Chem 226 — Problem Set #6 —
"Fundamentals of Organic Chemistry," 4th edition, John McMurry.
Chapter 6

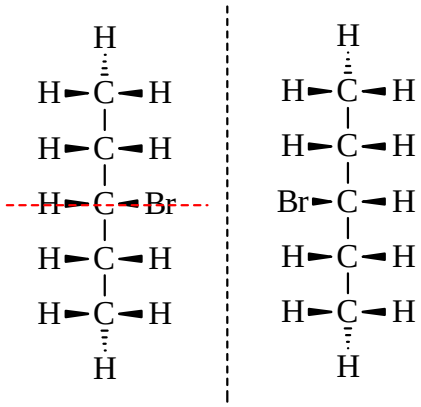
I would urge you to read through this entire document because issues that are treated more fully in the earlier problems may be treated in a more cursory manner in later problems.

2. Which of the following compounds are chiral?

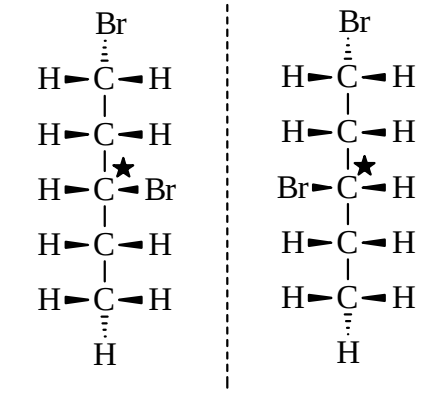
(a) 3-bromopentane, (b) 1,3-dibromopentane, (c) 3-methyl-1-hexene,
(d) cis-1,4-dimethylcyclohexane

A compound is chiral if it is not superimposable on its mirror image. This is the acid test. To this we might add the following embellishments:
(1) if the compound and its mirror image are superimposable in any conformation accessible to the molecule, then the molecule is achiral,
(2) if the molecule exhibits a plane of symmetry in any conformation accessible to it, it is achiral, and (3) if the molecule exhibits a center of symmetry in any conformation accessible to it, it is achiral. Also, if a compound has only one stereogenic center it will be chiral. If a compound has more than one stereogenic center it is likely to be chiral but may be achiral because it is a meso structure.

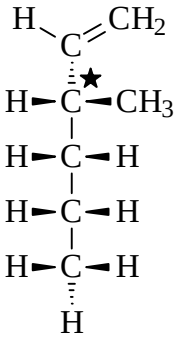
(a) Note the plane of symmetry that bisects this molecule, shown as the dotted red line. The existence of this plane of symmetry is a sufficient, but not necessary, condition to make this molecule achiral. To apply the acid test we can rotate the mirror image on the right 180° around an axis that passes through the third carbon and is perpendicular to the page. When we have done this, we recognize that the original and mirror image are superimposable. Hence, the molecule is achiral.

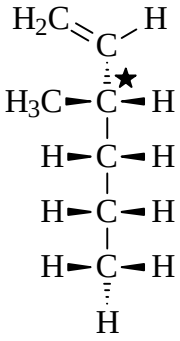


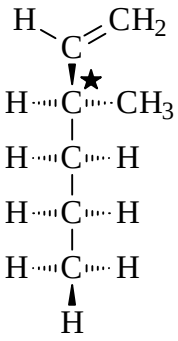
(b) In this case if we try to superimpose the molecule and its mirror image by just sliding the mirror image to the left there is not a match around carbon-3. On the other hand, if we rotate the mirror image by 180°, as we did in (a), we find that things match up at carbon-3, but now the original compound has a bromine at the top, while the mirror image has this bromine at the bottom. Again, there is a mismatch. The original and its mirror image are not superimposable and are, therefore, enantiomers of each other and each is chiral. Finally, we might note that the starred carbon is the one and only stereogenic center in the molecule.



(c) This compound has one and only one stereogenic center – the starred carbon. [Carbons 4 through 6 each have at least two identical hydrogens attached – they are not stereogenic centers. Carbons 1 and 2 are planar/trigonal and, therefore, cannot be stereogenic centers.] Hence, the compound will be chiral. To apply the acid test of superimposability we can see that sliding the mirror image to the left will leave groups attached to the stereogenic center mismatched. We would not be tempted to rotate the mirror image on the right 180° in an attempt to superimpose it on the original as we did in (a) because we are now experienced enough to see that the double bond would wind up at the bottom. But, how about rotating the mirror image on the right by 180° around an axis that passes through carbons 3-6. That would produce the situation shown to the right. Clearly, this is not superimposable on the original.

