Module 3, Lecture 5

Structure and Reactions of Organic Molecules

Part 2 – Stereochemistry
Chirality, Enantiomers and Diastereomers

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References to Brown *et al* text shown in BLUE

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Learning Objectives:

- **to have an understanding of chirality and why it is important**
- **to have an understanding of enantiomers**
- **to be able to identify *R* and *S* isomers (enantiomers)**
- **to have an understanding of what a diastereomer is**

Textbook: **Chapter 25, sections 25.1-25.6, Brown**

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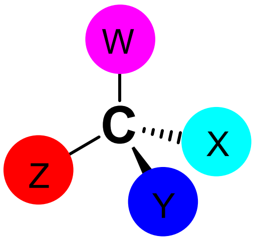
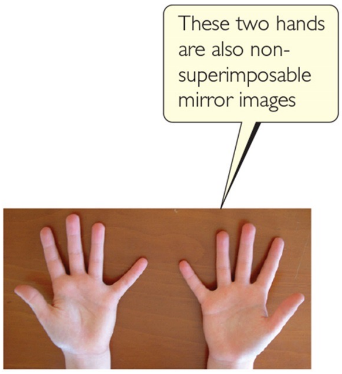
Chirality (25.3)

A compound (object) that is not superimposable on its mirror image is described as being *chiral*.

Most chiral organic compounds contain an asymmetric carbon atom (stereocentre), i.e. a carbon atom with four *different* groups attached.





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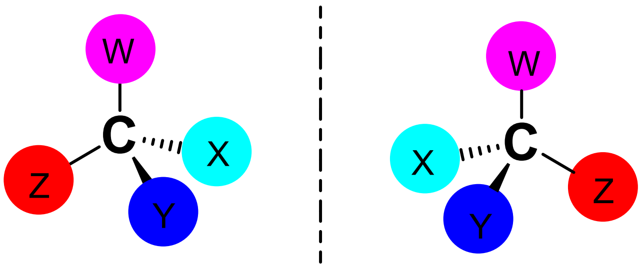
Chirality…..

A compound (object) that is not superimposable on its mirror image.



The object and its mirror image are **enantiomers**.

Possess identical chemical and physical (i.e. b.p. & m.p.) properties and differ only in their interactions with other chiral compounds (eg. biological systems).

4

Chirality…..

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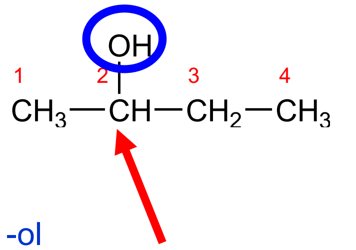
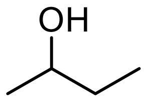
Possess identical chemical and physical (i.e. b.p. & m.p.) properties and differ only in their interactions with other chiral compounds (eg. biological systems).

e.g.

Enantiomers of 2-butanol





4 – carbon chain butan-

alcohol -ol

position 2 2-

Asymmetric C
stereocentre

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Chirality…..

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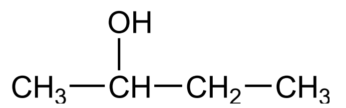

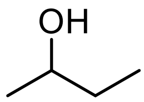

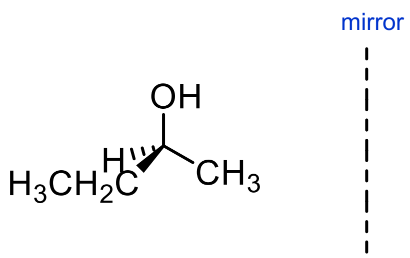

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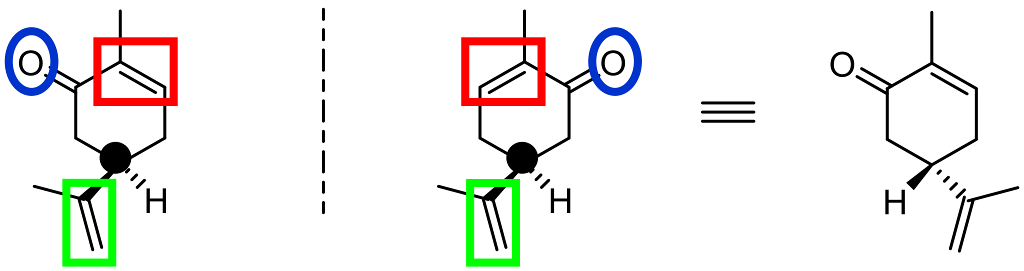
Nature can distinguish enantiomers



