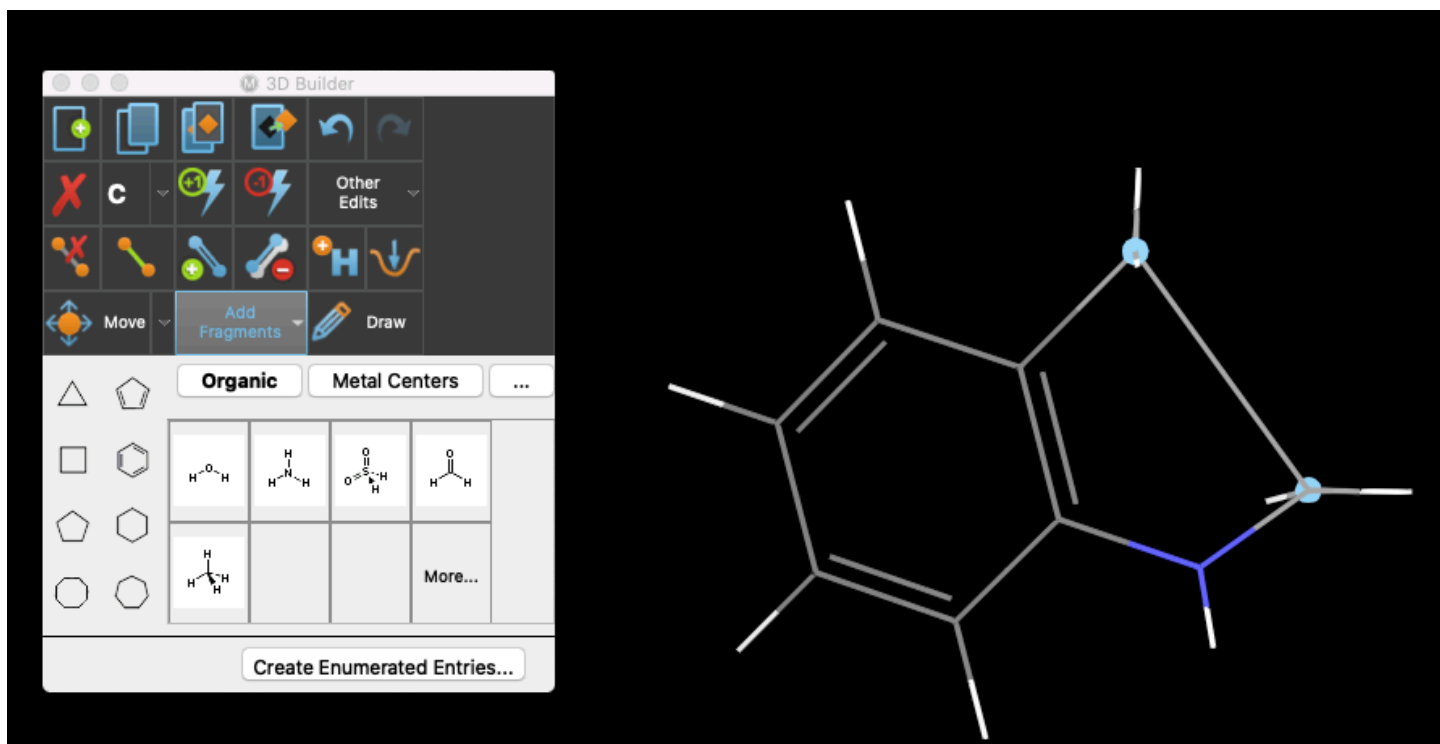


I suggest you take these steps to draw strychnine.



For each step, we are going to minimize the structure. To link the two atoms, one can select the two atoms with shift+left mouse click, then click the button with two orange circles with a green line.





Once we have this ugly looking dihydro indole, we are going to minimize the structure. From the tabs, click minimization, then click run.

M Minimization

Use structures from:

Workspace (included entries)

File name:

Browse...