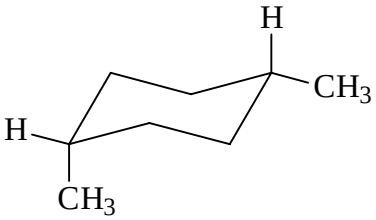


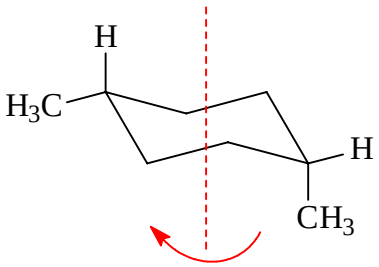




An Aside – Representing three-dimensional molecules in two dimensions on a planar surface is a topological nightmare. If you want to see what is really going on USE YOUR MOLECULAR MODEL KIT.

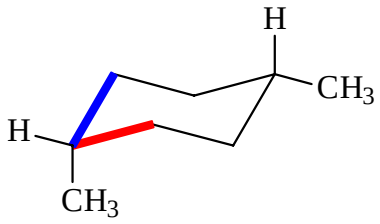
(d) Well, there they are – the original and its mirror image to the right. If we rotate the mirror image around the (red) axis, as shown, by 120° the mirror image will superimpose on the original. This molecule is achiral.





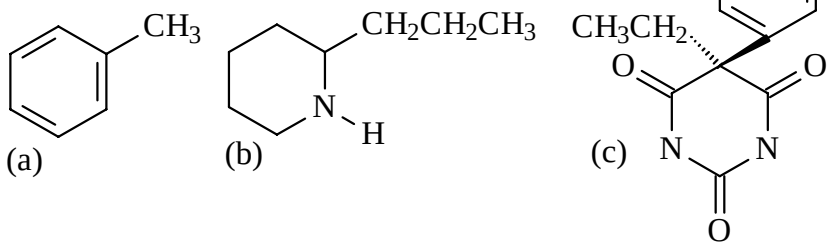
An Aside – It might be noted that there are no stereogenic centers in this molecule. This does not *guarantee* that the molecule is achiral; however, the absence of stereogenic centers would make us suspect that the molecule is achiral. But, how do we recognize a stereogenic center when the atom under consideration is part of a ring? First, the atom must be tetrahedral. Next, the two groups attached to the atom that are exocyclic to the ring must be different. So, the four $CH_2$ groups around the ring are not contenders. But, what about, for example, the lower-left carbon in the ring of the structure shown to the left above. It has an H and a $CH_3$ group exocyclic to the ring. Now we need to know if the two ring connections to this carbon constitute two identical groups or two different groups. If these connections are equivalent to two identical groups, the carbon is not a stereogenic center. On the other hand, if these connections are equivalent to two different groups, the carbon is a stereogenic center.

To determine whether the ring connections – shown in bold red and blue on the right – are equivalent to identical groups or different groups we need to traverse the ring in the clockwise direction (blue bond, then around the ring) and then in the counterclockwise direction (red bond, then around the ring). If we encounter the same groups in the same order going both ways, the ring is equivalent to two identical groups – the atom is not a chiral center. If we encounter the groups in different order, the ring is equivalent to two different groups – the atom is a stereogenic center.

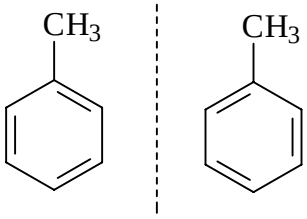



In this case going clockwise (blue bond first) we get $CH_2$, $CH_2$, $CHCH_3$, $CH_2$, $CH_2$. Going counterclockwise (red bond first) we get $CH_2$, $CH_2$, $CHCH_3$, $CH_2$, $CH_2$. Going in either direction gives us the same result. The ring, therefore, is equivalent to two identical groups and the atom under question is not a stereogenic center.

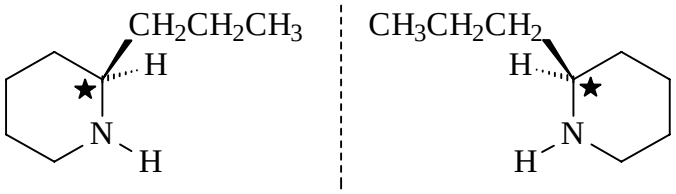
3. Which of the following molecules are chiral? Identify the stereocenter(s) in each.



