Tutorial

Molecular Docking Simulations Using ArgusLab

Prof. Dr. Walter Filgueira de Azevedo Jr.

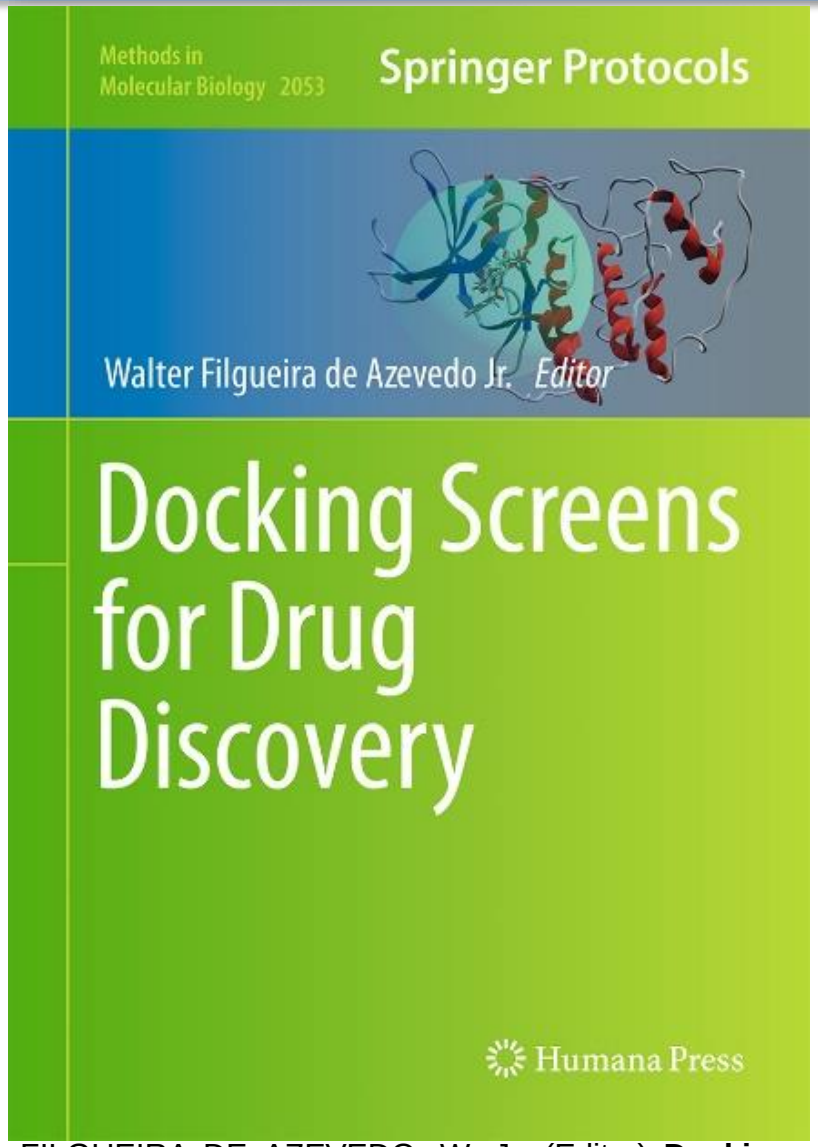
walter@azevedolab.net

azevedolab.net

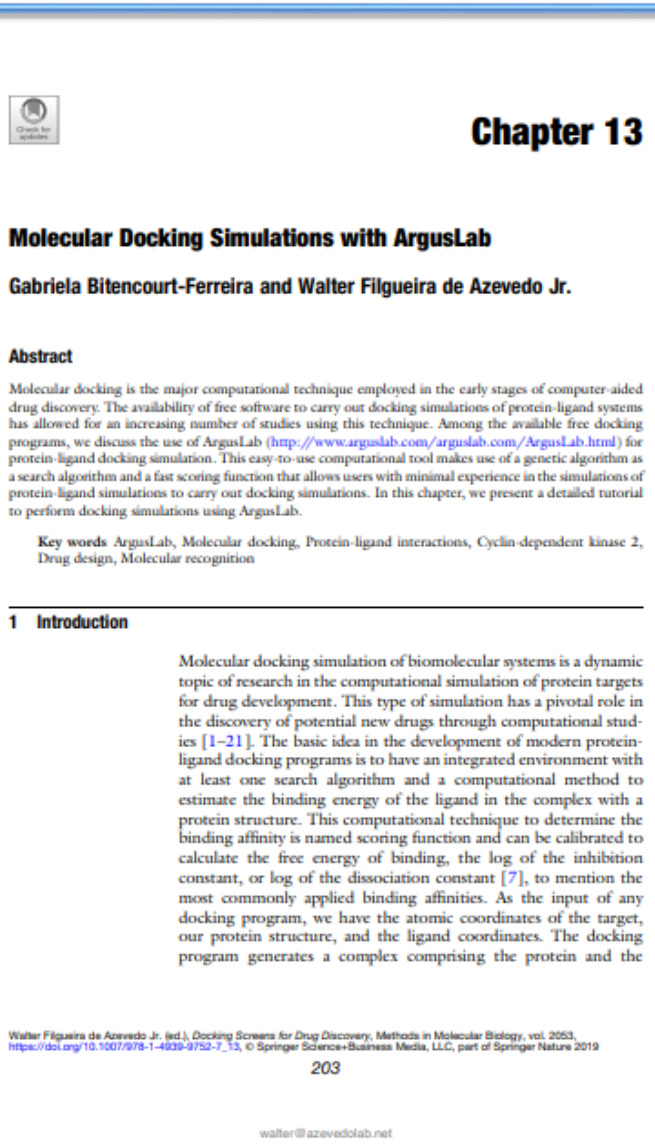
© 2020 Dr. Walter F. de Azevedo Jr.

Molecular Docking Simulations with ArgusLab

In this tutorial you will learn how to carry out docking simulation using the ArgusLab docking program (Joy *et al.,* 2006; Bitencourt-Ferreira & de Azevedo Jr., 2019). This docking software is freely available at www.arguslab.com. We used the atomic coordinates of cyclin-dependent kinase 2 in complex with 3-amino-6-(4-{[2-(dimethylamino)ethyl]sulfamoyl}phenyl)- n-pyridin-3-ylpyrazine-2-carboxamide (PDB access code: 4ACM.) (Berg *et al.,* 2012).



FILGUEIRA DE AZEVEDO, W. Jr. (Editor) **Docking Screens for Drug Discovery. Methods in Molecular Biology. Vol. 2053.** Springer Science+Business Media, 2019.



Chapter 13

Molecular Docking Simulations with ArgusLab

Gabriela Bitencourt-Ferreira and Walter Filgueira de Azevedo Jr.

Abstract

Molecular docking is the major computational technique employed in the early stages of computer-aided drug discovery. The availability of free software to carry out docking simulations of protein-ligand systems has allowed for an increasing number of studies using this technique. Among the available free docking programs, we discuss the use of ArgusLab (http://www.arguslab.com/arguslab.com/ArgusLab.html) for protein-ligand docking simulation. This easy-to-use computational tool makes use of a genetic algorithm as a search algorithm and a fast scoring function that allows users with minimal experience in the simulations of protein-ligand simulations to carry out docking simulations. In this chapter, we present a detailed tutorial to perform docking simulations using ArgusLab.

Key words ArgusLab, Molecular docking, Protein-ligand interactions, Cyclin-dependent kinase 2, Drug design, Molecular recognition

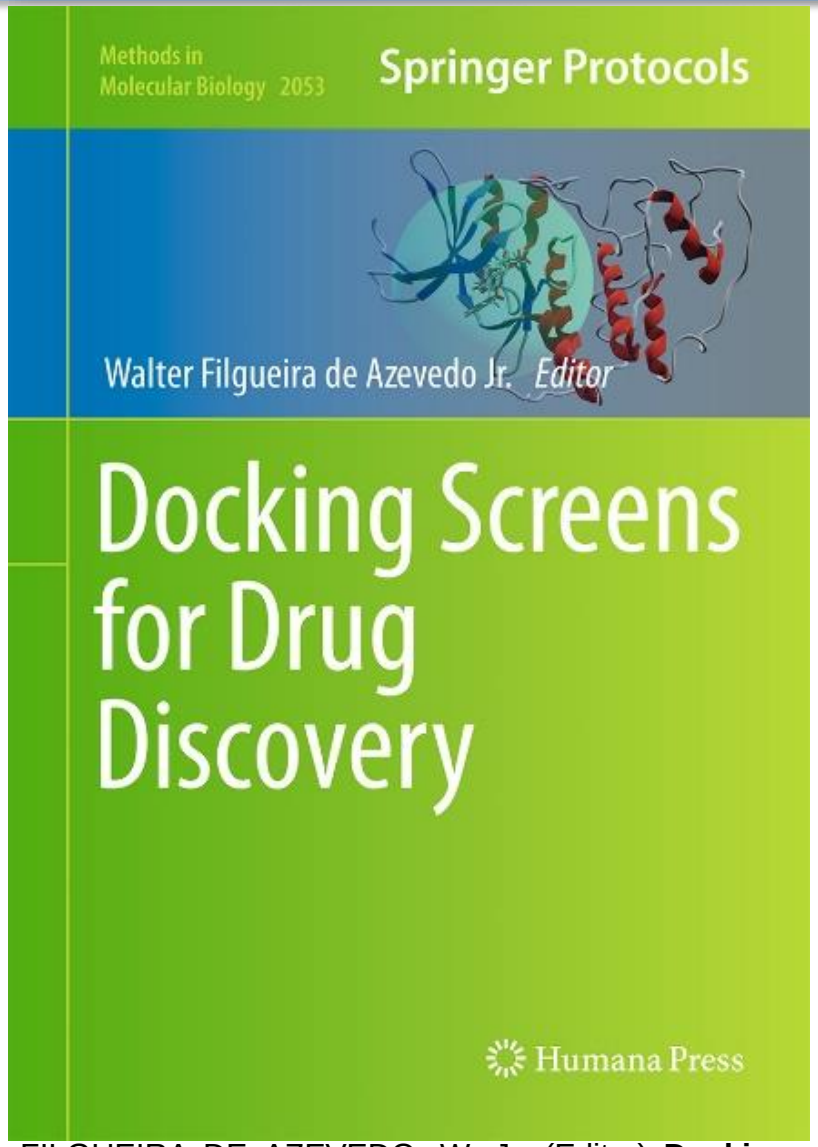
1 Introduction

Molecular docking simulation of biomolecular systems is a dynamic topic of research in the computational simulation of protein targets for drug development. This type of simulation has a pivotal role in the discovery of potential new drugs through computational studies [1–21]. The basic idea in the development of modern protein-ligand docking programs is to have an integrated environment with at least one search algorithm and a computational method to estimate the binding energy of the ligand in the complex with a protein structure. This computational technique to determine the binding affinity is named scoring function and can be calibrated to calculate the free energy of binding, the log of the inhibition constant, or log of the dissociation constant [7], to mention the most commonly applied binding affinities. As the input of any docking program, we have the atomic coordinates of the target, our protein structure, and the ligand coordinates. The docking program generates a complex comprising the protein and the

Walter Filgueira de Azevedo Jr. (ed.), *Docking Screens for Drug Discovery*, Methods in Molecular Biology, vol. 2053,
https://doi.org/10.1007/978-1-4939-9752-7_13, © Springer Science+Business Media, LLC, part of Springer Nature 2019

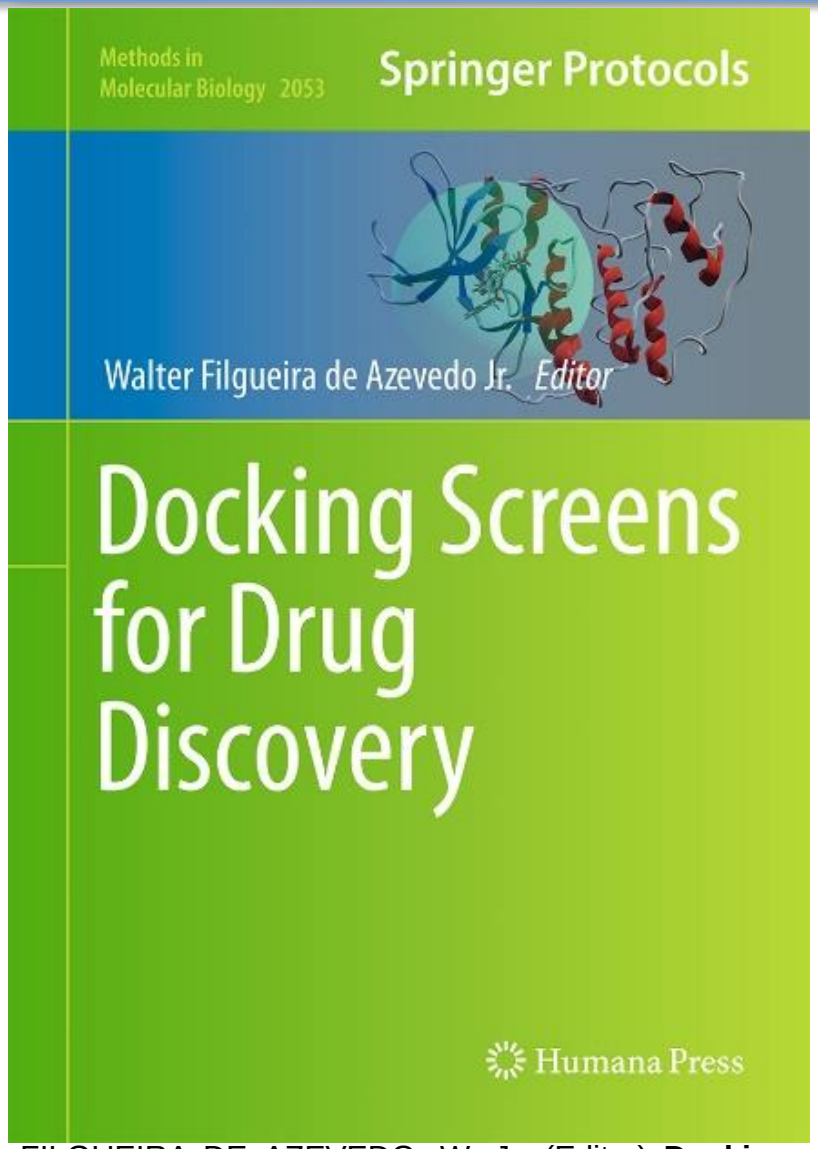
walter@azevedolab.net

Bitencourt-Ferreira G, de Azevedo WF Jr. Molecular Docking Simulations with ArgusLab. Methods Mol Biol. 2019; 2053: 203–220.



available at amazon

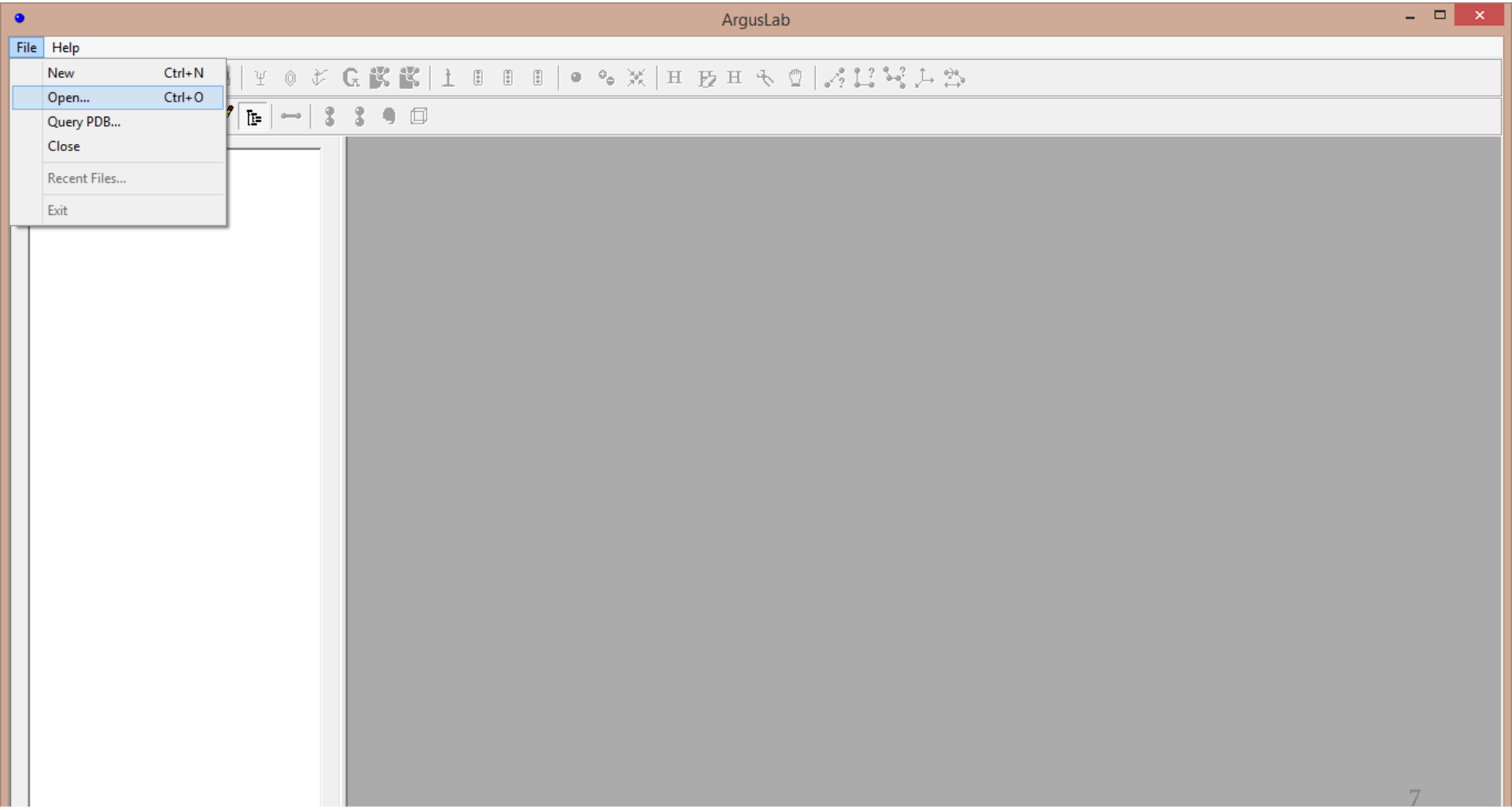
FILGUEIRA DE AZEVEDO, W. Jr. (Editor) **Docking Screens for Drug Discovery. Methods in Molecular Biology. Vol. 2053.** Springer Science+Business Media, 2019.



FILGUEIRA DE AZEVEDO, W. Jr. (Editor) **Docking Screens for Drug Discovery. Methods in Molecular Biology. Vol. 2053.** Springer Science+Business Media, 2019.

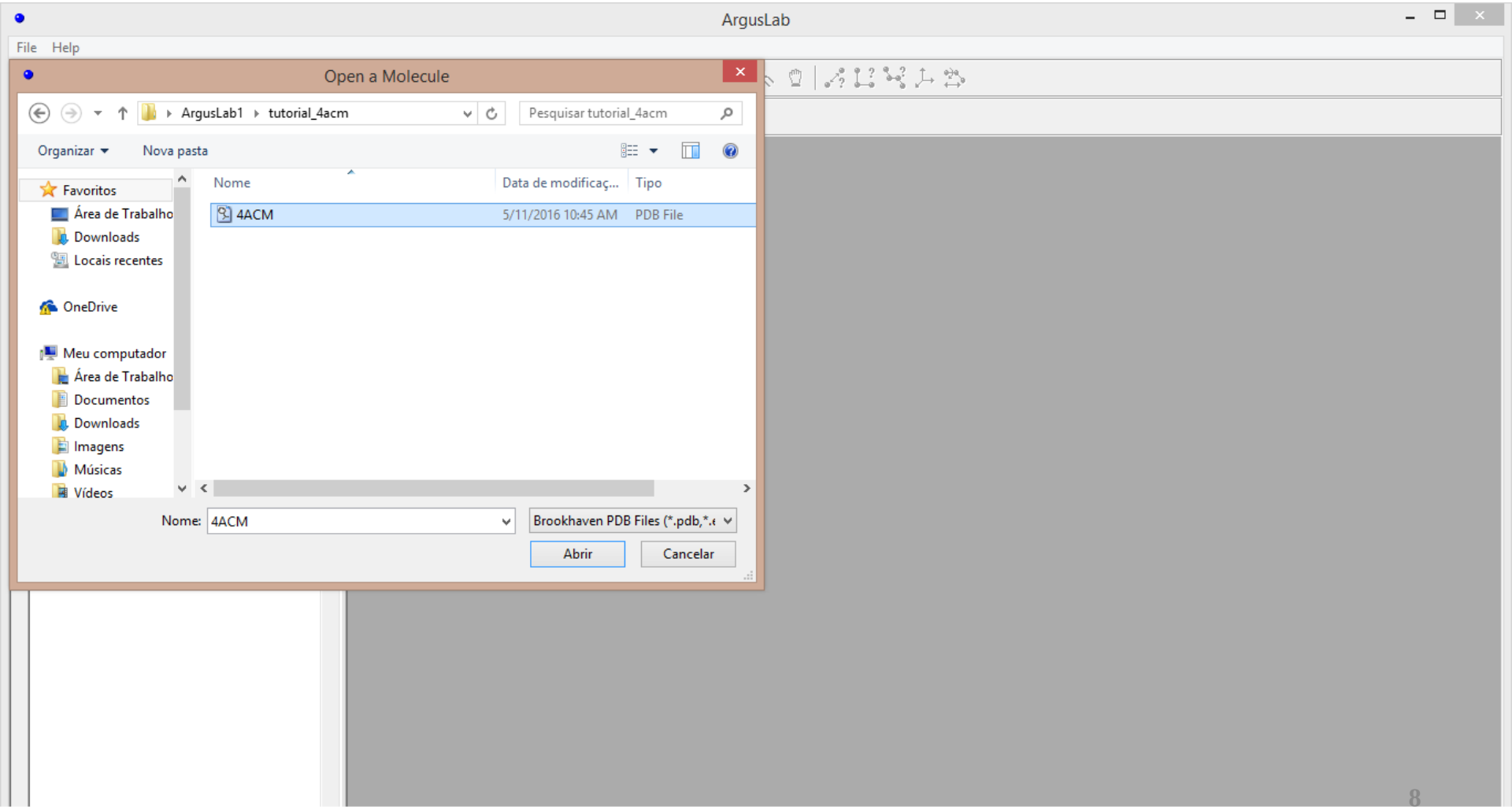
Loading PDB file

To open a PDB file click: File>Open..., as show below.