Potential

Constraints (0)

Substructure

Mini

Comparison

Method:

PRCG

Maximum iterations:

2500

Converge on:

Gradient

Convergence threshold:

0.05

Job name:

mmod_mini_118

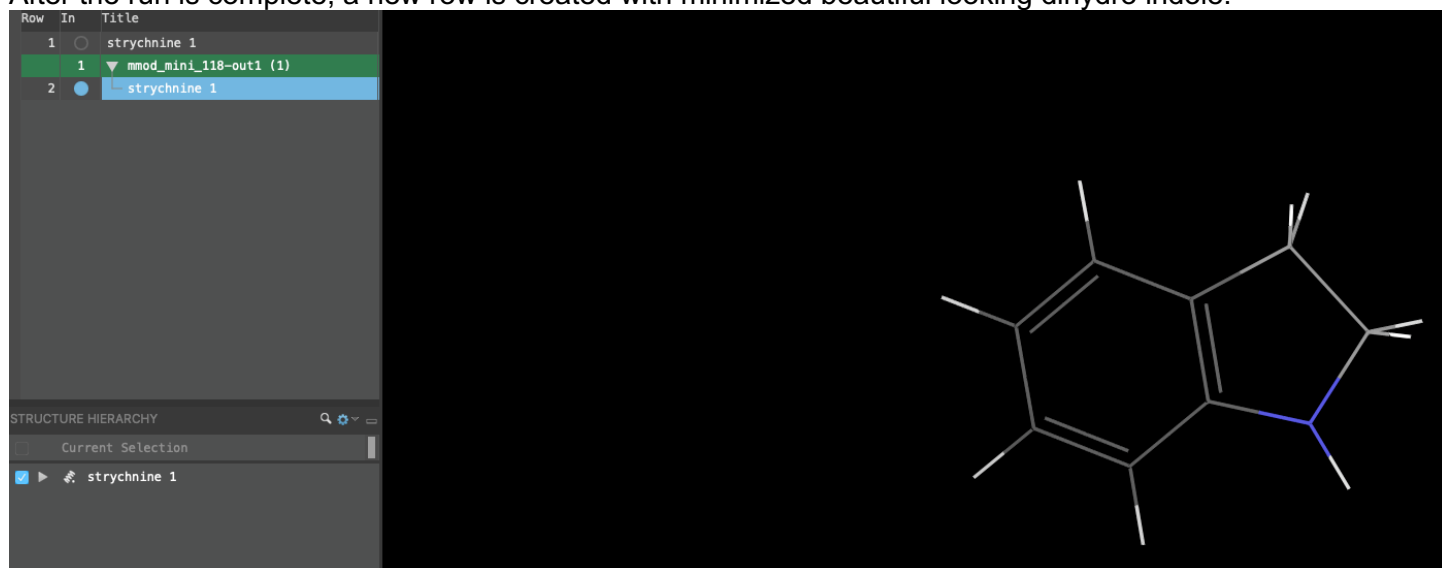
⚙️ ▾ ⌛

Run

MacroModel: Minimization, Host=localhost:4 Subjobs=1, Incorporate=Append new entries as a new group

?

After the run is complete, a new row is created with minimized beautiful looking dihydro indole.



After each minimization run, you want to check that the minimization converged by going to the folder. For MAC OS, it is in the maestro folder. (Users\YOUR COMPUTER NAME\mmod_mini_xxx{or your choice of Job name}) In the folder, you will see five files. If you open the log file in text editor, you will see that the minimization converged (highlighted in the picture below).

If your structure is big and did not converge, you want to increase the maximum iterations from 2500 to higher number.

The screenshot shows two windows. The left window is a file explorer for the folder 'mmod_mini_118', displaying the following files:

Name	Date Modified	Size
mmod_mini_118-out.maegz	Today at 4:04 PM	1 KB
mmod_mini_118.com	Today at 4:04 PM	990 bytes
mmod_mini_118.log	Today at 4:04 PM	7 KB
mmod_mini_118.mae	Today at 4:04 PM	2 KB
mmod_mini_118.sbc	Today at 4:04 PM	Zero bytes

