INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION

国际创新药学院

Fundamentals of Medicinal and Pharmaceutical Chemistry

FUNCHEM.16 Alkanes and Alkenes: structure, properties and isomers

Professor Dan Wu

DATE:13 November 2024

Learning outcomes

At the end of this lecture, the learner will be able to

- Recall and apply the rules of IUPAC method of nomenclature to name and identify cycloalkanes.
- Recall and explain the structural features of cycloalkanes and factors affecting their stability.
- Identify and explain geometric (cis/trans) isomers in cycloalkanes.
- Identify and describe the axial and equatorial positions in a cyclohexane chair conformer.
- Identify and explain factors affecting the stability of substituted cyclohexane in chair and boat conformer structures.
- Recall and explain the oxidation of alkanes

Recommended reading

McMurry, ‘Organic Chemistry with Biological Applications’, 3rd Edition, 2015, Cengage Learning

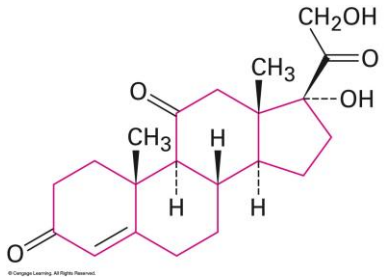
- ✓ Chapter 4
- ✓ Section 4.1 – Naming cyclic alkanes
- ✓ Section 4.2 – Cis-trans isomerism in cycloalkanes
- ✓ Section 4.3 – Stability of cycloalkanes: Ring strain
- ✓ Section 4.4 – Conformations of cycloalkanes
- ✓ Section 4.5 – Conformations of cyclohexane
- ✓ Section 4.6 – Axial and equatorial bonds in cyclohexane
- ✓ Section 4.7 – Conformations of monosubstituted cyclohexan
- ✓ Section 4.8 – Conformations cyclohexanes

Cycloalkane

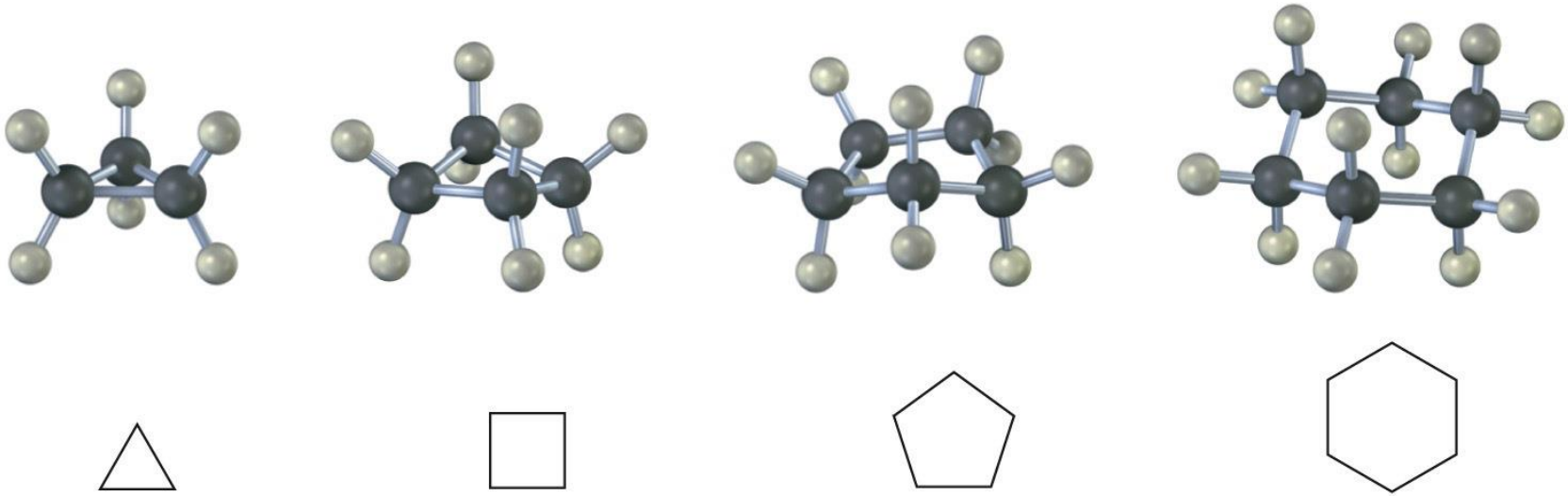
Very important structural feature of many biological compounds, e.g. steroids

General molecular formula: $\mathbf{C_nH_{2n}}$

Saturated hydrocarbons that have at least one ring of carbon atoms



Cortisone



Cyclopropane

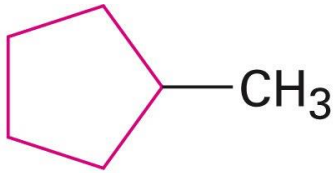
Cyclobutane

Cyclopentane

Cyclohexane

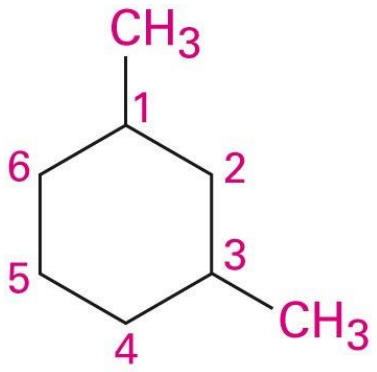
IUPAC Cycloalkane Nomenclature

1. Place the prefix cyclo– before the name of the straight chain alkane that has the same number of carbon atoms as there are in the ring
2. No number is needed before a substituent when there is only one attached to the ring
3. Number substituents around the ring in whichever direction gives them the lowest numbers
4. With different substituents, the one with highest alphabetic priority is located at C1



