Stereochemistry

Compound with same formula and structure but different configuration, spatial arrangement. Non-spherical orbitals have greater concentration in a particular direction leading to directional bonds.

Two types; Optical and geometrical
Optical stereoisomerism: due to asymmetry they rotate the plane of polarisation of plane polarised light.
Types of optical isomer; enantiomer, diastereomer and mesomer.
Enantiomer: optical isomers rotating the plane of light in equal and opposite direction by the same amount.
Diastereomer: When they rotate by different amount than it is called diastereomer.
Mesomer: optical isomer with no rotation

Assymetry: non super imposition on the mirror image. No element of symmetry.
Disssemtry: Non superimposition on mirror image. have some element of symmetry.

Optical activity may be due to crystalline form or molecular firm called anatiomorphous.
Quartz, benzil, sodium chlorate etc are aptically active in crystal form due to assymmetry in spiral structure. evaporation disolution or fusion leads to loss of optical isomerism.

Chirality or handedness, Kelvin (1884)
asymmetry is also called Chirality.

Conventions in stereochemistry
d or *l* for dextrorotatory and laevorotatory. useful in case of one chiral centre.

van't Hoff (1874)
+/- based on solid model and projection from the centre of the molecule.
diastereomer with two chiral centres can be --/ ++/+-/+-.
useful in case of two chiral centres.

Fischer (1891)
projection of mechanical model in plane.
useful for more than 2 chiral centres.
D/ L notation to show the stereo-chemical relationship between the compound.
A standard was chosen and then rest were related to it if the stereo-centre is not affected.
Disadvantage
D-mannose gave D-Mannoic acid and L-Mannose gave L-mannoic acid but both the mannoic acids were same.
Rosanoff (1906)
instead of arbitrary standard D-Glyceraldehyde was taken as the standard and rest were related to it.
e.g. glyceraldehyde was used as standard and then sugar molecules were related to it.

Conventions of drawing

Three groups are above the paper and one below
for D-(+)-glyceraldehyde H was at left bottom, OH at right bottom, and aldehyde at the top of the traingle

if the tetrahedron is rotated so that the group behind appears below front triangle. Top and bottom is shown in broken vertical line. asymmetric carbon is at the point where lines intersect.

Fischer projection: vertical line is behind whereas the horizontal line is in front of the paper.

Absolute configuration: Bijvoet (1951) sodium rubidium tartarate by x-ray crystallography.

Correlation of configuration

Configuration of unknown compound was related to the compound with known configuration.

Correlation of Glyceraldehyde with tartaric acid

D(+)-glyceraldehyde → *meso*-tartaric acid + (-) tartaric acid

so (-)-tartaric acid is D(-)-tartaric acid

(+)-tartaric acid → D(-)-glyceric acid

so (+)-tartaric acid is D(+)-tartaric acid

Methods of correlation

Chemical reaction without displacement at chiral centre
Chemical reaction with displacement at chiral centre.
X-ray analysis
asymmetric induction
Optical rotation
Quasi racemic compound
Enzyme action

Absolute configuration

Cahn (1956)

groups attached to chiral carbon is arranged as per the sequence rule

1) Sequence rule

- Atoms attached to the asymmetric carbon is prioritized as per atomic number
- If atoms have same atomic number, then comparison is made between the next atom attached to group. This continues till the sequence is clear.
- Multiple bonds are replicated with same atom. duplication for double bond, triplication for triple bond.
  e.g. -CHO becomes CH(O)-O(C)
- Rings are treated as branch
- Unsaturation in ring is treated by duplication of branch

2) conversion rule

when viewed from outside, with lowest priority group hiding behind the chiral carbon, the clockwise or right handed sequence is termed R (Rectus) and antilock or left handed sequence as S (sinister)

D(+)-Glyceraldehyde

From Fischer convention: H on left, OH on right, CHO on top and CH_2OH below.

Step 1: Lowest priority at the bottom.

interchange of H and OH makes it L (-) glyceraldehyde and
interchange of H and CH_2OH again restores D(+)-Glyceraldehyde.

sequence rule designated this as right handed, clock wise or R configuration

Optical isomerism in molecule without chiral carbon

optical activity due to **chiral axis**

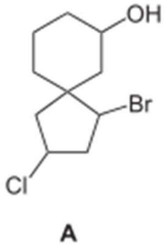
biphenyls (Christie and Kenner, 1922)
conditions
- 1) neither ring should have vertical plane of symmetry.
- 2) Ortho position should be substituted with large group prevent free rotation and forces two benzene ring to be perpendicular to each other.

