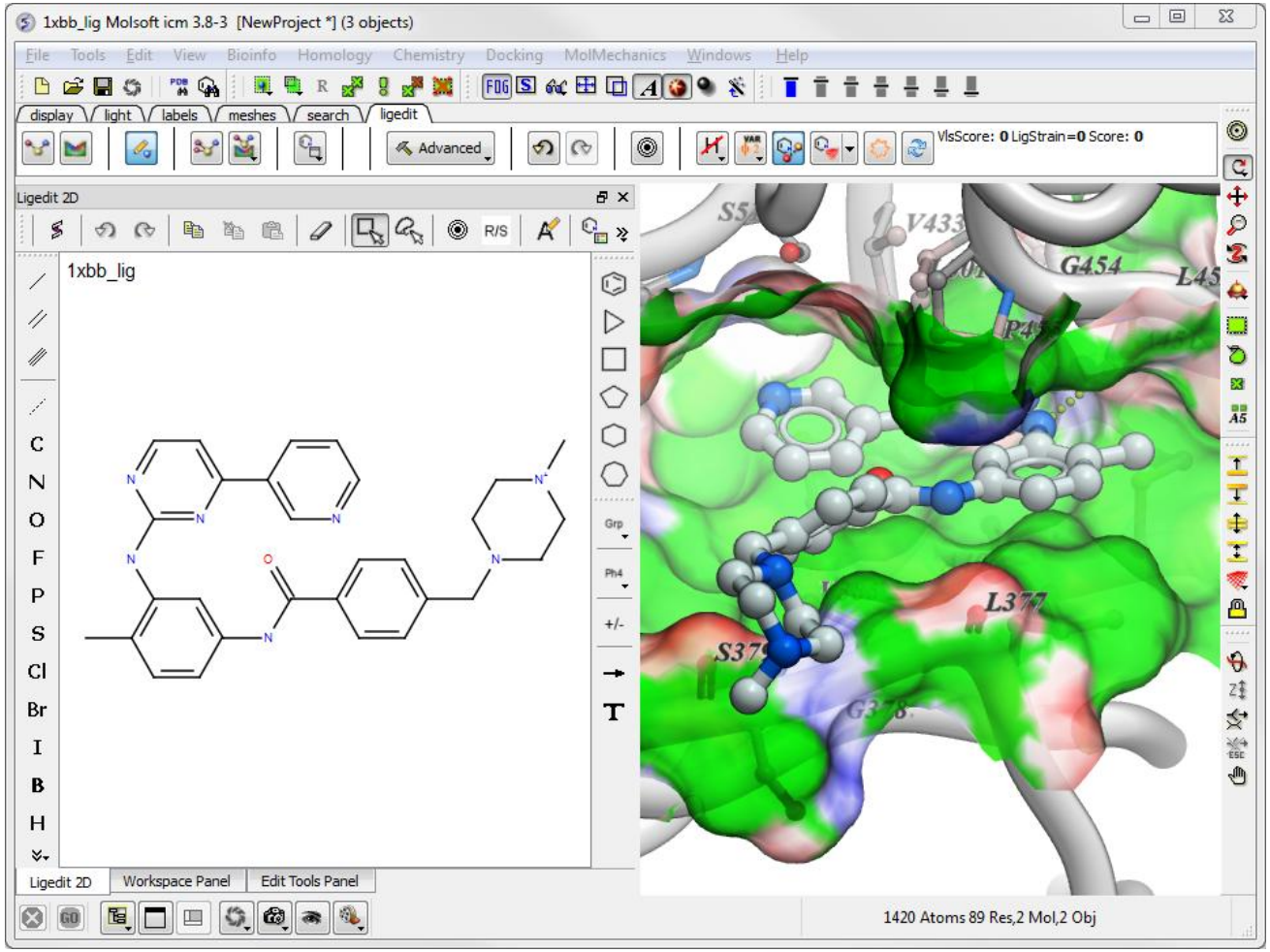
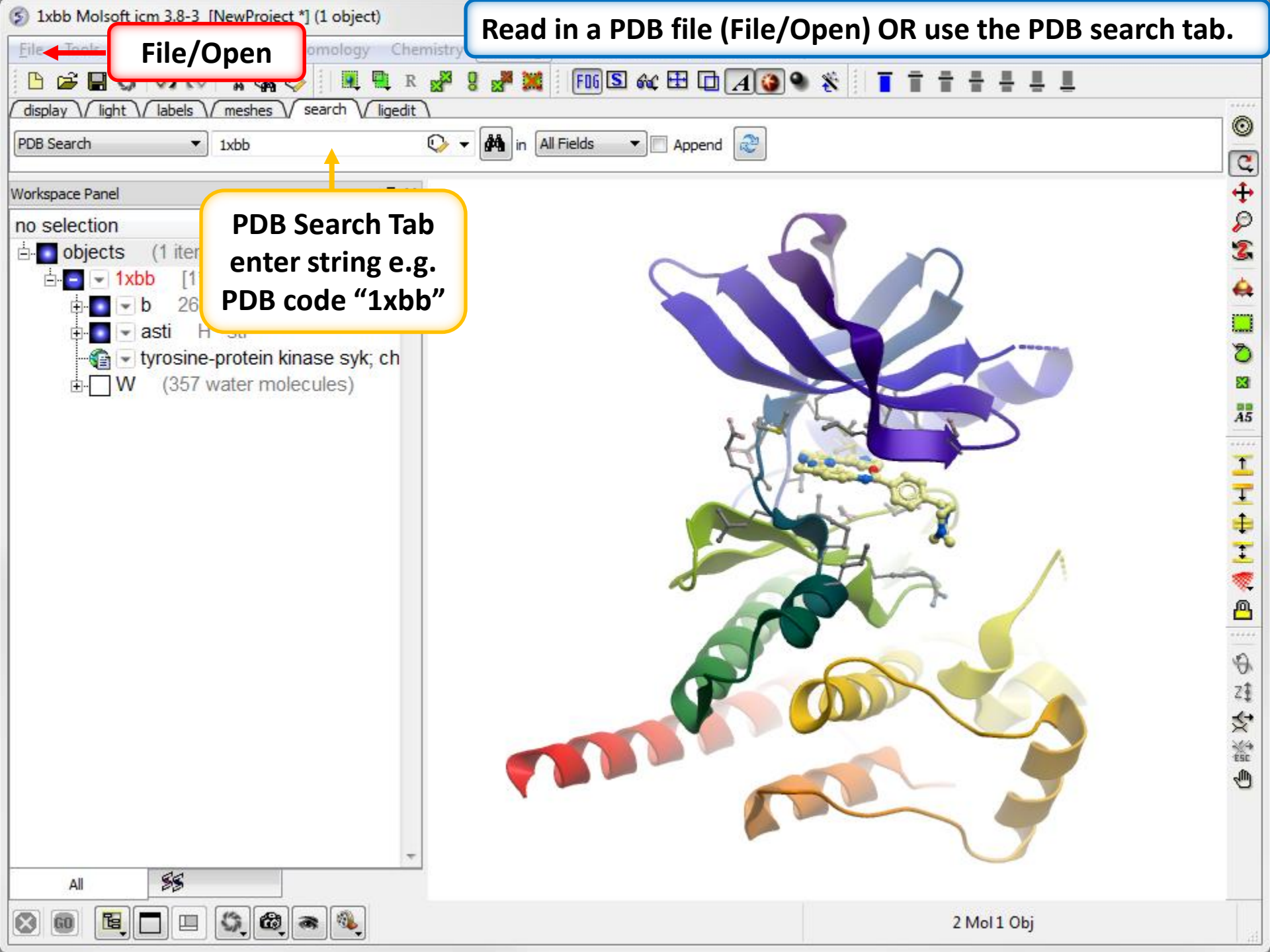
