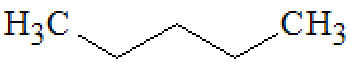
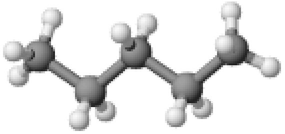
Formal representation
Molecular structures

a) Molecular formula (Ex. C_5H_{12}): *type and number of atoms*

b) Structure: *definition of chemical bonds*





c) Tridimensional formula (absolute molecular configuration) :
spatial distribution, bond length & angles
(allows us to identify isomers)

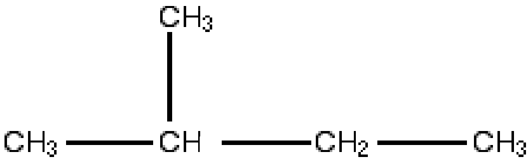
“Isomery” means “equal parts”

Isomery
property by which
Two or more compounds have identical molecular formula,
Same type and numer of atoms,
but
different structure;
i.e. different reciprocal position
of atoms and bonds.

Example C_5H_{12}

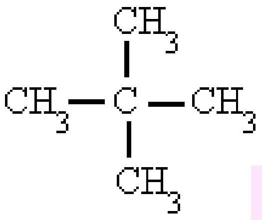
$CH_3 - CH_2 - CH_2 - CH_2 - CH_3$

pentane



$CH_3 - CH(CH_3) - CH_2 - CH_3$

iso-pentane, 2-methyl-butane

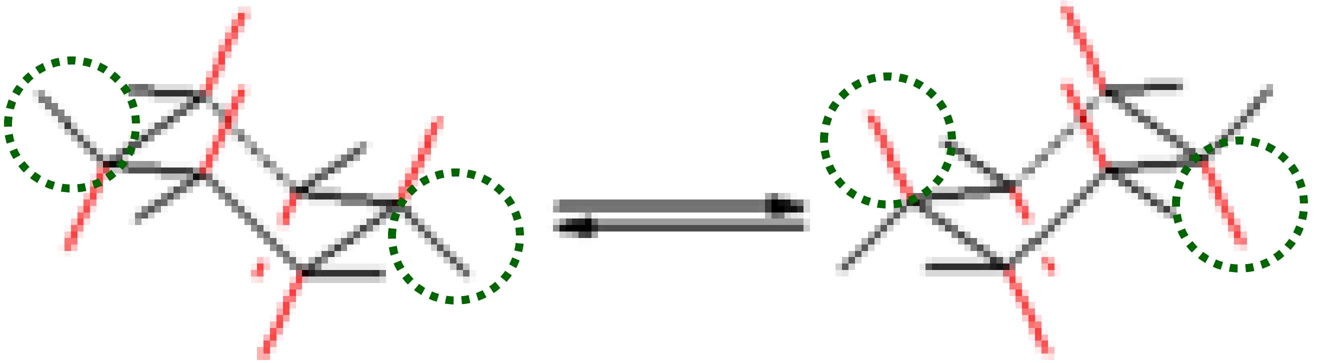


$CH_3 - C(CH_3)_2 - CH_3$

di-methyl-propane

cyclohexane

C_6H_{12}

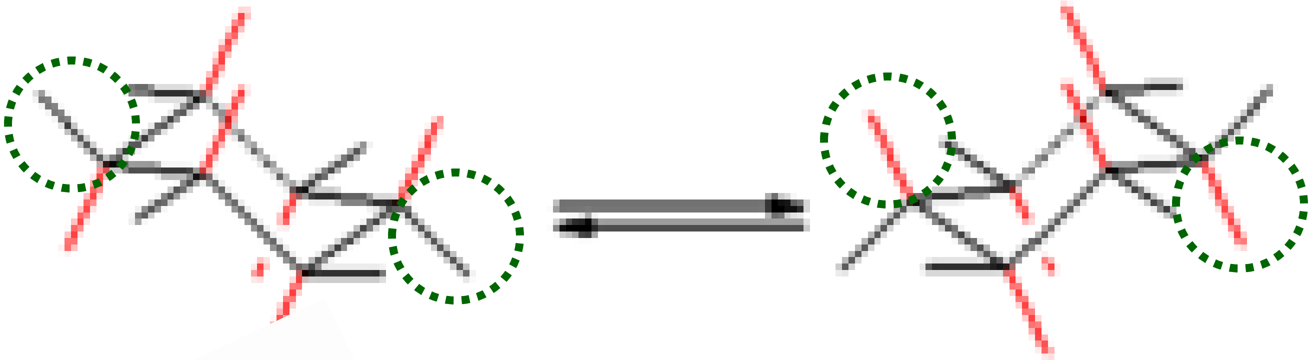


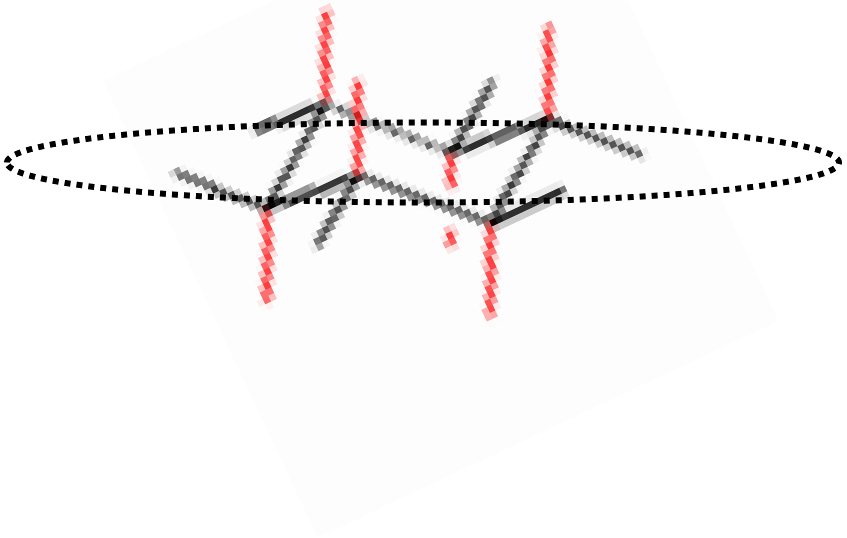
🟥 axial

■ equatorial

cyclohexane

C_6H_{12}

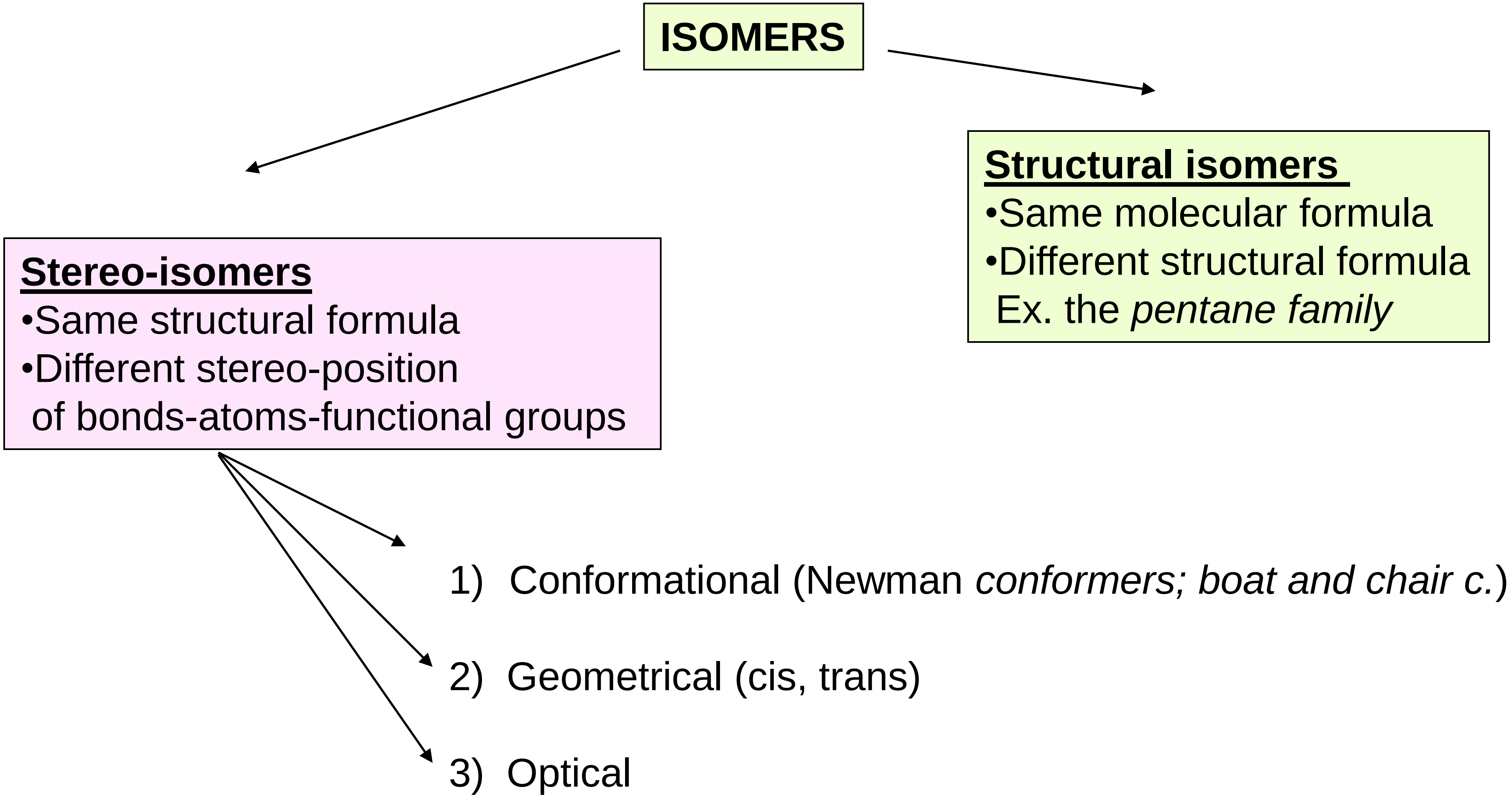




— axial

— equatorial

Structural, functional domains- absolute configuration – Xray crystallography



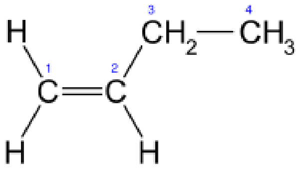
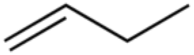
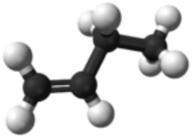
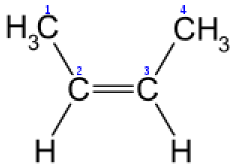
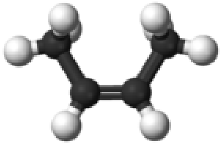
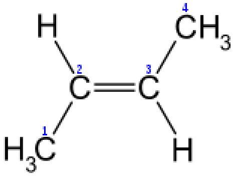
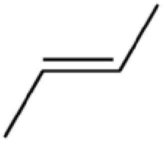
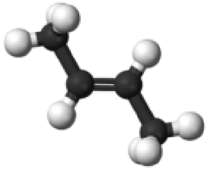
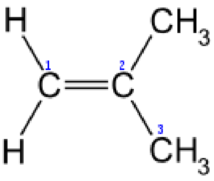
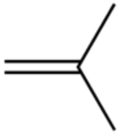
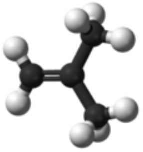
ISOMERS

