STEREOISOMERISM

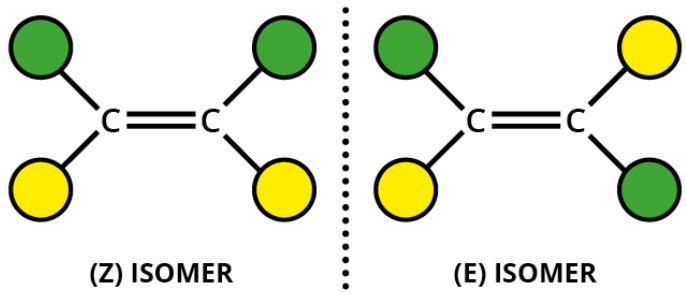
Stereoisomerism occurs when atoms are joined in identical manner but they have different spatial relationships to each other.

There are two main types of stereoisomerism – geometric isomerism, and optical isomerism. These, as the difference in name suggests, aren't to do with any large scale rearrangements of the structure of molecules; instead, they involve different arrangements of parts of the molecule in space. They're a little more complicated to think about than the structural isomers, so let's have a look at each of them in turn.

Geometric Isomers

Geometric isomerism is actually a term that is 'strongly discouraged' by IUPAC (the International Union of Pure & Applied Chemistry), who prefer 'cis-trans', or 'E-Z' in the specific case of alkenes. However, 'geometric isomerism' is still consistently used to refer to both, so for that reason I've used that name here.

This type of isomerism frequently involves carbon-carbon double bonds (shown by two lines joining each carbon instead of one) or cyclic compounds. Rotation about double bonds, or about single bonds in rings is difficult, compared to single bonds, which can rotate freely. This means that, if there are two different atoms, or groups of atoms, attached to each carbon of the carbon carbon double bond, they can be arranged in different ways to give different molecules. These atoms or groups can be given 'priorities', with atoms with higher atomic numbers given higher priorities. If the highest priority groups for each carbon are on the same side of the molecule, that molecule is denoted as the '*cis*-' or 'Z' isomer. If they're on opposite sites, it's denoted as the '*trans*-' or 'E' isomer.

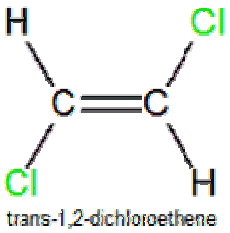


The two different nomenclatures are a little confusing – cis/trans is now less commonly used, with E/Z instead being favoured. E stands for 'entgegen' ('opposite' in german) whilst Z stands for 'zusammen' ('together' in german). The letter is simply added in brackets at the start of the molecule's name in order to indicate which isomer it is.

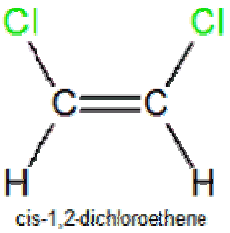
Summary

- Occur when rotation is restricted
  - Multiple bonds
  - Cyclic compounds
- There are two different groups on each of the rotation-restricted C atoms.
- Focus on what is attached at C=C bonds

Eg. 1,2-dichloroethene - build models of the molecules below:



trans-1,2-dichloroethene



cis-1,2-dichloroethene

Are these two molecules the same ? _____

Is there any way you can rotate one to form the other? _____

Note: *In the model, the reason that you can't rotate a carbon-carbon double bond is that there are two links joining the carbons together. In reality, the reason is that you would have to break the pi bond. Pi bonds are formed by the sideways overlap between p orbitals. If you tried to rotate the carbon-carbon bond, the p orbitals won't line up any more and so the pi bond is disrupted. This costs energy and only happens if the compound is heated strongly.*

There are two possible isomers:

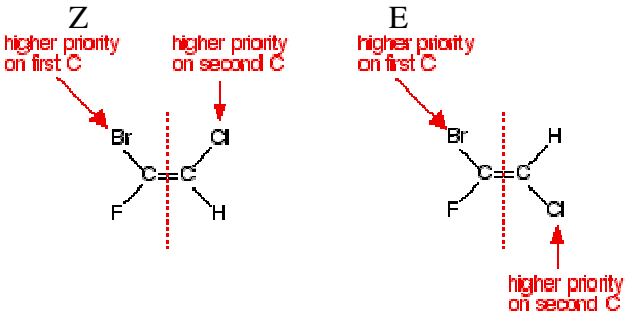
trans- (latin for ACROSS) groups are on opposite sides

cis- (latin for "ON THIS SIDE") groups are on the same side.

The E-Z system

What happens when there are FOUR different groups involved? cis-/trans- doesn't seem to work!

Consider the atomic numbers of the attached atoms either side of the C=C bond, and identify those with the higher value on each C atom in turn. The ones with the higher atomic number are given higher priority.



Build models of the Z and E isomers.

This method of assigning priorities to substituents by reference to atomic number is known as the CIP (Cahn-Ingold-Prelog) system.

Cahn-Ingold-Prelog (CIP) Priorities

Apply the following rules to decide the priority of an atom or group "X"under the CIP system.

Rule 1: The higher the atomic number of the first atom in X, the higher the priority of X.

e.g. for typical non-metals encountered in organic compounds we have:

$X = {}_{53}I > {}_{35}Br > {}_{17}Cl > {}_{16}S > {}_{15}P > {}_{8}O > {}_{7}N > {}_{6}C > {}_{1}H$

Rule 2: If the relative priorities of two groups cannot be decided by Rule 1, it is determined by applying Rule 1 to the next atom or atoms in the group 'X'.

e.g. for groupings in organic molecules where X is more than one atom ....Hence for X = alkyl:

$-CH(CH_3)_2 > -CH_2CH_2CH_3 > -CH_2CH_3 > -CH_3 > -H$

i.e. the longer the hydrocarbon carbon chain, and the more branched it is, the higher its priority.

Also, for a greater variety of groups we would have:

$-I > -Br > -Cl > CHBr_2 > -CH_2Br > -CH_2Cl > -CH_2OCH_3 > -CH_2OH > -CH_2CH_2Br > -CH_2CH_2Cl > -CH_2CH_3 > -CH_3 > -H$

These two rules will be applied both in the case of geometrical isomers (E/Z notation), and optical isomers (R/S notation.

Rules for Applying E/Z designation

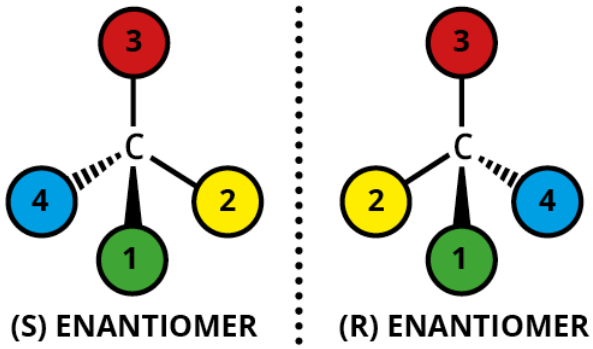
- Examine the atoms attached to the carbon atoms either side of the double bond (or adjacent to one another on a ring).
- Give each one a priority based on the CIP system.
- If high priority groups are on opposite sides you have the E isomer .(German entgegen = opposite)
- If high priority groups are on the same side you have the Z isomer (German zusamen = together).

