The Cahn-Ingold-Prelog rules

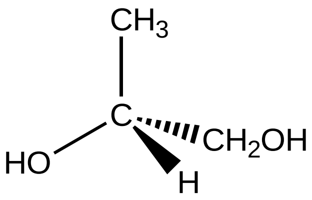
These rules give the absolute configuration, R- and S- for each chiral center within a compound. The chiral centers are names either R- or S-.

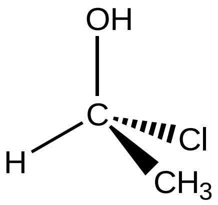
To name a chiral center using the Cahn-Ingold-Prelog rules:

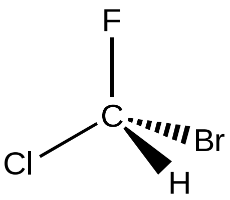
1) Identify a carbon with four different groups attached to it
2) Put the lightest group at the back (i.e. pointing away from you)
3) Give the heaviest group attached the highest priority (number 1)
4) Give the second heaviest group attached the number 2
5) Give the third heaviest group attached the number 3
6) If, with the lightest group or atom pointing away from you, the highest priority to the lowest priority (1→2→3) goes clockwise, the center is named R- , counterclockwise it's called S-

When looking for the heaviest group/atom you start with the atom joined to the chiral centre, if they are all different, just put them in order of atomic mass. If you have two the same, you work outwards one atom at a time until you reach an atom which differs which will allow you to prioritise the groups.

Some examples to try:

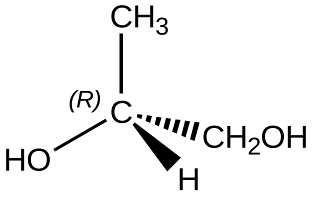


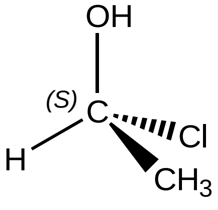


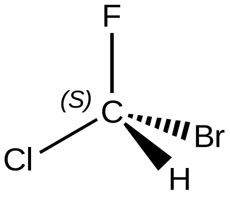


If you have trouble working out whether the centre is R- or S- try making a model of the molecule. Seeing it in 3D often helps.

And the answers….

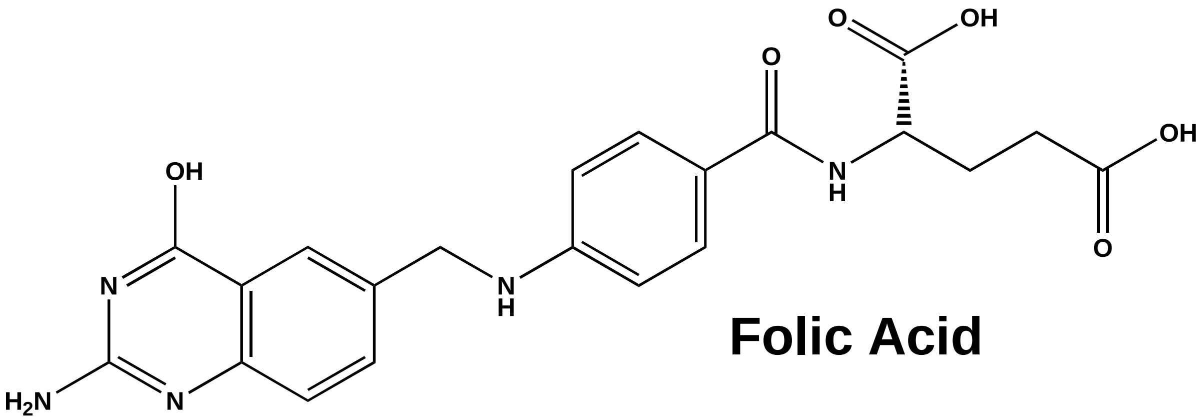




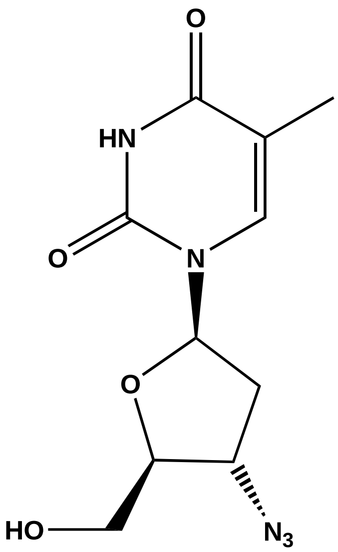


Some more complex examples:

You will need to work out which are the chiral centres and then whether they are R- or S-



Folic Acid



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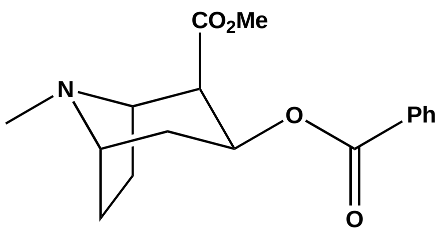
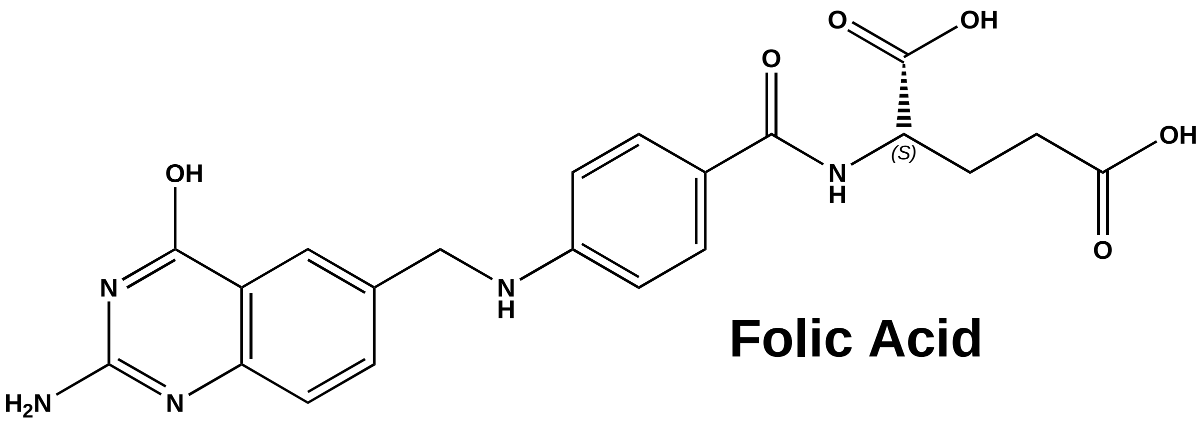


Cocaine

Answers:



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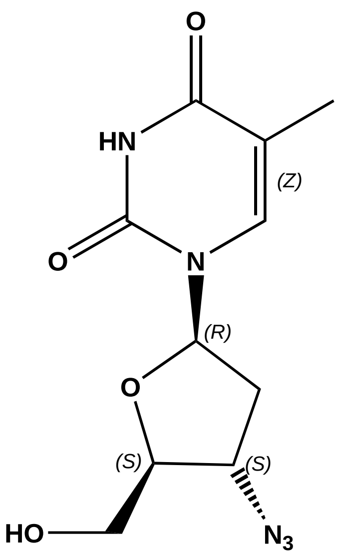

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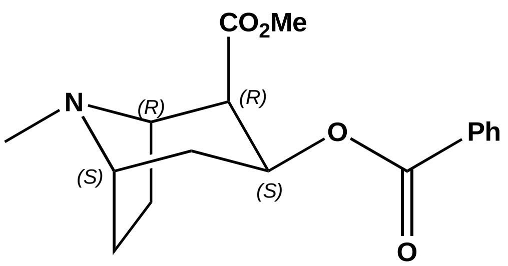


