ICM-Chemist-Pro How-To Guide

Version 3.6-1h

Last Updated 12/29/2009

ICM-Chemist-Pro

ICM 3D LIGAND EDITOR: SETUP

How to setup the ligand in the ICM 3D Ligand Editor.

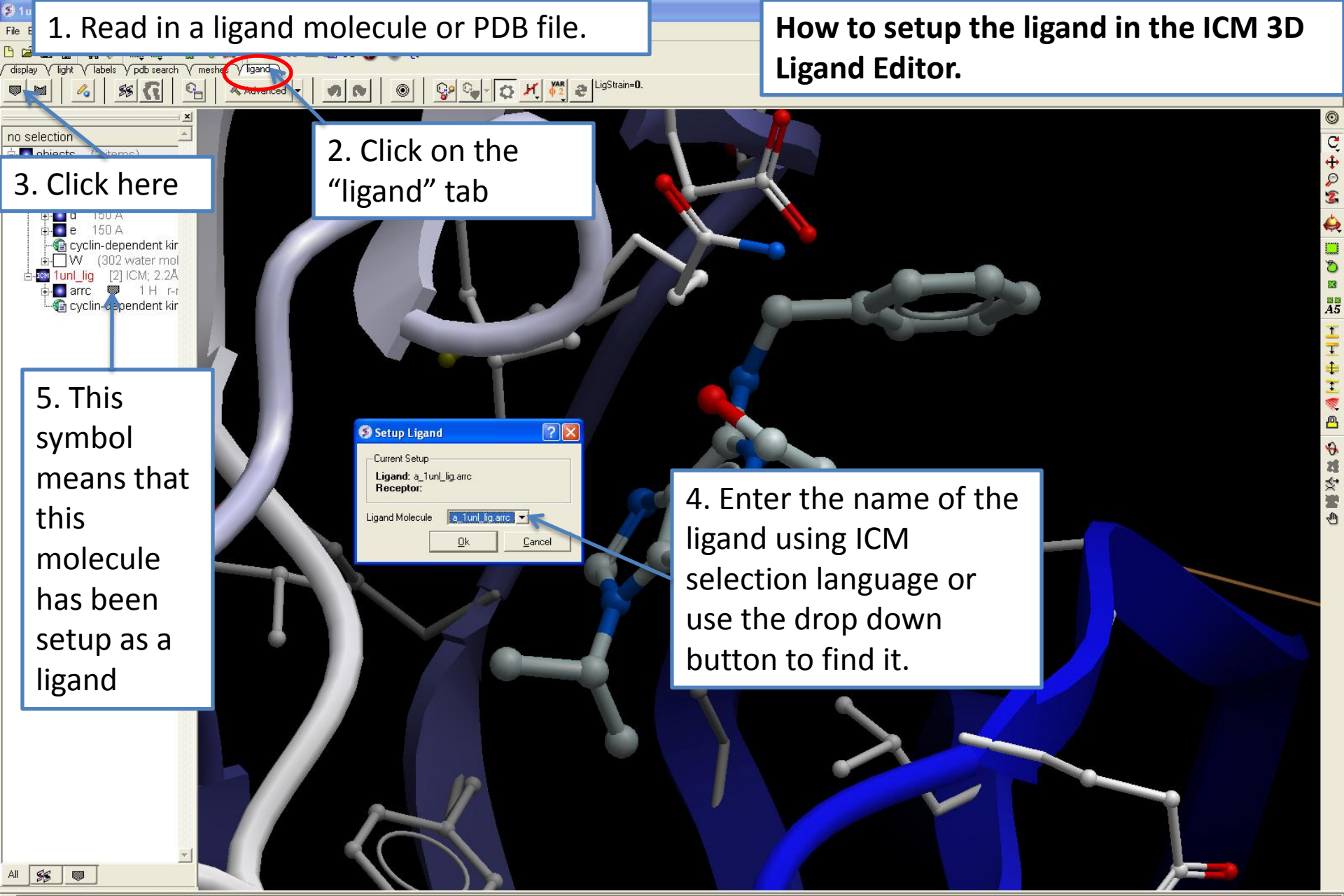
1. Read in a ligand molecule or PDB file.

2. Click on the “ligand” tab

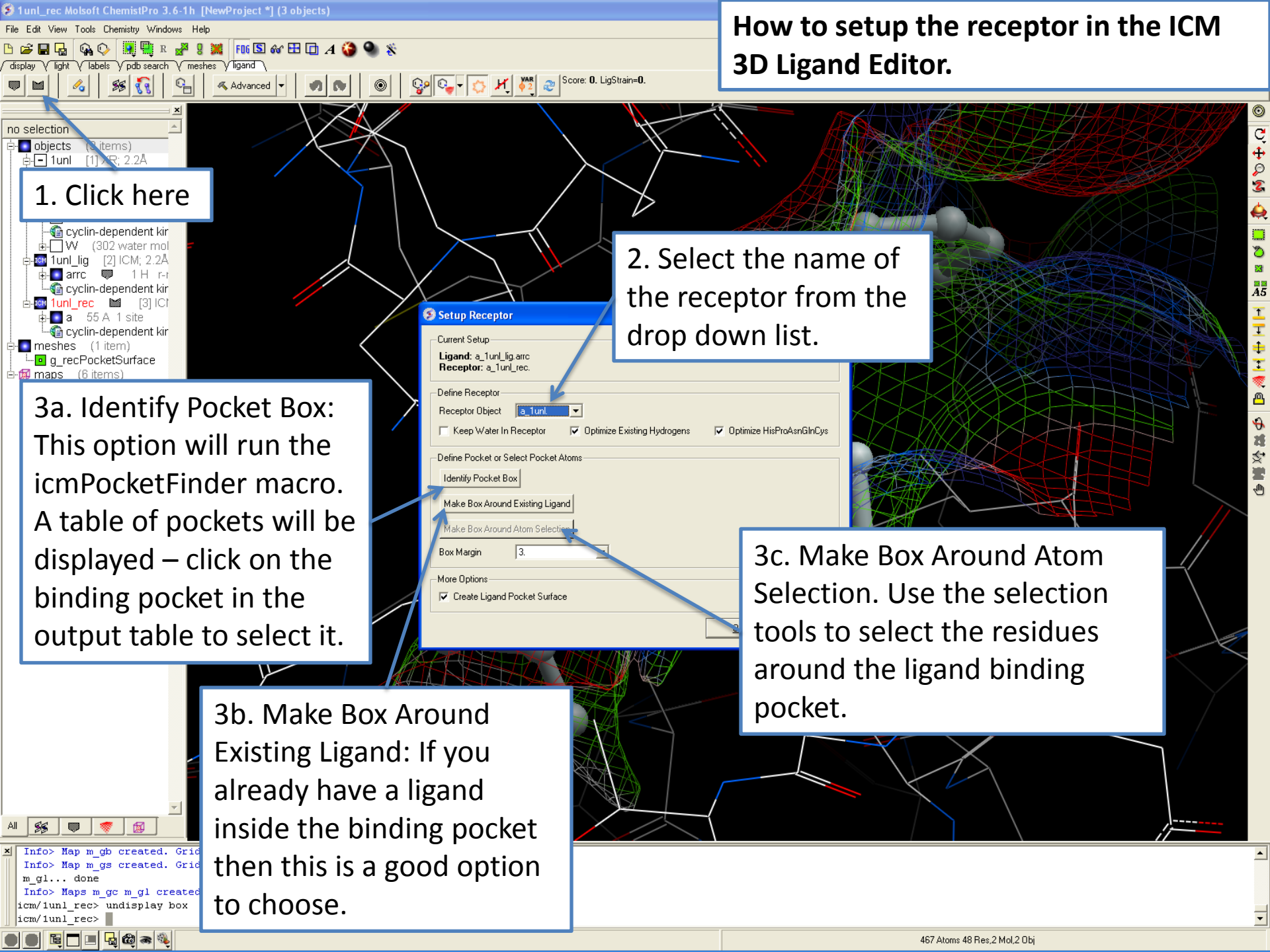
3. Click here

4. Enter the name of the ligand using ICM selection language or use the drop down button to find it.

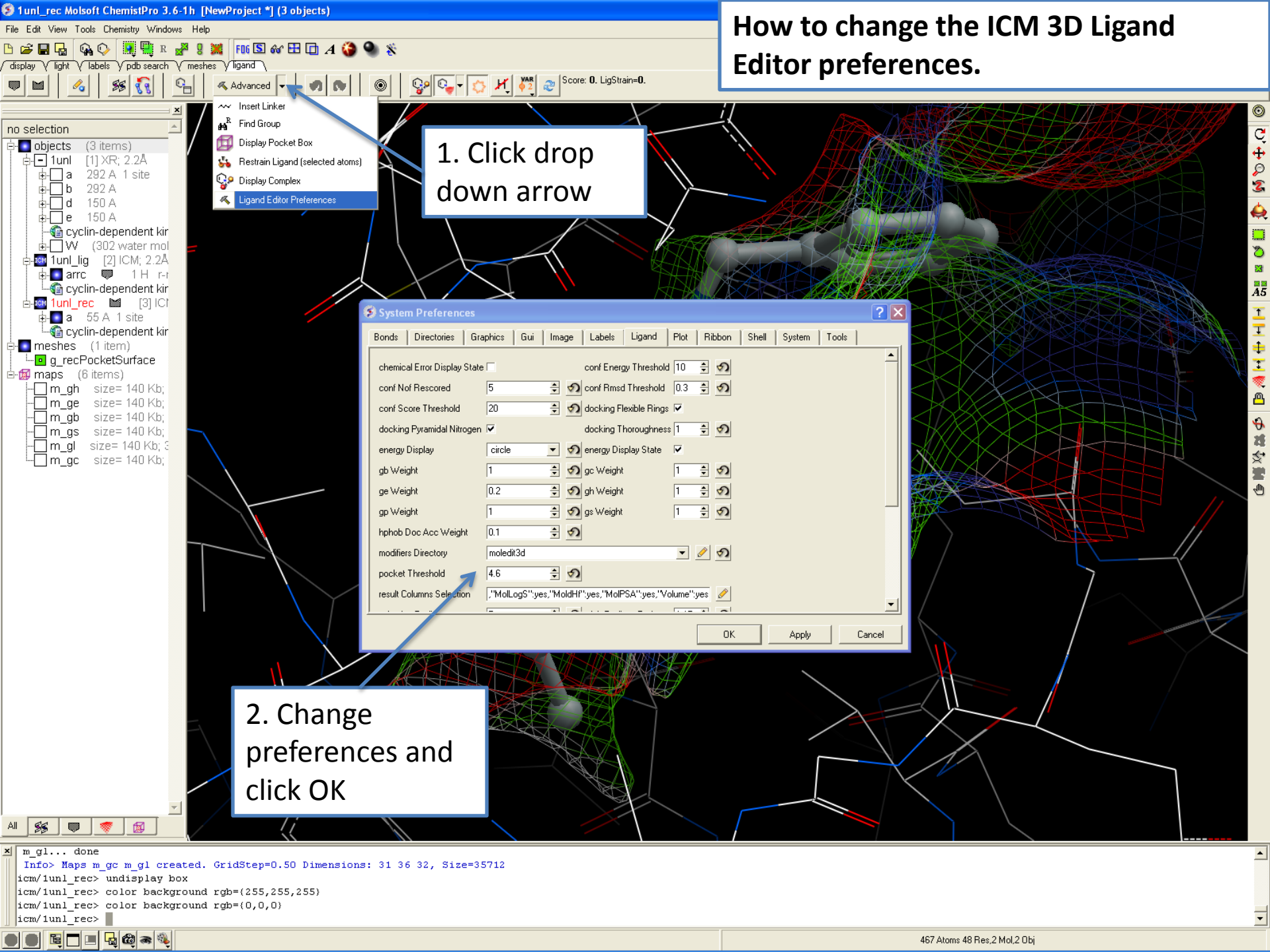
5. This symbol means that this molecule has been setup as a ligand

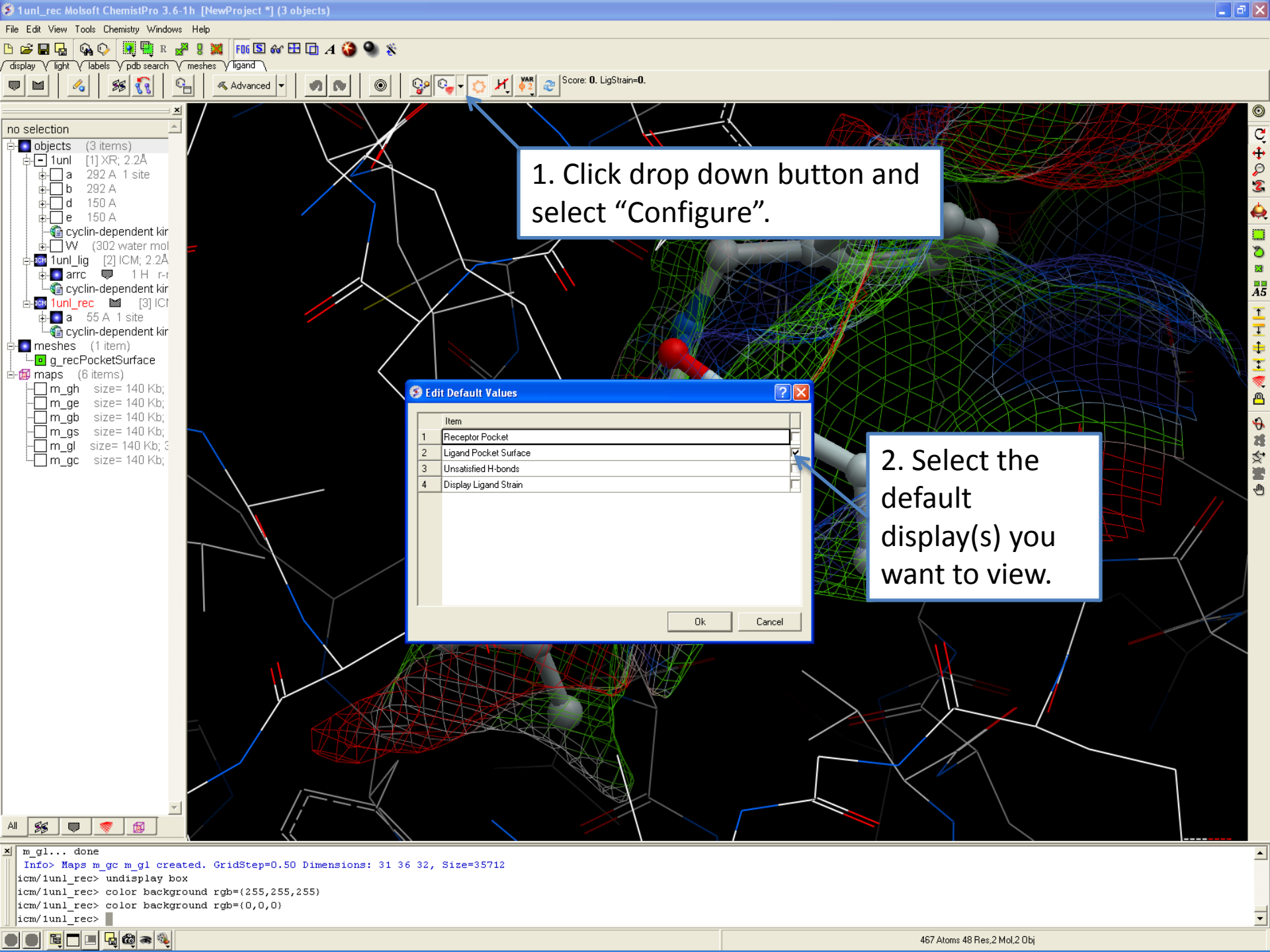


How to setup the receptor in the ICM 3D Ligand Editor.