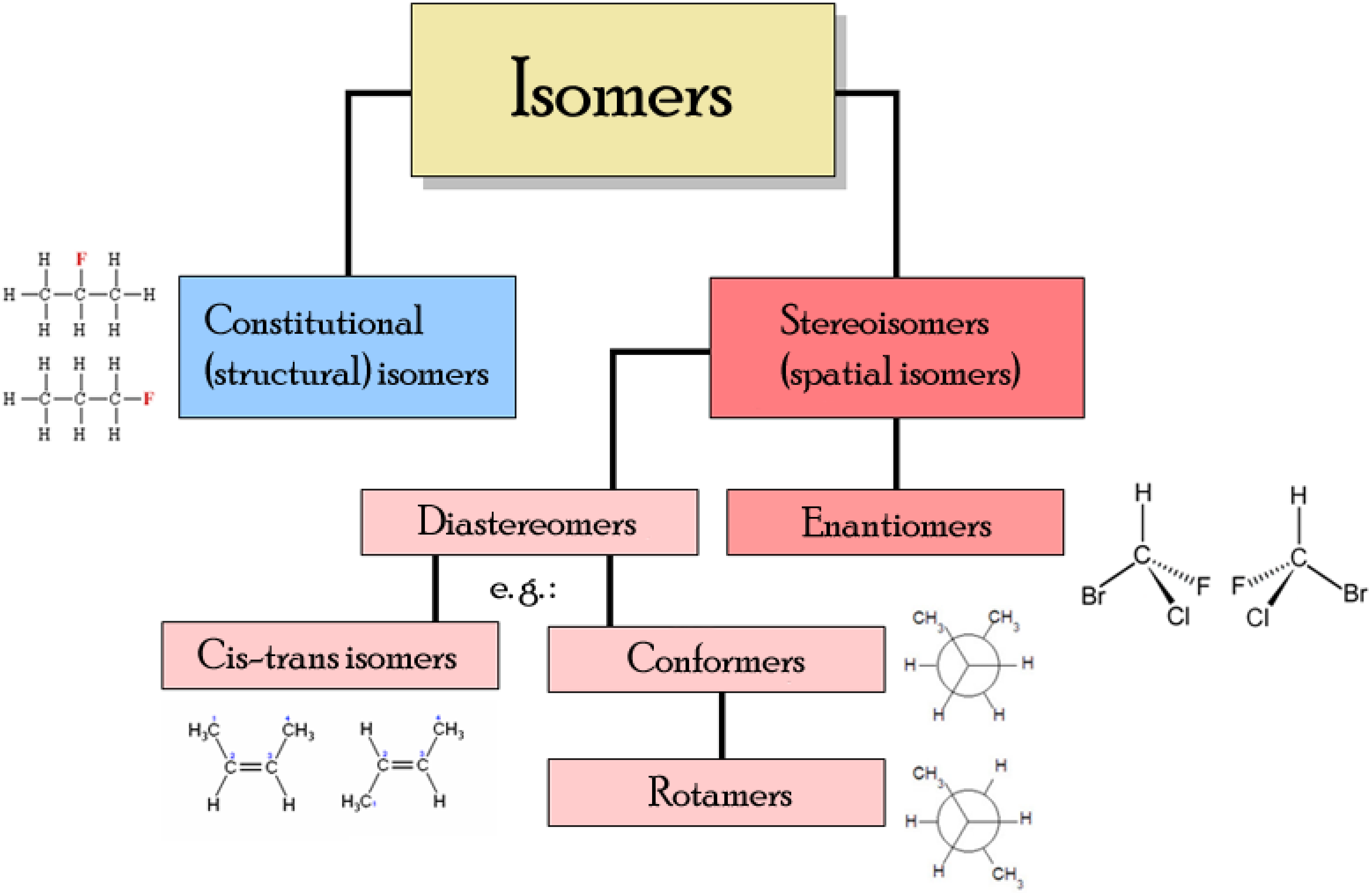
Stereo-isomers
- Same structural formula
- Different stereo-position of bonds-atoms-functional groups

Structural isomers
- Same molecular formula
- Different structural formula

Ex. the *pentane family*

1) Conformational (Newman *conformers; boat and chair c.*)
2) Geometrical (cis, trans)
3) Optical

IUPAC	common	structure	skeletal	3-D ball & stick
1-Butene	α-butylene			
cis-2-butene	Z-β-butylene			
trans-2-butene	E-β-butylene			
2-methylpropene	isobutylene			



Isomers

Constitutional (structural) isomers

Stereoisomers (spatial isomers)

Diastereomers

Enantiomers

e.g.:

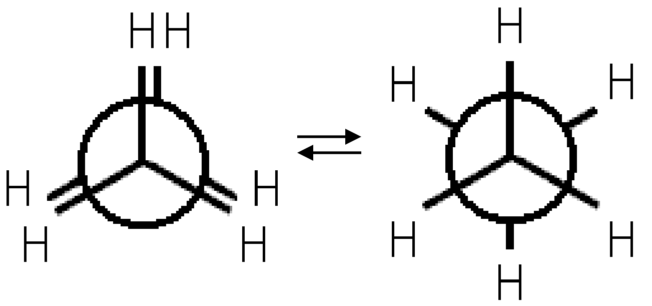
Cis-trans isomers

Conformers

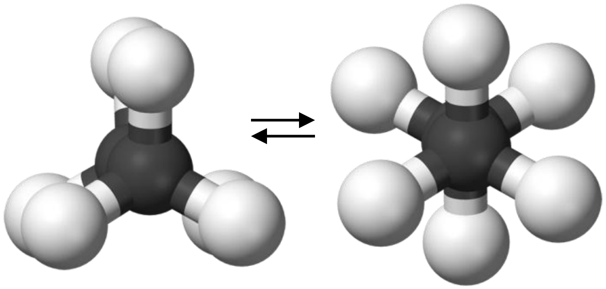
Rotamers

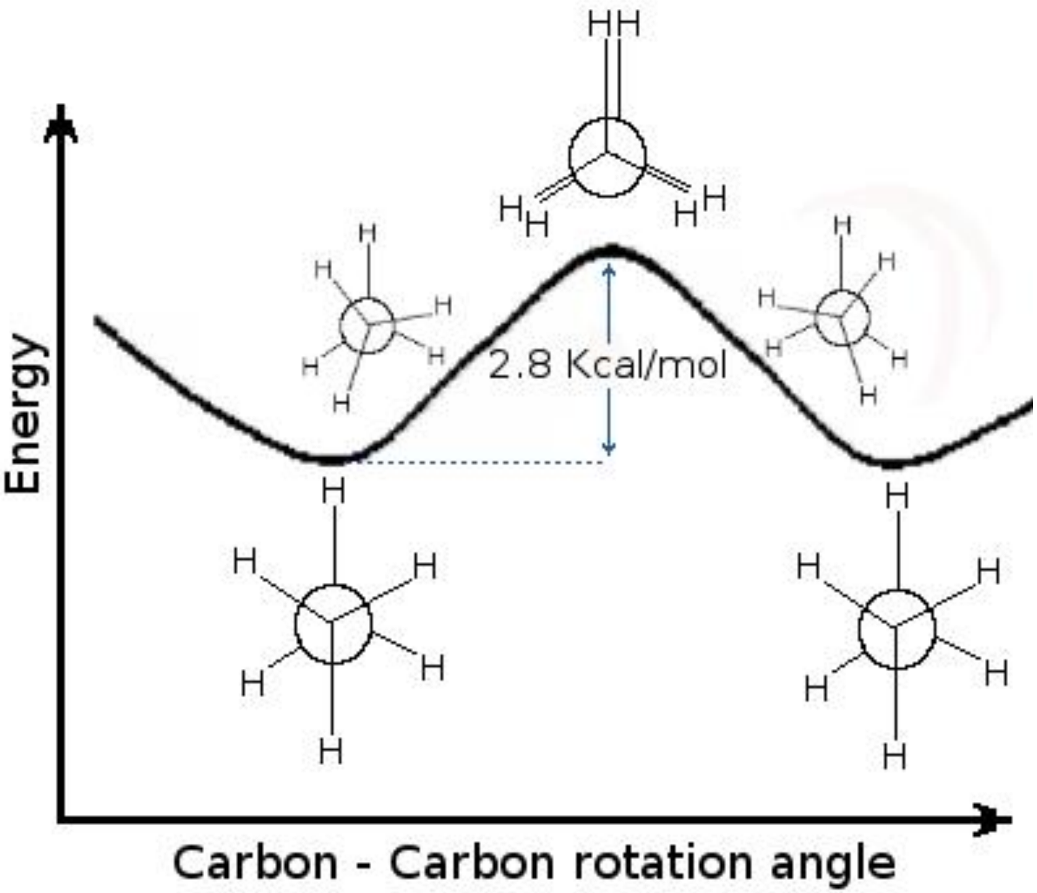
Conformational Isomerism

Newman conformers



Eclipsed **Staggered**

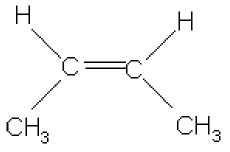




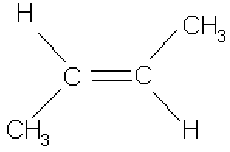
At T = 298 K, equilibrium reached within 10^{-11} s

Geometric isomers (cis, trans)