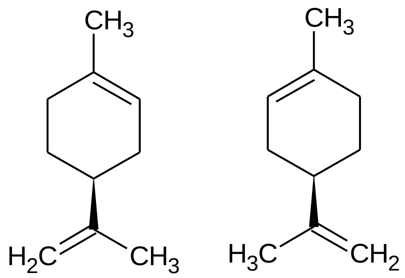
Cocaine

<u>Question: Find some other organic compounds and name the chiral centres as R- or S-</u>

Chirality and smells:

As well as chiral molecules interacting differently with enzymes depending on their chirality, they can also interact differently with receptors in our sense organs, such as our smell receptors in our noses. Two really nice examples of this which you can experience yourself are those of limonene and carvone.

To smell the two enantiomers of limonene, get an orange and a lemon. Scratch the skin of both and see if you can tell the difference between the two chemicals:

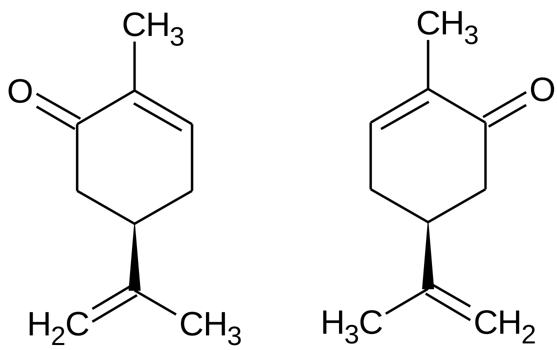


D- L-

The smells of Lemon (L-) and Orange (D-).

<u>Question: can you name the chiral centres using the Cahn-Ingold-Prelog rules?</u>

The two enantiomers of carvone are more distinct for most people, these can be found in spearmint, such as toothpaste or chewing gum, and caraway seeds.



R S

Here the R- enantiomer is responsible for the spearmint smell, whereas the S- enantiomer for the caraway smell.

Chirality and Drugs

As well as molecules which cause smells interacting differently with our sense receptors, drugs also interact differently with the body depending on the handedness.

This difference comes about due to a number of reasons:

1. Different rates of metabolism
    - The different isomers can be broken down at different speeds
2. Different effects on the body
    - Sometimes one isomer doesn't have any effect, sometimes it can have an adverse effect

One classic example of the effect of different enantiomers is that of the use of thalidomide, which is shown below:

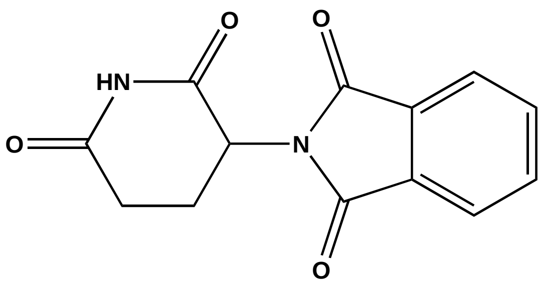


Figure 1. Thalidomide, how many chiral centres does this have?

The two isomers here were originally given together as an anti-morning sickness drug. One of the enantiomers did indeed stop morning sickness, however the other was found to cause severe deformity in the foetus.

Once it was discovered that the different isomers could have such different effects, the laws on new drugs being made were changed such that the different enantiomers had to be separately licenced (i.e. separately tested to make sure that they would not cause these, or other, significant side effects).

One drug you may well have taken which has different isomers which have different effects on the body is ibuprofen. Here it is found that the S- enantiomer is over 100 times more effective a COX inhibitor (inhibiting the COX enzyme is how ibuprofen reduces pain) than the R- enantiomer. In this case, though, the R- enantiomer does not cause any unwanted side effects, so in fact, the tablets you may have taken contain equal amounts of the two enantiomers.

<u>Question: Ibuprofen is one drug where the enantiomers have different effects, three other examples are methadone, verapamil and citalopram Can you find out the structure of these drugs, identify and name the chiral centres and find out how the enantiomers have different effects on the body?</u>