How to change the ICM 3D Ligand Editor preferences.




1unl_rec Molsoft ChemistPro 3.6-1h [NewProject *] (3 objects)
File Edit View Tools Chemistry Windows Help
display light labels pdb search meshes ligand
Advanced
Score: 0. LigStrain=0.
no selection
objects (3 items)
1unl [1] XR; 2.2Å
a 292 A 1 site
b 292 A
d 150 A
e 150 A
cyclin-dependent kir
W (302 water mol
1unl_lig [2] ICM; 2.2Å
arrc 1 H
cyclin-dependent kir
1unl_rec [3] ICM
a 55 A 1 site
cyclin-dependent kir
meshes (1 item)
g_recPocketSurface
maps (6 items)
m_gh size= 140 Kb;
m_ge size= 140 Kb;
m_gb size= 140 Kb;
m_gs size= 140 Kb;
m_gl size= 140 Kb;
m_gc size= 140 Kb;
1. Click drop down button and select “Configure”.
Edit Default Values
Item
1 Receptor Pocket
2 Ligand Pocket Surface
3 Unsatisfied H-bonds
4 Display Ligand Strain
Ok
Cancel
2. Select the default display(s) you want to view.
m_gl... done
Info> Maps m_gc m_gl created. GridStep=0.50 Dimensions: 31 36 32, Size=35712
icm/1unl_rec> undisplay box
icm/1unl_rec> color background rgb=(255,255,255)
icm/1unl_rec> color background rgb=(0,0,0)
icm/1unl_rec>
467 Atoms 48 Res,2 Mol,2 Obj

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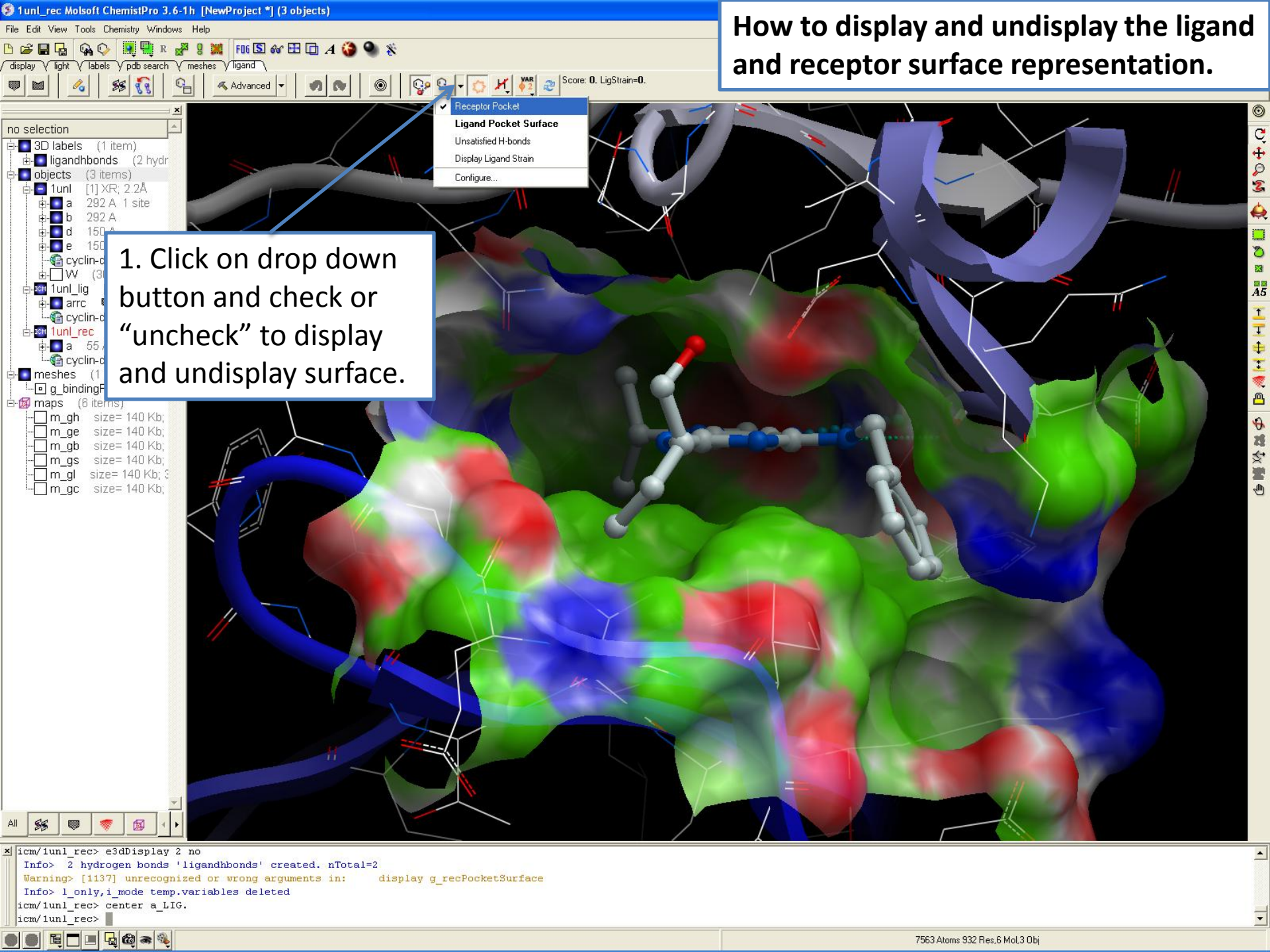
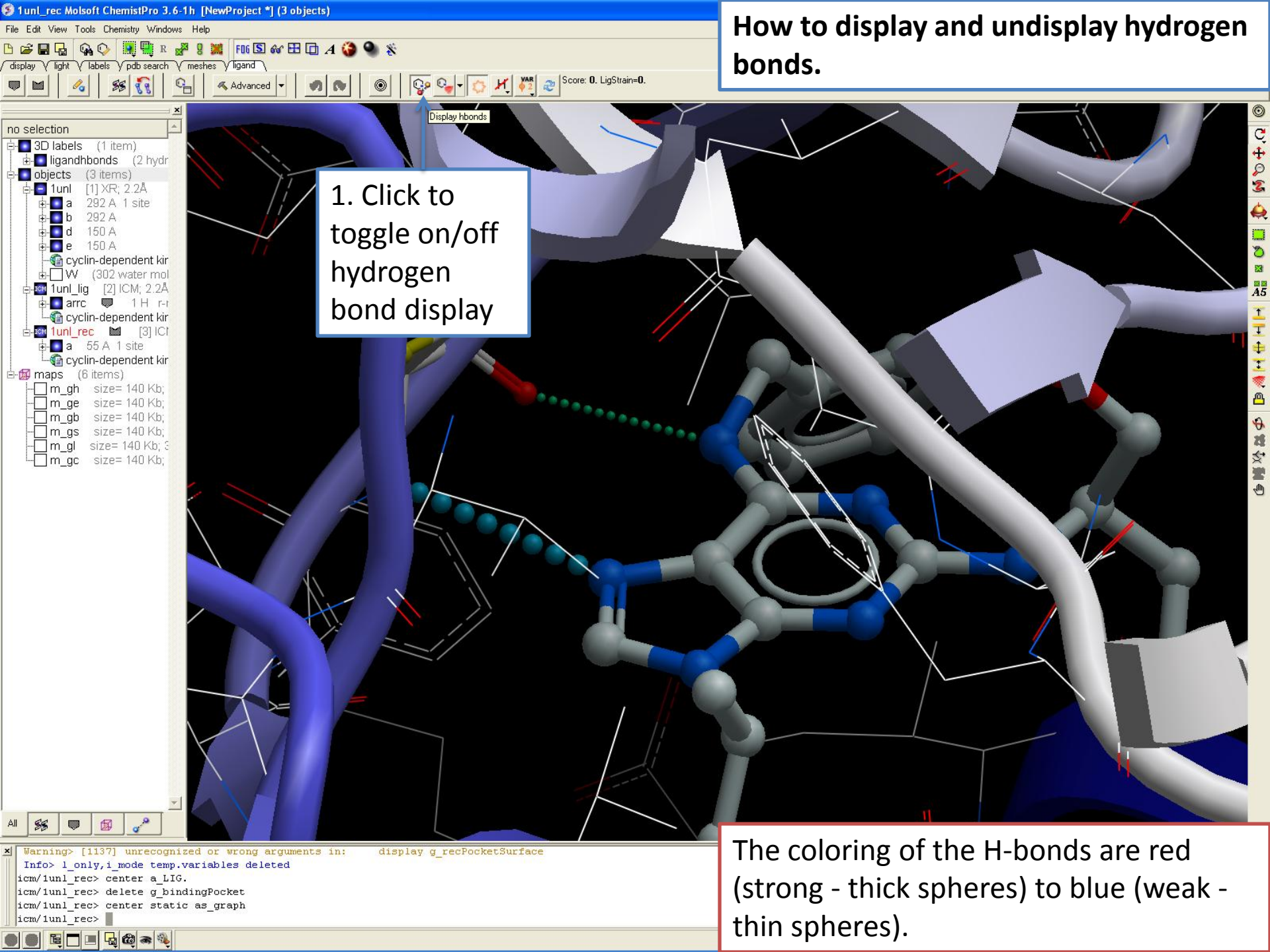
ICM 3D LIGAND EDITOR: DISPLAY

How to display and undisplay the ligand and receptor surface representation.

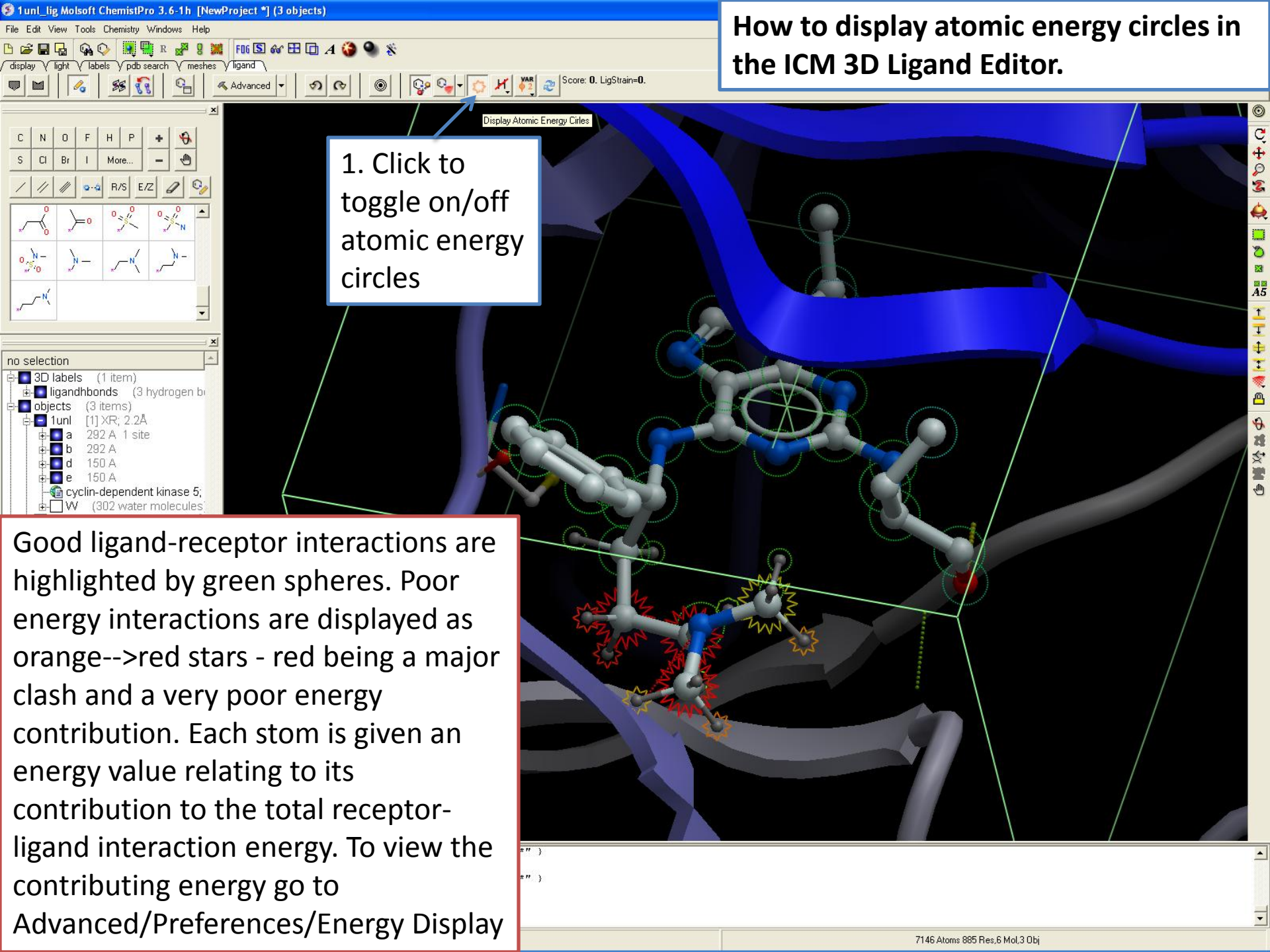


How to display and undisplay hydrogen bonds.