The right window shows the contents of the 'mmod_mini_118.log' file:

```

T.E. for cross-checking: 2335.1194 kJ/mol
Iter= 20 Move(A)= 7.161148 E(kJ/mol)= 13.96396 Grad= 30.13462
Iter= 40 Move(A)= 3.607890 E(kJ/mol)= -8.369245 Grad= 21.37401
Iter= 60 Move(A)= 1.108510 E(kJ/mol)= -11.48474 Grad= 3.065503
Iter= 80 Move(A)= 0.185340 E(kJ/mol)= -11.55962 Grad= 0.3780869
Iter= 100 Move(A)= 0.081095 E(kJ/mol)= -11.56963 Grad= 0.9717010
Iter= 120 Move(A)= 0.138657 E(kJ/mol)= -11.57419 Grad= 0.1161521
Iter= 140 Move(A)= 0.006392 E(kJ/mol)= -11.57432 Grad= 0.2109144E-01
Minimization converged; gradient = 0.211E-01 .LT. 0.500E-01
Total Energy = -12.6026 kJ/mol
Stretch = 3.5753 kJ/mol
Bend = 11.4163 kJ/mol
Torsion = 1.4427 kJ/mol
Improper Torsion = 0.0004 kJ/mol
VDW = 34.5827 kJ/mol
Electrostatic = -38.2581 kJ/mol
Explicit Hydrogen Bonds = 0.0000 kJ/mol
Cross Terms = 0.0000 kJ/mol
Solvation = -25.3620 kJ/mol

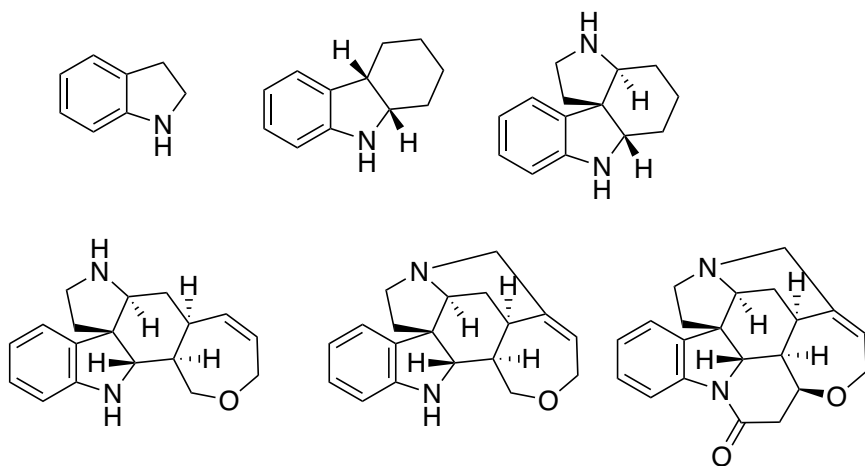
T.E. for cross-checking: -12.6026 kJ/mol
Iterations = 140 out of 2500
Conf 1 E = -12.603 ( 0.021) kJ/mol
Total number of structures processed = 1

BatchMin: normal termination 12-Feb-2021 16:04:38

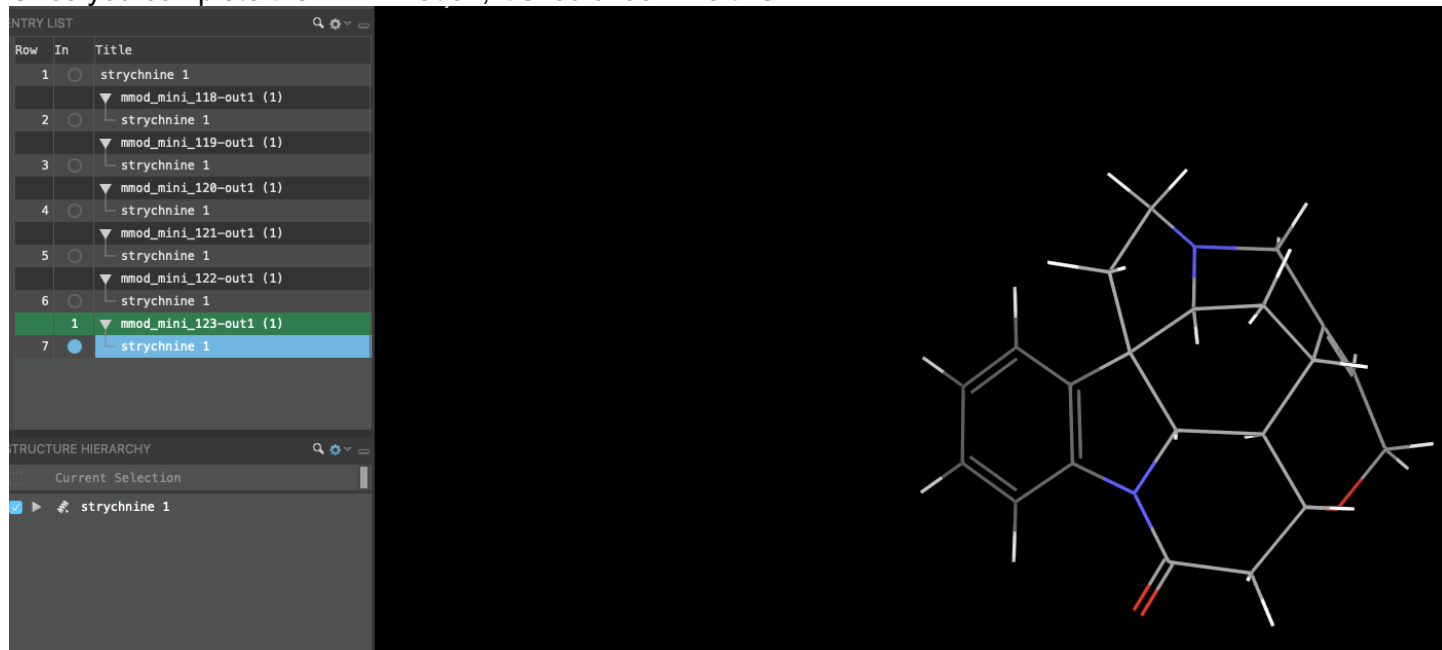
real 0m5.037s
user 0m4.139s