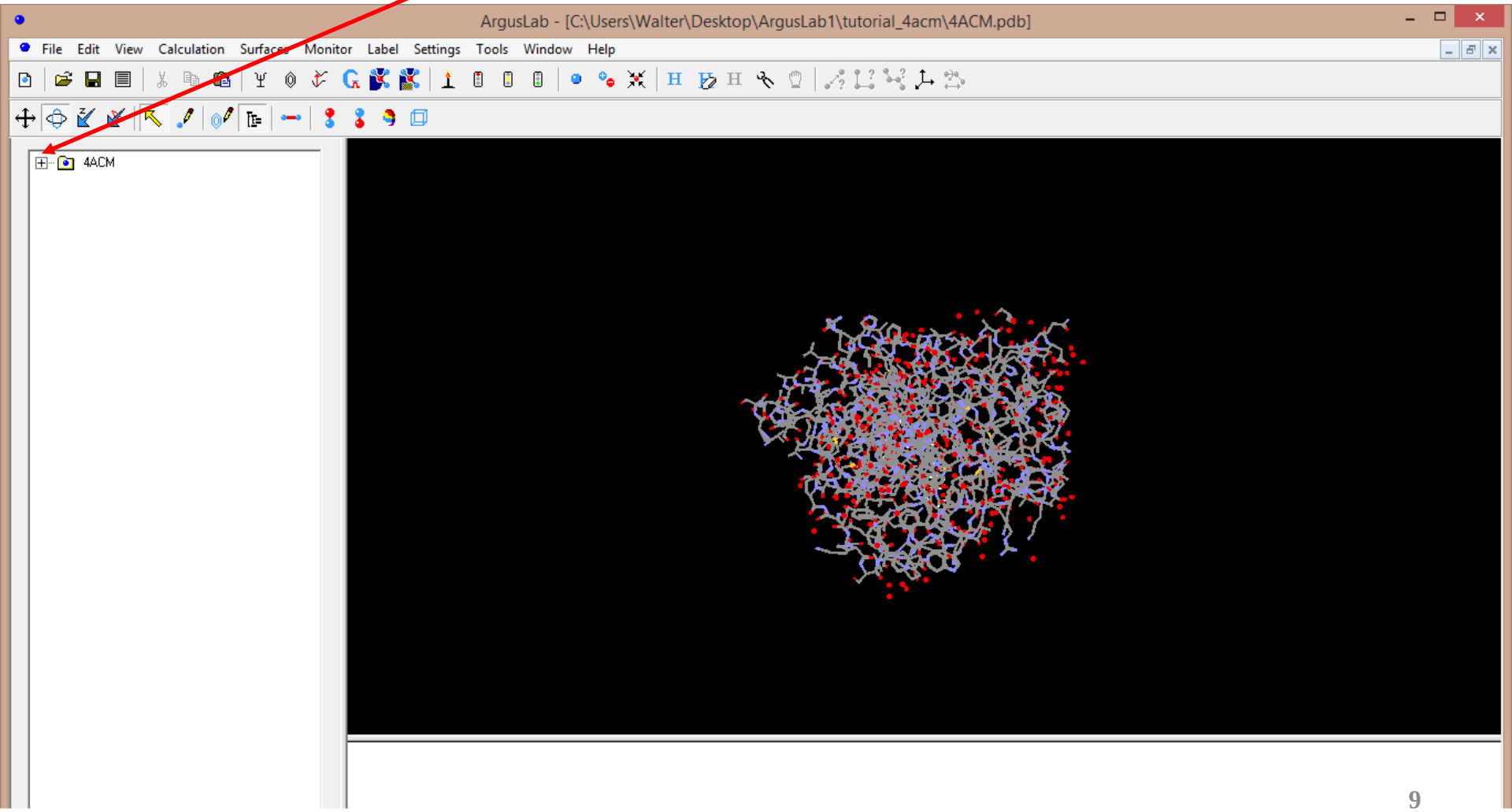
Loading PDB file

Then browse the folder where you have the PDB file.



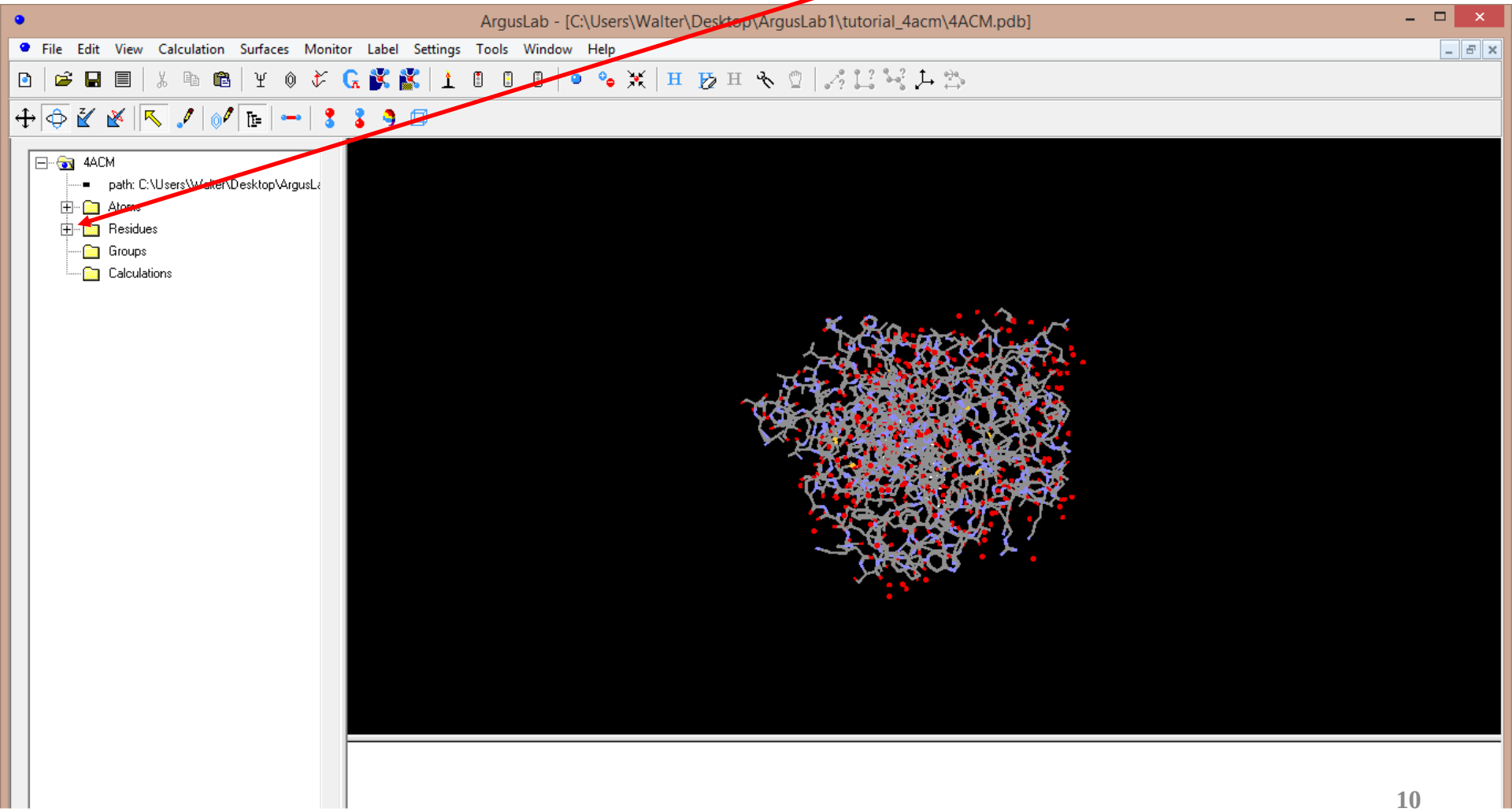
THOMSON REUTERS SCOPUS

You will have the structure in the graphical screen. On the left, you have the Tree View tool. Click on the “+” to expand the tree.

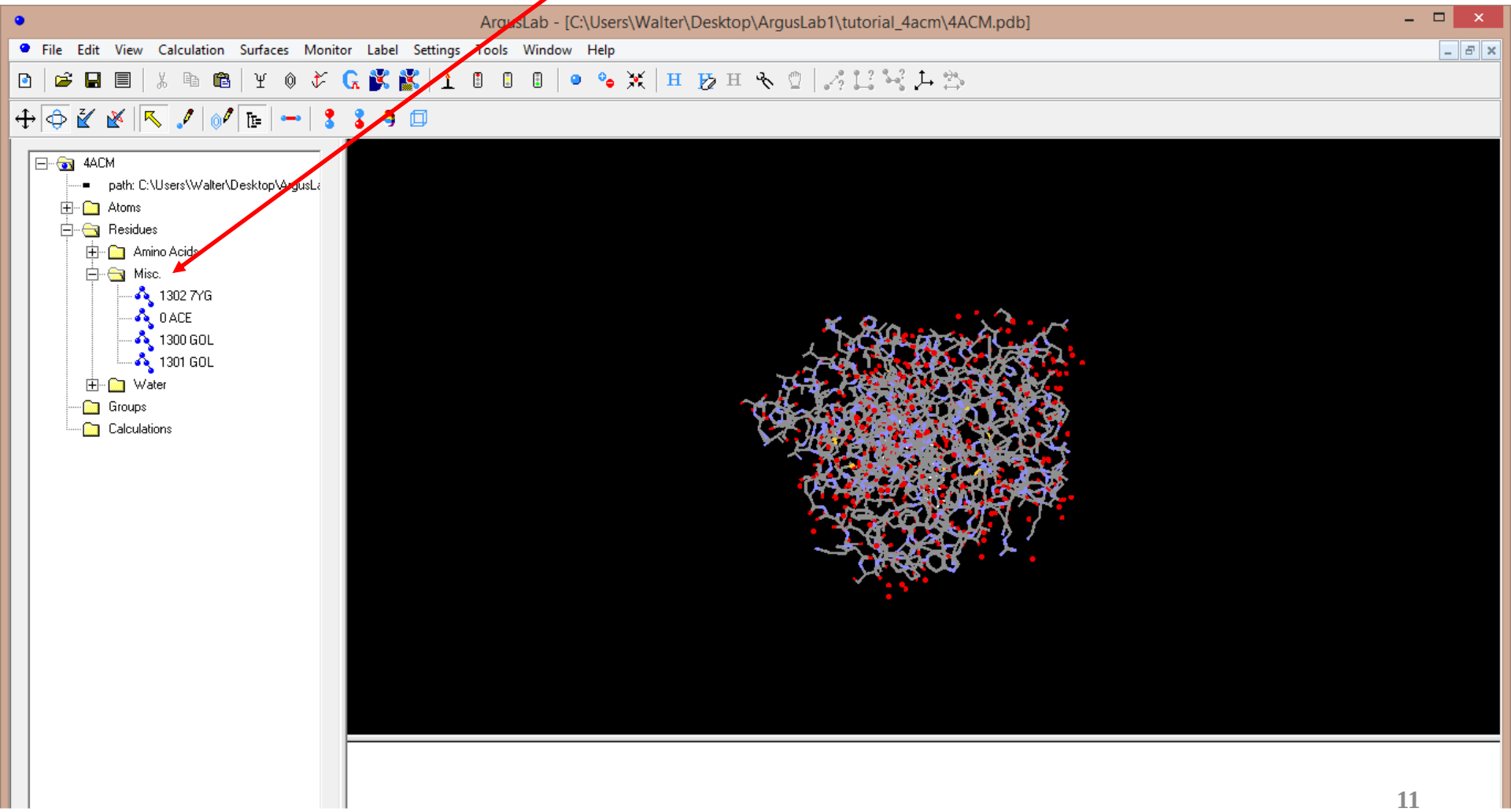


THOMSON REUTERS SCOPUS

Expand the Tree View of 4ACM and open up the Residues/Misc. folder to show the ligands.

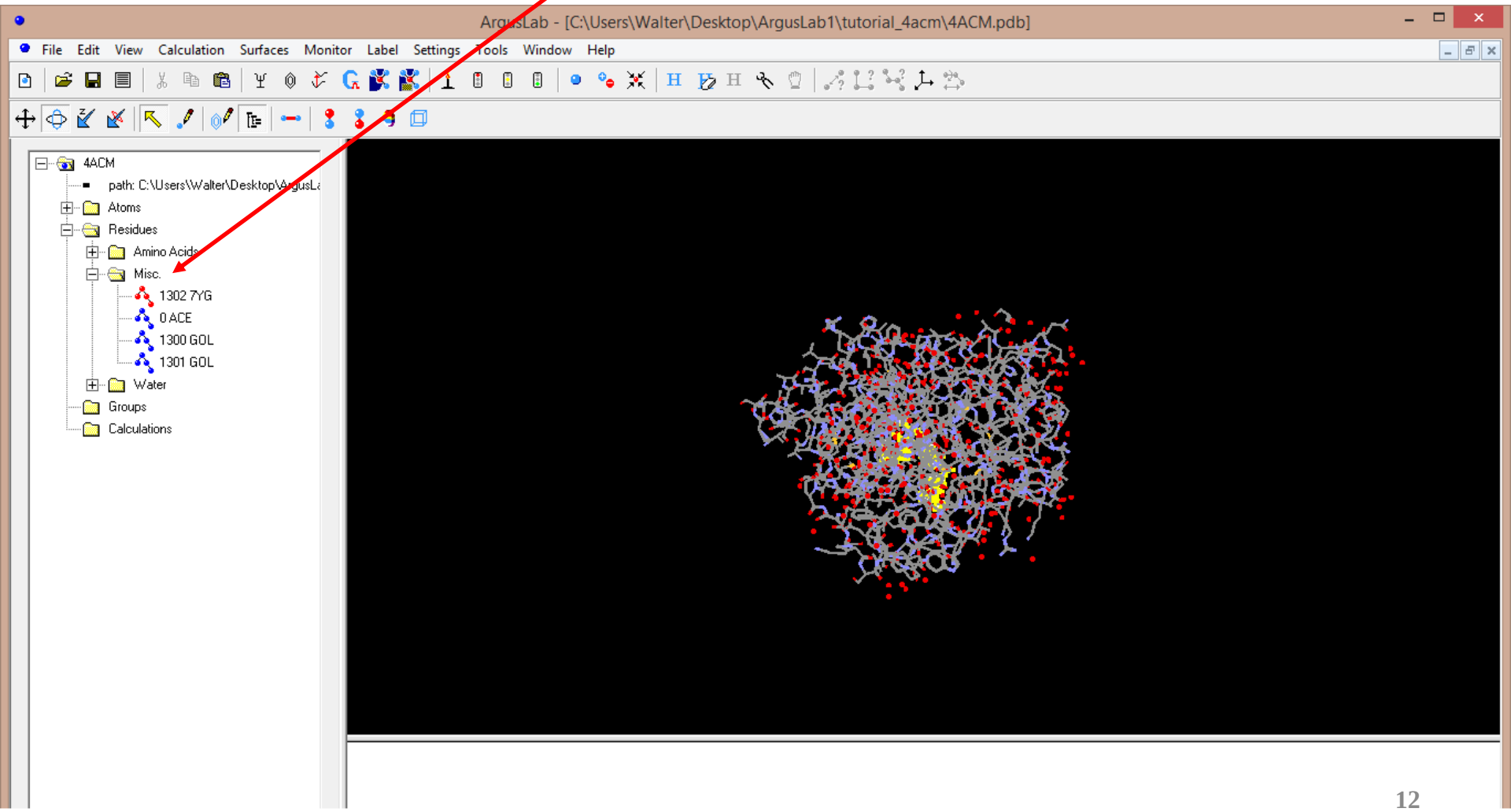


You should have something like this. The active ligand in “1302 7YG”, which will be used in the docking simulations.



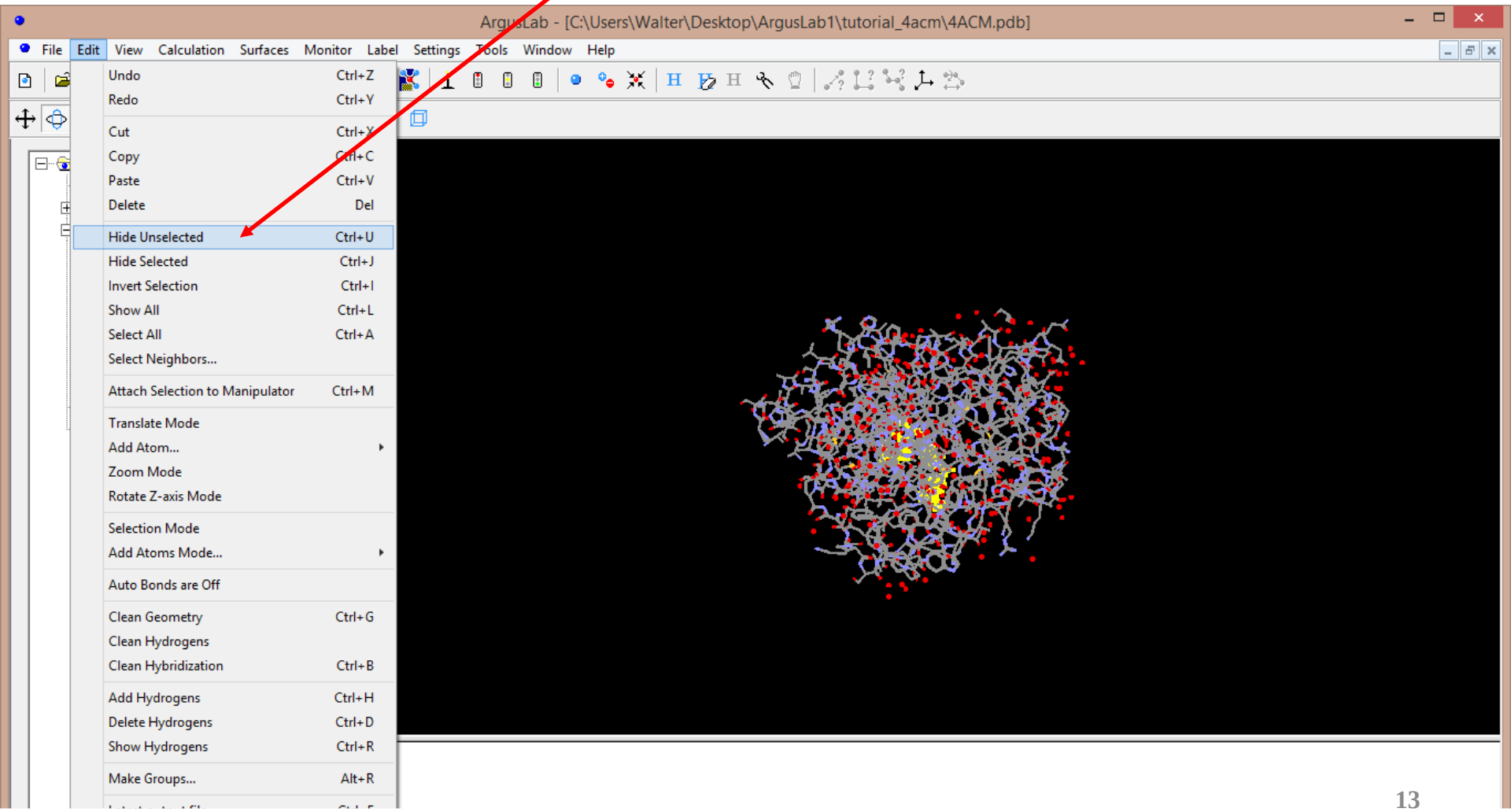
THOMSON REUTERS SCOPUS

Left click on “1302 7YG” in the Tree View to select the active ligand. It should appear in yellow on the graphical screen.



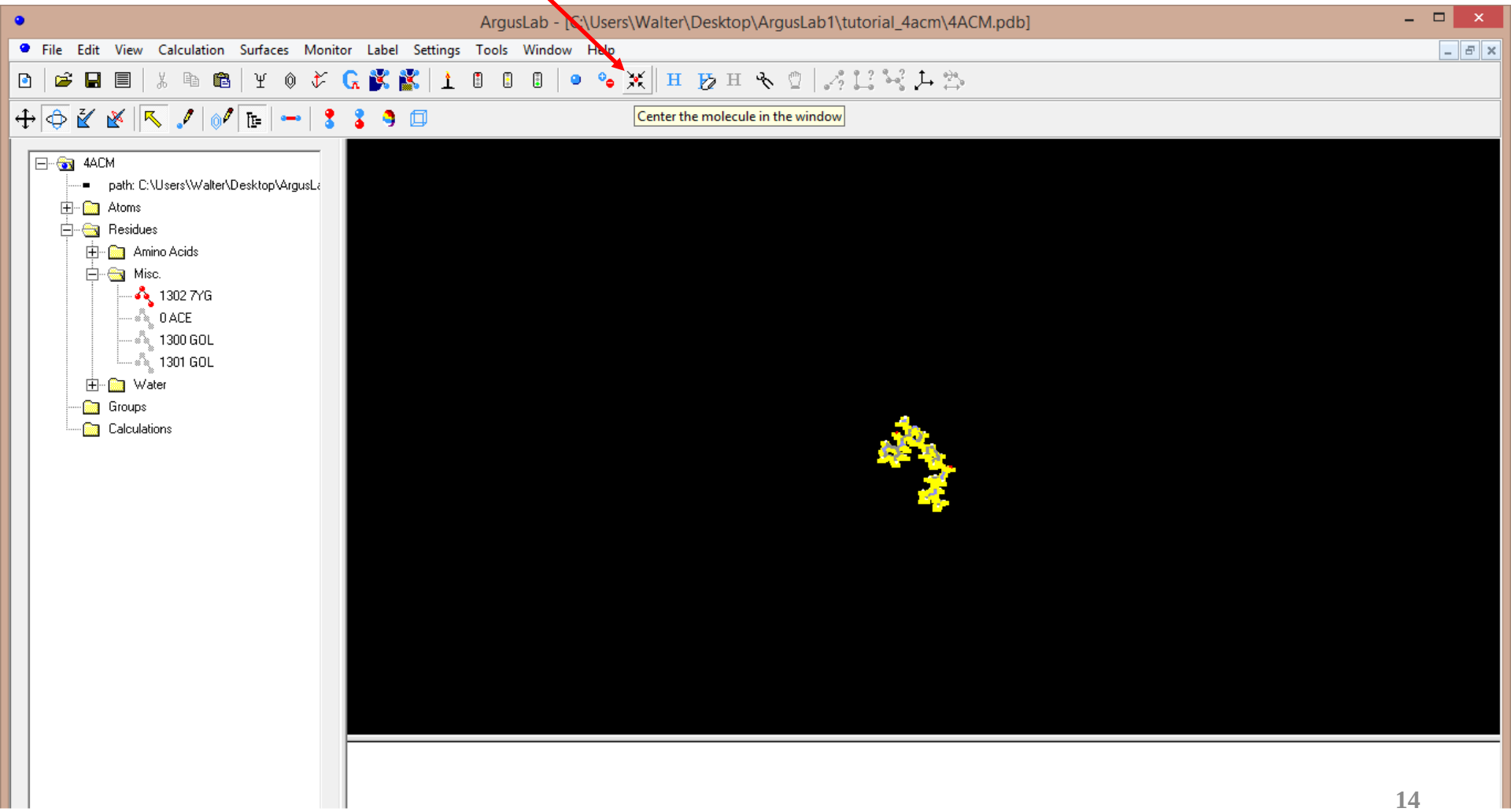
THOMSON REUTERS SCOPUS

Now click on Edit>Hide Unselected, as shown below. You will have only the active ligand on the graphical screen.