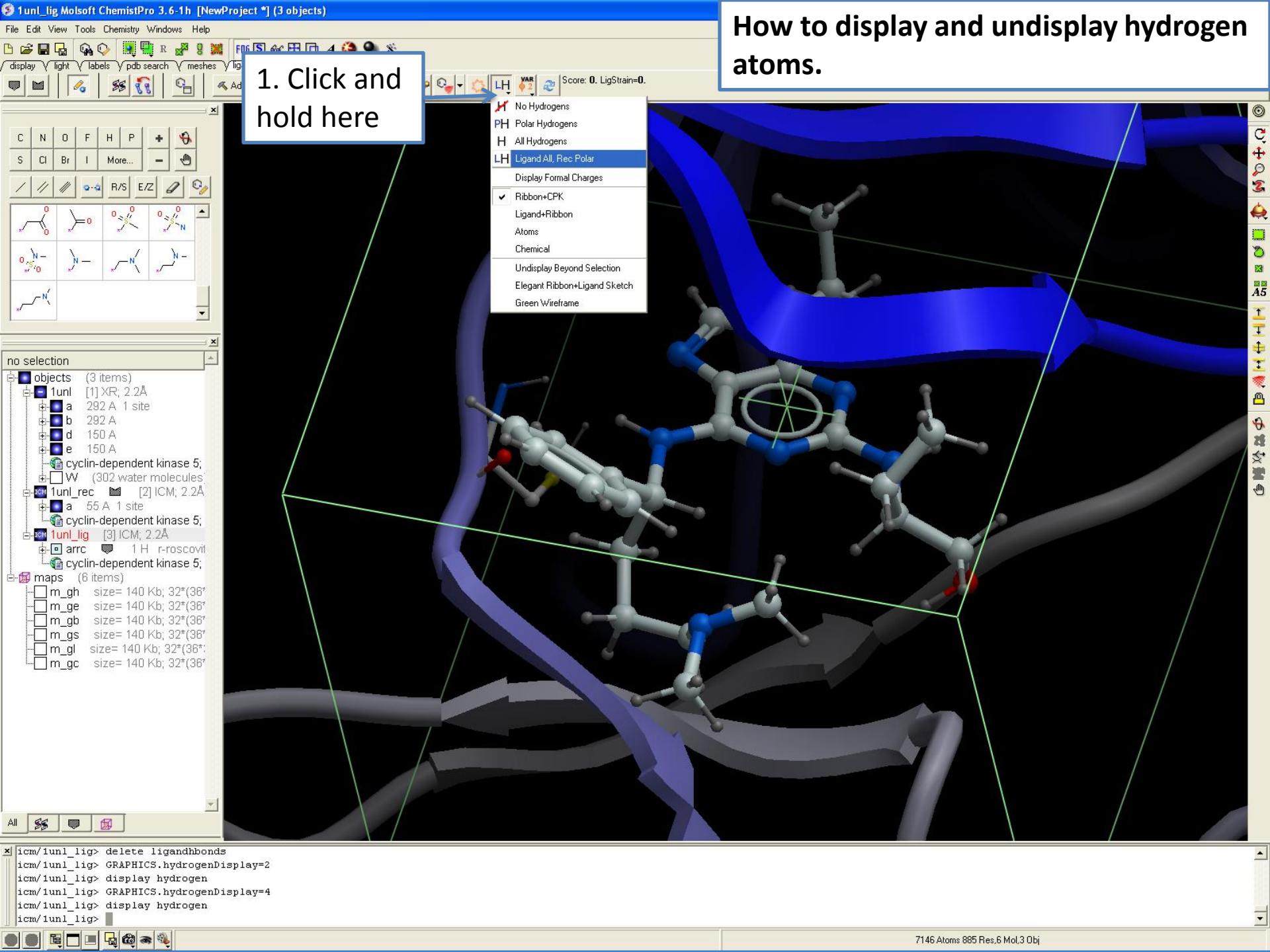
The coloring of the H-bonds are red (strong - thick spheres) to blue (weak - thin spheres).

How to display atomic energy circles in the ICM 3D Ligand Editor.

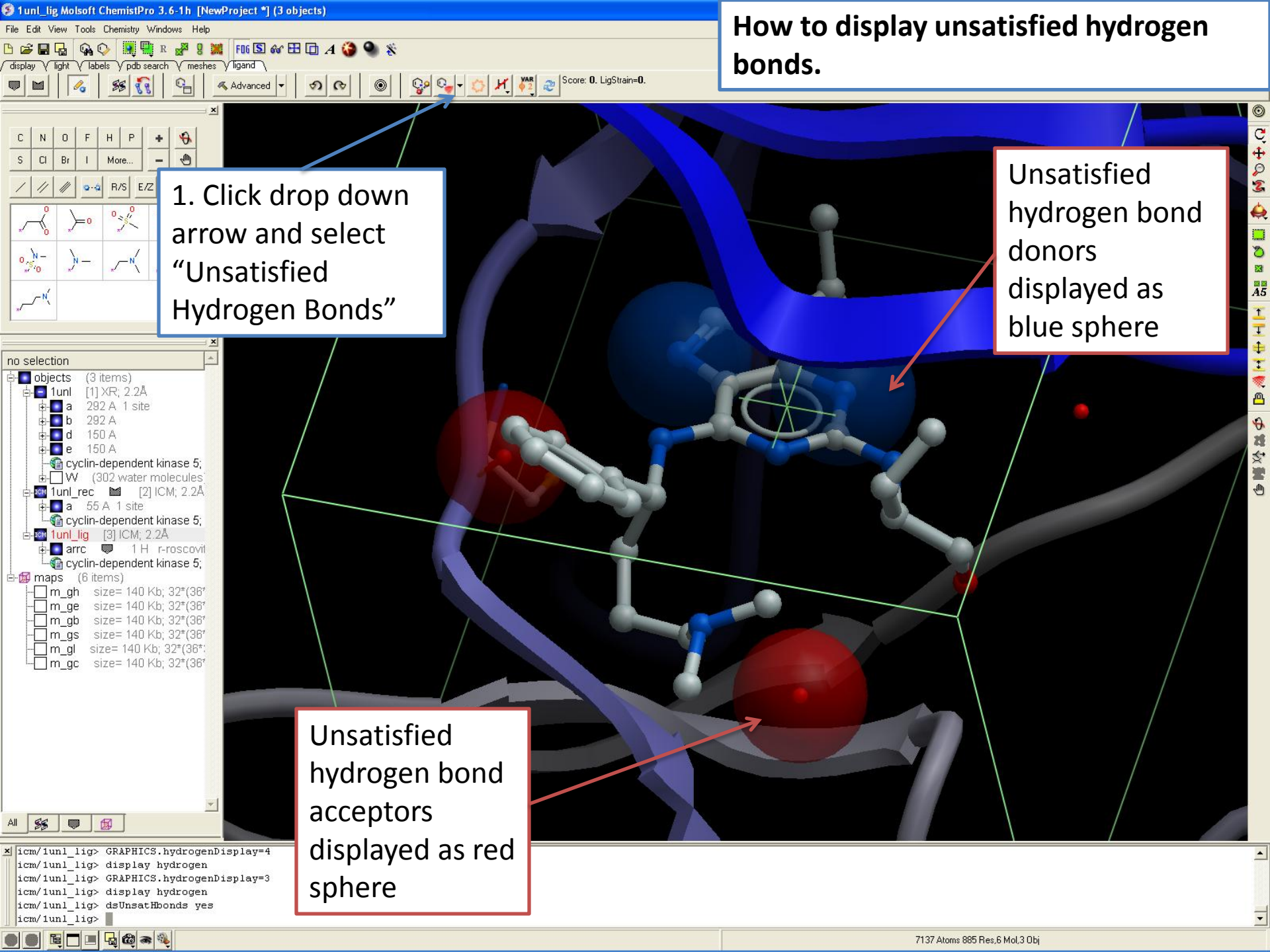


Good ligand-receptor interactions are highlighted by green spheres. Poor energy interactions are displayed as orange-->red stars - red being a major clash and a very poor energy contribution. Each stom is given an energy value relating to its contribution to the total receptor-ligand interaction energy. To view the contributing energy go to Advanced/Preferences/Energy Display

How to display and undisplay hydrogen atoms.



How to display unsatisfied hydrogen bonds.

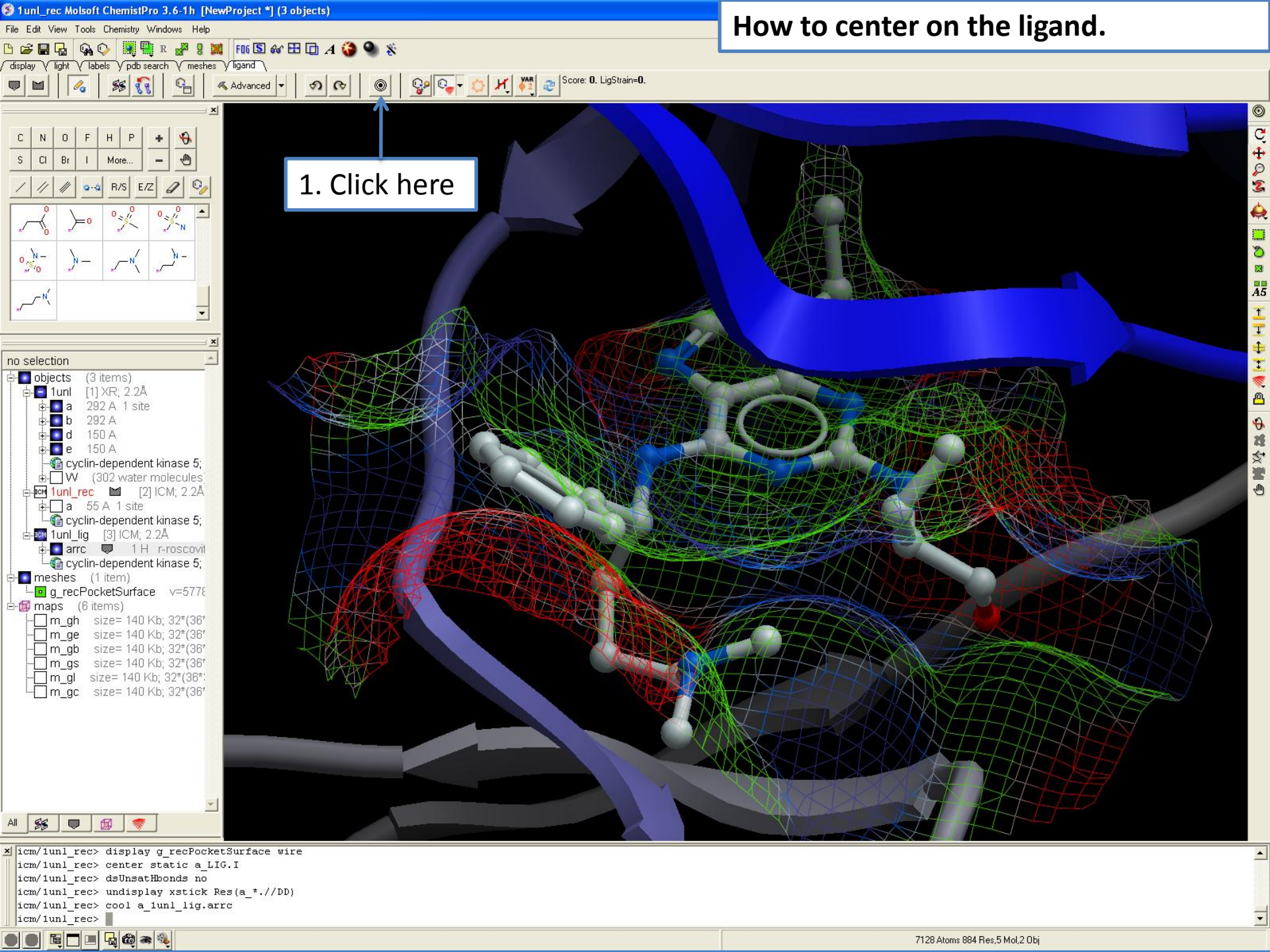


1. Click drop down arrow and select “Unsatisfied Hydrogen Bonds”

Unsatisfied hydrogen bond donors displayed as blue sphere

Unsatisfied hydrogen bond acceptors displayed as red sphere

How to center on the ligand.