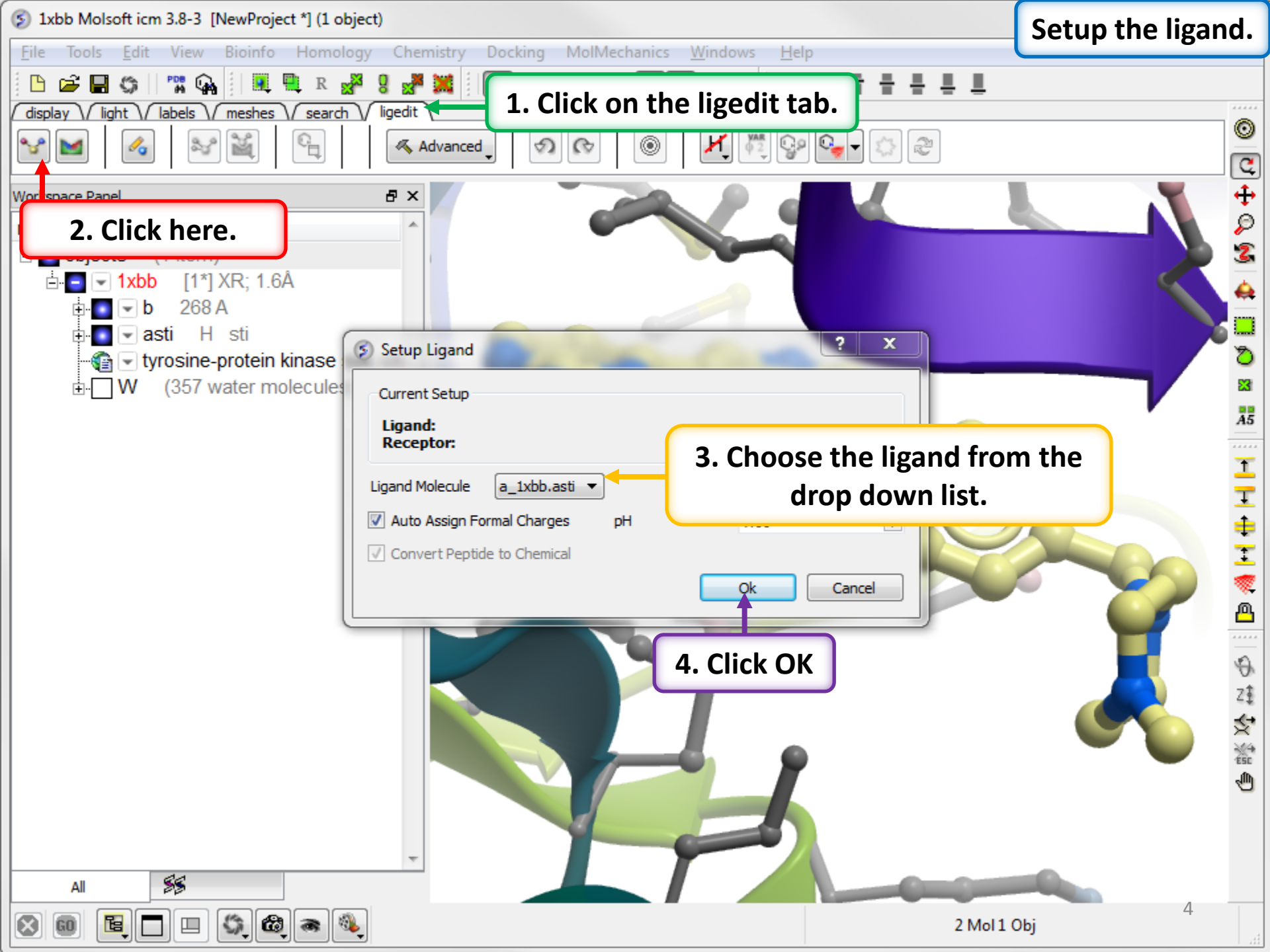
ICM Interactive Ligand Editor Getting Started Guide