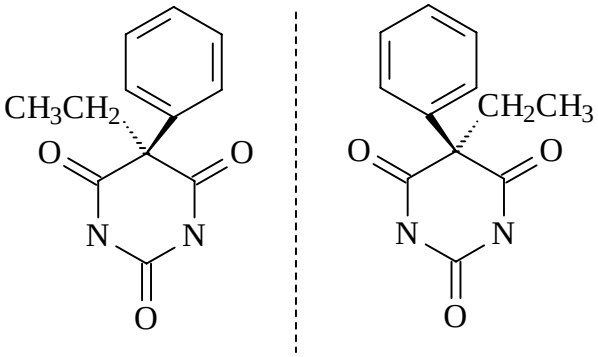

(a) Just slide the mirror image onto the original and they superimpose as long a you remember that there are two resonance structures for the benzene ring, making each bond around the ring identical. Even if you didn't remember that the bonds around the ring are all equivalent, you can see that flipping the mirror image over like a pancake superimposes it exactly onto the original. This molecule is achiral. It has no stereocenters.



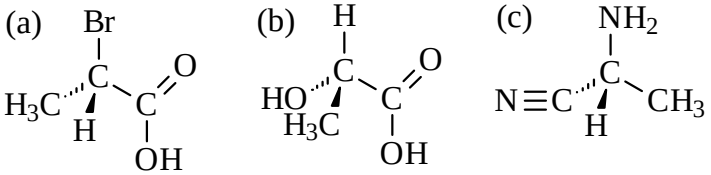
(b) [The molecule was redrawn to emphasize its three-dimensional structure.] The mirror image is not superimposable on the original; this molecule is chiral. It has one stereocenter (starred). This stereocenter is part of the ring. The two exocyclic groups are different (hydrogen and propyl) and going around the ring clockwise gives NH, $CH_2$, $CH_2$, $CH_2$, $CH_2$, while going around counterclockwise gives $CH_2$, $CH_2$, $CH_2$, NH; thus, the ring is equivalent to two different groups.



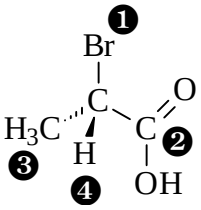

(c) [The molecule was redrawn to emphasize its three-dimensional structure. Actually, the phenyl group on top is right in front of the ethyl group, eclipsing it; they are drawn alongside each other only so you can see both.] The molecule and its mirror image are superimposable, so the molecule is achiral. There is a vertical plane of symmetry bisecting the phenyl and ethyl groups, the ring-carbon to which they are both attached, and the C=O group at the bottom. There are no stereocenters.




9. Assign R,S configurations to the following molecules.



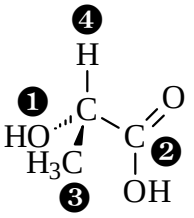

(a) The molecule is shown to the right with priorities assigned to the four groups around the stereocenter. Bromine has the highest atomic number (35) and hydrogen has the lowest (1). The two carbons are identical at 6, but the carboxyl carbon has, in effect, three oxygens (8) attached, while the methyl carbon has three hydrogens (1). Since 8 > 1, the carboxyl group is 2 and the methyl is 3.




❶ 35
❷ 6: 8,8,8
❸ 6: 1,1,1
❹ 1

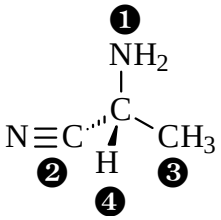
To place the group of lowest priority back we need to rotate the molecule or look at it from behind the page. Doing this and counting 1, 2, 3, moves us in a counterclockwise direction: S.

(b) In this case to get the right point of view (H behind stereocenter), we need to look up from the bottom. Counting 1, 2, 3 is counterclockwise: S.




1 8
2 6: 8,8,8
3 6: 1,1,1
4 1

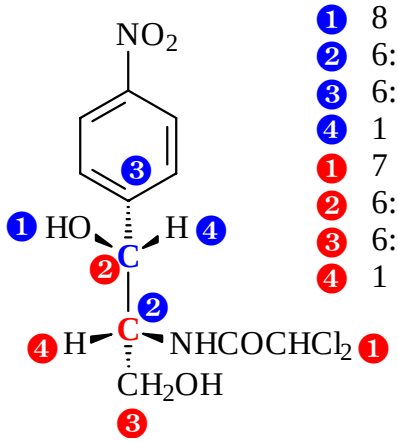
(c) In this case our point of view should be from behind the page (to place group 4 behind the stereocenter). From this perspective counting 1, 2, 3 goes clockwise: R.