Methylcyclopentane

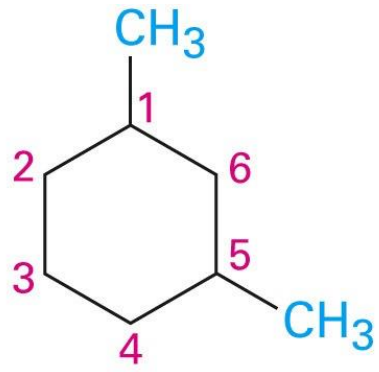
Number substituents around the ring in whichever direction gives them the lowest numbers



1,3-Dimethylcyclohexane

Lower

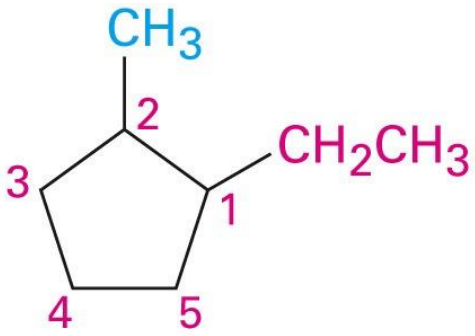
NOT



1,5-Dimethylcyclohexane

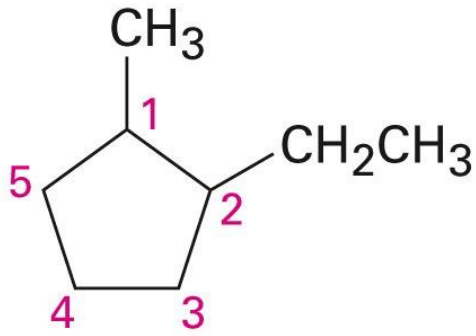
Higher

With different substituents, the one with highest alphabetic priority is located at C1



1-Ethyl-2-methylcyclopentane

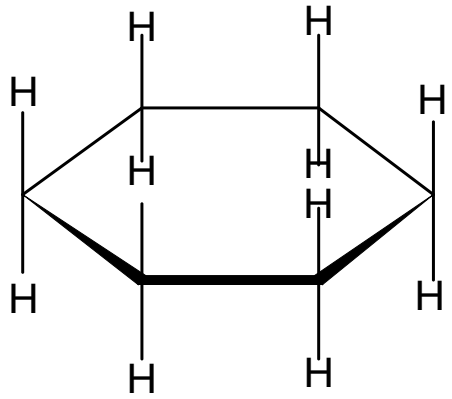
NOT



2-Ethyl-1-methylcyclopentane

Conformations of Cyclohexane

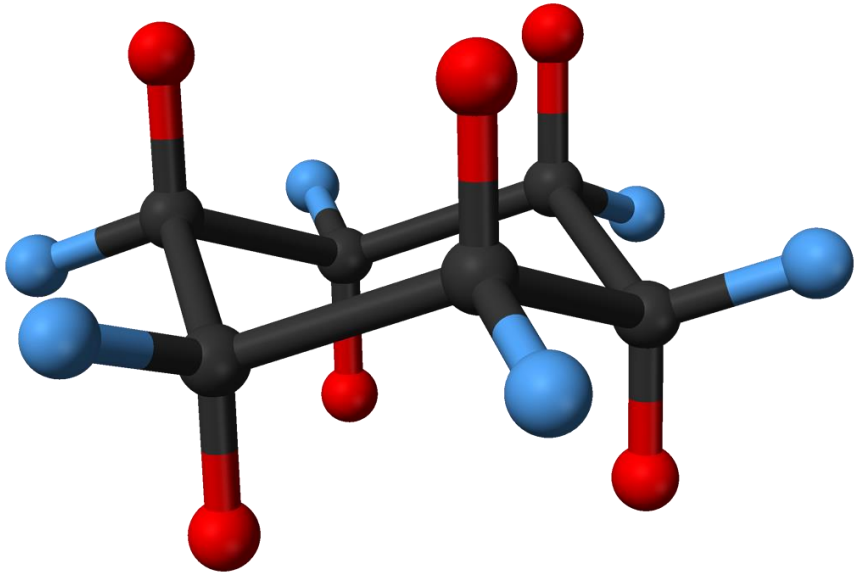
Cyclohexane is not planar



If cyclohexane were planar all of the hydrogens would be eclipsed, resulting in steric strain.

There would also be angle strain
- a hexagon has 120° internal angles.

