

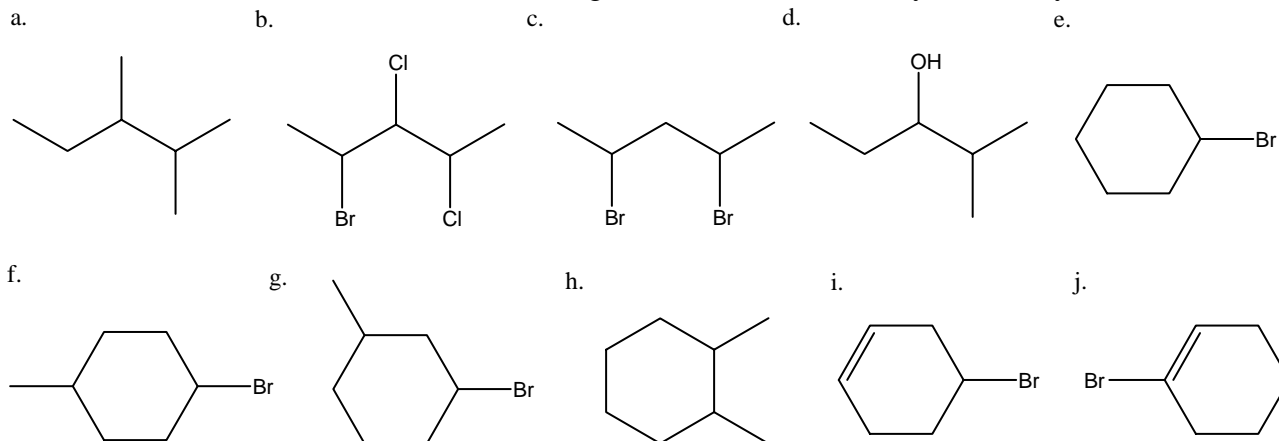
Lecture 16

Problem 1 - Draw a 3D structure and its mirror image for each of the following molecules. Are they different (enantiomers) or identical (superimposable)? Build models of each and see if your pencil and paper analysis is correct. See if you can use your hands to help your analysis.

- a. 1-bromopentane
b. 2-bromopentane
c. 3-bromopentane

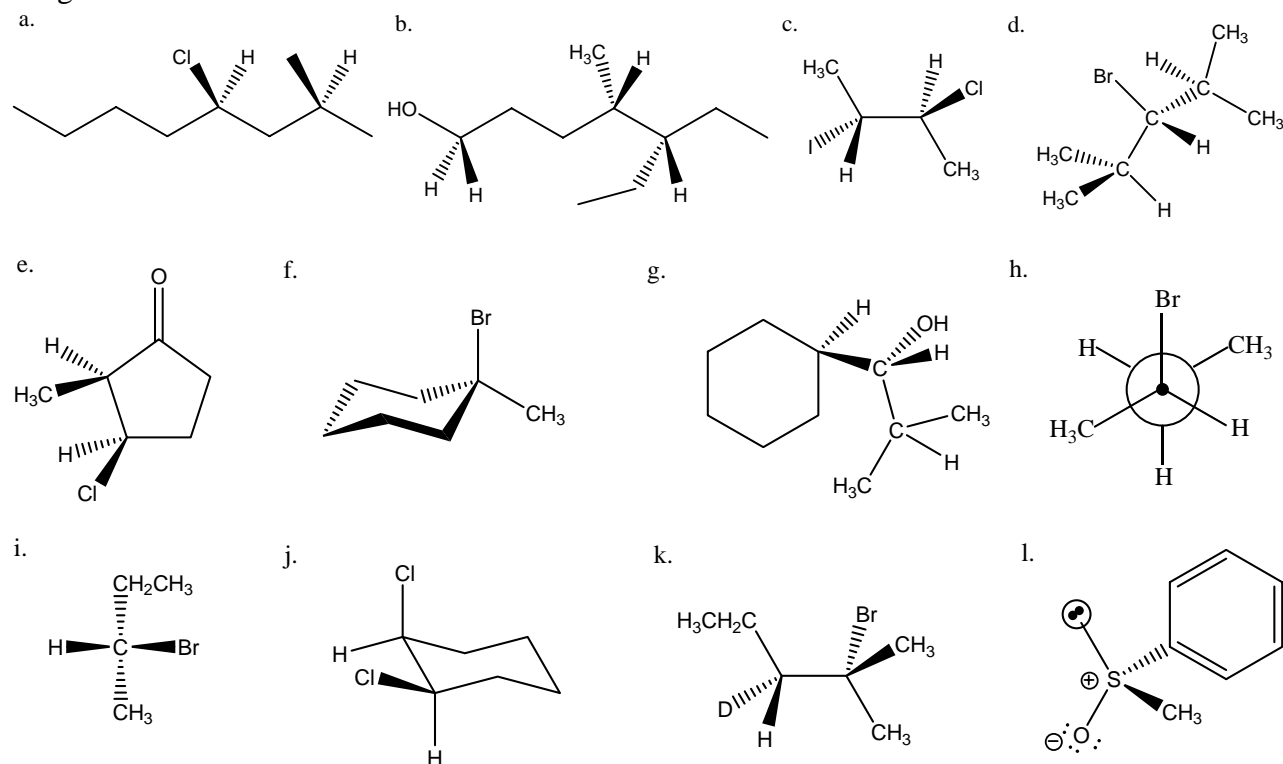
- d. 1,1-dibromocyclopentane
e. *cis*-1,2-dibromocyclopentane
f. *trans*-1,2-dibromocyclopentane

Problem 2 - Which molecules below have stereogenic centers? How many? Are they all chiral centers?



R and S Nomenclature

Problem 3 - Classify the absolute configuration of all chiral centers as R or S in the molecules below. Use hands (or model atoms) to help you see these configurations whenever the low priority group is facing towards you (the wrong way). Find the chiral centers, assign the priorities and make your assignments.



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5. Add in the other two groups in specified order (R would have 2 to the right and S would have 2 to the left.)



6. If a second stereogenic center (3rd, 4th...etc.) exists, add in groups in a similar way. With one group fixed, it may be difficult to follow the above procedure. In such cases, you can randomly put in groups 2 and 3 and then do a quick check of absolute configuration. This should be easy because you placed “4” away from you in the first step (or you can use your arms and hands if “4” is towards you). If the assignment is correct, you are finished. If it is incorrect, then interchange any two convenient groups and it will be correct.

Problem 6 - Write a three dimensional structure for each of the following names.