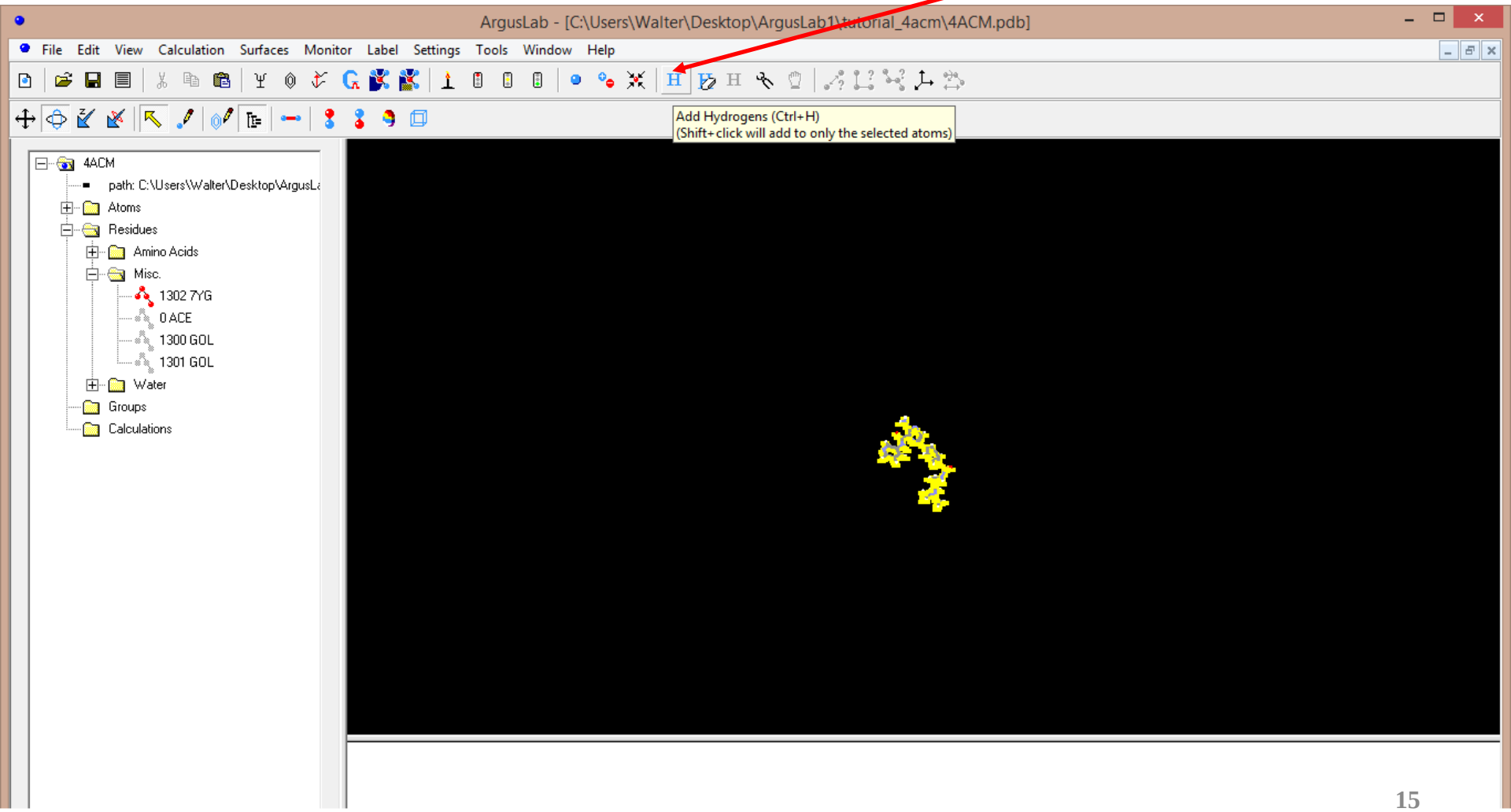
THOMSON REUTERS SCOPUS

To center the ligand click here.



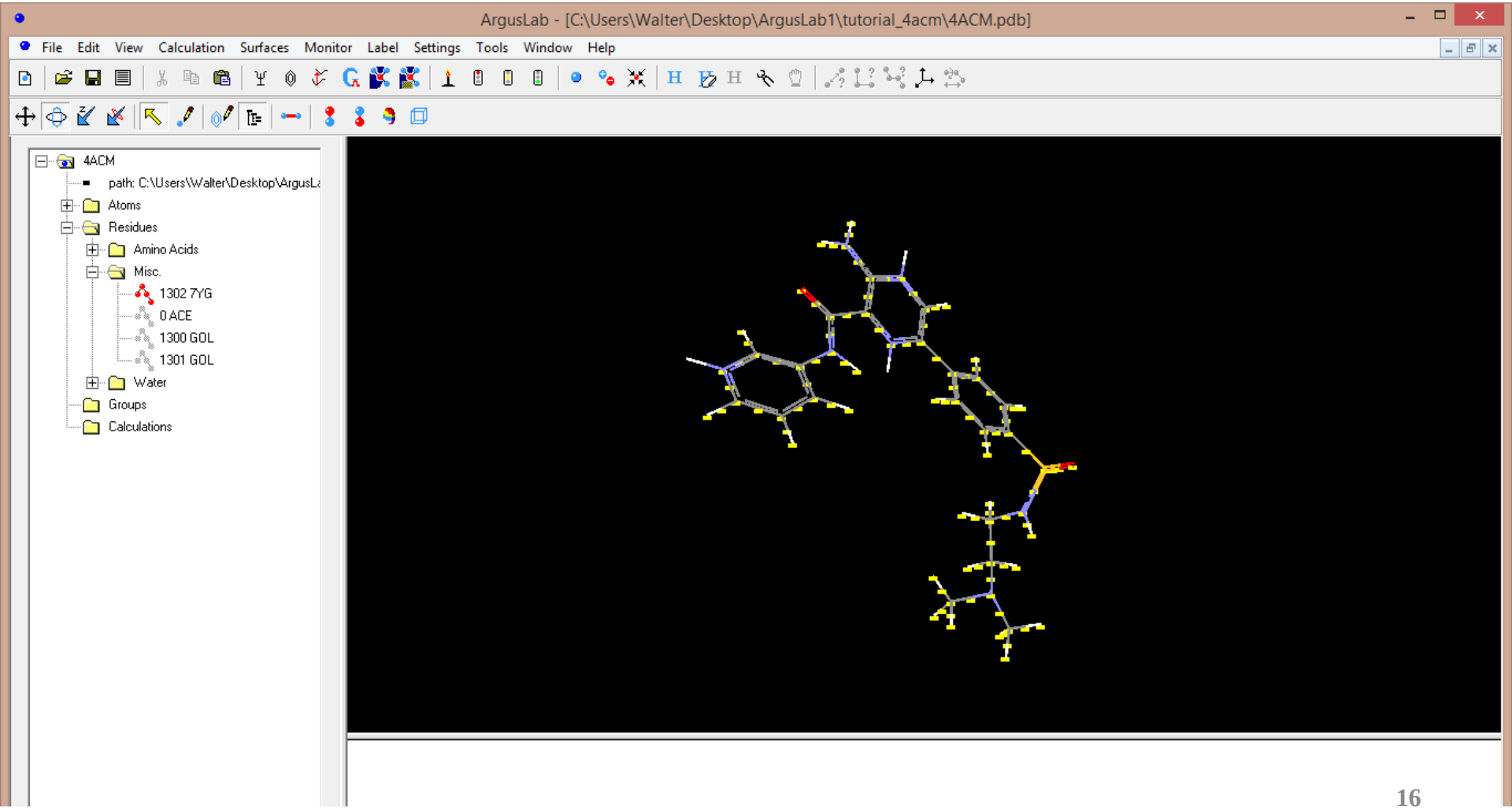
THOMSON REUTERS SCOPUS

To add hydrogens to the ligand hold down the shift key and click here.

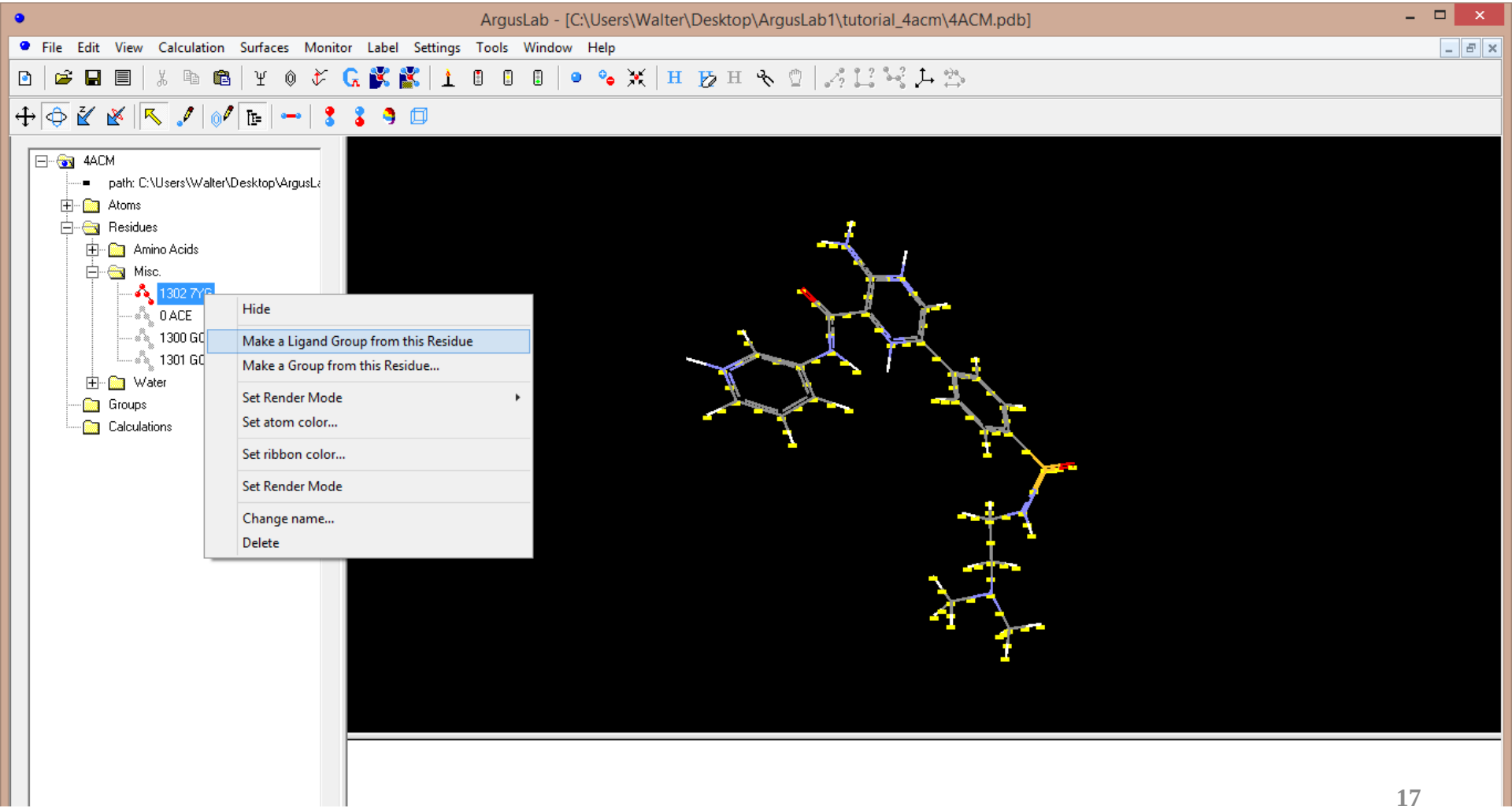


THOMSON REUTERS SCOPUS

Here we have the ligand with hydrogens added to the structure.

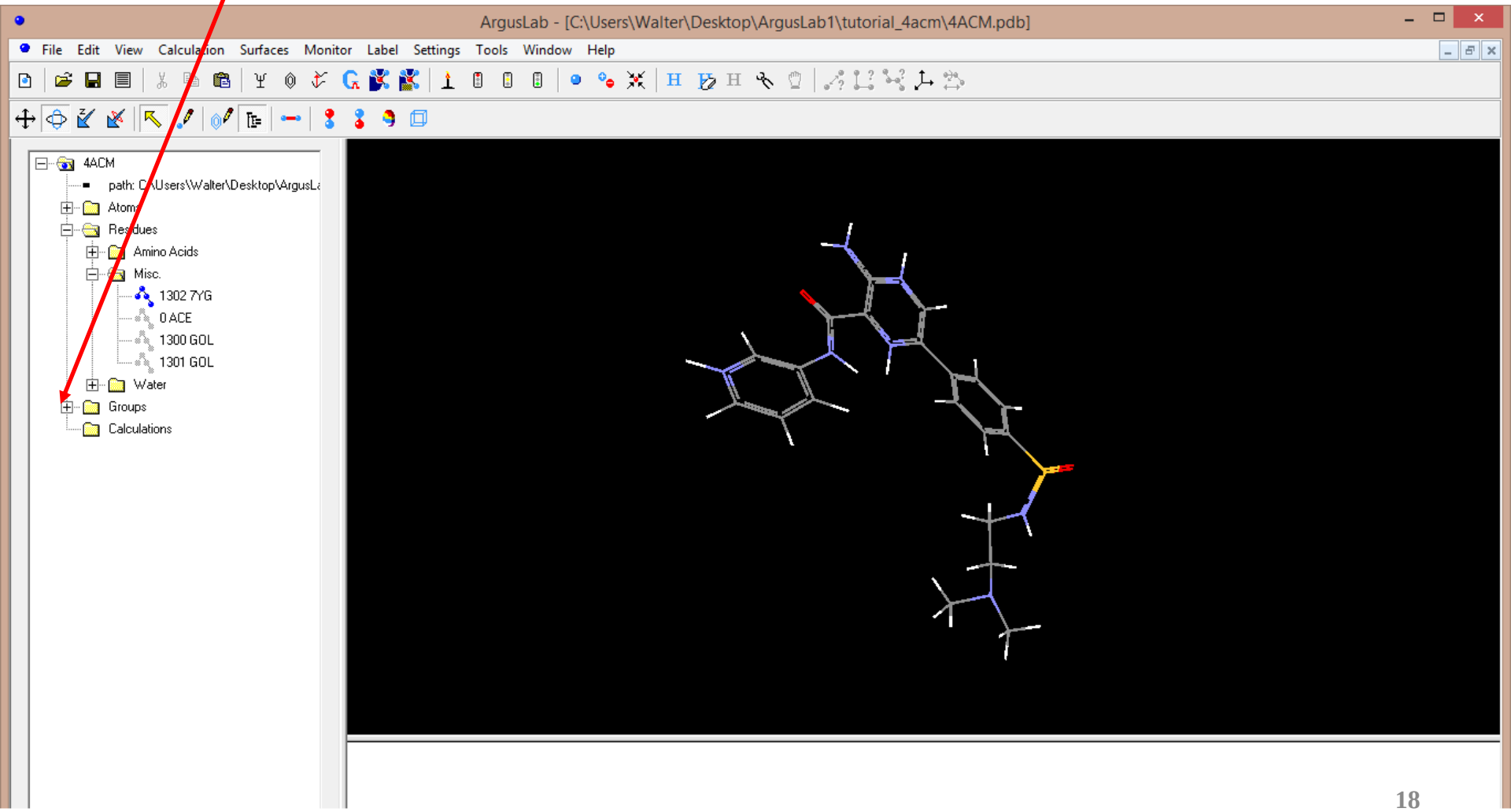


Here we have the ligand with hydrogens added to the structure. Right click on “1302 7YG” on the Tree View and select “Make a Ligand Group from this Residue” option.



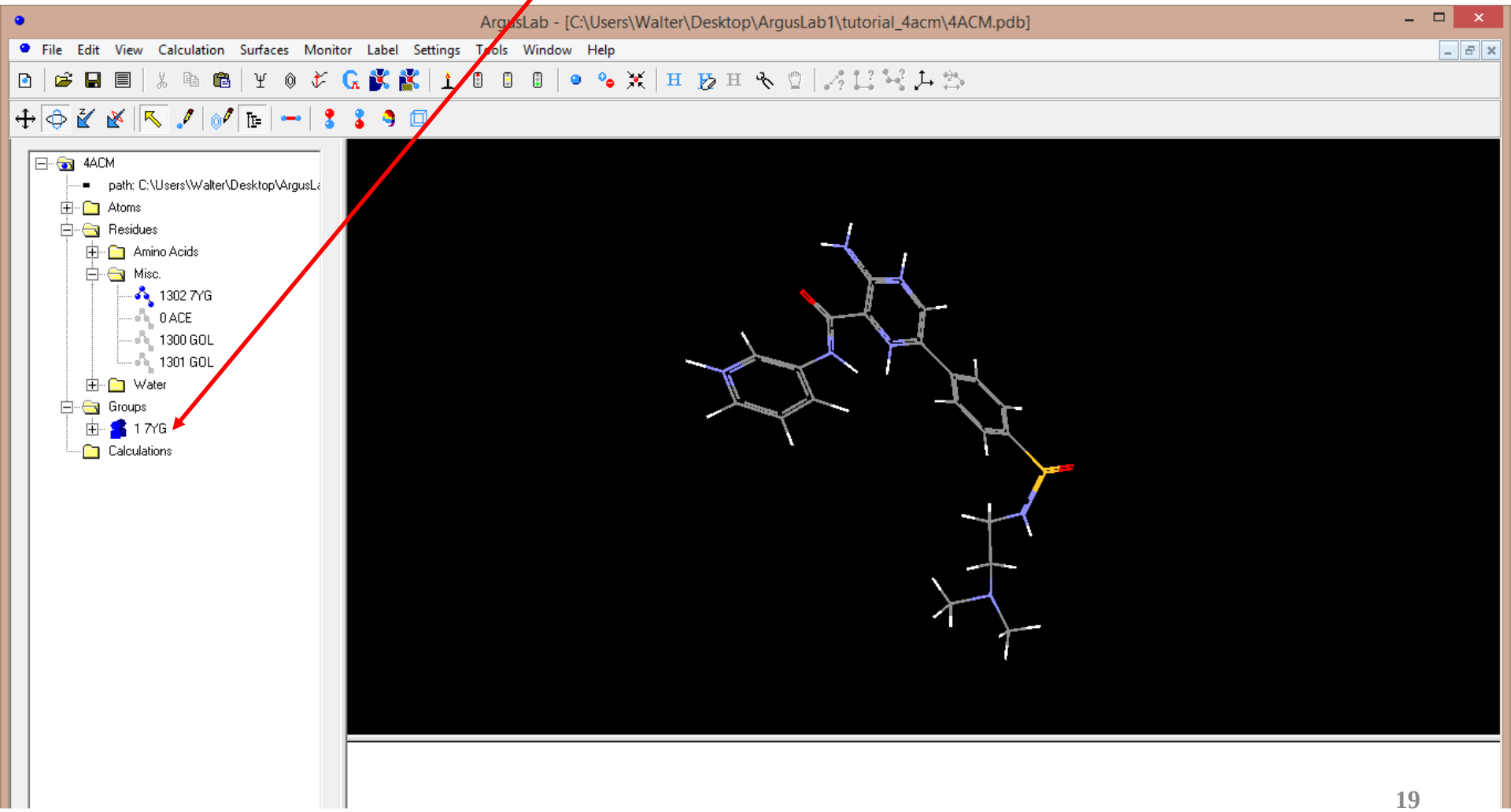
THOMSON REUTERS SCOPUS

Expand Groups folder in the Tree View.

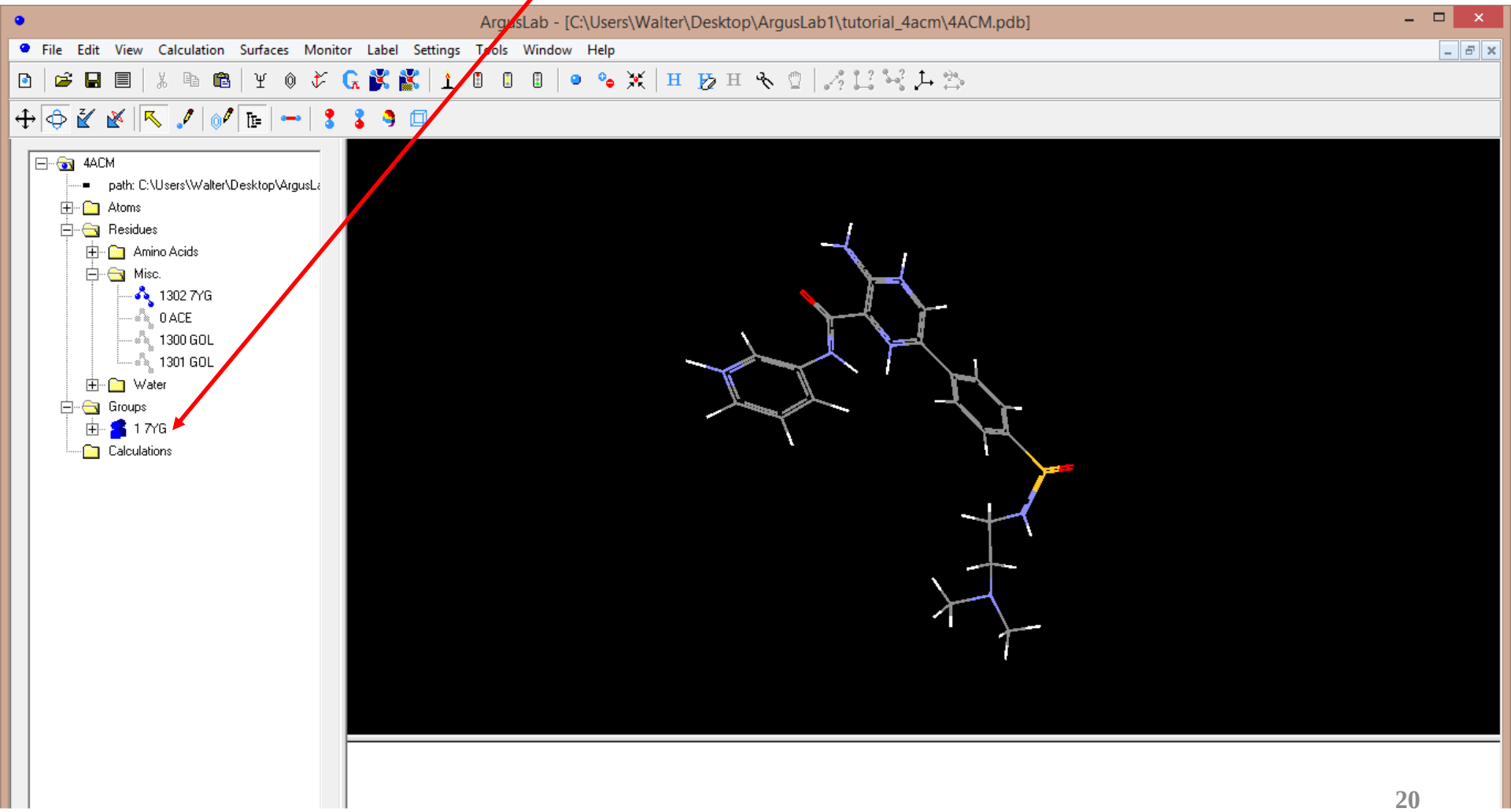


THOMSON REUTERS SCOPUS

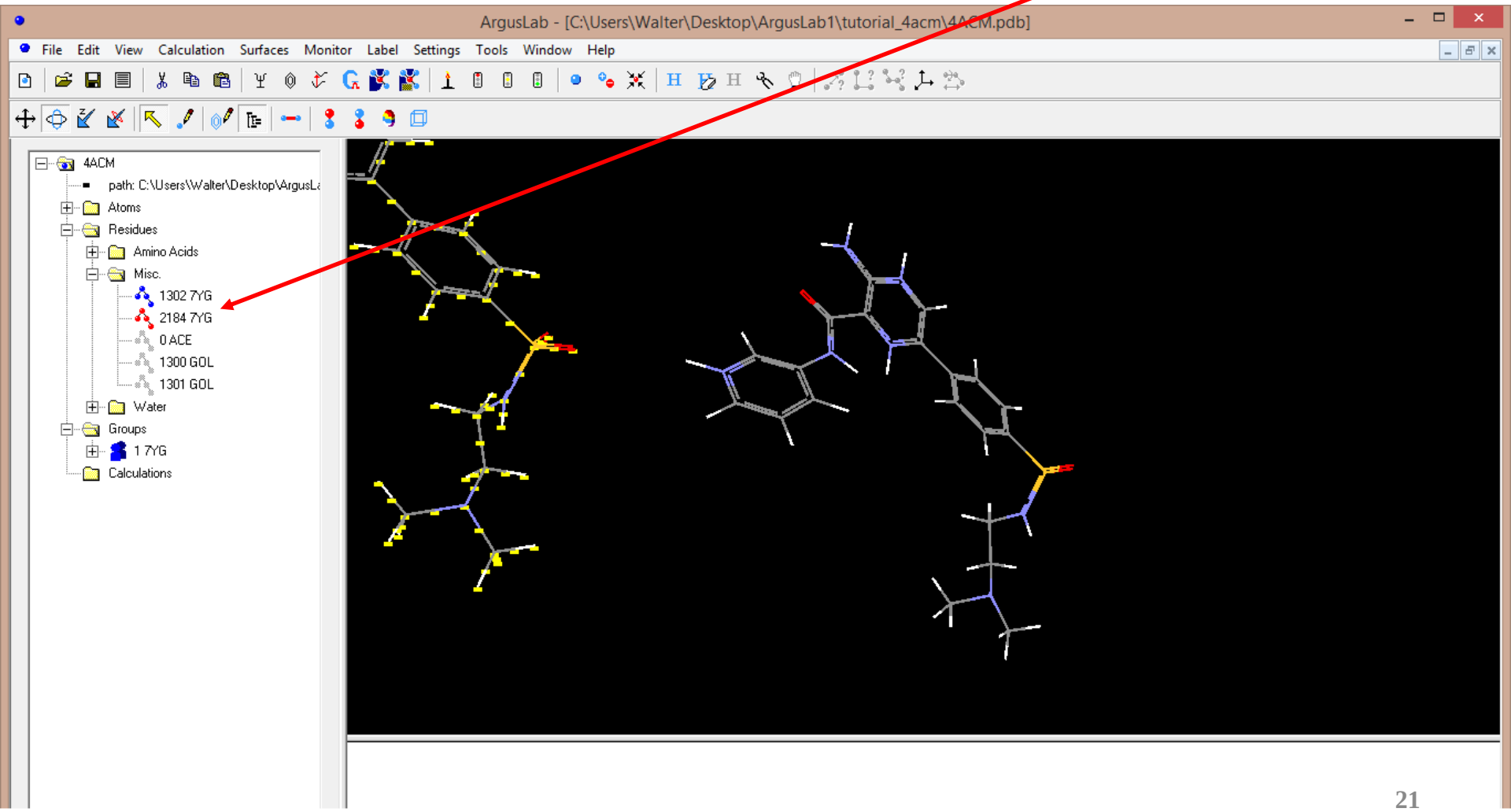
Now we have access to the ligand in the Groups folder.