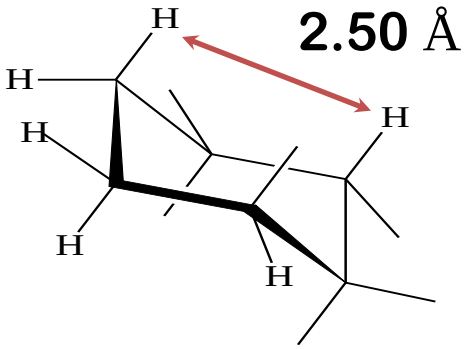
Cyclohexane is puckered



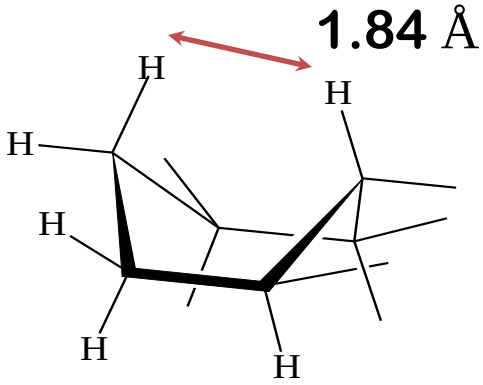
all bond angles are 109.5°

all hydrogens on adjacent carbons are staggered (lower energy than eclipsed)

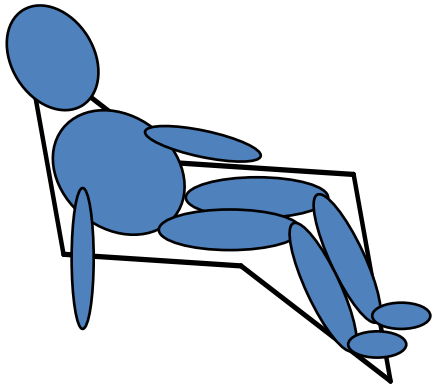
Two Conformations of Cyclohexane

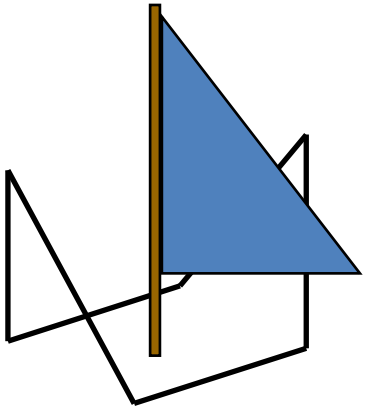


Chair



Boat

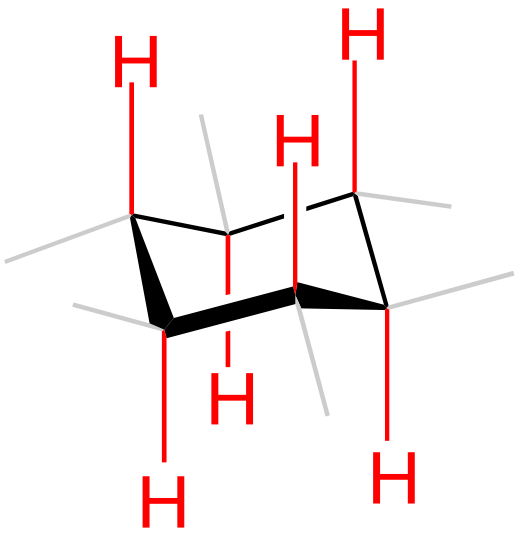


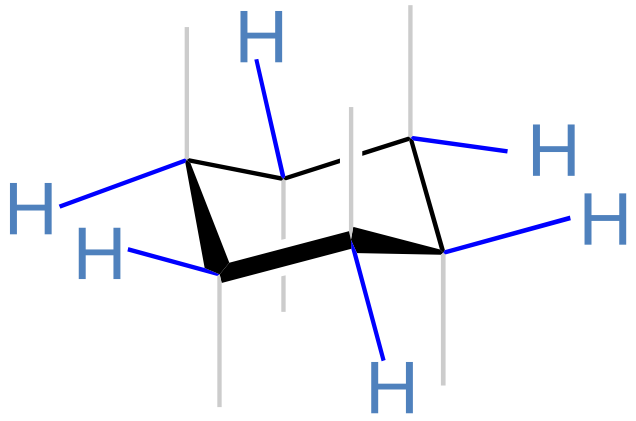


The boat conformations are usually higher in energy than any chair

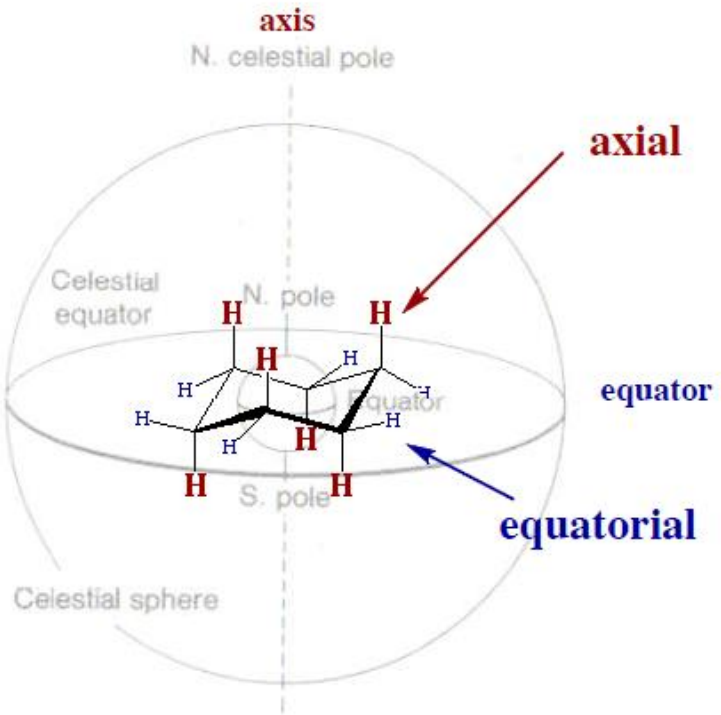
Chair Conformations: Axial and Equatorial Hydrogens