Ex. 1

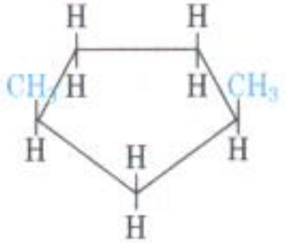


cis-2-butene

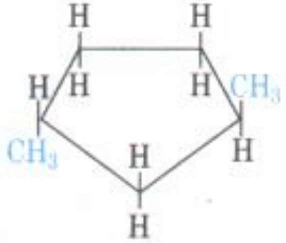


trans-2-butene

Ex. 2

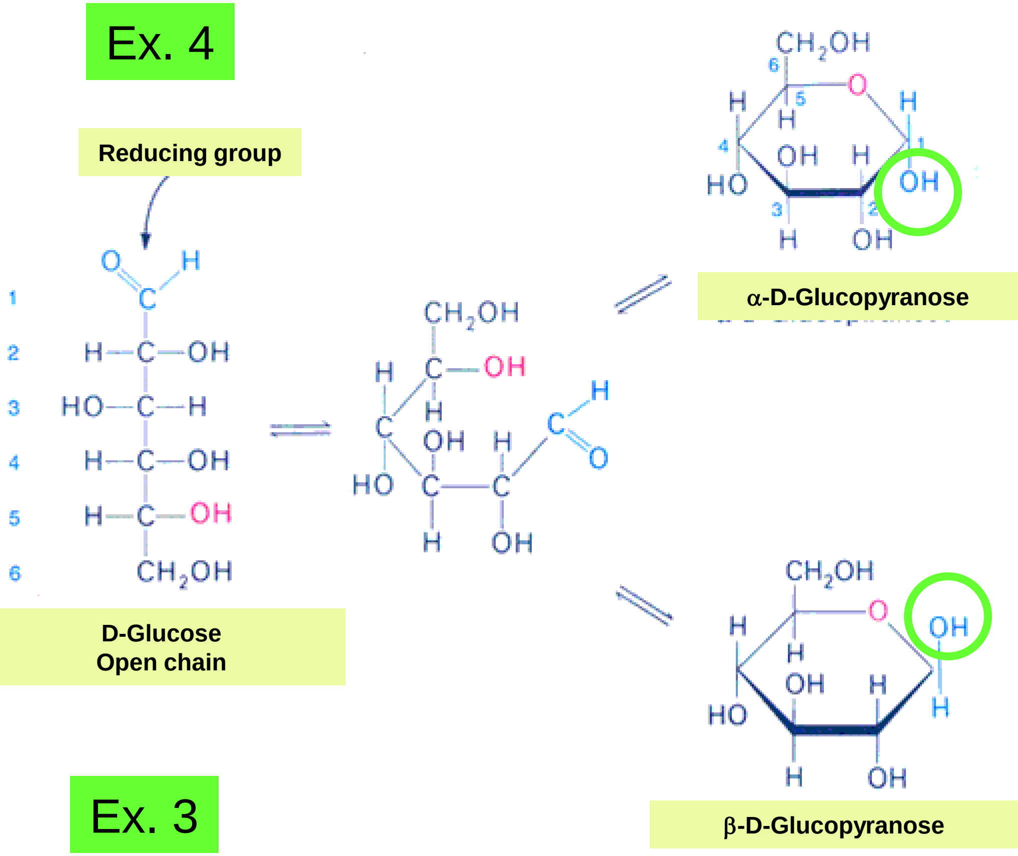


cis-1,3-dimethylcyclopentane



trans-1,3-dimethylcyclopentane

Ex. 4



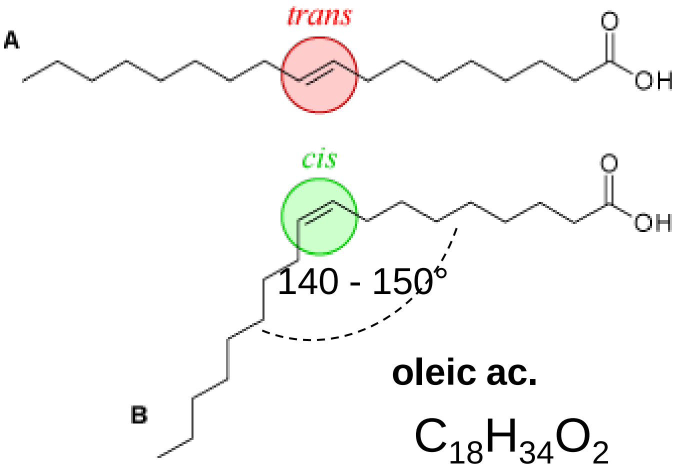
Reducing group

D-Glucose
Open chain

α-D-Glucopyranose

β-D-Glucopyranose

Ex. 3



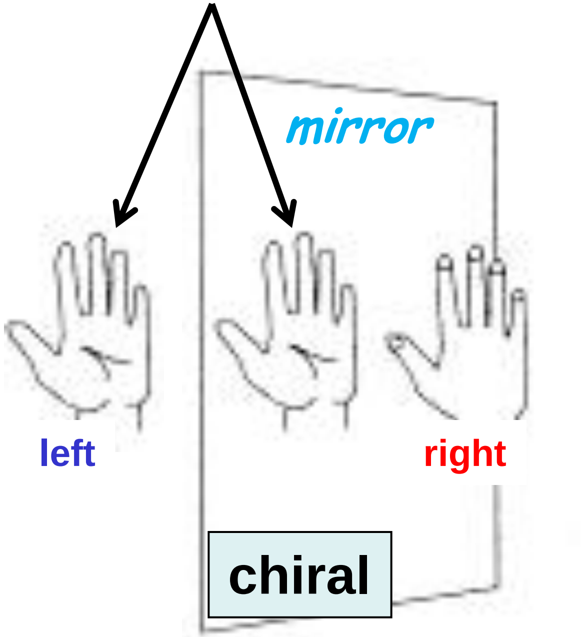
oleic ac.

$C_{18}H_{34}O_2$

Optical Isomerism

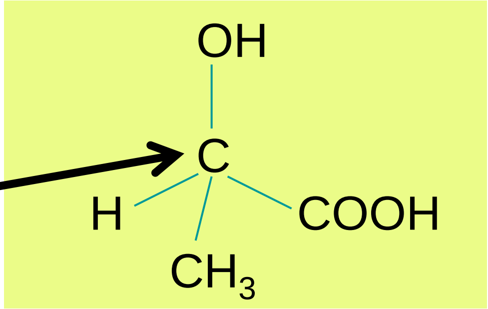
Requisites:
- C sp3
- 4 different substitutes

These can be overimposed !!



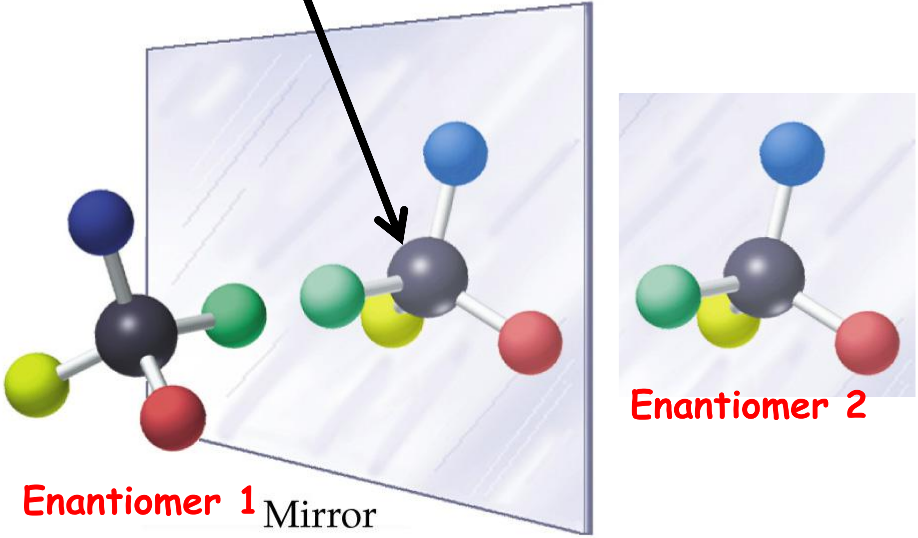
chiral

Lactic acid



$$\begin{array}{ccc} & OH & \\ & | & \\ H - & C & - COOH \\ & | & \\ & CH_3 & \end{array}$$

Stero-centre

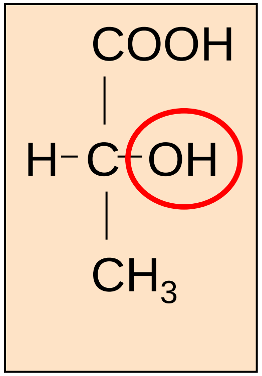


Enantiomer 1

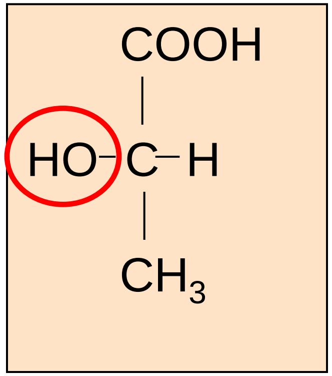
Enantiomer 2

Convention/Notation

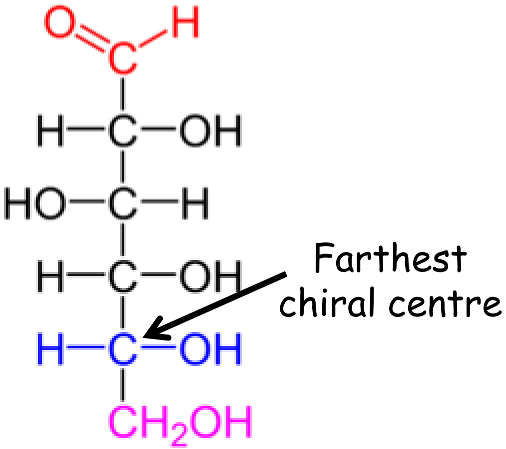
Fischer 1852 -1919:
D - L



D-lactic ac.



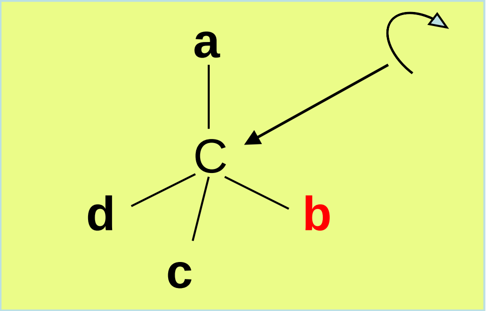
L-lactic ac.