1 7
2 6: 7,7,7
3 6: 1,1,1
4 1

13. Chloramphenicol is a powerful antibiotic isolated from the Streptomyces venezuelae bacterium. It is active against a broad spectrum of bacterial infections and is particularly valuable against typhoid fever. Assign R or S configuration to the stereocenters in chloramphenicol.

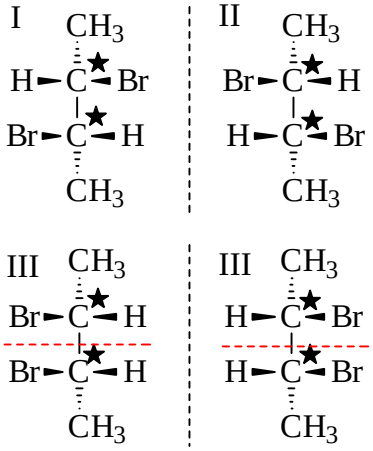
Since the low priority groups attached to both stereocenters are poking out toward us we will need a point of view from behind the page to get this right. The top (blue) stereocenter is R. The bottom one (red) is also R.




1 8
2 6: 7,6,1
3 6: 6,6,6
4 1
1 7
2 6: 8,6,1
3 6: 8,1,1
4 1

14. Which of the following substances have meso forms?
(a) 2,3-dibromobutane, (b) 2,3-dibromopentane, (c) 2,4-dibromopentane

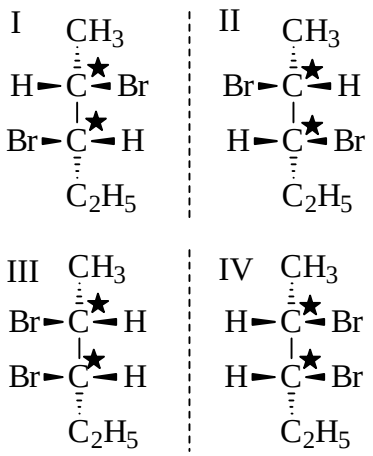
(a) I and II, non-superimposable mirror images, are enantiomers of each other. Each has two stereocenters and each is a chiral molecule. III is superimposable on its mirror image even though it has stereocenters. A molecule that has stereocenters and is superimposable on its mirror image is a meso structure. Meso structures often have a plane or center of symmetry *in at least one of the molecule's conformations*. III has a plane of symmetry in the conformation shown; this plane is perpendicular to the page and is shown as a red dotted line.




We might note in passing that I and III and also II and III are diastereomers: stereoisomers that are not enantiomers.

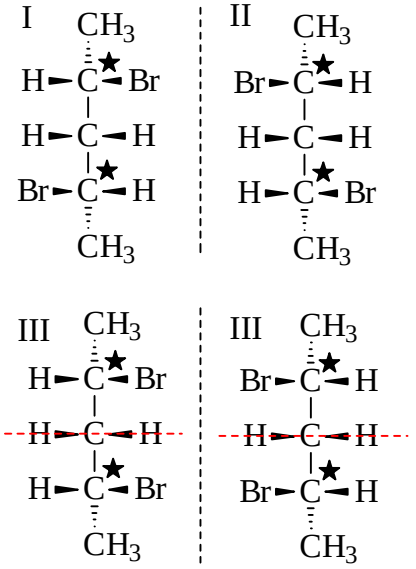
(b) There are four stereoisomers here. I and II are enantiomers. III and IV are enantiomers. There are no meso forms here.

Also, we might note in passing that the following pairs are diastereomers: I&III, I&IV, II&III, and II&IV.



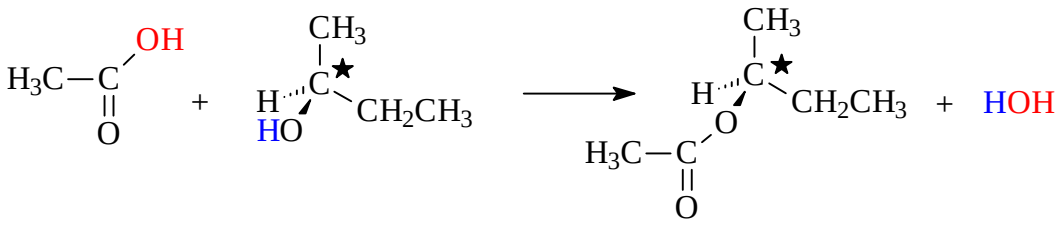
(c) I and II are enantiomers; they are non-superimposable mirror images. III is superimposable on its mirror image. Since III has stereocenters and is superimposable on its mirror image it is a meso structure. In the conformation of III that is shown there is a plane of symmetry perpendicular to the page (dotted red line).