- | | |
|---|---|
| a. (4R,6S)-4,6-dimethylnonane | b. (1R,3R)-3-methyl-1-cyclohexanol |
| c. (4R)-4-phenyl-5-methyl-1-hexyne | d. (2R)-2,3-dihydroxypropanal |
| e. (3S)-4-methyl-3-bromo-1-pentene | f. methyl (2R)-2-aminopropanoate |
| g. (1R,3S)-1,3-cyclohexanediol | h. (1R)-1-fluoro-1-chloropropane |
| i. (2S)-2-amino-2-phenylethanoic acid | j. (2R)-2-isopropylcyclohexanone |
| k. (2R,3R,4S,5R)-2,3,4,5-tetrahydroxyhexane | l. (1R,2S)-1-chloro-2-ethenylcyclopentane |

Molecules with more than one chiral center and Fischer Projections

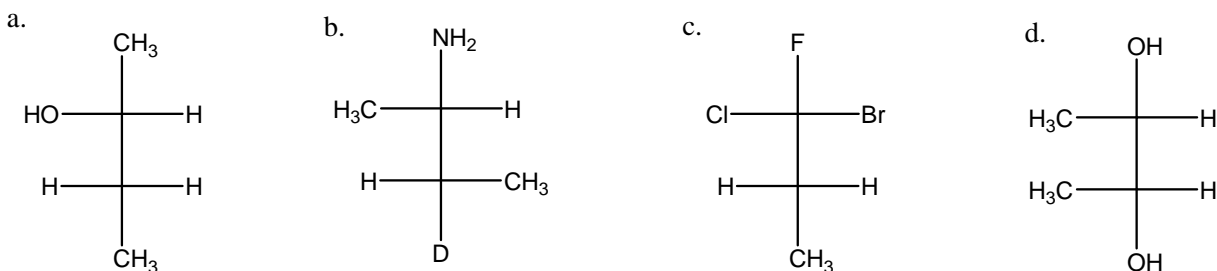
Basic Rules of Fischer Projections

1. Place the longest chain in vertical direction
2. Put the highest priority (nomenclature priority) in the top half of your representation.
3. Horizontal groups project toward the front (in front of the page/surface)
4. Vertical groups project away from the viewer (in back of the page/surface)
5. A carbon atom is indicated at each intersection of vertical and horizontal lines.

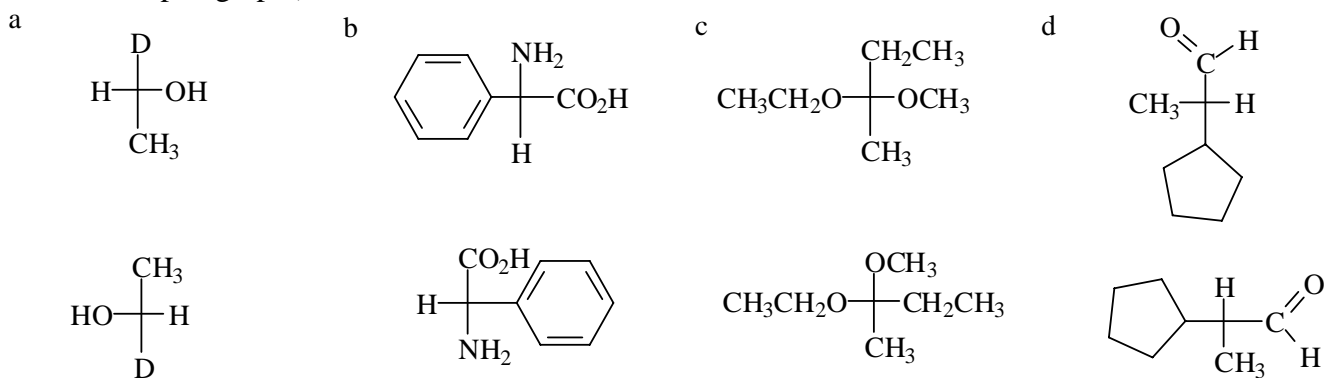
Problem 7 - Place glyceraldehyde (2,3-dihydroxypropanal) in the proper orientation to generate a Fischer projection. Can you find any stereogenic centers? Is the molecule as a whole chiral? If so, draw the enantiomer and classify all stereogenic centers as R or S.

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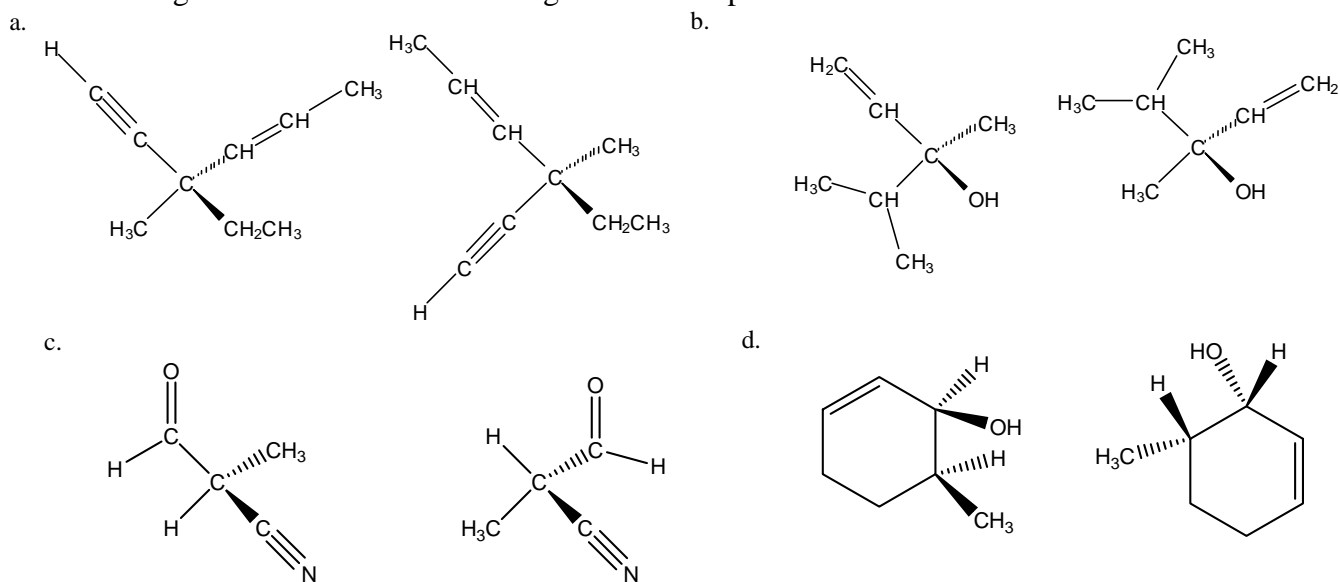
Problem 8 - Draw a 3D Newman projection and a sawhorse representation for each the following Fischer projections. Redraw each structure in a sawhorse projection of a stable conformation. Identify stereogenic atoms as R or S.



Problem 9 - Determine how many switches it takes to make the second stereogenic center appear identical to the first and identify whether the configurations at the two stereogenic centers are identical or opposite. Specify the absolute configurations as R or S. (There is another way to compare absolute configurations. (See the next paragraph.)

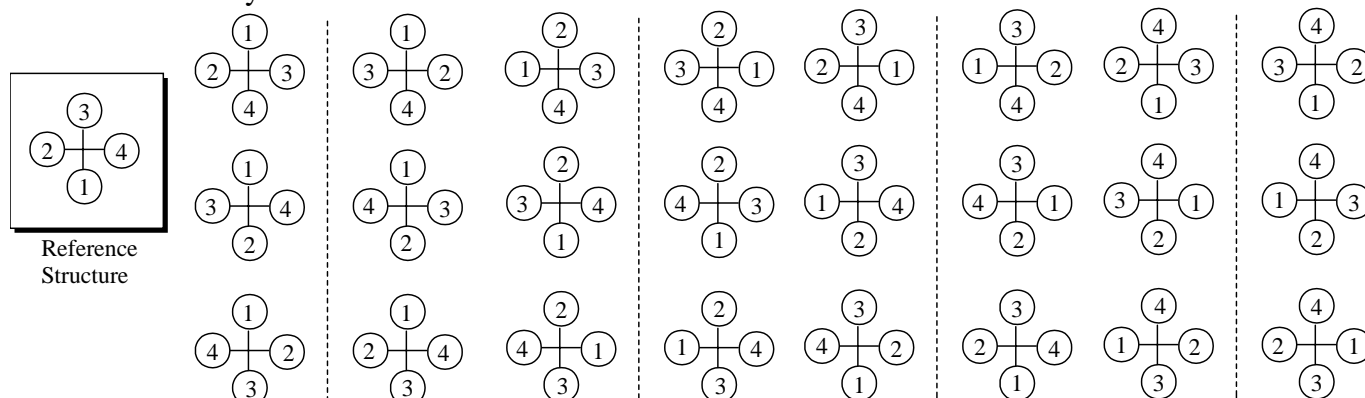


Problem 10 - Decide which are identical and which are enantiomers using your hands and arms. Specify absolute configuration as R or S. First assign the correct priorities.

