Diastereomers are stereoisomers that are not mirror images of each other.

Diastereomers can be divided into two categories:

(a) Configurational Diastereomers: A relationship between stereoisomers of a chiral molecule, but ones that are not enantiomers.

(b) Cis-Trans Diastereomers: These are stereoisomers, that usually arise due to restricted rotation within a molecule; commonly at a carbon-carbon double bond.
Diastereomers
Configurational Diastereomers

Configurational diastereoisomerism occurs in molecules that have more than one chiral center.

1 Chiral centre = 2 Stereoisomers

D-Glyceraldehyde
\[ \text{CHO} \]
\[ \text{H} \]
\[ \text{OH} \]
\[ \text{CH}_2\text{OH} \]

L-Glyceraldehyde
\[ \text{CHO} \]
\[ \text{H} \]
\[ \text{S} \]
\[ \text{CH}_2\text{OH} \]

Enantiomers

2 Chiral centres = 4 stereoisomers

D-Erythrose
\[ \text{CHO} \]
\[ \text{R} \]
\[ \text{H} \]
\[ \text{OH} \]
\[ \text{CH}_2\text{OH} \]

L-Erythrose
\[ \text{CHO} \]
\[ \text{H} \]
\[ \text{S} \]
\[ \text{H} \]
\[ \text{S} \]
\[ \text{CH}_2\text{OH} \]

Diastereomers

D-Threose
\[ \text{CHO} \]
\[ \text{S} \]
\[ \text{H} \]
\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{CH}_2\text{OH} \]

L-Threose
\[ \text{CHO} \]
\[ \text{H} \]
\[ \text{S} \]
\[ \text{H} \]
\[ \text{OH} \]
\[ \text{CH}_2\text{OH} \]

Enantiomers

Generally, a molecule with \( n \) chiral centers (stereochemical units) can have a maximum of \( 2^n \) stereoisomers.
Occasionally, exceptions occur. For example, whereas tartaric acid has 2 chiral centers and expected to have a maximum of 4 stereoisomers, it has only 3 stereoisomers.
Diastereomers

Meso Compound

A meso compound or meso isomer is an achiral member of a set of stereoisomers, at least two of which are chiral. Since a meso isomer has a superimposable mirror image, a compound with a total of $n$ stereocenters cannot have $2^n$ stereoisomers if at least one of the stereoisomers is meso. Although a meso compound passes the tests of same molecular formula, same connectivity of atoms, having a chiral centre and mirror image, it fails the test of non-superimposability since it is superimposable on its mirror image.
Diastereomers
Meso Compounds

Other examples of stereoisomers that have corresponding meso compounds include:
(a) cis-1,2-disubstituted cyclopropane has a meso cis-isomer.

(b) cis-1,2-disubstituted cycloalkanes are meso if the two substituents are identical. cis stereoisomers of 1,2-substituted cyclohexanes behave like meso compounds since they can undergo rapid ring flipping.
Diastereomers Assignment

Determine which of the following compounds are chiral and which ones are not. Give reasons to support each choice you make.

\[ \text{CN} \quad \text{H-C-OH} \quad \text{HO-C-H} \quad \text{CN} \]

\[ \text{OH} \quad \text{OH} \]

\[ \text{CO}_2\text{H} \quad \begin{array}{c} \text{Ph} \\ \text{Ph} \end{array} \]

\[ \text{CO}_2\text{H} \]

\[ \text{C}_5 \text{H}_5 \text{NC} \]
Diastereomers
Assignment/Answers

To determine if a compound is chiral or meso, assign the stereochemistry at the chiral centres and then assess if there is a plane of symmetry in the molecule.

Chiral. No plane of symmetry

Meso. Has plane of symmetry

Chiral. No plane of symmetry
Diastereomers
Properties of Configurational Diastereomers

Configurational diastereomers have different chiral and achiral properties in any environment and are thus different compounds. They have different:

- Melting and boiling points
- Solubility and ease of crystallization
- Spectroscopic characteristics (NMR, IR, UV)
- Chromatographic retention times
- Specific rotations
- Rates of reactions with any reagents
- Biological properties
Diastereomers

Properties of Diastereomers of Tartaric Acid

- **Dextrotartaric acid**
  - $[\alpha]^{D} = +12.7$
  - Melting point: **171-174°C**
  - Density: **1.76 g/mL**
  - Solubility in water: **139 g/100 mL**

- **Mesotartaric acid**
  - Melting point: **146-148°C**
  - Density: **1.66 g/mL**
  - Solubility in water: **125 g/100 mL**

Being different compounds, diastereomers can be separated through conventional techniques such as distillation, selective crystallization and chromatography.
Molecular Structure Relationships

The Roadmap

After the configurational diastereomers, the next set of stereoisomers to discuss are the *cis-trans* diastereomers. The family tree below relates these diastereomers.
Diastereoisomers

**Cis-Trans** diastereomers or geometric isomers usually arise when there is restricted rotation in a molecule; commonly at a carbon-carbon double bond.

Due to the restricted rotation at the double bond, groups attached to it could be positioned either on the same or opposite sides of the alkene leading to stereoisomerism.
By applying the CIP rules, the configuration of a double bond is specified with a prefix (E or Z) based on whether the high priority substituents are on opposite or same side of the double bond.

If both high priority substituents are on the same side of the double bond, then the stereoisomer is assigned a Z or \textit{Zusammen} configuration.

If, by contrast they are on opposite sides, then the stereoisomer is assigned an E or \textit{Entgegen} configuration.
Types of Diastereoisomers
Assigning Configuration of Geometric Isomers

$Z$ comes from the German word *Zusammen* for 'together', while $E$ is derived from the word *Entgegen* meaning 'in opposition to'.

Fumaric Acid

Maleic acid

Note that for fumaric acid and maleic acid, the stereochemistry of the compounds is implied in these common names.
By determining the symbol generated in the movement, high-low-high-low, one can identify the developing symbol (E or Z).

E-But-2-enedioic acid  Z-But-2-enedioic acid

The application of the CIP rules allows for the assignment of a configuration that can be used in the systematic name of the alkene.
Diastereoisomers

Physical Properties of Geometric Isomers

Cis-trans diastereomers are different compounds. They have different physical, chemical and biological properties. For example, the cis and trans isomers of butenedioic acid show large differences in their melting points.

- Fumaric Acid: Mpt = 287 °C
- Maleic acid: Mpt = 135 °C
Diastereoisomers
Chemical Properties of Geometric Isomers

They also have different chemical properties. Whereas maleic acid readily undergoes dehydration, fumaric acid is resistant to dehydration.

\[
\text{Maleic acid} \xrightarrow{\text{Heat}} \text{succinic anhydride} + \text{H}_2\text{O}
\]

\[
\text{Fumaric Acid} \xrightarrow{\text{Heat}} \text{No Reaction}
\]
Diastereoisomers

Biological Activity of Geometric Isomers

Cis-trans diastereomers have different biological properties.

**Triprolidine**, an antihistamine drug used to combat symptoms associated with allergies and provides general relief for flu-like symptoms, is more effective in the E-configuration.

E-Triprolidine (Actifed) (1000 times more active than Z)