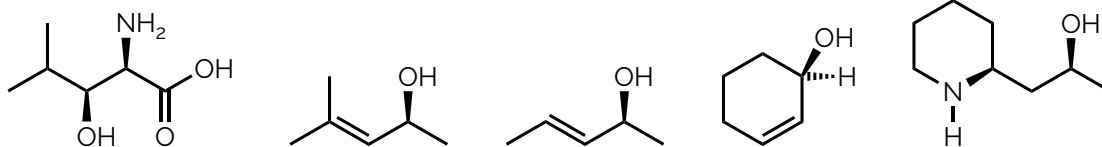


# Stereochemistry 1 - Worksheet

## Question 1

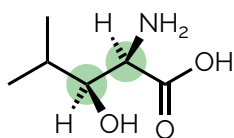
Identify the stereocentre(s) in the following molecules:



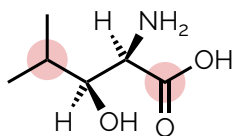
## Answer 1

Molecule 1

For first year chemists there are two possible stereocentres, those based on tetrahedral or  $sp^3$  hybridised atoms and those based on  $sp^2$  hybridised atoms as found in alkenes (or imines). For an  $sp^3$  atom to be a stereocentre it must have four different substituents (or groups of atoms) coming off the atom. If we look at the first molecule, there are two such stereocentres. The key is to remember the hydrogen atom that is omitted from skeletal representations. The stereocentres are shown below:

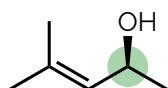


The two most common mistakes are thinking the atoms marked in red (below) are stereocentres. The  $sp^3$  carbon on the left is not a stereocentre as the two methyl groups are identical, exchanging these would not lead to a new stereoisomer. The carbonyl group is not a stereocentre as the atom at the other end of the double bond must have two different groups if we are to form stereoisomers (unless the molecule is an allene but you will not meet this functional group at first year) and here we have two identical lone pairs of electrons.

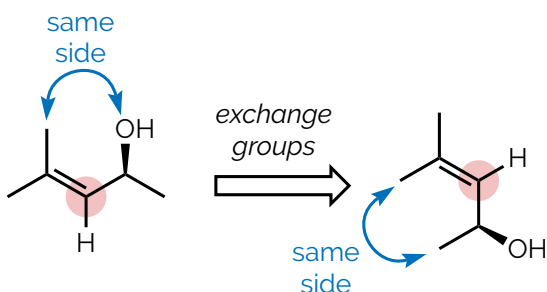


Molecule 2

There is only one stereocentre in this molecule (shown in the green circle).

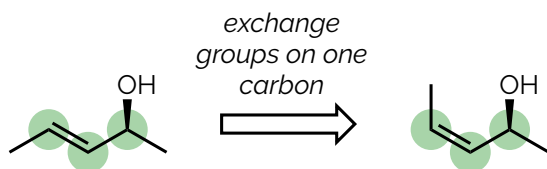


The alkene isn't a stereocentre as there are two identical groups on one of the carbon atoms. This means we can exchange these groups and we are left with an identical molecule not a stereocentre (this is also the case if the alcohol substituent is exchanged at the other end of the alkene. It is currently on the same side as a methyl group and if it was swapped to the other side of the alkene it would still be next to a methyl group (see below).



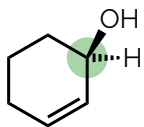
Molecule 3

Now there are three stereocentres. The original alcohol with  $sp^3$  hybridised atom with four groups attached, and now the two carbon atoms of the alkene. Swapping the substituents on either of these carbon atoms would change the alkene from a trans alkene to a cis alkene or would change the stereoisomer.



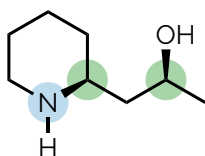
#### Molecule 4

There is only one stereocentre in this molecule, the carbon with the alcohol. The alkene carbons are not stereocentres. The alkene cannot exist as a trans isomer as it would be impossible to close the six-membered ring. There simply are not enough atoms to allow the two ends to join up. The smallest cyclic system that can accommodate a trans alkene is cyclooctene (eight carbons in a ring).



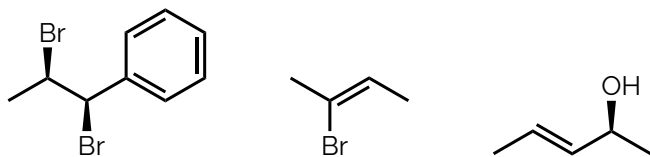
#### Molecule 5

And we'll finish question one with a nasty example. There are definitely two stereocentres in this molecule (marked in green). Both carbon atoms have four different groups coming off them (don't forget the hydrogen atoms omitted from skeletal diagrams). The problematic atom is the nitrogen. It has four groups attached to it; two carbon atoms, a hydrogen atom and a lone pair of electrons. As such it is a stereocentre. So why have we mentioned it? The problem is that you would not be able to isolate the two stereoisomers that could be formed by exchanging two groups. The lone pair on nitrogen can burrow through the atom and swap sides of the molecule in a process known as pyramidal inversion. If you can't isolate a stereoisomer does it exist? We'll leave that question to your professor (but we'd accept it if we were marking your work).