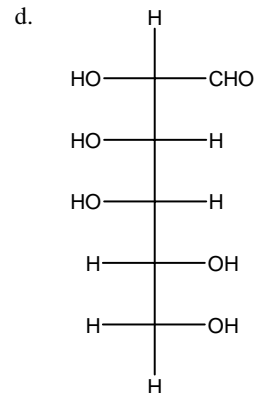
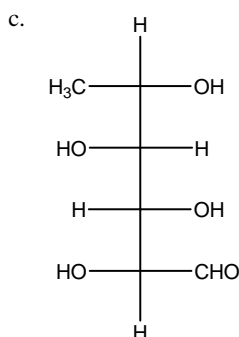
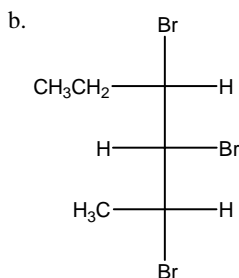
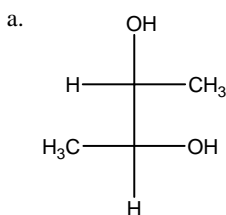


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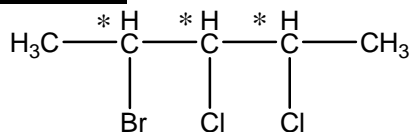
Problem 11 – For a single chiral center, Fischer projections seem almost more trouble than they are worth. There are 12 different representations of enantiomeric pairs having a single chiral center. Use the first Fischer projection drawn as a reference structure and compare the 24 different representations drawn to determine if they are identical or the enantiomer.



Problem 12 - Rearrange the Fischer projections below to their most acceptable form. You may have to rotate the top and/or bottom atom(s). You also may have to twist a molecule around 180° in the plane of the paper. Assign the absolute configurations of all stereogenic centers. Using your arm and fingers is helpful here. Write the name of the first structure.



Three Stereogenic Atoms

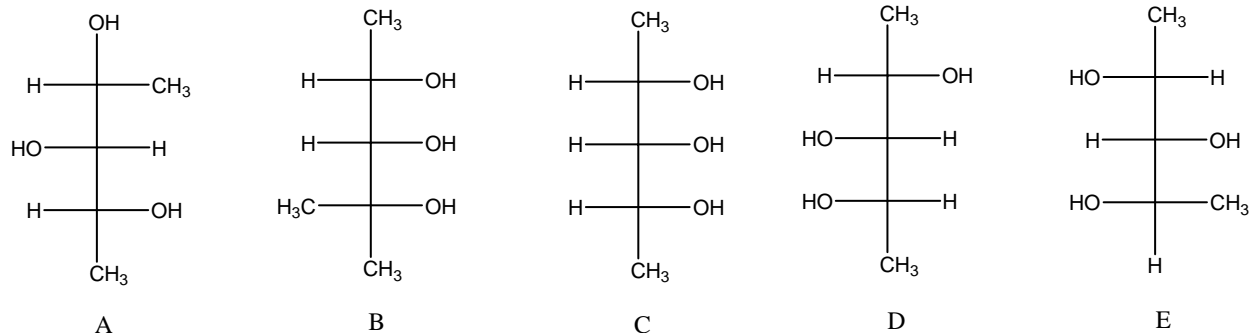


Three stereogenic centers with $2^3 = 8$ possible stereoisomers.

Problem 13 - For each of the following structures, draw only the stereoisomer Fischer projection(s) with all chlorines on one side. Is there a potentially stereogenic atom at the center of 2,3,4,5-tetrachlorohexane? What about 2,3,4,5,6-pentachloroheptane? If so draw the two stereoisomers that result from a switch only at that atom. Are the stereoisomers chiral or achiral? Are they meso, enantiomers or diastereomers?

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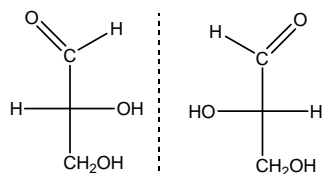
Problem 14 - For the following set of Fischer projections answer each of the questions below by writing the appropriate letter(s) or letter combination(s). Hint: Redraw the Fischer projections with the longest carbon chain in the vertical direction.



- Which are optically active?
- Which are meso?
- Which pairs are enantiomers?
- Which pairs are identical?
- Which pairs are diastereomers?
- Which, when mixed as a 50/50 mixture, will not rotate plane polarize light (optically inactive)?
- Draw any stereoisomers of 2,3,4-pentanetriol as Fischer projections, which are not shown above.

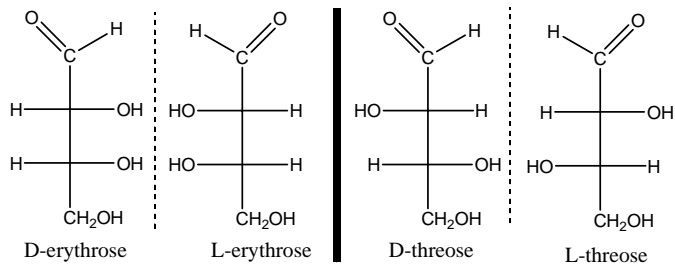
How does Nature do it?