If rotational barrier is > 75 KJ/mol. separable rotaional isomer is possible. such isomers are called atropisomers
Chiral axis is derived from chiral centre (with aba'b' groups) by elongating the tetrahedron with a and b on one end and a' and b' on end.
for chiral centre all four group should be different but for chiral axis $a \neq b$ is sufficient
Rule for assignment of absolute configuration
groups at the near end are given preference over far end for example a and b are at the near end
if a>b and a'>b' then a=1, b=2, a'=3, b'=4
in the conventional tetrahedron the b' will be behind
with a partial rotaion the b' will be brought down and shown in the fischer projection

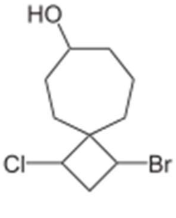
molecular over crowding
nonbonded carbon atom cannot approach closer than 3 Å. if atom approach each other then there will be out of plane buckling and helix is formed
optical activity *due to helicity*. e.g benzophenanthrene
the buckling is distributed all over the structure

Spiran
if both double bond of allene is replaced with ring systems. two rings perpendicular to each other and chirality due to asymmetry of molecule as whole.

Nomenclature
- prefix spiro-
- Number of carbon atom in the nucleus
- Number placed in square bracket indicating the number of carbon atom joined to the junction C atom
- total number of atom denoted as in any hydrocarbon
- numbring begin with the smaller ring
- substitution is indicated before the ring



A



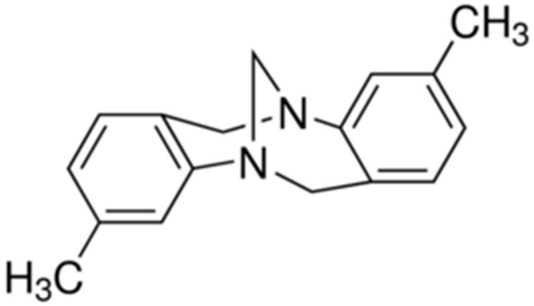
B

compound A is called *1-bromo-3-chlorospiro[4.5]decan-7-ol*, and
compound B is called *1-bromo-3-chlorospiro[3.6]decan-7-ol*

Adamentane
centre of chirality is *unoccupied centre*. this may be considered as analogue of chiral carbon.

compounds with nitrogen

quadricovalent unielectrovalent like carbon
but unresolvable due to fast racemisation
if anchored in fixed confirmation then resolvable. e.g troger base



oximes
oxime of cuclohexanone-4-carboxylic acid

phosphorus compounds
teritiary phosphines

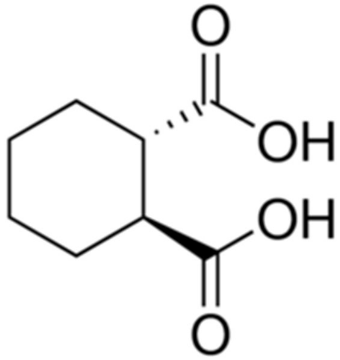
Arsenic compounds

silicon compounds
tin compounds

Geometrical isomerism

Maleic acid and fumaric acid $C_4H_4O_4$
they are not structural isomer because both
on catalytic reduction produce succinic acid
on addition of Br_2 produce dibromosuccinic acid
with $KMnO_4/OH^-$ give tartaric acid
no free rotation of double bond
2 H and 2 -COOH are in same plane. they are not optically active due to superimpossibility of the mirror image.
Cis-trans isomerism
when identical group are on same side then it is *cis*, maleic acid,
when on opposite side it is *trans*, fumaric acid.
3 groups

- double bond, C=C, C=N, N=N
- cyclic structure, homocyclic, heterocyclic, fused ring
- restricted rotation about single bond. hexahydrophthalic acid.



disadvantage

when four groups are different

deviates from alphabatical nomenclature

italicisation of group poses difficulty in pronunciation

E-Z nomenclature

Double bond is considered as UXC=CYZ

U,X,Y and Z are arranged as the sequence rule.

U>X and Y>Z

if U and Y are on same side then it is seqcis or Z (Zussamen; together) otherwise it is seqtrans or E (entgegen; opposite)

number of geometrical isomer possible

2^n, where n is number of double bonds when ends are different

2n-1 + 2p-1, where p = n/2 when n is even and p = (n+1)/2 when n is odd.

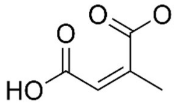
cumulene C=C=C also show geometrical isomerism

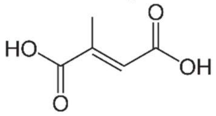
determination of configuration

ease of intramolecular cyclization

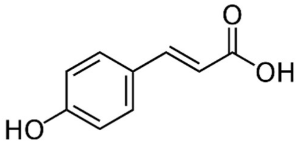
maleic gives maleic anhydride so cis

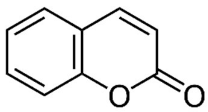
citraconic acid forms anhydric but not mesaconic so citraconic is cis

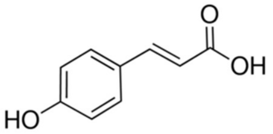




caumaric forms form coumarin, lactone but not coumarinic acid former is cis







conversion to compound with known configuration

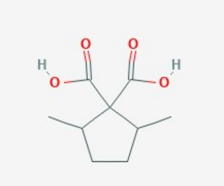
on hydrolysis one form of trichorocrotonic acid five fumaric so it is trans

on reduction it gives crotonic acid so it is trans and isocrotonic is cis

less symmetrical derivative

2,5-dimethylcyclopentane-1,1-dicarboxylic acid in two forms

on decarboxylation trans gives single product but cis give two product



Optical activity

cis-hexahydrophthalic acid is optically inactive due to plane of symmetry

trans- form is active

Dipole moment

when groups have linear moment cis-1,2-dicloroethylene 1.85 D, of trans is Zero.

disadvantage

in case of nonlenear moment of diethyl maleate 2.54 D and of fumarate is 2.38 D

X-ray crystallography

Spectroscopic

UV: if better conjugation or planarity then longer absorption wavelength (λ_{max}) and larger molar extinction coefficient (ε).