axial



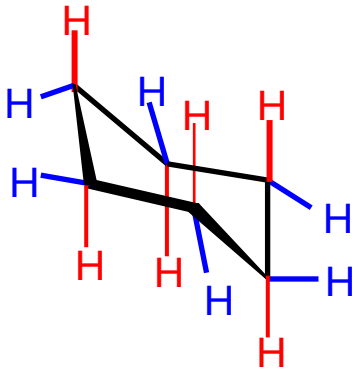


equatorial



Conformations of Cyclohexane

Chair conformation



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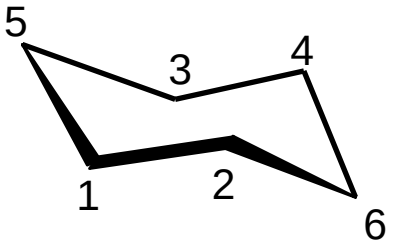
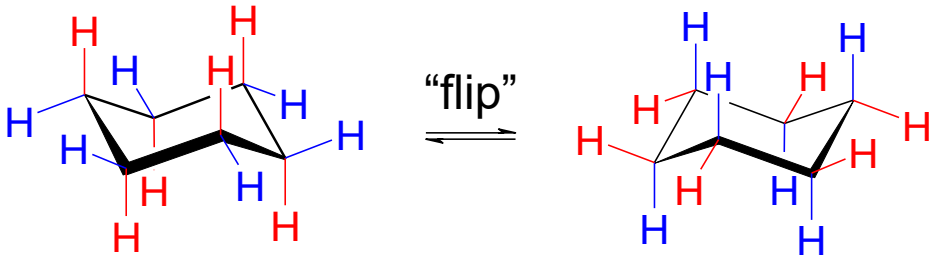


Six axial (red) and six equatorial (blue) hydrogens

Four carbons in same plane (1,2,3,4) one up (5) and one down (6)

Axial and equatorial groups can exchange positions by a ring flip

(keep 1-4 in the same position and push 5 down and 6 up)