Three carbon aldose carbohydrates



D-glyceraldehyde L-glyceraldehyde

Four carbon aldose carbohydrates



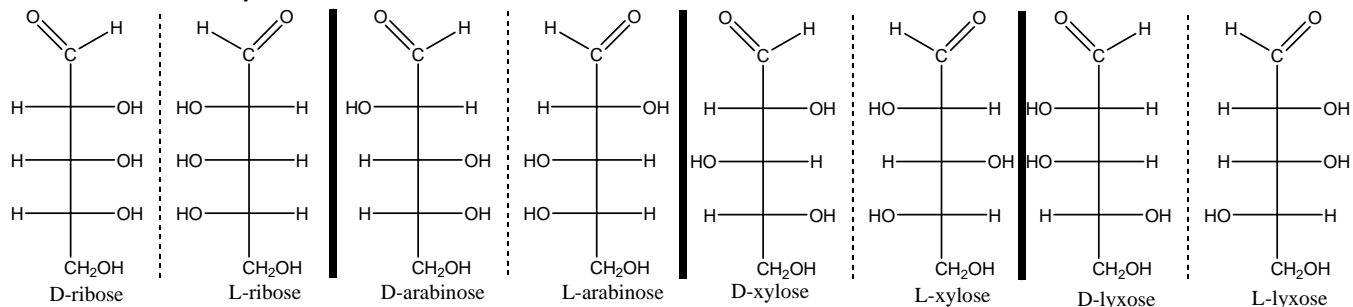
D-erythrose

L-erythrose

D-threose

L-threose

Five carbon aldose carbohydrates



D-ribose

L-ribose

D-arabinose

L-arabinose

D-xylose

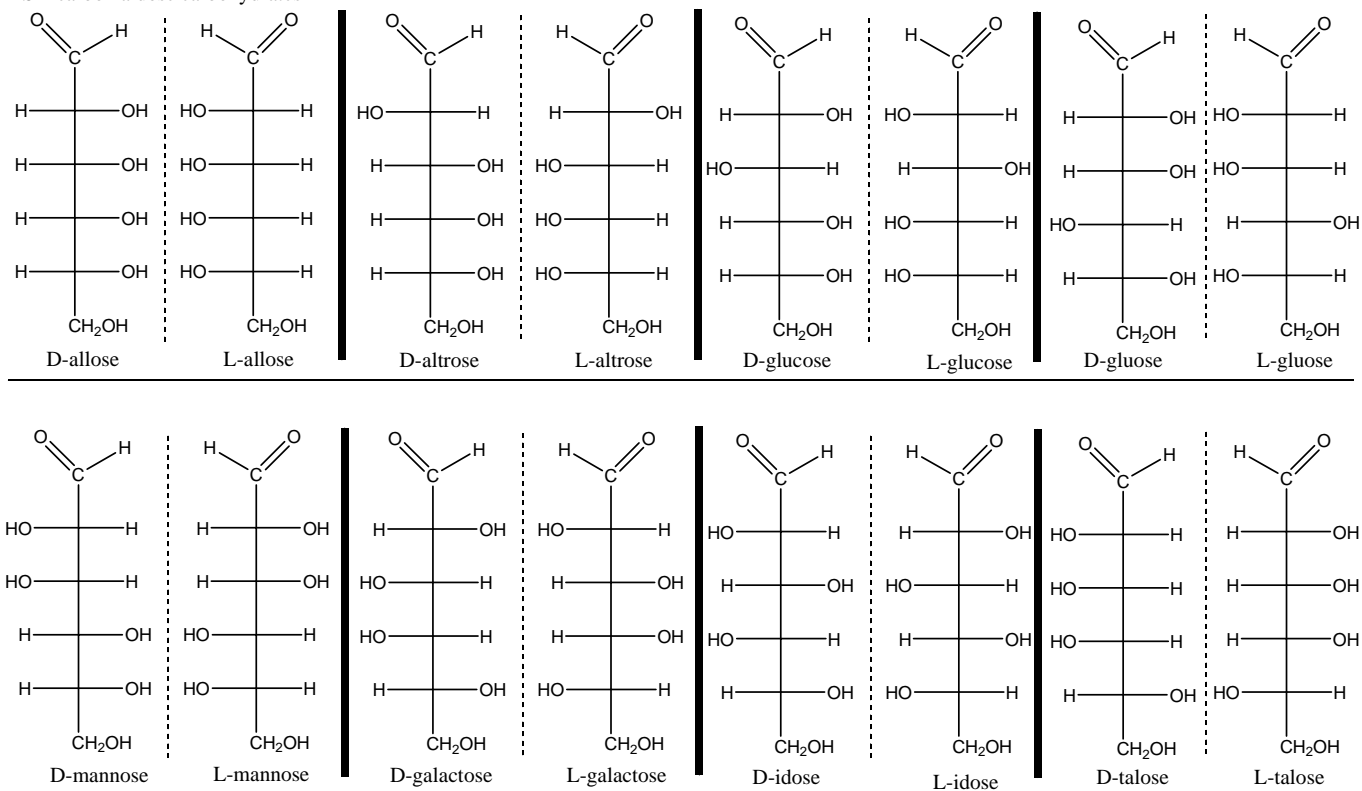
L-xylose

D-lyxose

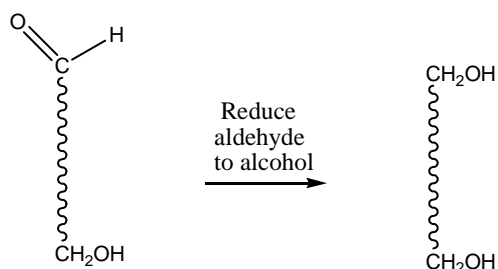
L-lyxose

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Six carbon aldose carbohydrates

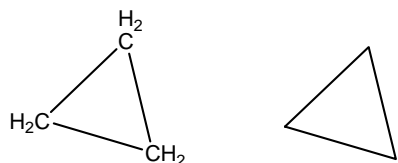


Problem 16 – What would happen to the number of stereoisomers in each case above if the top aldehyde functionality were reduced to an alcohol functionality (a whole other set of carbohydrates!)? A generic structure is provided below to show the transformation.

**Cyclic Systems**

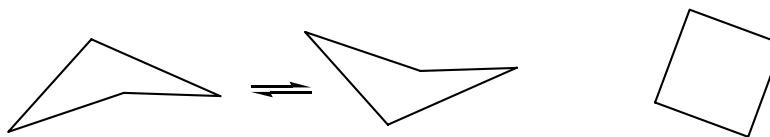
An extension of this approach to cyclic systems (rings) is straight forward, if you have understood the material presented thus far. Some of our more commonly encountered ring systems include the small ($n = 3$ and 4) and normal ($n = 5, 6$ and 7) sized rings. Remember, except for cyclopropane, rings have the ability to make partial rotations (conformational changes) about their single bonds and have a certain floppiness to them. These movements occur on the order of tens of thousands of times per second and no single representation of our ring system will accurately describe all possible conformations. Our approach in drawing rings depends on what we are emphasizing. If we want to try and show relationships of the ring and its substituents, then we need to draw approximate 3D structures that focus on a single possible conformation. Other conformations may be drawn as well for a more complete analysis. However, if we just want to show that the structure is a ring with a top and a bottom, a flat 2D structure may be sufficient. We often choose to represent the rings as time-averaged flat structures even though none of them actually exists in a flat shape, except for cyclopropane.

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cyclopropane



Cyclopropane is a flat, three point planar structure. No other shape is possible.

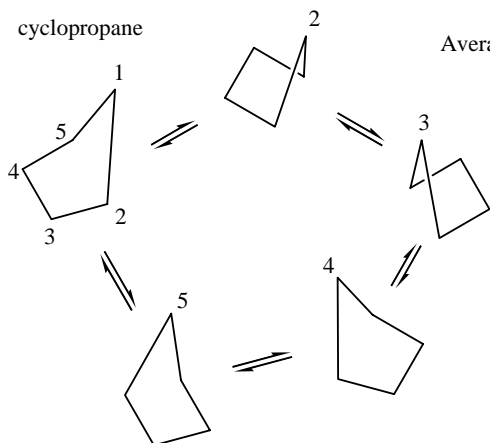
cyclobutane



Cyclobutane has a puckered conformation that flip-flops back and forth.

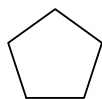
Average cyclobutane is flat.

cyclopentane

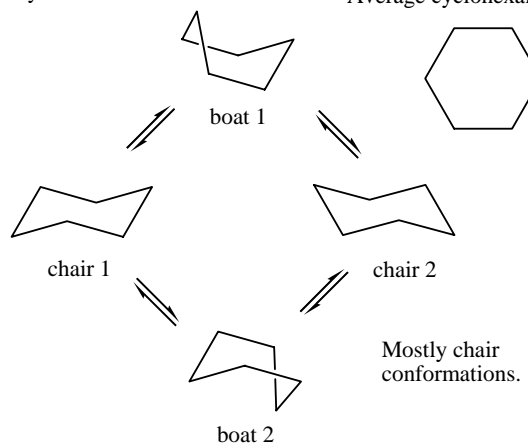


Cyclopentane has many envelope conformations via pseudorotations. Tip of flap can be up or down.

Average cyclopentane is flat.



