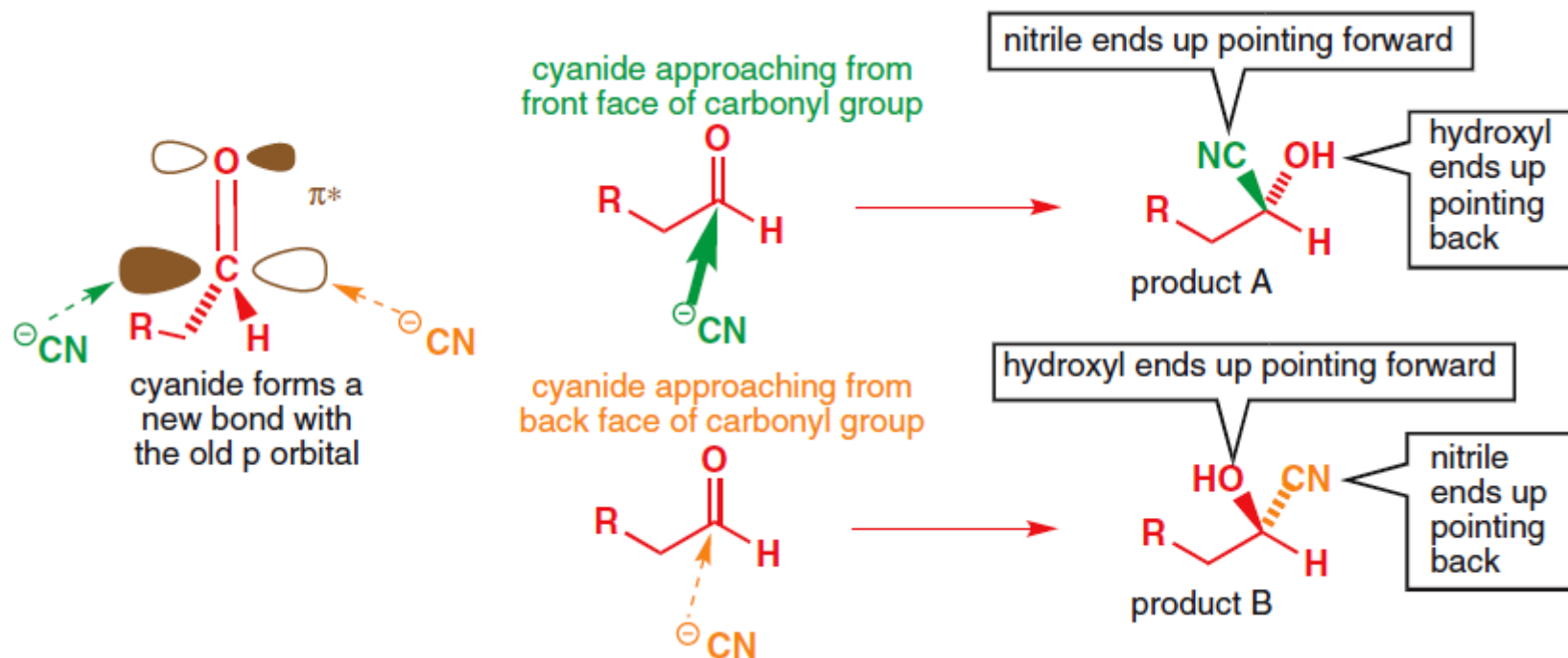
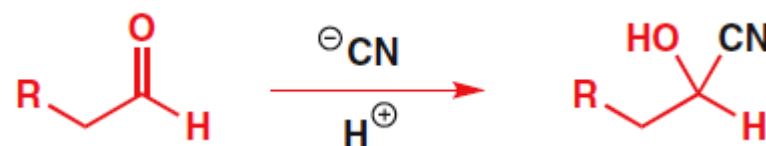
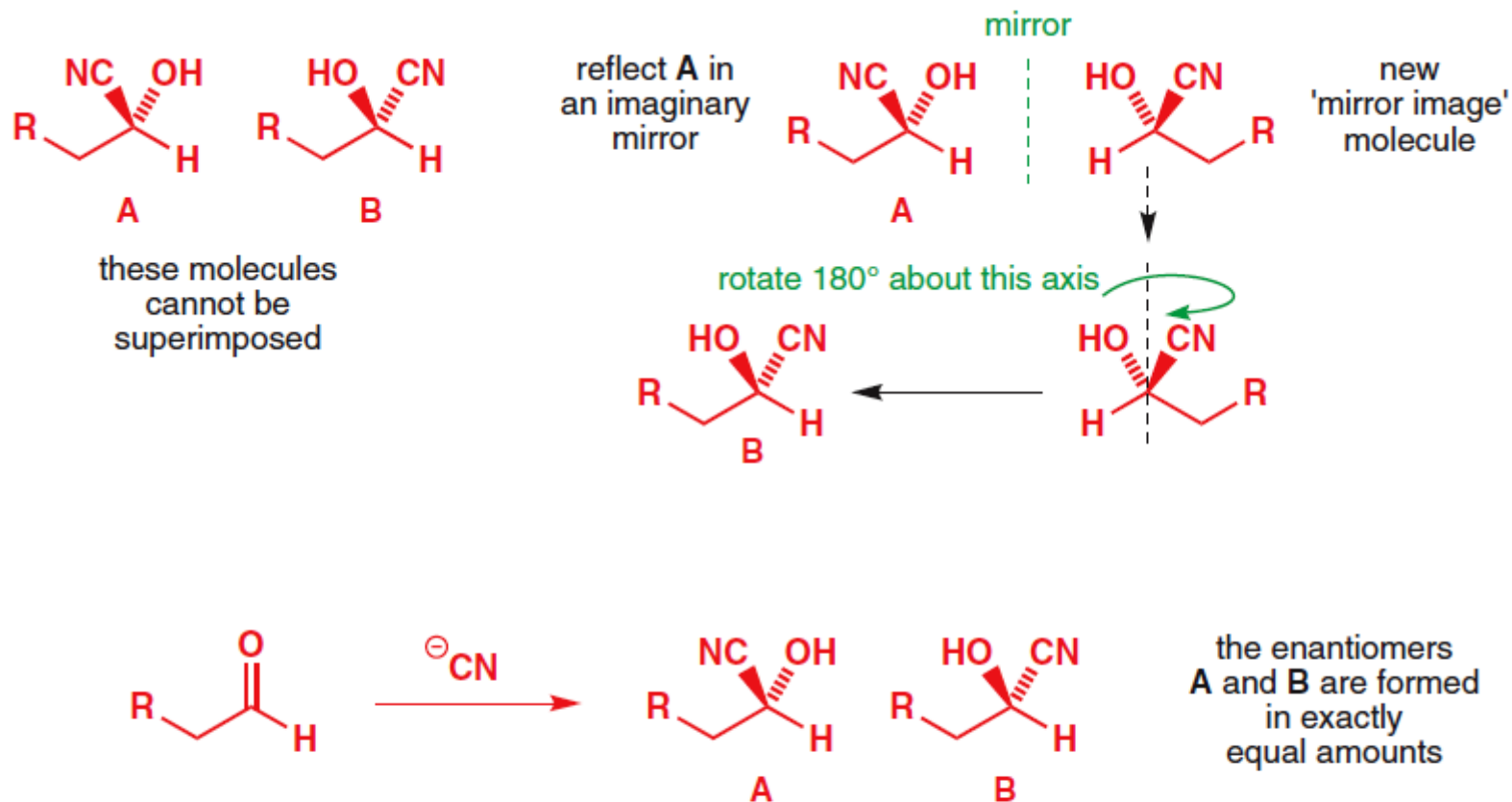


Stereochemistry

Some compounds can exist as a pair of mirror-image forms



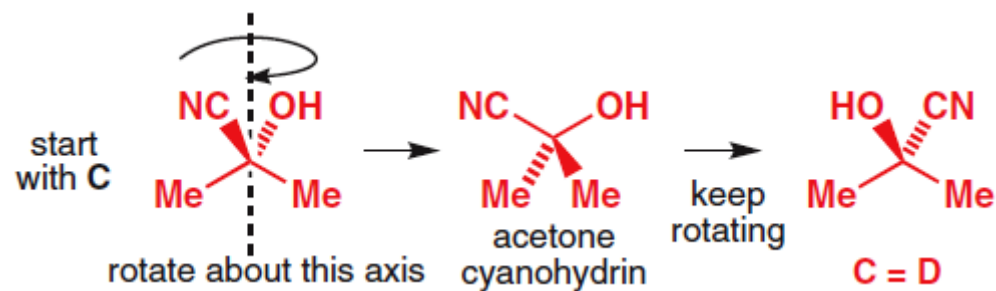
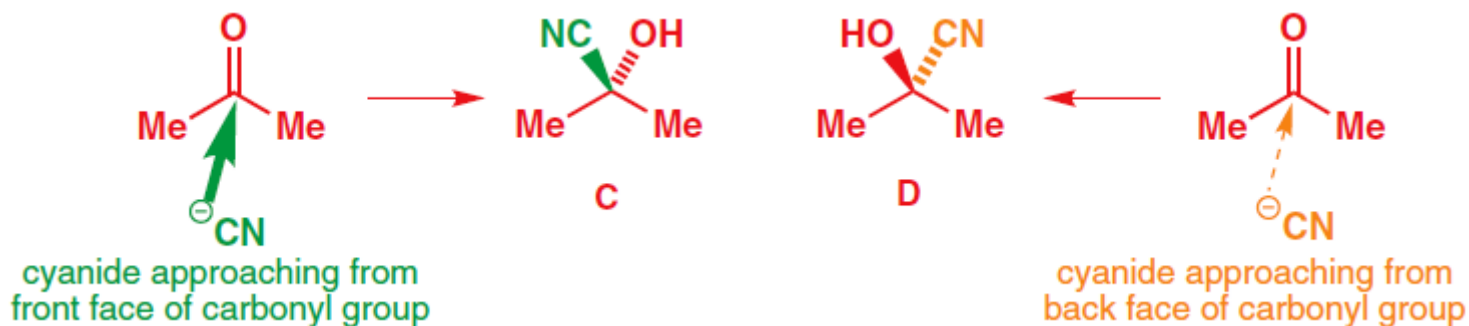
Some compounds can exist as a pair of mirror-image forms



