

Molecular Overlay Exercise

Due October 5, 2010

Cocaine versus Procaine

This exercise is based on Ch. 13 qu. 6 in Patrick's An Introduction to Medicinal Chemistry.

*Note: only PC computers at Bryn Mawr College have Chem3D!

1. Open Chem3D

**Note: the display has many windows or panels which can be removed or added. You can click on the 'X' in the upper right corner of each panel/window to remove that panel. To restore the panel, choose 'View' in the upper menu and select the desired panel: for example, Model Explorer; Structure Browser; ChemDraw Panel; Output Box; etc.*

2. Bring up structures of cocaine and procaine by typing their names in Chem/SMILES box in upper right corner of screen. Since you can only draw one structure at a time with this function, you will need to open two files/windows to generate each compound and then copy/paste one into the window with the other.

**Note: a second window can be generated by clicking on the blank paper icon in the upper left corner of the screen.*

**Note: structures are manipulated on the screen with the three object moving tools in the upper left corner of the screen. These three icons are the black arrow, the hand and the rotating ball (with curved arrow). Click on each to explore their use. To separately move procaine or cocaine, click on their name (Fragment 1, etc.) in the Model Explorer window. A molecule is selected when all the atoms turn yellow.*

3. When combined in the same window, minimize the energy of both structures by clicking on the icon: MM2→ (black arrow beneath). The output window at the bottom of the screen will display the energy minimization outcome.

4. Click on 'Help' in the top menu and select 'Contents'. Select 'Tutorial 6: Overlaying Models' and read the instructions. Using the description as a template, perform an overlay with procaine and cocaine. Substitute procaine/cocaine for epinephrine/methamphetamine to perform the analogous procedure.

**Note: the structures can be magnified or shrunk by holding down the right button of the mouse and spinning the mouse wheel.*

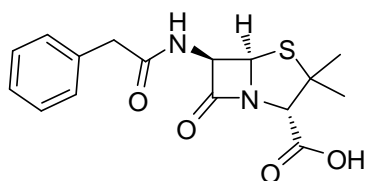
5. Rotate the overlaid structures to find an acceptable depiction. Print the screen.

6. Measure the distance between the two tertiary amines in the different molecules by using the selection icon (black arrow in top left corner) to chose one nitrogen atom. Move the selection arrow to the other N and read the distance in angstroms. Do the same for two carbon atoms in the benzene ring and write the distances (in angstroms) on the overlay printout for both measurements.

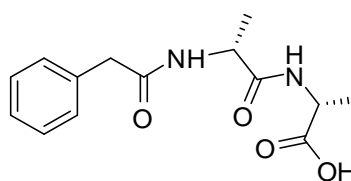
Penicillin versus N-Phenylacetyl-D-ala-D-ala

This exercise is based on figure 19.18 in Patrick's An Introduction to Medicinal Chemistry (p. 434)

1. Perform the same process as described above for cocaine/procaine with penicillin and N-phenylacetyl-D-ala-D-ala. You will need to draw penicillin since Chem3D does not recognize it by name. Use the left ChemDraw panel and the tools palette to draw the structure (you may need to click in the ChemDraw window to get the tools palette). Be sure to draw the correct stereochemistry. Note: sometimes the Chem3D program will invert the molecule or stereocenters and create the enantiomer or a diastereomer. An enantiomer can be corrected by selecting 'Structure', then 'Reflect Model', and then choose a plane (anyone should work). Otherwise individual stereocenters may need to be adjusted in the ChemDraw panel.



penicillin G



N-phenylacetyl-D-Ala-D-Ala

2. Follow the 'fast overlay' procedure as described above. Rotate the overlaid structures to find an acceptable depiction. Print the screen.

3. Measure the distance between the two N-terminal nitrogen atoms in the different molecules by using the selection icon (black arrow in top left corner) to chose one nitrogen atom. Move the selection arrow to the other N and read the distance in angstroms. Do the same for the two carboxylic acid carbon atoms and write the distances (in angstroms) on the overlay printout.