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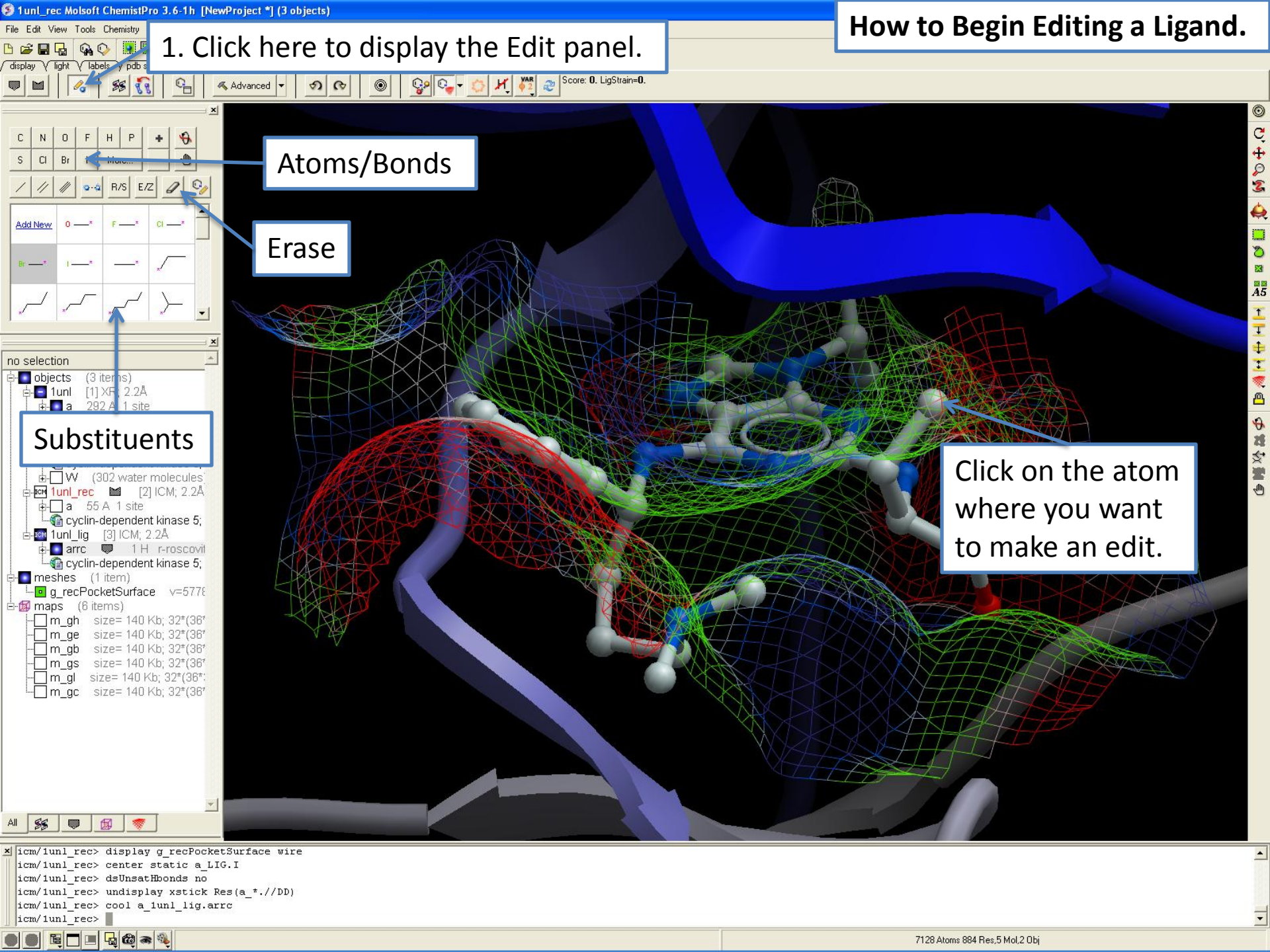
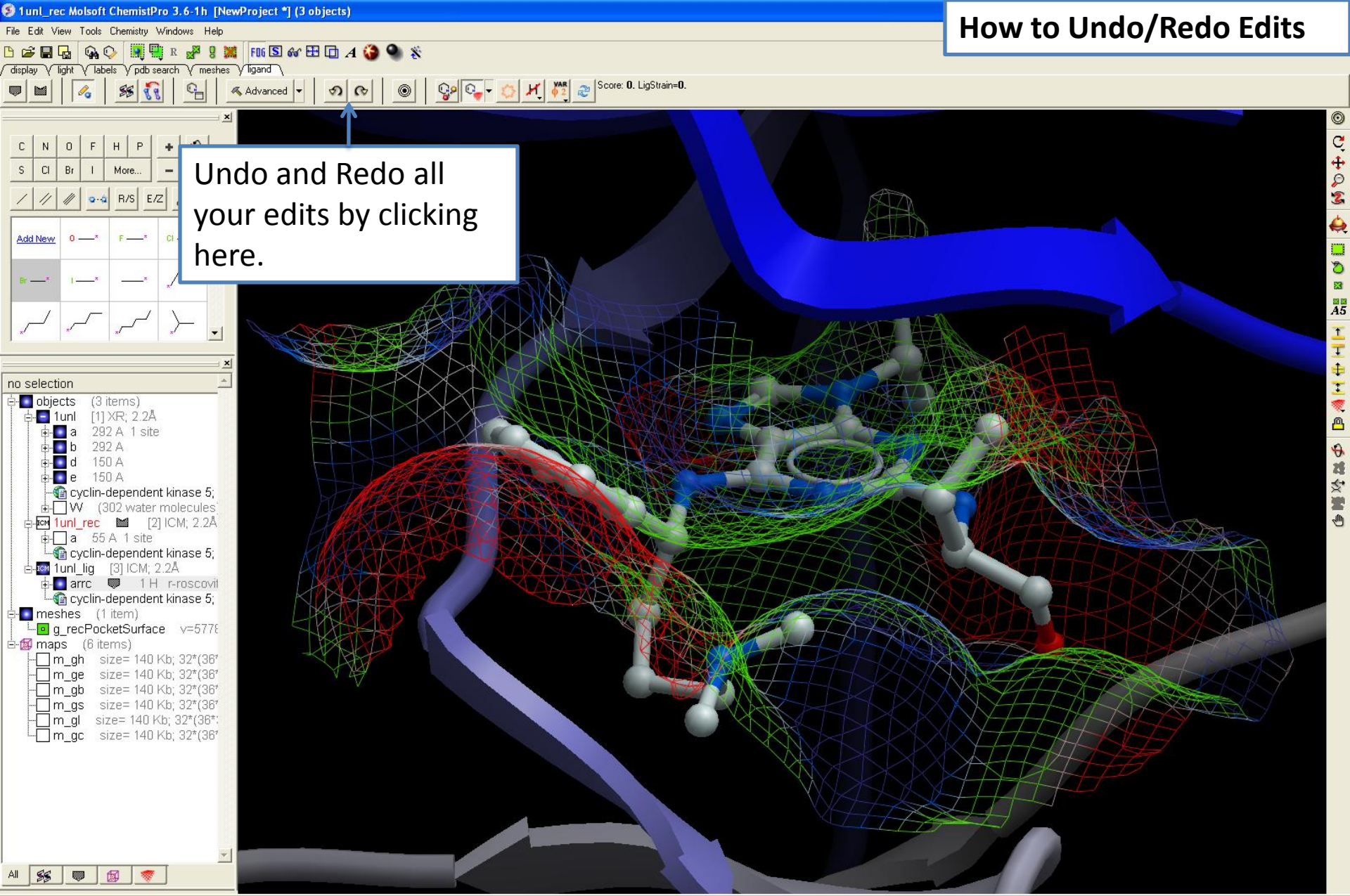
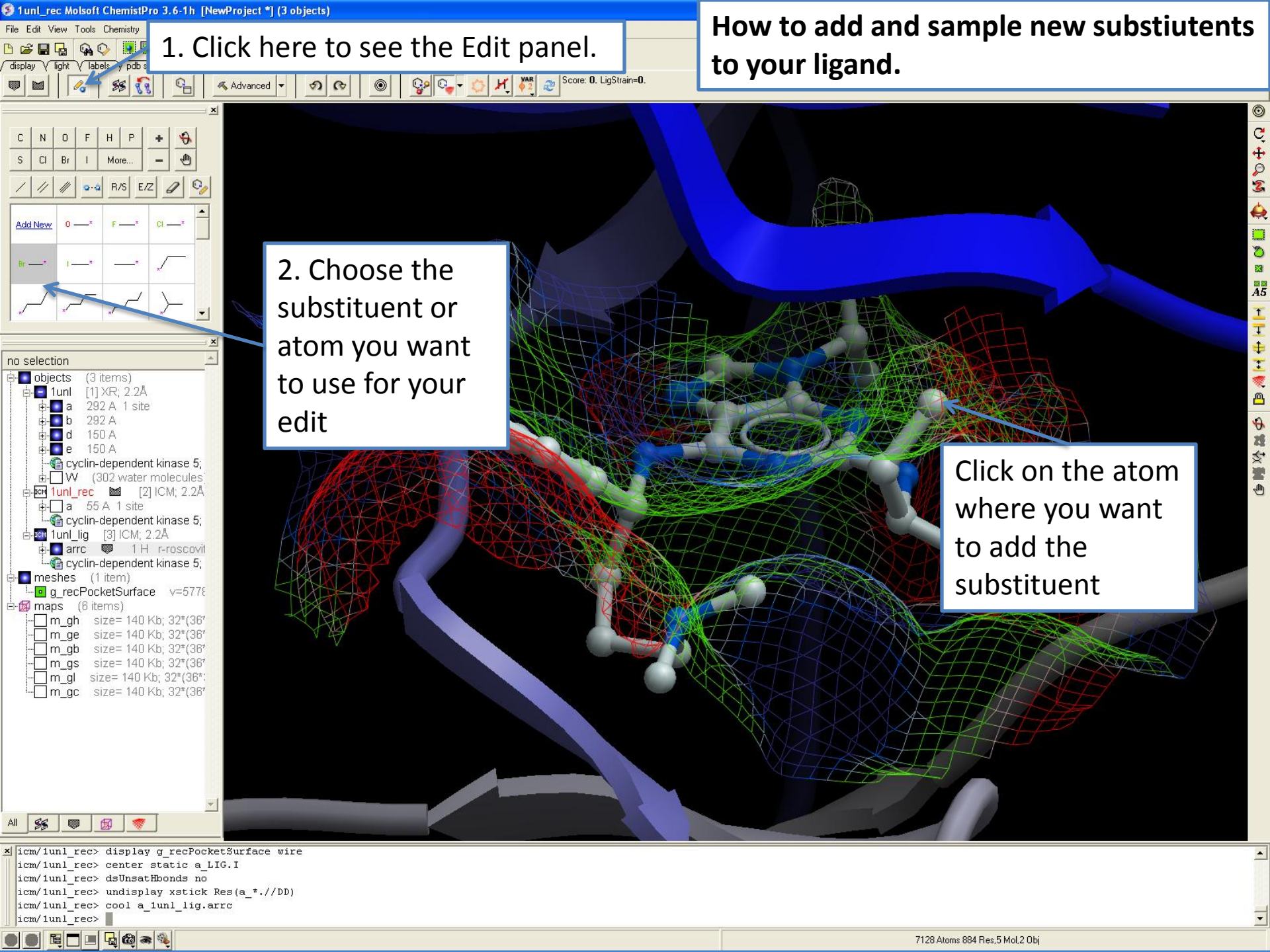
ICM 3D LIGAND EDITOR: EDIT LIGAND

How to Begin Editing a Ligand.