```

With these, please complete drawing the strychnine minimizing each structure below;

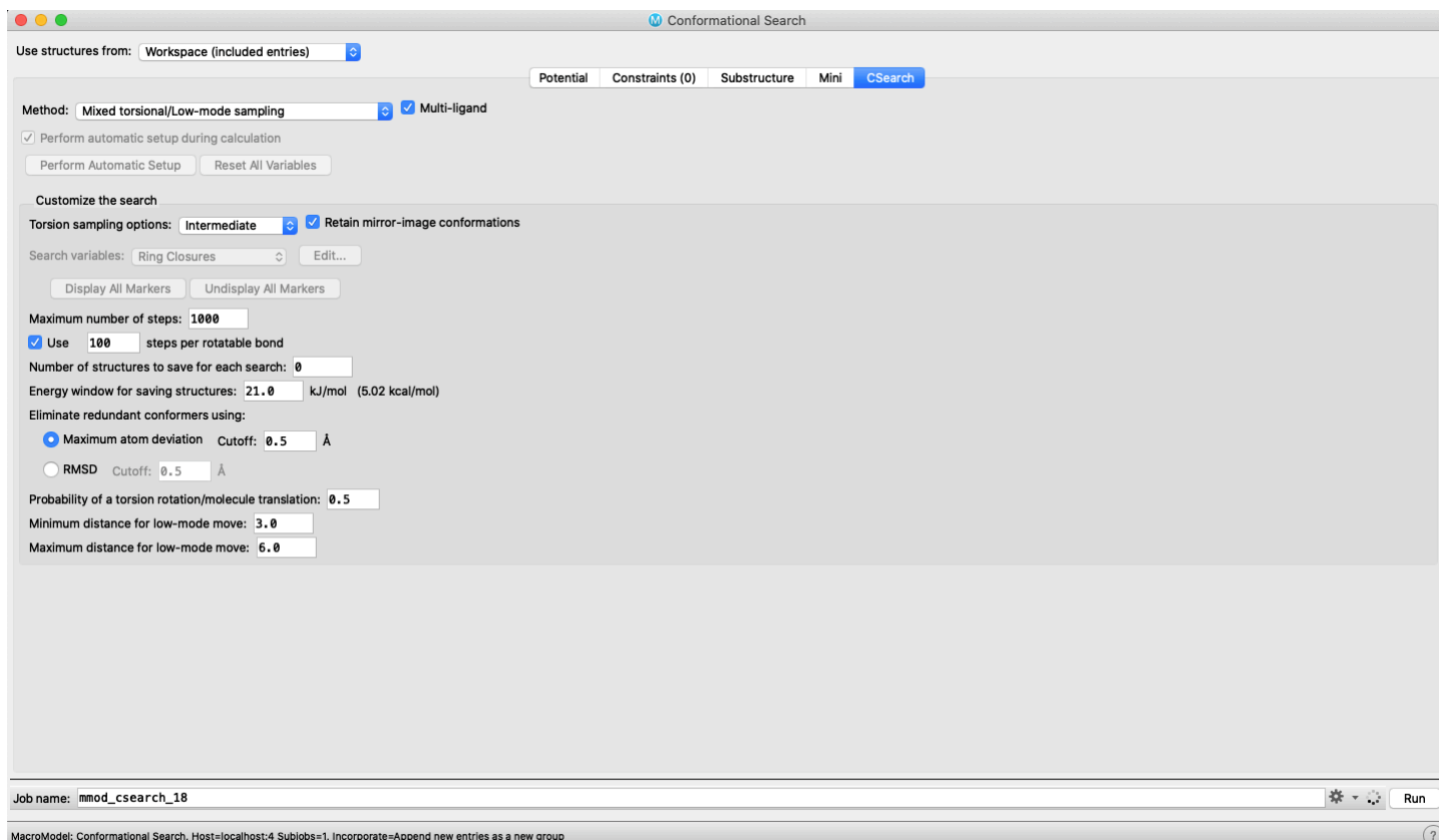


Once you complete the minimization, it should look like this.