● Enantiomers and chirality

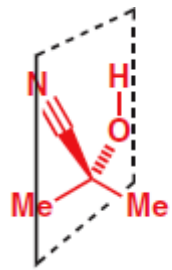
- Enantiomers are structures that are not identical, but are *mirror images* of each other.
- Structures are *chiral* if they cannot be superimposed on their mirror image.

Some compounds can exist as a pair of mirror-image forms



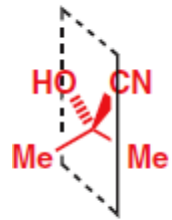
- *Achiral* structures are superimposable on their mirror images.

Chiral molecules have no plane of symmetry

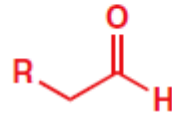


plane of symmetry runs through central carbon, OH and CN

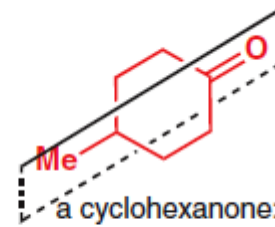
molecules with planes of symmetry



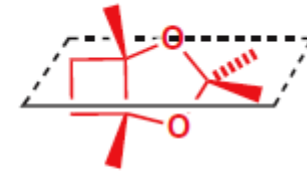
acetone cyanohydrin



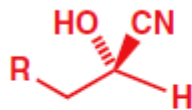
any planar molecule: the plane of the paper is a plane of symmetry



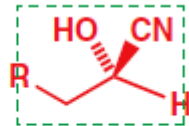
a cyclohexanone: plane of symmetry is orthogonal to the paper



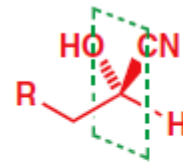
a bicyclic acetal: plane of symmetry is orthogonal to the paper



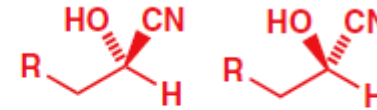
aldehyde cyanohydrin



plane of paper not a plane of symmetry



plane through OH and CN not a plane of symmetry



so the molecule is chiral with two enantiomers

Planes of symmetry and chirality

- Any structure that has no plane of symmetry is chiral and can exist as two mirror-image forms (*enantiomers*).
- Any structure with a plane of symmetry is not chiral and cannot exist as two enantiomers.

To summarize

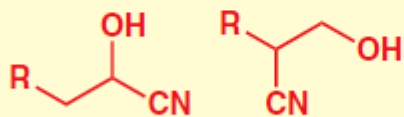
- A structure *with* a plane of symmetry is *achiral* and *superimposable* on its mirror image and *cannot* exist as two enantiomers.
- A structure *without* a plane of symmetry is *chiral* and *not superimposable* on its mirror image and *can* exist as two enantiomers.

Stereogenic centres

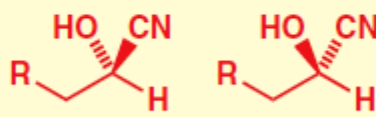
• Stereoisomers and constitutional isomers

Isomers are compounds that contain the same atoms bonded together in different ways. If the connectivity of the atoms in the two isomers is different, they are constitutional isomers. If the connectivity of the atoms in the two isomers is the same,

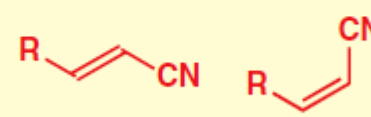
they are stereoisomers. Enantiomers are stereoisomers, and so are *E* and *Z* double bonds. We shall meet other types of stereoisomers shortly.



constitutional isomers: the way the atoms are connected up (their *connectivity*) differs



enantiomers

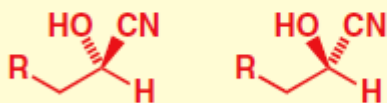


E/Z isomers (double bond isomers)

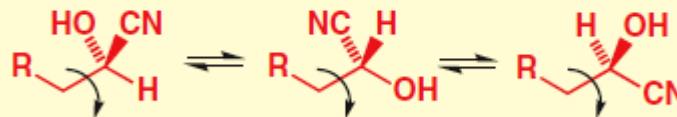
stereoisomers: the atoms have the same connectivity, but are arranged differently

• Configuration and conformation

- Changing the *configuration* of a molecule always means that bonds are broken.
- A different configuration is a different molecule.
- Changing the *conformation* of a molecule means rotating about bonds, but not breaking them.
- Conformations of a molecule are readily interconvertible, and are all the same molecule.

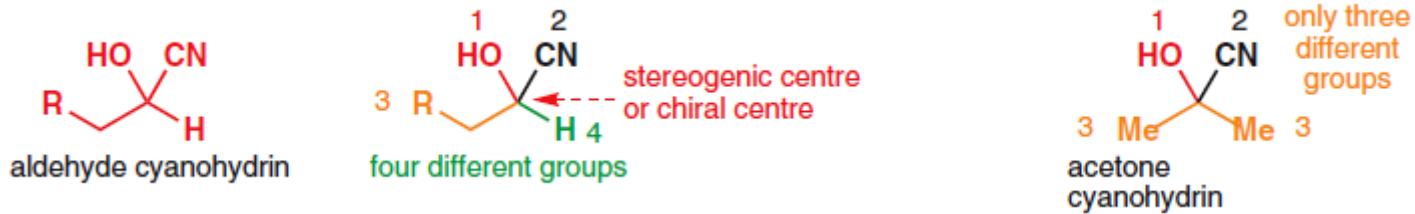


two configurations: going from one enantiomer to the other requires a bond to be broken

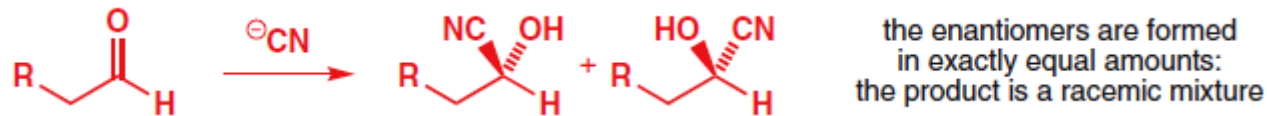


three conformations of the same enantiomer: getting from one to the other just requires rotation about a bond: all three are the same molecule

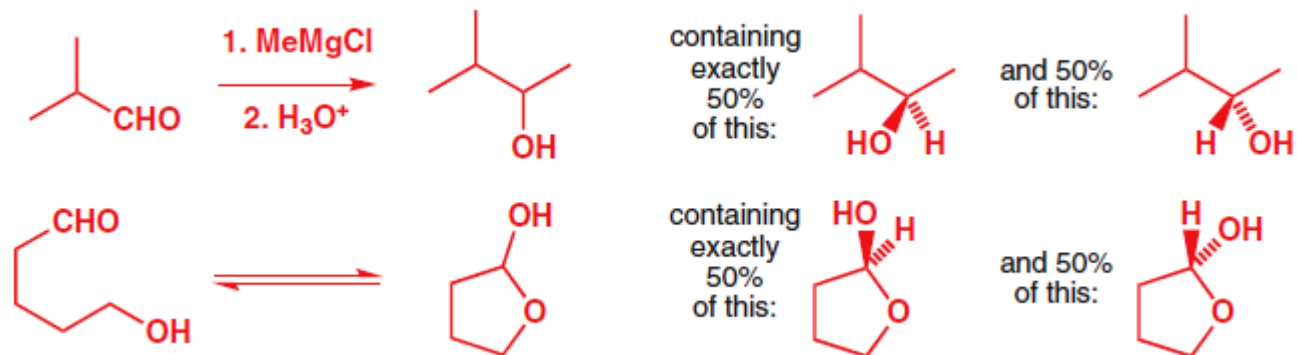
Stereogenic centres



● If a molecule contains one carbon atom carrying four different groups it will not have a plane of symmetry and must therefore be chiral. A carbon atom carrying four different groups is a stereogenic or chiral centre.