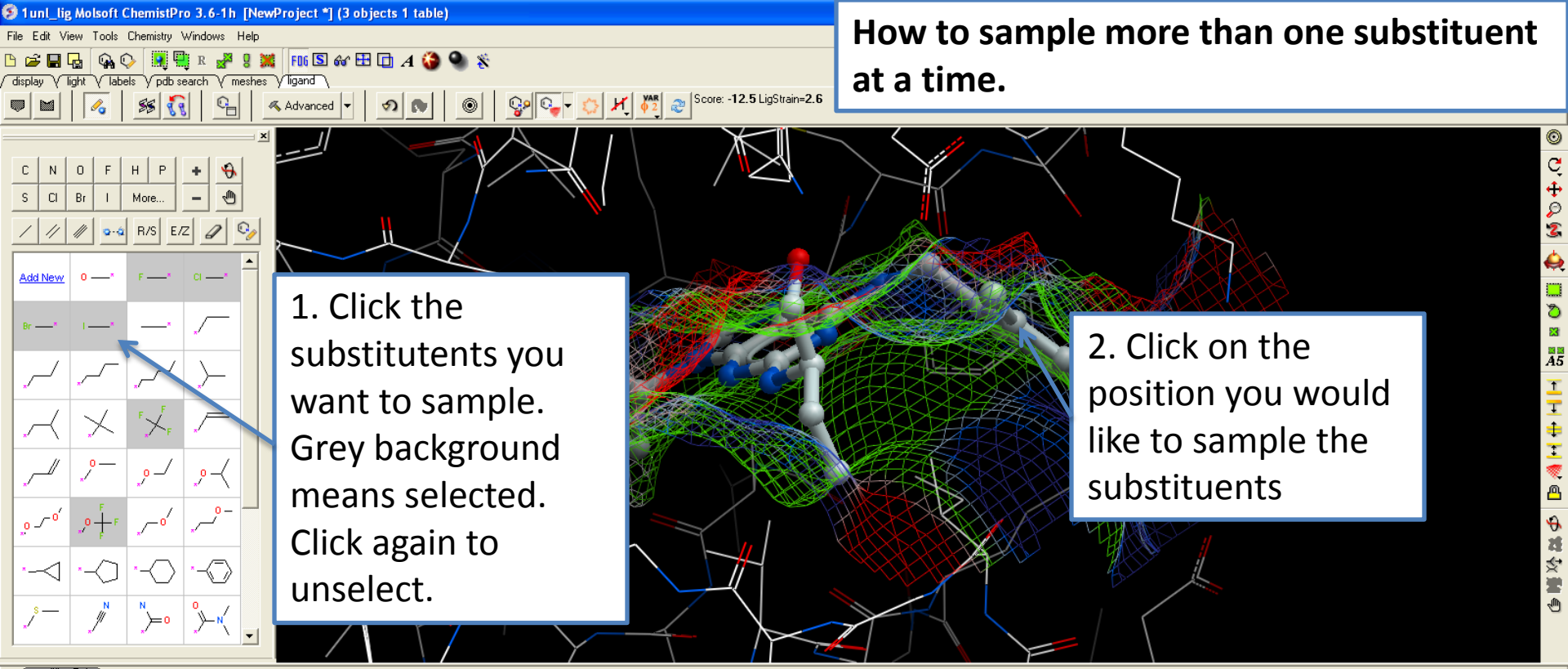


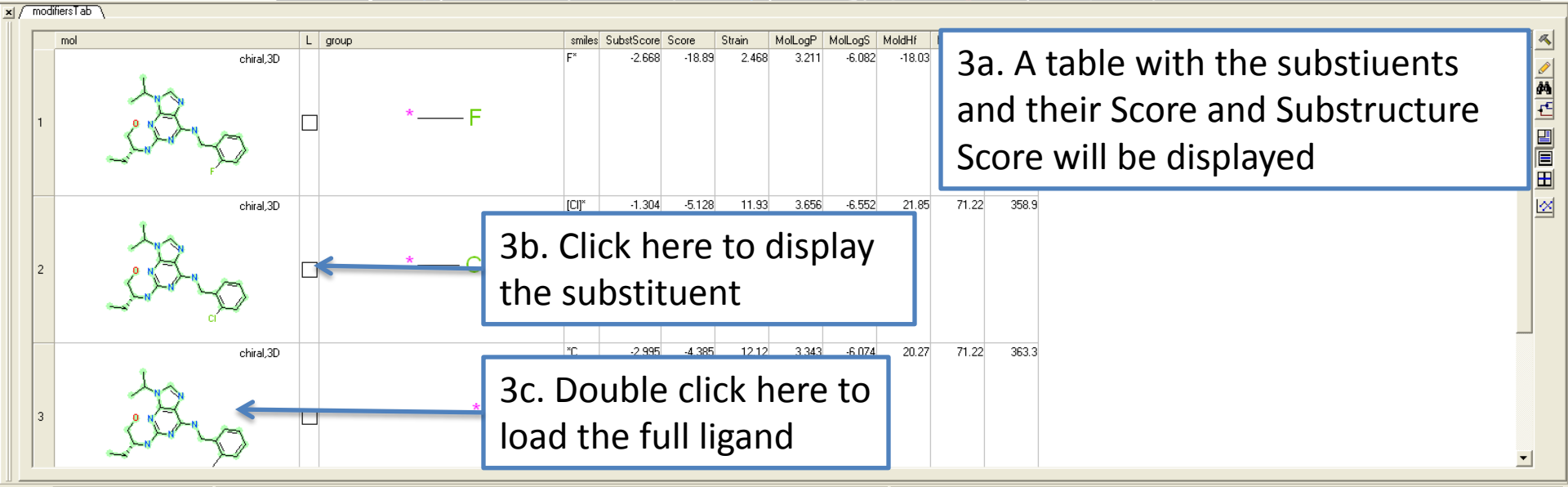
How to Undo/Redo Edits



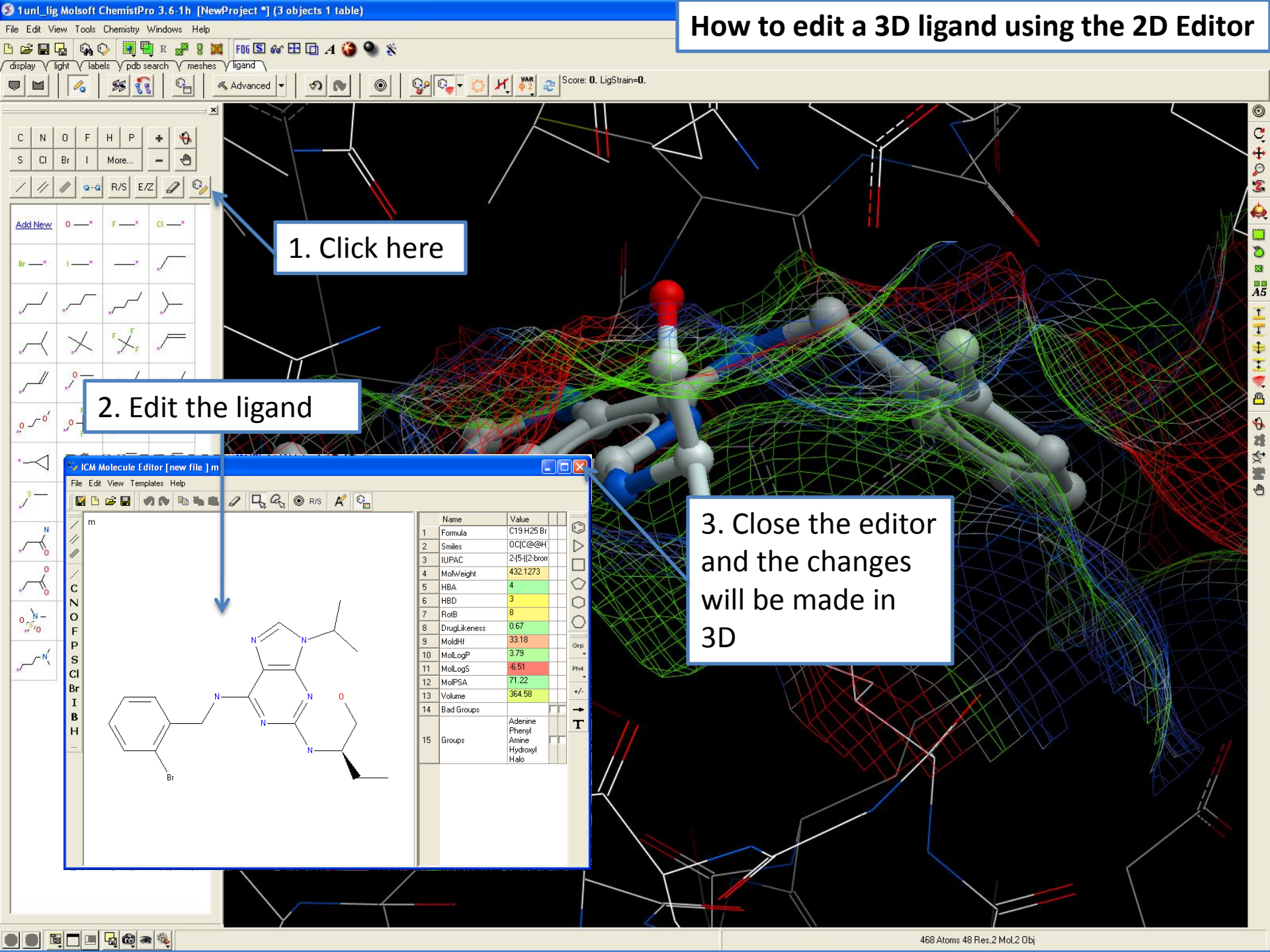

1unl_rec Molsoft ChemistPro 3.6-1h [NewProject *] (3 objects)
File Edit View Tools Chemistry
1. Click here to see the Edit panel.
How to add and sample new substiutents to your ligand.
Advanced
Score: 0. LigStrain=0.
C N O F H P
S Cl Br I More...
R/S E/Z
Add New
2. Choose the substituent or atom you want to use for your edit
Click on the atom where you want to add the substituent
no selection
objects (3 items)
1unl [1] XR; 2.2Å
a 292 A 1 site
b 292 A
d 150 A
e 150 A
cyclin-dependent kinase 5;
W (302 water molecules)
1unl_rec [2] ICM; 2.2Å
a 55 A 1 site
cyclin-dependent kinase 5;
1unl_lig [3] ICM; 2.2Å
arrc 1 H r-roscovi
cyclin-dependent kinase 5;
meshes (1 item)
g_recPocketSurface
maps (6 items)
m_gh size= 140 Kb; 32*(36
m_ge size= 140 Kb; 32*(36
m_gb size= 140 Kb; 32*(36
m_gs size= 140 Kb; 32*(36
m_gl size= 140 Kb; 32*(36
m_gc size= 140 Kb; 32*(36
All
icm/1unl_rec> display g_recPocketSurface wire
icm/1unl_rec> center static a_LIG.I
icm/1unl_rec> dsUnsatHbonds no
icm/1unl_rec> undisplay xstick Res(a_*.//DD)
icm/1unl_rec> cool a_1unl_lig.arrc
icm/1unl_rec>
7128 Atoms 884 Res,5 Mol,2 Obj

How to sample more than one substituent at a time.

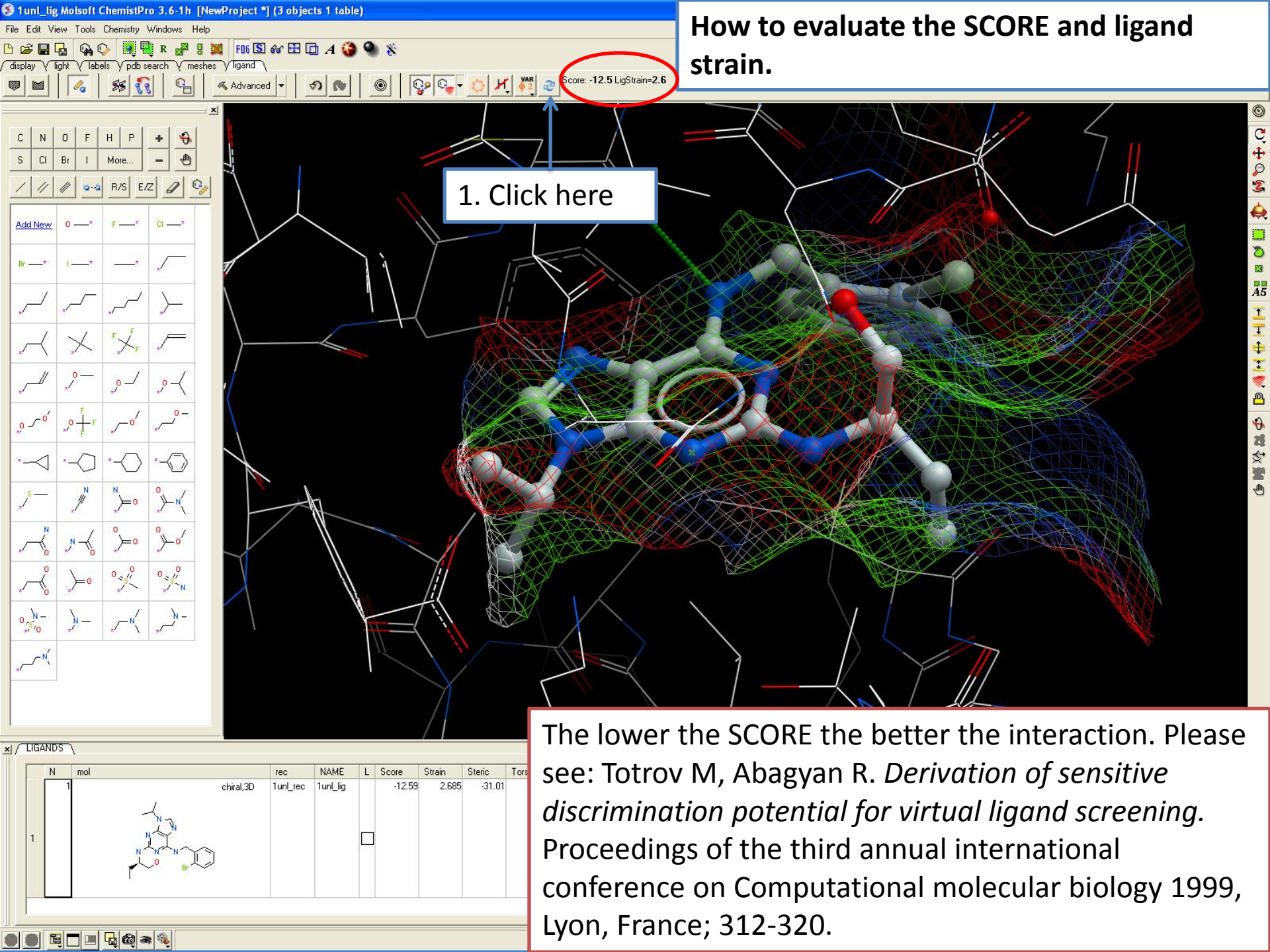




How to edit a 3D ligand using the 2D Editor

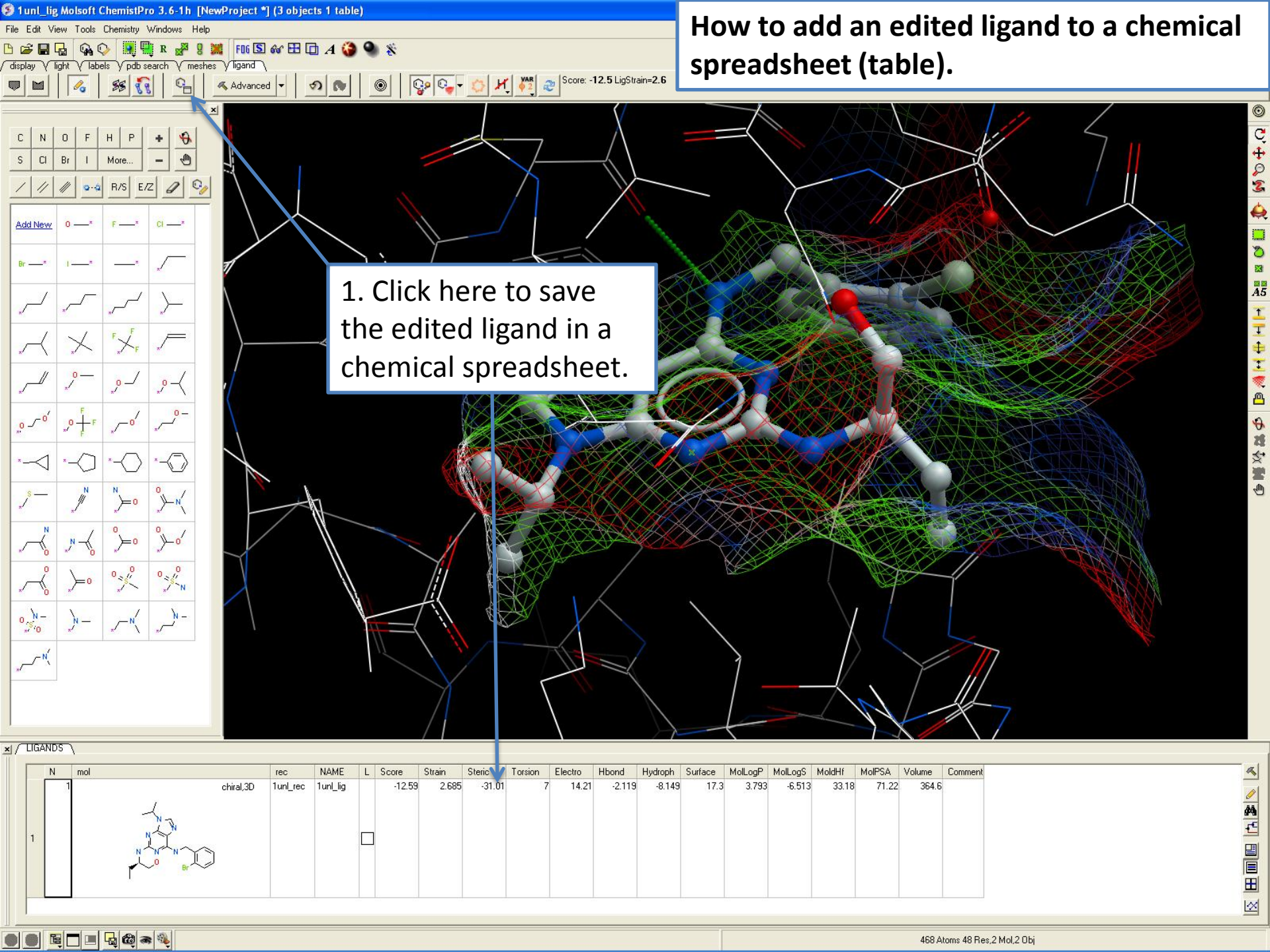


How to evaluate the SCORE and ligand strain.

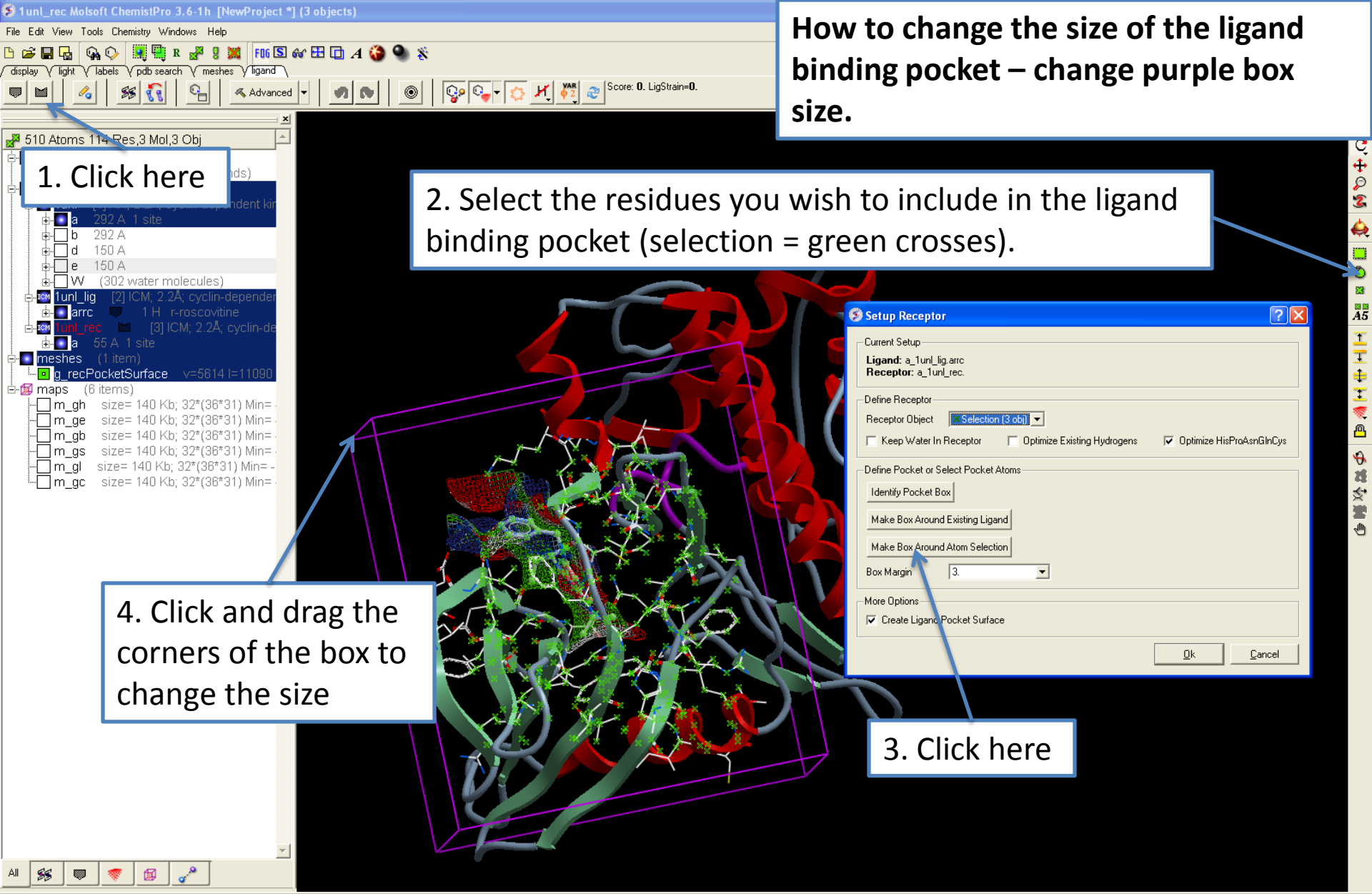


The lower the SCORE the better the interaction. Please see: Totrov M, Abagyan R. *Derivation of sensitive discrimination potential for virtual ligand screening.* Proceedings of the third annual international conference on Computational molecular biology 1999, Lyon, France; 312-320.

