Chemistry I (Organic)

Stereochemistry
LECTURE 4
CIP for axially chiral molecules & diastereoisomers

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Format & scope of lectures

- ***Recap of CIP nomenclaure – extension to axially chiral molecules***

- ***Diastereoisomers***
  - (*Z*) & (*E*) alkenes
  - molecules containing multiple stereogenic elements (*e.g.* centres)
  - *meso* compounds & *epimers*

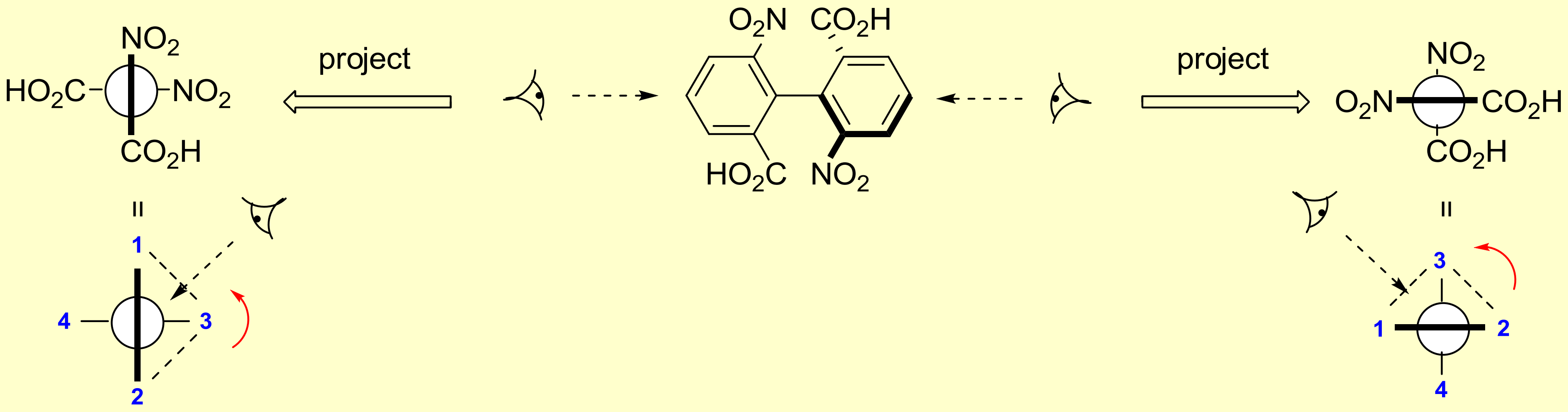
- ***Case study 1: pentane-2,3-diol***
  - *i.e.* two stereogenic centres (different sets of groups attached)

- ***Case study 2: 2,3-dihydroxybutan-1,4-dioic acid***
  - *i.e.* two stereogenic centres (same sets of groups attached)

NB. For 3D Jmol models of molecules **A & B** see link @ http://www.ch.ic.ac.uk/spivey/?q=firstyear

Extension of the notation to axial stereogenicity

- ***The (R)/(S) notation has also been extended to allow assignment of the configurations of chiral molecules without a stereogenic centre***
  - For example, ***axially chiral molecules*** like allenes and hindered biaryls can be assigned provided that a couple of additional conventions are implemented. ***The molecule must be viewed along the chiral axis*** (from either end, it doesn't matter which) with the substituents giving rise to the chirality projected onto a plane at right angles to the chiral axis. The priorities of the four substituents are then assigned in the usual manner with the proviso that ***the near groups always take precedence over the far groups***
  - For example, for (-)-6,6'dinitrobiphenyl-2,2'-dicarboxylic acid is (*S*)-configured:

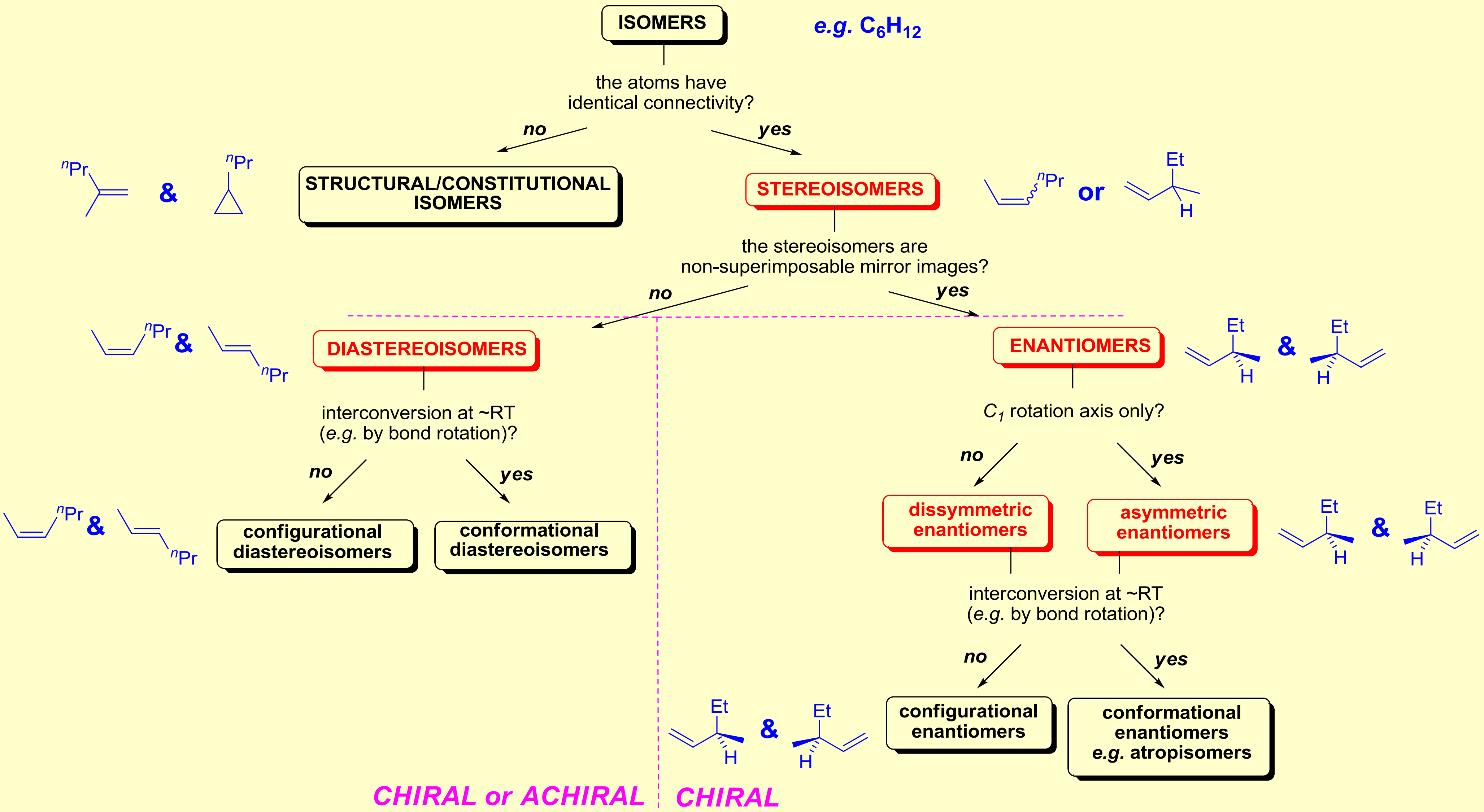


anti-clockwise = (*S*) **anti-clockwise = (*S*)**

- ***The (R)/(S) notation has also been extended to allow assignment of enantiotopic and diastereotopic groups etc. This will be explored later in the degree course***

Diastereoisomers

- recall - ***Diastereoisomers*** ***(= diastereomers) are stereoisomers that are NOT enantiomers:***



ISOMERS

e.g. **C_6H_{12}**

the atoms have identical connectivity?

no → **STRUCTURAL/CONSTITUTIONAL ISOMERS**

yes → **STEREOISOMERS**

the stereoisomers are non-superimposable mirror images?