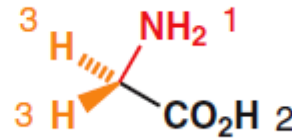
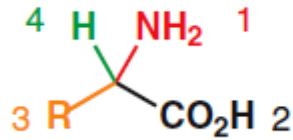


● A racemic mixture is a mixture of two enantiomers in equal proportions. This principle is very important. If all the starting materials and reagents in a reaction are achiral and the products are chiral they will be formed as a racemic mixture of two enantiomers.



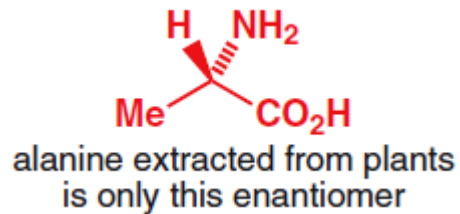
Many chiral molecules are present in nature as single enantiomers

amino acids
are chiral



except glycine—
plane of paper is a
plane of symmetry
through C, N, and CO₂H

laboratory synthesis of racemic alanine from acetaldehyde

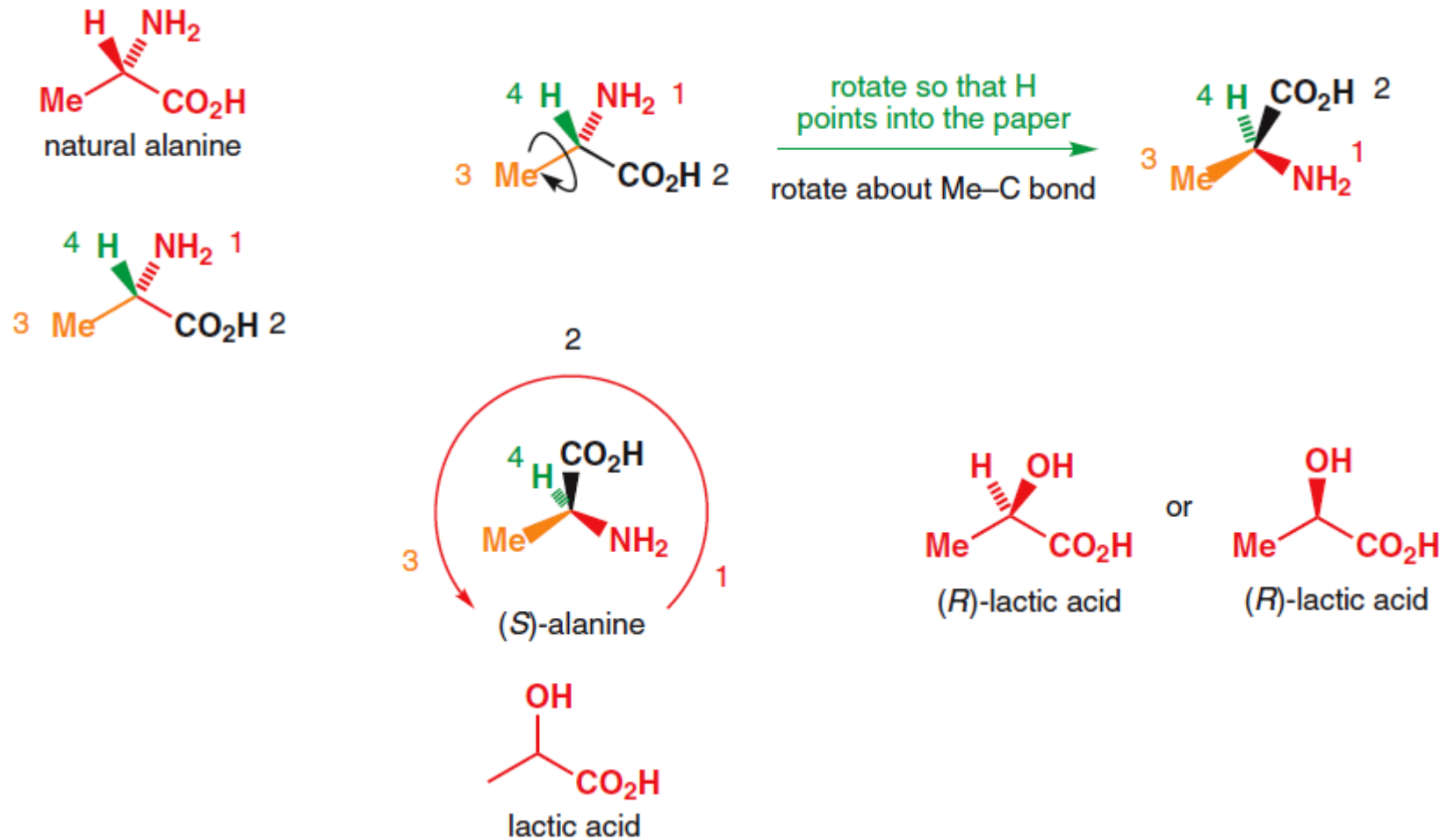


Enantiomeric alanine

In fact, nature does sometimes (but very rarely) use the other enantiomer of alanine, for example in the construction of bacterial cell walls. Some antibiotics (such as vancomycin) owe their selectivity to the way they can recognize these 'unnatural' alanine components and destroy the cell wall that contains them.

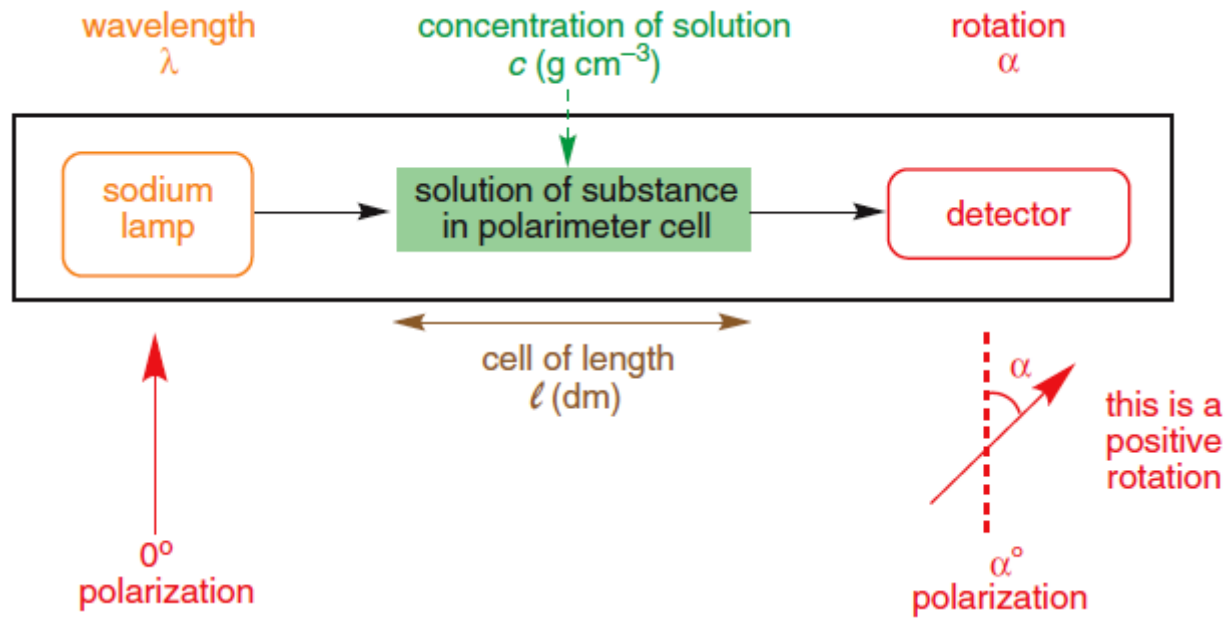
● 'Chiral' does not mean 'enantiomerically pure'.

R and S can be used to describe the configuration of a chiral centre

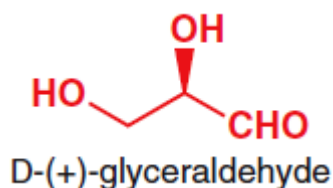


Is there a chemical difference between two enantiomers?

The rotation of plane-polarized light is known as optical activity



$$[\alpha] = \frac{\alpha}{c \cdot \ell} \quad [\alpha]_{\text{D}}^{20} = \frac{\alpha}{c \cdot \ell} = \frac{-4.35}{0.028 \times 1} = -155.4$$



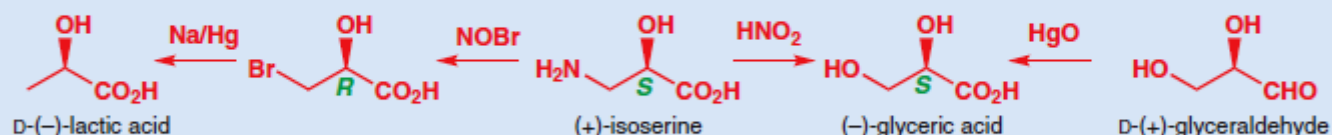
Enantiomers can be described as (+) or (–)

Enantiomers can be described as D or L

- Remember that the *R/S*, *+/-*, and *D/L* nomenclatures all arise from different observations and the fact that a molecule has, say, the *R* configuration gives no clue as to whether it will have + or – optical activity or be labelled *D* or *L*. Never try and label a molecule as *D/L* or *+/-* simply by working it out from the structure. Likewise, never try and predict whether a molecule will have a + or – specific rotation by looking at the structure.

