

TERMINOLOGY FOR ISOMERS AND REACTIONS OF ISOMERS

STRUCTURAL ISOMERISM

Structural isomers (sometimes called constitutional isomers) have the same molecular formula but different atom connectivity.

Differences in Structure

carbon skeleton: "straight", branched, positional; ring size
functional group: alcohol, ether; aldehyde, ketone, enol; alkene, cycloalkane; etc.

Differences in Reaction

Regioselective: one direction or site of bond-breaking or bond-making occurs preferentially. Examples: addition of HBr to propene to form 1- and 2-bromopropane, dehydration of 2-butanol to give 1- and 2-butene. Regioselectivity is usually caused by the mechanistic characteristics of the reaction responding to small differences between the possible reaction sites.

Regiospecific: one direction or site of bond-breaking or bond-forming occurs exclusively. Regiospecificity probably never occurs; used sometimes for strongly regioselective reactions.

STEREOCHEMICAL ISOMERISM

Differences in Structure

Stereoisomers are compounds with the same formula and connectivity but different spatial relationships between atoms.

Configurational Stereoisomers: those that require breaking a bond to interconvert.

enantiomers: mirror images not superimposable (sometimes called optical isomers)

nomenclature: **R, S** (also: *d, l; D, L*)

other terms:

chiral = dissymmetric

achiral = mirror symmetric

racemic, resolution

enantiomeric excess, enantioenriched, enantiopure

optically active, non-racemic

diastereomers: all other stereoisomers

geometric (about a double bond, or sometimes a ring)

nomenclature: **E, Z** (also: *cis, trans; syn, anti*)

with chiral centers

nomenclature **R, S** (for each of several chiral centers)

meso, epimer

Note that enantiomers have the same physical and chemical properties unless they are examined with a chiral tool. Plane polarized light is rotated the same amount but in opposite directions. Chemical reactivity is different if and only if the other reagent is also chiral; this is almost always true in living creatures, whose enzymes are highly chiral. (**S**)-ibuprofen is a potent analgesic and (**R**)-ibuprofen is inert; the enantiomers of carvone are the flavors mint and caraway. Now that synthetic techniques the lab synthesis of pure enantiomers easier, many drugs currently sold as racemates will soon be available as "chiral drugs", to prevent any

possible side effects of the inactive enantiomer.

Diastereomers have different physical and chemical properties, although they may not be very different because they have the same connectivity. They can be separated by crystallization, distillation, chromatography. The separation of enantiomers always involves converting them to diastereomers; in most modern techniques, no covalent bonding is needed, only diastereomeric interactions, e.g. chromatography on a chiral phase like cellulose.

Conformational Stereoisomers: those that are interconverted by rotations about one or more single bonds.

open chain compounds

staggered (anti or gauche), eclipsed

cyclic compounds, esp. cyclohexane

chair (axial or equatorial), boat, twist boat

can also be classified as enantiomers and diastereomers

In general, conformational isomers cannot be separated, but an understanding of the conformation of the starting materials can help estimate conformations of transition states and thus help make sense of reactivity patterns. There are some conformational changes that require so much energy that the conformers can be stored in separate bottles at room temperature, e.g. *o*-substituted biphenyls, natural and denatured proteins.

Differences in Reactions

Stereospecific: different stereoisomers of starting material yield different stereoisomers of product. Usually the mechanism of the reaction controls the stereochemistry with little influence by substrate structure. Examples: S_N2 (enantiomers), bromination or epoxidation of alkenes (diastereomers).

Stereoselective: one stereoisomer formed or destroyed preferentially. Usually the stability of the starting material or the product (and thus the transition state) controls the reaction, with the mechanism a minor influence. Examples: dehydration of 2-butanol to give (*E*)- and (*Z*)-2-butene, Diels Alder reaction preference for *endo*.

Stereochemical Outcomes for chiral centers

inversion - new group on opposite side (stereospecific)

retention - new group on same side (stereospecific)

racemization - equal amounts of both enantiomers (not stereospecific or stereoselective)

FOR FURTHER READING

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