spearmint caraway

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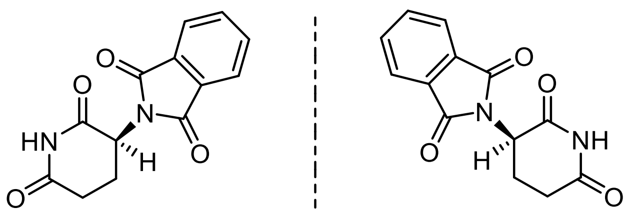
Nature can distinguish enantiomers: Very important as many drugs are chiral

Thalidomide

Used in the late 1950s and 1960s as a sedative and to combat nausea in pregnant women. **Sold as a mixture of enantiomers**.

One enantiomer was later found to be teratogenic in fetal development. About 12000 were born with birth defects.

Banned for use with pregnant women but is still sold for other applications.
The scientific community is now acutely aware of the potential contrasting biological activities of stereoisomers.



Many children in the 1960's, were born with phocomelia as a side effect of the drug thalidomide, resulting in the shortening or absence of limbs. (Photo by Leonard McCombe//Time Life Pictures/Getty Images)

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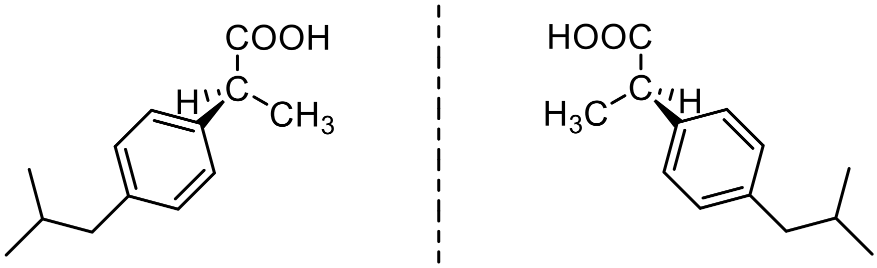
Nature can distinguish enantiomers: Very important as many drugs are chiral

Ibuprofen (Nurofen®)

Sold as a mixture of enantiomers. The inactive form is converted to the active form in the body.



anti-inflammatory inactive

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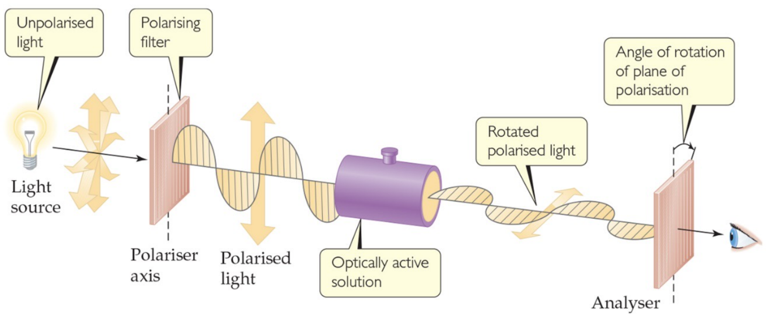
Optical rotation (25.4)

One way of distinguishing between enantiomers involves their interaction with plane polarized light.

The rotation, α, may be measured in a polarimeter. *{Optical activity}*

▶ **FIGURE 23.8 Optical activity.** Effect of an optically active solution on the plane of polarisation of plane-polarised light. The unpolarised light is passed through a polariser. The resultant polarised light then passes through a solution containing a dextrorotatory optical isomer. As a result, the plane of polarisation of the light is rotated to the right relative to an observer looking towards the light source and so the optically active compound is dextrorotatory.