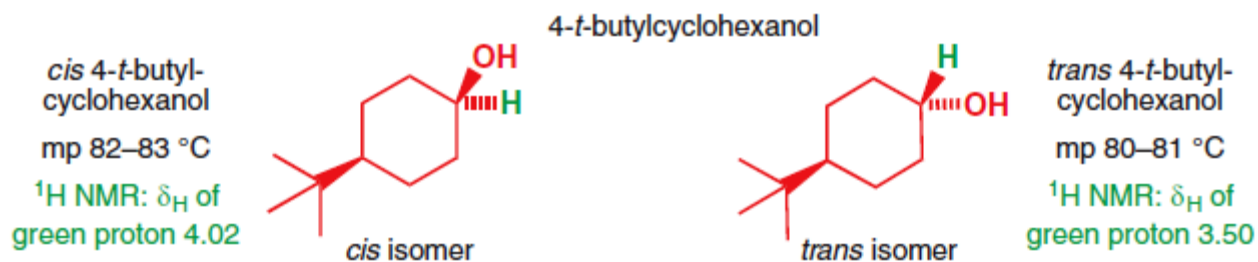
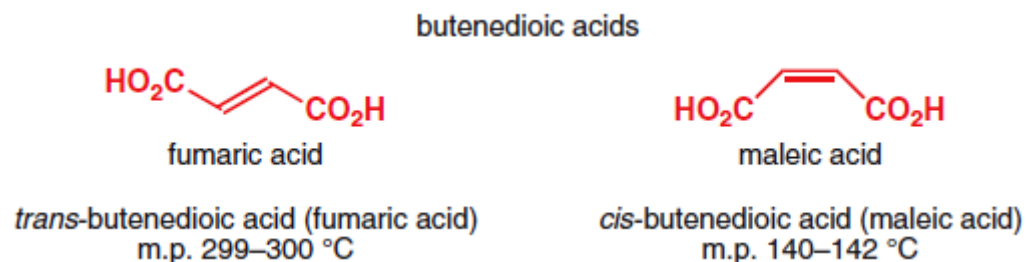
The correlation between D-(–)-lactic acid and D-(+)-glyceraldehyde

Here, for example, is the way that (–)-lactic acid was shown to have the same configuration as D-(+)-glyceraldehyde. We do not expect you to have come across the reactions used here.



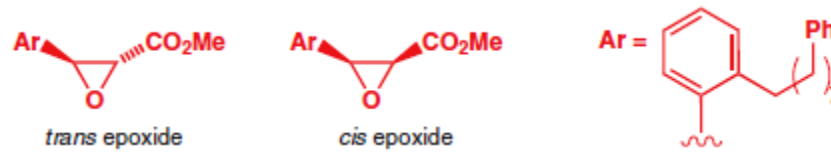
Notice from this scheme that the three intermediates all have the 'same' stereochemistry and yet one is (*R*) and two are (*S*). This is merely the consequence of the priority of the elements. (*R*) can be *D* or *L* and (+) or (–).

Diastereoisomers are stereoisomers that are not enantiomers

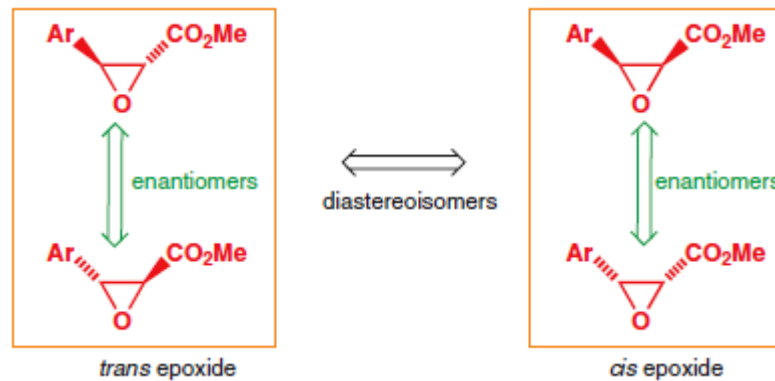
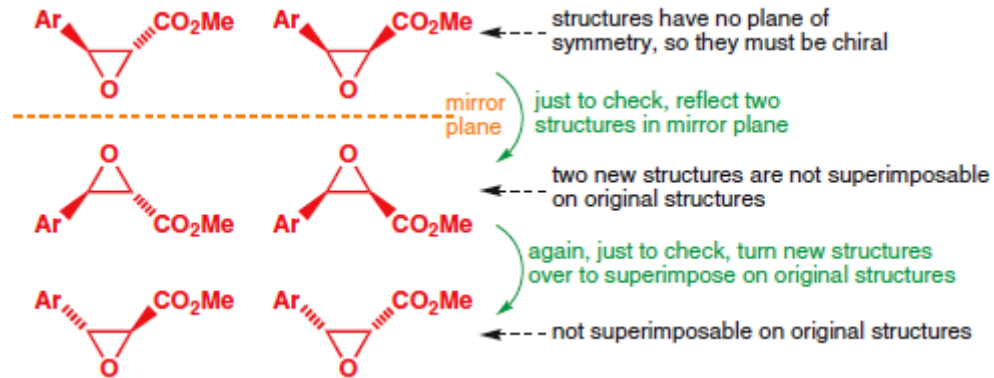
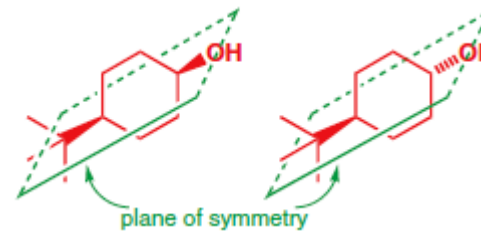
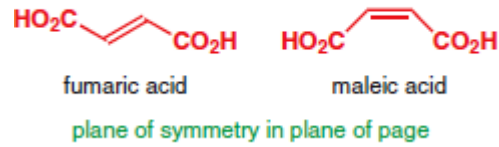


- The physical and chemical properties of enantiomers are identical; the physical and chemical properties of diastereoisomers differ. 'Diastereoisomer' is sometimes shortened to 'diastereomer'.

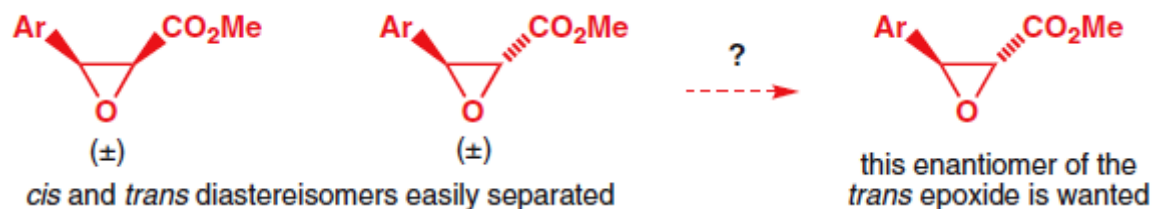
Diastereoisomers can be chiral or achiral



two pairs of achiral diastereoisomers

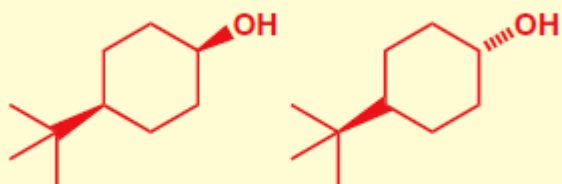


Absolute and relative stereochemistry

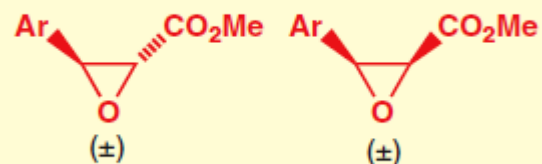


● Enantiomers and diastereoisomers

- Enantiomers are stereoisomers that are mirror images. A pair of enantiomers are mirror-image forms of the same compound and have opposite absolute stereochemistry.
- Diastereoisomers are stereoisomers that are not mirror images. Two diastereoisomers are different compounds, and have different relative stereochemistry.
- Diastereoisomers may be achiral (have a plane of symmetry) or they may be chiral (have no plane of symmetry).