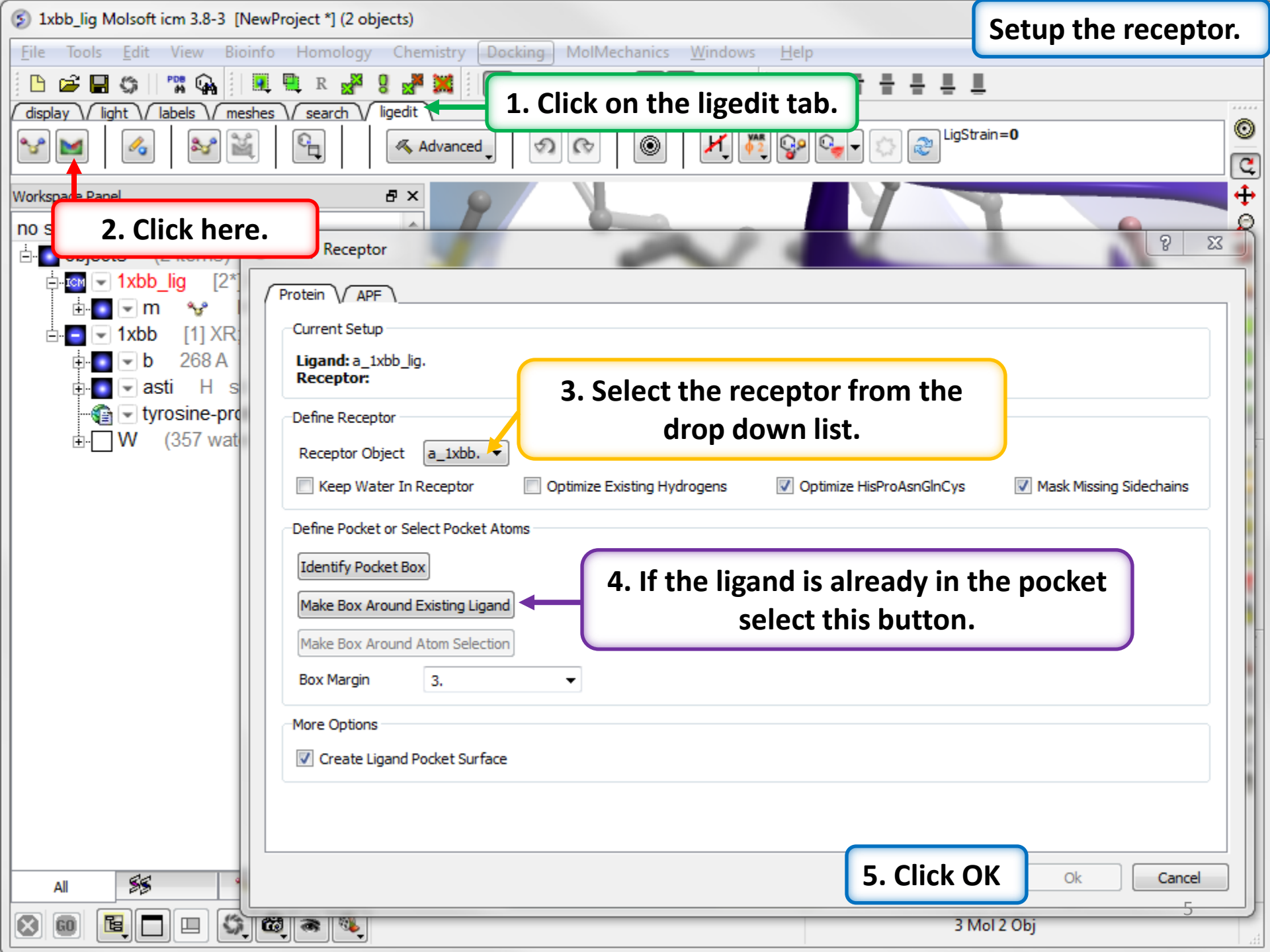


molsoft
molecules *in silico*

Reading in a PDB file and Setting up the Ligand and Receptor

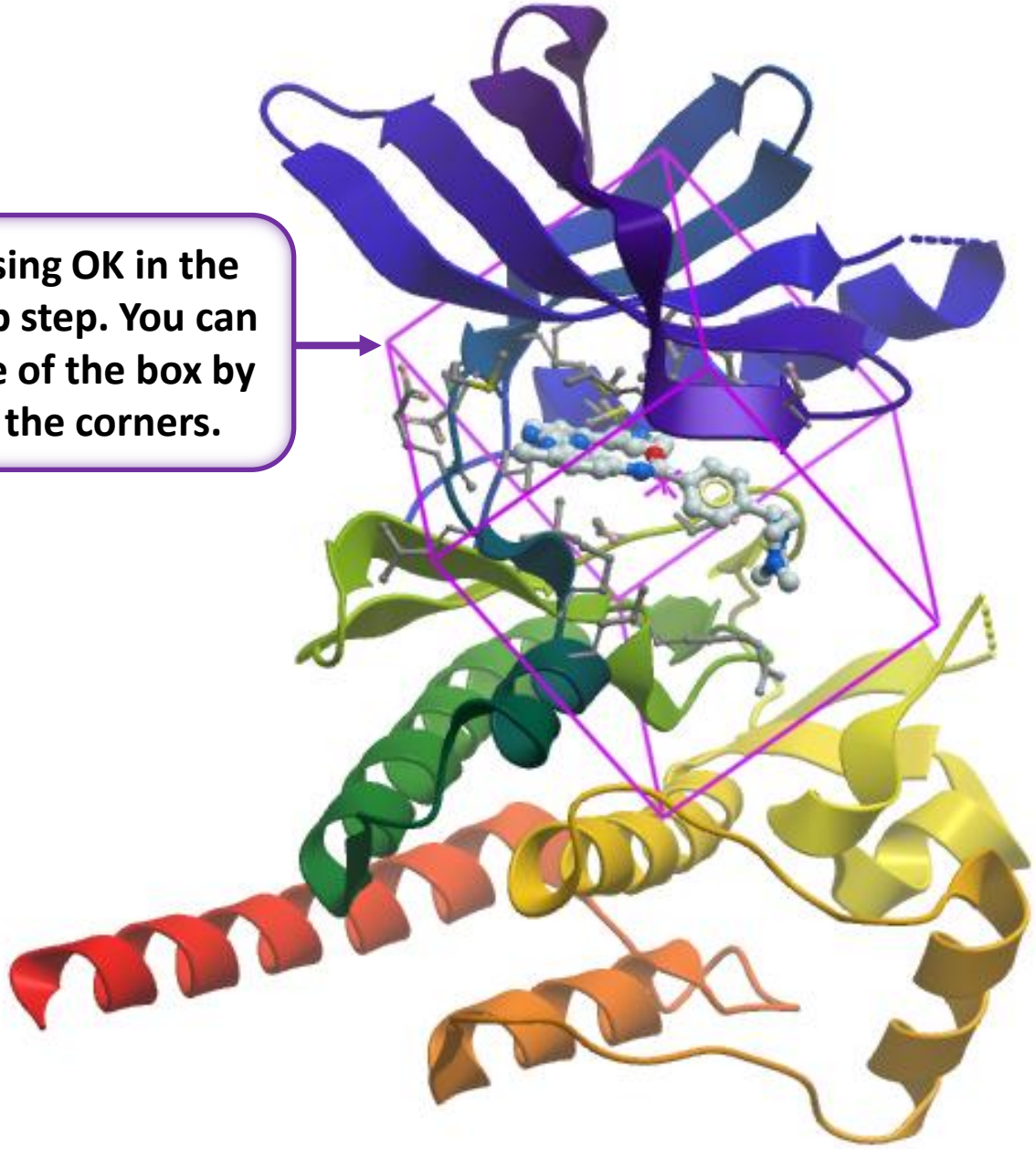

1xbb Molsoft icm 3.8-3 [NewProject *] (1 object)
File/Open
Read in a PDB file (File/Open) OR use the PDB search tab.
display
light
labels
meshes
search
ligedit
PDB Search
1xbb
in
All Fields
Append
Workspace Panel
PDB Search Tab
enter string e.g.
PDB code “1xbb”
no selection
objects
1xbb
b
asti
tyrosine-protein kinase syk; ch
W
(357 water molecules)
All
2 Mol 1 Obj