IR: = C-H bend cis is lower wavenumber (ν) than trans

NMR: coupling constants are disfferent

MS: Trans have higher intensity of molecular ion due to steric effect.

Surface film formation by trans form of long chain unsaturated fatty acid.

Solid solution: Fumaric acid (trans) forms solid solution with Succinic acid (saturated) but maleic acid does not. due to similarity in structure.

Physical properties

Melting point of *cis* is lower than trans

Boiling point, density, refractive index, solubility, heat of combustion ($\Delta_{combustion}H$), heat of hydrogenation ($\Delta_{Hydrogenation}H$), dipole moment, dissociation constant of *cis* are more than *trans*.

Auwers Skita rule states trends in boiling point, density, refractive index,

Comparision with similarly ortho and para substituted benzene with *cis* and *trans*.

cis-crotonic acid (m.p; 15.5°C) *trans*-crotonic acid (m.p.; 72°C) *o*-toulic acid (105°C) and *p*-toulic acid (180°C)

Stereoselective reaction and analysis of the product

- Addition
  - Catalytic reduction give *cis* addition
    - *cis*-2,3-diphenylbutene gives meso isomers
    - *trans*- gives pair of enantiomer
  - Hydroxylation stereochemistry depends on reaction
    - *cis* ($KMnO_4$, OsO_4, H_2O_2-OsO_4) and
    - *trans* (H_2SO_4, C_6H_5COOOH, H_2O_2-SeO_2)
  - Diel-Alder reaction *cis* addition
  - Methelyne or carbene addition *cis* addition in photolysis method
  - Addition of halogen and halogen acid in polar medium gives *trans* product due to nonclassical carbocation formation with bridge bond
  - HBr addition with peroxide at low temp gives *trans* product.
- Elimination
  - E2cB mechanism is faster in trans than in cis. *Trans* goes through slower E2
    - hexaclorocyclohexane has β form with all *cis* configuration so

elimination is slow.

pyrolytic elimination of ester, Xanthates or amine oxide (cope reaction) is *cis*

Interconversion of isomers

phocatalysed transition singlet (cis) $\rightleftarrows$ triplet (cis) $\rightleftarrows$ triplet (trans) $\rightleftarrows$ triplet (trans)

trans is of lower energy than cis catalysed by Br_2 and BF_3.

Conformational analysis

Principle of rotation about the single bond produces different forms called conformers.
The study of existence of preferred conformations in molecules and the relating of physical and chemical properties of a molecule to its preferred conformation

best viewed in Newman projection
Torsion or dihedral angle: angle off ratio
Torsional energy; Energy required to move one energy minima to another energy minima

Ethane
one methyl group is rotated while other is fixed
Eclipsed position: when dihedral angle is zero. energy is maximum
staggered: when angle is 60°. energy is minimum
energy difference 12.55KJ/mol

1,2-dichloroethane
staggered ; C-Cl bonds are 180° (transoid, anti)
Fully eclipsed: C-Cl bonds are 0° (cisoid, syn periplanar)
Eclipsed partially; C-Cl bonds are 120°
Gauche or Skew: C-Cl bonds are 60°
Staggared (0 KJ/mol) < gauche (4.6 KJ/mol) < Eclipsed (11.72 KJ/mol) < fully eclipsed (18.83 KJ/mol)

Butane
Staggared (0 Kcal/mol) < gauche (0.8 Kcal/mol) < Eclipsed (3.4 Kcal/mol) < fully eclipsed (4.4-6.1 Kcal/mol)

1,2-diol
Gauche < Staggard due to H-bond < Eclipsed < fully eclipsed

cyclic compounds
Cyclohexane

two set of six H
Chair,
- all C-H bond on adjacent carbon is skew,
- two types of H, axial (*a* with) and equatorial (*e*)
- two chair forms possible with interchanging axial and equatorial H

boat
- 4 C-H skew and 2 C-H in eclisped
- four types of H, flagpole (*fp*), bowspirit (*bs*) boat-equatorial (*be*) and boat-axial (*ba*)

Conformation	Position	H-H distance in (Å)
Chair	1e,2e	2.49
	1e,2a	2.49
	1a,2a	3.06
	1a3a	2.51
Boat	2a,3a	2.27
	2e,3e	2.27
	1fp4fp	1.83

twist-boat

reduced fp interaction and reduced eclipsed conformations.

chair-boat 28.9 KJ/mol
chair-twist boat 22.2 KJ/mol
chair to twist boat energy barrier 37.7 KJ/mol