How to add an edited ligand to a chemical spreadsheet (table).



How to change the size of the ligand binding pocket – change purple box size.



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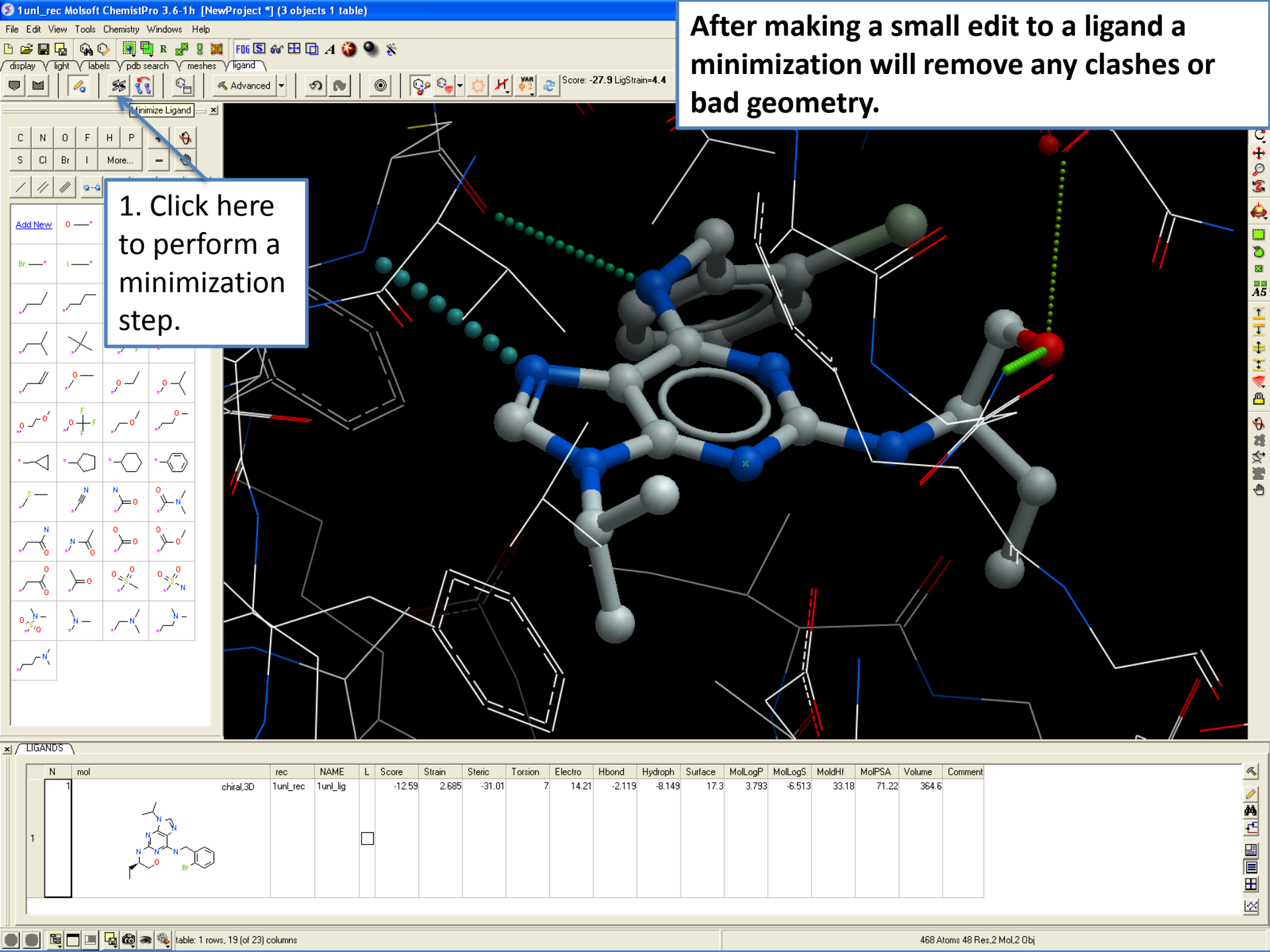
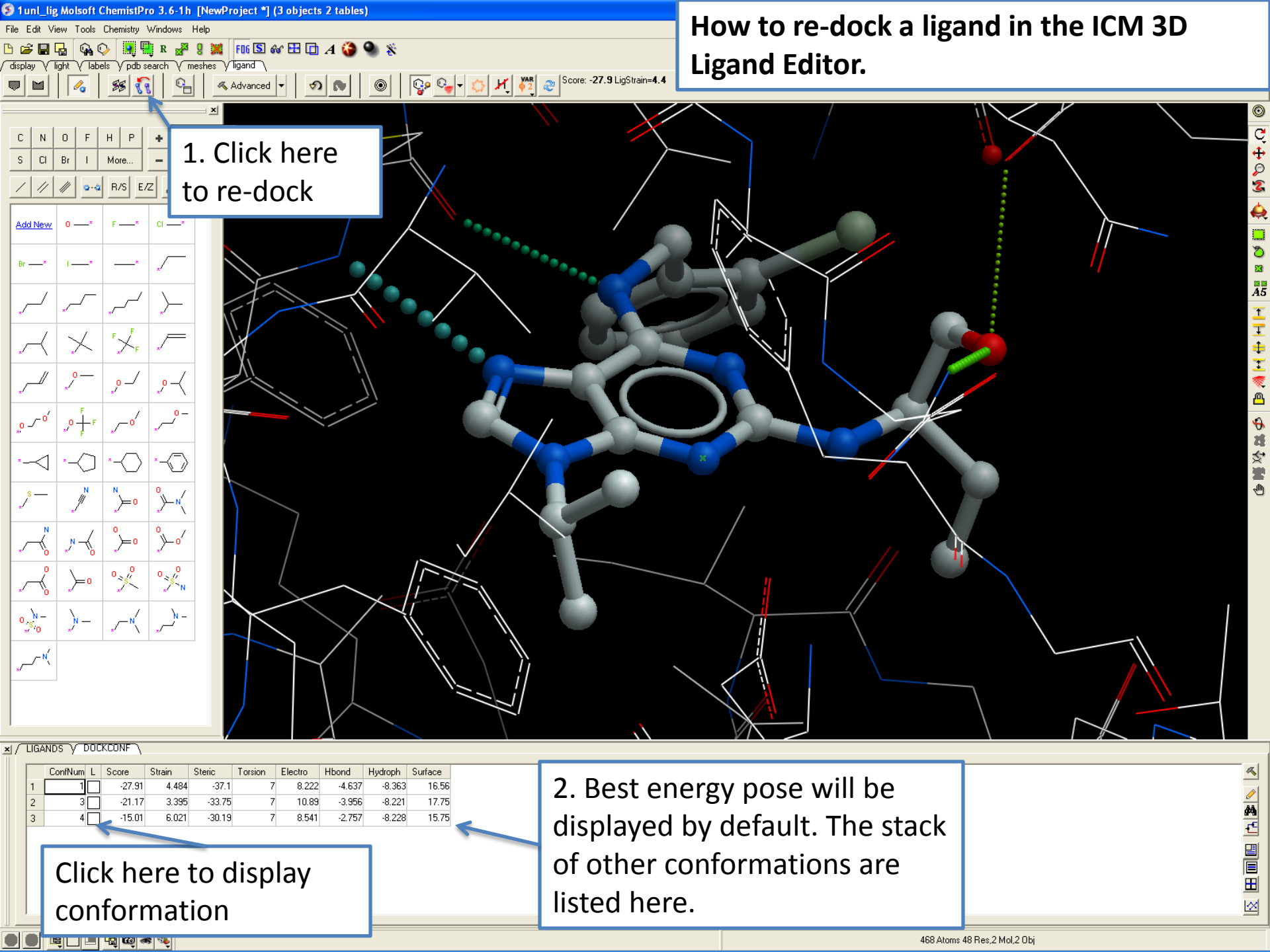
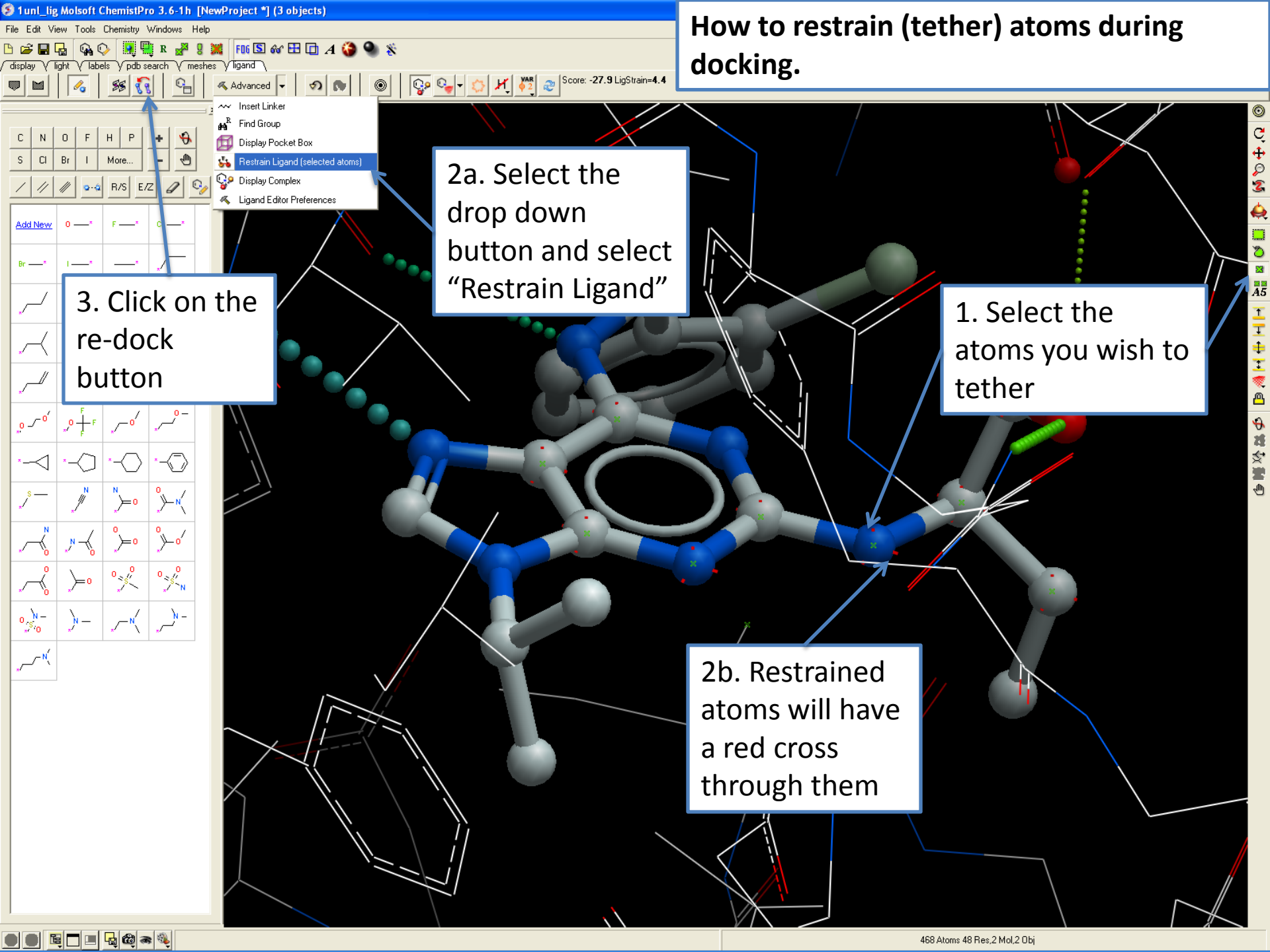
ICM 3D LIGAND EDITOR: MINIMIZATION AND DOCKING

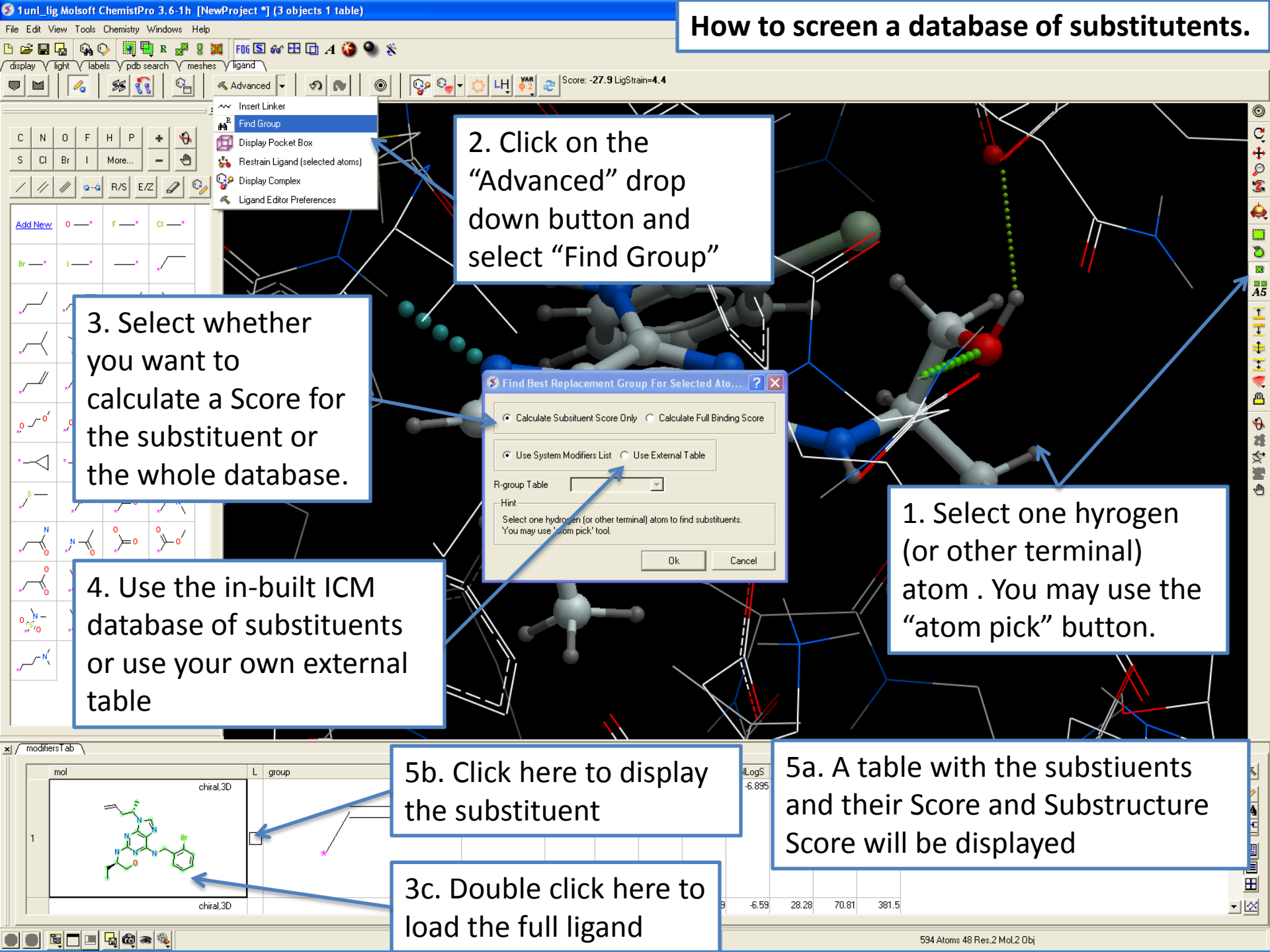

1unl_rec Molsoft ChemistPro 3.6-1h [NewProject *] (3 objects 1 table)
File Edit View Tools Chemistry Windows Help
display light labels pdb search meshes ligand
Advanced
Score: -27.9 LigStrain=4.4
Minimize Ligand
After making a small edit to a ligand a minimization will remove any clashes or bad geometry.
1. Click here to perform a minimization step.
LIGANDS
N mol rec NAME L Score Strain Steric Torsion Electro Hbond Hydroph Surface MolLogP MolLogS MolHf MolPSA Volume Comment
1 chiral,3D 1unl_rec 1unl_lig -12.59 2.685 -31.01 7 14.21 -2.119 -8.149 17.3 3.793 -6.513 33.18 71.22 364.6
table: 1 rows, 19 (of 23) columns
468 Atoms 48 Res,2 Mol,2 Obj

How to re-dock a ligand in the ICM 3D Ligand Editor.