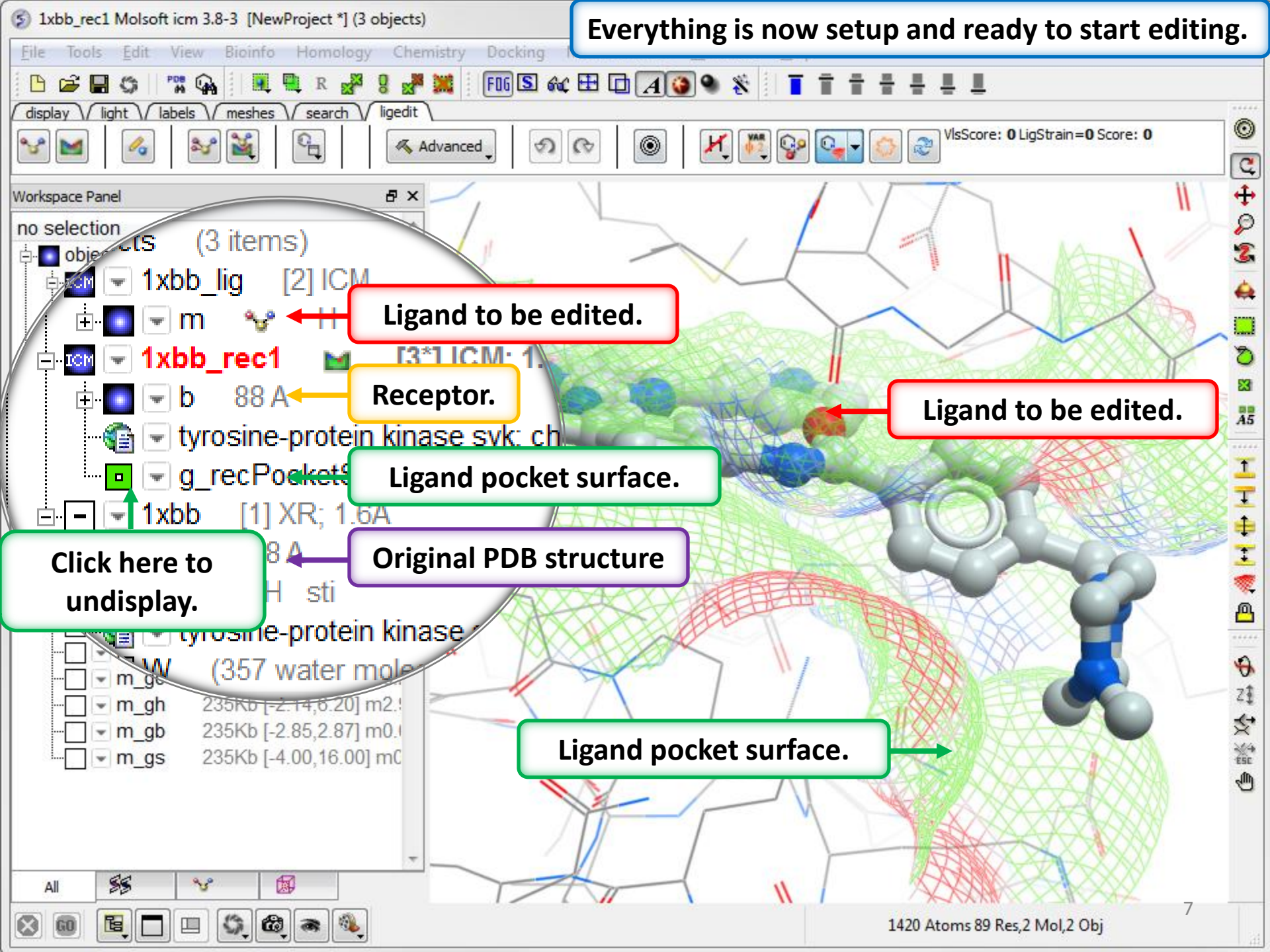

Setup the ligand.
1xbb Molsoft icm 3.8-3 [NewProject *] (1 object)
File Tools Edit View Bioinfo Homology Chemistry Docking MolMechanics Windows Help
display light labels meshes search ligedit
1. Click on the ligedit tab.
Advanced
2. Click here.
Workspace Panel
1xbb [1*] XR; 1.6Å
b 268 A
asti H sti
tyrosine-protein kinase
W (357 water molecules
Setup Ligand
Current Setup
Ligand:
Receptor:
Ligand Molecule
a_1xbb.asti
3. Choose the ligand from the drop down list.
Auto Assign Formal Charges
pH
Convert Peptide to Chemical
Ok
Cancel
4. Click OK
All
2 Mol 1 Obj


Setup the receptor.
1xbb_lig Molsoft icm 3.8-3 [NewProject *] (2 objects)
File Tools Edit View Bioinfo Homology Chemistry Docking MolMechanics Windows Help
display light labels meshes search ligedit
1. Click on the ligedit tab.
Advanced
LigStrain=0
2. Click here.
Workspace Panel
1xbb_lig
m
1xbb
b
asti
tyrosine-pro
W
Receptor
Protein APF
Current Setup
Ligand: a_1xbb_lig.
Receptor:
3. Select the receptor from the drop down list.
Define Receptor
Receptor Object
a_1xbb.
Keep Water In Receptor
Optimize Existing Hydrogens
Optimize HisProAsnGlnCys
Mask Missing Sidechains
Define Pocket or Select Pocket Atoms
Identify Pocket Box
Make Box Around Existing Ligand
Make Box Around Atom Selection
Box Margin
3.
4. If the ligand is already in the pocket select this button.
More Options
Create Ligand Pocket Surface
5. Click OK
Ok
Cancel
All
3 Mol 2 Obj
5

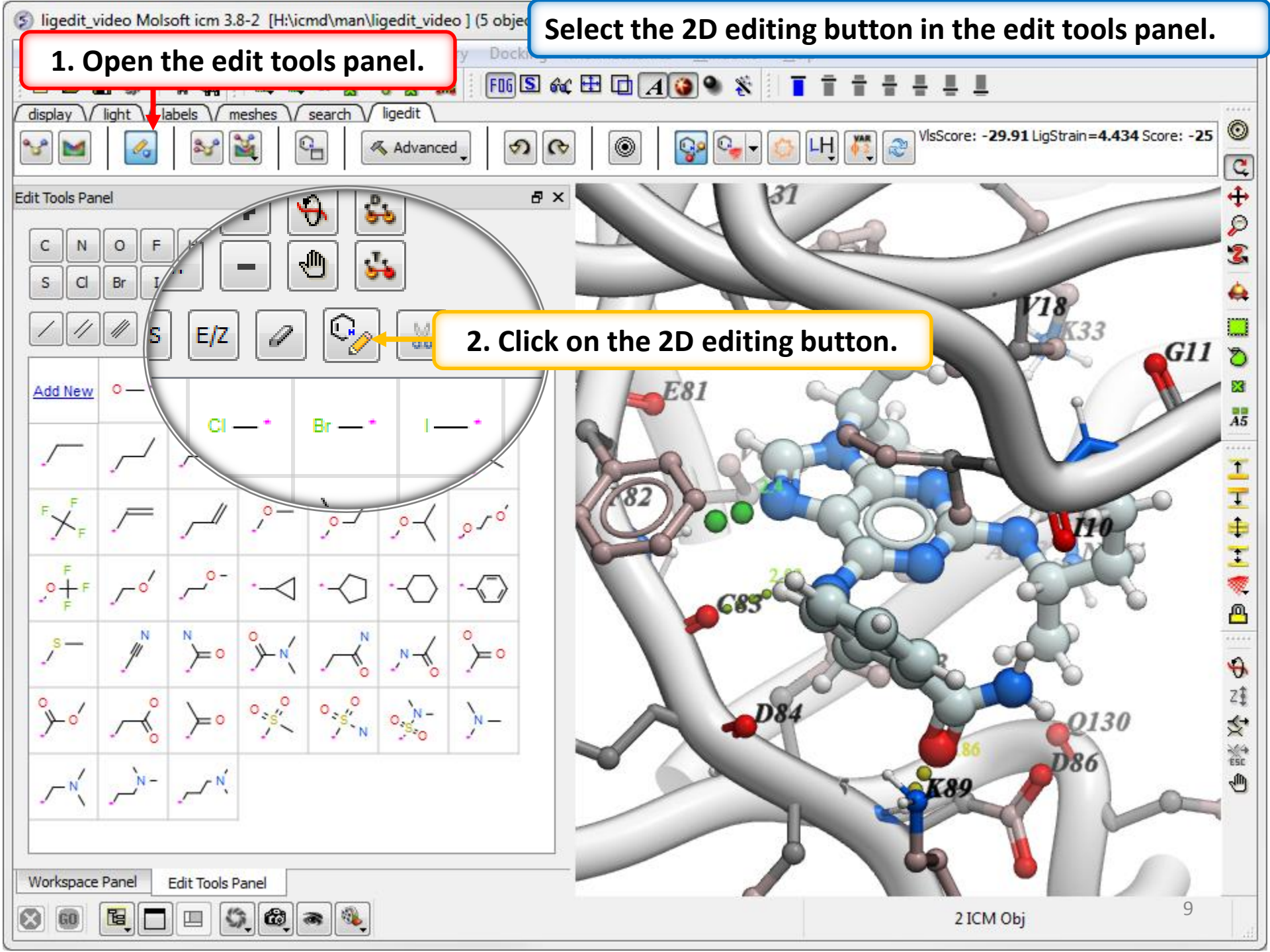
The energy maps are made inside the purple box.