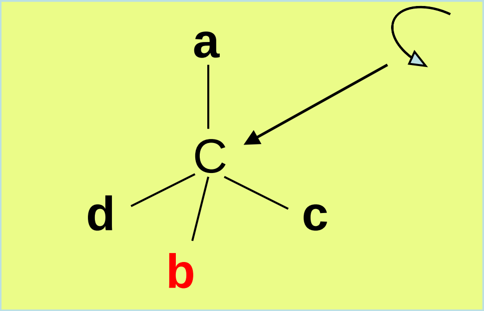
Farthest chiral centre

D-glucose

Cahn-Ingold-Prelog : R - S



Rectus - R



Sinister - S

Priority (P) – roules:
a → b → c → d

P Increases with Z
P Increases with n° of bound atoms
H = the lowest P (**d**)

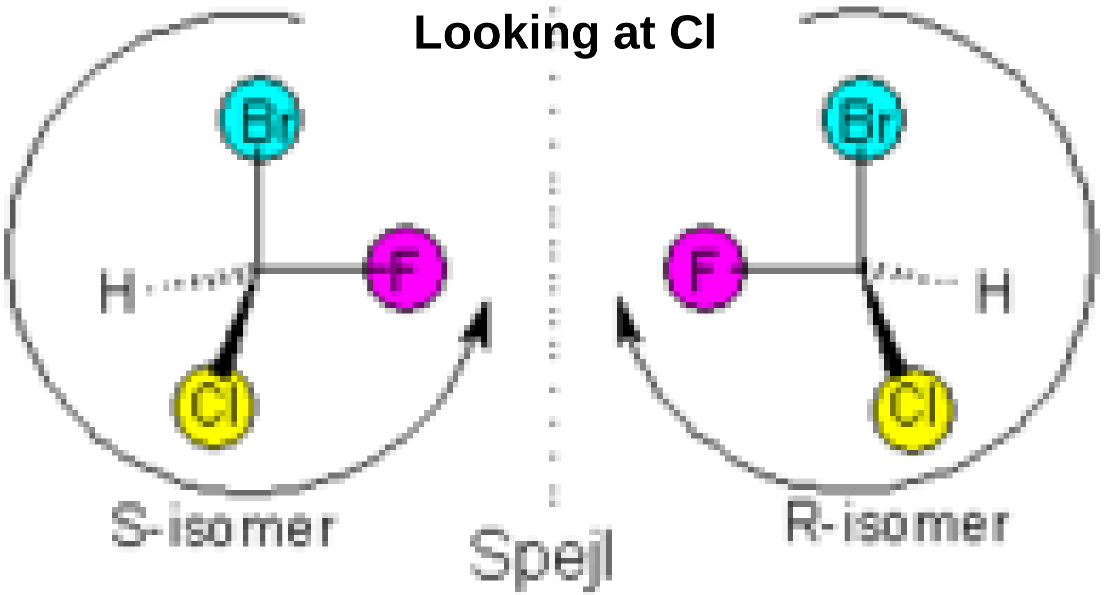
Priority scale: $-OH > -COOH > -COH > -CH_2OH > -CH_3 > -H$

Cahn-Ingold-Prelog (Example)

Bromine- Chlorine- Fluorine- Methane

Lactic acid

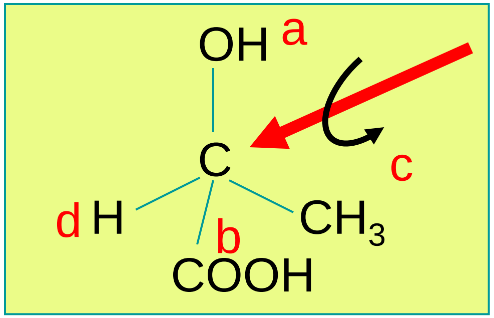
1966



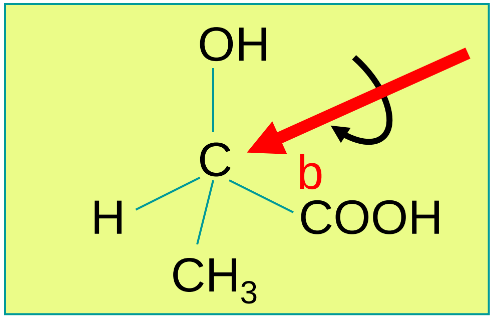
Looking at Cl

priorità

a = Br
b = Cl
c = F
d = H



S – lactic acid

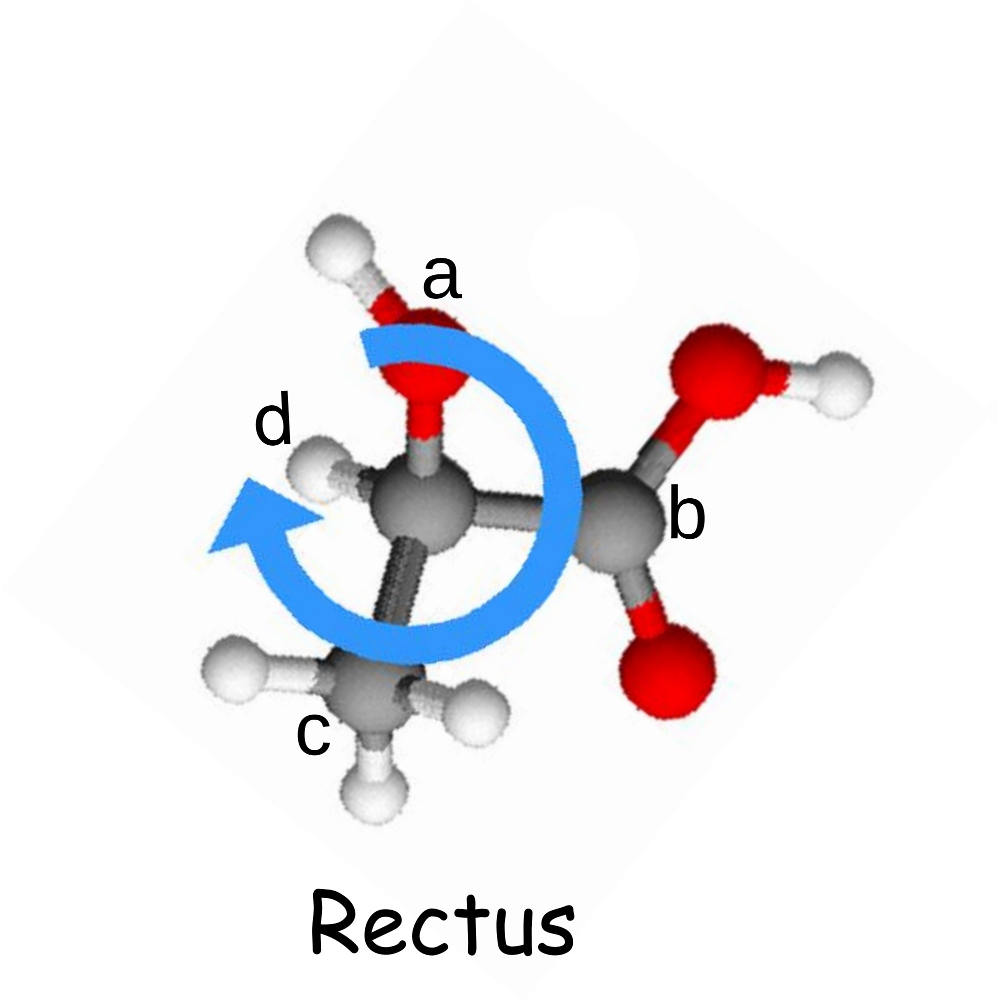


R – lactic acid

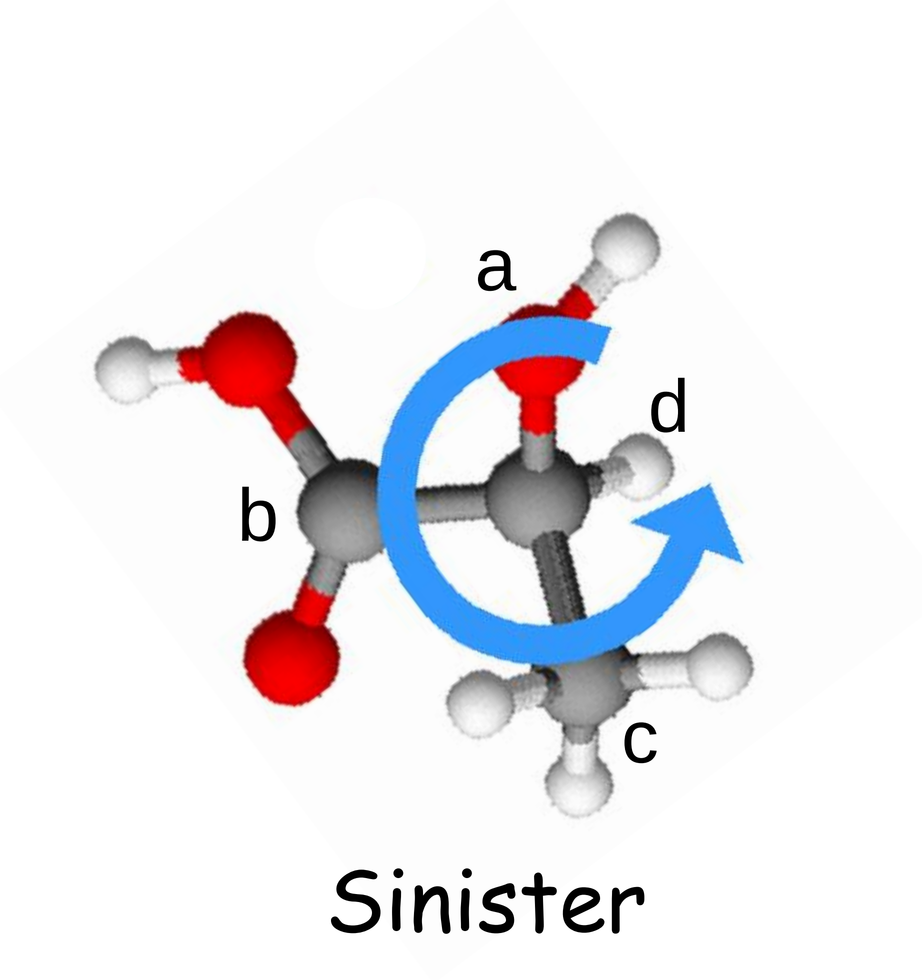
priority

a = OH
b = COOH
c = CH3
d = H

Cahn-Ingold-Prelog (lactic acid)