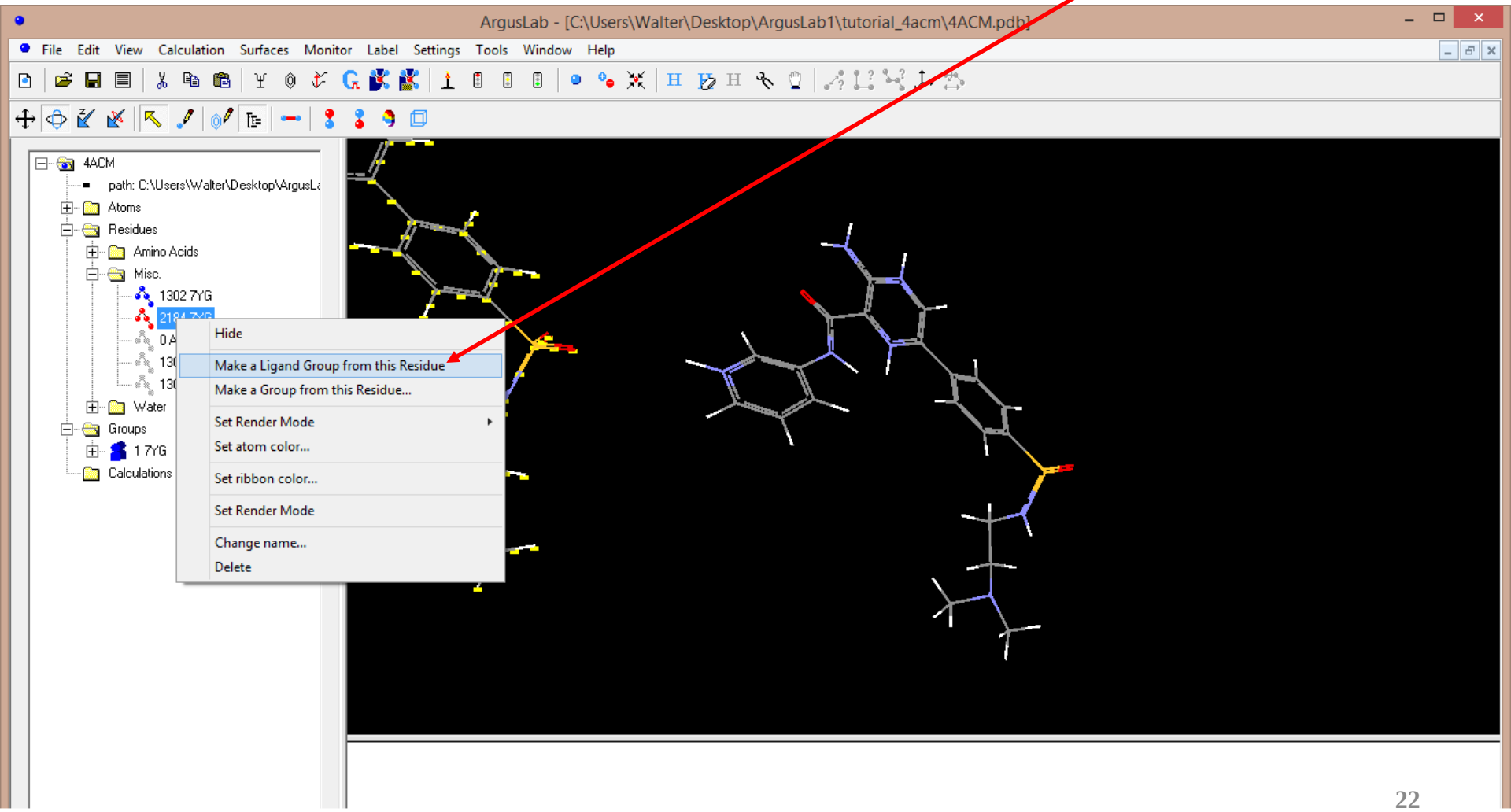
Left-click on “17YG” in the Groups folder to select the atoms of the ligand on the screen. Copy (Ctrl+C) and paste (Ctrl+V) the selected ligand.



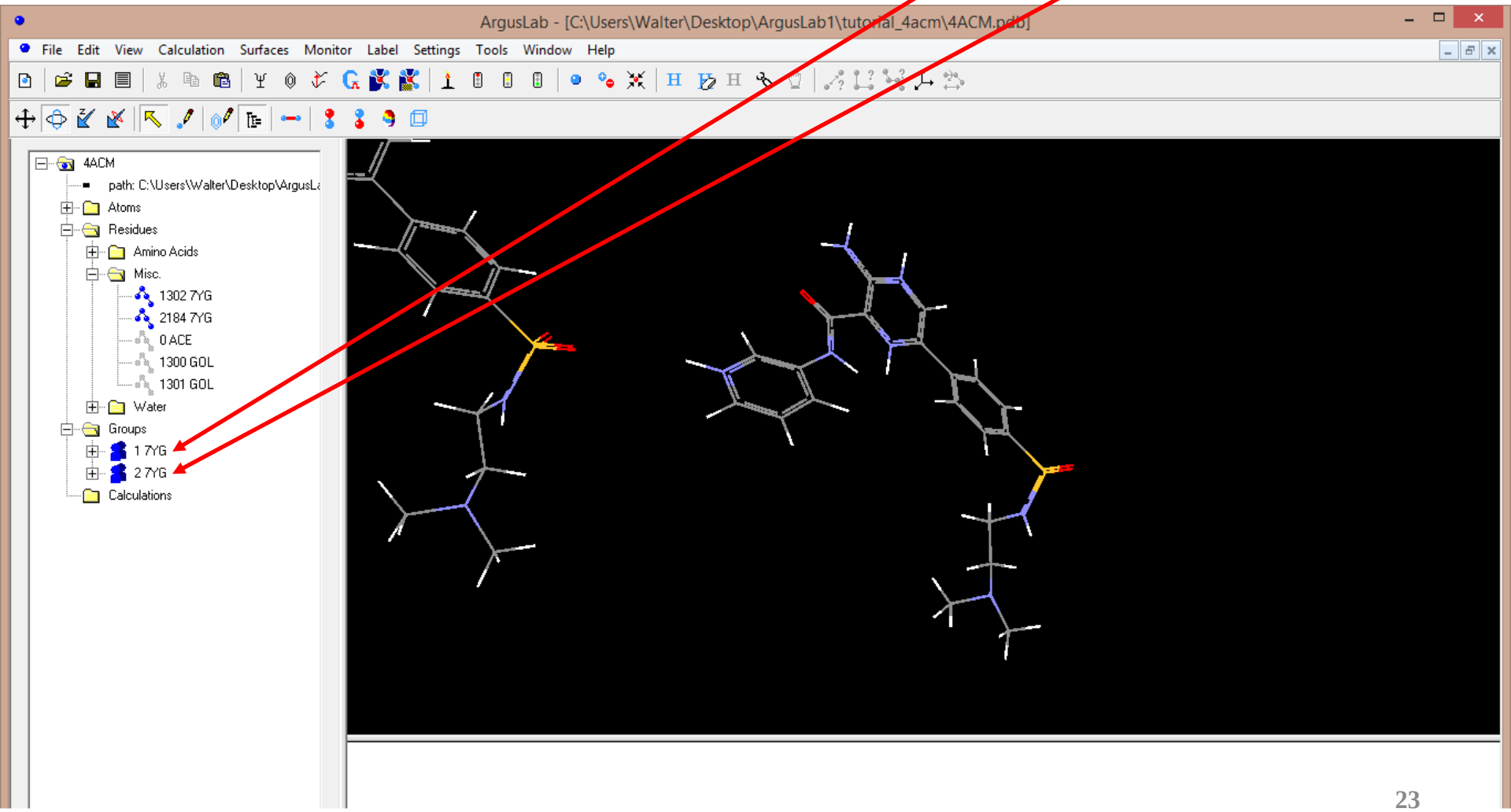
Expand the Misc. folder and you will see the copy of the ligand named “2184 7YG”.



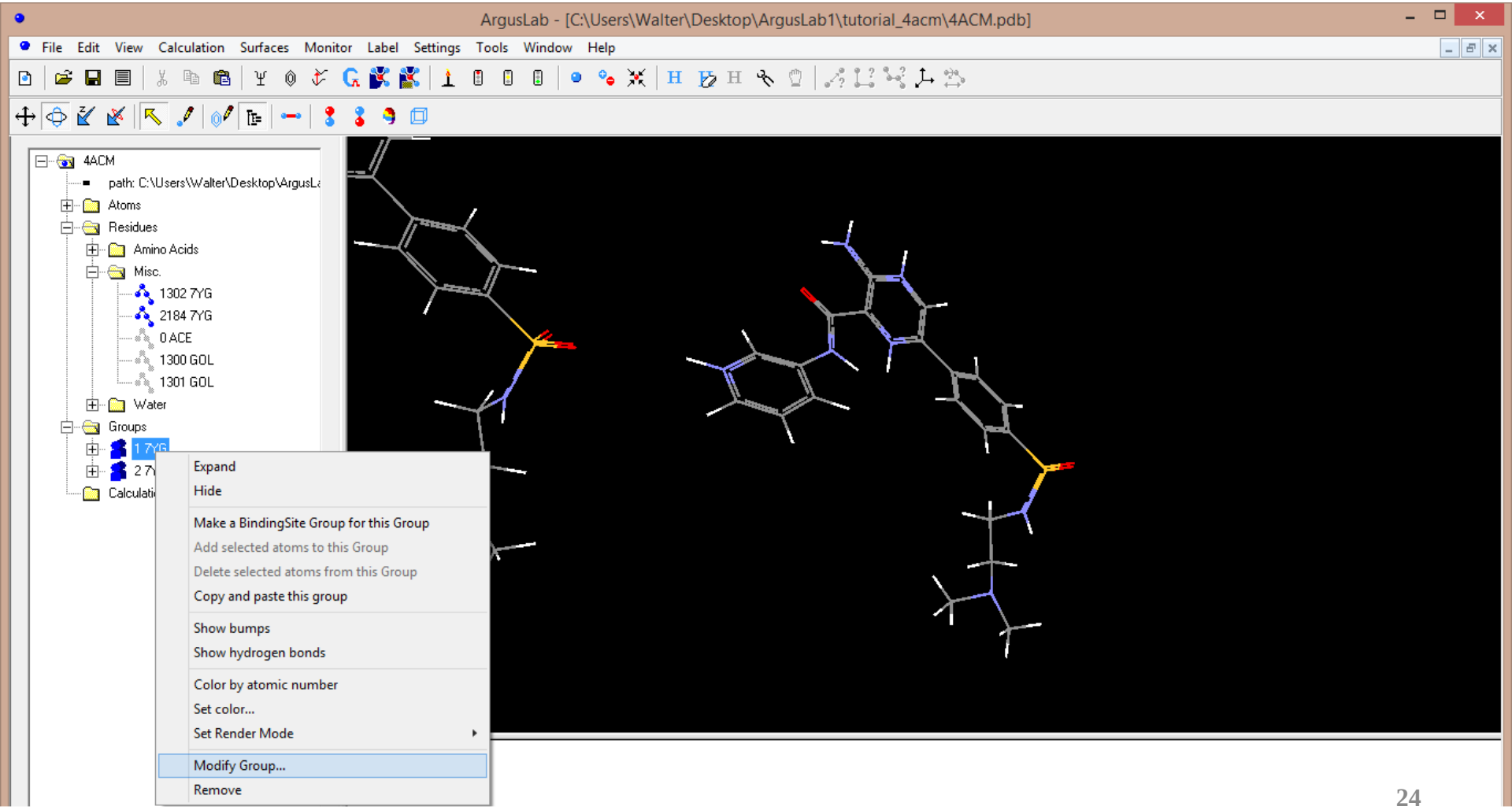
Right click on “2184 7YG” on the Tree View and select “Make a Ligand Group from This Residue” option, as shown below.



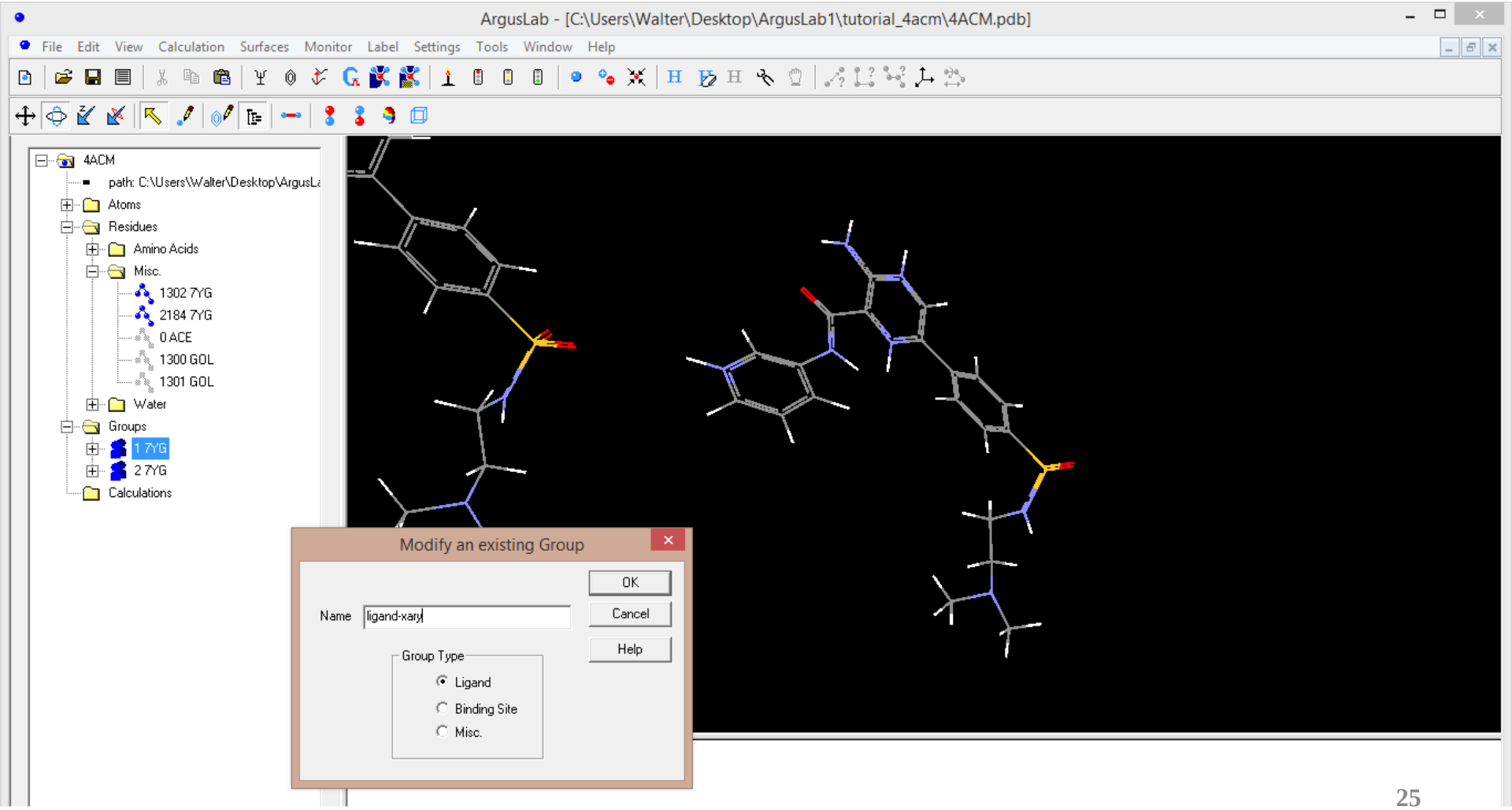
Now we have two ligands in the Groups folder named “1 7YG” and “2 7YG”. We have to rename these ligands to “ligand-xray” and “ligand”, respectively.



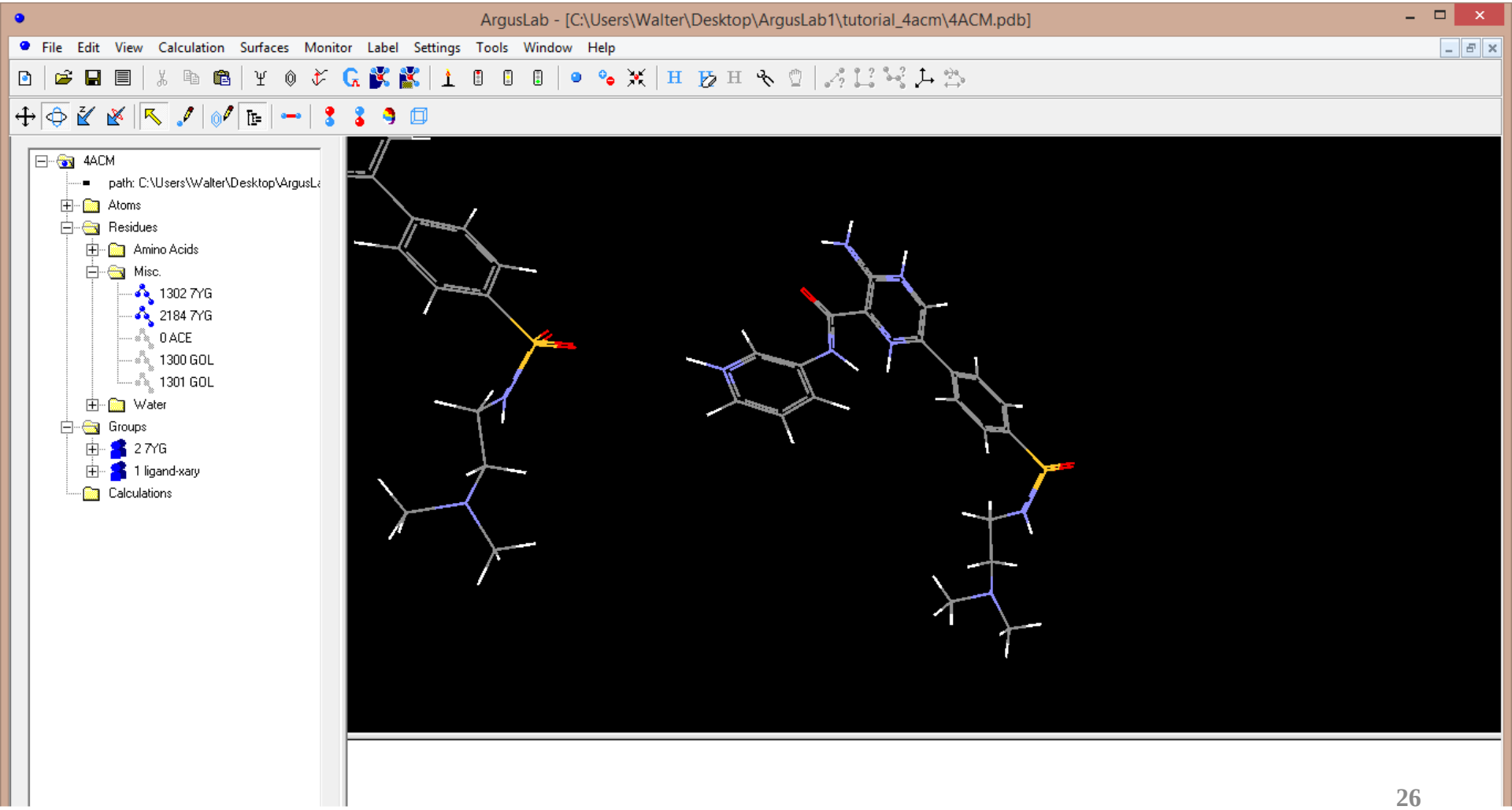
Right-click on “1 7YG” in the Groups folder and select “Modify group...” option, as shown below.