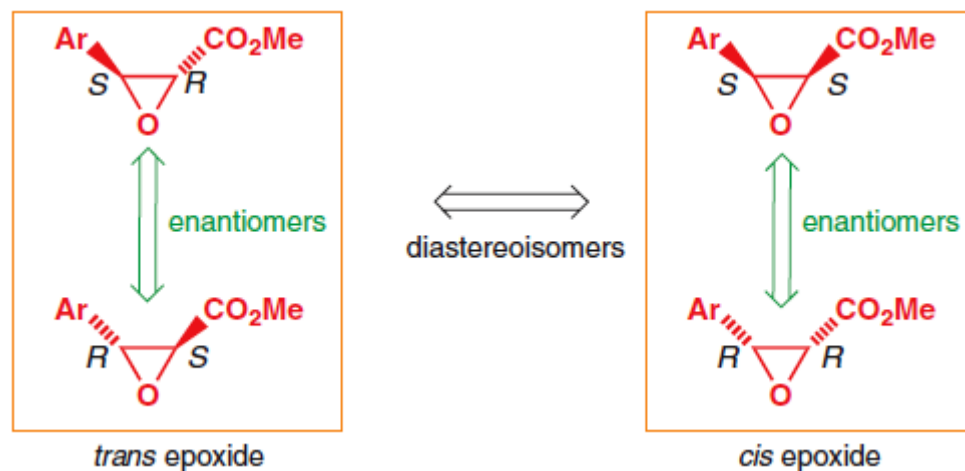


these diastereoisomers are *achiral*



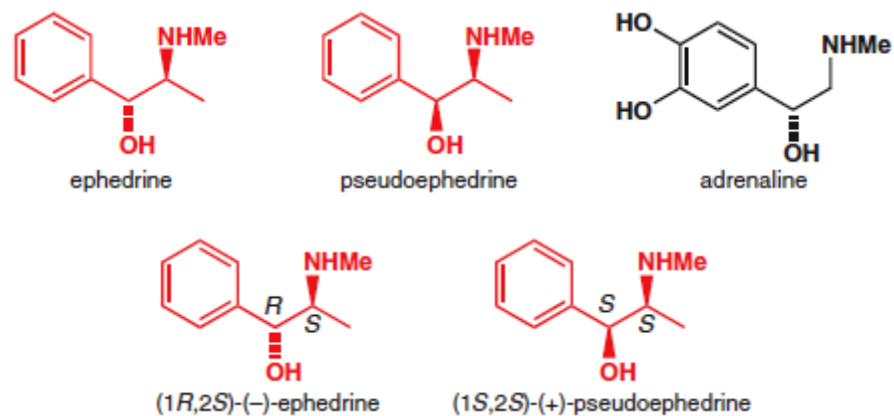
these diastereoisomers are *chiral*

Diastereoisomers can arise when structures have more than one stereogenic centre



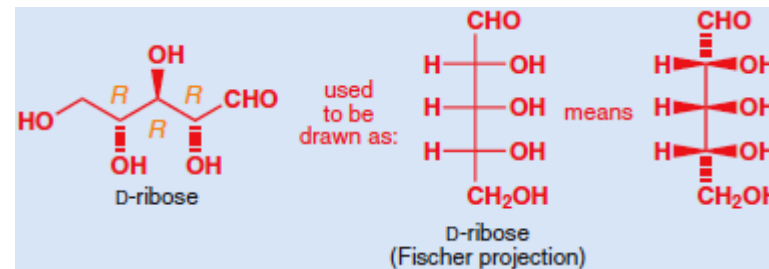
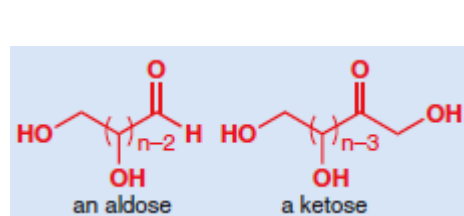
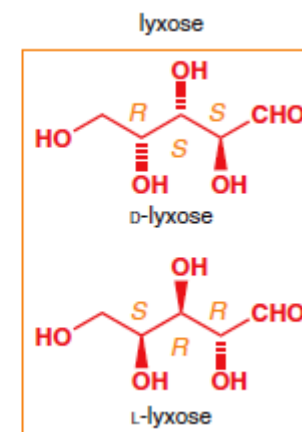
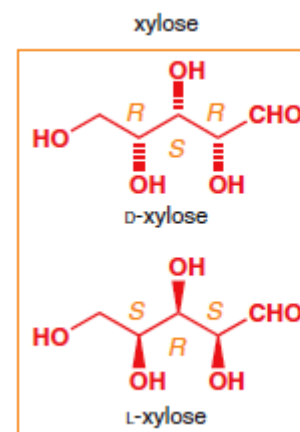
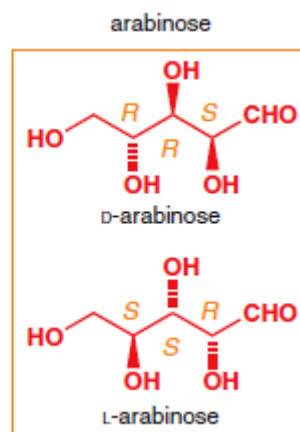
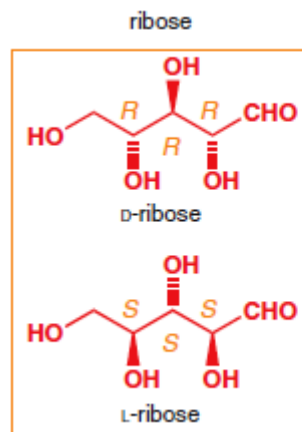
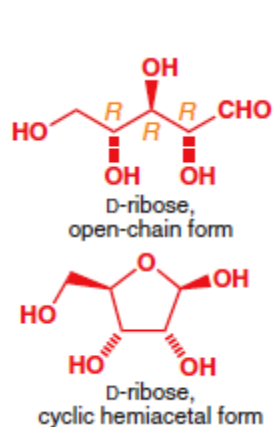
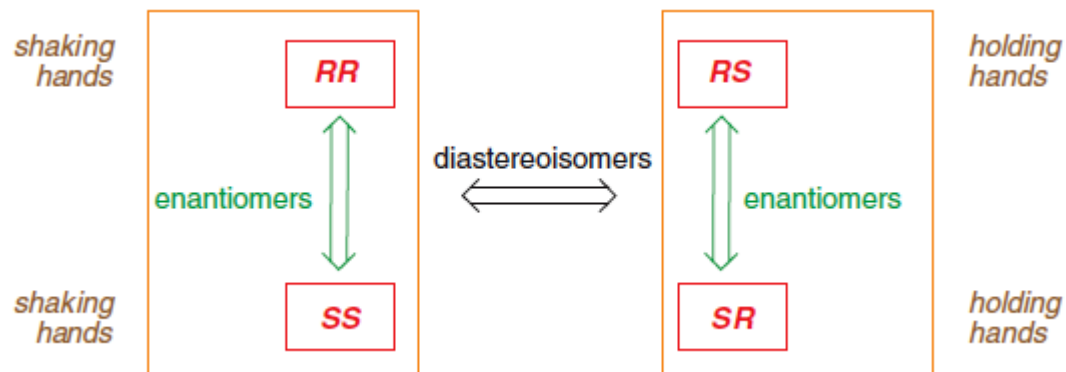
● **Converting enantiomers and diastereoisomers**

- To go from one *enantiomer* to another, *both* stereogenic centres are inverted.
- To go from one *diastereoisomer* to another, only *one* of the two is inverted.