no → **DIASTEREOISOMERS**

yes → **ENANTIOMERS**

interconversion at ~RT (*e.g.* by bond rotation)?

no → **configurational diastereoisomers**

yes → **conformational diastereoisomers**

C_1 rotation axis only?

no → **dissymmetric enantiomers**

yes → **asymmetric enantiomers**

interconversion at ~RT (*e.g.* by bond rotation)?

no → **configurational enantiomers**

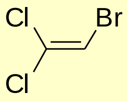
yes → **conformational enantiomers *e.g.* atropisomers**

CHIRAL or ACHIRAL

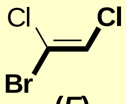
CHIRAL

Diastereoisomers – *(Z) & (E) alkenes*

- ***Cis (Z) and trans (E) alkenes are diastereoisomers***
  - the *Z* ('zusammen' = together) & *E* ('entgegen' = opposite) descriptors relate to the CIP priority assignments for the alkene substituents:

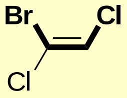


no stereoisomers



(*E*)

&



(*Z*)

diastereoisomers

- ***Alkene diastereoisomers are <u>achiral</u> (i.e. their mirror images are superimposable) – because they have a plane of symmetry through the plane of the double bond (i.e. S_1 improper axis)***

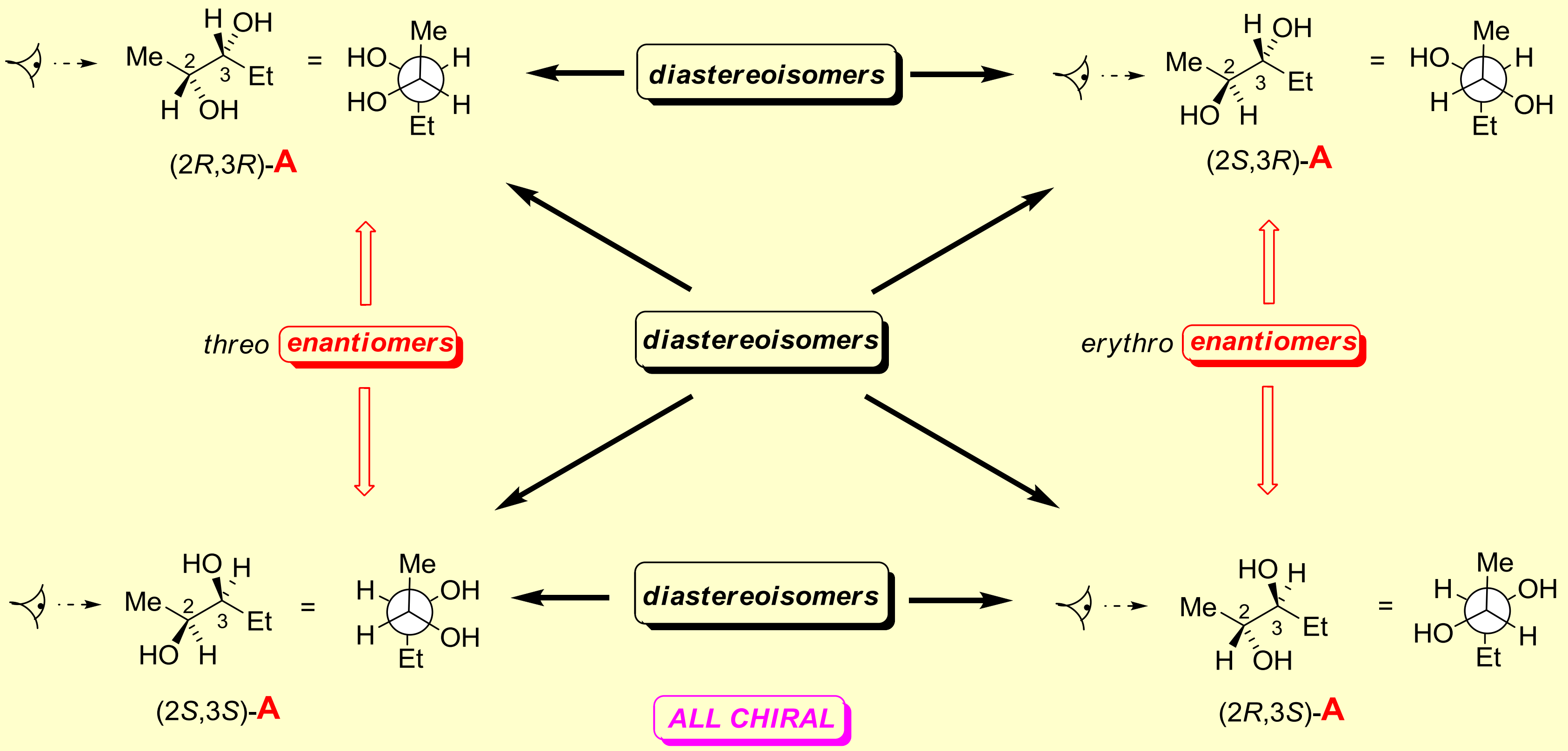
- Unlike enantiomers, ***<u>diastereoisomers</u> have different chemical and physical properties*** (*e.g.* melting points, solubilities, reactivities *etc*.)
  - This is because the ways in which the electrons associated with the various groups buttress against each other are different in the different diastereoisomers, giving rise to different energies and different shapes *etc*.