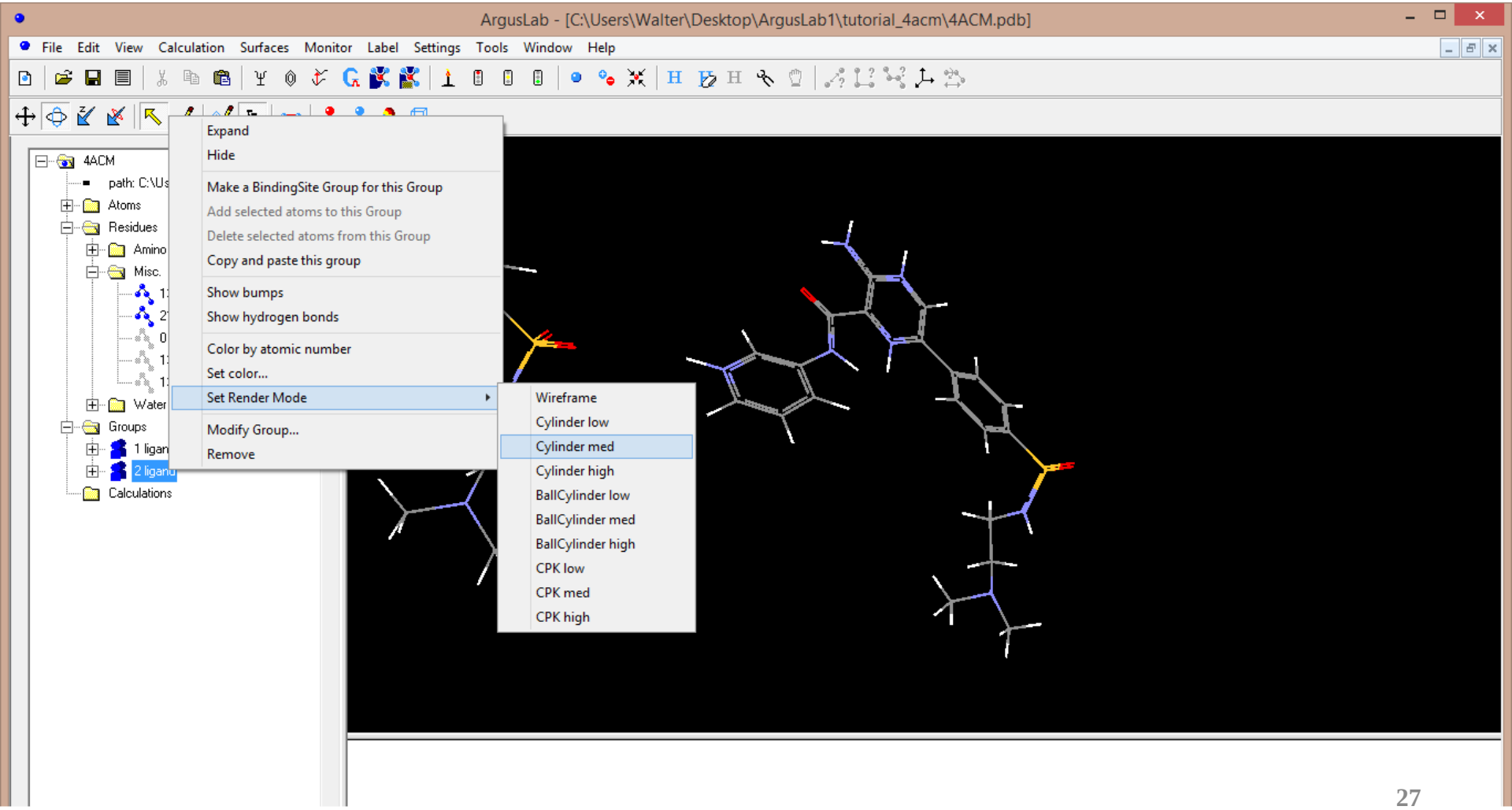
In the “Modify group...” Dialog box, type in the “ligand-xray”. Don’t change the Groups type.



Do the same to the “2 7YG” and rename it to “ligand”.

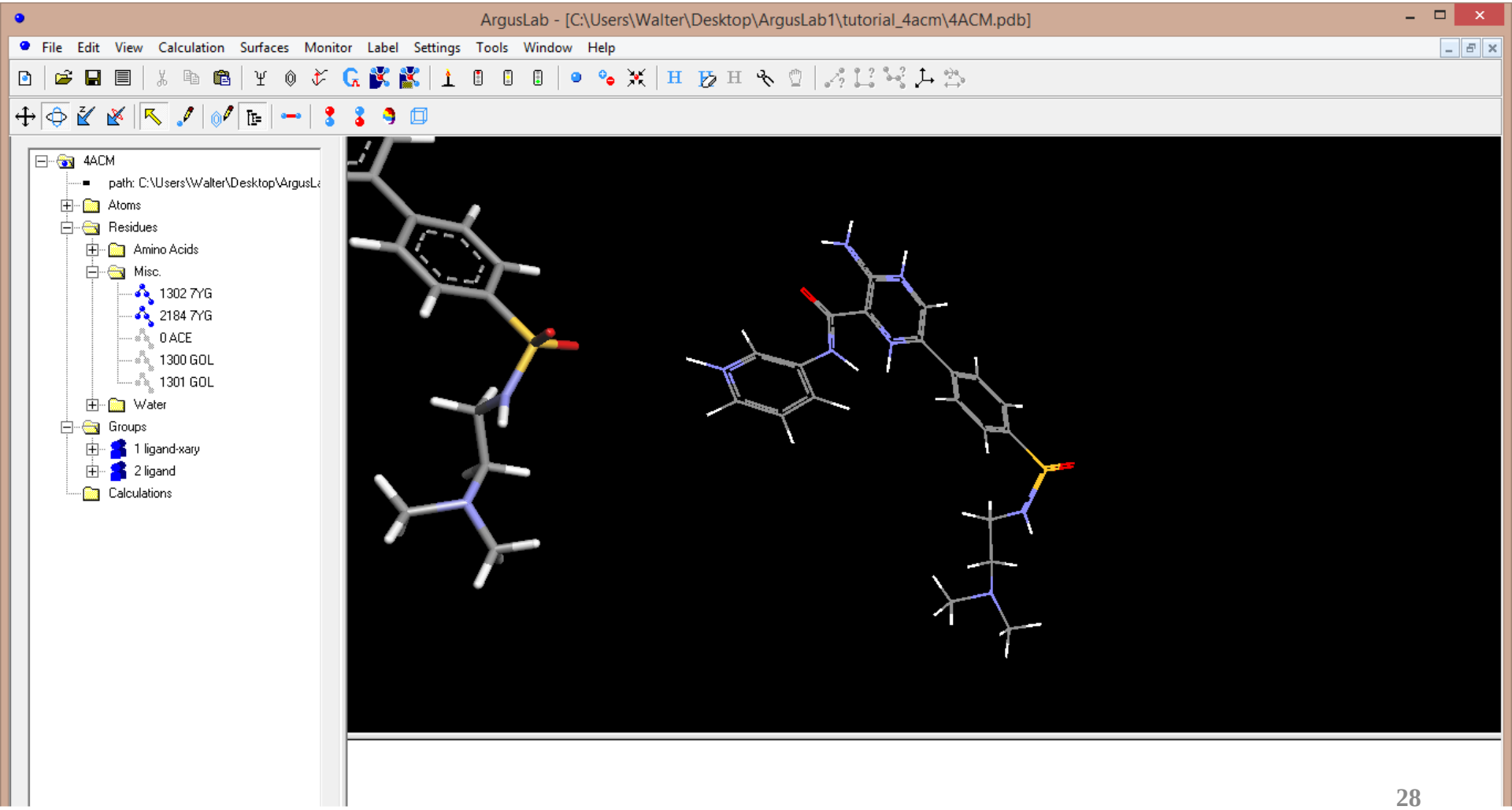


Right-click on the ligand and select “Set Render Mode” and choose “Cylinder med” option, as shown below.

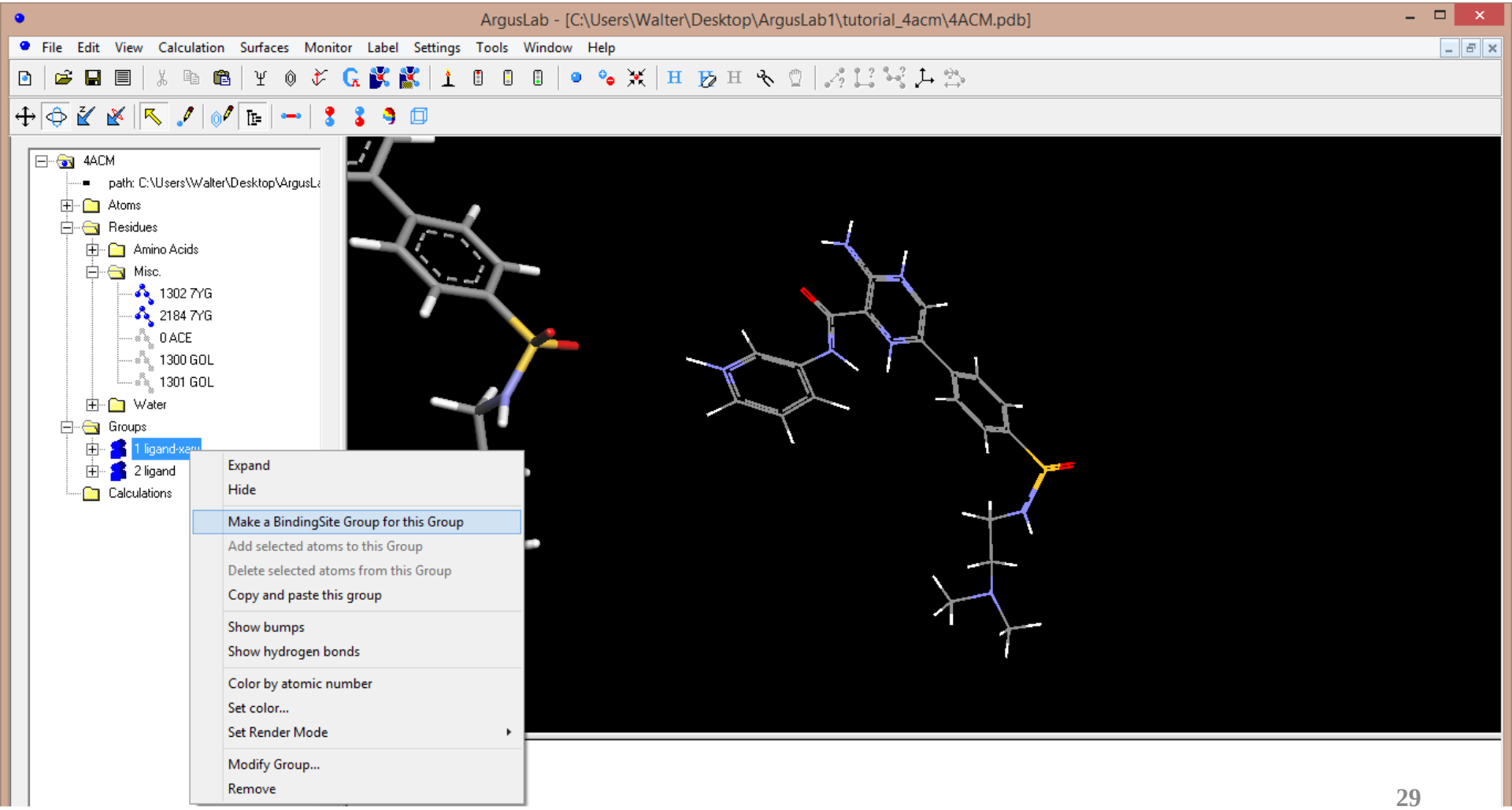


THOMSON REUTERS SCOPUS

You will have the following view.

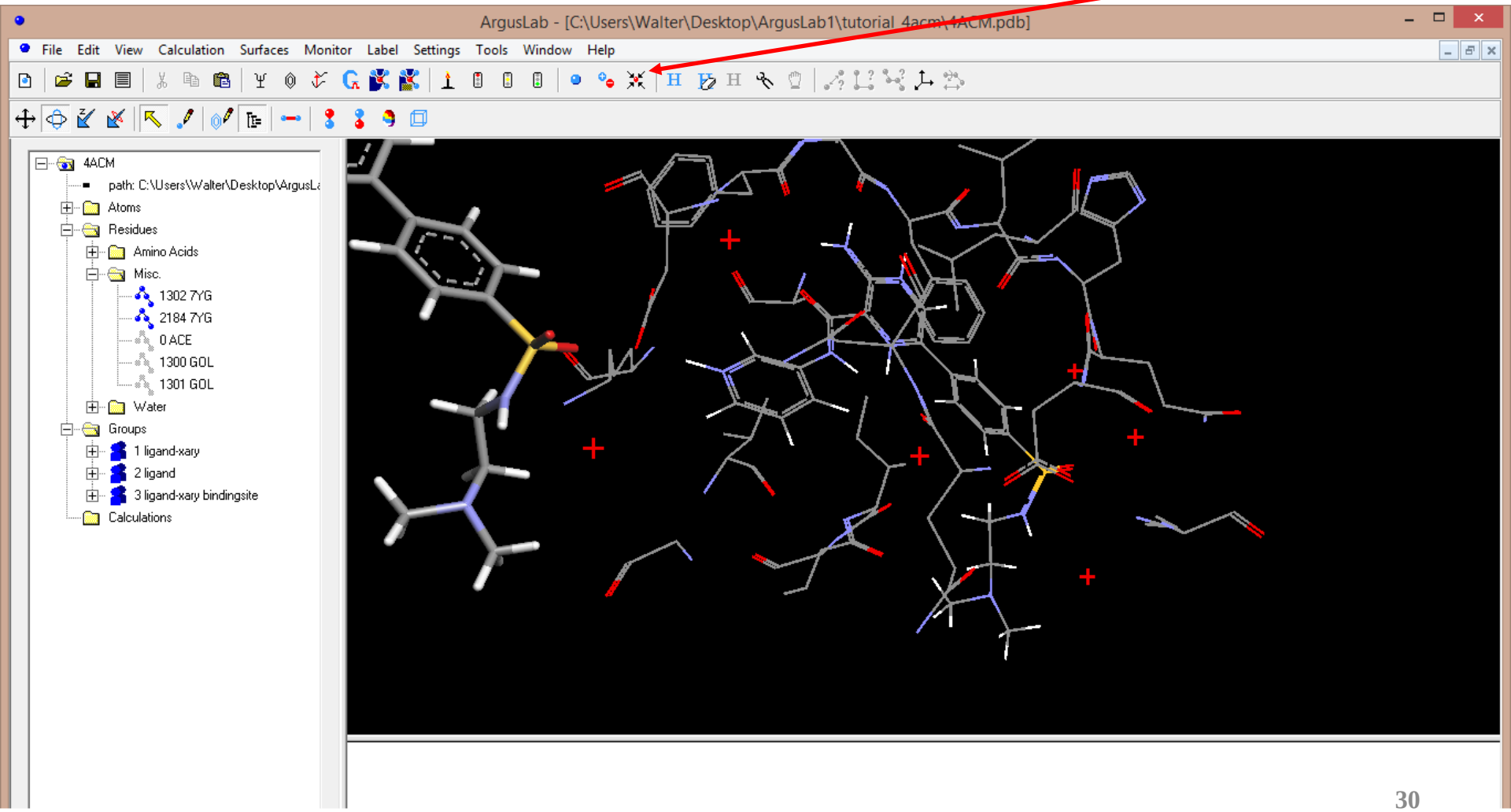


Right-click on the ligand-xray in the Groups folder and choose “Make a BindingSite Group for this Group”, as shown below.



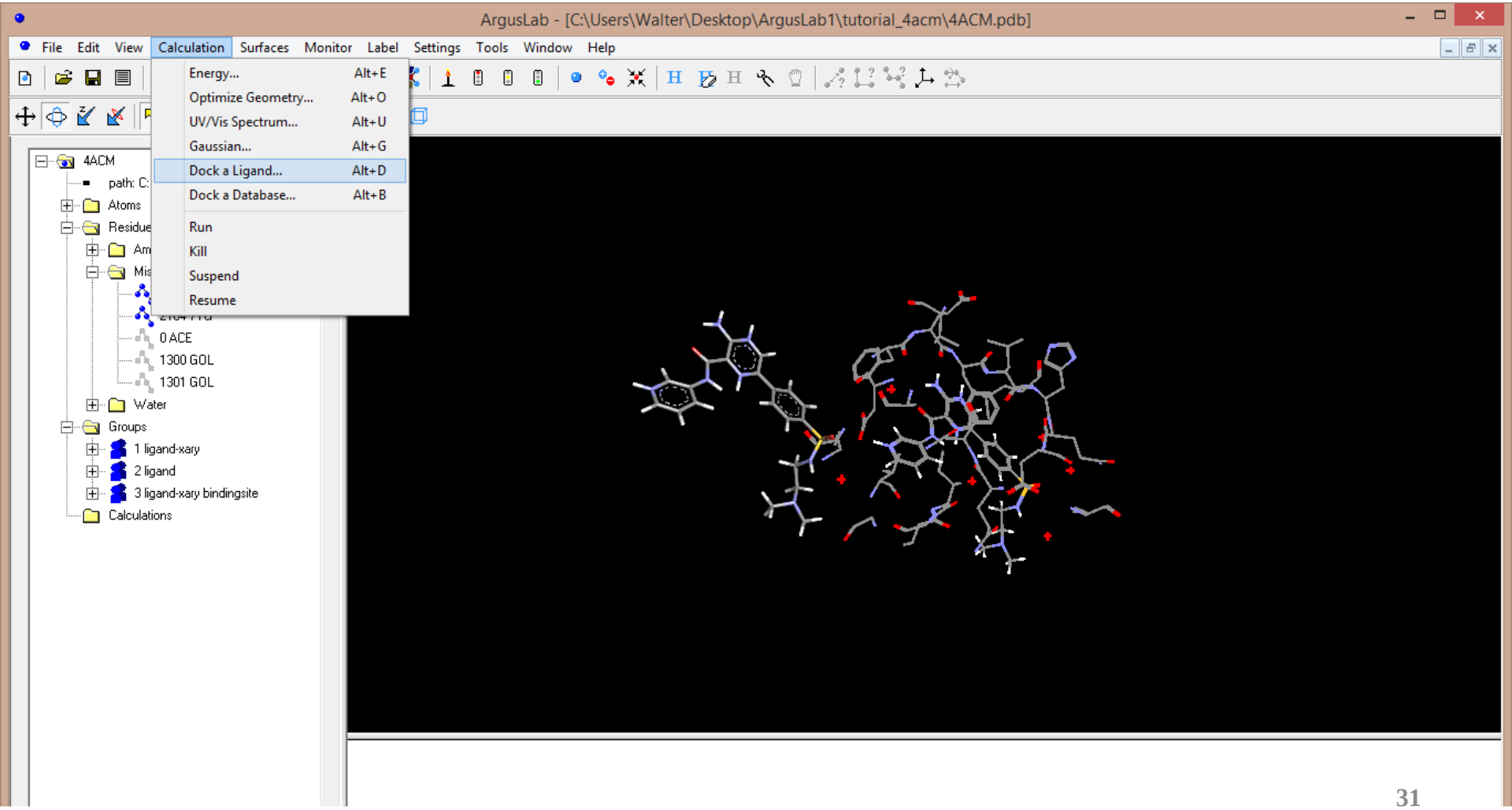
THOMSON REUTERS SCOPUS

Now we have the binding site as show below. Center the molecules by clicking here.



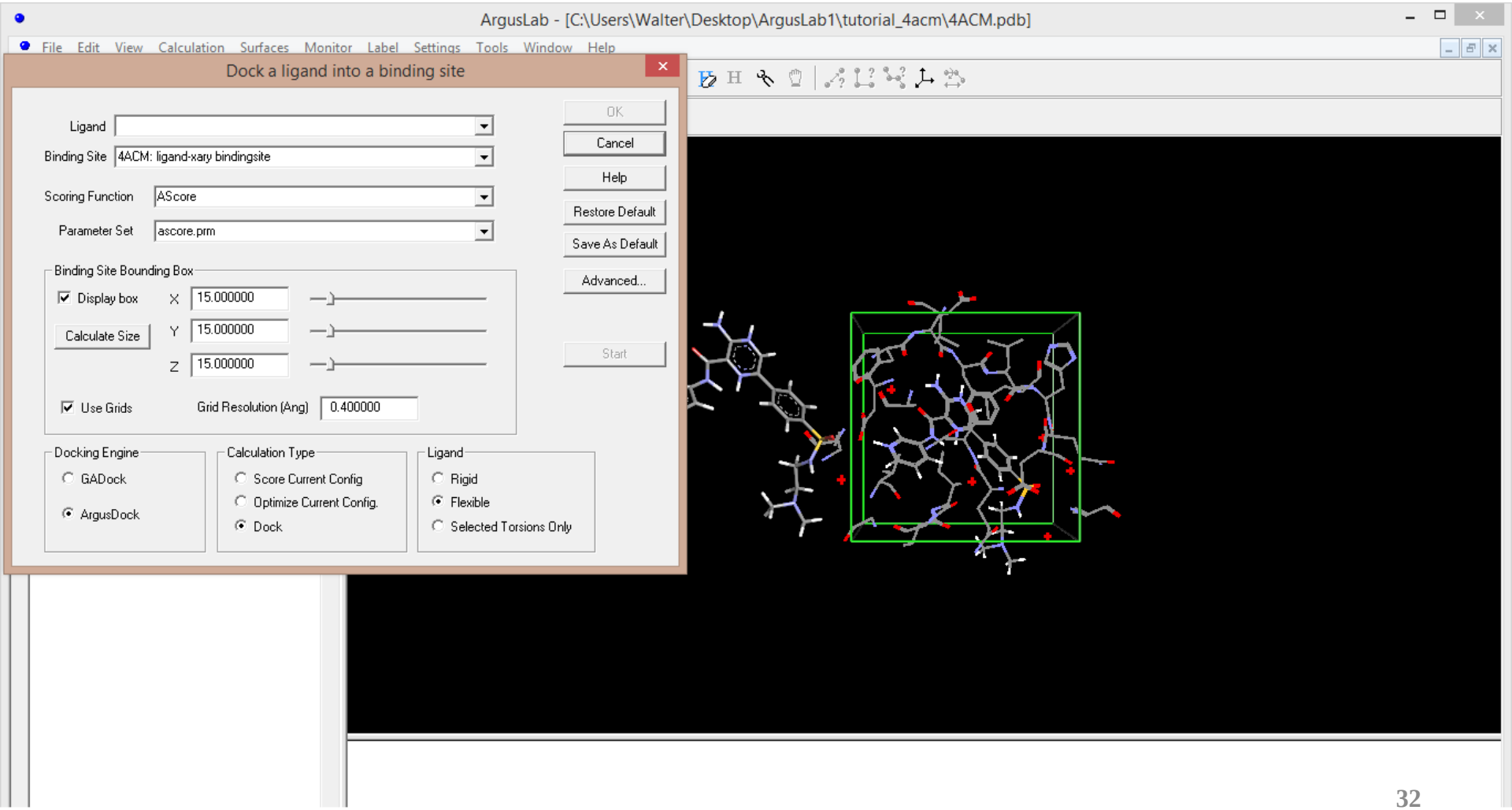
THOMSON REUTERS SCOPUS

Click on Calculation>Dock a Ligand...