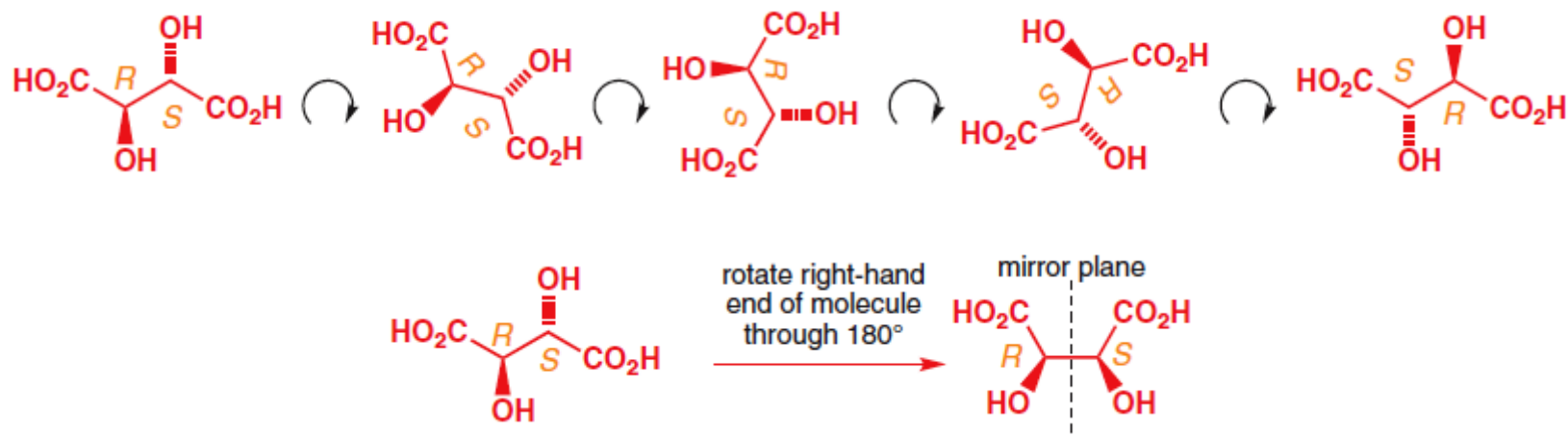
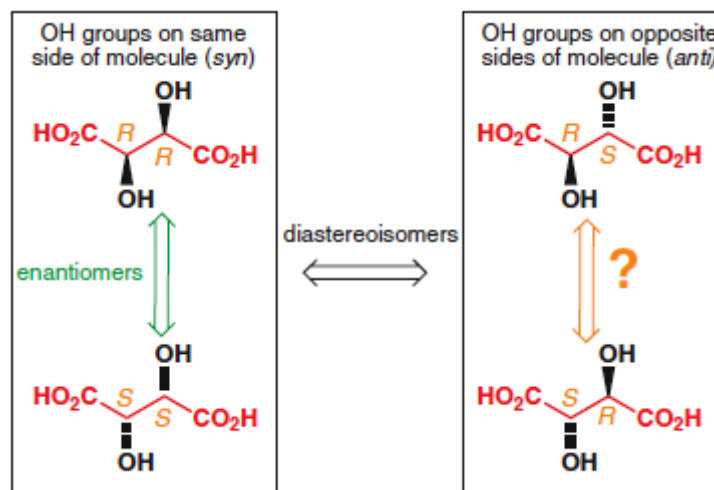
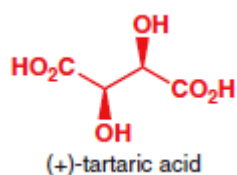


- The two diastereoisomers are different compounds with different names and different properties, while the pairs of enantiomers are the same compound with the same properties, differing only in the direction in which they rotate polarized light.

Diastereoisomers can arise when structures have more than one stereogenic centre

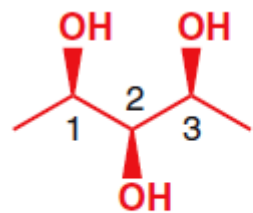
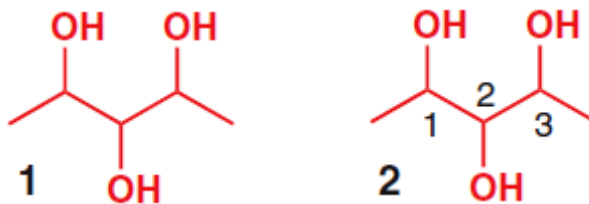


Why only usually?—achiral compounds with more than one stereogenic centre

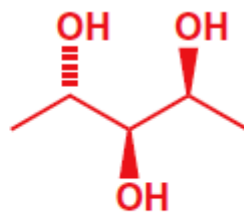


- Compounds that contain stereogenic centres but are themselves achiral are called *meso compounds*. This means that there is a plane of symmetry with *R* stereochemistry on one side and *S* stereochemistry on the other.

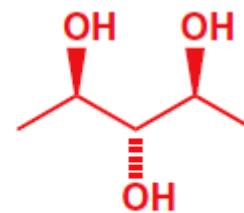
Investigating the stereochemistry of a compound



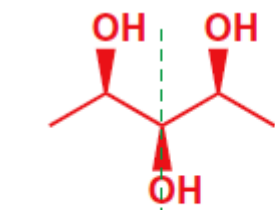
all up or *syn, syn*



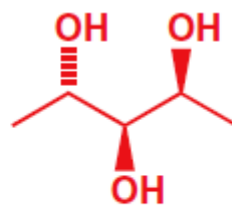
outside one down,
others up or *anti, syn*



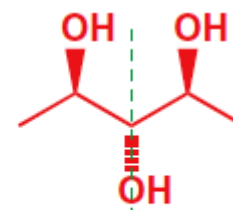
inside one down,
others up or *anti, anti*



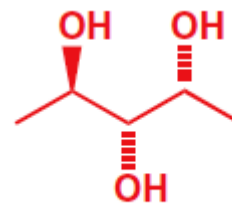
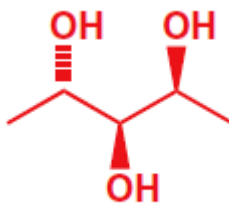
plane of symmetry
achiral (*meso*)



chiral

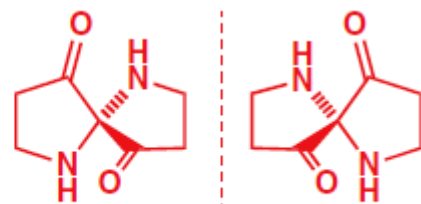
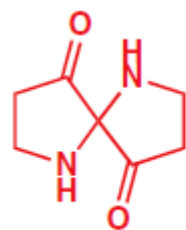
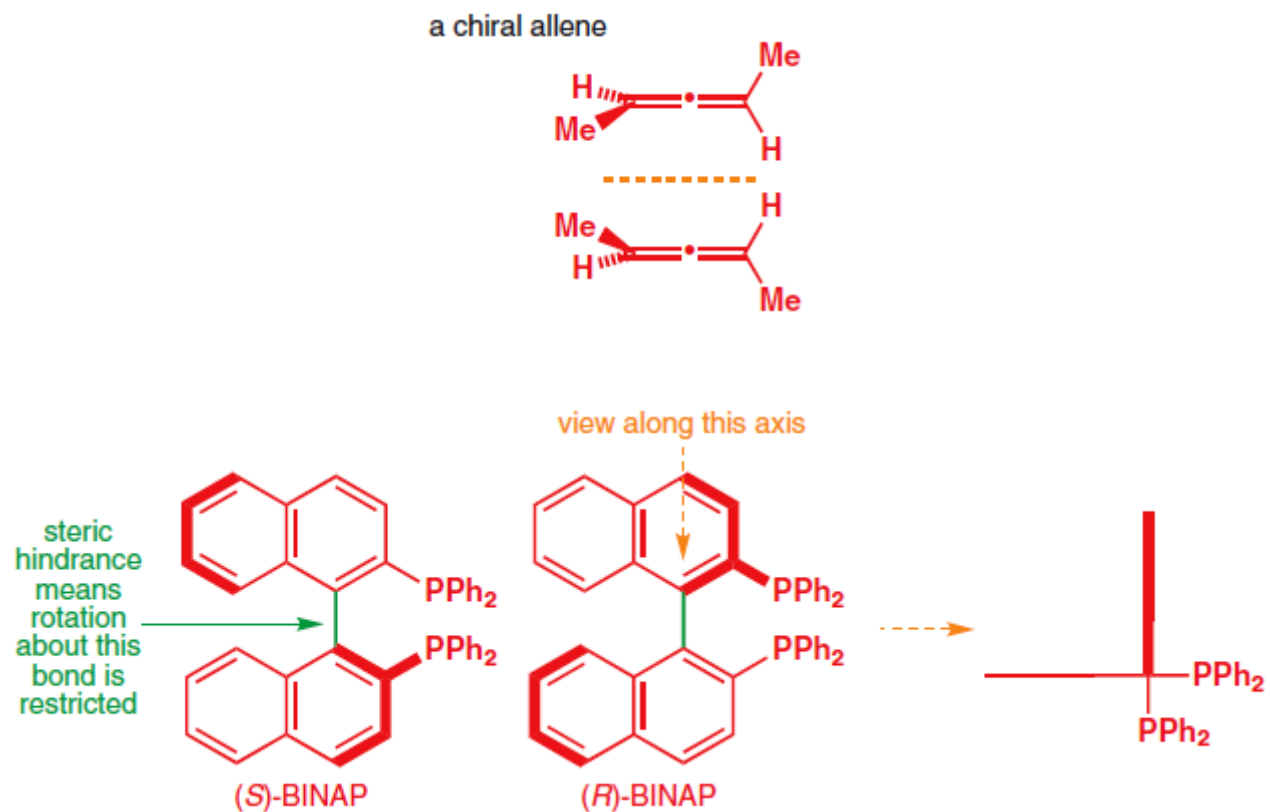


plane of symmetry
achiral (*meso*)



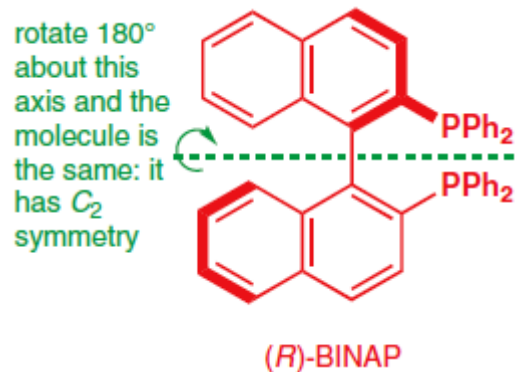
the two enantiomers of the *anti, syn* diastereoisomer

