

In-class Practical 2

Introduction to Avogadro


Today we'll be building, optimizing, and deforming molecules using Avogadro. This is a neat tool for exploring energies and geometries of small molecules and short proteins. We'll also be looking at chemically interesting questions that involve multi-dimensional surfaces.

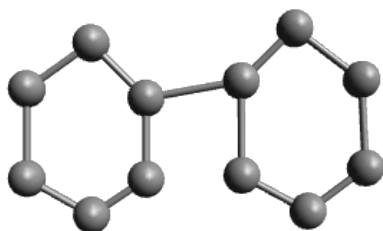
Drawing Structures:

1. First, make sure you have downloaded a copy of Avogadro to your laptop. To get the software, go to:

<http://avogadro.cc/>

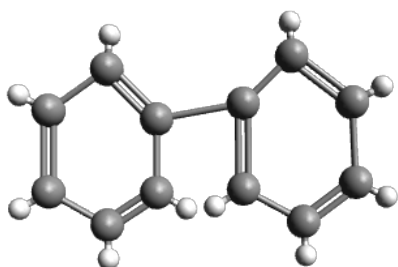
and open the Download link. Install it as you would any other software.

2. Open Avogadro.
3. Use the draw tool , and go to the **Tool Settings...** to *uncheck* the **Adjust Hydrogens** button.
4. Click in the main window to place a carbon atom.
5. Drag from one atom to another location to make a carbon-carbon bond.
6. Sketch out the skeleton of the biphenyl structure:



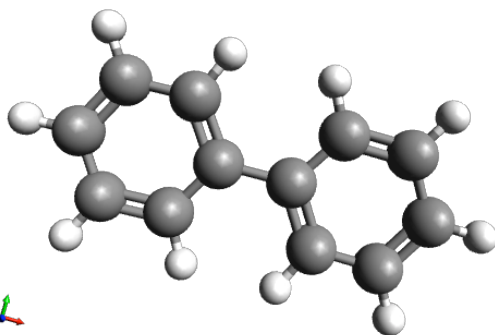
7. Click the **Bond Order** drop-down and select "Double". Also, re-enable the "Adjust Hydrogens" check-box.


8. Click alternating bonds to convert the system to two conjugated rings:



This is a very uncomfortable geometry for biphenyl, so we want to allow the molecule to relax into a lower energy conformation.

9. Go to **Extensions** → **Molecular Mechanics** → **Setup Force Field...**, Pick the **MMFF94** Force Field, the **Steepest Descent** Algorithm, and a convergence criteria of $10e-2$. Click **OK**.
10. Go to **Extensions** → **Optimize Geometry**. You should get a structure that looks like this:



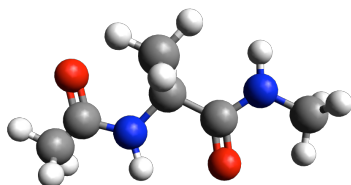
11. The measure tool  allows you to measure distance, angles, or dihedral angles.
- Click on two atoms to measure a distance.
 - Click on three atoms to measure the angle between them.
 - Click on four atoms to measure the dihedral angle between them. (Measure the dihedral or torsion angle between the two phenyl rings).
 - Right click (or Ctrl-click or ⌘-click) to clear the measurement and the list of selected atoms.



12. The bond-centric manipulation tool provides a “chemically-oriented” way to change bond lengths, angles, and dihedral angles.
- Click on the bond between the two phenyl rings. A rectangle will be drawn with the bond at the center. You can rotate this plane about the bond by clicking on the bond and dragging.
 - Right click (or ⌘-click) on one of the atoms in the selected bond and drag to change the bond length. The current bond length is listed in the bottom left corner.
 - Left click on one of the atoms in the selected bond and drag to change the bond angle. The atom you click on will move in the highlighted plane, with the other atom as the center of rotation. The appropriate angles will update interactively.
 - Click on an atom *neighboring the bond* and drag to change the dihedral angle. Adjust the phenyl-phenyl ring dihedral until it is near 90°.
13. Re-optimize the geometry. What is the optimum phenyl-phenyl dihedral angle now? What does your chemical intuition say about the *correct* phenyl-phenyl angle?

