

Enantiomers and Diastereomers

A Introduction

B Relationship Between Optical Rotation and Enantiomeric Excess

Optical Rotations

excess of one enantiomer over another are optically *active*
those containing only one enantiomer are optically *active and pure*.

Optically active molecules *can* rotate the plane
Rarely, there *may* be wavelengths of that plane of polarized light

rotation for a sample is called its *observed optical rotation*; it is measured in *degrees* on an instrument called a *polarimeter*.

plane to the right is called *dextrorotatory / positive*

rotate light to the right *are not* always *R*-, and *S*-enantiomers *are not* always levorotatory.

solvent / wavelength of the plane polarized light / temperature
pathlength of the sample container (cell) /
concentration of the sample

optically active impurities *do not* lead to reproducible readings.

variables specified are called *specific* rotations.
These values *do* facilitate comparisons of data

which are the temperature of the sample (in *centigrade*)

$$a = -21^\circ$$

$$[a]_{\lambda}^T = \frac{a \cdot 100}{l \cdot c} = -8.5^\circ$$

observed optical rotation

specific rotation

determine which enantiomer is in abundance, *and* how much it is in excess or the other.

Enantiomeric Excess

prepared *a different* enantiomer to the one made in the US, and it was *optically pure*.

the specific rotation of the mixture solution was $+8^\circ$ (same solvent, temperature, and light wavelength).

The enantiomeric excess of the solution featured above was **33%**.

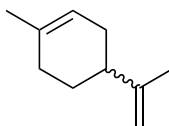
$$\text{enantiomeric excess} = \frac{[S] - [R]}{[S] + [R]} \cdot 100\%$$

then the enantiomeric excess would be **50%**.

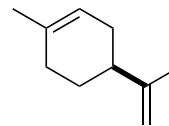
enantiomeric excess values are often abbreviated to *ee*, and they *are* proportional to the optical rotation of the sample measured using a *polarimeter*.

shown that the Jabberwock excretes *R*-bong-tree essence.

oranges (*R*-enantiomer) and lemons (*S*-), and it was given another name: *limonene*.



bong-tree essence
(stereochemistry
not defined)



bong-tree essence
(stereochemistry
defined)

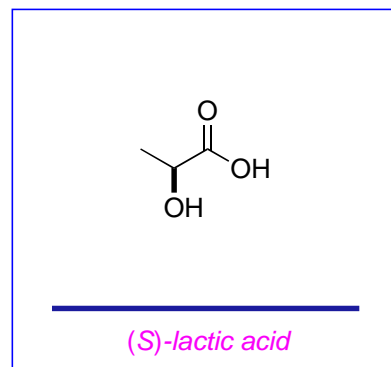
C Properties Of Enantiomers

(*R*)- and (*S*)-lactic acid *do* rotate plane-polarized light

(*S*)-Lactic acid is dextrorotatory, so it rotates plane polarized light *counterclockwise*, *ie* to the *left*, otherwise denoted (-).

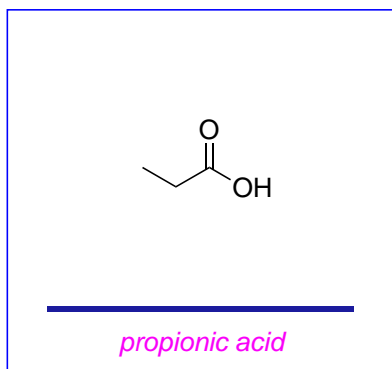
(*S*)- and (*R*)-lactic acid have:

- *the same* boiling points
- *the same* melting points
- *the same* infra-red (IR), nuclear magnetic resonance (NMR), ultra-violet spectra (UV)
- *the same* molecular ion in mass spectrometry (MS)
- *the same* chromatographic elution rates featuring solid and liquid phases that are not chiral (*ie* are *achiral*)



These generalities would apply to *all* sets of enantiomers.

1:1 is called *racemic* mixture or a *racemate*.



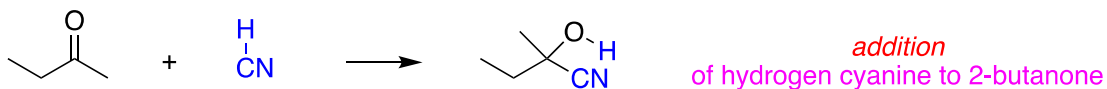
(*R*)-lactic acid by replacement of the *pro-R* this would be a *substitution* reaction.

activation energy barrier to substitute the *pro-S* and *-R* hydrogens would be *the same* and the product would be a *racemate*.

