Chapter 1. Stereoisomerism

- symmetry elements

  symmetry planes, symmetry axes, inversion centers

- point groups

  chiral point groups

- enantiomers and diastereomers

  in chiral point groups: chiral centers

  chiral axes

  planes of chirality

- notation: Fischer D,L

  Cahn, Ingold, Prelog R,S

- resolution of a racemic mixture

Little Eliel
"Symmetry"
p. 45-58   …

For symmetry, also check out http://www.reciprocalnet.org/edumodules/symmetry,
a very nice site.

3. Stereoisomers

- original subdivision: configurational
                            conformational   not always clear cut (energy criterion)
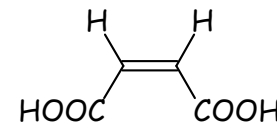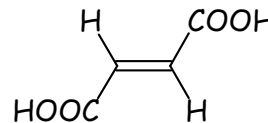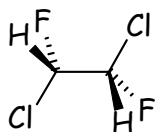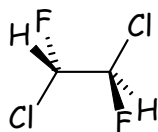
- configurational subdivision: enantiomers
                                   diastereomers   unambiguous

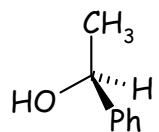- enantiomers: molecule and its non-superposable mirror image
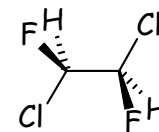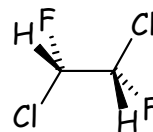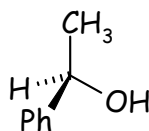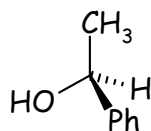
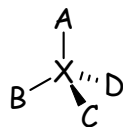- diastereomers: two stereoisomers not related as object and mirror image
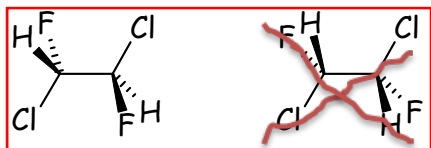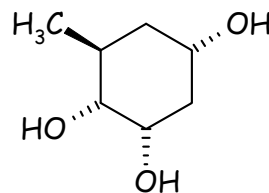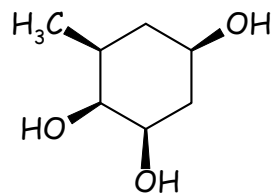
a) Center of chirality
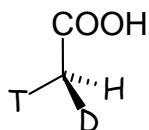
- "asymmetric C-atom"

 or, in general , where X = C, N, P, Si, Ge, As

- 4 different substituents on a tetrahedral central atom

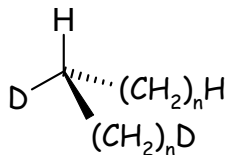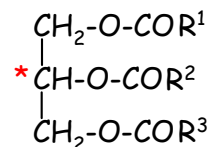- isotopes count as being different

 chiral acetic acid

C&E News

- differentiation might not be sufficient: chiral compound might not show

optical activity: it is "crypto-chiral"

real-life example: a fat (glycerol triester)

$$CH_2-O-COR^1$$
$$* CH-O-COR^2$$
$$CH_2-O-COR^3$$

a) Center of chirality continued
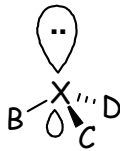
- configurational subdivision: enantiomers
  diastereomers ⎤ unambiguous, but still

1. Small E_a
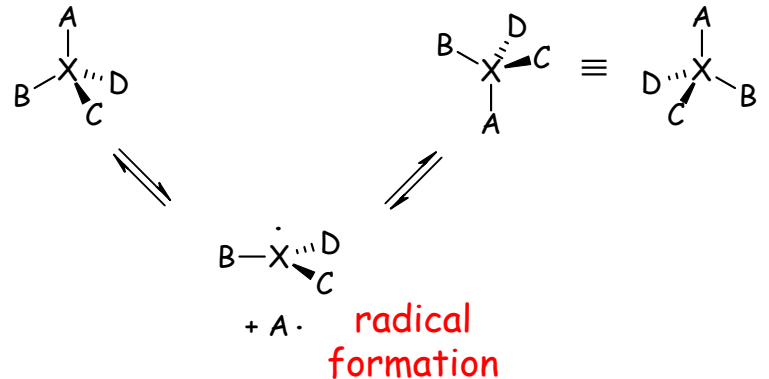
for X = N, P, As:

- enantiomer through inversion

- configurationally not stable

Similar examples for diastereomers.