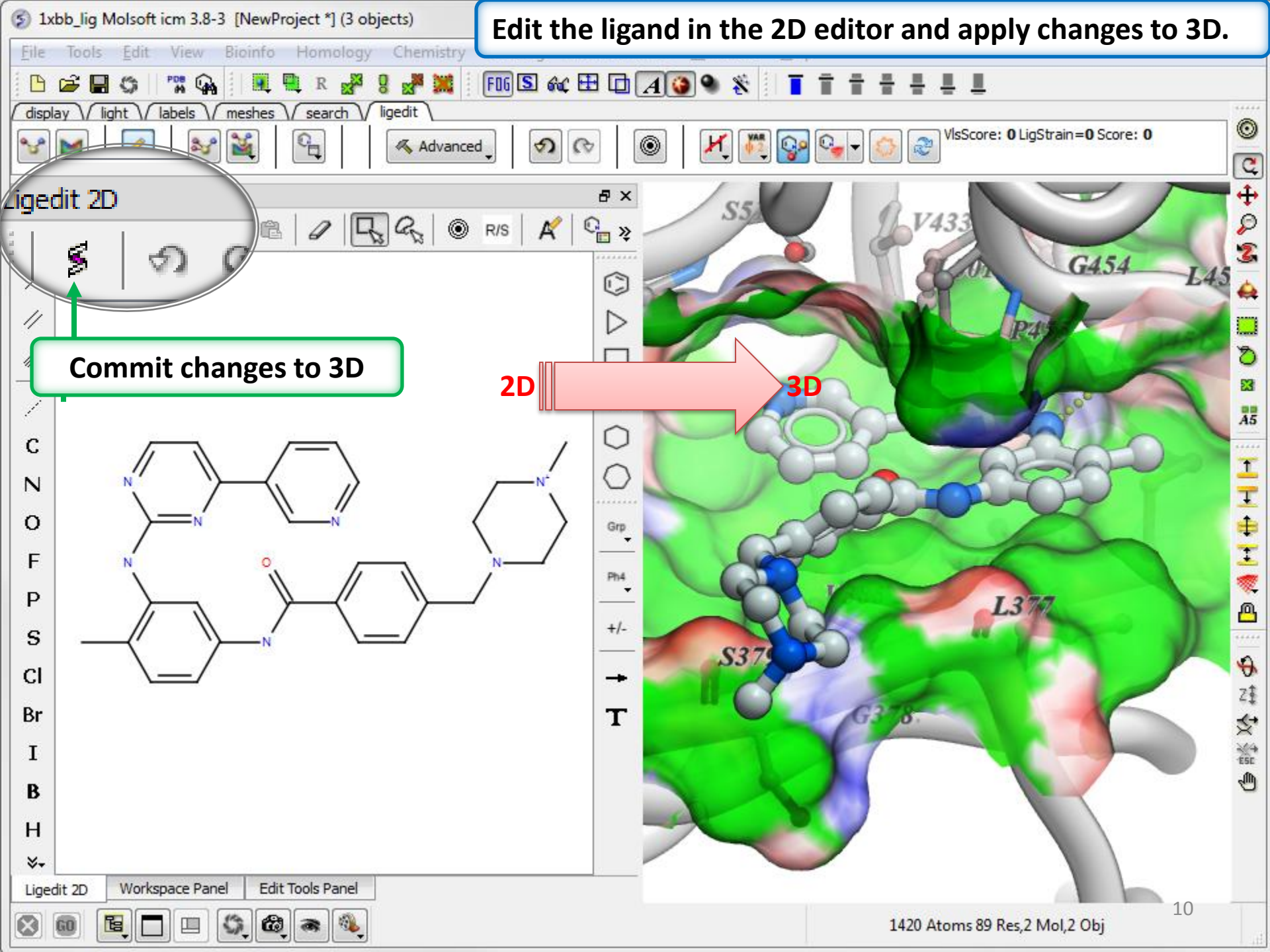
Prior to pressing OK in the receptor setup step. You can adjust the size of the box by dragging on the corners.

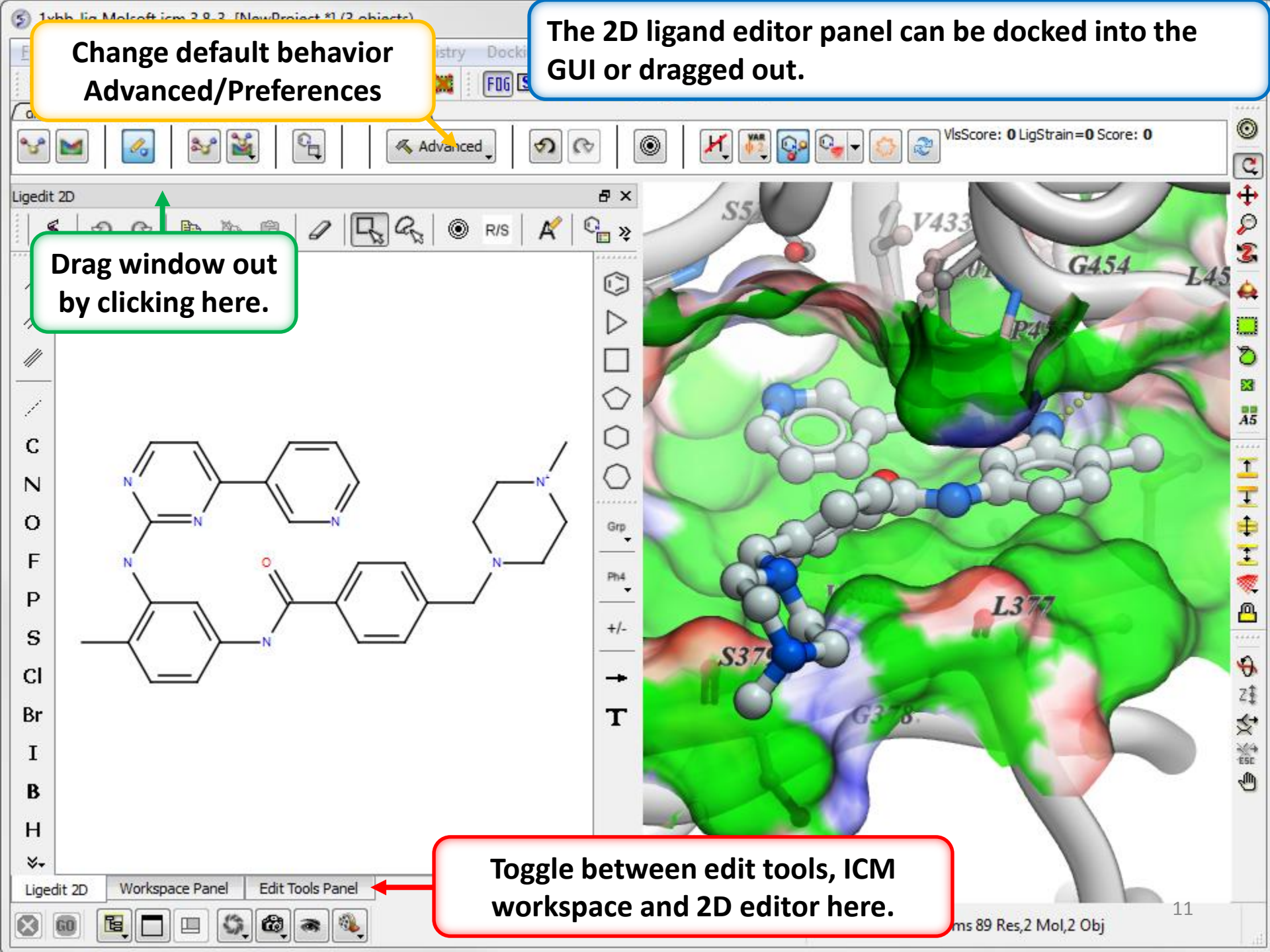



1xbb_rec1 Molsoft icm 3.8-3 [NewProject *] (3 objects)
Everything is now setup and ready to start editing.
File Tools Edit View Bioinfo Homology Chemistry Docking
display light labels meshes search ligedit
Advanced
VlsScore: 0 LigStrain=0 Score: 0
Workspace Panel
no selection
(3 items)
1xbb_lig [2] ICM
Ligand to be edited.
1xbb_rec1
Receptor.
b 88 A
tyrosine-protein kinase svk; ch
Ligand pocket surface.
1xbb [1] XR; 1.6A
Original PDB structure
Click here to undisplay.
(357 water mole
m_gh 235Kb [-2.14,6.20] m2.
m_gb 235Kb [-2.85,2.87] m0.
m_gs 235Kb [-4.00,16.00] mC
Ligand to be edited.
Ligand pocket surface.
All
1420 Atoms 89 Res,2 Mol,2 Obj