I and III and also II and III are diastereomers.

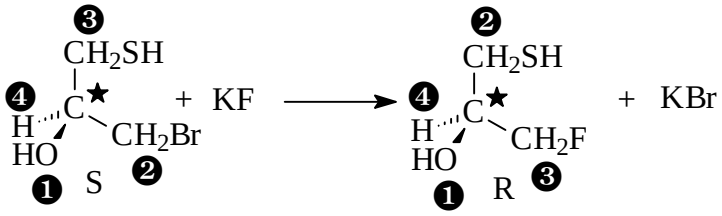



17. Suppose that acetic acid ($CH_3COOH$) reacts with (S)-2-butanol to form an ester (see Practice Problem 6.7). What stereochemistry would you expect the product(s) to have? What is the relationship of the products?

From the practice problem we learn the following:



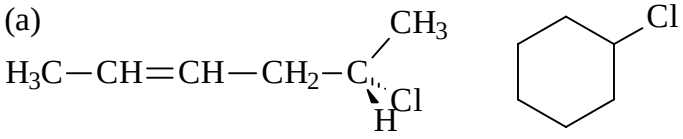
In other words the C-O breaks in the carboxylic acid and the O-H bond breaks in the alcohol to form the ester product and water. Since none of the bonds around the stereocenter is broken in this reaction the configuration in the product must be the same as in the reactant. In this case it is S in both. [It might be noted that when we say the configuration is retained in a reaction, or, equivalently, that the configuration is the same in reactant and product, we mean that the arrangement of atoms around the stereocenter has not changed. It is possible (although not common) that R may become S or vice versa, even though the configuration is the same. This would result from a change in the priorities of the groups that determine R and S, not from a change in the configuration around the stereocenter. An example of this is shown below.]




Note that the configuration around the stereocenter is the same in both reactant and product, but S has become R by virtue of a change in the group priorities.

18. What kinds of isomers are the following pairs?
(a) (S)-5-chloro-2-hexene and chlorocyclohexane,
(b) (2R,3R)-dibromopentane and (2S,3R)-dibromopentane.

(a)

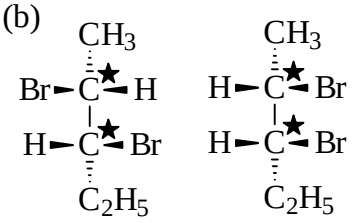






These are constitutional or structural isomers.

(b)



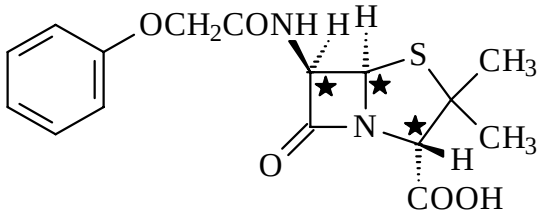

2R,3R 2S,3R

These are diastereomers, stereoisomers that are not mirror images.

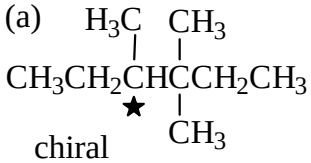
21. Define the following terms.
(a) chirality, (b) stereocenter, (c) diastereomer, (d) racemate, (e) meso compound,
(f) enantiomer.

(a) Chirality is a molecular property. If a molecule is chiral it is not superimposable on its mirror image.
(b) A stereocenter is a tetrahedral atom that has four different groups attached.
(c) Diastereomers are stereoisomers that are not enantiomers.
(d) A racemate or racemic mixture is a 1 to 1 mixture of a pair of enantiomers.
(e) A meso compound is one that has stereocenters but is not chiral.
(f) Enantiomers occur in pairs; they are mirror image stereoisomers.

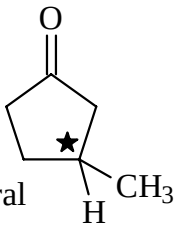
24. Penicillin V is a broad-spectrum antibiotic that contains three stereocenters. Identify them with asterisks.