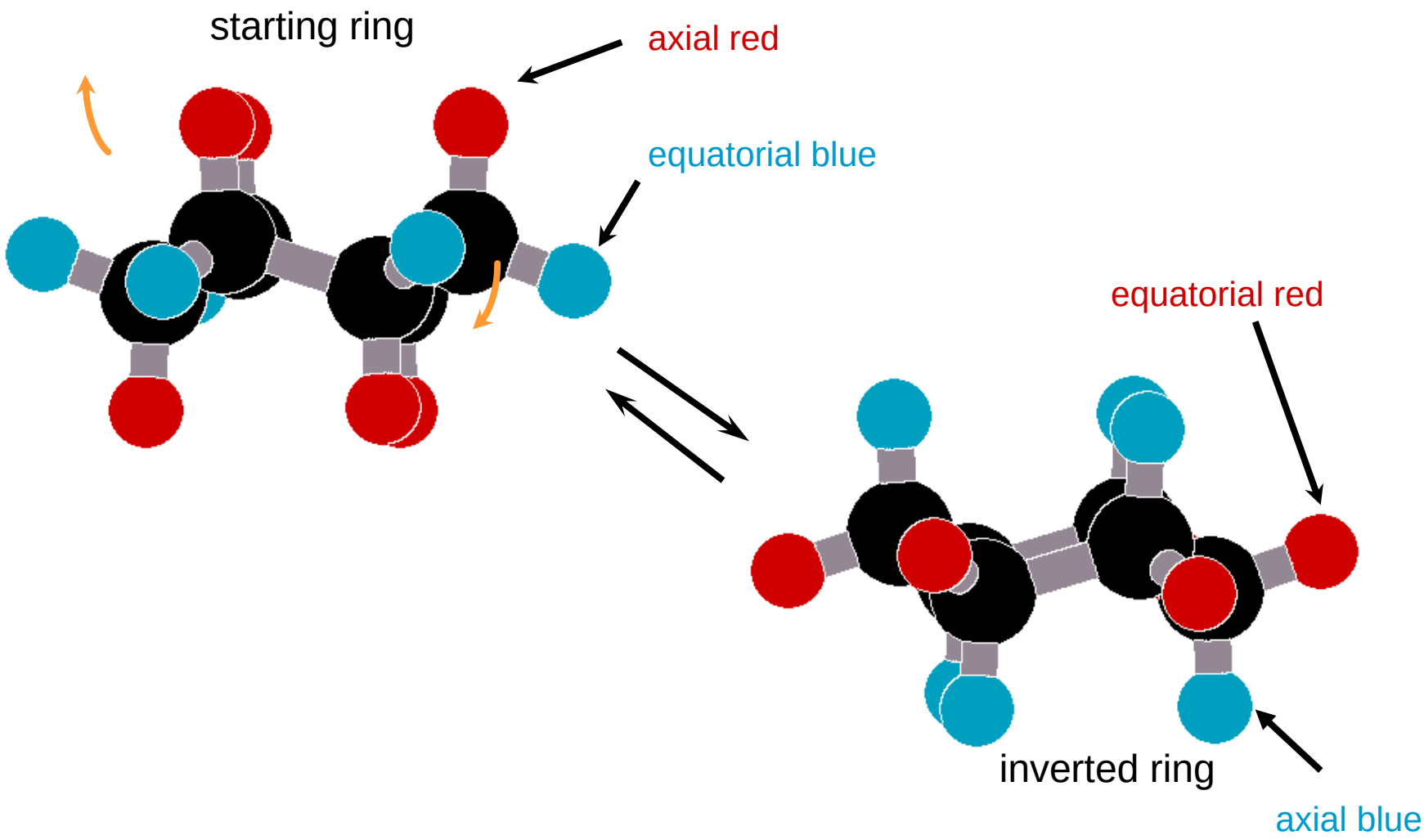


Axial bonds in the left structure become equatorial bonds in the right structure when the ring "flips"

Groups (other than H) prefer to be in an equatorial position

Chair Conformations: Ring Inversion

axial and equatorial hydrogens are interchanged when the ring is inverted



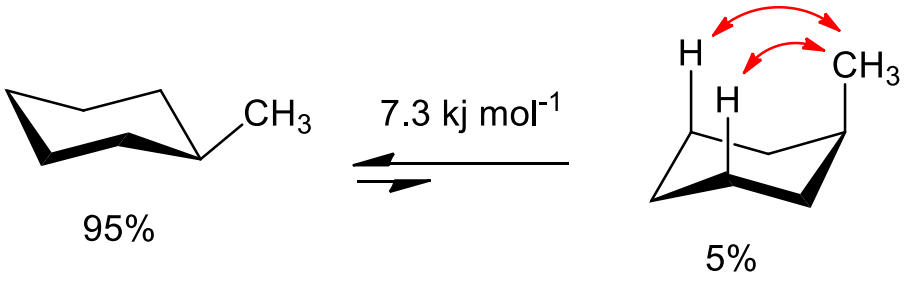
Try it yourself at

https://www.chemtube3d.com/stcyclohexane-ring-flip/

Chair Conformations of Methylcyclohexane

Methyl equatorial

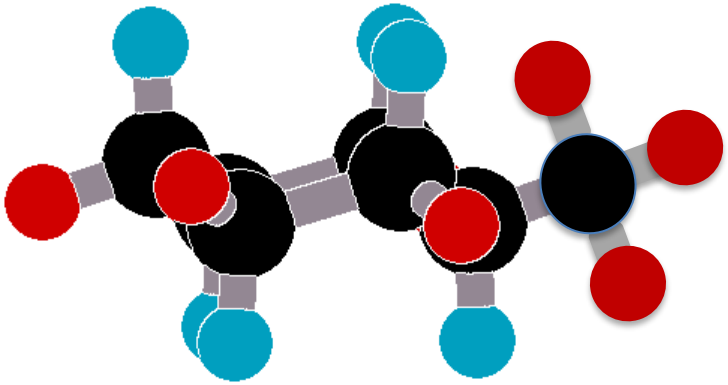
Methyl axial



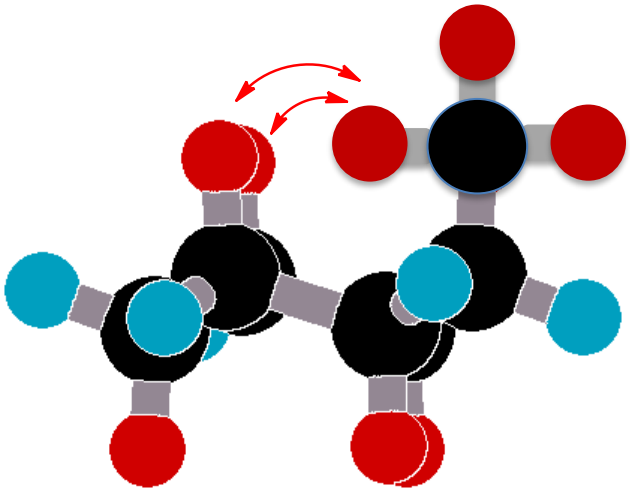
95%

5%

red arrows shown unfavourable interaction between the methyl group and the axial hydrogens