Ligand Editing in 2D

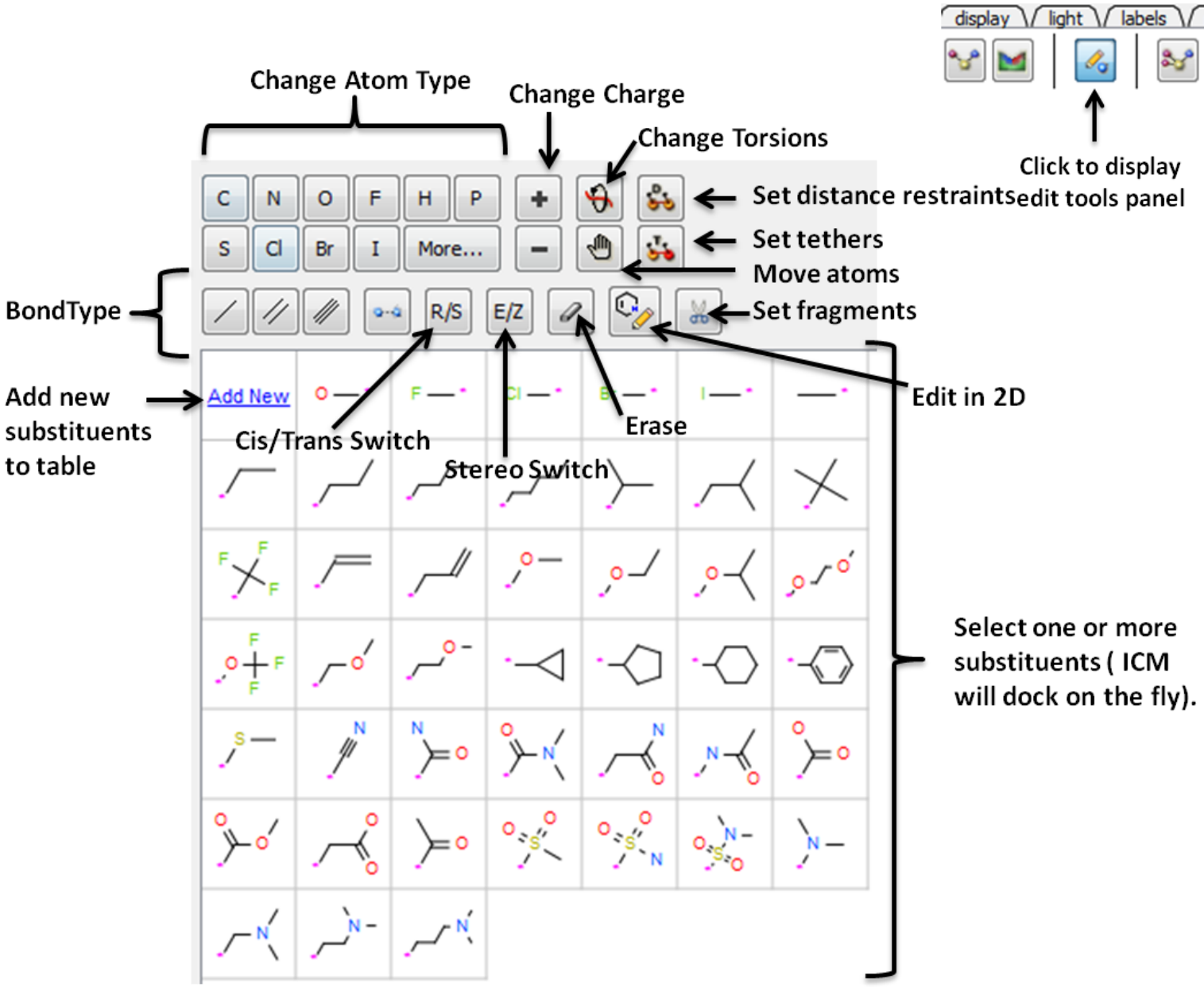

1. Open the edit tools panel.
Select the 2D editing button in the edit tools panel.
2. Click on the 2D editing button.
display
light
labels
meshes
search
ligedit
Advanced
Edit Tools Panel
Add New
Workspace Panel
Edit Tools Panel
2 ICM Obj
V18
K33
G11
E81
I10
G83
D84
Q130
D86
K89

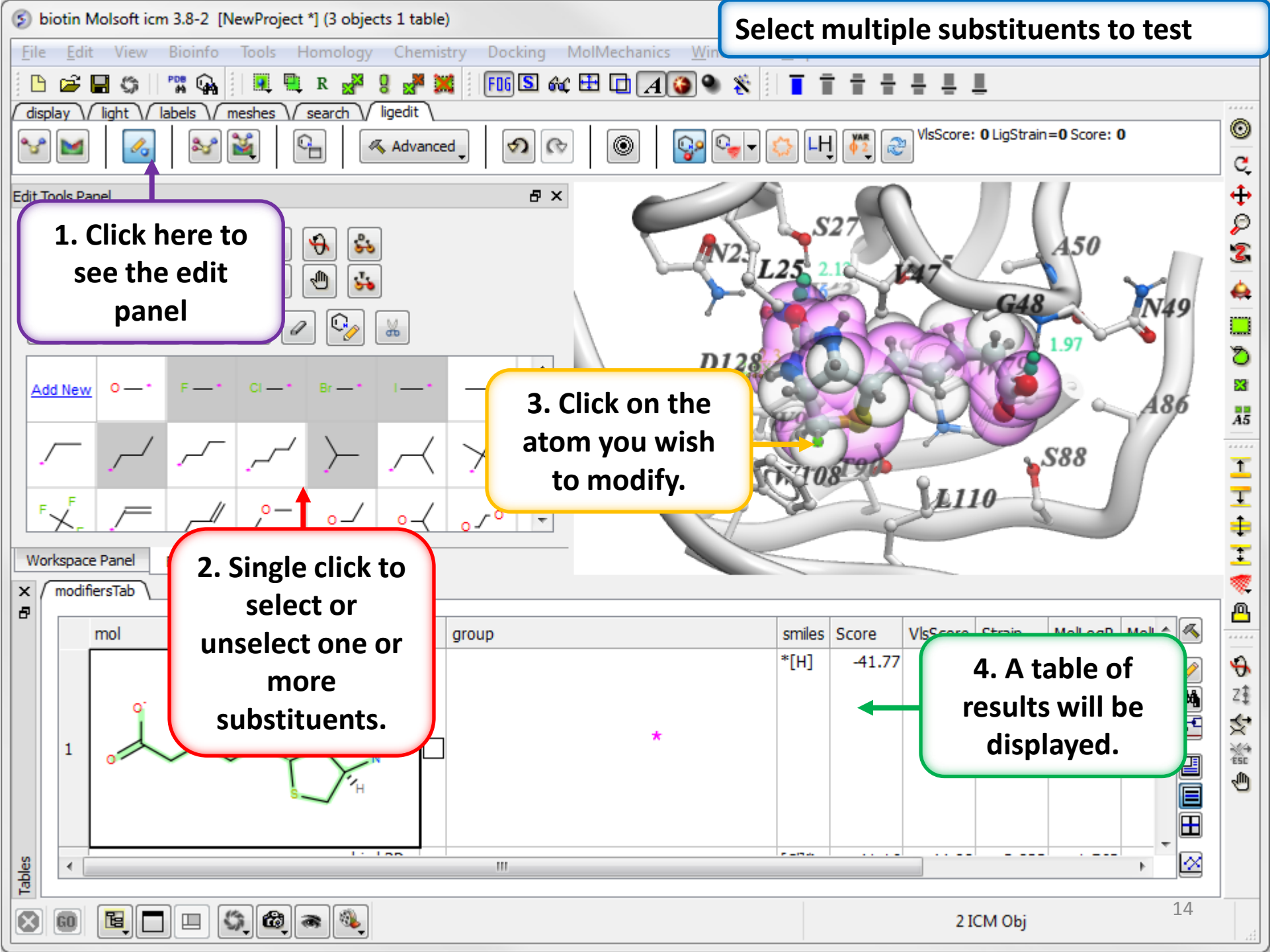

Edit the ligand in the 2D editor and apply changes to 3D.
1xbb_lig Molsoft icm 3.8-3 [NewProject *] (3 objects)
File Tools Edit View Bioinfo Homology Chemistry
display light labels meshes search ligedit
Advanced
VlsScore: 0 LigStrain=0 Score: 0
Ligedit 2D
R/S
Commit changes to 3D
2D
3D
C N O F P S Cl Br I B H
Grp
Ph4
+/-
T
S5
V433
G454
L45
L377
S37
G378
A5
Ligedit 2D
Workspace Panel
Edit Tools Panel
GO
1420 Atoms 89 Res,2 Mol,2 Obj


Change default behavior
Advanced/Preferences
The 2D ligand editor panel can be docked into the GUI or dragged out.
Advanced
VlsScore: 0 LigStrain=0 Score: 0
Ligedit 2D
Drag window out by clicking here.
R/S
Grp
Ph4
+/-
C
N
O
F
P
S
Cl
Br
I
B
H
L377
G454
Ligedit 2D
Workspace Panel
Edit Tools Panel
Toggle between edit tools, ICM workspace and 2D editor here.