Rectus



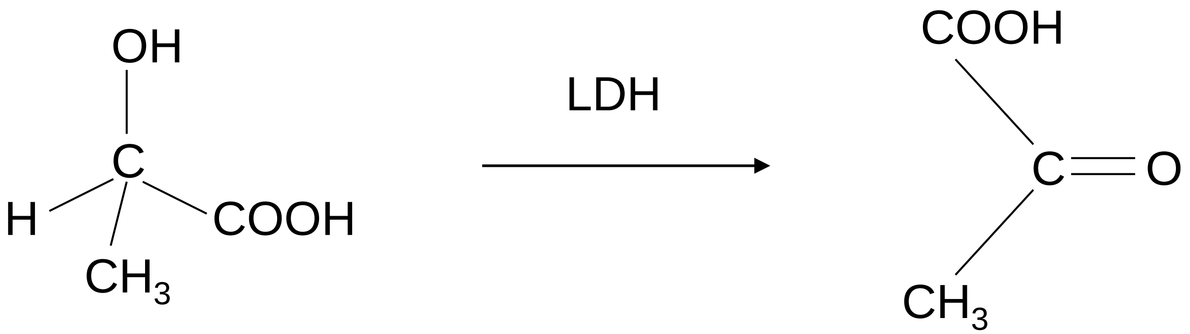
Sinister

Enantìomers properties

Non-chiral: fusion p. –boiling p. – density – spectroscopic prop. ,etc.

Chiral: functional prop. **(enzymatic activity**) – optical prop. (analytical) etc.

Ex. LDH (lactic-dehydrogenase)



R (+) lactic ac.

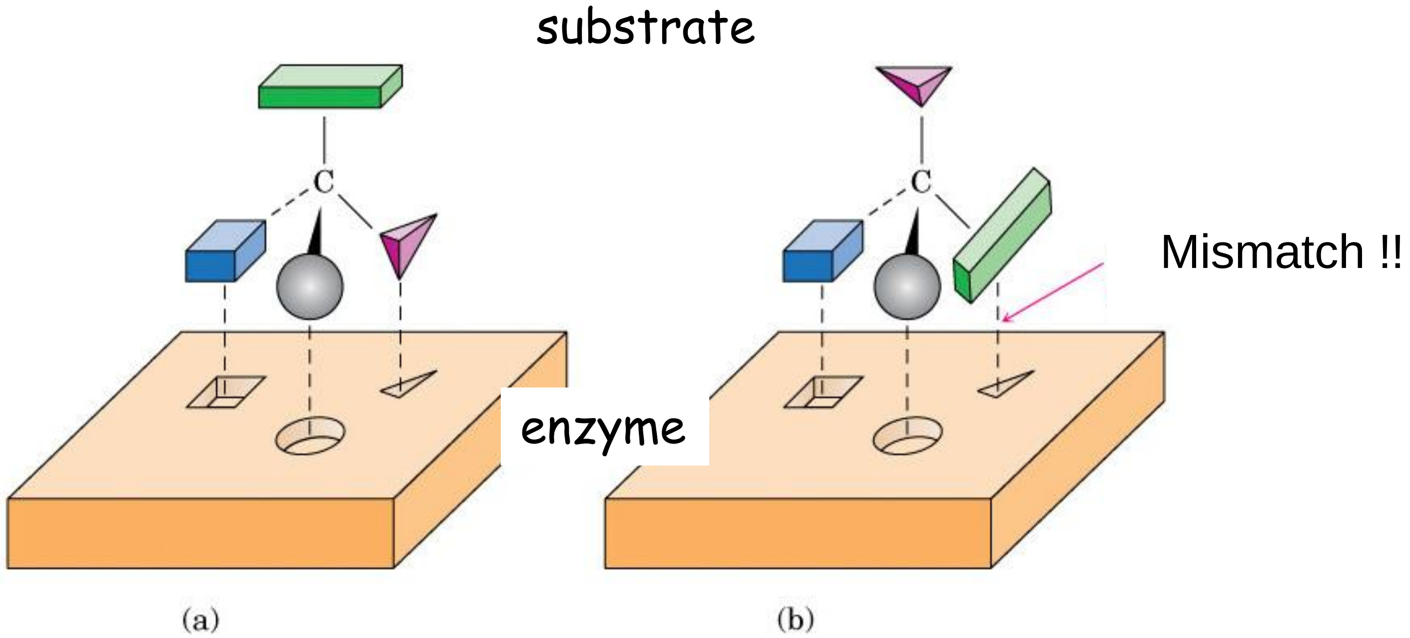
Pyruvic ac.

Reaction

Allowed with **R (+)**

Denied with **S (-)**

Stereochemistry at work !



substrate

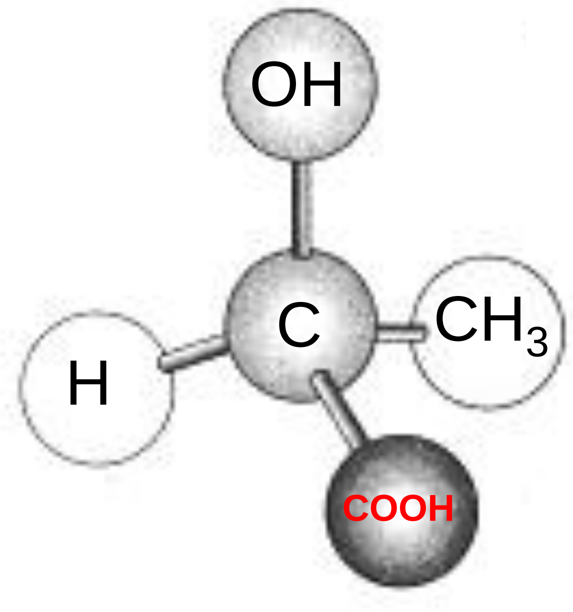
enzyme

Mismatch !!

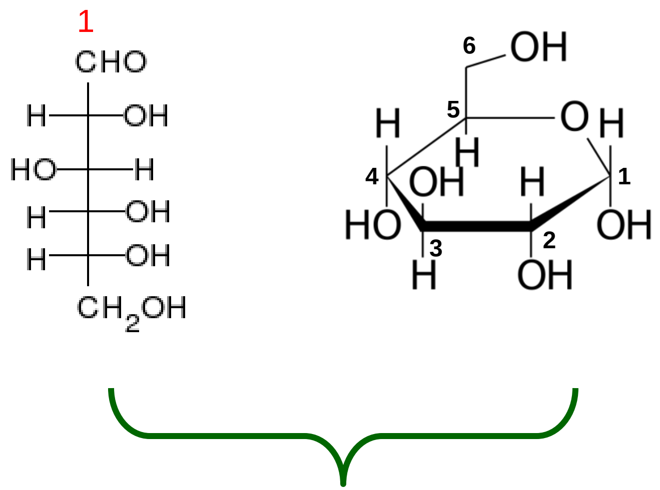
(a)

(b)

Chirality

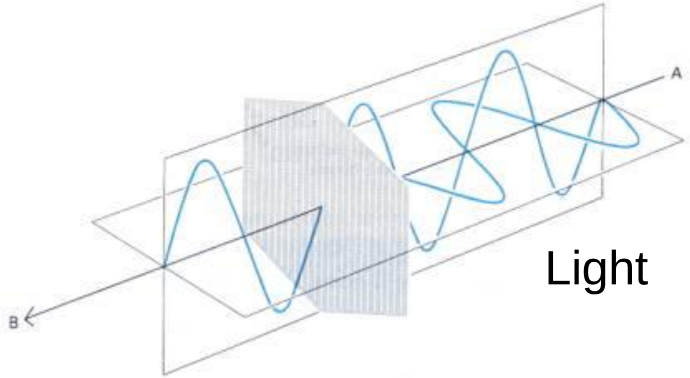


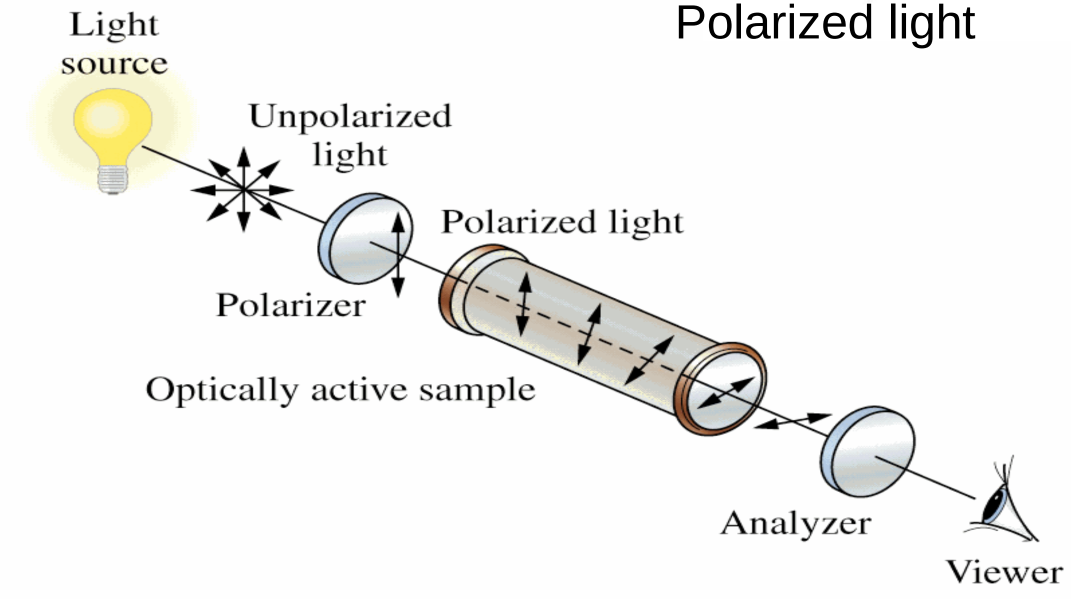
Lactic ac.
1 chiral carbon



Glucose

The Polarimeter: reveals optical activity of a solution (1 or more chiral centres)