Methyl equatorial

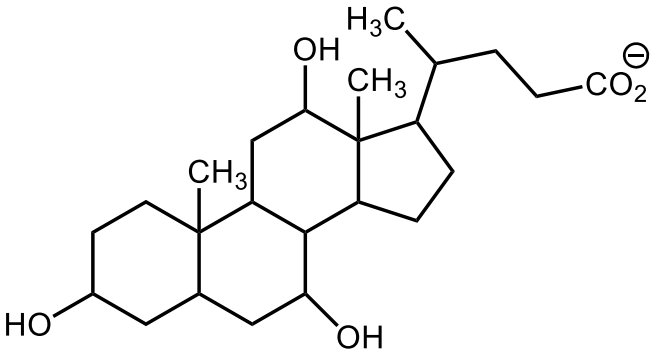


Methyl axial

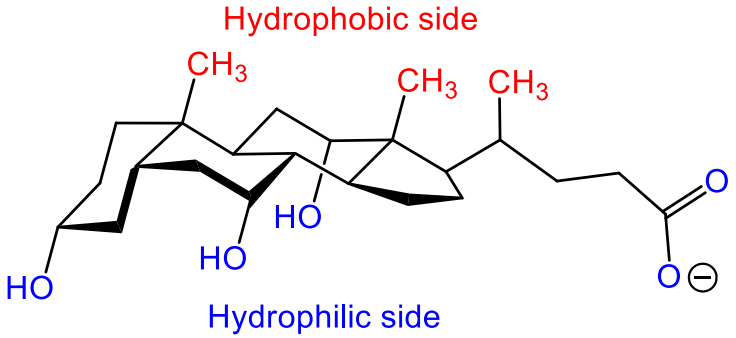
Cyclohexanes in Biology

Cholic acid is the major bile acid and acts as a key lipid emulsifier which allows their hydrolysis by pancreatic lipases

Cholic acid



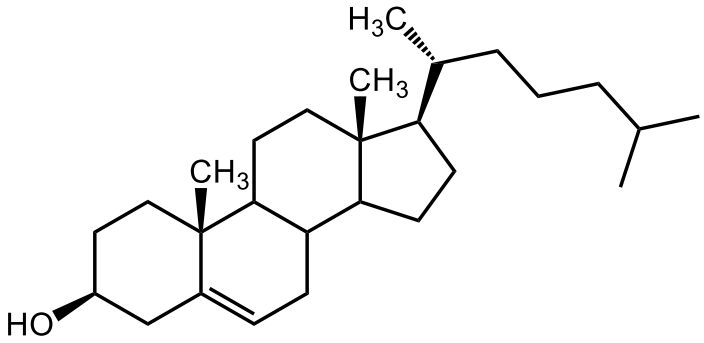
Cholic acid

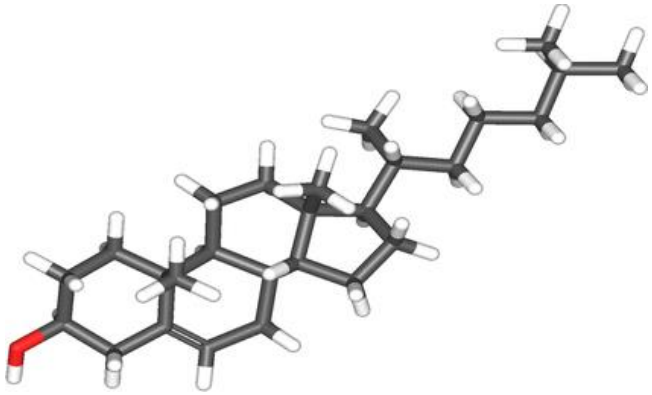


"soap-like" nature of cholic acid gives it the emulsifying properties

Cholesterol

Important roles in membrane structure



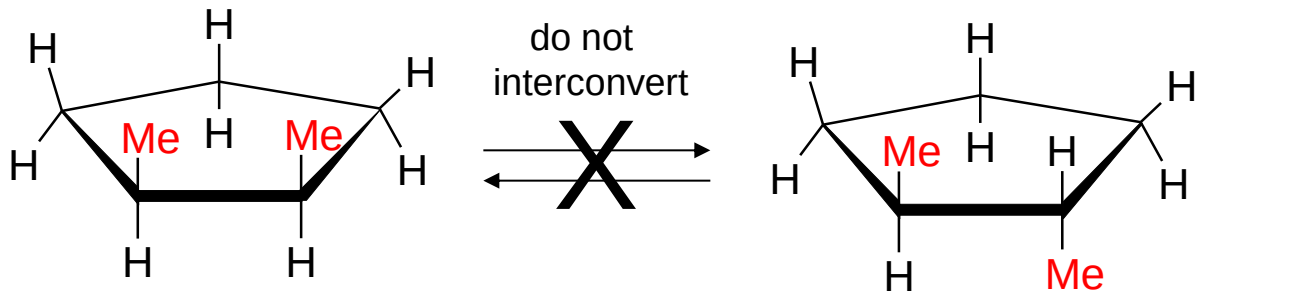


Cis-Trans Isomerism in Disubstituted Cycloalkanes

(Geometric isomerism)

cis and trans are relationships relative to a plane
cis – “same side”
trans – “opposite side”