Optical Isomers

Optical isomers are so named due to their effect on plane-polarised light, (read more at this link), and come in pairs. They usually (although not always) contain a chiral centre – this is a carbon atom, with four different atoms (or groups of atoms) attached to it. These atoms or groups can be arranged differently around the central carbon, in such a way that the molecule can't be rotated to make the two arrangements align. Since one arrangement can't line up to look exactly like the other, we refer to them as 'non-superimposable mirror images' –the isomers are mirror images of each other. your hands are like this – you can't exactly superimpose one hand on top of the other, because your thumbs will stick out in opposite directions. That's why we sometimes use the expression "handed" when referring to similar objects. The technical term in chemistry is *chiral.*

Optical isomers can be allocated an identifying letter, based on the same CIP system of priority as with E-/Z-. The molecule is rotated so that the lowest priority group (usually hydrogen) is oriented pointing away. Looking at the remaining groups, if they decrease in priority going in an anti-clockwise direction, then the isomer is designated "S" (from the Latin 'sinister', meaning 'left'). If they decrease

in priority going in a clockwise direction, "R"is used (from the Latin 'rectus', meaning 'right'). The "S" or "R" letter is simply added in front of the isomer's name in order to indicate which one it is.



Terms to Note

Chiral
Molecules which CANNOT be superimposed on their mirror images are described as chiral.

Achiral
Molecules which CAN be superimposed on their mirror images are described as achiral.

Enantiomers or optical isomers
These are isomers which are non-superimposable mirror-images of one another. Enantiomers behave in an identical manner EXCEPT in a chiral environment. (Such as in the presence of enzymes.)

Chiral/stereogenic centre
A carbon with 4 different atoms or groups attached.

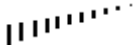
Meso-
Describes a molecule which has more than one stereocentre, but which is nevertheless identical to its mirror image and so shows no optical activity.

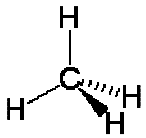
Racemic
Describes a mixture which contains equal amounts of the R and the S forms of a molecule, and therefore shows no net optical activity.

Stereochemical Formulae

This is a formula which shows the relative orientation in space of the bonds around an atom or a group of atoms. Two conventions are important:

 for a bond which comes out towards the front of the molecule, towards one, and:

 (or a simple dotted line) for a bond which goes towards the rear of the molecule, away from one. This stereochemical formula shows the shape of the methane molecule:



Stereochemistry activities

1) Make a model of dichloromethane. Draw two views of the molecule. Use stereochemical formulae.

a) Are they inter-convertible? _____
b) Hold the model in the mirror.
   i) Can the model be superimposed on its mirror image? _____
   ii) Is this molecule CHIRAL or ACHIRAL ? underline.

2) Make a model of bromochlorofluoromethane. CHBrClF
   a) Hold the model next to a mirror.
      i) Can the model be superimposed on the mirror image ? _____
      ii) Draw the model in the box below.

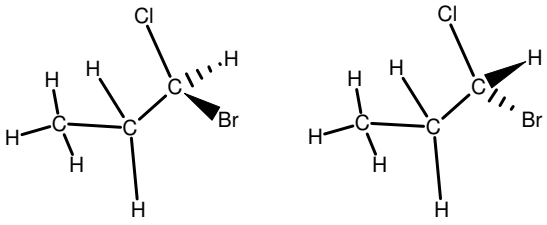
b) Draw the mirror image of the model in the second box.

Is this molecule CHIRAL or ACHIRAL ? (underline)

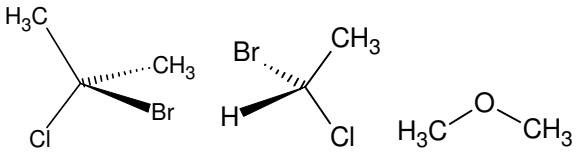
Use models as necessary to complete the following activities. Classify each as either R or S enantiomers according to the method given below.

Rules for Applying R/S designation

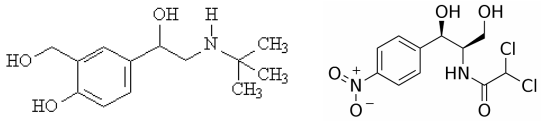
- Assign priorities according to the CIP rules above.
- Turn the molecule so that the lowest priority group is pointing away from you.
- Consider an imaginary circle from the highest priority to the lowest via the one of intermediate priority.
- If the path goes to the left (counter clockwise) the enantiomer is **S**
- If the path goes to the right (clockwise) the enantiomer is **R**.