Ligand Editing in 3D

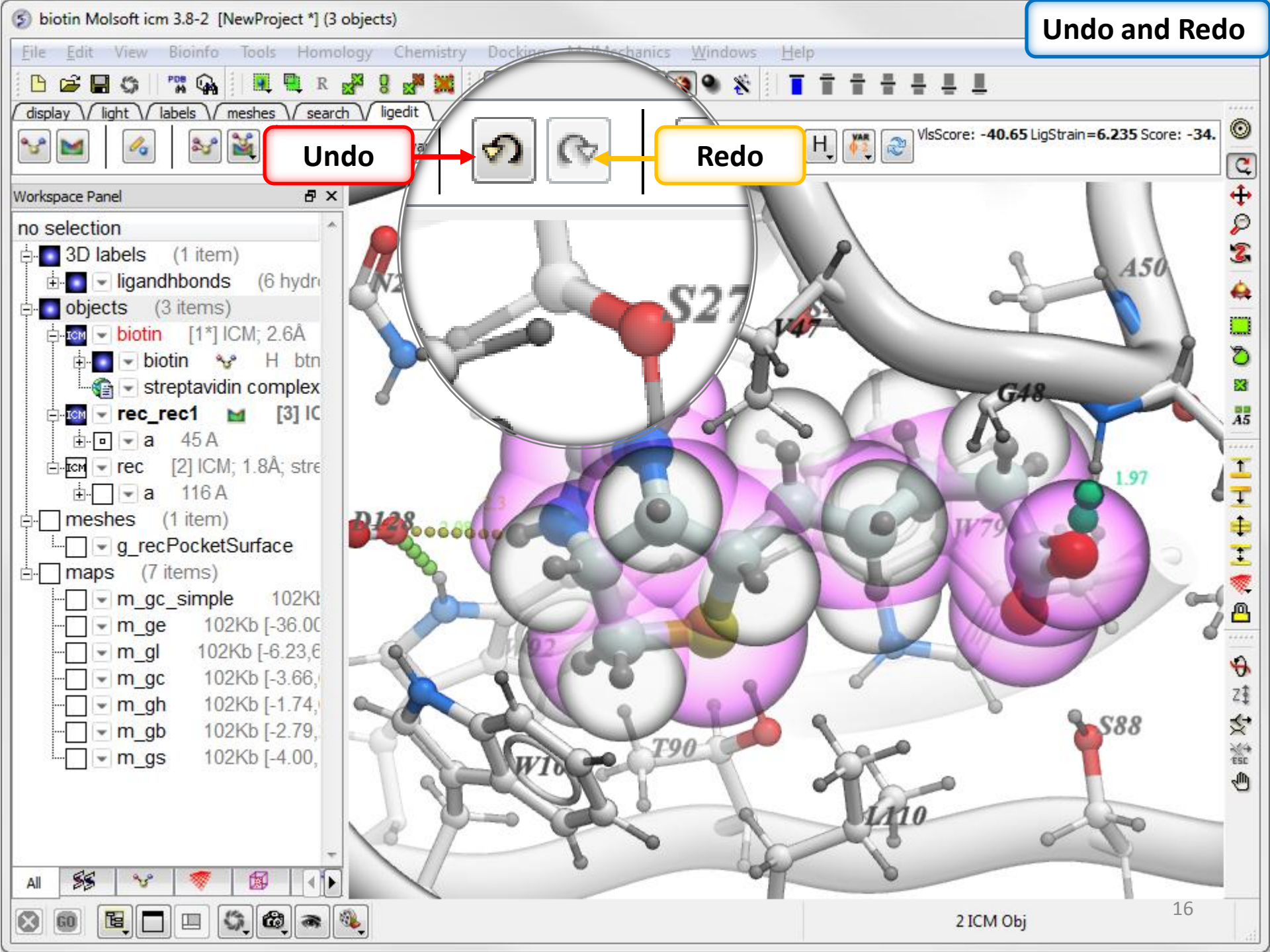
Select the modification you want to make from the panel below and then click on the ligand in the 3D display. One or more substituents can be screened.