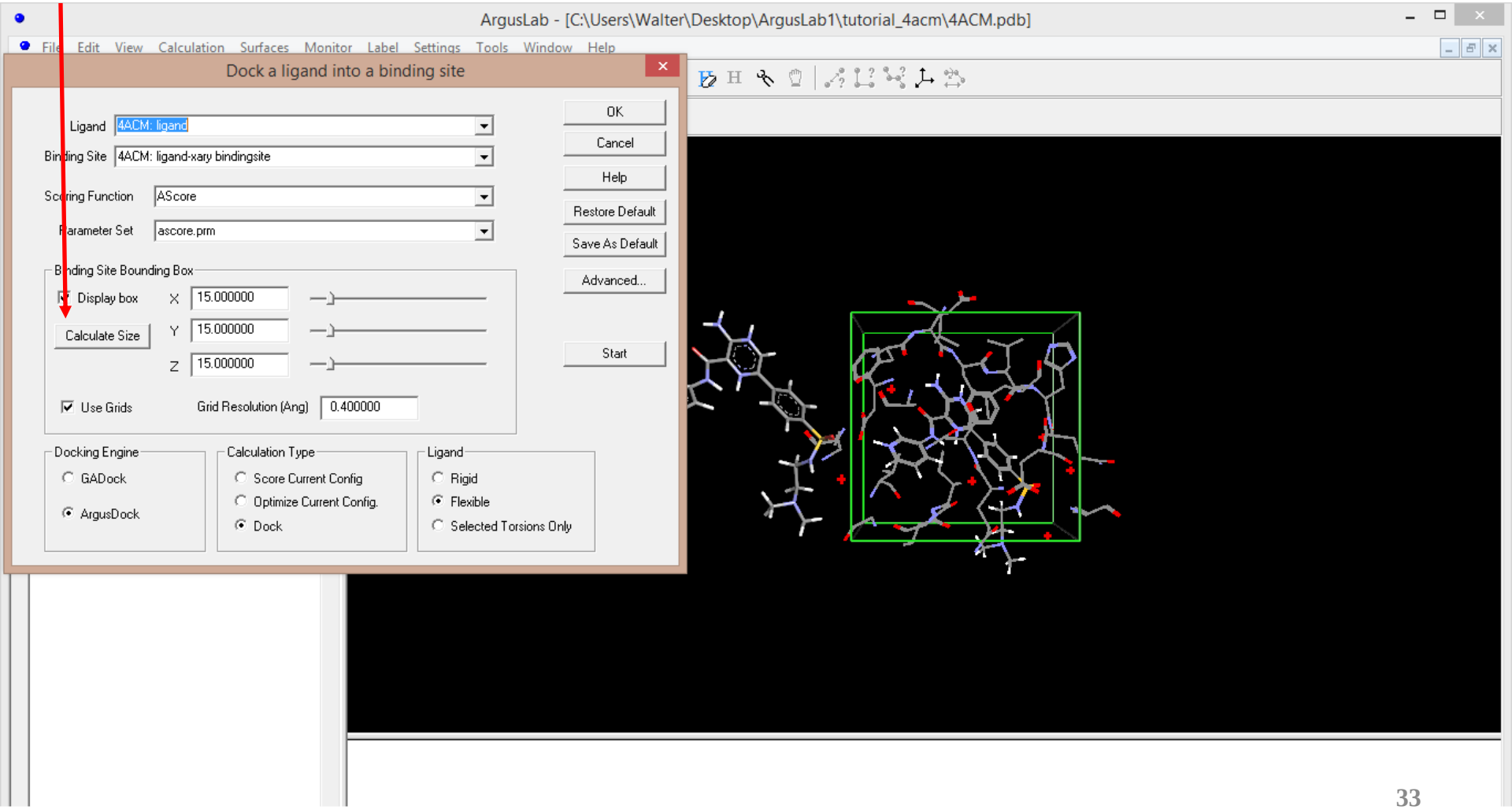


THOMSON REUTERS SCOPUS

We have the dialog box to enter docking parameters.

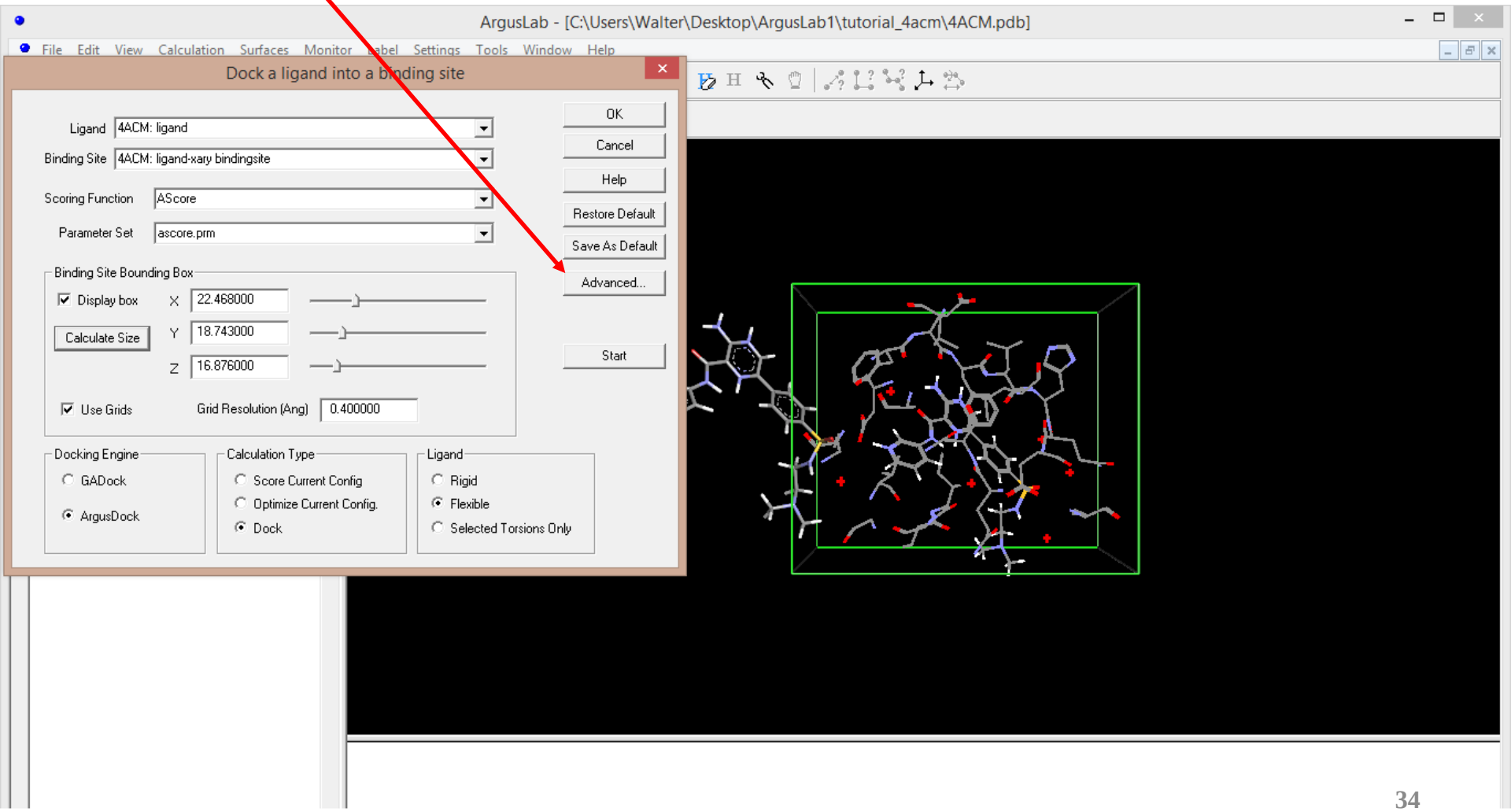


Select “4ACM: ligand” on Ligand drop box, as shown below. Then press “Calculate Size” button.



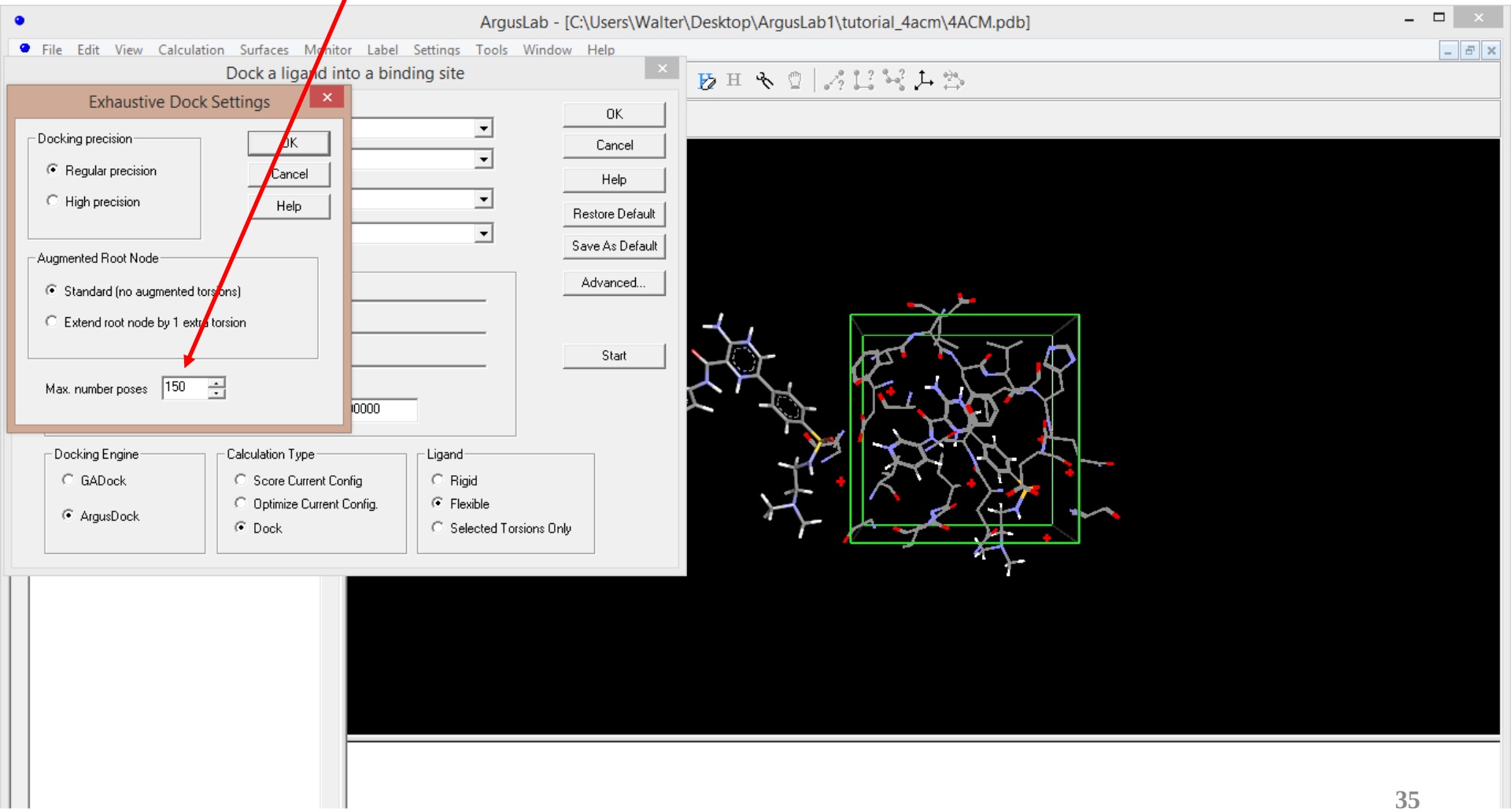
THOMSON REUTERS SCOPUS

Press the “Advanced...” button.



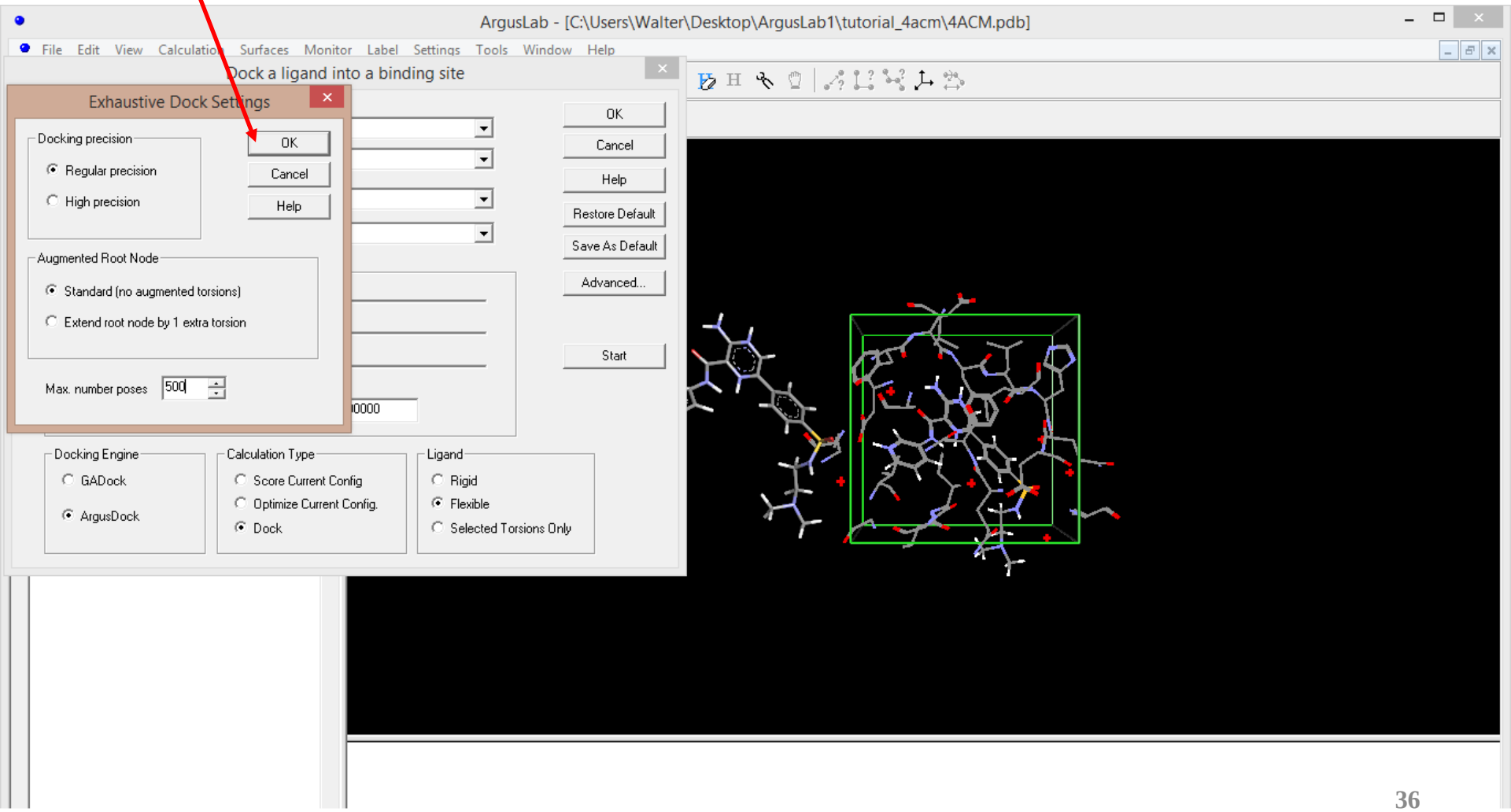
THOMSON REUTERS SCOPUS

Change “Max. number of poses” to 500.



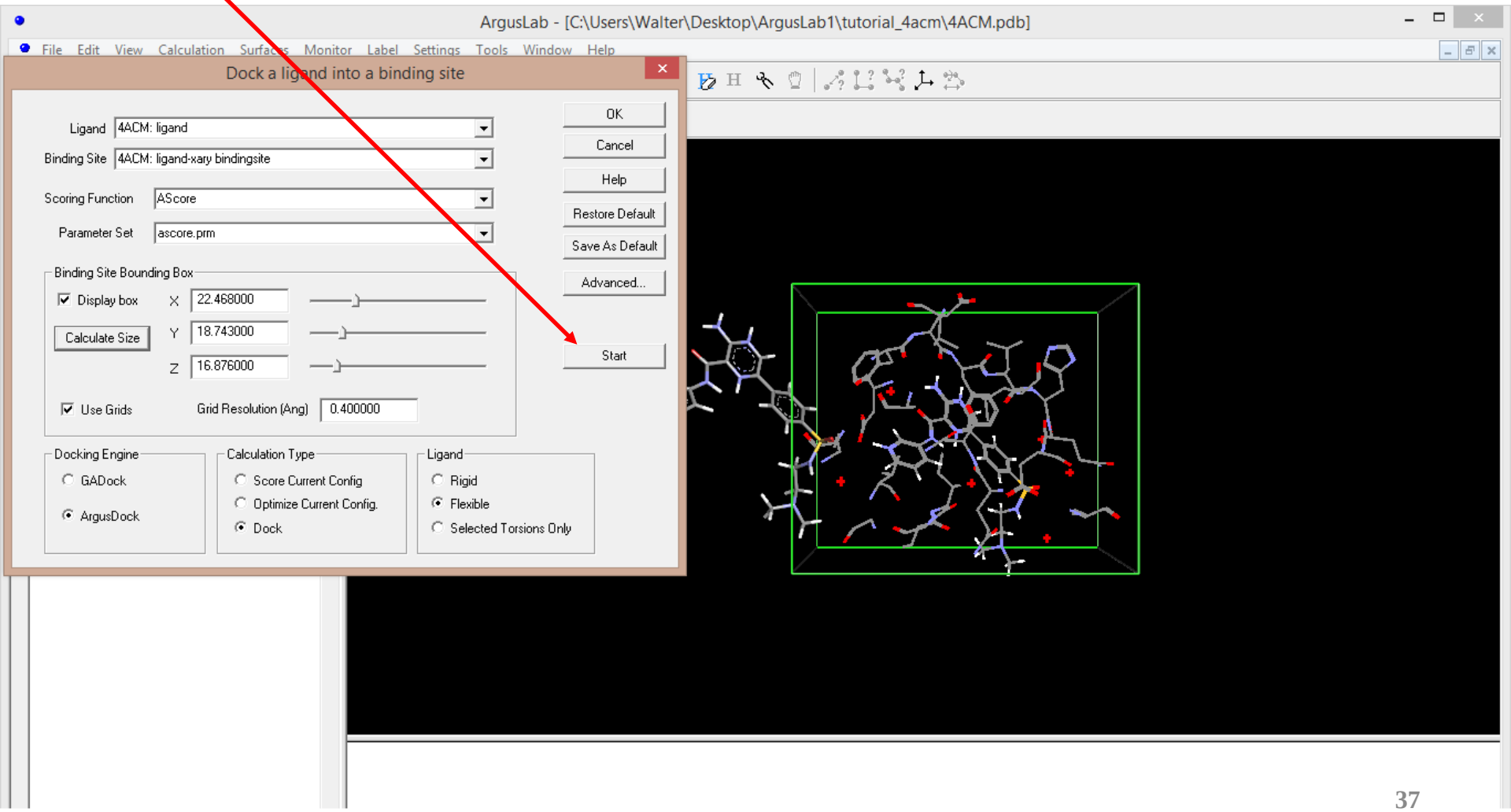
THOMSON REUTERS SCOPUS

Press “OK” button.



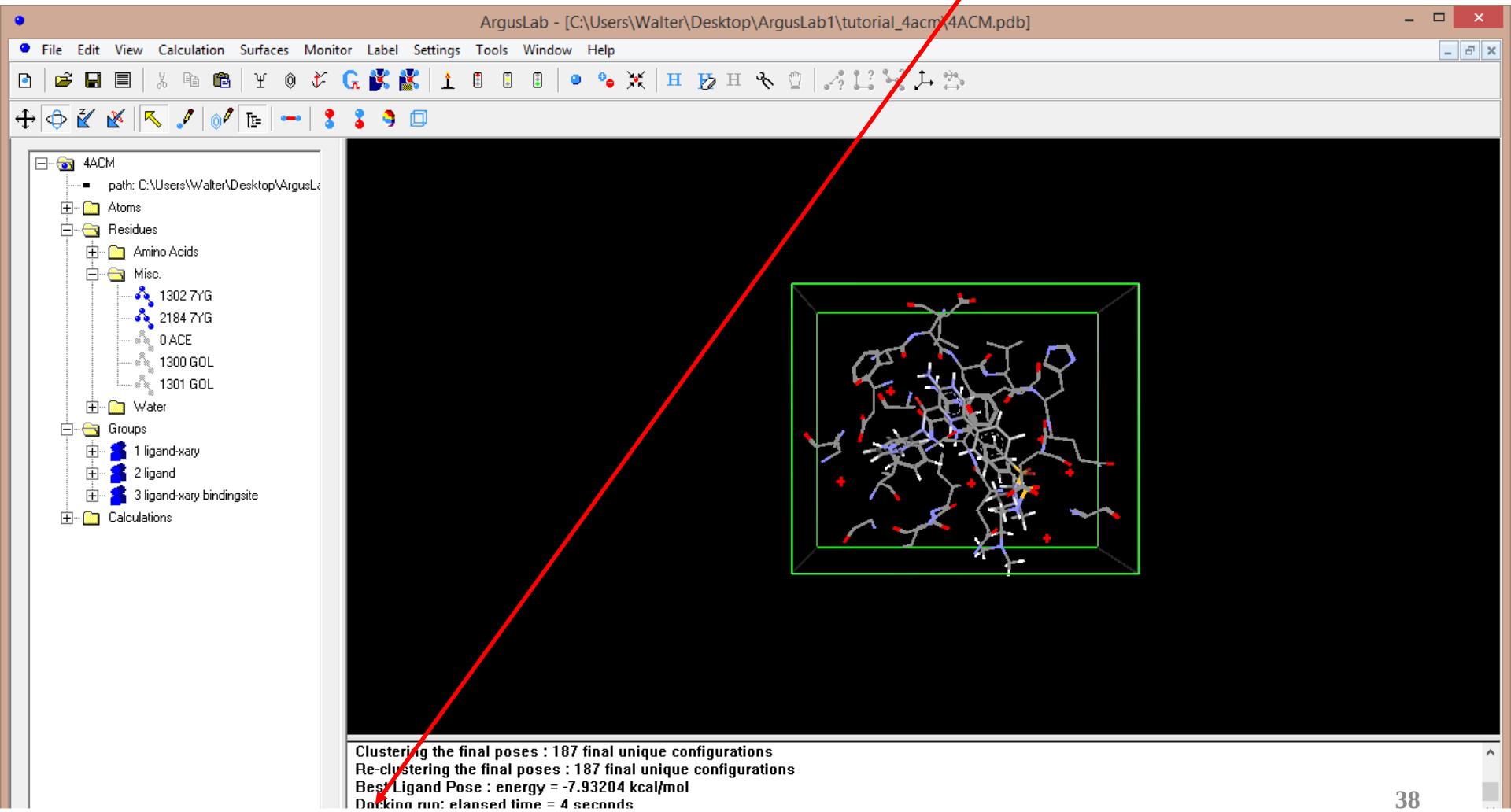
THOMSON REUTERS SCOPUS

Press “Start” button to initiate docking simulation.

