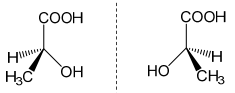
Stereochemistry review

Stereoisomers: Molecules having the same atom connections, but different 3-dimensional orientations of atoms in space

Enantiomers: Two stereoisomers that are non-superimposable mirror images



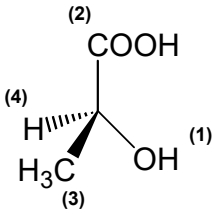
Chiral center: A tetrahedral C atom bonded to four different substituents

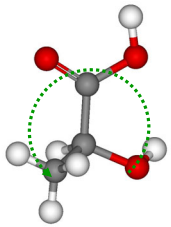
Fischer projection: horizontal bonds come out of the plane of the board; vertical bonds go back into the plane of the board

R,S nomenclature for sp^3 chiral centers

- Assign priority to functional groups in order of decreasing atomic number
  - O > N > C > H
  - T > D > H
  - C-OH > C-CH_3
- Place lowest priority group in rear and note the order of rotation of the other groups in order of decreasing priority
  - R = clockwise
  - S = counterclockwise

Example: L-lactic acid

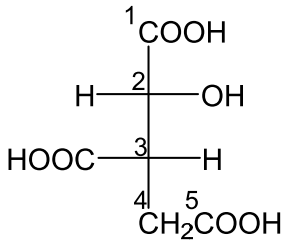




≡ S

Stereochemistry review

Molecules with two chiral centers have four possible stereoisomers



2R, 3S

Diastereomers are stereoisomers that are not enantiomers (not non-superimposable mirror images)

An easy way to assign stereochemistry without having molecular models at hand

- Begin with a correct Fischer projection
- Focus on chiral center of interest
- Assign priorities of groups bonded to chiral carbon
- Assume a Fischer projection with the lowest priority substituent in the bottom position by rotating any 3 attached groups stepwise, keeping the position of the central atom and the 4th group fixed
- Note direction of rotation of the three highest priority groups from highest to lowest priority. R=CW, S=CCW

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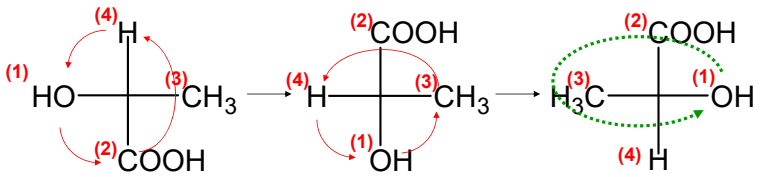
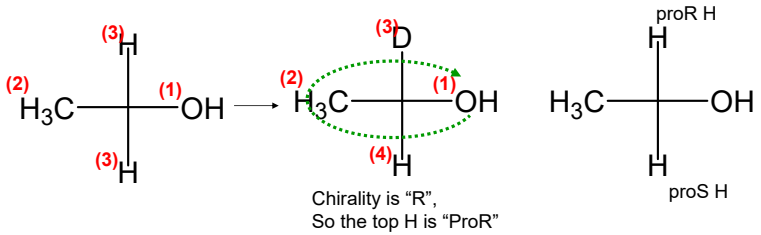


Counterclockwise rotation of three groups with H in the bottom means the chiral center is “S”

Prochirality in sp^3 centers (C_{aacd})

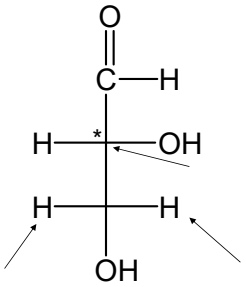
- A prochiral center becomes chiral if one of identical groups “a” in C_{aacd} is replaced by a group “b” (C_{abcd})
- To assign a prochiral center, replace one of identical groups “a” with a higher priority group “b”. So as not to change the nature of the molecule, use a heavy isotope (D for H)
- Assign chirality of the carbon center. If it is S, then the group “a” which was replaced by “b” is a “proS” group. If it is “R”, then the group is “ProR”

Prochirality example: ethanol

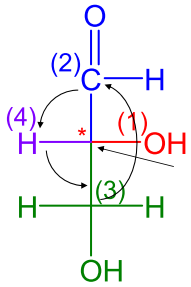


Chirality is “R”,
So the top H is “ProR”

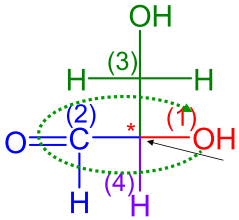
Assign the chirality and prochirality of D-glyceraldehyde



Assign the chirality of D-glyceraldehyde

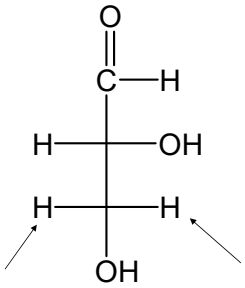


Assign the chirality of D-glyceraldehyde

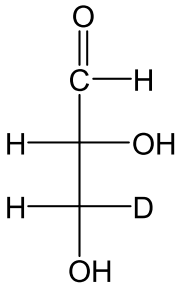


Clockwise rotation by priority of groups 1, 2, 3 means chirality is "R"