3) Classify each of the following molecules as chiral or achiral.



4) Mark all stereogenic centres in the compounds shown below:



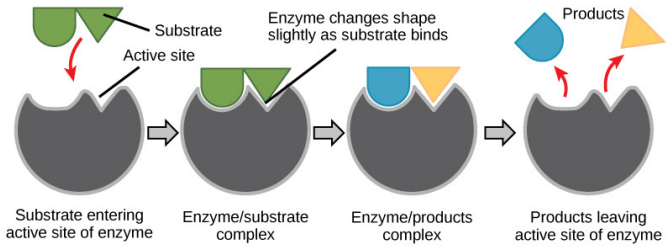
5) a) Build a chiral molecule using a larger ball as carbon and four smaller balls of different colours as substituents.

b) Draw your structure. Classify your structure as R or S.

c) Draw a triangle on a piece of paper. Label each corner with one of the colours you have used to make your model. Attempt to place your model on the triangle so that the colours match. (This is like a molecule fitting into the *active site* of an enzyme.)

d) Swap the positions of two of the coloured balls (substituents) in your model and attempt the placement of the model on the triangle again. What conclusions can you draw about the acitivity of enzymes with regard to chiral molecules?

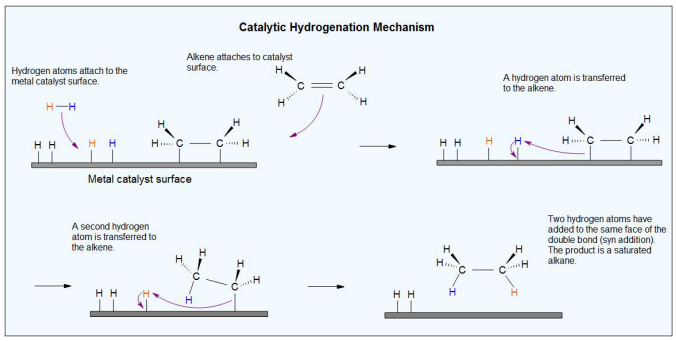
The diagram below shows how enzyme catalysis works, but does not show that the active site is usually chiral.



Source: https://www.boundless.com/biology/textbooks/boundless-biology-textbook/metabolism-6/enzymes-72/enzyme-active-site-and-substrate-specificity-350-11576/

Stereochemistry of Selected Reactions

1) Hydrogenation of an alkene on the surface of a Ni catalyst. Two hydrogen atoms add to the same side of the molcule. This is called "syn" addition.



Source: http://chemwiki.ucdavis.edu/Organic_Chemistry/Hydrocarbons/Alkenes/Reactions_of_Alkenes/Catalytic_Hydrogenation

a) Construct (E)-1,2-dichloro-1,2-difluoroethene and draw a stereochemical formula for your molecule.

b) Lay the molecule down flat and add a hydrogen to each carbon from above, moving the halogen atoms down to accommodate the hydrogens with the proper tetrahedral bond-angles.

c) You might have any of the following molecules:
(1R,2S)-1,2-dichloro-1,2-difluoroethane,
(1R,2R)-1,2-dichloro-1,2-difluoroethane or
(1S,2S)-1,2-dichloro-1,2-difluoroethane.
Which one do you have? (Underline)

d) Draw a stereochemical formula for your molecule:

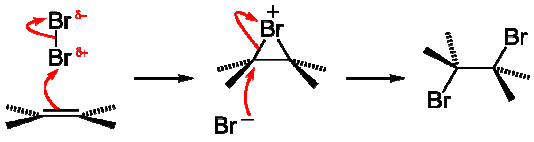
e) Is your molecule chiral or meso? _____

f) Repeat steps (a) to (d) starting with (Z)-1,2-dichloro-1,2-difluoroethene.
Formula:

Name _____

Chiral or meso? _____

2) Halogenation of an alkene using Cl_2 or Br_2. The halogen atoms add to *opposite* sides of the molecule. This is called "anti" addition.



http://en.wikipedia.org/wiki/Halogen_addition_reaction

a) Repeat exercise (1), but now with anti addition of bromine.
Formula:

Name _____

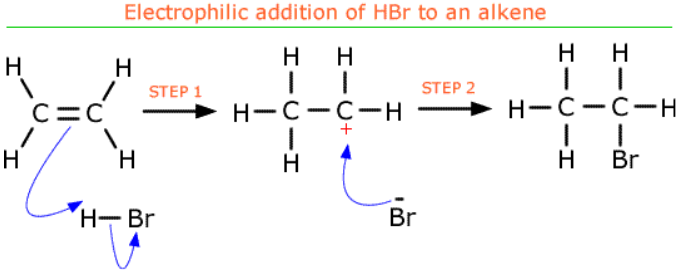
Chiral or meso? _____

Formula

Name _____

Chiral or meso? _____

3) Hydrohalogenation (HX) where X=Cl, Br or I. racemic mixture produced, both syn & anti addition.



Source:
http://alevelchem.com/aqa_a_level_chemistry/unit3.2/sub3209/02.htm

a) Start with (E)-1,2-dichloro-1,2-difluoroethene again.

b) Add a hydrogen to either carbon. Note that this will give two different optical isomers for the carbocation intermediate depending on exactly how the hydrogen is added, either from the top or the bottom. The intermediate is planar about the positively charged carbon.

c) Add bromine to the intermediate, from either the top or the bottom.

d) Satisfy yourself that 4 different product molecules will be formed, draw their formulae and name them, using the names given in (1c) above as your model.

e) Why were there only 3 compounds for (1c) whereas there are 4 in this case?

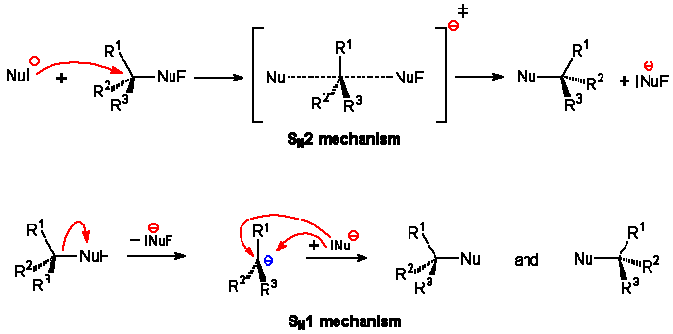
_____

_____

_____

4) Nucleophilic substitution, the S_N1 and S_N2 mechanisms.

In the diagram below, "NuI" represents an incoming "nucleophile". NuI could be Br, so that the negatively charged attacking species is Br^-. NuF represents what is known as a "leaving group". I and Br are good leaving groups.



Source: http://myibchemistry.blogspot.com/2014_04_01_archive.html

a) Build a model of bromochlorofluoromethane and represent it with a stereochemical formula. We will assume that only one istope of bromine is used, ^{79}Br.

b) Is it R or S? _____

c) If the nucleophile is $^{81}Br^-$ (remember different isotopes of an element have the same chemical properties) carefully construct the molecule that results from the S_N2 attack of $^{81}Br^-$ on the molecule. The leaving group is the ^{79}Br, which turns into $^{79}Br^-$.

Is the product R or S? _____

d) Why do we refer to "inversion of configuration" regarding the S_N2 mechanism?

e) Compare the S_N1 mechanism. Note the carbocation intermediate. Explain why this gives a *racemic mixture* of products.

Other sources

http://www.compoundchem.com/2014/05/22/typesofisomerism/

http://www.docbrown.info/page07/isomerism2.htm