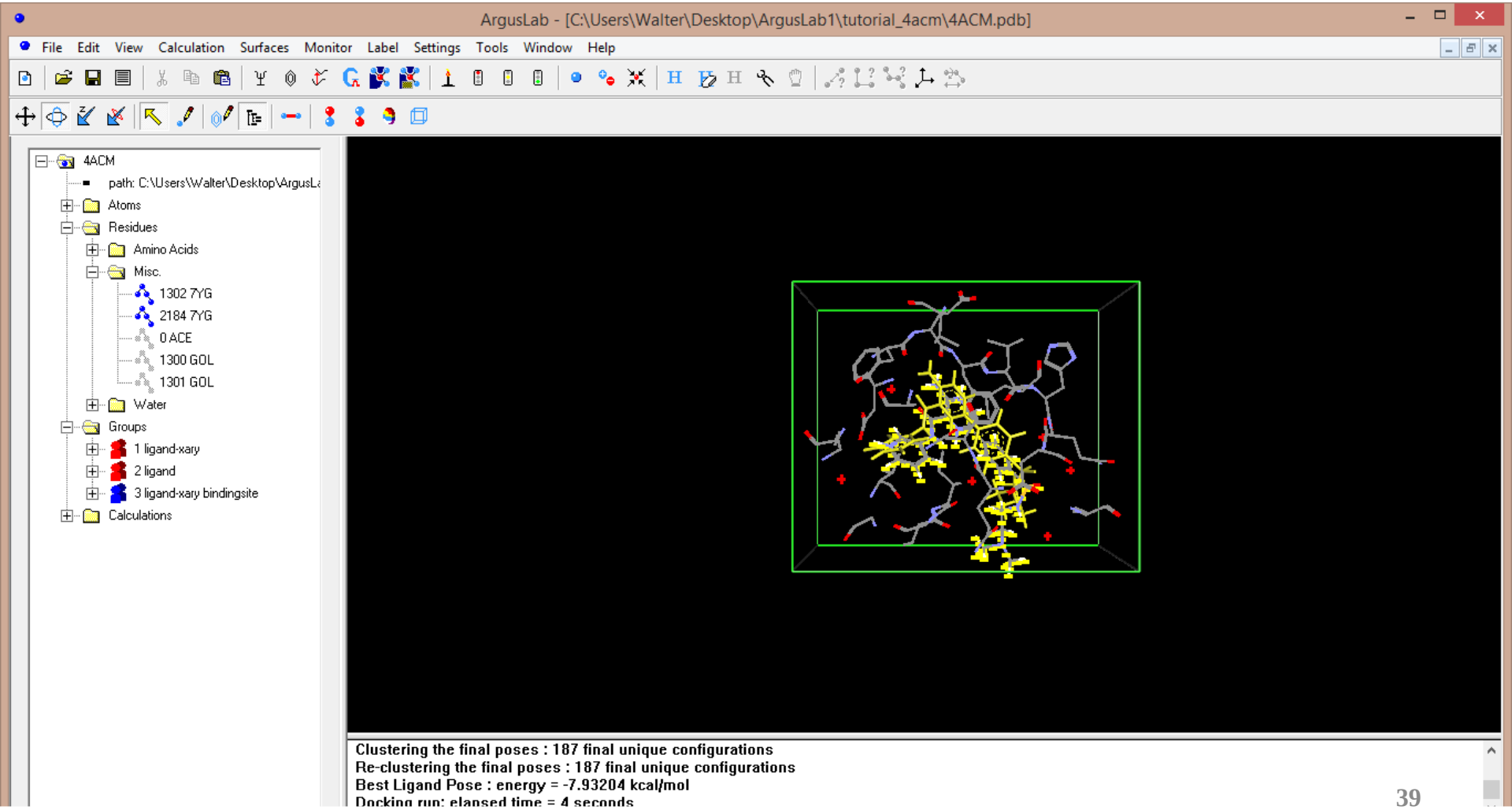


THOMSON REUTERS SCOPUS

After few seconds you will see the message “Docking run: elapsed time...”

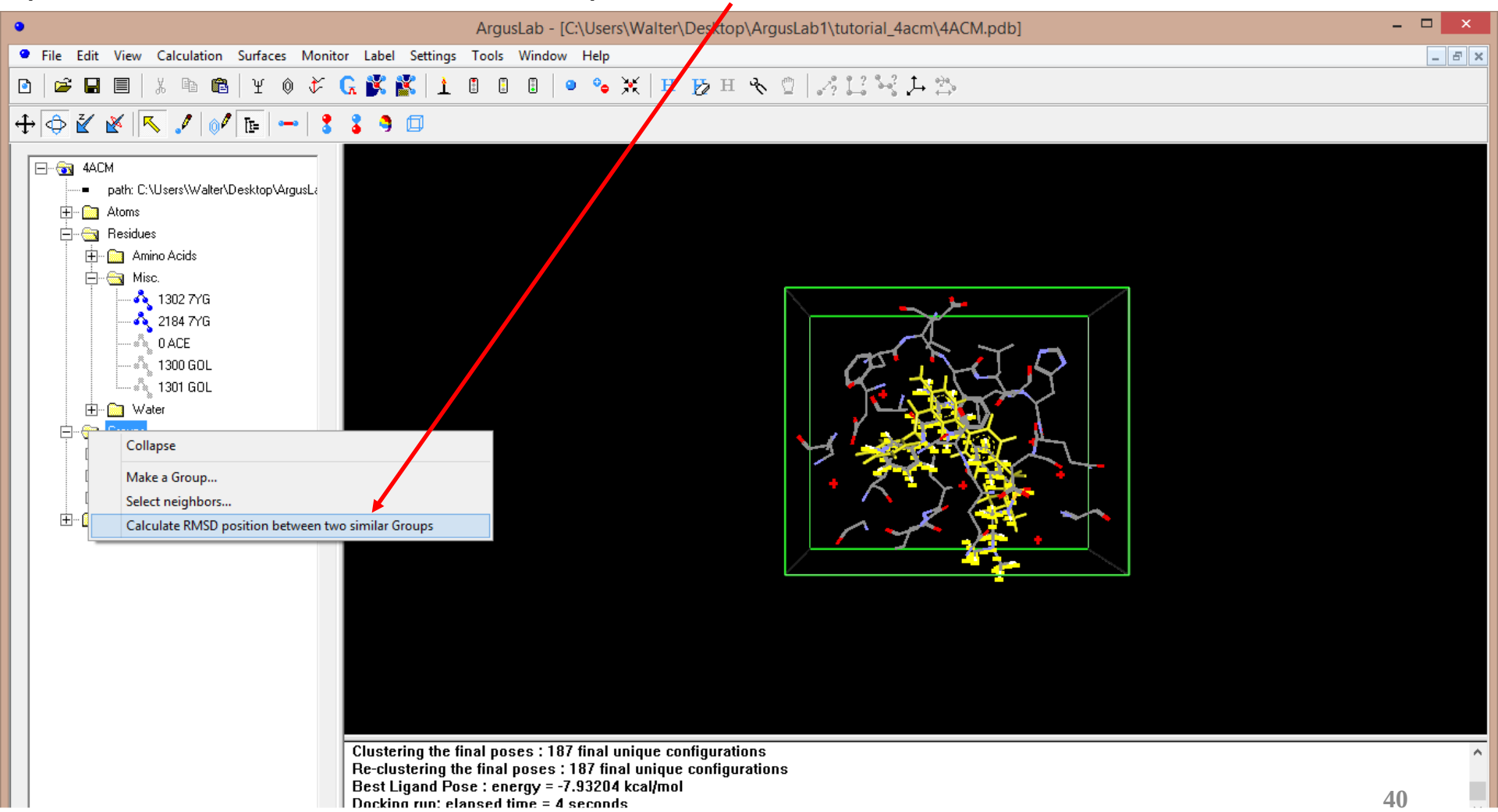


In the Tree View tool, select ligand and ligand-xray by holding down the “Ctrl” key and left-clicking on both groups. You will have the following screen.



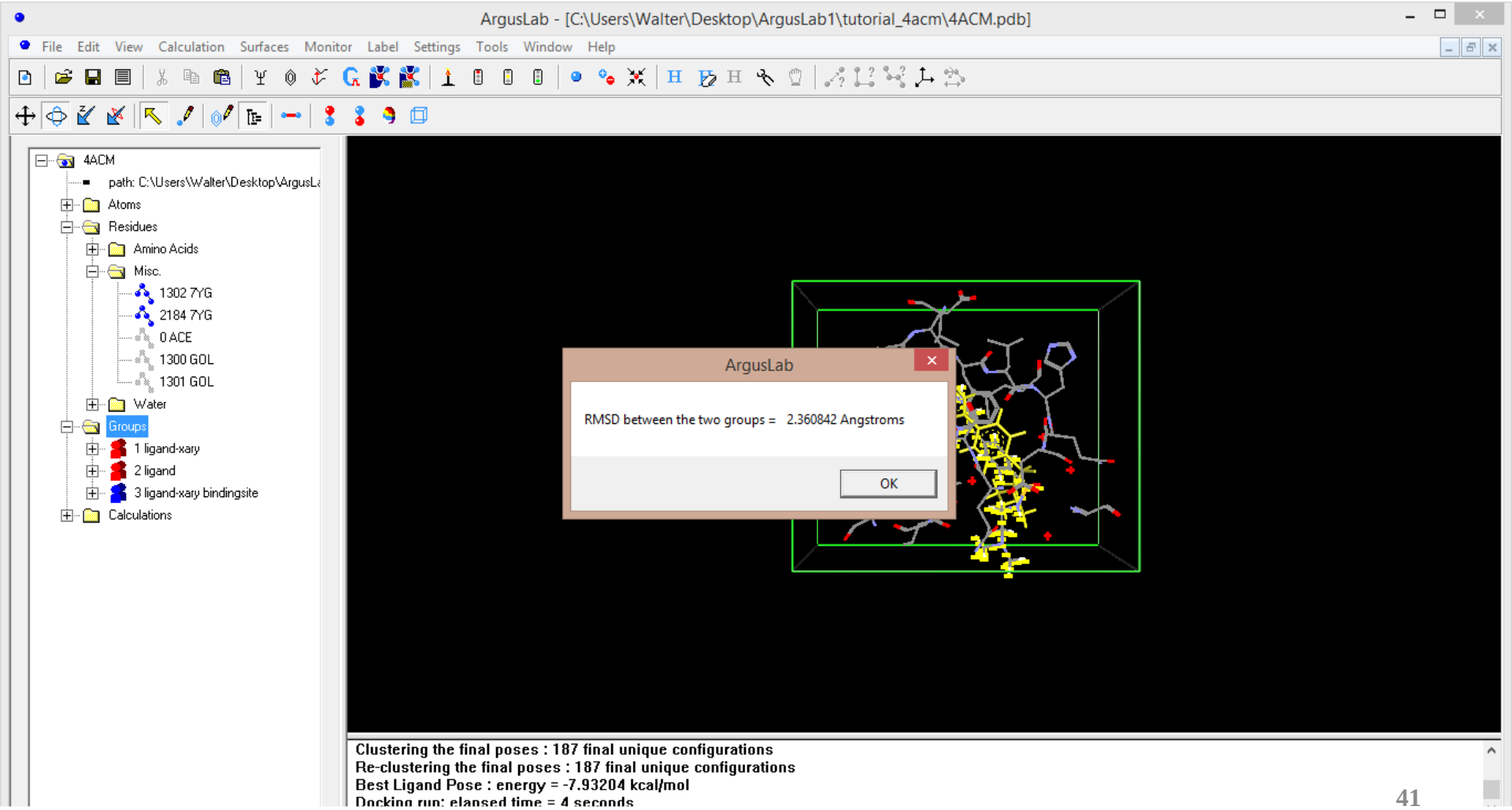
THOMSON REUTERS SCOPUS

Right-click on the “Groups” folder tab in the Tree View and select “Calc RMSD position between two similar Groups”, as shown below.



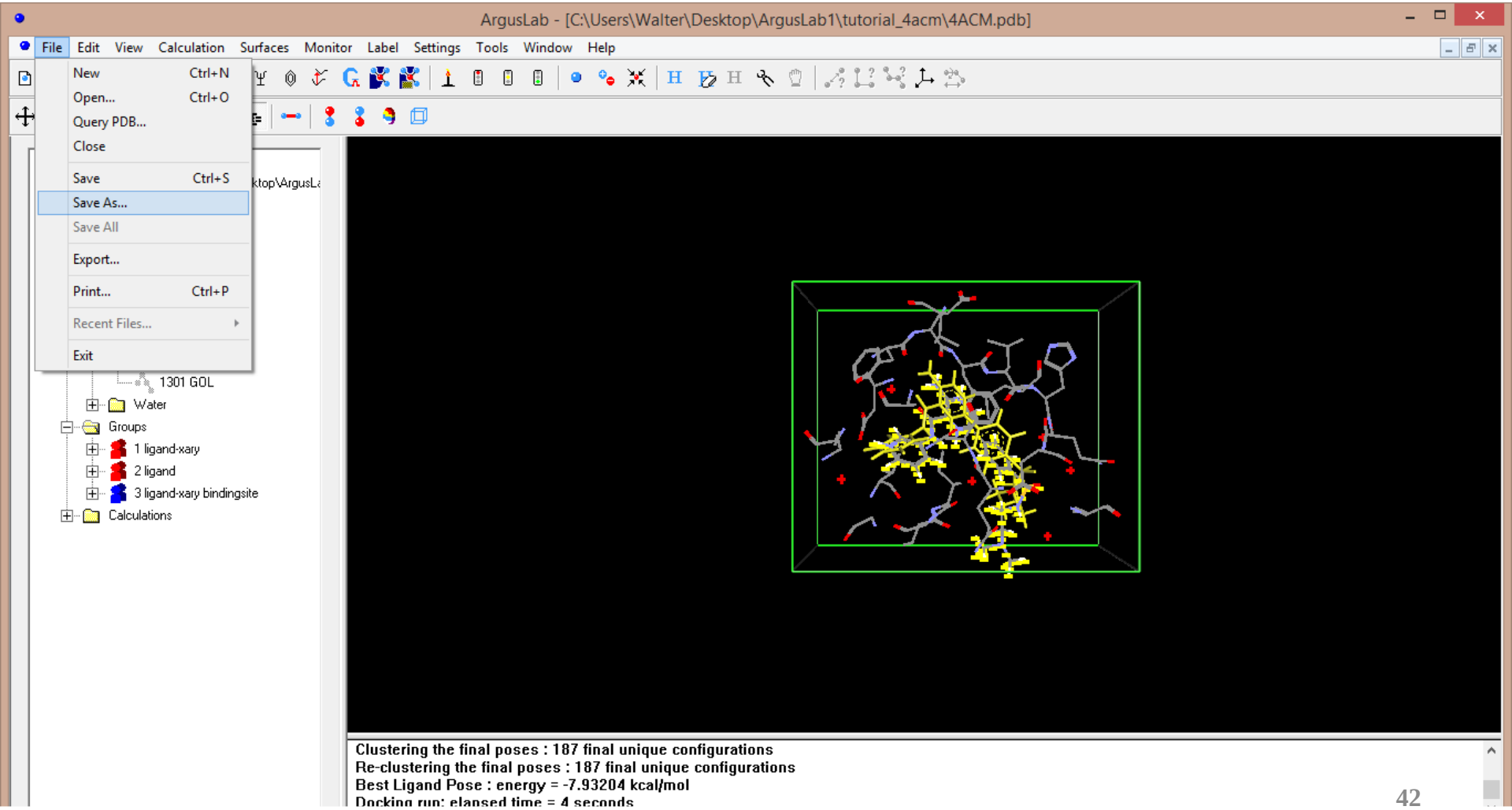
THOMSON REUTERS SCOPUS

We have the docking RMSD between crystallographic position and pose.



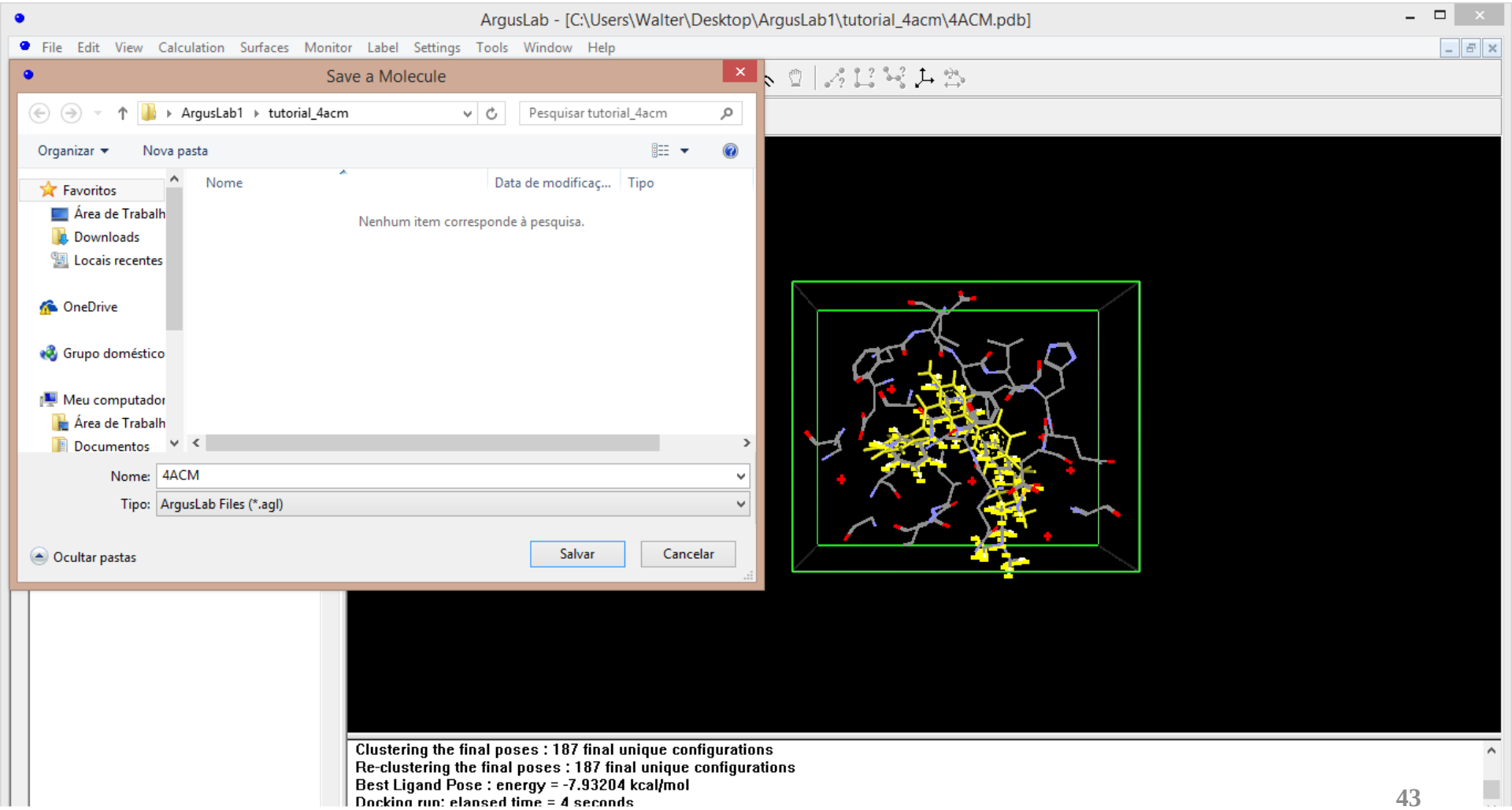
THOMSON REUTERS SCOPUS

Click on File>Save as..., as shown below.



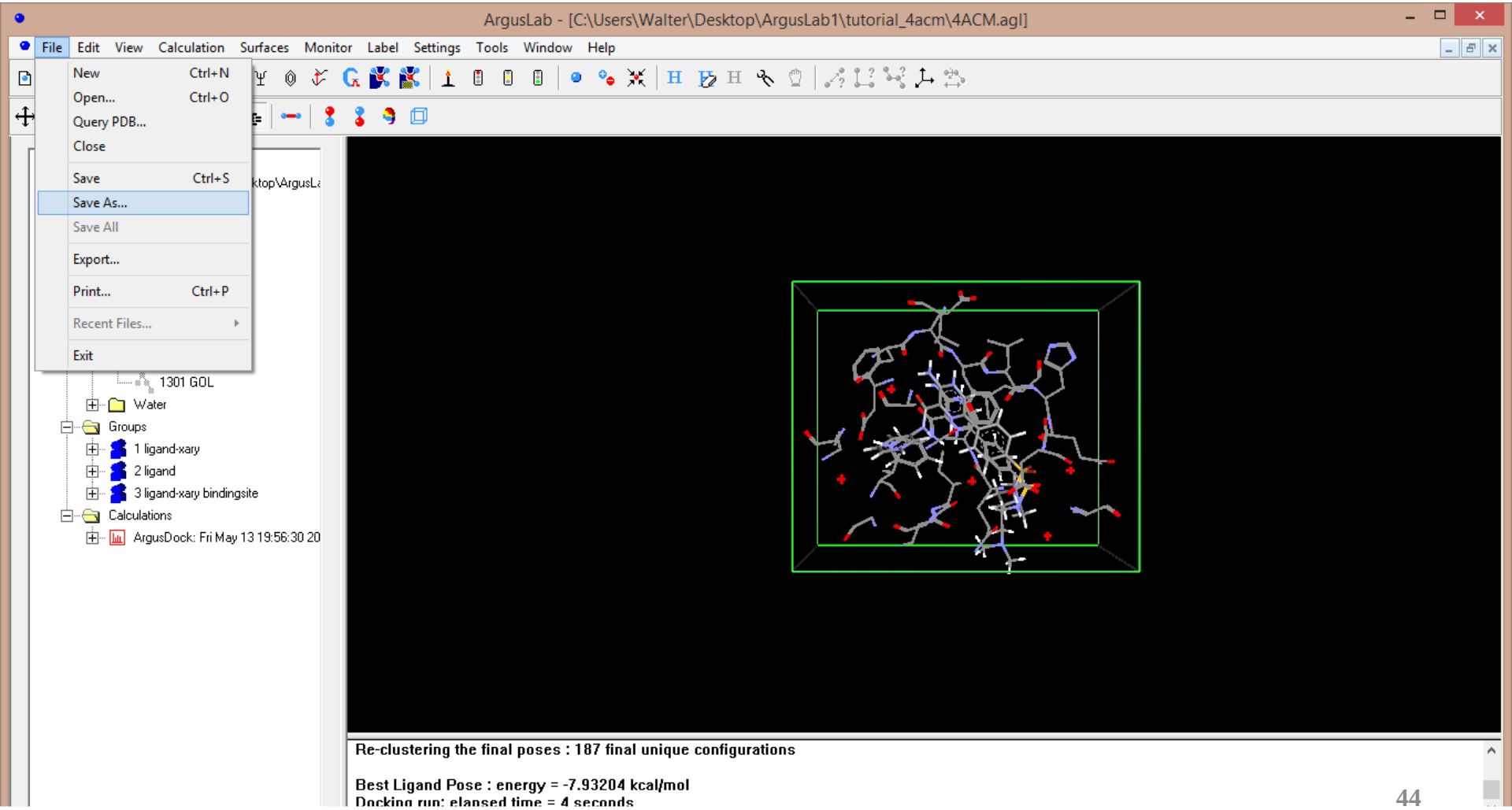
THOMSON REUTERS SCOPUS

Then choose ArgusLab Files (*.agl).