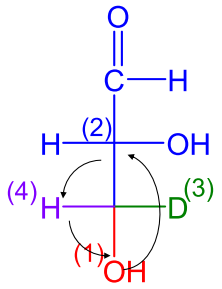
Assign prochirality of D-glyceraldehyde



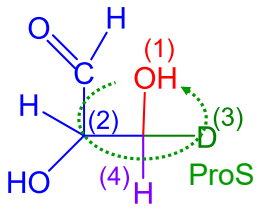
Assign prochirality of D-glyceraldehyde



Assign prochirality of D-glyceraldehyde

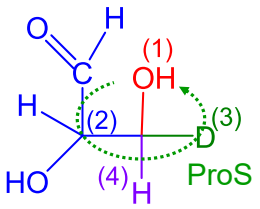


Assign prochirality of D-glyceraldehyde



Counter clockwise rotation by priority of groups 1, 2, 3 means prochirality of the hydrogen replaced by deuterium is “S”

Assign prochirality of D-glyceraldehyde



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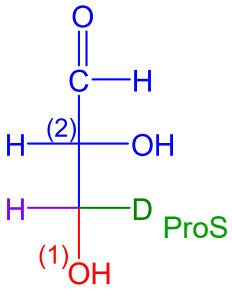
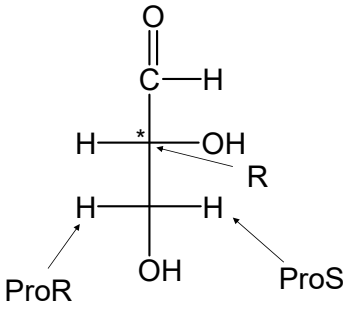
Assign prochirality of D-glyceraldehyde

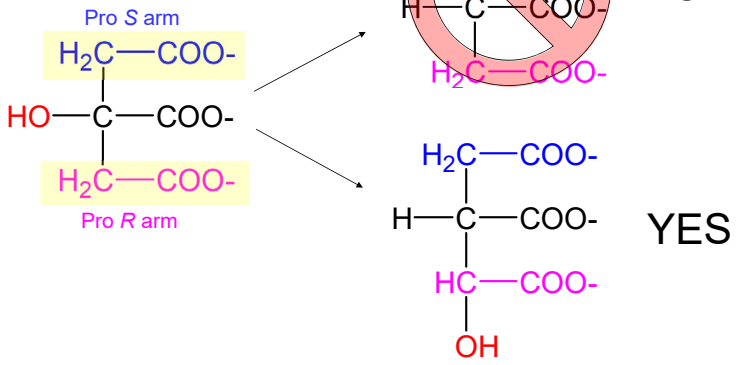


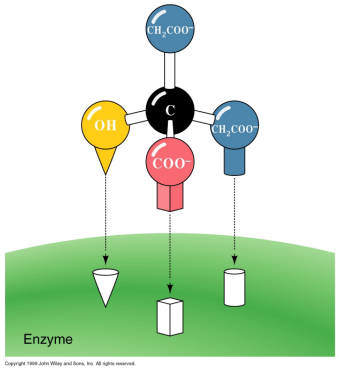
Assign the chirality and prochirality of D-glyceraldehyde



Since enzymes are chiral, they can, in general, discriminate between prochiral groups on substrate molecules. The classic example is citrate in the Krebs cycle

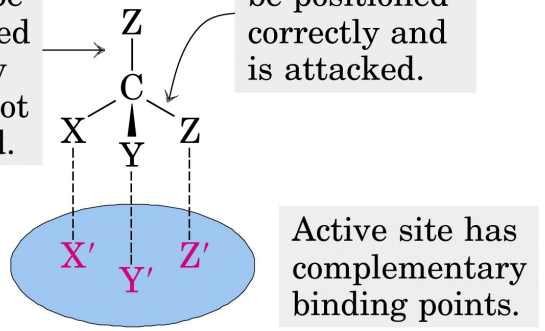
Discrimination between the two arms of citrate by aconitase





This bond cannot be positioned correctly and is not attacked.

This bond can be positioned correctly and is attacked.

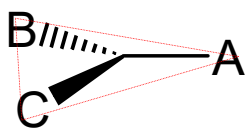


Active site has complementary binding points.

(c)

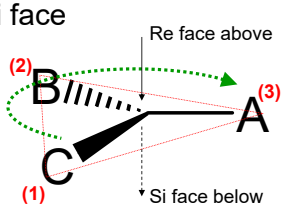
sp^2 prochiral centers

- Trigonal carbon atoms with 3 different substituents (C_{abc}) are prochiral
- The two faces of a trigonal planar prochiral molecule are sterically nonequivalent



sp^2 prochiral centers

- Assign substituents in order of decreasing priority
- Orient the planar sp^2 center so that you are looking down at one of the faces of the four bonded atoms
- If priority is clockwise in this orientation, then you are looking down on (closest to) re face; if priority is counterclockwise then you are looking down on si face



Which face of NAD^+ is this?