Optical Isomers in Pharmaceutical Products

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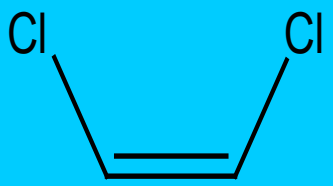
Definition of Isomers

- Stereoisomers are compounds that have identical chemical components but differ in the way the atoms or groups are arranged in space.
- Stereoisomers fall into two broad classes:
  - 1) Geometric isomers and
  - 2) Optical isomers

Definition of Isomers (Cont'd)

- Geometric isomers are a type of stereoisomer in which a chemical group or atom occupies different spatial positions in relation to the double bonds. If the double bond is between two carbon atoms, the isomers are called cis or trans.

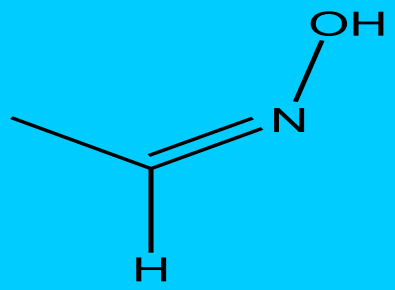


cis-1,2-dichloroethene

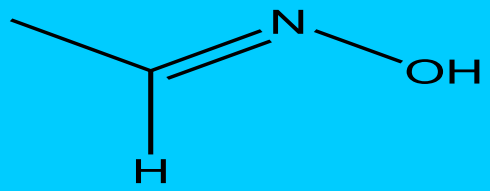
trans-1,2-dichloroethene

Definition of Isomers (Cont'd)

- If the double bond is between a carbon and a nitrogen atom, the isomers are called anti and syn.
- Example



syn-acetaldoxime



anti-acetaldoxime

Definition of Isomers (Cont'd)

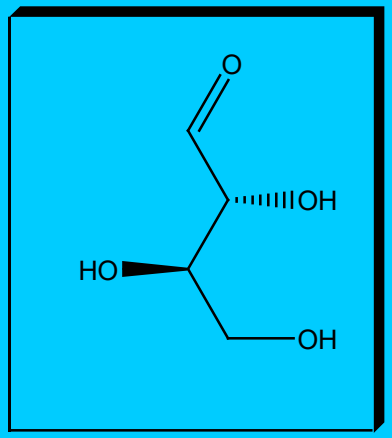
- An optical isomer is compound which rotates the plane of polarized light.

Definition of Isomers (Cont'd)

- There are two kinds of optical isomers:
  - 1) Diastereomers and
  - 2) Enantiomers

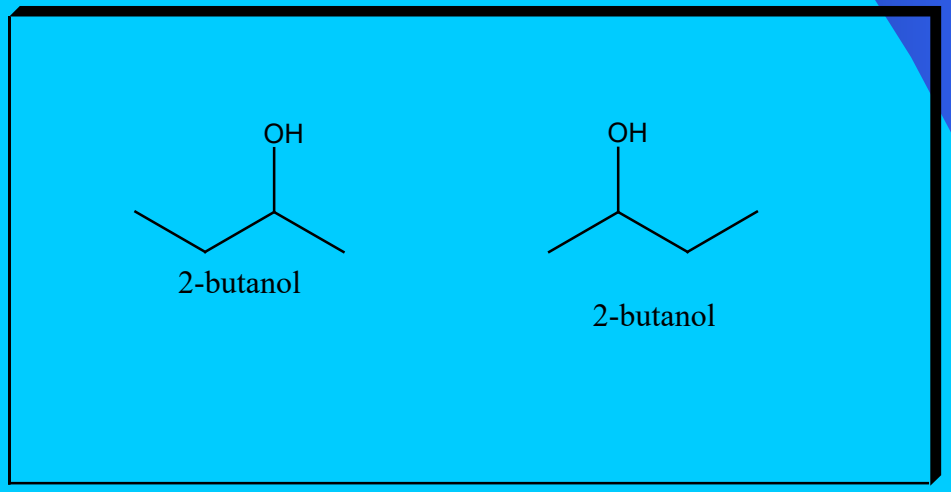
Definition of Isomers (Cont'd)

- Diastereomers are not mirror images and occur in compounds having two or more asymmetric carbon atoms or chiral center.
- Said another way, diastereomers are stereoisomers which are not enantiomers.
- Example: Erythrose



Definition of Isomers (Cont'd)

- Enantiomers are mirror image structures that result from the presence of one or more asymmetric carbon atoms in the compound.
- Example



Pharmacokinetic Properties

- Stereoisomers may possess different pharmacokinetic properties, such as adsorption, distribution, biotransformation, and excretion.
- They may also possess, quantitatively or qualitatively, different pharmacologic or toxicologic effects.

Technological Advances

- Technological advances now allow for the separation of most racemates into the corresponding enantiomers, and for large scale production of a single enantiomer.

Technological Advances (Cont'd)

- As a result, it is now the accepted practice to separate racemates into the corresponding enantiomers early in drug development, and to do pharmacokinetic studies on the enantiomer that is identified as having the predominant biological activity.

Claiming an Enantiomer

- Include the name or the structure of the enantiomeric chemical compound.
- Apply a “standard” convention to designate and name the enantiomer.
- Incorporate as much as possible of comparative, and especially, pharmacokinetic data into the specification.

Examining the Claim

- In examining the claim to the enantiomer, the existence of the racemic mixture has to be considered.
- Because it is no longer unexpected for one enantiomer to posses the predominant biological activity, a prima facie case of obviousness may be made in cases where the prior art enables the separation of the racemic mixture into the corresponding enantiomer.

Examining the Claim

- This is not a general rule and every case has to be weighed and considered according to the specific facts.
- However, an application would be more complete if the specification includes as much pharmacokinetic data as possible.
- Simply showing that one enantiomer possesses the predominant biological activity will normally not be considered sufficient to rebut a prima facie finding of obviousness.

Examining the Claim

- For Example, applicants may compare the potential for inter-conversion, absorption, distribution, biotransformation, altered metabolic function, drug-drug interaction, and toxicity.

QUESTIONS