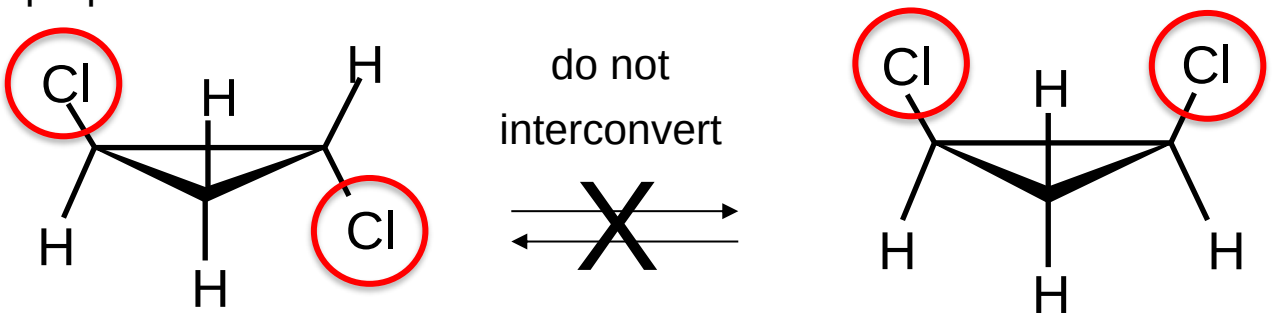
Example: cyclopentane



cis-1,2-dimethylcyclopentane

trans-1,2-dimethylcyclopentane

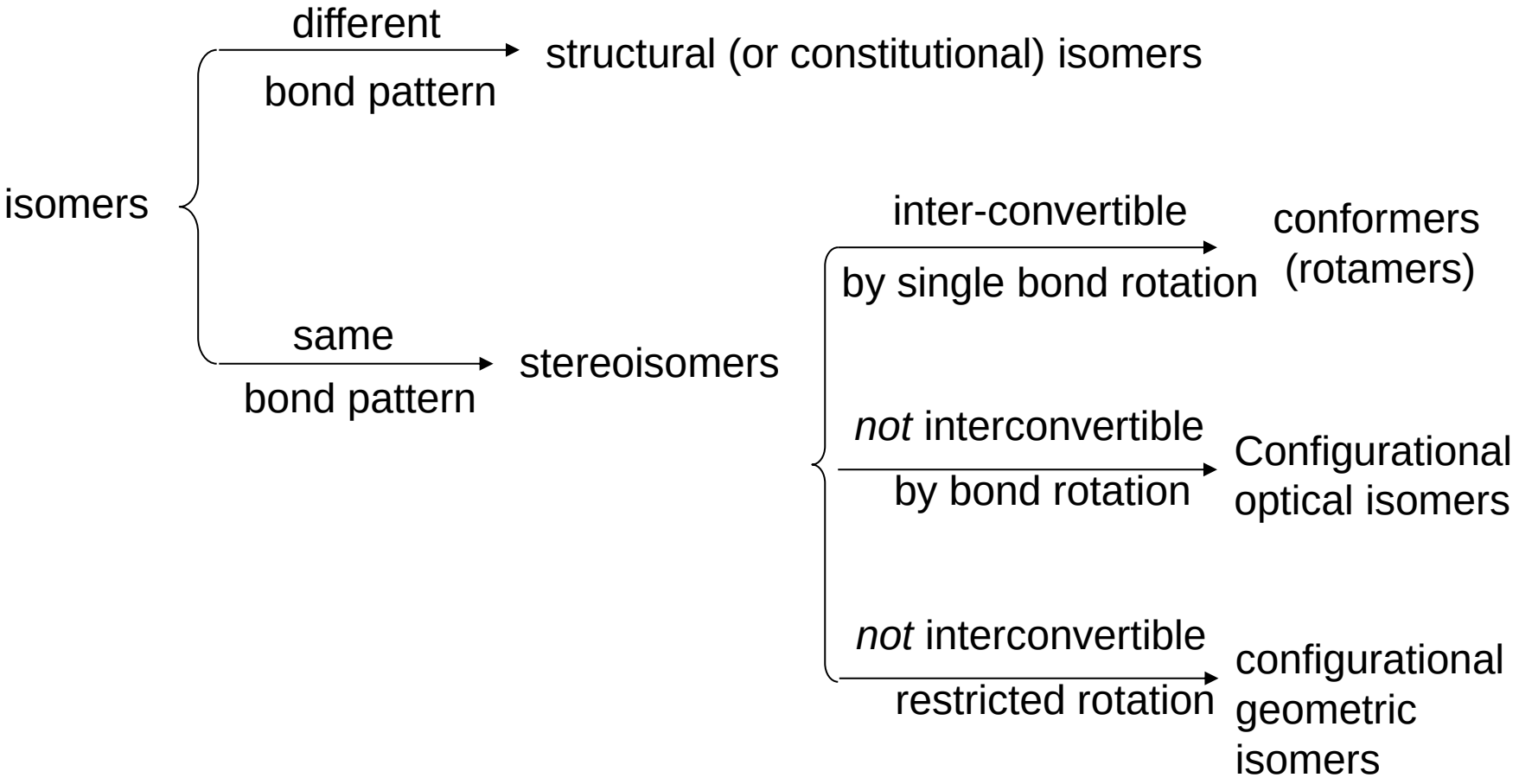
Example: cyclopropane



trans-1,2-dichlorocyclopropane

cis-1,2-dichlorocyclopropane

Summary of Isomer Types in Alkanes



Chemical Properties of Alkanes

Extremely unreactive

unreactive towards strong acids; strong alkalis; mild oxidising agents; halogens in the dark

Main chemical reactions:

Oxidation (addition of O or removal of H)

Halogenation (using light) [**no longer in course content**]

Oxidation or Combustion of Alkanes

hydrocarbons burn to form carbon dioxide, water and heat.
The heat can be used to heat homes or run engines.