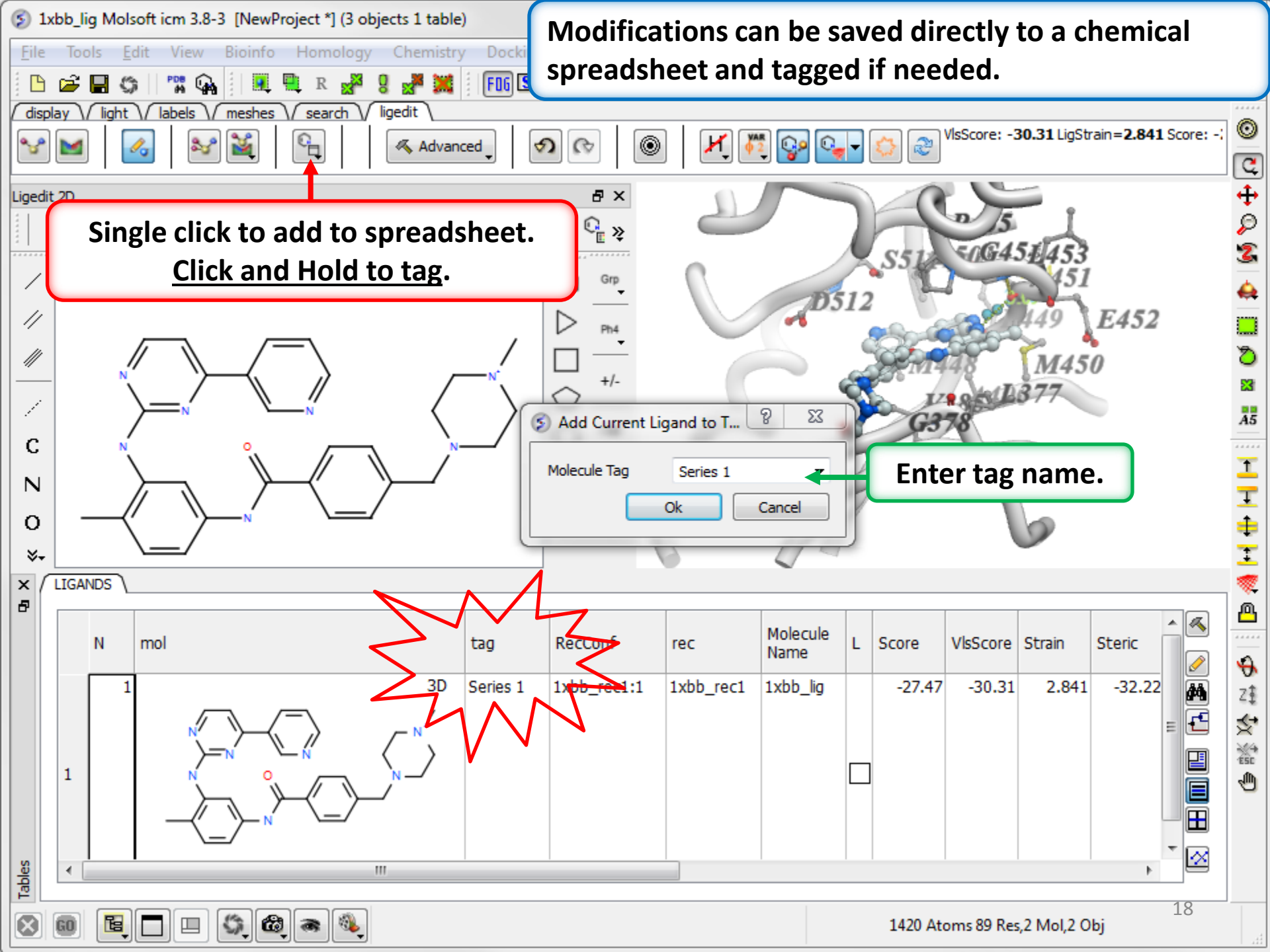

biotin Molsoft icm 3.8-2 [NewProject *] (3 objects 1 table)
Select multiple substituents to test
File Edit View Bioinfo Tools Homology Chemistry Docking MolMechanics
display light labels meshes search ligedit
Advanced
VlsScore: 0 LigStrain=0 Score: 0
Edit Tools Panel
1. Click here to see the edit panel
Add New
3. Click on the atom you wish to modify.
2. Single click to select or unselect one or more substituents.
Workspace Panel
modifiersTab
mol
group
smiles
Score
*[H]
-41.77
4. A table of results will be displayed.
Tables
2 ICM Obj

All modifications to the ligand can be undone or redone.

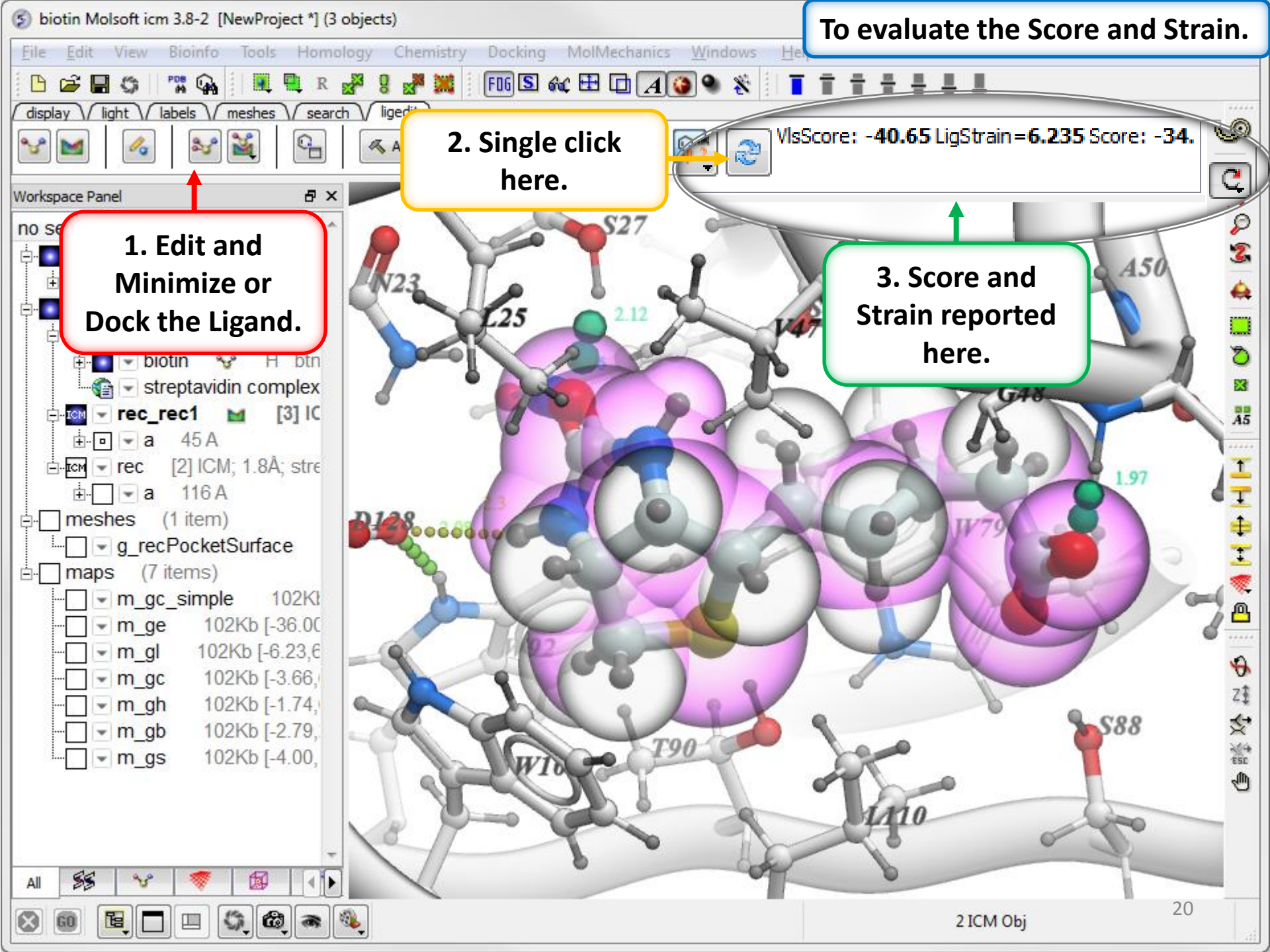
Undo and Redo



If you like a modification you can store it in a chemical spreadsheet and load it again later.


1xbb_lig Molsoft icm 3.8-3 [NewProject *] (3 objects 1 table)
Modifications can be saved directly to a chemical spreadsheet and tagged if needed.
File Tools Edit View Bioinfo Homology Chemistry
display light labels meshes search ligedit
Advanced
VlsScore: -30.31 LigStrain=2.841 Score:
Ligedit 2D
Single click to add to spreadsheet.
Click and Hold to tag.
Add Current Ligand to T...
Molecule Tag
Series 1
Ok
Cancel
Enter tag name.
LIGANDS
N mol tag RecConf rec Molecule Name L Score VlsScore Strain Steric
1 3D Series 1 1xbb_rec1:1 1xbb_rec1 1xbb_lig -27.47 -30.31 2.841 -32.22
Tables
1420 Atoms 89 Res,2 Mol,2 Obj

Evaluate how well the modifications fit into the pocket. The lower the score the better the predicted fit.


biotin Molsoft icm 3.8-2 [NewProject *] (3 objects)
To evaluate the Score and Strain.
File Edit View Bioinfo Tools Homology Chemistry Docking MolMechanics Windows
display light labels meshes search
2. Single click here.
VlsScore: -40.65 LigStrain=6.235 Score: -34.
Workspace Panel
1. Edit and Minimize or Dock the Ligand.
3. Score and Strain reported here.
biotin
streptavidin complex
rec_rec1
a 45 A
rec [2] ICM; 1.8Å; stre
a 116 A
meshes (1 item)
g_recPocketSurface
maps (7 items)
m_gc_simple
m_ge 102Kb [-36.0
m_gl 102Kb [-6.23,6
m_gc 102Kb [-3.66,
m_gh 102Kb [-1.74,
m_gb 102Kb [-2.79,
m_gs 102Kb [-4.00,
S27
N23
L25
A50
G48
D128
W79
T90
S88
L110
2.12
1.97
All
2 ICM Obj

Visualizing ligand strain.