## Question 2

Draw a diastereomer (diastereoisomer) of each of the following molecules:

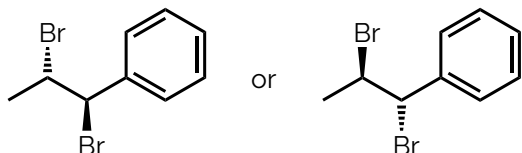


## Answer 2

#### Molecule 1

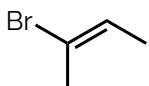
A diastereomer is a stereoisomer that is not a mirror image of the original compound. This means you must change the relative stereochemistry of the molecule. This means one stereocentre within the molecule must stay the same and at least one must change. You cannot change all the stereocentres as this would either give you an enantiomer or, if the molecule is achiral, the original compound.

For the first molecule this means we can change either bromo substituent but not both. In the original molecule both bromo substituents were on the same side. In the diastereomer they are on opposite sides of the molecule.



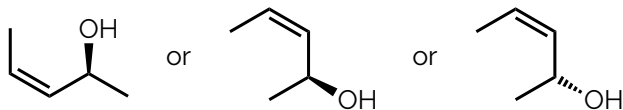
#### Molecule 2

Alkenes are just the same. We can change either stereocentre but not both, the latter would return the original molecule. We have to change the alkene from a Z-alkene to an E-alkene.



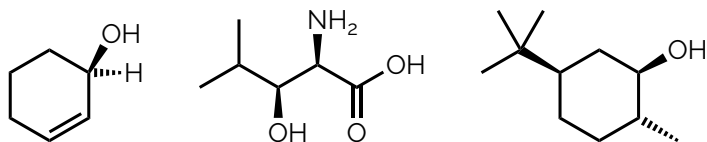
### Molecule 3

In this example, we have to be slightly careful. Changing the configuration of the alcohol leads to an enantiomer not a diastereomer. So, in order to draw a diastereomer, we have to change the configuration of the alkene. We could change both the alkene and the alcohol (the last drawing) but the key is the alkene must change.



### Question 3

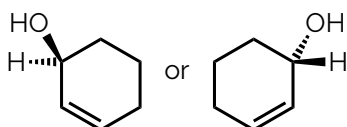
Draw the enantiomer of each of the following molecules:



### Answer 3

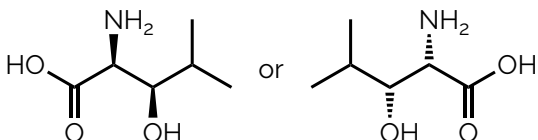
#### Molecule 1

This question requires you to draw the non-superposable mirror image of the molecules. This means changing the absolute configuration of every stereocentre within the molecule. The first molecule only has a single stereocentre (remember, the alkene cannot be changed as the ring is too small). The enantiomer can be drawn either as if the mirror had been placed to the side of the molecule or above the molecule (drawing on the right). Both drawings below are the same enantiomer.



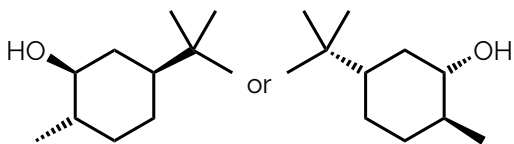
#### Molecule 2

If there are multiple stereocentres, you must change them all. Again, you can either draw the mirror image (left-hand side) or invert the stereocentres (right-hand side).



#### Molecule 3

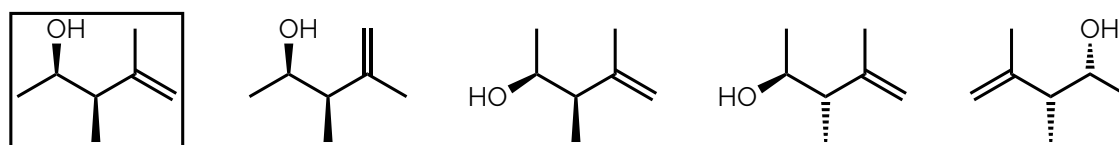
The ring makes no difference, you have to change all the stereocentres. The two representations of the other enantiomer are below:



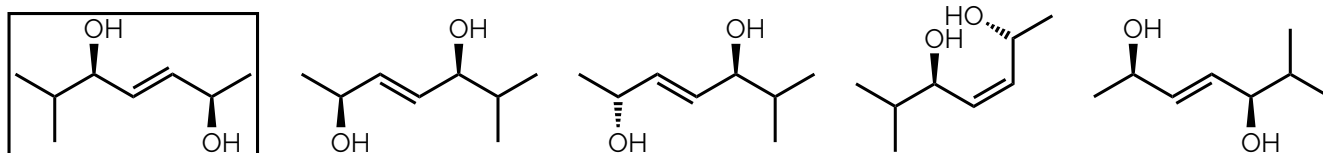
### Question 4

Describe the relationship between each of these molecules and the original, circled molecule. Are they the same, enantiomers or diastereomers?

a)



b)

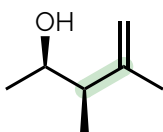


#### Answer 4

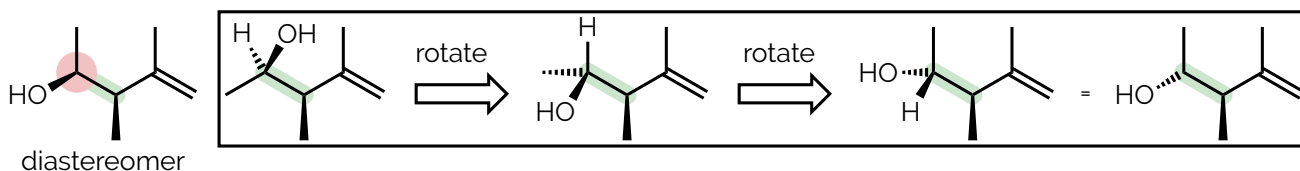
a)

The purpose of this question is to practice manipulating representations of molecules, so that you twist, rotate and flip a molecule without losing sight of the three-dimensional structure. It is a hard skill to develop and, if we're brutally honest, learning the naming system of stereoisomers (the next summary) is a useful fall back position as it allows you to check that your manipulations of the molecule are correct.

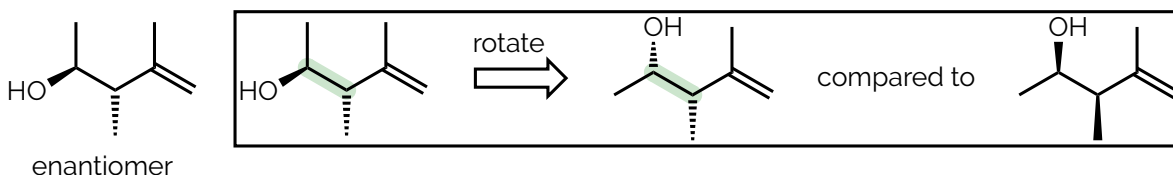
The first molecule is the **same** molecule. The C-C bond (in green) adjacent to the alkene has been rotated but no stereocentres have been altered.



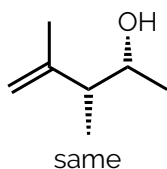
The second molecule is a **diastereomer** of the molecule in a box. Rotation around the C-C bond in green has been coupled with inversion of the stereocentre in red. If we had simply rotated the C-C bond clockwise, then the alcohol (OH) would be on the lower face away from you. If you don't believe us, make a model.



The third molecule builds upon the second. Now both stereocentres have been inverted or changed. This means this molecule is an **enantiomer** or non-superposable mirror image. We have redrawn the third molecule by rotating the green bond. Now its relation to the original should be more obvious.

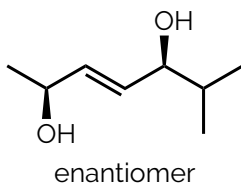


The final molecule is the **same** as the original. It is not a mirror image but rather has been flipped through 180° (imagine turning drawing the molecule on a piece of paper and then turning the paper over ... that would produce the same representation).



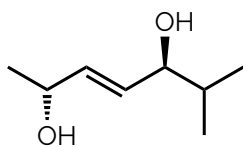
b)

The first molecule is the **enantiomer**. It is the mirror image (with the mirror placed to the right-hand side of the original).



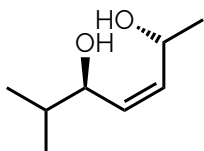
The second molecule is a **diastereomer** of the molecule in a box. Don't be fooled by the fact the molecule has been flipped as well, the give away that this is a diastereomer is that the two alcohols that were both up in

the first molecule are now on different faces of the molecule (one up one down), so the relative stereochemistry has changed and you have a diastereomer. The stereocentre that has been inverted is highlighted, the other is unchanged. Compare this molecule to the previous diagram, the enantiomer, and the change in relative stereochemistry should be more apparent.



diastereomer

The third molecule is also a **diastereomer**. The change of shape of the alkene (often described as a change in geometry) is the give away. It can't be a mirror image or the same molecule if the central alkene is changed from trans to cis.



diastereomer

The final molecule is the **same** as the original. It has simply been rotated by 180° like a Tetris brick.