D Combinations Of Chiral Centers

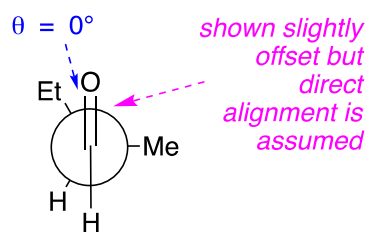
Diastereomers

The following is an *addition* reaction.



add to the *Si*- and *Re*- faces of the ketone would be *the same*, and a *racemate* would be produced.

implying, in this case, that a *racemate* would be produced.

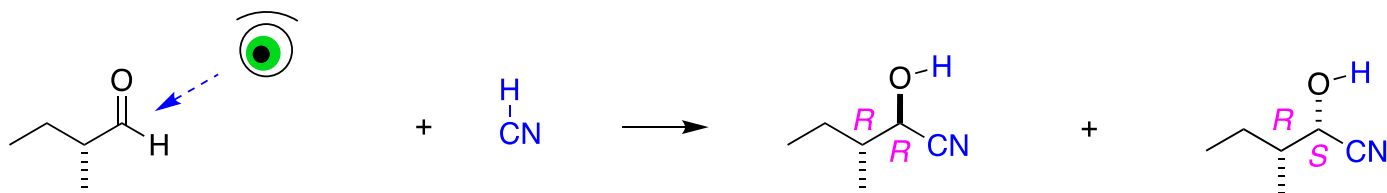


addition of hydrogen cyanide to this aldehyde will be *different* as it

(*R,R*) and (*R,S*) *diastereomers* formed will be *different*.

This reaction therefore will have *diastereoselectivity*.

complete this
Newman projection



addition
of hydrogen cyanide to *R*-2-methylbutanal

diastereomers
eg ratio of *R,R* to *R,S* 9:1

diastereomeric excess would be: 80 %

$$\text{diastereomeric excess} = \frac{[R,S] - [R,R]}{[R,S] + [R,R]} \cdot 100\%$$

products formed would be *enantiomers* of those shown in the reaction above, and they would be produced in *the same* ratio.

diastereomer would be formed as *a racemate* of those shown in the reaction above.
diastereoselectivity would be *the same* as the reactions starting

Diastereoselectivity *is* a particular form of stereoselectivity.

It *is not* possible to measure the diastereoselectivity of a reaction starting with a racemic substrate.

In general, diastereomers have:

- *different* boiling points
- *different* melting points
- *different* infra-red (IR), nuclear magnetic resonance (NMR), ultra-violet spectra (UV)
- *the same* molecular ion in mass spectrometry (MS)
- *different* chromatographic elution rates featuring solid and liquid phases that are not chiral (*ie* are *achiral*)

it *is* possible to measure the diastereoselectivity

can have a *S,S-* configuration.

its enantiomer is always *S,S-*.

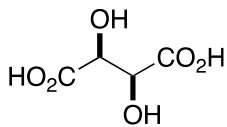
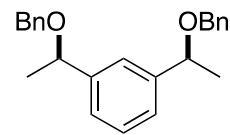
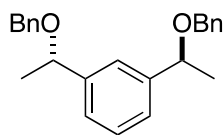
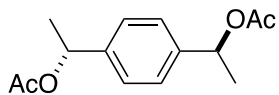
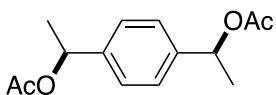
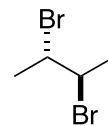
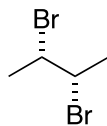
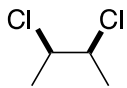
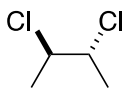
Optical rotations and enantiomeric excess *are* directly correlated

Optical rotations and diastereomeric excess *are not* directly correlated

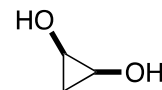
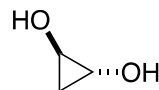
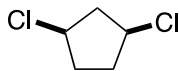
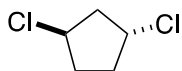
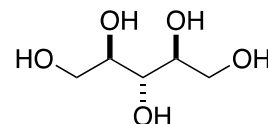
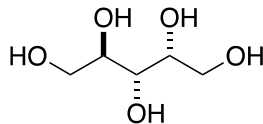
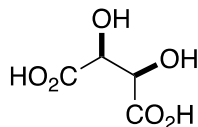
Meso Compounds

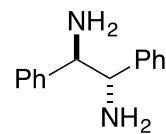
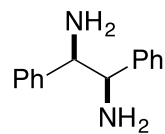
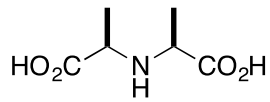
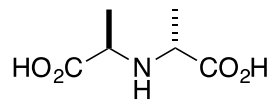
This stereoisomer of 2,3-butandiol (left) has *R* configuration at C^2 and *S* at C^3 . C^2 -chiral center will *cancel* that at C^3 hence the molecule *is not* optically active.

