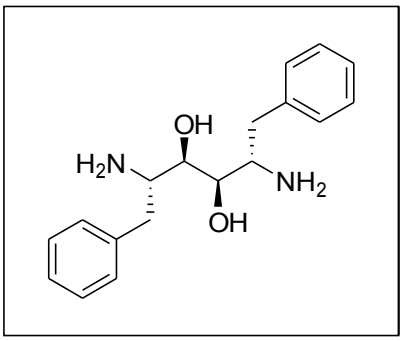
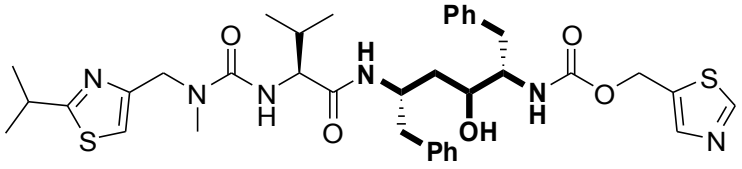
9. Below is the structure of a lead compound that was key in the development of Ritonavair. Ritonavir inhibits HIV protease, a key enzyme involved in the lifecycle of the human immunodeficiency virus. The "core" of the lead compound that was retained in the final drug has been bolded.

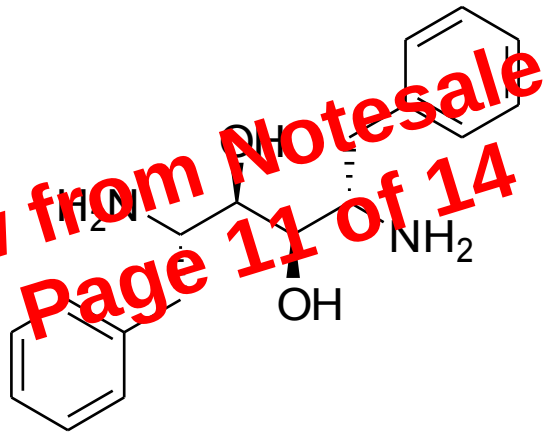


Lead Compound



Ritonavir

a. Assign each stereocenter in this lead compound (it is redrawn below) as R or S.
b. Is this a meso compound? If so, clearly indicate the internal mirror plane.

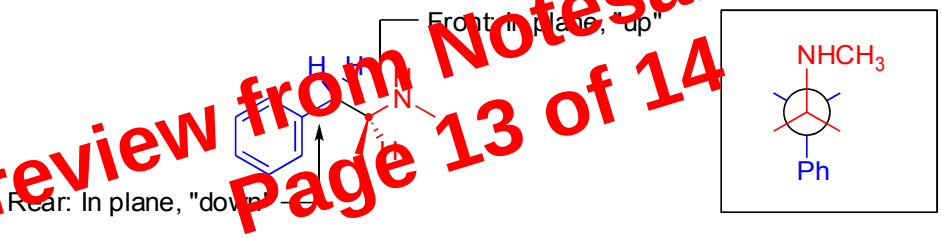


Drawing Newman projections of chiral molecules is an important skill that we will be using very often in this course. This requires a little more work than drawing a Newman projection of an achiral molecule. To start with, remember what the different types of bonds mean – bonds drawn as flat lines are in the plane of the page, wedges are out of the plane of the page, and dashes are back into the plane of the page. Knowing this enables us to construct a correct Newman projection for chiral molecules.

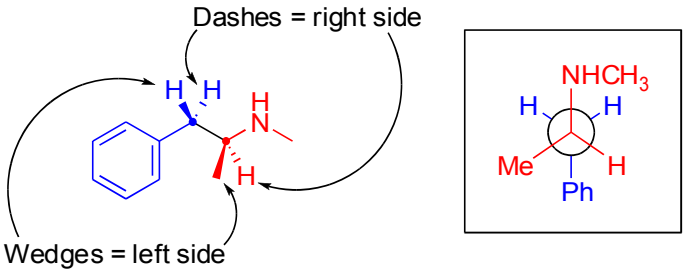
As an example, take (+)-methamphetamine, as viewed down the bond shown. Start by filling in the implicit hydrogens.

Next, look at the two groups that lie in the plane of the page on the front and rear carbons. In this case, they are the -NHCH3 group and the phenyl group. Now, imagine the molecule being rotated 90 degrees. In effect, this is like picking up your paper from the right side, and looking at it edge-on.

If you did so (or if you built a model, which you should do), you would notice that the -NHCH3 group is now bound to the "front" carbon (red), and is facing up. Conversely, the phenyl group is bound to the rear carbon (blue), and is facing down. These two groups are anti to each other. Now, this can be filled in on the Newman projection.



If you pick up a piece of paper from the right side and look at it edge-on, you will also notice that what was the "front" side of the paper is now on your left, and what was the "back" side of the paper is now on your right. This means that the wedge-bond groups can be put on the left side of the Newman projection, and the dashed-bond groups can be put on the right.



11. Try rotating the Newman projection to one of the eclipsed conformers, and go backwards (from the projection to the skeletal structure). Verify that it is correct by assigning the absolute configuration!