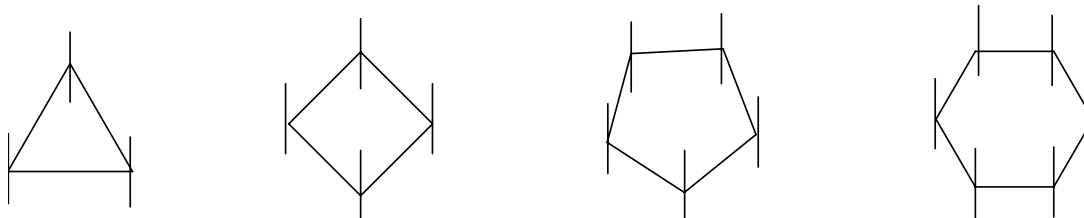
cyclohexane



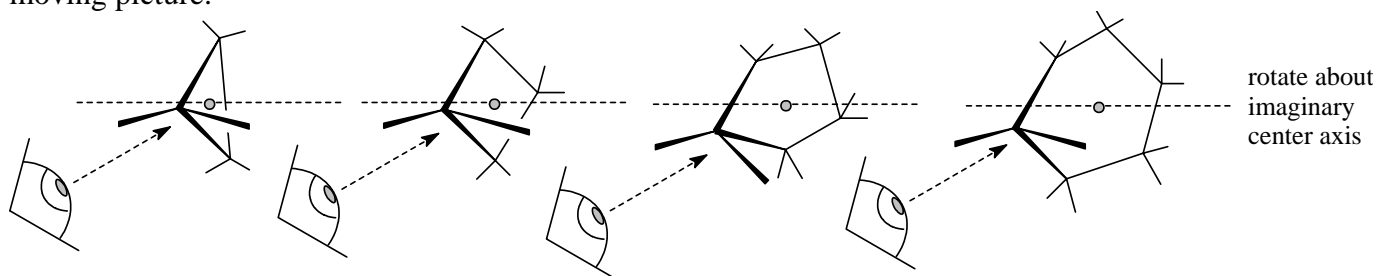
Average cyclohexane is flat.

Mostly chair conformations.

One can quickly evaluate whether substituents are on the same side (*cis*) or opposite sides (*trans*) using this approach. The two additional substituents at each carbon atom of the ring are often drawn in with simple straight lines perpendicular to the ring to indicate top and bottom (this is called a **Haworth structure** in biochemistry). Of course, real 3D structures are much more complex than this simplistic representation (i.e., cyclohexane chair conformations have axial and equatorial positions on both top and bottom that can interchange, and boat, twist boat and half chair conformations are also possible).

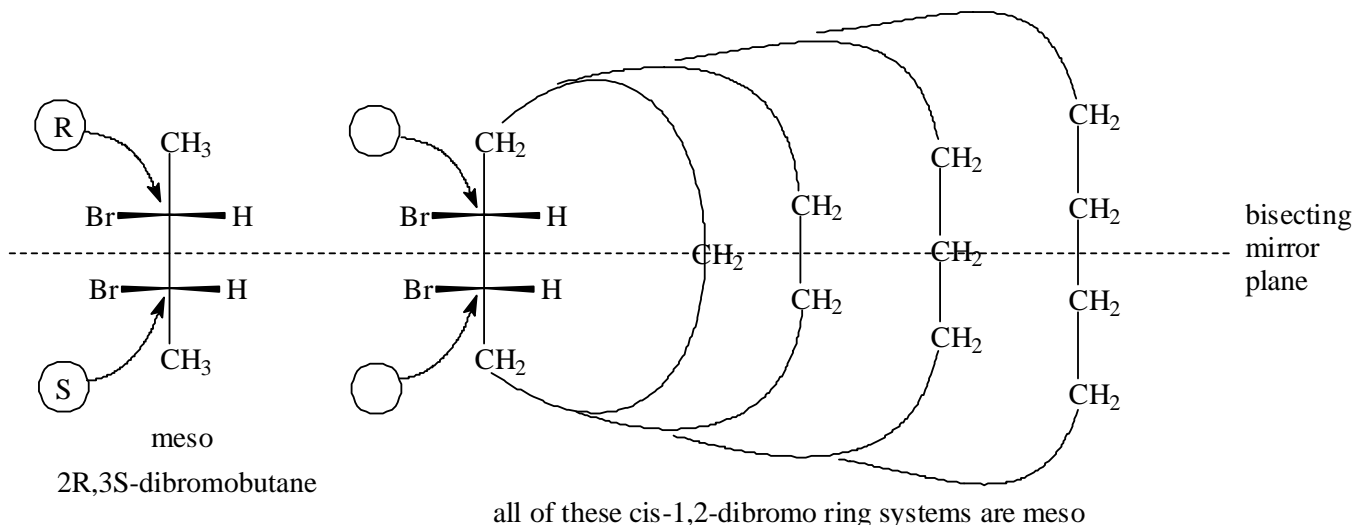


Modified Fischer projections are workable with the ring systems. We can tilt the rings on their sides and rotate the ring about an imaginary axis through the middle of the ring. The horizontal groups will continually face you as they rotate by and the vertical groups (the ring connections) will always be away. There is not really any longest, vertical carbon chain, rather each rotation is like a frame of a moving picture.



Meso Rings

If two bromine atoms were at vicinal positions (vicinal = adjacent, which comes from vicus, Latin = village, neighbors) and on the same side of the ring (*cis*), we would have a very similar picture to the meso 2,3-dibromobutane example presented earlier.

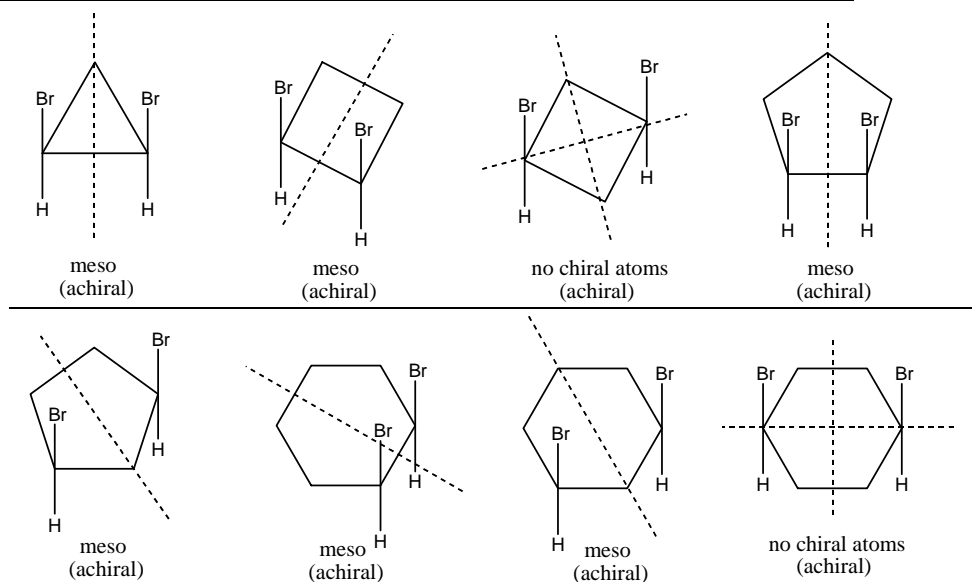


All of the *cis*-1,2-dibromo ring structures have two chiral atoms with mirror plane symmetry and so are meso (achiral and superimposable on their mirror image). Confirm the top and bottom stereogenic centers as R and S in the ring structures.

When two *cis* substituent groups are identical in any simple positional disubstituted cycloalkane examples, the stereoisomers will either be meso (achiral with chiral atoms present) or achiral (no chiral atoms present). All of these molecules have a bisecting mirror plane reflecting one half of the molecule into the other half.

When there is an even number of carbon atoms in a ring and two *cis* substituent groups are exactly opposite one another, the substituted carbon atoms are stereogenic, but not chiral.