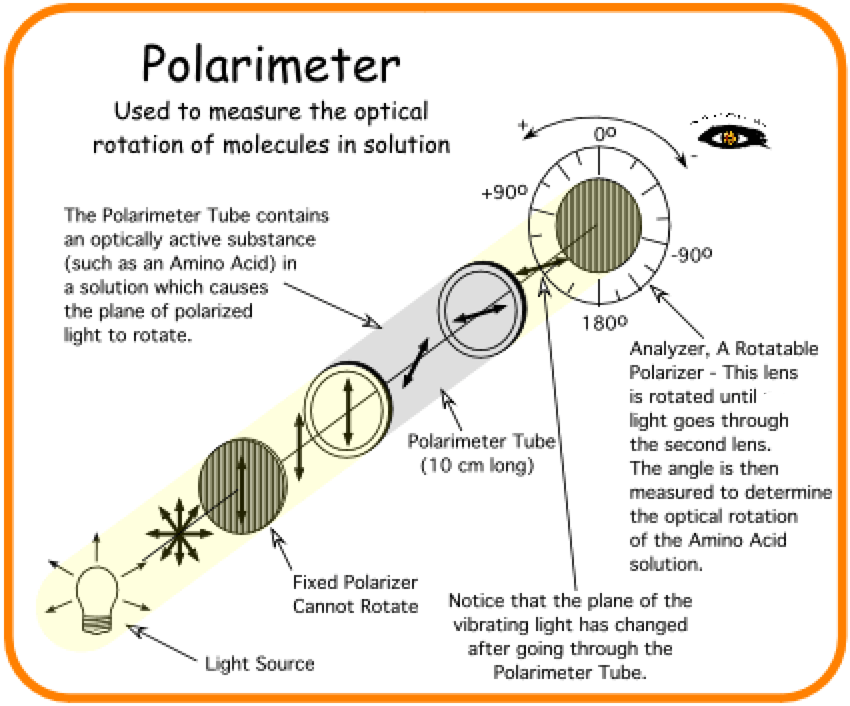


Specific rotation angle $= [\alpha]^{t}_{\lambda} = \dfrac{\alpha}{l \times c}$ (given solvent)

$\lambda =$ Na, D band = 589.3 nm

l = 1 dm ; C = 1g/ml (w/v)

Polarimeter



Polarimeter

Used to measure the optical rotation of molecules in solution

The Polarimeter Tube contains an optically active substance (such as an Amino Acid) in a solution which causes the plane of polarized light to rotate.

Analyzer, A Rotatable Polarizer - This lens is rotated until light goes through the second lens. The angle is then measured to determine the optical rotation of the Amino Acid solution.

Polarimeter Tube (10 cm long)

Fixed Polarizer Cannot Rotate

Light Source

Notice that the plane of the vibrating light has changed after going through the Polarimeter Tube.

+ -

Specific rotation angle (+):
Clockwise (right) rotation of polarized light …

Specific rotation angle (-):
Counter-Clockwise (left) rotation of polarized light …

All chiral substances display optical activity

Glucose ; specific optical activity

α pure *(methanol crystallized)*
$[\alpha] = 112°$

β pure *(acetic ac. crystallized)*
$[\alpha] = 19°$

$$36\,\% = \frac{(53 - 19)}{93}$$

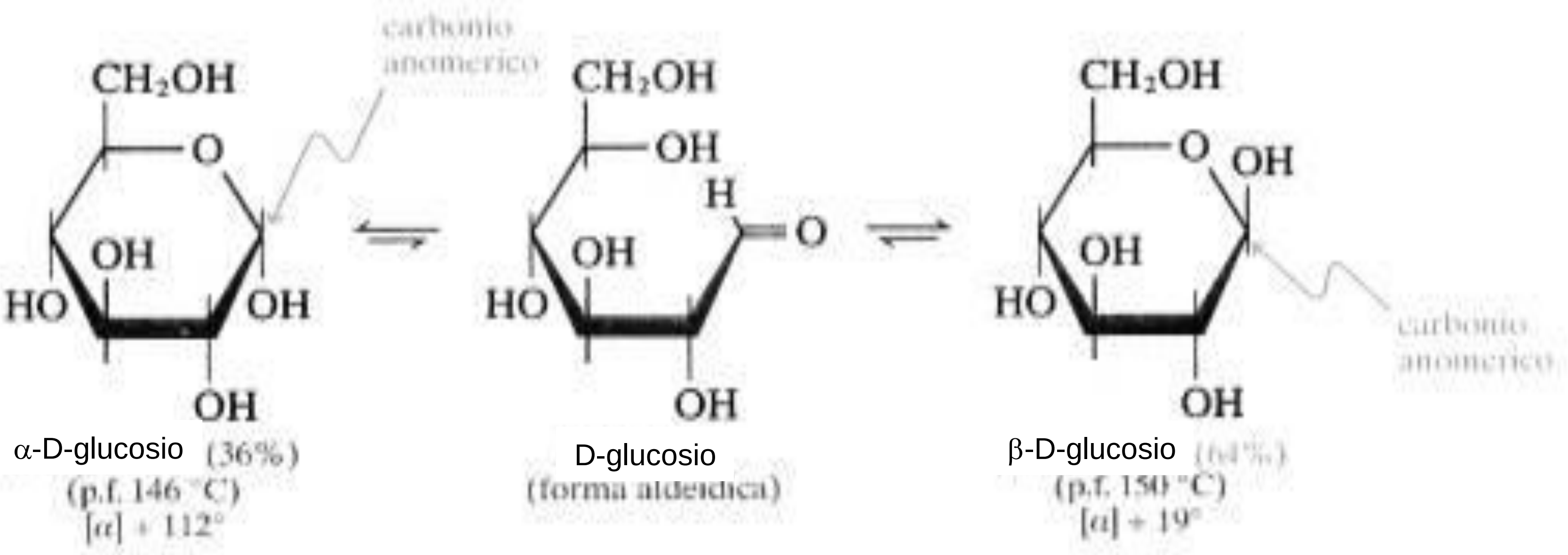
(gain in α)

$[\alpha] = 53°$

at time = t_{eq}

$$64\% = \frac{(112 - 53)}{93}$$

(gain in β)



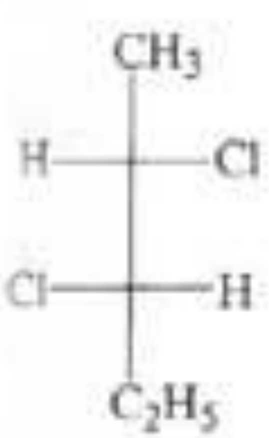
α-D-glucosio

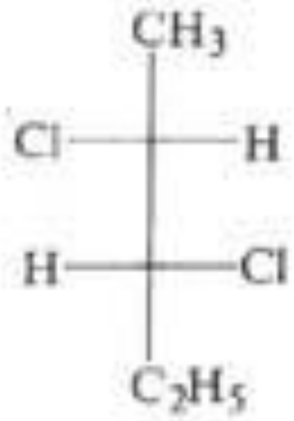
D-glucosio

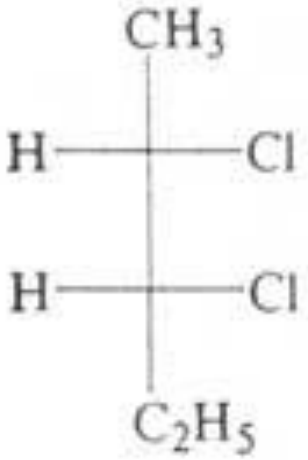
β-D-glucosio

Diastereomers

2 molecules, with more than 1 stereocentre, which are not mirror images of each other.


I

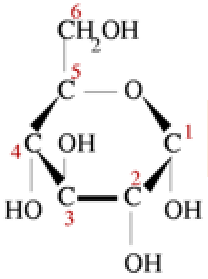

II

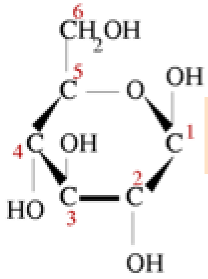


Enantiomers
whose mirror image cannot overlap

Check this one!

Glucose: the anomeric carbon 1
glucopyranose, diastereomers


α


β

Organic compounds: reactivity

Organic compounds: reactivity

Generally:

- Most organic molecules (of the type C_nH_m) are characterized by a low dipole moment, $D \approx 0$
- organic reactions are based on **breaking** and **re-formation** of covalent bonds
- H replacement produces the so called “**inductive effects**” with D variation

X = elettron-acceptor

X-R

X ← R

(δ–) (δ+)

negative inductive effects (on R) (-1)

X = elettron-donor

X-R

X → R

(δ+) (δ–)

positive inductive effects on R (+1)

How do covalent bonds cleave ?!

$A \cdots\!:\!\cdots B \longrightarrow A^{\bullet} + B^{\bullet}$ Homolytic fission- *radicalic*

$A \,\vdots\, : \quad B \longrightarrow A^{+} + B{:}^{-}$ Heterolytic fission- *ionic*

$A \quad : \,\vdots\, B \longrightarrow A{:}^{-} + B^{+}$ Heterolytic fission- *ionic*

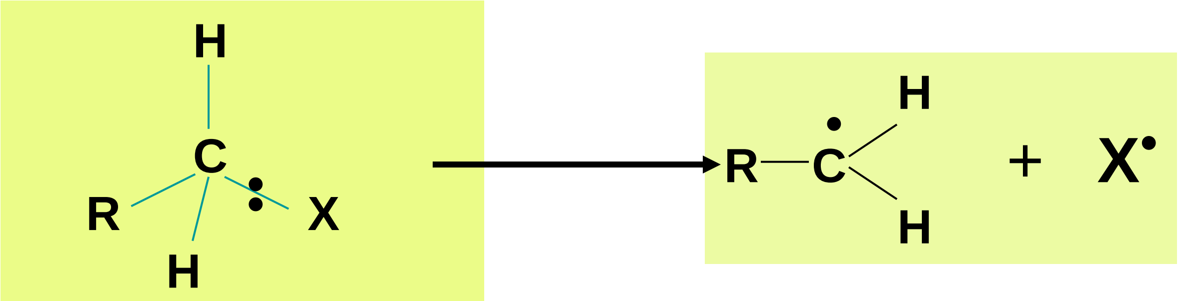
$A\bullet \quad B\bullet$ **are electroneutral radicalic species (1 unpaired e- in the valence shell)**