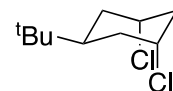
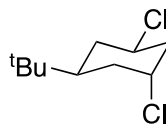
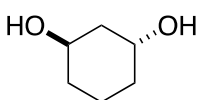
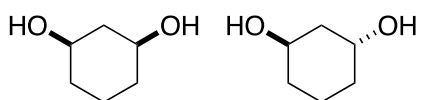
All meso-isomers have *a plane of symmetry* and they *do not* rotate plane polarized light.

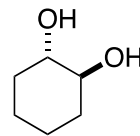
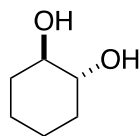
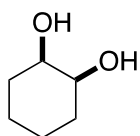
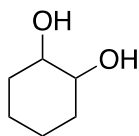


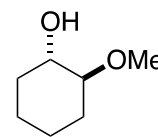
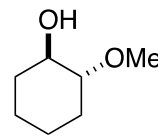
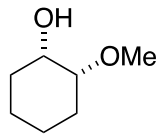
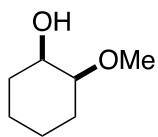
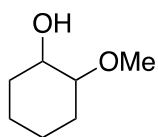
tartaric acid



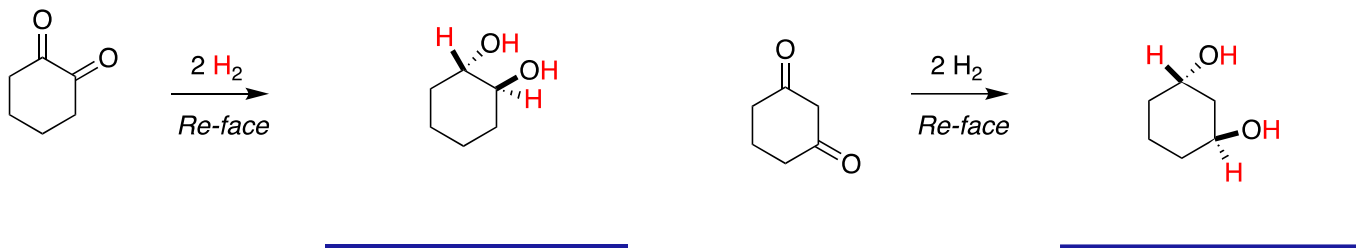








In general, a compound has n chiral centers will have 2^{n-1} diastereomers, and 2^n enantiomers of these: *true*.



The diol products formed in the reactions above will be *optically active* stereoisomers.

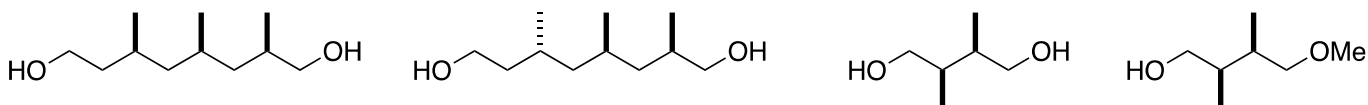
Epimers

Epimers *are / are not* a sub-set of diastereomers that are configurationally different at one chiral centers. Classify the following (choose all options that are correct):