Chiral compounds with no stereogenic centres

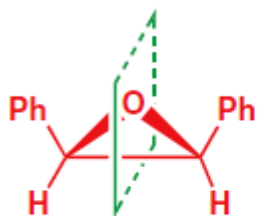


non-superimposable enantiomers

Axes and centres of symmetry

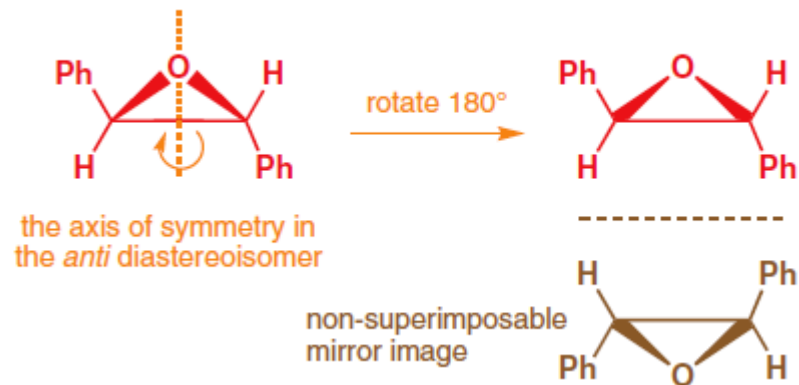


this diastereoisomer is achiral

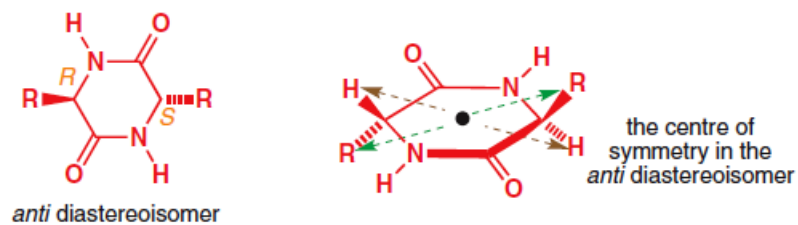
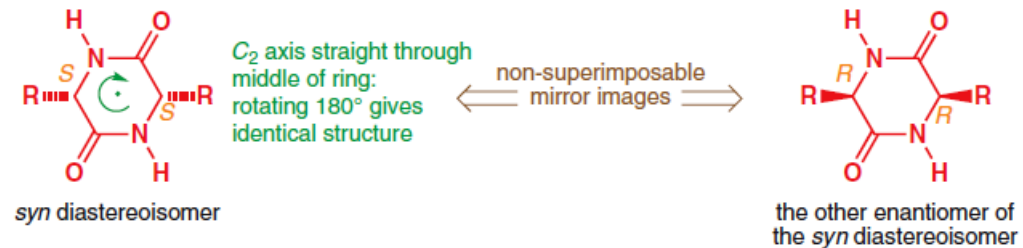
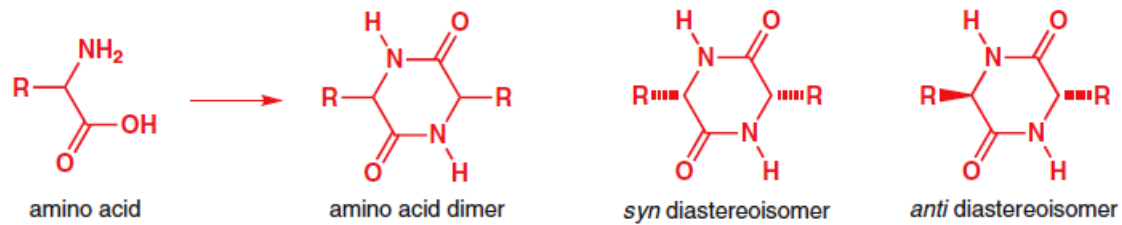
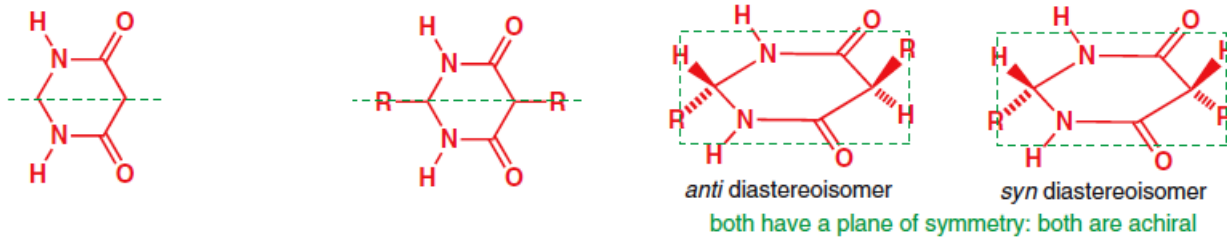