$A{:}^{-} \quad B{:}^{-}$ **1 lone pair donors , nucleophiles, (Nu:)**

$A^{+}, \ B^{+}, \ R^{\bullet}$ **these species are electrophiles (E^{+})**

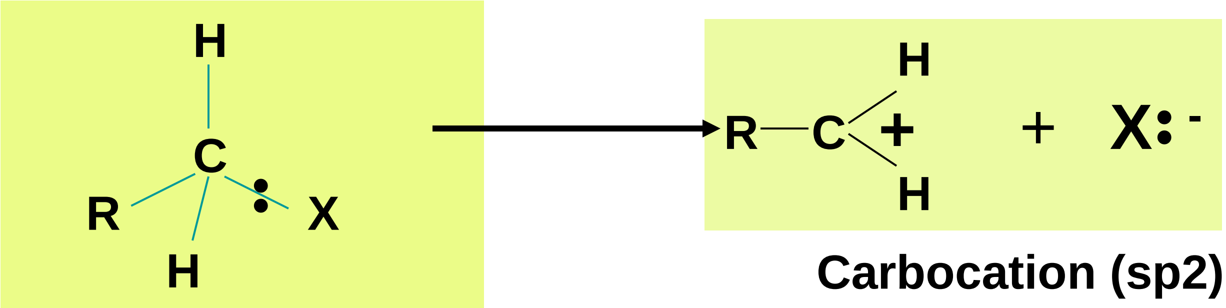
Reactive states of carbon

The structure



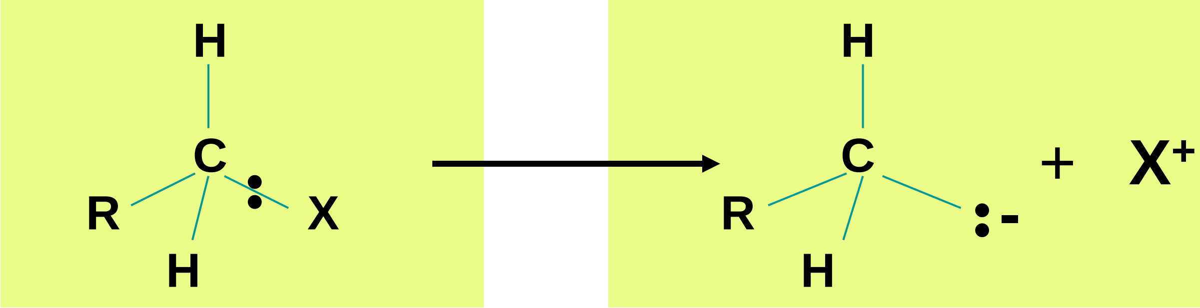
Free radical (sp2), R$^\bullet$

Trigonal planar



Carbocation (sp2), E$^+$

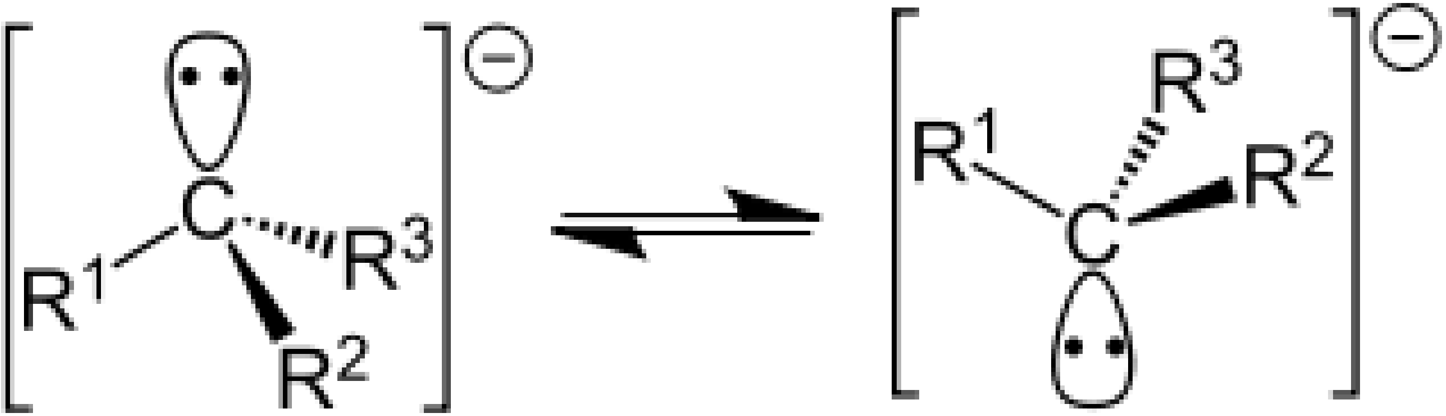
Trigonal planar



Carbanion (sp3), Nu:

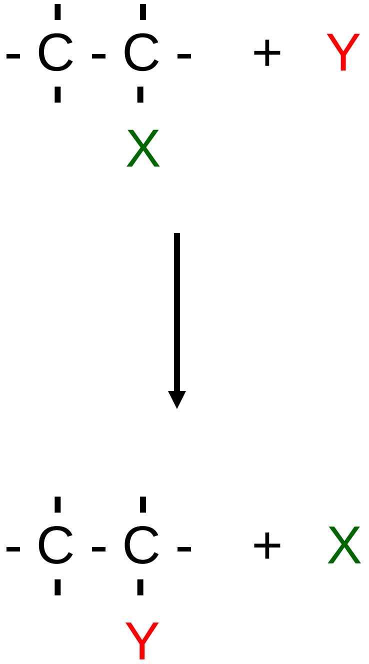
Tetrahedron

Two carbanions in rapid equilibrium



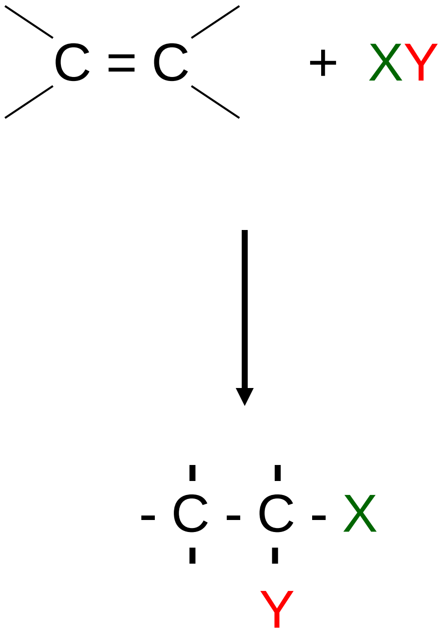
Organic reactions

Substitution



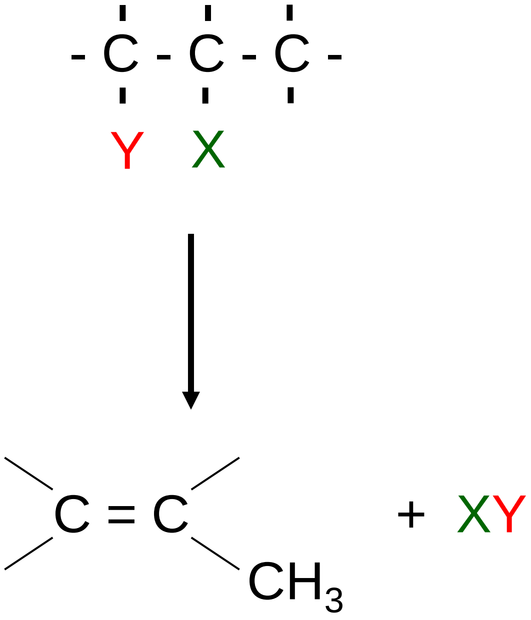
σ cleavage
&
new σ bond

Addition



π cleavage
&
new σ bonds (2)

Elimination



(X Y) elimination (2 σ bonds)
&
new π formation

even with $\Delta G < 0$, if Ea is high, then
CATALYSIS

Acid, H^+

Basic, OH^-

The H+ will attack the most
Electron dense region of substrate
Thus varying charge delocalization

The OH- will attack the most
Electron deficient region of substrate
Thus varying charge delocalization

A few examples of *substitution reactions* (SN_1 - SN_2)

$$R\text{-}X + Nu \longrightarrow R\text{-}Nu + X^-$$

Substrate alkyl ↓ **Nu :** ↓ **product** ↓

$$R\text{-}X + H\ddot{\underset{..}{O}}\!:^- \longrightarrow R\text{-}OH + X^-$$ **(alcohol)**

$$R\text{-}X + R\ddot{\underset{..}{O}}\!:^- \longrightarrow R\text{-}O\text{-}R + X^-$$ **(ether)**

$$R\text{-}X + \ddot{N}H_3 \longrightarrow R\text{-}NH_3^+ + X^-$$ **(alkyl-ammonium ion)**

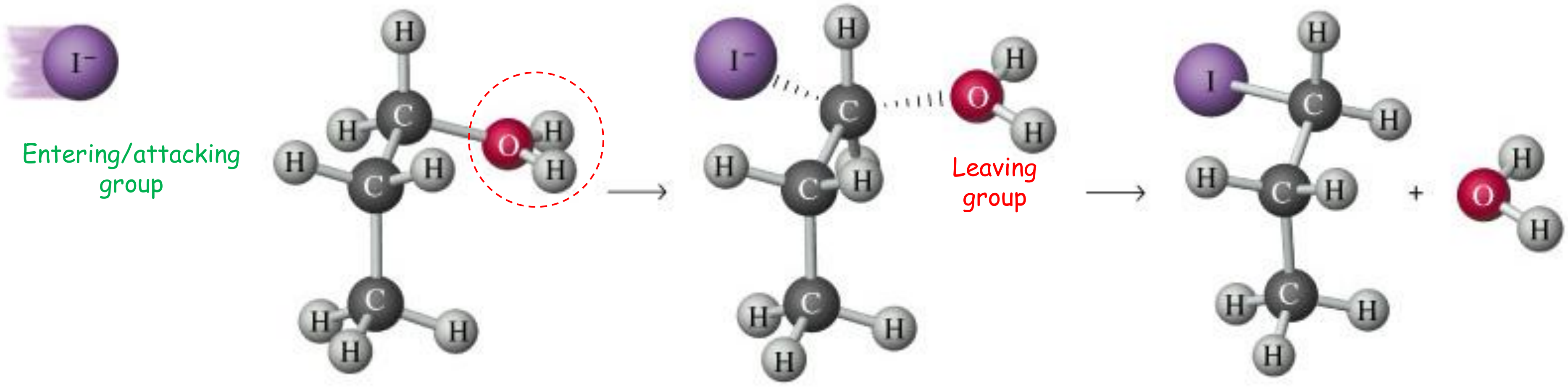
$$R\text{-}X + H\ddot{\underset{..}{S}}\!:^- \longrightarrow R\text{-}SH + X^-$$ **(thiol)**