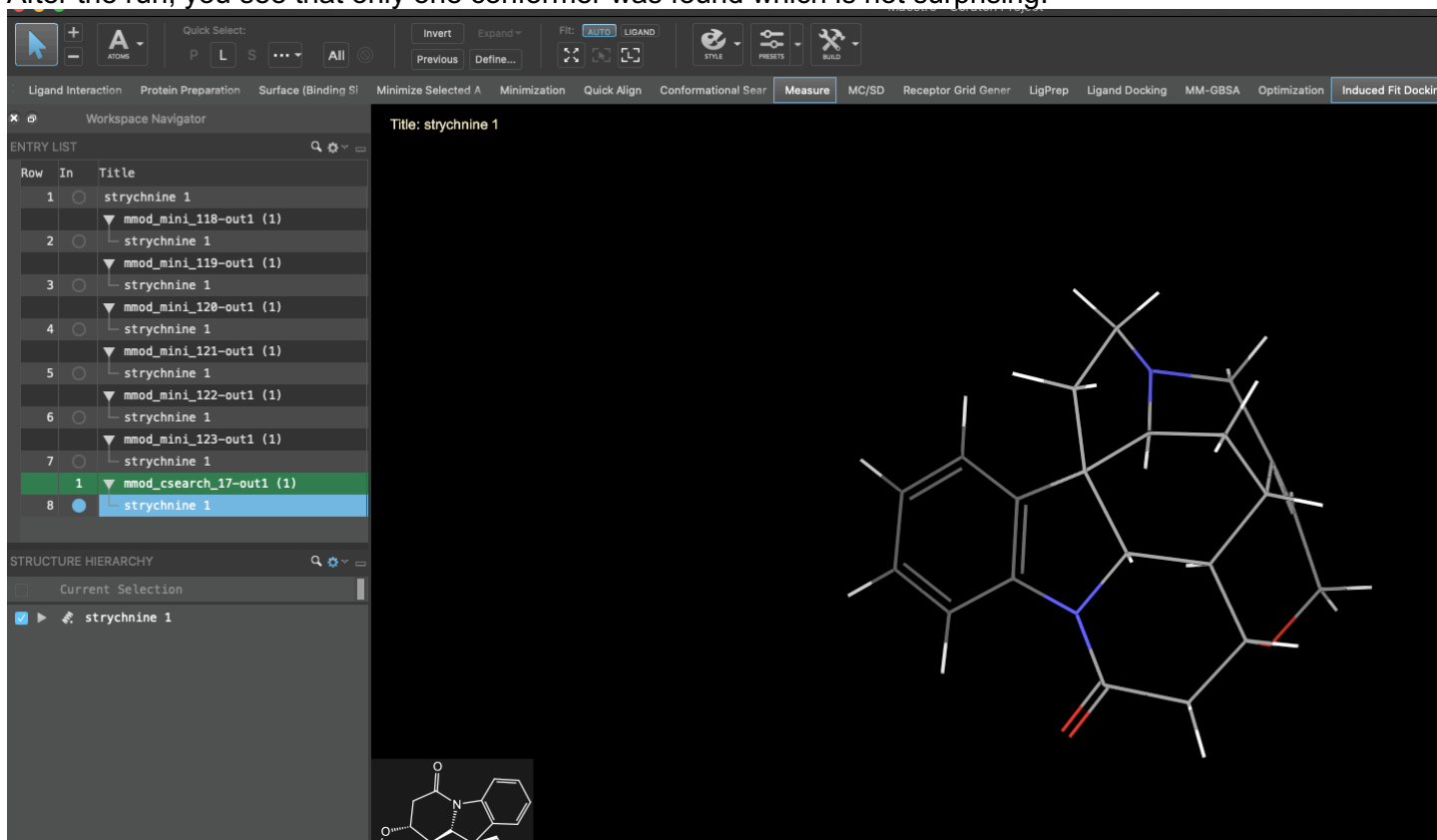


If you want to look at the structure in PyMOL, you go to Workspace→Send to PyMOL→Selected Entries and PyMOL session will open up with your structure.

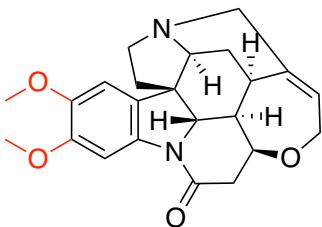