the plane of symmetry in
the *syn* diastereoisomer

this diastereoisomer is chiral



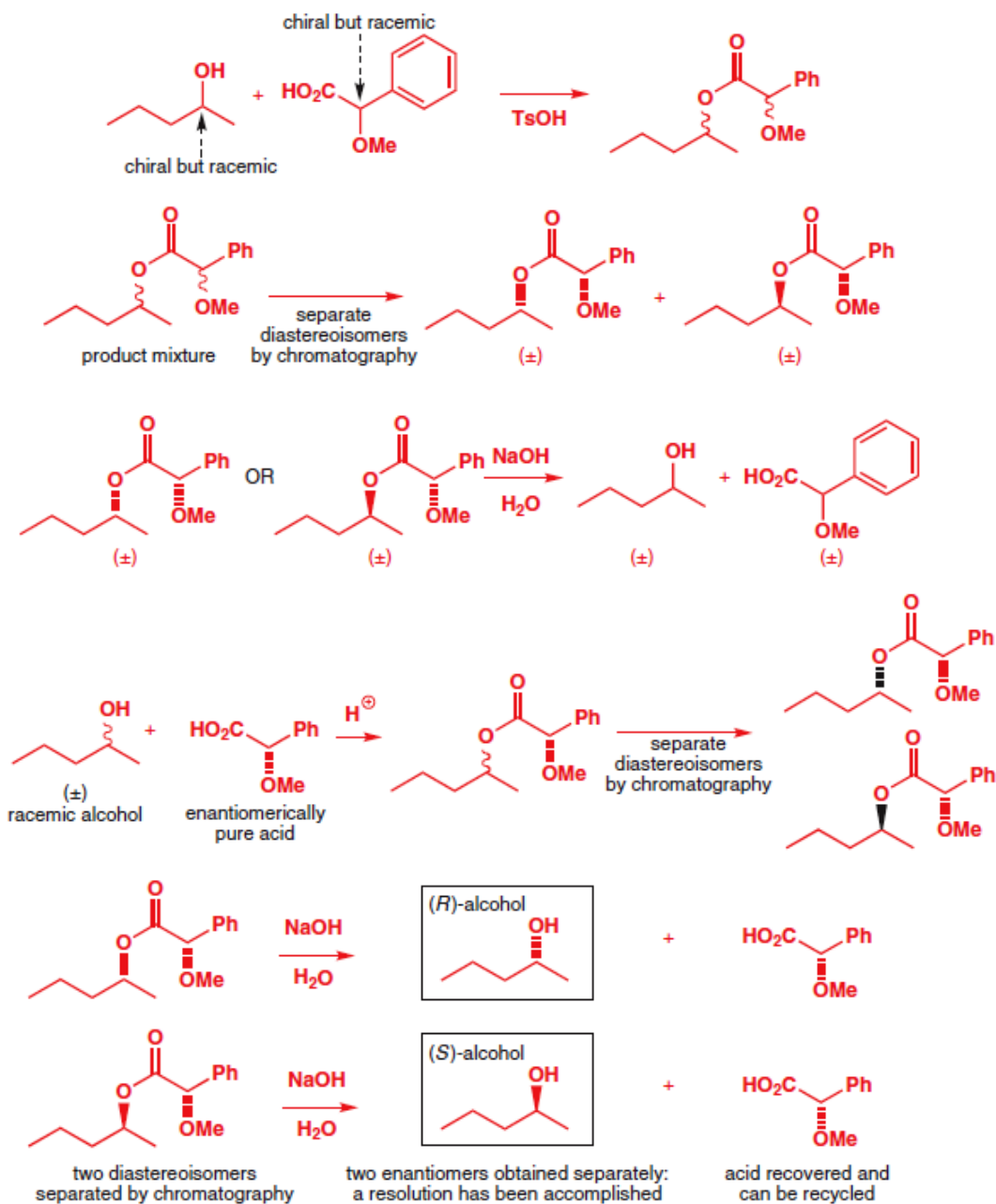
Axes and centres of symmetry



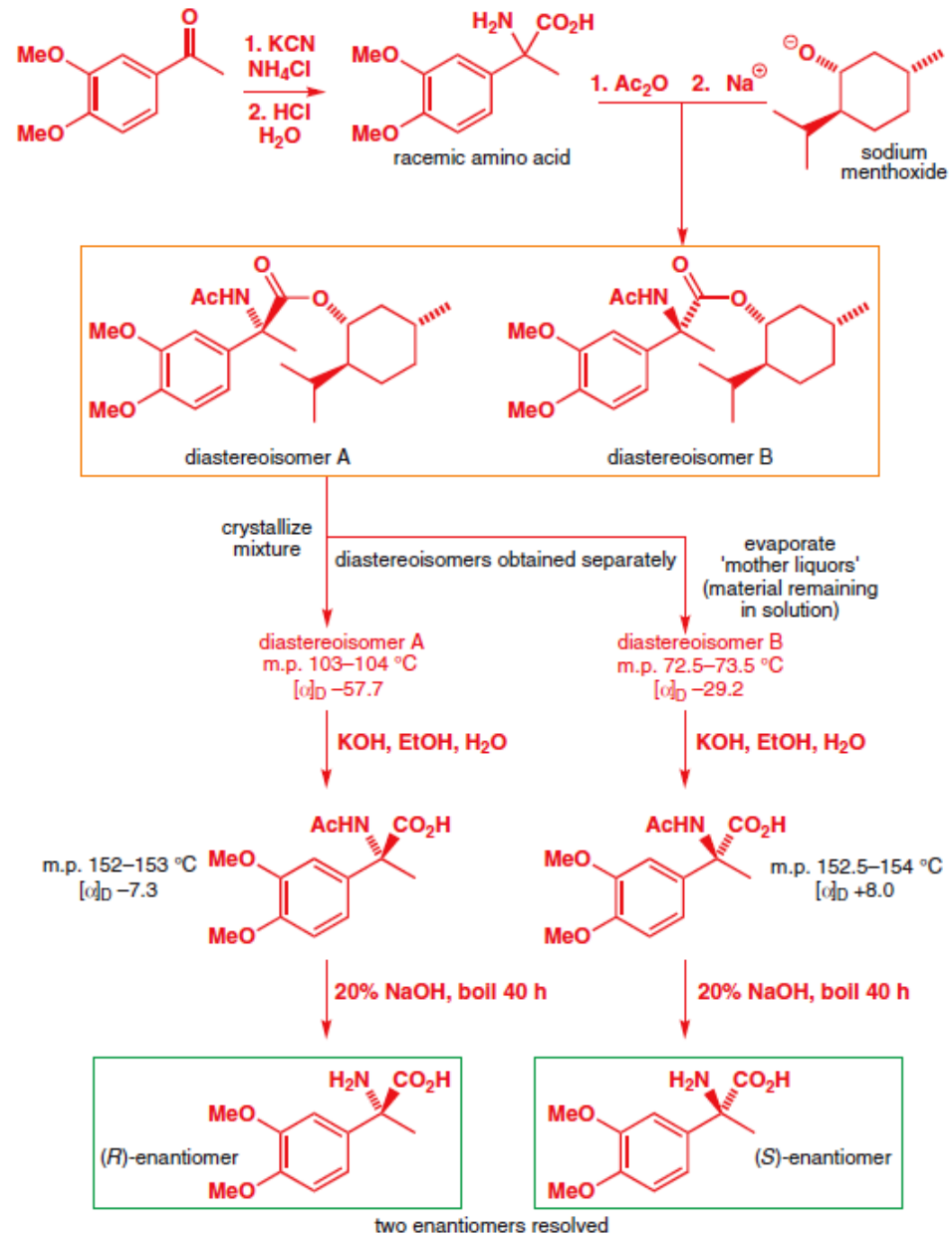
● Chirality in terms of planes, centres, and axes of symmetry

- Any molecule which has a *plane* of symmetry or a *centre* of symmetry is *achiral*.
- Any molecule which has an axis of symmetry is *chiral*, provided it does not also have a plane or a centre of symmetry. An axis of symmetry is the only symmetry element compatible with chirality.

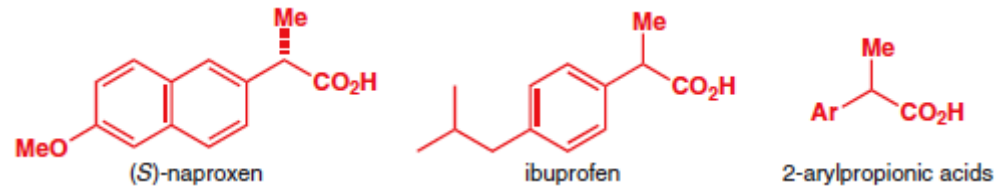
Separating enantiomers is called resolution



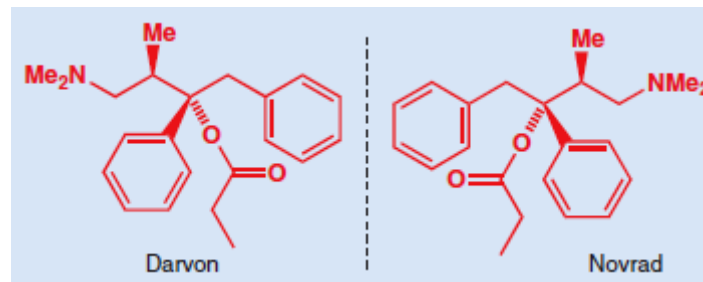
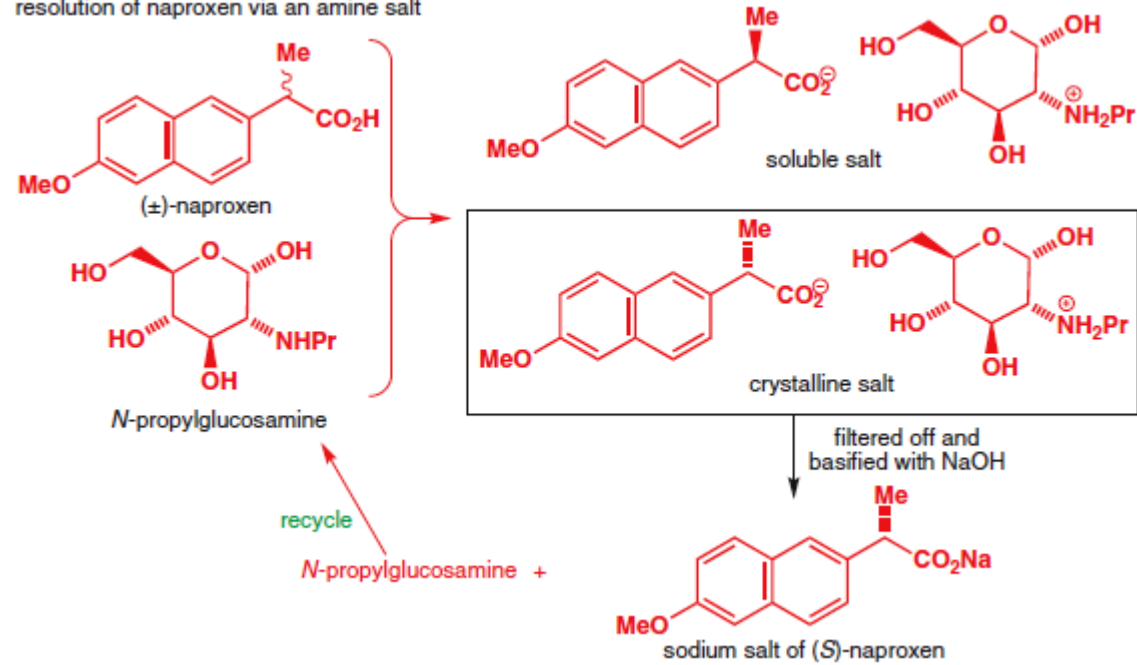
Separating enantiomers is called resolution



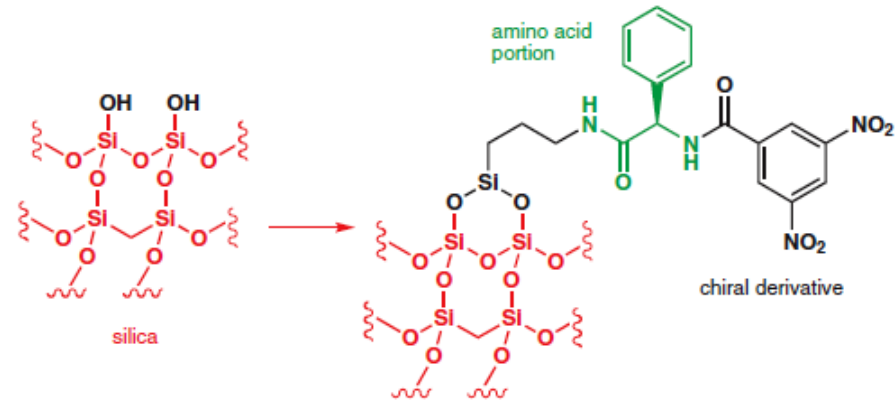
Resolutions using diastereoisomeric salts



resolution of naproxen via an amine salt



Resolutions can be carried out by chromatography on chiral materials



an analogue of the tranquillizer Valium