SUBSTITUTIONS

SN2 (mechanism)

bimolecular collision

Nu: Propyl alcohol Single step intermediate Iodine-propane



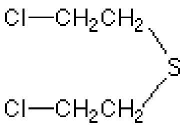
Entering/attacking group

Leaving group

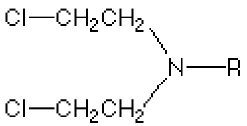
SN1 (mechanism)

1st event (slow) *bimolecular => carbocation formation*
2nd event (rapid) Nu attack => product formation

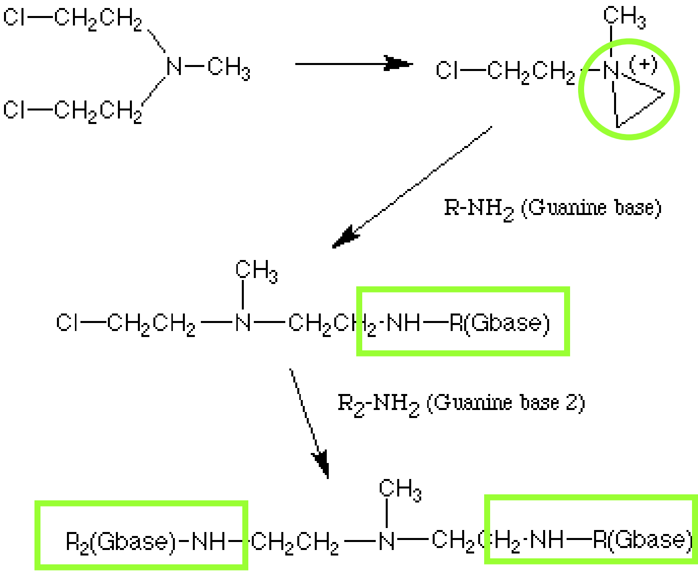
Mustard = **Alkylating agent**



Bischloroethylsulfide
(sulfur mustard)

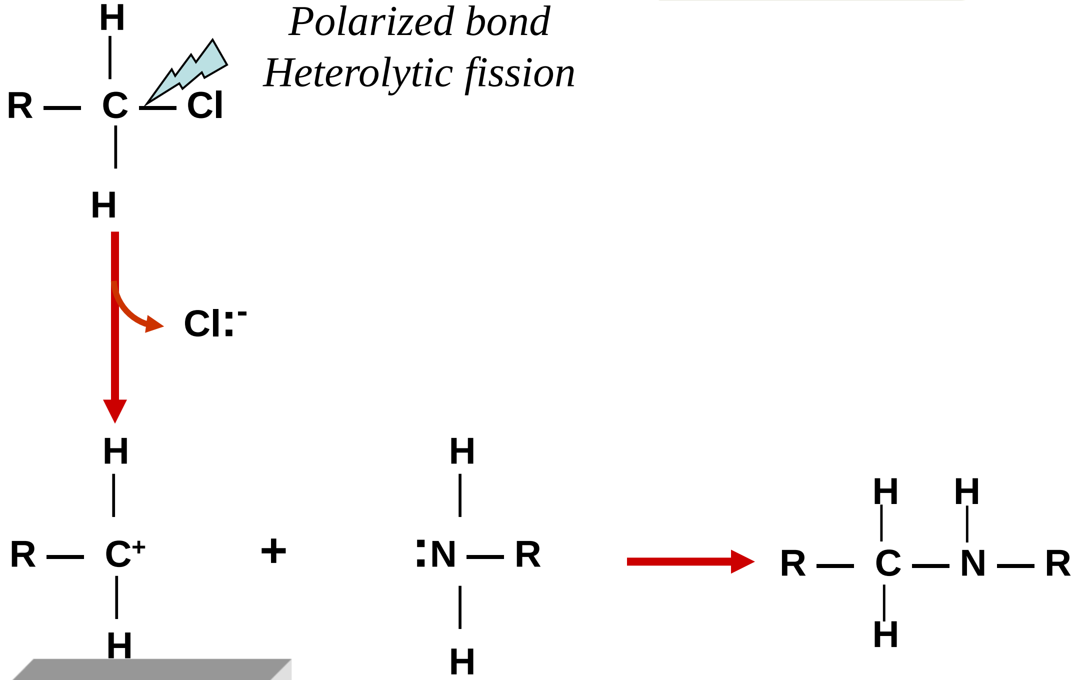


Bischloroethylamine
(nitrogen mustards)
R = $-CH_3$
R = $-CH_2CH_2Cl$



Alkylating agent

alkylation



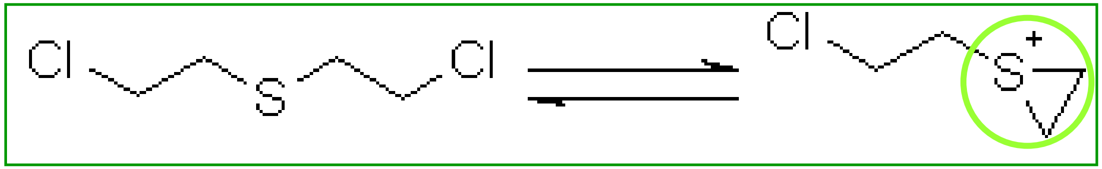
Polarized bond
Heterolytic fission

alkyl
carbocation

Ammine target
(Nu:)
(proteins, DNA)

Alkylated
product

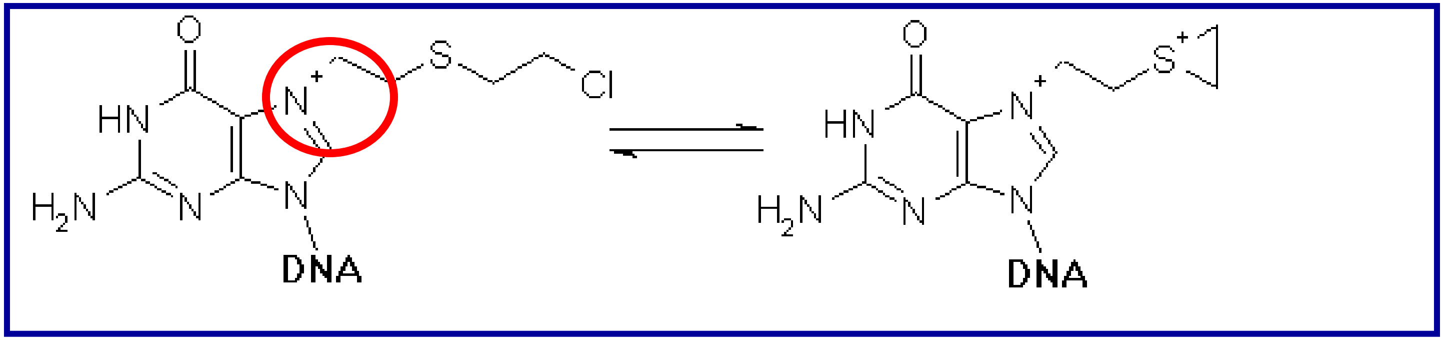
S-mustard binds DNA



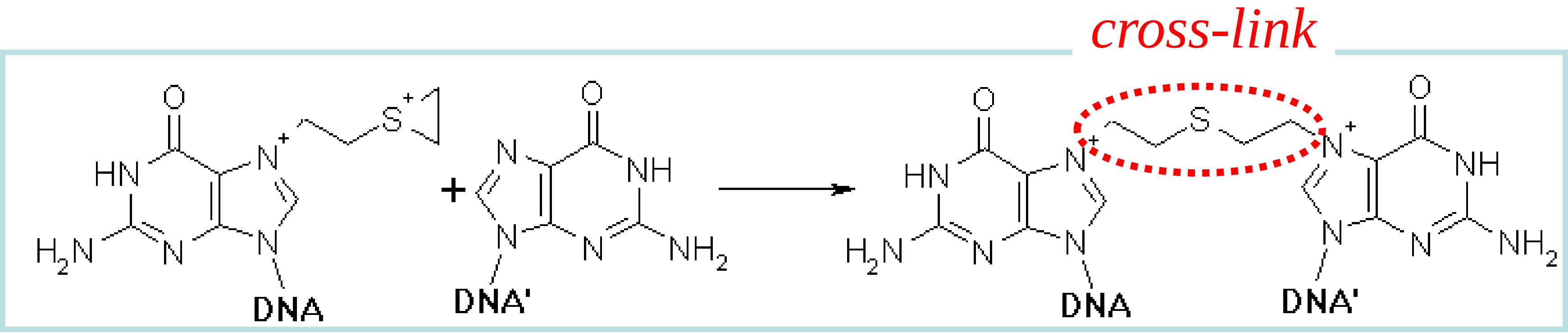
bis-2-chloroethyl sulfide

$Cl-CH_2-CH_2-S-CH_2-CH_2-Cl$

guanine



Bonding a single DNA chain

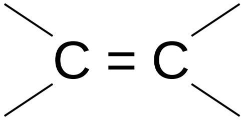


Bonding two DNA chains

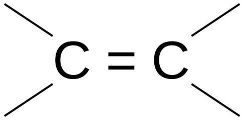
Paolo Sarti 2008
Dip. Scienze Biochimiche
La Sapienza

Skin injures by mustards

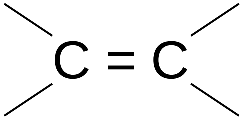
Addition reaction examples



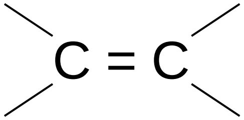
$C=C + H_2 \longrightarrow C_2H_6$ *hydrogenation of unsaturated chains*



$C=C + I_2 \longrightarrow C_2H_4I_2$ *halogenation of unsaturated chains*



$C=C + H_2O \longrightarrow CH_3CH_2\text{-}OH$ *hydration of alkenes*



$C=C + HCl \longrightarrow CH_3CH_2\text{-}Cl$ *halo-hydrogenation of alkenes*