With the strychnine molecule, let's run conformational search. Click conformational search in one of your favorite tabs and click run. (This may take a long time)



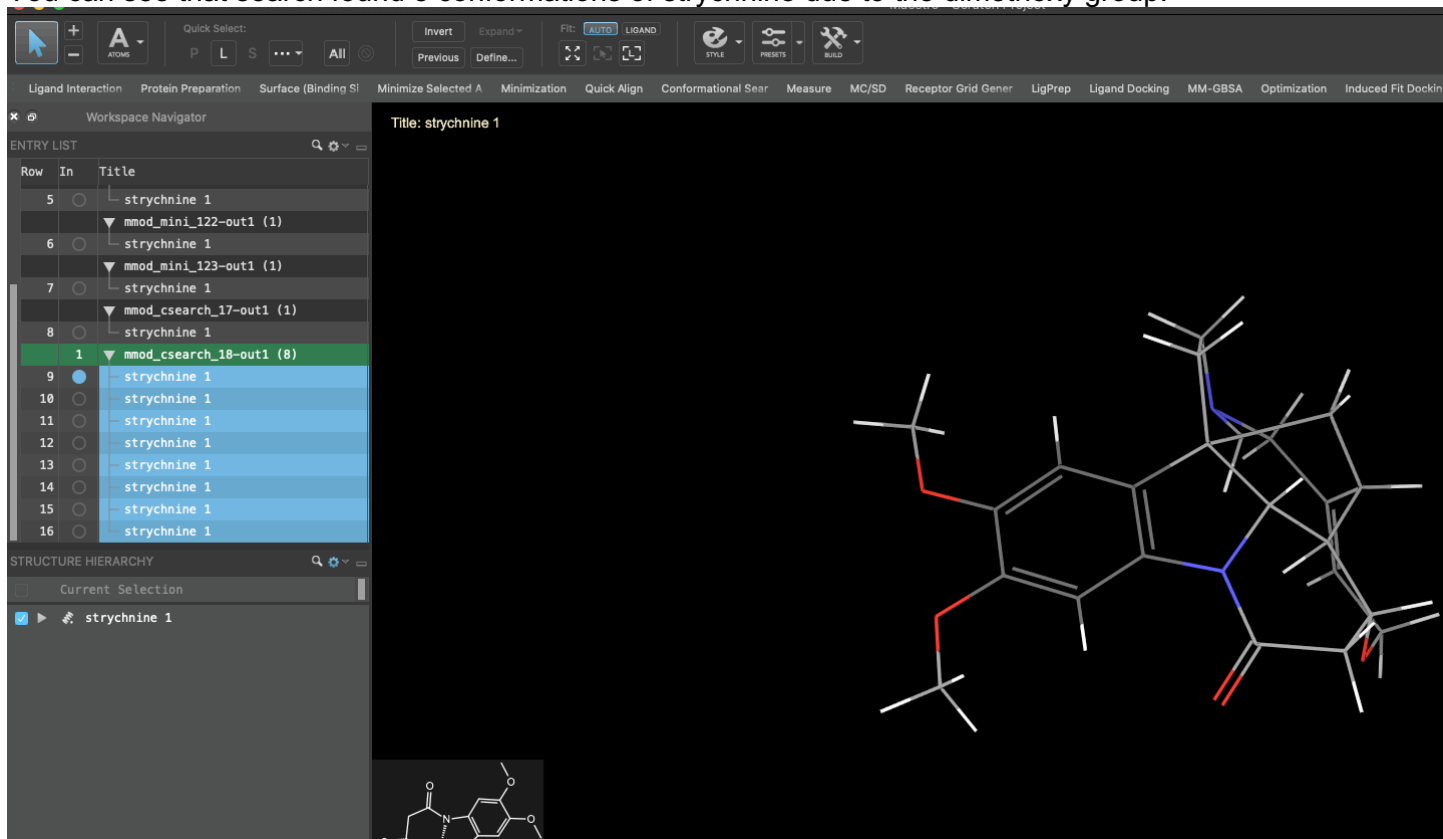
After the run, you see that only one conformer was found which is not surprising.