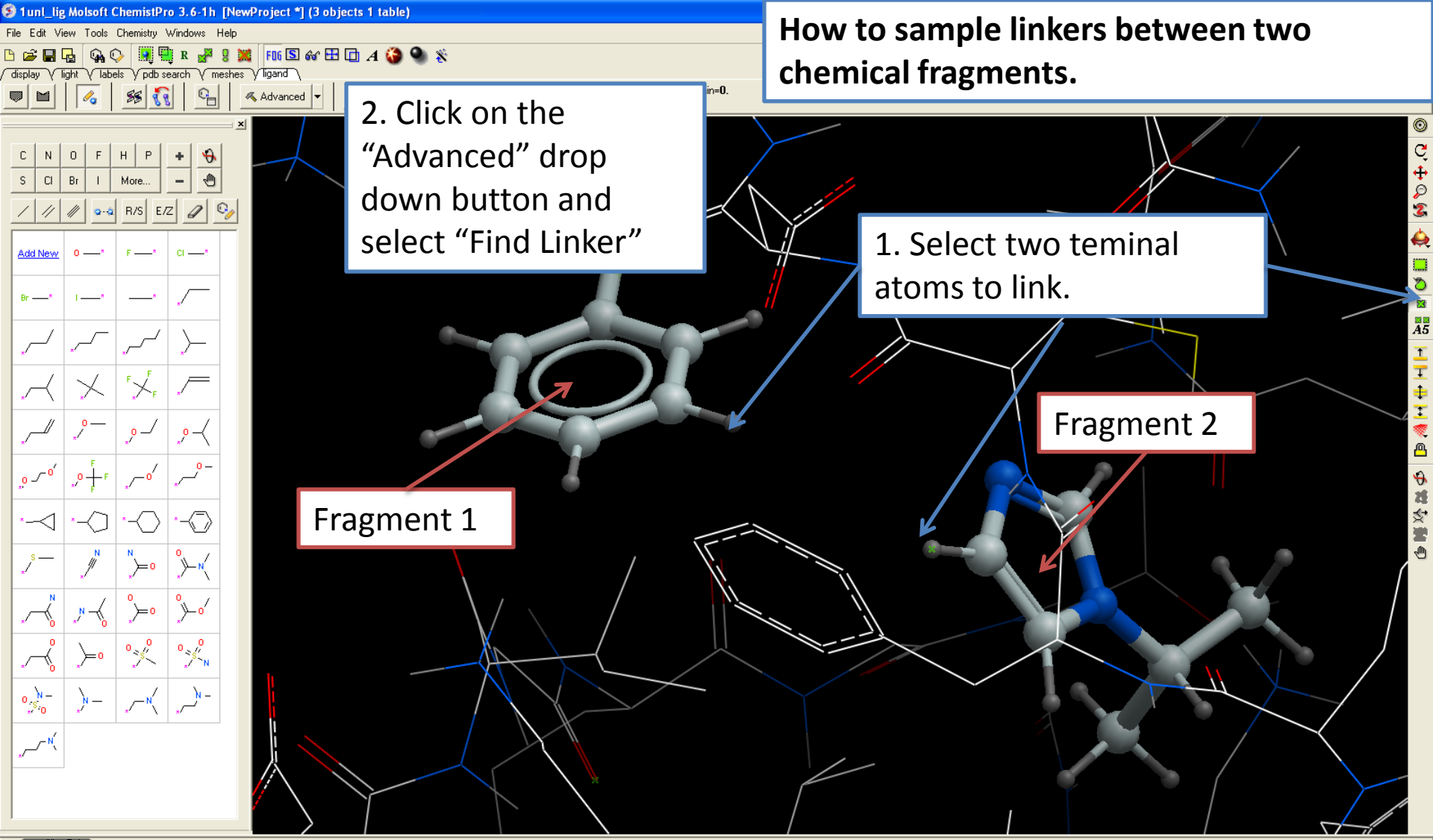



How to restrain (tether) atoms during docking.
1unl_lig Molsoft ChemistPro 3.6-1h [NewProject *] (3 objects)
File Edit View Tools Chemistry Windows Help
display light labels pdb search meshes ligand
Advanced
Score: -27.9 LigStrain=4.4
Insert Linker
Find Group
Display Pocket Box
Restrain Ligand (selected atoms)
Display Complex
Ligand Editor Preferences
2a. Select the drop down button and select “Restrain Ligand”
3. Click on the re-dock button
1. Select the atoms you wish to tether
2b. Restrained atoms will have a red cross through them
468 Atoms 48 Res,2 Mol,2 Obj

How to screen a database of substitutents.



How to sample linkers between two chemical fragments.



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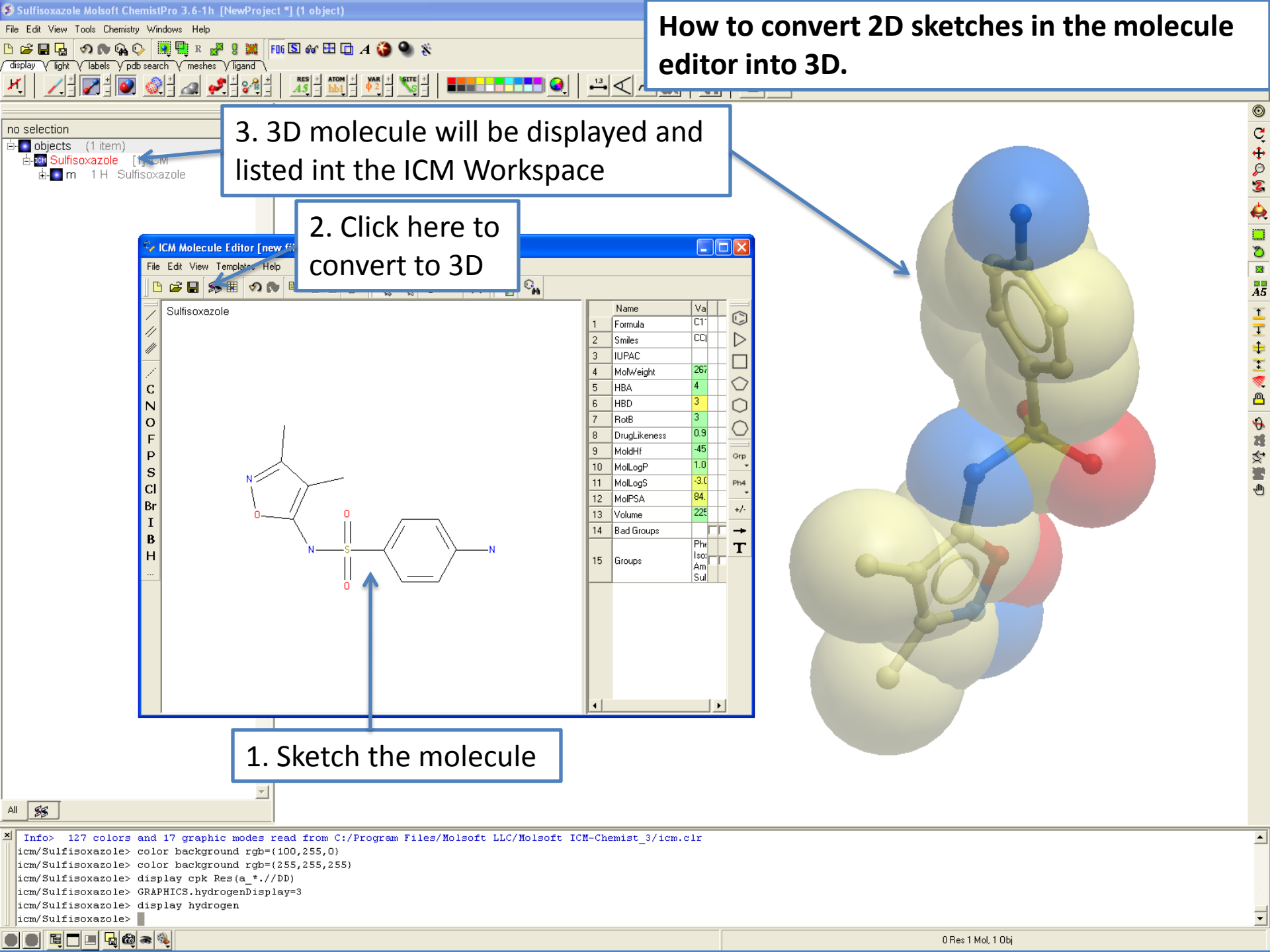
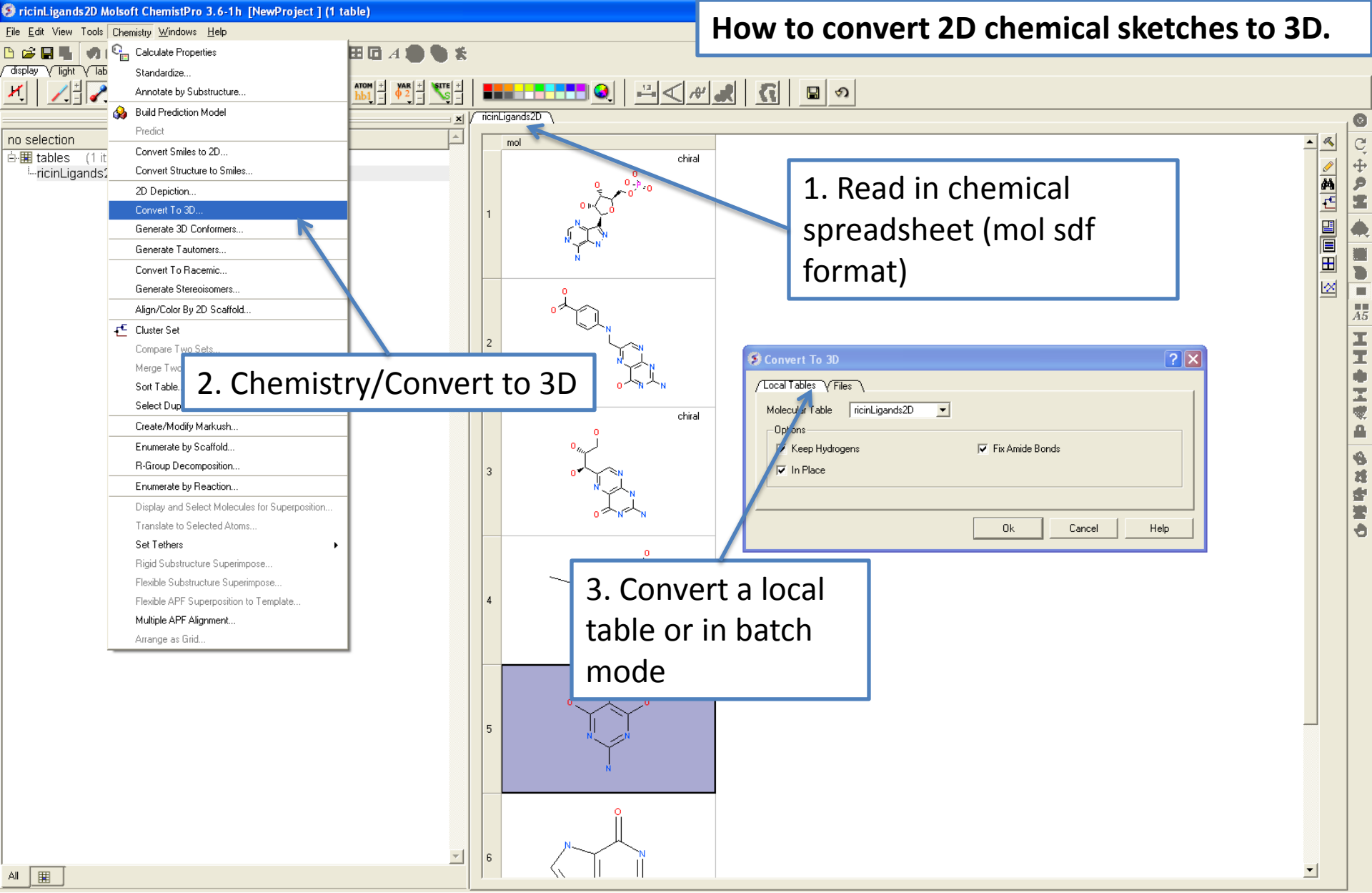
ICM 3D LIGAND EDITOR: CONVERT CHEMICALS TO 3D