Building a Peptide

- Start a new molecule (⌘N on a Mac) and close the window with your biphenyl system (or just quit and restart Avogadro).
- Go to **Build** → **Insert** → **Peptide**
- We’re going to create a peptide analogue which contains a single amino acid residue, alanine (Ala), flanked by two peptide bonds and capped at each end with methyl groups. To do this, insert the peptide sequence Gly-Ala-Gly. Close the “Insert Peptide” window.
- The main window will contain the peptide, but it will have all of the atoms selected (surrounded by a blue halo). Use the selection tool to pick only a few atoms to delete with the “Delete” key. Then use the build tool, to modify the structure until you get the capped alanine structure:



Note that you may need to add hydrogens back to the structure with the drawing tool to make it look like the capped alanine in this picture.

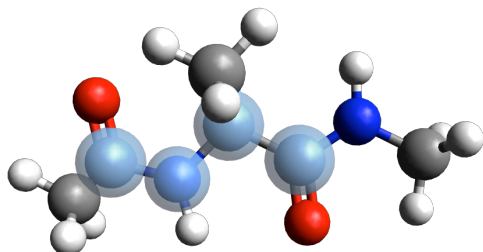
5. We will use the methyl group side chain of the Ala residue as our visual anchor point. Conformations will generally be oriented so that the Ala methyl group is at the top and slightly rotated forward. The Ala methyl group is attached to the Ala alpha-carbon ($C_{\alpha 1}$) at the center of the peptide.

In this view, the Ala amide nitrogen (N_{H1}) is attached to the left of $C_{\alpha 1}$. The carbonyl carbon (C_{O-1}) to the left of N_{H1} represents the C-terminal end of the preceding residue.

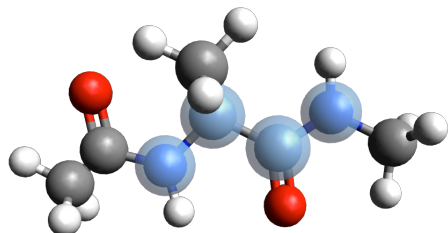
Also in this view, the Ala alpha-carbonyl carbon (C_{O1}) is attached to the right of $C_{\alpha 1}$. The amide nitrogen (N_{H+1}) to the right of C_{O1} represents the N-terminal end of the succeeding residue. It may help to label the previous diagram.

The methyl carbons at each end correspond to the alpha-carbons of the preceding and succeeding residues.

6. The ϕ angle is the torsion angle specified by the spatial positions of C_{O-1} , N_{H1} , $C_{\alpha 1}$ and C_{O1} . These atoms are highlighted below. C_{O-1} is the left-most highlighted atom and C_{O1} is the right-most highlighted atom. In this conformation, $\phi = 180^\circ$.



7. The ψ angle is the torsion angle specified by the spatial positions of N_{H1} , C_{a1} , C_{O1} and N_{H+1} . These atoms are highlighted below. N_{H1} is the left-most highlighted atom and N_{H+1} is the right-most highlighted atom. In this conformation $\psi = 180^\circ$.



Energy related to torsional rotation

1. By using the measure tool and bond centered manipulation, change both the ϕ and ψ to 0° . Why is this a high-energy conformation?



2. Turn on the auto-optimization tool, select the GAFF force field, the “Steepest Descent” algorithm, and hit the start button. Drag around atoms until you find a low energy configuration (that is around -12 kJ / mol or so). What are the ϕ and ψ angles in this conformation?

Homework questions (turn these in with Problem Set 3):

1. The experimental phenyl-phenyl dihedral angle in biphenyl in the gas phase is 44 degrees. Chemically, why might biphenyl prefer that configuration? Why did you get two different results each time you did the calculation?
2. When you found a low-energy structure for the capped alanine, what interactions were stabilizing the structure? What do your values of ϕ and ψ correspond to on the Ramachandran plot?
3. **Extra Credit** Cookie Challenge! This week's Extra Credit / Cookie Challenge is to find the capped-alanine structure that is closest to the global minimum of energies for this molecule. To get the extra credit points:
 - Use the GAFF forcefield
 - Export your lowest energy structure as an XYZ file

- Attach that XYZ file to an *email* to Dr. Gezelter along with a description of how you looked for that structure.
- The person who submits the best (i.e. closest to the global minimum) structure to me by Friday at 5:00 p.m. will win the cookie.