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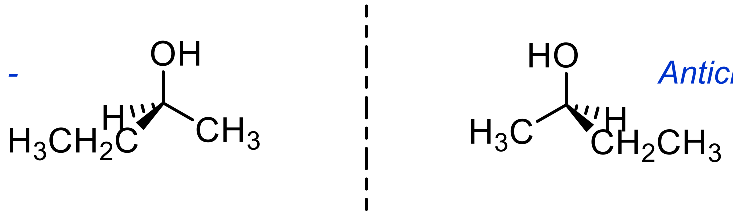
Optical rotation (23.4)

Usually reported as the specific rotation:

$[\alpha]^{20}_{D}$ ← temperature, 20 °C

← sodium D line, 589 nm

Clockwise rotation - to the right



Anticlockwise rotation - to the left

(+)-2-butanol

$[\alpha]^{20}_{D} = 13°$

(-)-2-butanol

$[\alpha]^{20}_{D} = -13°$

Enantiomers have equal rotation but in opposite directions.

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Optical rotation – a racemic mixture (25.4)

A 1:1 mixture of two enantiomers is called a *racemate*, or a *racemic mixture*.

A racemate:

- is designated ($\pm$), [*eg*. ($\pm$)-2-butanol]
- has no specific rotation, *ie* $\alpha = 0^\circ$ (or "*not optically active*").

Separation of a racemic mixture into the enantiomers requires interaction with a chiral molecule. In lab or in nature

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Absolute Configuration of Asymmetric Carbon (25.5)

The convention for labelling chiral carbon atoms and assigning the absolute three dimensional configuration uses sequence rules similar to that described for labelling (Z)- and (E)-isomers of alkenes.

1. identify the asymmetric C atom;
   Carbon with four different singly-bound groups
2. assign priorities to the four substituents (Highest = 1, lowest = 4);
   On the basis of highest atomic number
3. draw (or visualise) the structure of the molecule viewed down the bond from C to the substituent with the lowest priority (often H);
4. If the arrangement of the remaining bonds from 1 to 3 appears clockwise (*right handed*), assign *R* configuration; if anticlockwise (*left handed*) assign *S* configuration.

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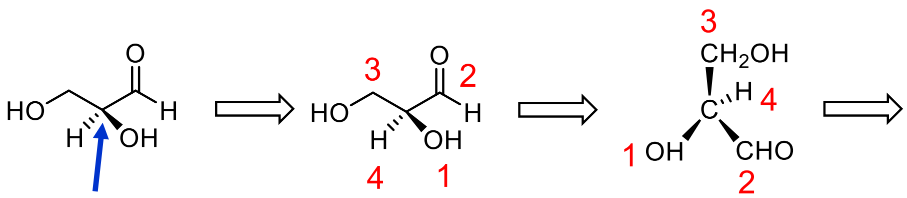
Absolute Configuration of Asymmetric Carbon (25.5)

eg. for one enantiomer of glyceraldehyde:



asymmetric carbon

$OH > CHO > CH_2OH > H$

(O,O,H) (O,H,H)

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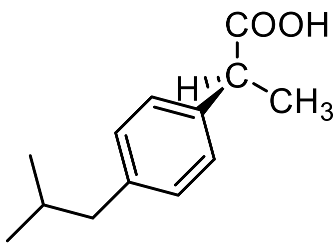
Absolute Configuration of Asymmetric Carbon (25.5)

Ibuprofen (Nurofen®)



anti-inflammatory

COOH > ring > CH_3 > H

Answer later in the lecture!!!!!