Now let's try the derivative of strychnine, Brucine 3 and run conformational search.



You can see that search found 8 conformations of strychnine due to the dimethoxy group.



Further, you can click the “table” button located on the right top and look at the relative potential energy to determine the energy levels of various conformations.

Project Table --- Scratch Project

File Table Data Select Window ePlayer

Import Export 2D Viewer Plot Sort Find/Replace Show Props Color Rows Calculator Columns Tree Show 2D Structure Show Family Hide Family

Row	In	Title	Stars	Entry ID	Date Added	Date Modified	Potential Energy-OPLS3e	RMS Derivative-OPLS3e	Job Name	Relative Potent.
		▼ mmod_mini_119-out1 (1)								
3		strychnine 1	☆☆☆	3	16:11	16:14	12.293	0.049	mmod_mini_1_	
		▼ mmod_mini_120-out1 (1)								
4		strychnine 1	☆☆☆	4	16:14	16:16	68.489	0.017	mmod_mini_1_	
		▼ mmod_mini_121-out1 (1)								
5		strychnine 1	☆☆☆	5	16:16	16:17	52.947	0.044	mmod_mini_1_	
		▼ mmod_mini_122-out1 (1)								
6		strychnine 1	☆☆☆	6	16:17	16:18	644.691	0.029	mmod_mini_1_	
		▼ mmod_mini_123-out1 (1)								
7		strychnine 1	☆☆☆	7	16:18	16:19	579.531	0.045	mmod_mini_1_	
		▼ mmod_csearch_17-out1 (1)								
8		strychnine 1	☆☆☆	8	16:23	16:34	579.506	0.026	mmod_csearc_	
		▼ mmod_csearch_18-out1 (8)								
9		strychnine 1	☆☆☆	9	16:40	16:40	628.286	0.024	mmod_csearc_	
10		strychnine 1	☆☆☆	10	16:40	16:40	636.842	0.035	mmod_csearc_	
11		strychnine 1	☆☆☆	11	16:40	16:40	637.358	0.025	mmod_csearc_	
12		strychnine 1	☆☆☆	12	16:40	16:40	637.483	0.023	mmod_csearc_	
13		strychnine 1	☆☆☆	13	16:40	16:40	637.579	0.045	mmod_csearc_	
14		strychnine 1	☆☆☆	14	16:40	16:40	639.948	0.043	mmod_csearc_	
15		strychnine 1	☆☆☆	15	16:40	16:40	646.017	0.041	mmod_csearc_	
16		strychnine 1	☆☆☆	16	16:40	16:40	646.559	0.030	mmod_csearc_	

Property Tree

Search

All

Entries: 16 total, 8 selected, 1 included Groups: 8 total, 1 selected Properties: 20 total, 8 shown

CC12CC3C(C1)N(C2)C4=CC(OC)=CC(OC)=C4C3

***** few other notes;

(A) For running peptides, I suggest you use the MMFFs force field as it accounts for the planarity of the amides.
 (B) one can add the constraints in the minimization and the conformation search to keep certain atoms frozen or keep next to certain atoms.