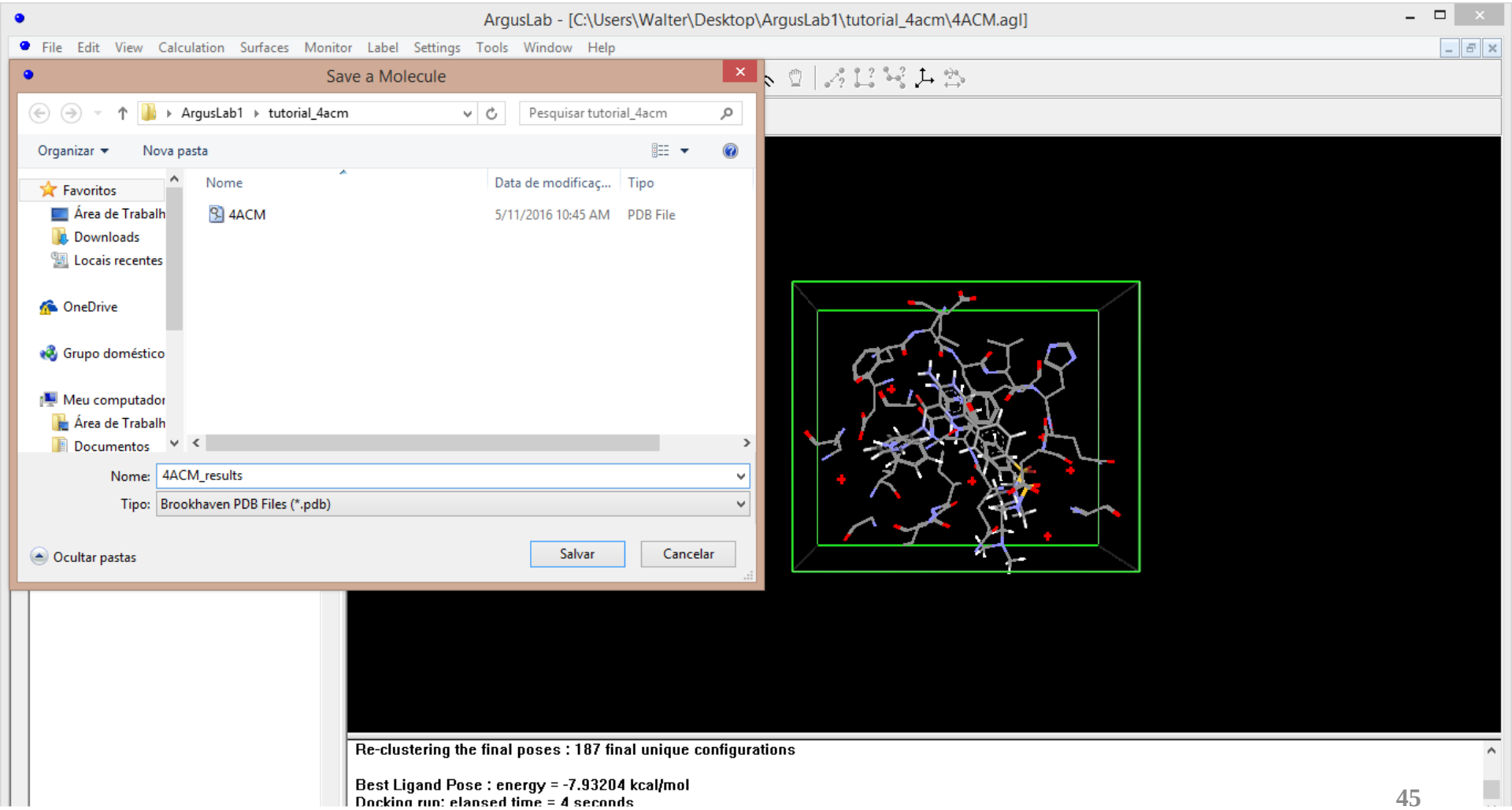


THOMSON REUTERS SCOPUS

Save your results as a PDB file.

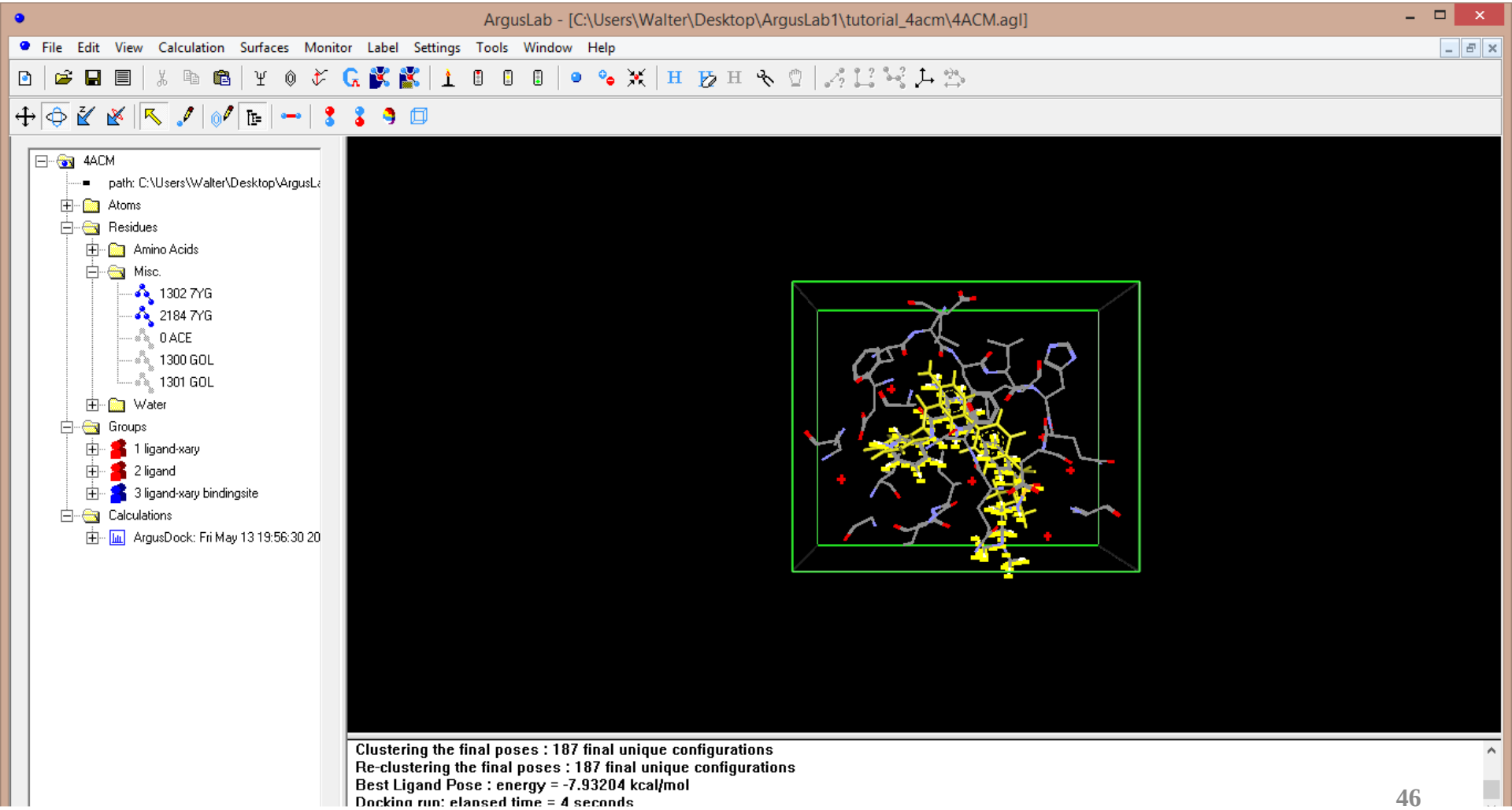


Choose the folder where to save your PDB file.



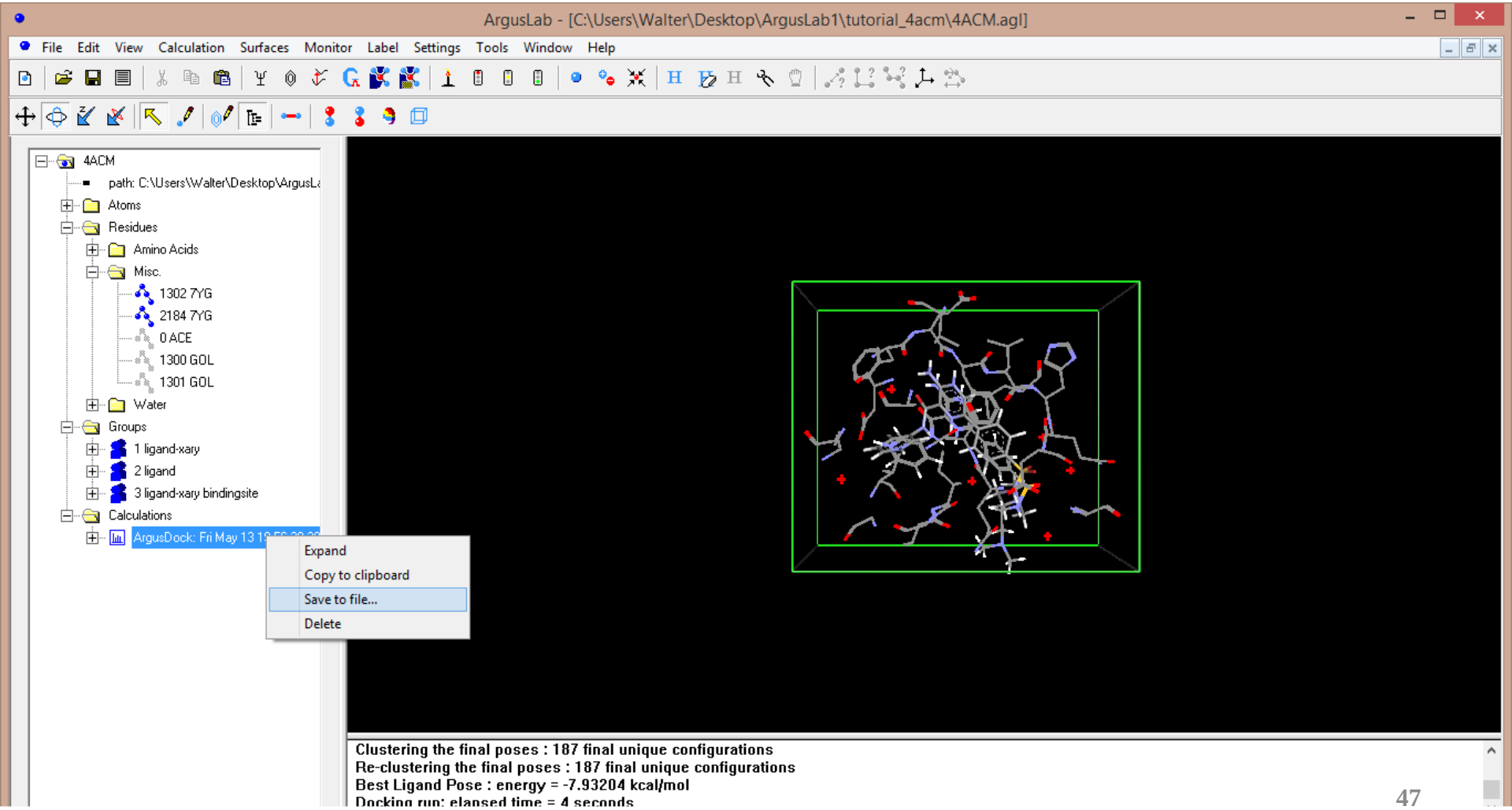
THOMSON REUTERS SCOPUS

In the Tree View expand Calculations folder

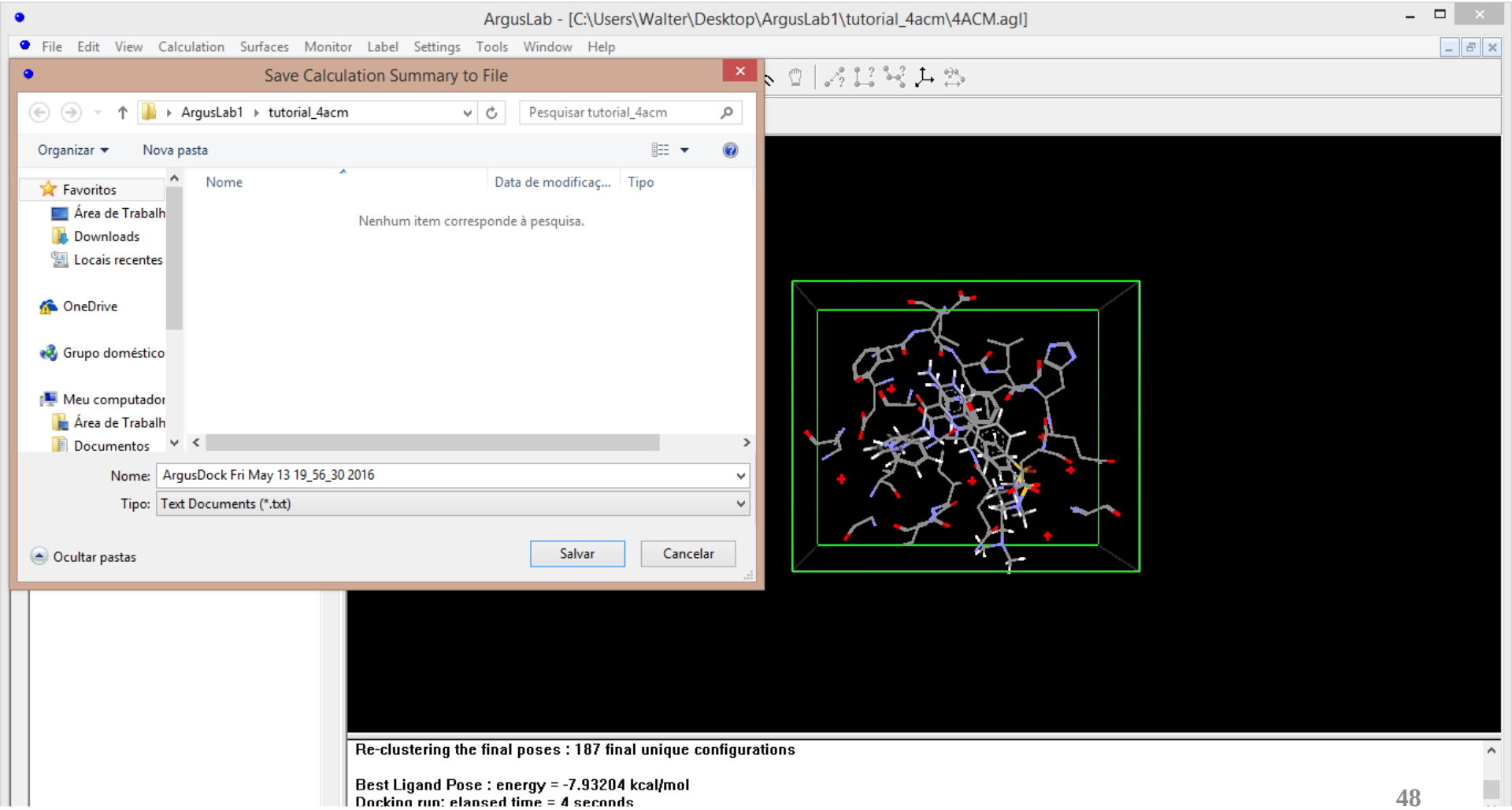


THOMSON REUTERS SCOPUS

Right-click on “ArgusDock...” and select “Save to file...”.

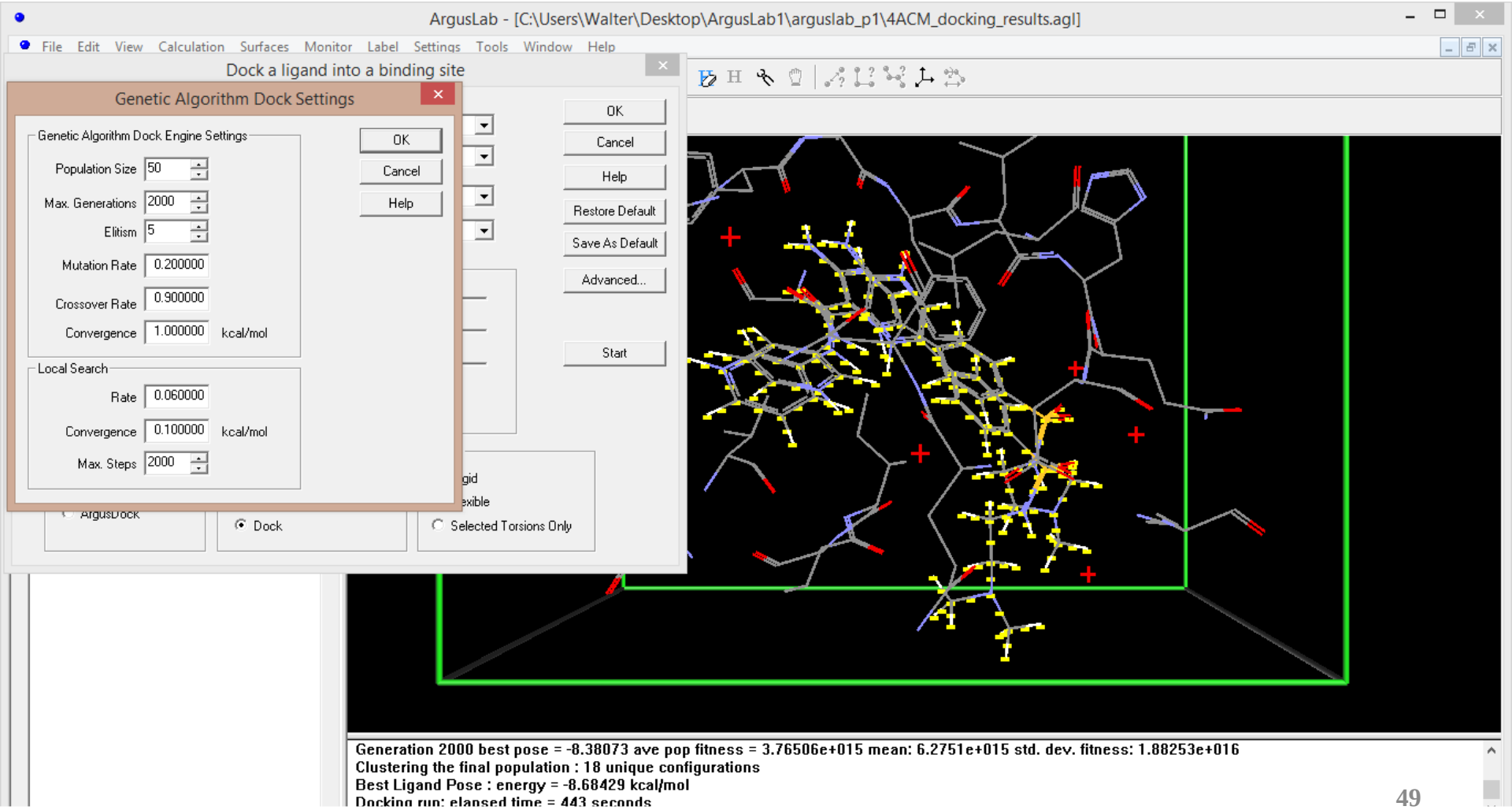


Select the folder where to save the docking results file.



Docking a ligand (Lamarckian genetic algorithm)

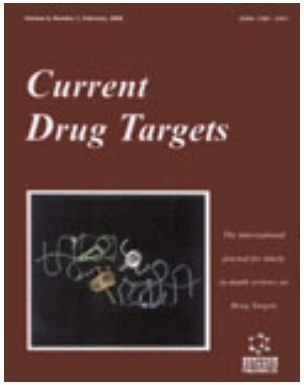
Alternative docking protocol using Lamarckian genetic algorithm is available in the ArgusLab.

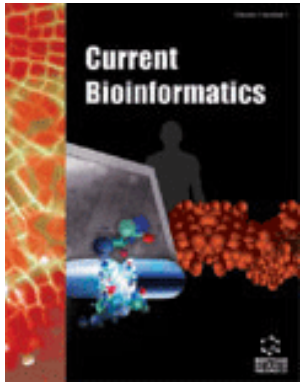


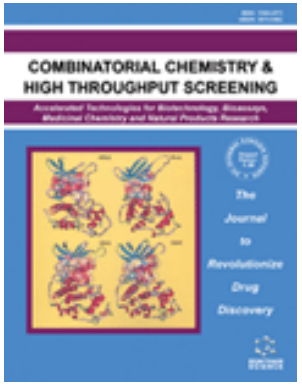
This tutorial was produced in a DELL Inspiron notebook with 6GB of memory, a 700 GB hard disk, and an Intel® Core® i5-3337U CPU @ 1.80 GHz running Windows 8.1. Text and layout were generated using PowerPoint 2013 and figures were captured from ArgusLab program. This tutorial uses Arial font.

Prof. Azevedo is Frontiers Section Editor (Bioinformatics and Biophysics) of the Current Drug Targets, section editor (Bioinformatics in Drug Design and Discovery) of the Current Medicinal Chemistry, section editor (Combinatorial/Medicinal Chemistry) for the Combinatorial Chemistry & High Throughput Screening, member of the editorial board of Current Bioinformatics, and editor of Docking Screens for Drug Discovery (Methods of Molecular Biology)(Springer Nature). He is also member of the editorial board of PeerJ, PeerJ Physical Chemistry, Organic & Medicinal Chemistry International Journal, and section editor in chief (Bioinformatics) of the Bioengineering International. He graduated in Physics (BSc in Physics) from the University of São Paulo (USP) in 1990. He completed a Master Degree in Applied Physics also from the USP (1992), working under the supervision of Prof. Yvonne P. Mascarenhas, the founder of crystallography in Brazil. His dissertation was about X-ray crystallography applied to organometallics compounds (De Azevedo Jr. et al., 1995). During his PhD, he worked under the supervision of Prof. Sung-Hou Kim (University of California, Berkeley), on a split Ph.D. program with a fellowship from Brazilian Research Council (CNPq)(1993-1996). His PhD was about the crystallographic structure of CDK2 (De Azevedo Jr. et al., 1996). His current position is coordinator of the Structural Biochemistry Laboratory at Pontifical Catholic University of Rio Grande do Sul (PUCRS). His research interests are interdisciplinary with two major emphases: molecular simulations and protein-ligand interactions. He published over 190 scientific papers about protein structures and computer models to assess intermolecular interactions involving biomolecules and potential ligands (H-index: 37, RG Index > 41.0). These publications have over 5000 citations in the Web of Science (Publons h-index: 37), more than 5600 citations in the Scopus (h-index: 41), and over 7200 citations in the Google Scholar (h-index: 44).

PROUD
to be
a Springer Author
Read a free
preview!







THOMSON REUTERS SCOPUS

https://www.facebook.com/azevedolab.net/

References

Berg S, Bergh M, Hellberg S, Högdin K, Lo-Alfredsson Y, Söderman P, von Berg S, Weigelt T, Ormö M, Xue Y, Tucker J, Neelissen J, Jerning E, Nilsson Y, Bhat R. Discovery of novel potent and highly selective glycogen synthase kinase-3ß (GSK3ß) inhibitors for Alzheimer's disease: design, synthesis, and characterization of pyrazines. J Med Chem. 2012; 55(21):9107-19.

Bitencourt-Ferreira G, de Azevedo WF Jr. Molecular Docking Simulations with ArgusLab. Methods Mol Biol. 2019; 2053: 203–220.

Joy S, Nair PS, Hariharan R, Pillai MR. Detailed comparison of the protein-ligand docking efficiencies of GOLD, a commercial package and ArgusLab, a licensable freeware. In Silico Biol. 2006;6(6):601-5.

Last update on June 12, 2020.