2. Large E_a

for X = C, Si, Ge:

- enantiomer through homolysis
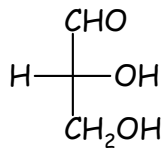
- configurationally stable

+ A· radical formation

a) Center of chirality continued

- notations:

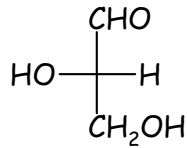## 1. Fischer D,L

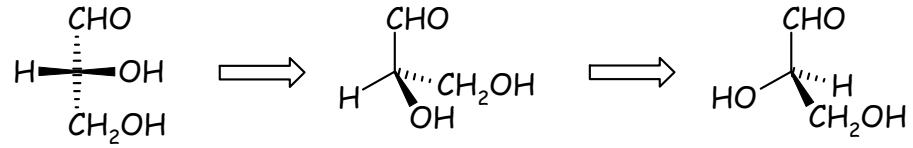- mostly for sugars (OH defining) and α-aminoacids (NH$_2$ defining)

- originally for glyceraldehyde

D
dexter

L
laevus
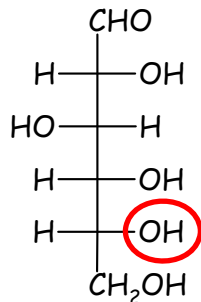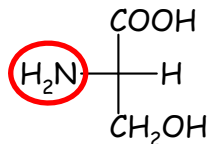
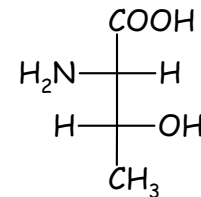Conversion from Fischer projection to 3D presentation

- sugar (D-glucose)

defining C*: D-configuration

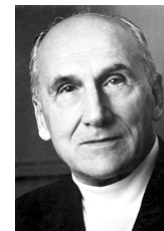- α-aminoacid (L-serine)

L-configuration

?-threonine

either
D$_G$: glucose reference
or
L$_S$: serine reference

a) Center of chirality continued

- notations:

2. Cahn, Ingold, Prelog R,S (Prelog, ETH, Nobel Prize 1975)
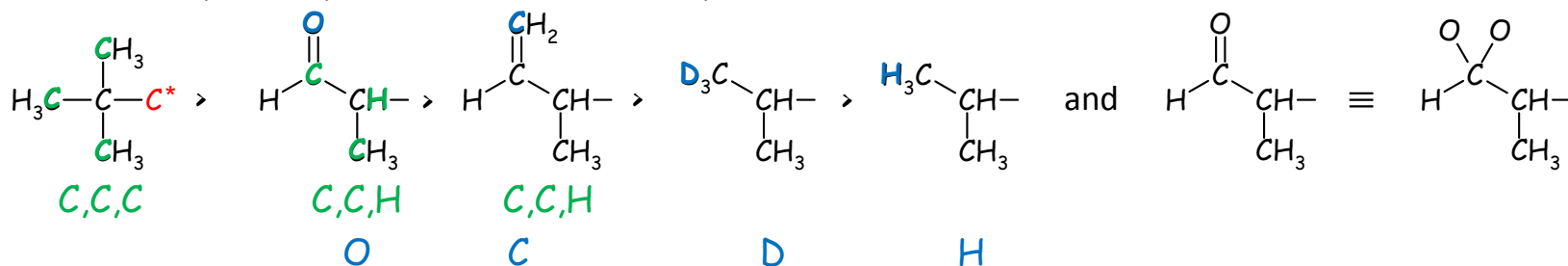
- chirality rule

  - The four substituents are given priorities.

  - The molecule is viewed with "4" to the back.

  - 1→2→3: clockwise is R (rectus), anticlockwise is S (sinister)

- sequence rules (determining the order of priority)
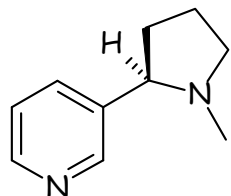
  - Priority increases with increasing atomic number.   lp<H<C<N<O<F<Cl

  - When two atoms directly attached are identical,

    use the "principle of outward exploration":

- For isotopes: Priority increases with increasing mass.   H<D<T

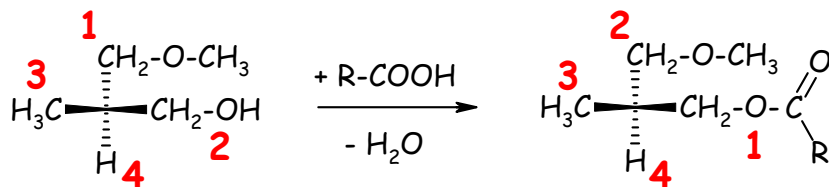# a) Center of chirality continued

- example:

H = 4
N = 1
sp^2-C = 2
sp^3-C = 3

$\longrightarrow$ (R)-nicotine

The CIP system is universal and unambiguous, but consider this:
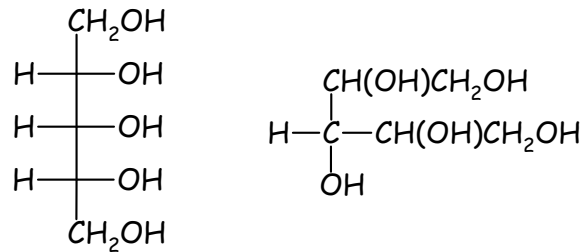

(R)-alcohol $\longrightarrow$ (S)-ester , but **not** through a Walden inversion
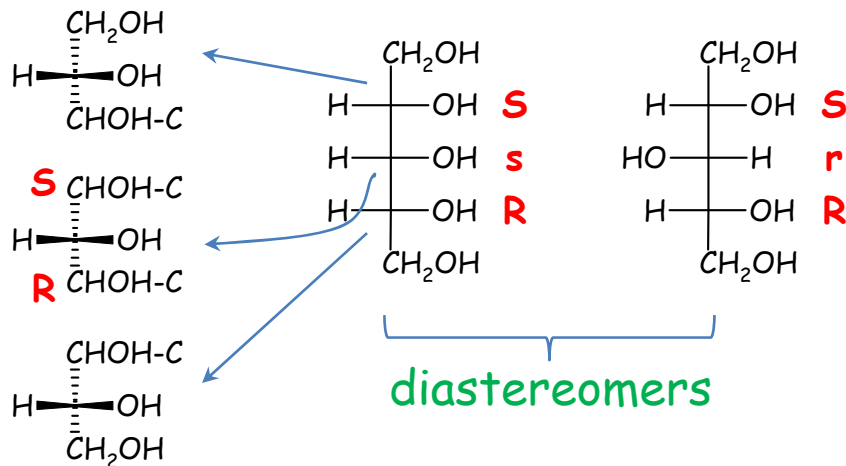
at C*,

just through a change of priorities!
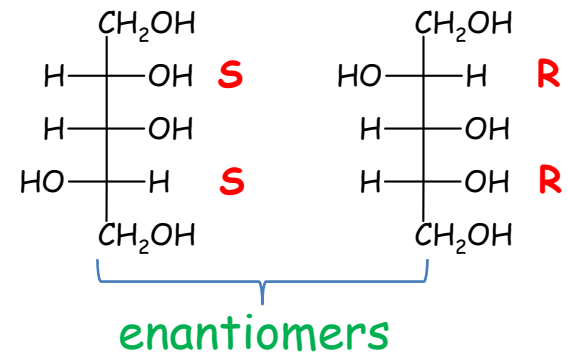
a) Center of chirality continued

- two special cases:

  1. The pseudo-asymmetric C-atom

C^3 is **not** a C*, but it is a stereogenic center ("pseudo-asymmetric")!
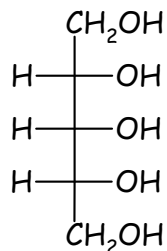

diastereomers

in contrast:

enantiomers

C^3 is **not** a C*, **nor** is it stereogenic!
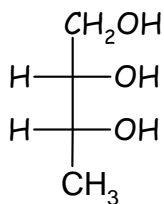
a) Center of chirality continued

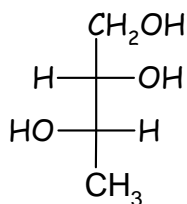- number of stereoisomers:

  for n C* there are 2^n stereoisomers

$2\ C^* = 2^2 = 4$ stereoisomers (maximum number possible)

- enantiomers: differ in configuration at all C*

- diastereomers: differ in configuration at least at one C* (but not at all)

- "epimers": differ in configuration at only one C* of multiple

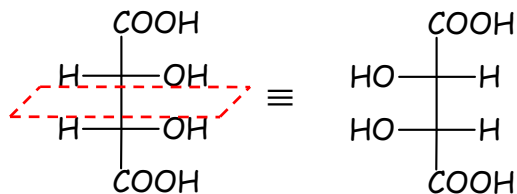 - for isomers with 2 C*, the old nomenclature is

erythro   threo

But this is often not without problems
and therefore discouraged.

a) Center of chirality continued
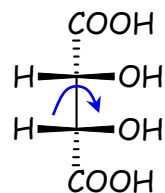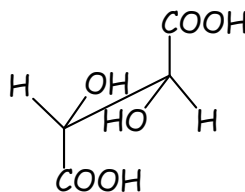
- two special cases:

2. The meso form

tartaric acid

Symmetry plane **only** in the Fischer projection!

twist about central bond:

eclipsed,
not a proper
representation

staggered,
proper
representation: center of inversion!

- achiral member in a set of diastereomers that also has chiral members

- reduces the number of actual stereoisomers (2 are identical)

- compare carefully to the pseudo-asymmetric C case!