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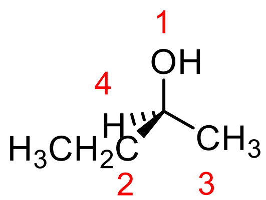
Absolute Configuration of Asymmetric Carbon (23.5)

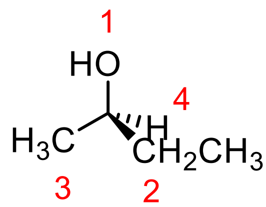
From earlier in the lecture: OH > CH_2CH_3 > CH_3 > H

Note: optical rotation (+/-) and the rotation that gives the absolute configuration (S/R) do not have to be in the same direction



(+)-2-butanol

***S*-(+)-2-butanol**



(-)-2-butanol

***R*-(-)-2-butanol**

The absolute configuration of one stereoisomer is inverted in the other.

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Diastereomers (25.6)

Stereoisomers that are NOT enantiomers.

Occur with compounds with more than one asymmetric carbon (stereocentre).

n Stereocentres have a *maximum* of 2^n stereoisomers.

Diastereomers do NOT have similar physical properties (i.e. bp, mp, etc.).

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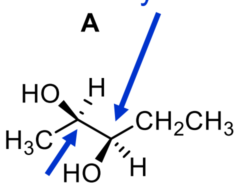
Diastereomers (25.6)

eg. For 2 chiral carbons there are 4 possible stereoisomers. For example:

asymmetric carbons 2^2



A and C, A and D, B and C, B and D are diastereomers

A and B, C and D, are related as enantiomers.

The absolute configuration at both stereocentres of one stereoisomer is inverted in the other.

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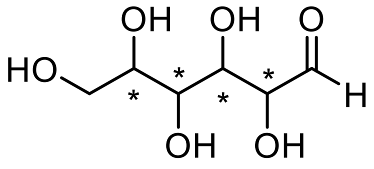
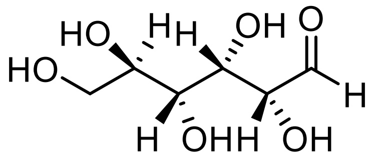
Diastereomers (25.6)

How many diastereoisomers are there for this molecule?



$2^n = 2^4 = 16$ stereoisomers

One of them is: **glucose**



The other diastereomers are : **allose, altrose, galactose, gulose, idose, mannose, and talose**

There are seven other named diastereomers and each one has an enantiomer, a total of 16 stereoisomers.

therefore **glucose** has one **enantiomer** and 14 **diastereomers**

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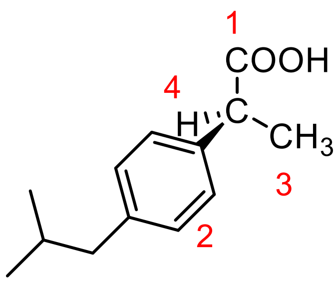
Absolute Configuration of Asymmetric Carbon (25.5)

Ibuprofen (Nurofen®)



anti-inflammatory

?

COOH > ring > CH_3 > H

S

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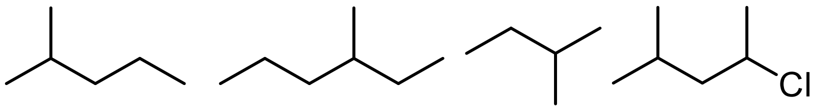
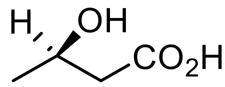
Questions

1. Which of these molecules are chiral?



2. (+)-2-Butanol has a boiling point of 99° C. What is the boiling point of (-)-2-butanol?

3. Assign the absolute configuration of this molecule.



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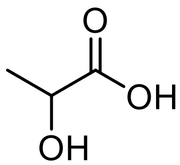
Questions

1. Lactic acid builds up during exercise and is often blamed for muscle soreness*. It is a chiral molecule, identify the chiral carbon.



2. Draw both the R and S enantiomers of Lactic acid.

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✱ Homework ✱

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Brown et al.

Problems 25.7, 25.9, 25.10, 25.11, 25.15, 25.20, 25.21, 25.25, 25.26, 25.41, 25.42

Answers on Blackboard