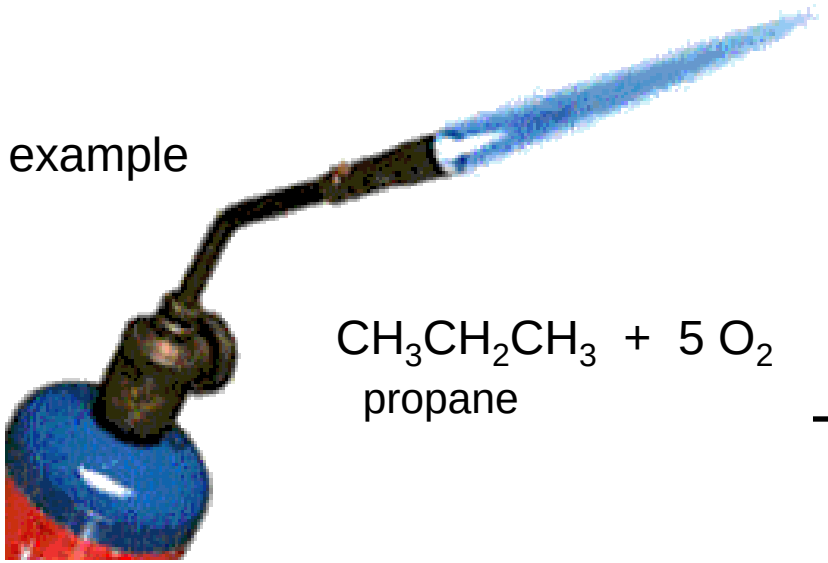
example

CH_4 Methane (natural gas)

$$CH_4 + 2\,O_2 \longrightarrow CO_2 + 2\,H_2O + \text{Heat}$$

Each carbon gives a CO_2 molecule and every two hydrogens give a water molecule

example



liquefied propane

$CH_3CH_2CH_3$ + 5 O_2 → 3 CO_2 + 4 H_2O + Heat

propane

Alkenes, Dienes, Polyenes Functional Groups

They contain the functional group C = C.

They are unsaturated because the carbons are attached to less than the maximum number of atoms.

Alkenes (linear) have the general formula C_nH_{2n}.

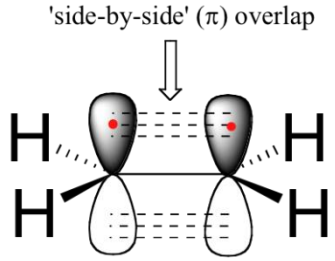
Compounds with two C = C groups are called dienes,

compounds with three C = C groups are called trienes,

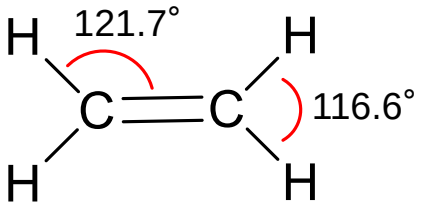
and with many C = C groups are called polyenes.

Alkenes: Shape and Bonding

The geometry around doubly bonded carbon is trigonal planar, bond angle ~120˚



A pi (π) bond is a covalent bond formed by sideways overlap of atomic orbitals, e.g. carbon-carbon double bonds contain one sigma bond and one pi bond formed by sideways overlap of two *p* orbitals.



carbon-carbon double bonds containing one sigma bond and one pi bond with length of 133 pm;
C-H bond angle of 121.7˚

Note: There is restricted rotation around the C=C bond.

Nomenclature

The names of alkenes end in –ene.

$H_2C{=}CH_2$ ethene

$H_2C{=}CH{-}CH_3$ propene

For longer chain alkenes C chain is numbered so that the (first) C of the double bond has the lowest number.

1 2 3 4
$H_2C{=}CHCH_2CH_3$

1-butene or but-1-ene

NOT

4 3 2 1
$H_2C{=}CHCH_2CH_3$

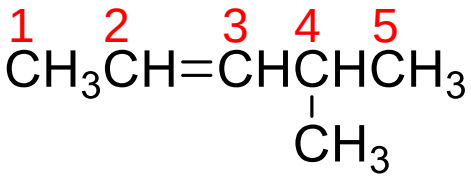
3-butene or but-3-ene

1 2 3 4
$CH_3CH{=}CHCH_3$

2-butene or but-2-ene

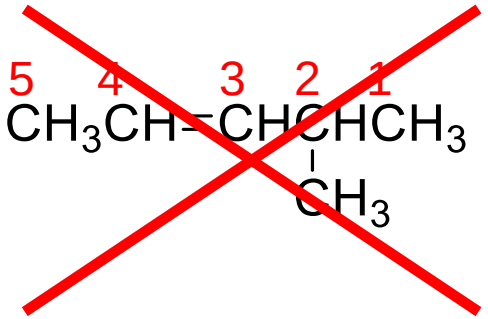
1-butene and 2-butene are structural isomers.

Example of Nomenclature



4-methyl-2-pentene

or



2-methyl-3-pentene

Double bond takes precedence over

alkyl substituent.

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