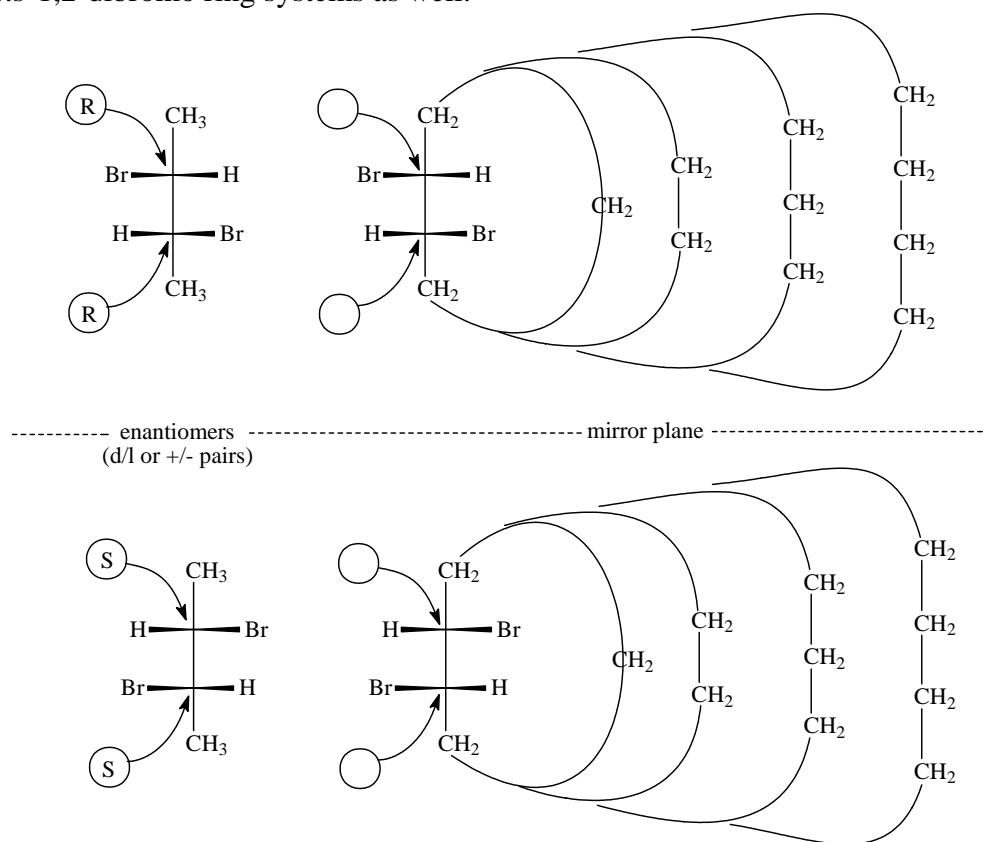
Cis possibilities - All are achiral, some are meso and some have no chiral centers



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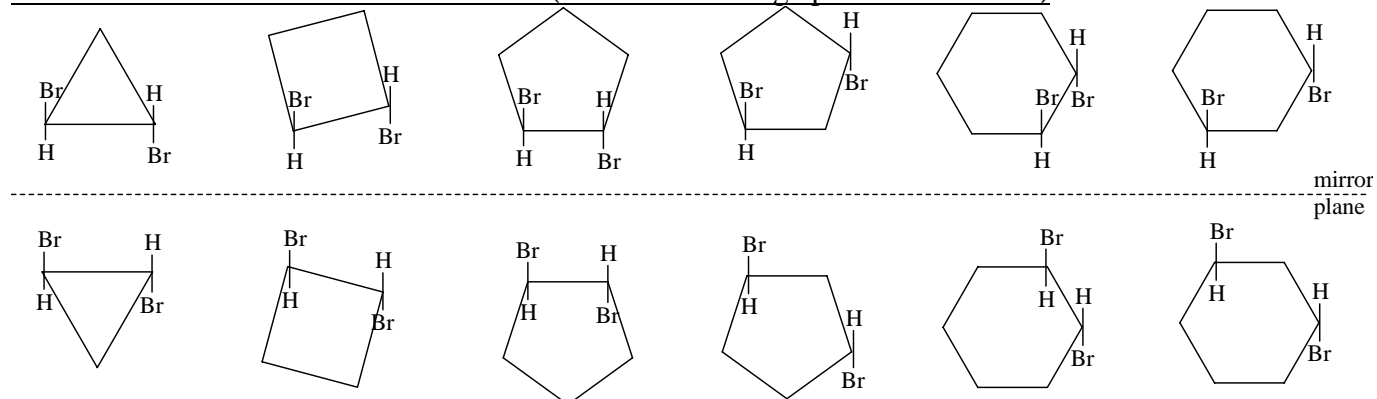
Enantiomeric Rings

The other 2,3-dibromobutane arrangement produced a (dl) enantiomeric pair. This turns out to be true in the *trans*-1,2-dibromo ring systems as well.



All of the *trans*-1,2-dibromo ring structures have two chiral atoms, with no mirror plane symmetry. They are chiral, and come in enantiomeric pairs. Confirm the top and bottom chiral centers as both R or both S in the ring structures.

When two *trans* substituent groups are identical in any simple positional disubstituted cycloalkane examples, the stereoisomers will either be enantiomeric pairs (with chiral atoms present) or achiral (no chiral atoms present). None of the enantiomeric pairs have a bisecting mirror plane reflecting.

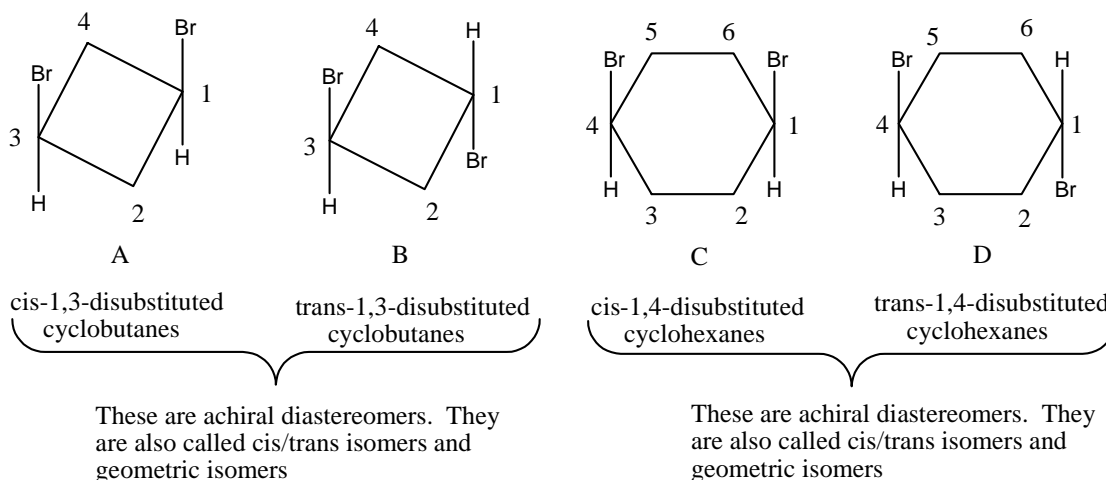
Trans Possibilities - Pairs of Enantiomers (these mirror image pairs are different)

The left bromine is on the top in all examples.