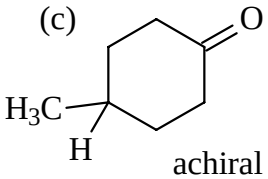

26. Which of the following compounds are chiral? Label all stereocenters.

(a) 

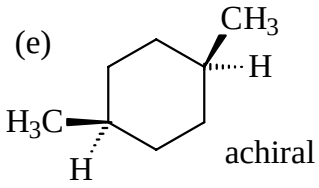
chiral

(b) 

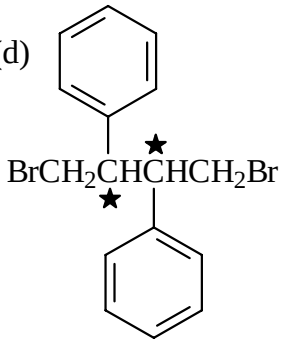
chiral

(c) 

achiral

(e) 

achiral

(d) 


This compound is stereochemically analogous to the 2,3-dibromobutane considered in question #14a. The $CH_2Br$ groups here take the place of the $CH_3$ groups there. Also, the phenyl groups here take the place of the bromines there. As was the case in 14a, there are a pair of enantiomers and a meso here.

34. What is the relationship between the specific rotations of (2R,3R)-dihydroxypentane and (2S,3S)-dihydroxypentane?

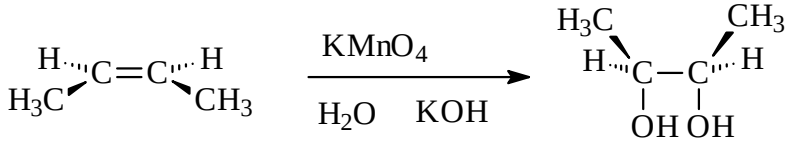
These compounds are enantiomers. Therefore, their specific rotations are equal but opposite, one is dextrorotatory, the other levorotatory by an equal number of degrees.

Between (2R,3S)-dihydroxypentane and (2R,3R)-dihydroxypentane?

These compound are diastereomers. Each is chiral and, therefore, each would be optically active. There is no relationship between their respective specific rotations.

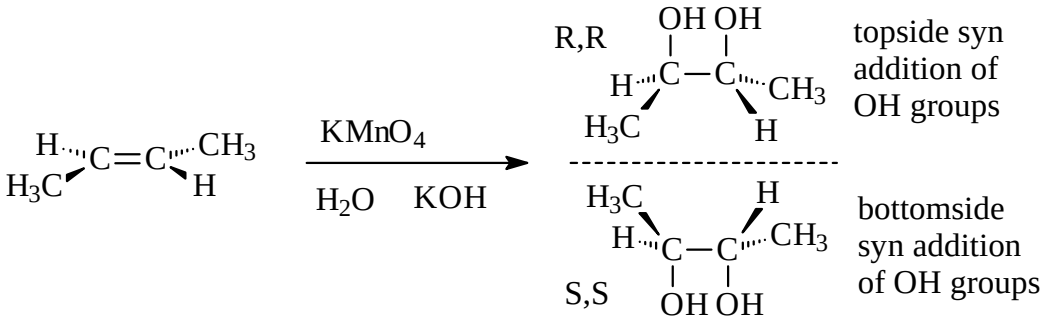
47. Hydroxylation of *cis*-2-butene with $KMnO_4$ yields 2,3-butanediol. What is the stereochemistry of the product?

The OH groups add in syn fashion to the double bond. This has a stereochemical consequence for the product as shown to the right.




The same product will be obtained whether the OH groups add to the top or bottom of the alkene. This product is a meso structure, (R,S)-2,3-butanediol.

48. Answer problem 47 for *trans*-2-butene.




The OH groups again add in syn fashion to the double bond. However, in this case the stereochemical consequence is different owing to the different starting material. In this case addition of the OH groups to the top of the molecule gives one enantiomer, while addition of the OH groups to the bottom of the molecule gives the other enantiomer. Since the addition of the OH groups is equally probable from top and bottom (there is no steric or electronic factor that favors one over the other) we would get a racemic mixture of the two products, (R,R)-2,3-butanediol and (S,S)-2,3-butanediol.

Problems 47 and 47 illustrate an important principle: When achiral reactants react to give compound that contain stereocenters, the products are racemic mixtures or meso compounds. More generally, we can say that optically inactive reactants give optically inactive products.