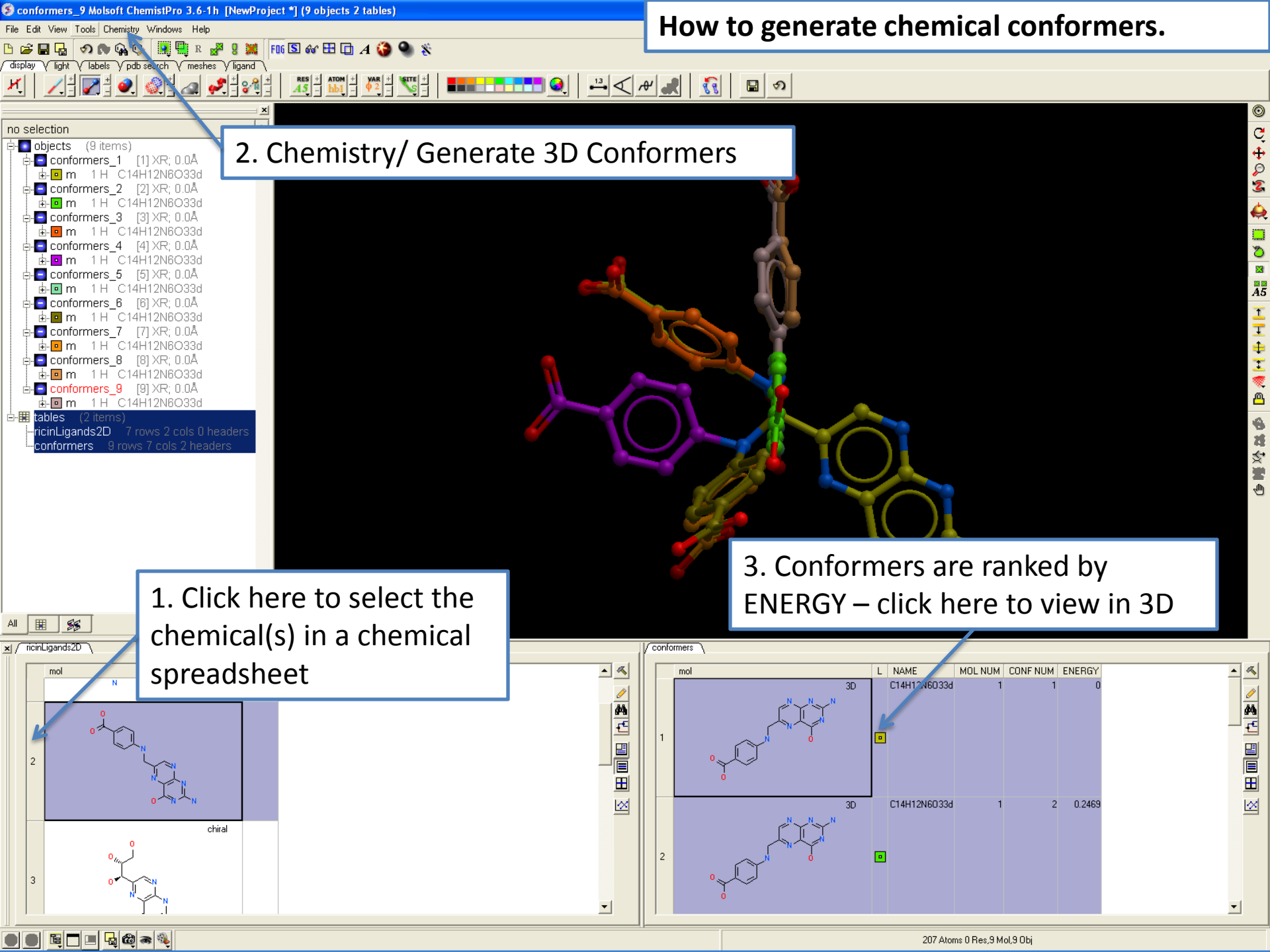
How to convert 2D sketches in the molecule editor into 3D.



How to convert 2D chemical sketches to 3D.



How to generate chemical conformers.



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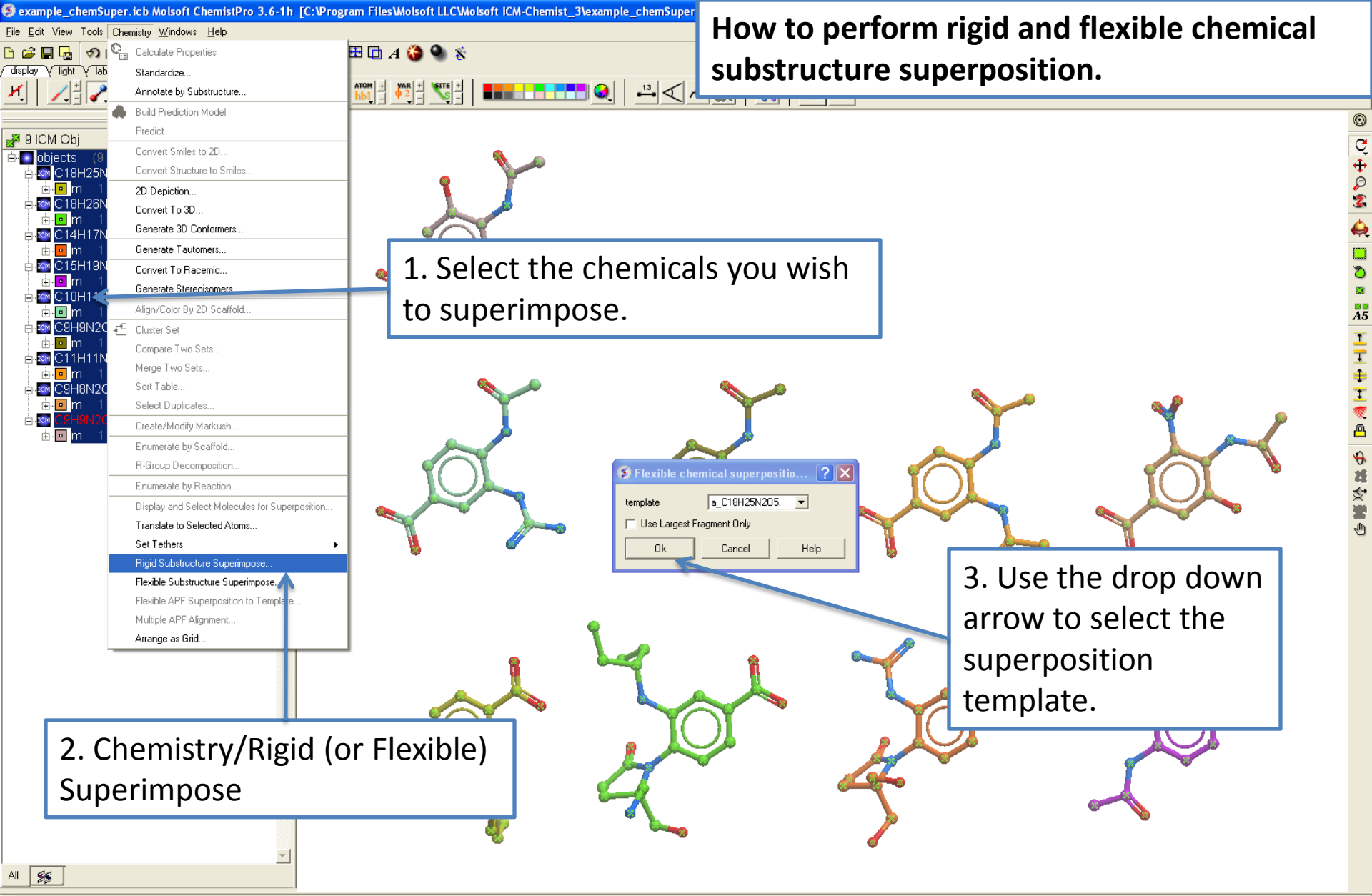
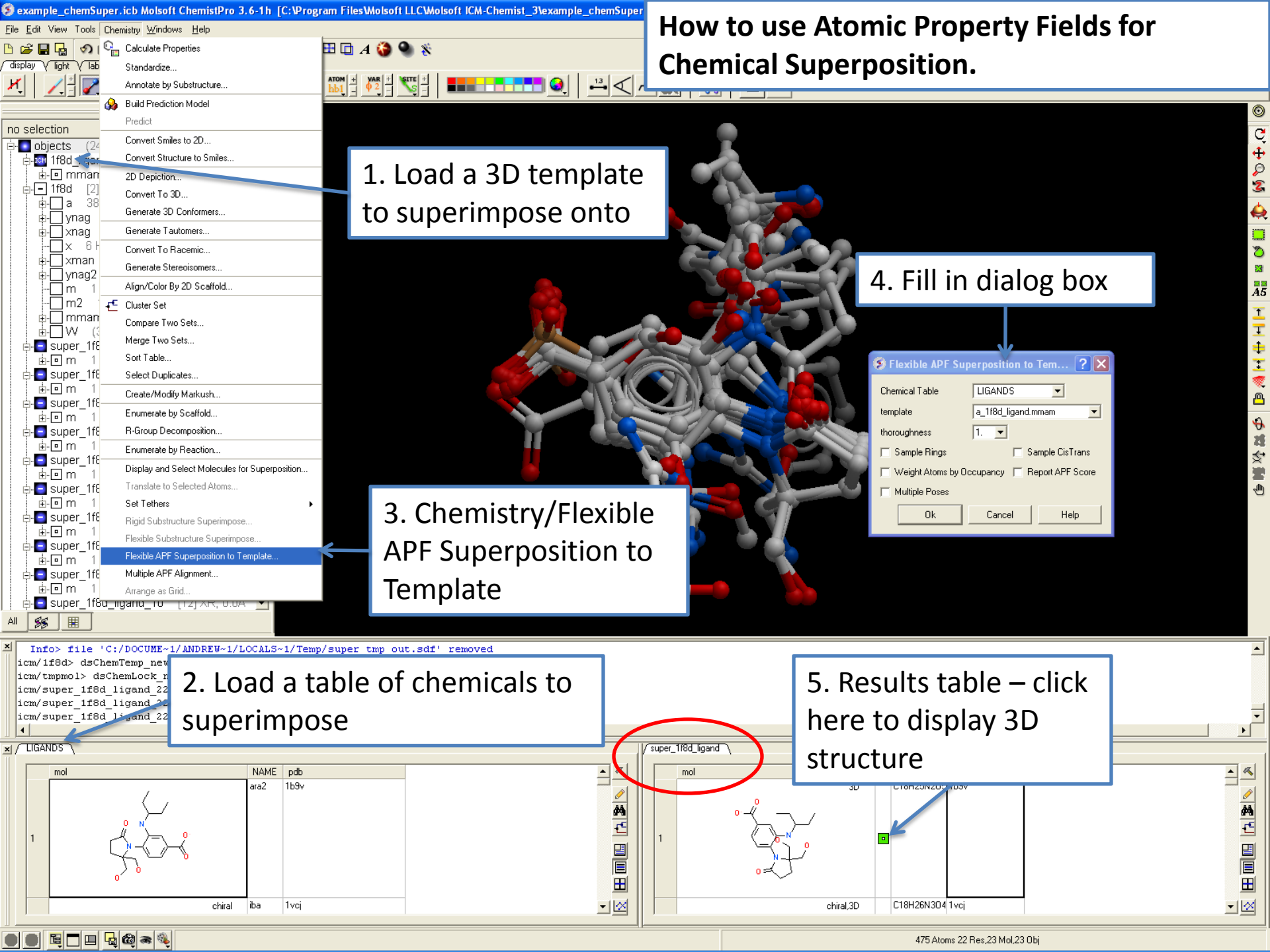
ICM 3D LIGAND EDITOR: CHEMICAL SUPERPOSITION

How to perform rigid and flexible chemical substructure superposition.



How to use Atomic Property Fields for Chemical Superposition.



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ICM 3D LIGAND EDITOR: QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP (QSAR)

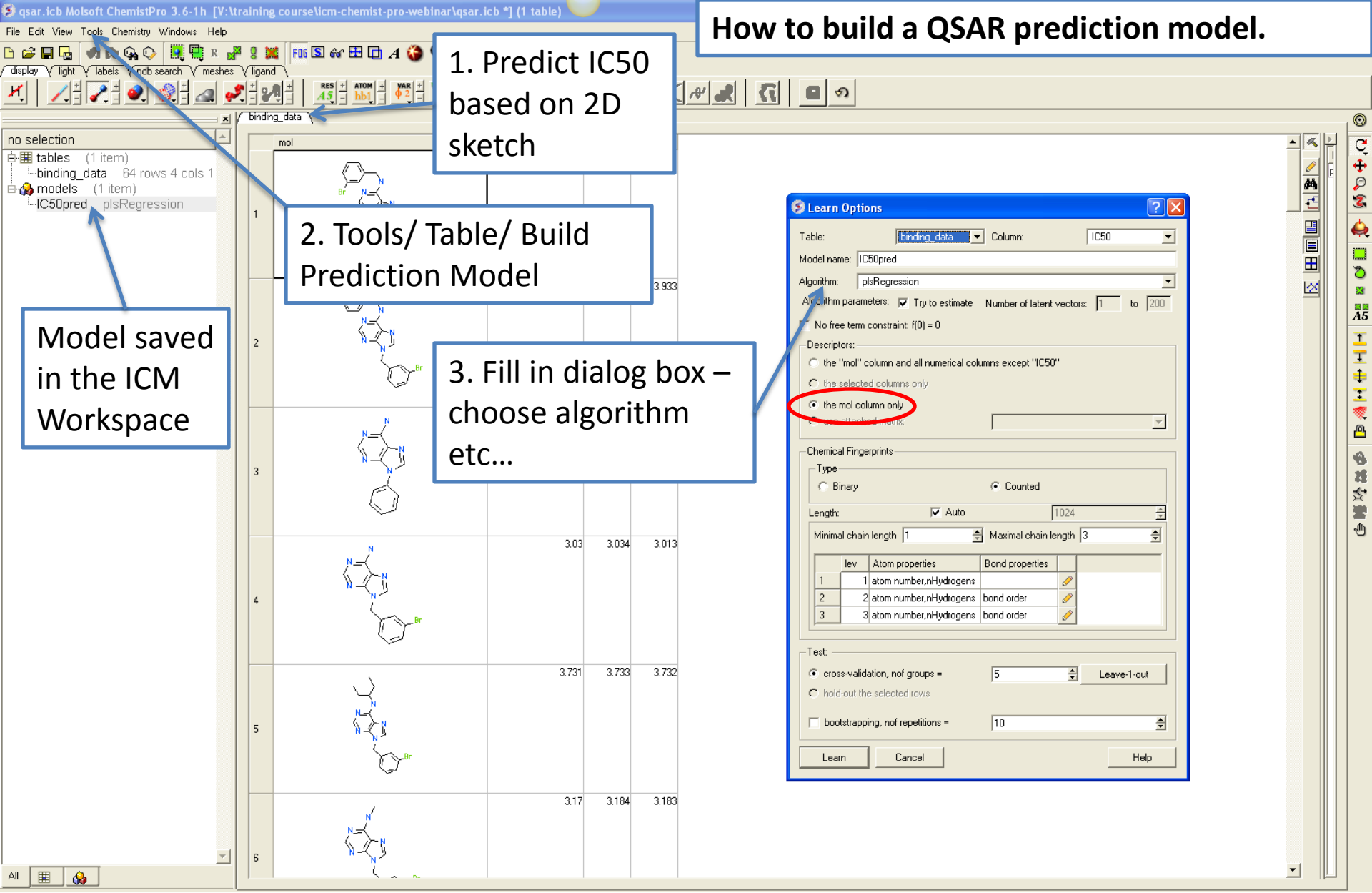
How to build a QSAR prediction model.

1. Predict IC50 based on 2D sketch

2. Tools/ Table/ Build Prediction Model

Model saved in the ICM Workspace

3. Fill in dialog box – choose algorithm etc…



How to apply a QSAR prediction model.