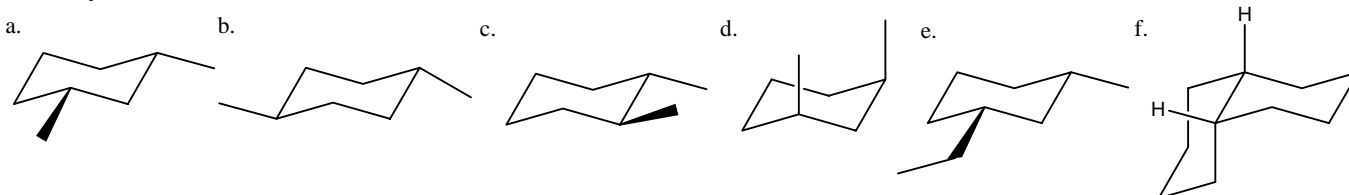
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As with the *cis* disubstituted isomers, when there is an even number of carbon atoms in a ring and two *trans* substituent groups are exactly opposite one another, the substituted carbon atoms are stereogenic, but not chiral.

Both *cis* and *trans*-1,3-disubstituted cyclobutanes and 1,4-disubstituted cyclohexanes illustrate this feature. They have stereogenic centers in the *cis/trans* sense, but not in the R/S sense, since the two paths traced about the ring are identical (two groups are the same). They are diastereomers that are also classified as geometric isomers and *cis/trans* isomers.



Problem 17 - Draw the mirror image for each of the following structures. Is the mirror image identical or different? (i.e. Is the molecule chiral?) Classify all stereogenic atoms as R or S absolute configuration. Are any of these structures meso?

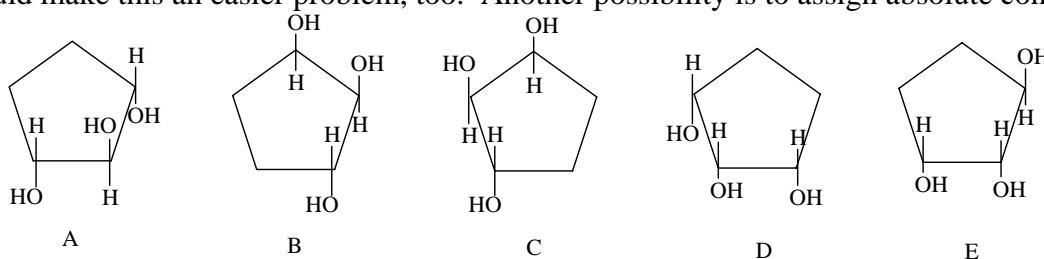


Problem 18 - a. Draw all possible isomers of dimethylcyclobutane (structural isomers and stereoisomers, there should be 9 of them). Label your structures A, B, C, D...and indicate which, if any, are enantiomers, diastereomers and/or meso structures. If stereogenic centers are present indicate the absolute configuration as R or S or an achiral stereogenic center. Decide which conformation is most likely preferred for each isomer.

b. How would the problem change if one of the methyl substituents had been changed to a Br substituent?

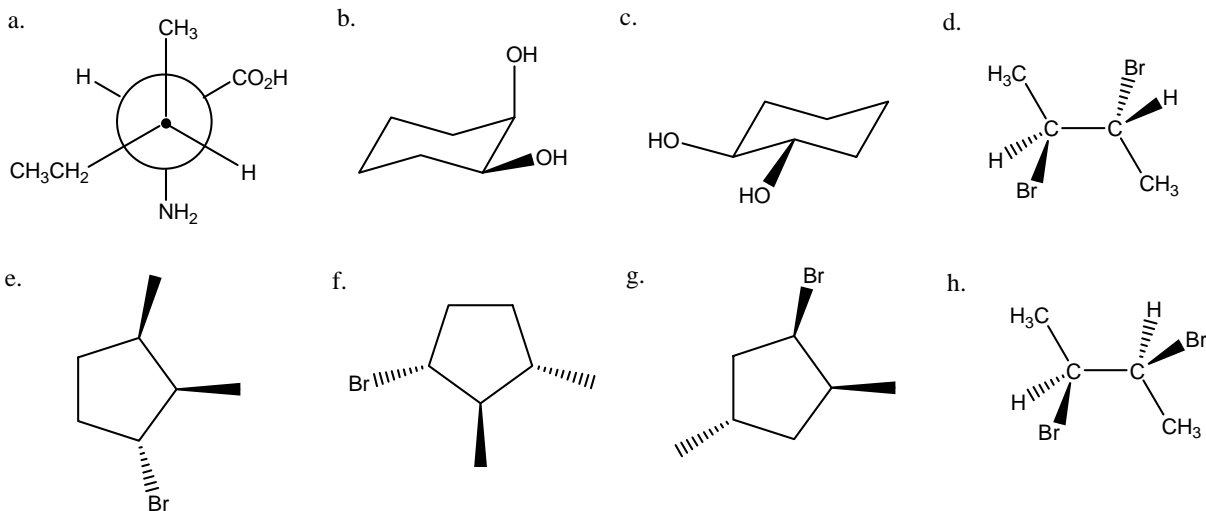
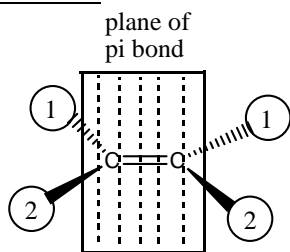
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Problem 19 - For the following set of stereoisomers answer each question by indicating the appropriate letter(s) or letter combination(s). It may help to rotate and/or flip the rings to alternate perspectives. Models would make this an easier problem, too. Another possibility is to assign absolute configurations.



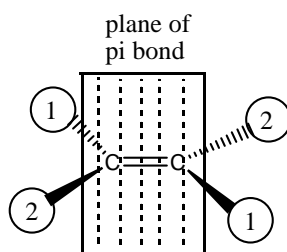
- Which stereoisomers can rotate plane polarize light (are optically active)?
- Which are meso?
- Which pairs are enantiomers?
- Which pairs are identical?
- Which pairs are diastereomers?
- Draw any stereoisomers of 2,3,4-cyclopentanetriol not shown above.

Problem 20 - Draw the mirror image structure for each of the following molecules. Is the mirror image identical or different? Is the molecule chiral? Classify all stereogenic centers as R or S absolute configuration. Are there any meso structures?

E and Z Isomers

Z = zusammen

The high priority groups are on the same side of a plane cutting through the pi bond.



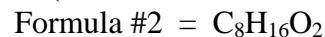
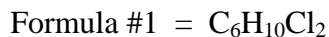
E = entgegen

The high priority groups are on opposite sides of a plane cutting through the pi bond.