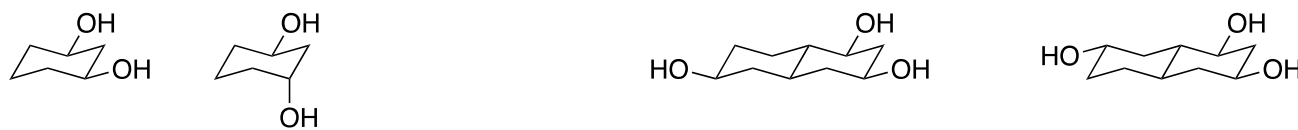
neither

epimers



diastereomers / epimers

neither



diastereomers

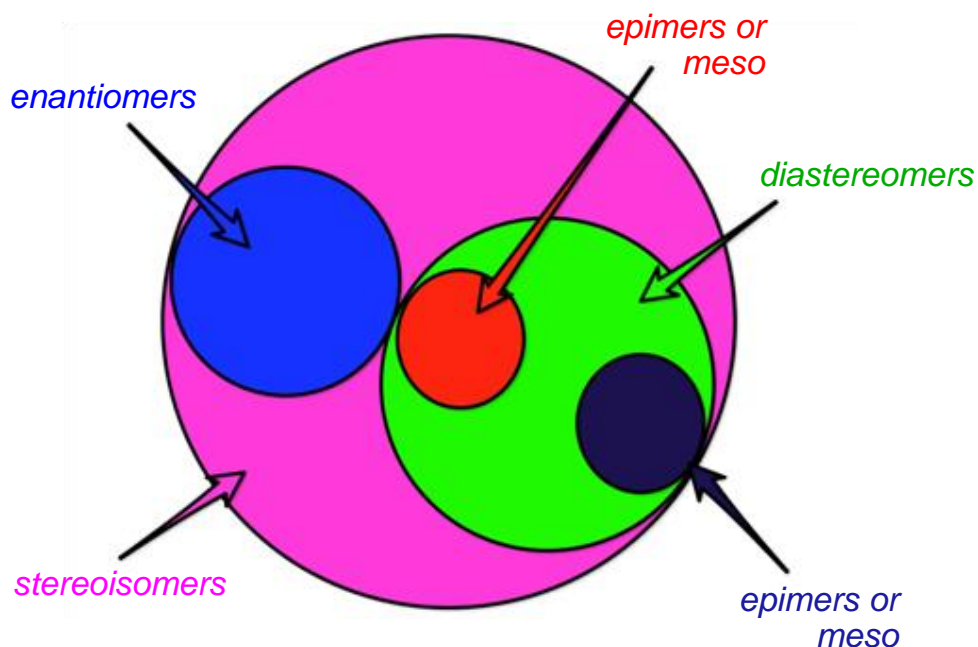
neither



enantiomers

diastereomers

Graphical Summary



E Enantioselectivity As An Example Of Kinetic Control

there could be some enantioselectivity in this reaction *until it reaches equilibrium*.

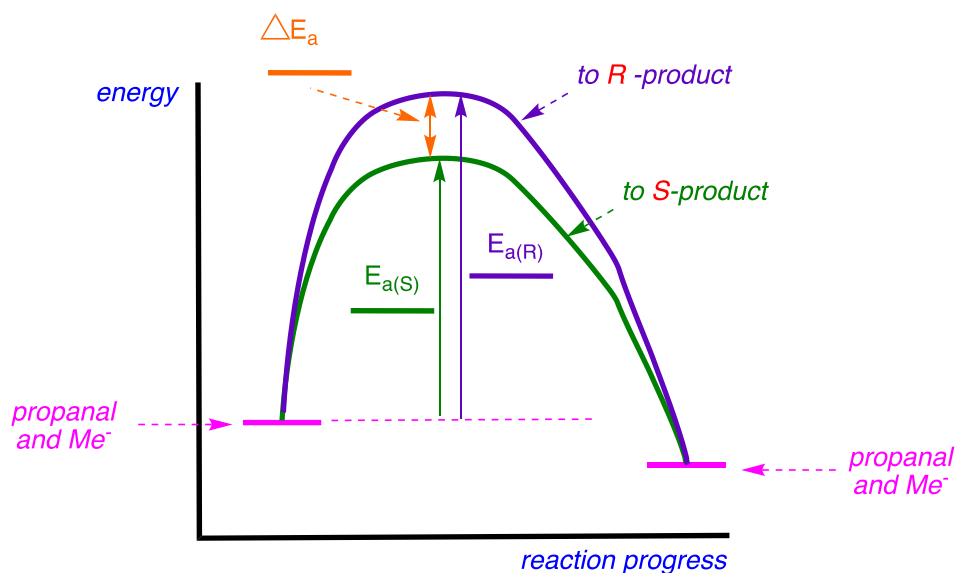
$$K_S = \frac{[S]}{[\text{propanal}][\text{HCN}]} \quad K_R = \frac{[R]}{[\text{propanal}][\text{HCN}]}$$

$$\frac{K_S}{K_R} = \frac{[S]}{[R]} = 1$$

expressed as concentrations of products only *numerical*

so suitable words to describe this are *thermodynamic* control.

Thermodynamically controlled reactions at equilibrium *can* be enantioselective.



transformation above, so it is *kinetically* controlled.

activation energy barrier E_a by the *Arrhenius* equation, where:

$$k = Ae^{-E_a/RT}$$

$$A = \frac{\text{pre-exponential factor}}{\text{name}} \quad \frac{s^{-1}}{\text{(units)}} \quad E_a = \frac{\text{activation energy}}{\text{name}} \quad \frac{J \text{ mol}^{-1}}{\text{(units)}}$$

$$R = \frac{\text{universal gas constant}}{\text{name}} \quad \frac{8.314 \text{ J mol}^{-1} \text{ K}^{-1}}{\text{numerical value (units)}} \quad T = \frac{\text{temperature}}{\text{name}} \quad \frac{\text{Kelvin}}{\text{(units)}}$$

$$\ln(k_R/k_S) = -\Delta\Delta G/RT + \ln(A_r/A_s)$$

$$\text{but } \ln(A_r/A_s) = \ln 1 = 0$$

For ee of 80 %, ratio of enantiomers is 9:1 thus $k_R/k_S = 9$.

$$\text{Solve then for } -\Delta\Delta G = RT \cdot \ln 9 = 0.008314 \cdot 298 \cdot 2.197 = 5.44$$