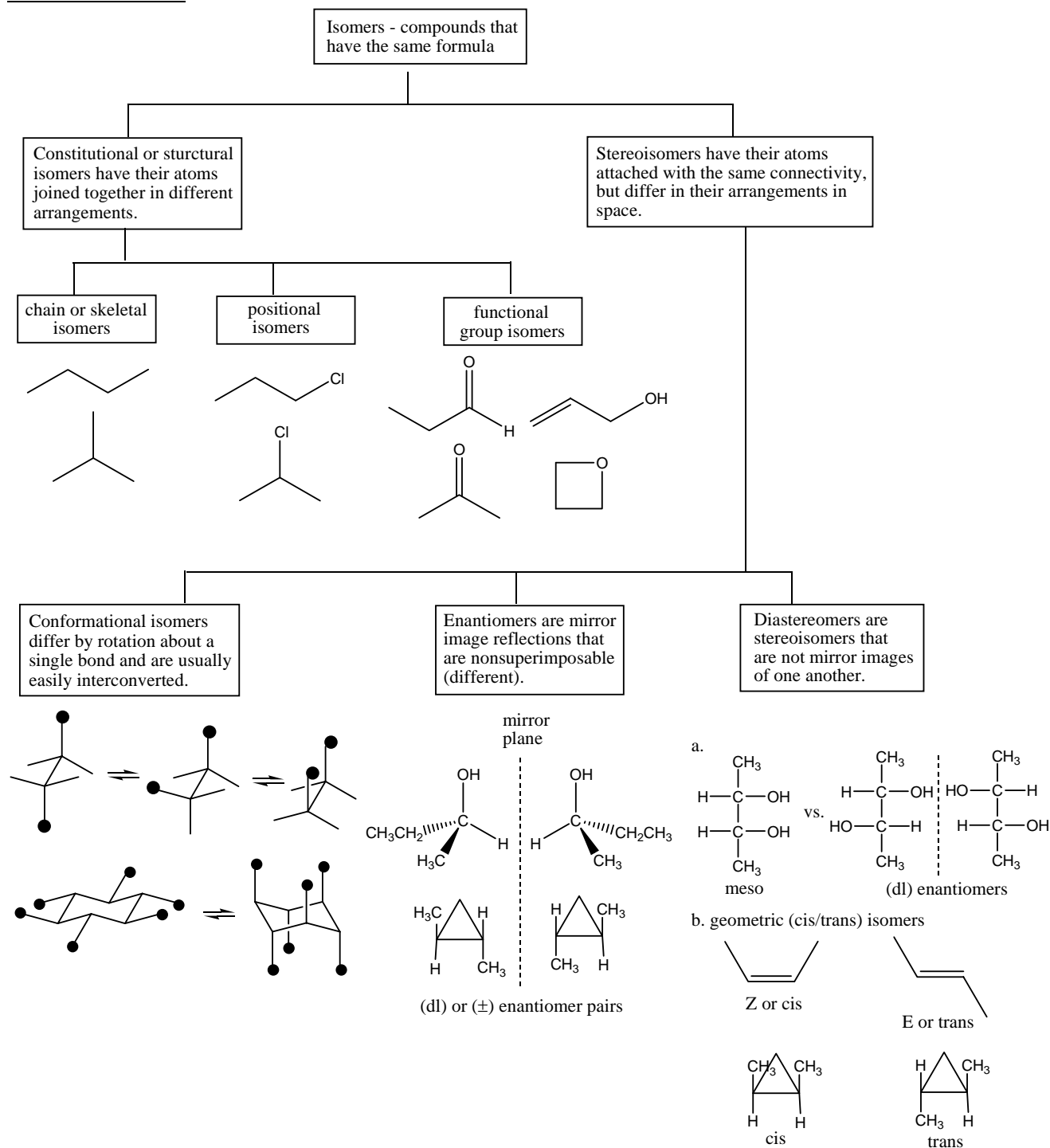
"1" and "2" are the priorities of the groups bonded to the atoms of the pi bond.

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Problem 21 - Using the formulas provided, draw an example illustrating each of the listed types of isomerism. To illustrate isomerism you have to draw at least two structures. (Hint - First calculate the degree of unsaturation.)

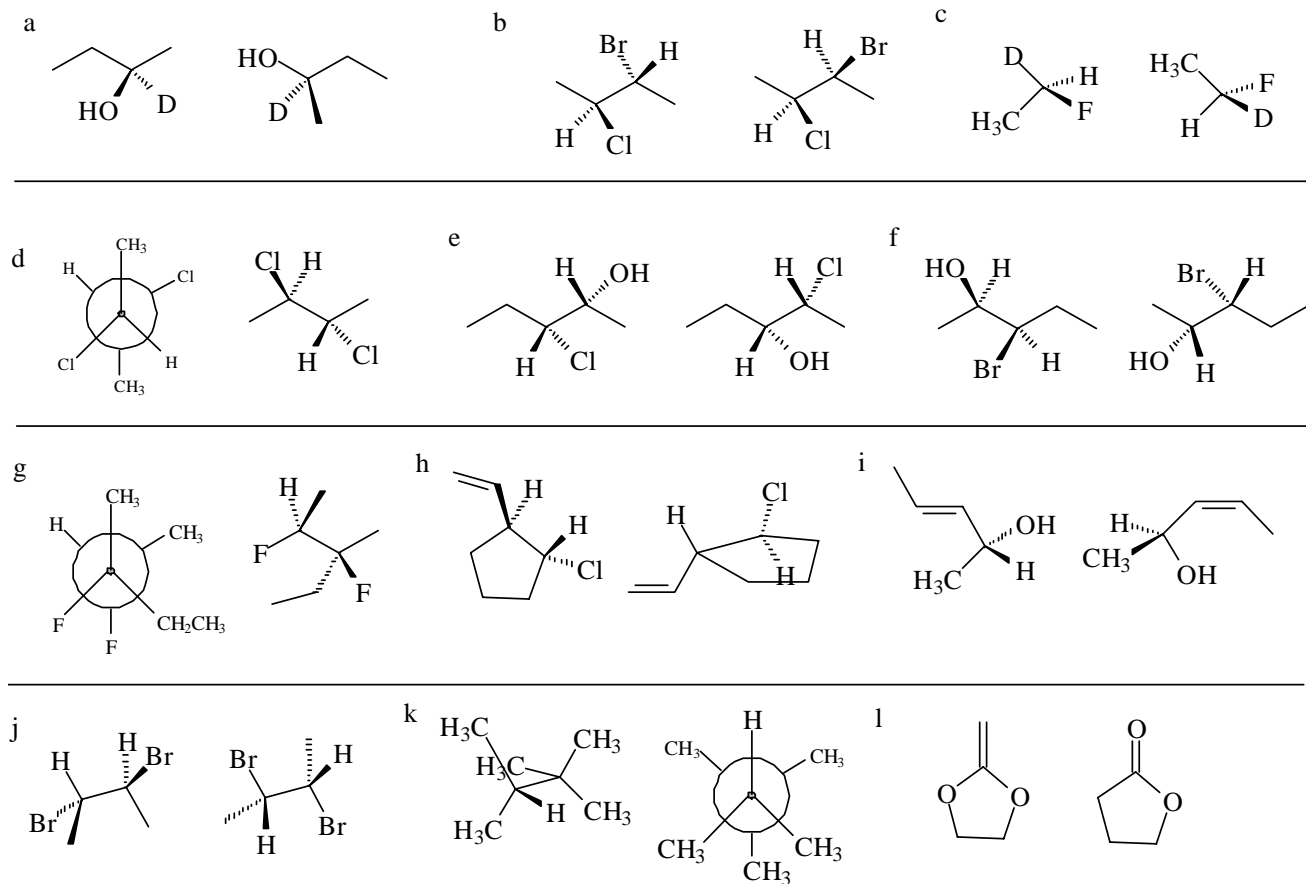


- a. chain or skeletal isomers
 b. positional isomers
 c. functional group isomers
 d. enantiomers
 e. diastereomers (not geometric)
 f. diastereomers (geometric)
 g. conformational isomers
 h. a meso compound (only one structure needed)

Isomer Overview

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Problem 22 - What is the relationship between the molecules in each of the following pairs? i. structural isomers ii. functional group isomers iii. positional isomers iv. enantiomers v. diastereomers (not geometric) vi. diastereomers (geometric, cis/trans) vii. conformational isomers viii. not isomers at all



Problem 23 - There are two possible stereoisomers at an E/Z double bond, just as there are two possible absolute configurations at an R/S stereogenic center (atom). Using this knowledge, predict how many stereoisomers are possible for each of the following structures. Draw a 3D structure of each stereoisomer. Provide an acceptable name for your stereoisomers in part a.