Diastereoisomers – *multiple stereogenic centres*

- ***Diastereoisomers* often result when two (or more) stereogenic centres are present in the same molecule**
- ***For a molecule containing n stereogenic centres there are a maximum of 2^n stereoisomers***
  - However, there are often fewer due to the occurrence of symmetry operations (*i.e*. S_n improper rotation axes) that render certain stereoisomers ***achiral*** (*i.e.* their mirror images are superimposable). These are designated as ***meso*** (see 'CASE 2' following slides)
- ***Meso is the term given to achiral members of a series of diastereoisomers in which at least one is chiral***
- ***Epimers are diastereoisomers differing in configuration at just one stereogenic centre***
- ***We will consider molecules containing two stereogenic centres. There are two cases:***

Diastereoisomers – *case 1*

- ***The two stereogenic centres have <u>different</u> sets of groups attached.***
  - *e.g.* pentane-2,3-diol



(2*R*,3*R*)-**A**

(2*S*,3*R*)-**A**

diastereoisomers

threo ***enantiomers***

diastereoisomers

erythro ***enantiomers***

diastereoisomers

(2*S*,3*S*)-**A**

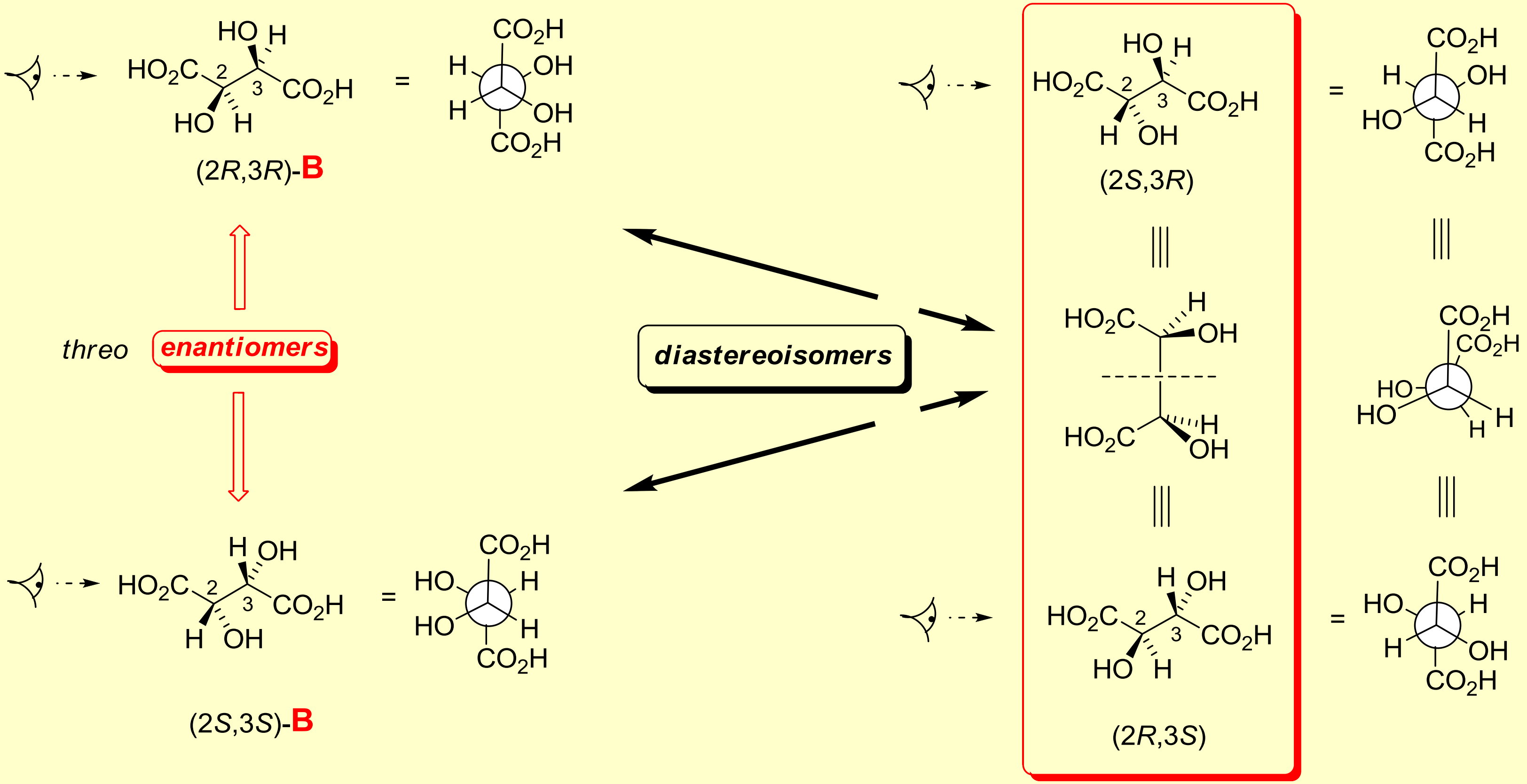
(2*R*,3*S*)-**A**

ALL CHIRAL

- ***i.e. 4 stereoisomers, two pairs of asymmetric enantiomers***
  - *NB.* designation of the (*R*,*R*)/(*S*,*S*) pair as ***threo*** (= ***syn***) & the (*R*,*S*)/(*S*,*R*) pair as ***erythro*** (= ***anti***)

Diastereoisomers – *case 2*

- ***The two stereogenic centres have <u>the same</u> set of groups attached***
  - *e.g.* tartaric acid (2,3-dihydroxybutan-1,4-dioic acid)



(2*R*,3*R*)-**B**

threo ***enantiomers***

diastereoisomers

(2*S*,3*S*)-**B**

(2*S*,3*R*)

(2*R*,3*S*)

meso-**B**

CHIRAL

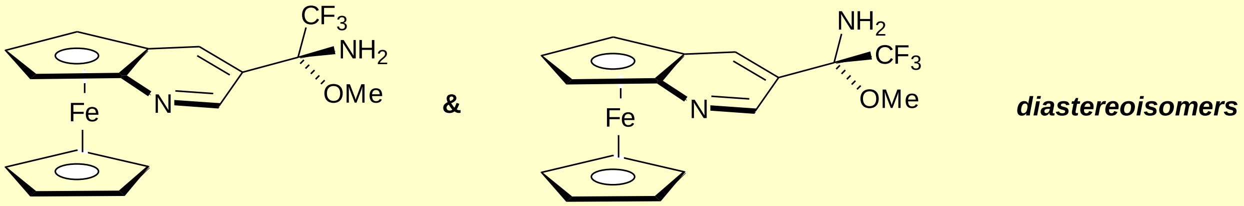
ACHIRAL

- ***i.e. 3 stereoisomers, one pair of dissymmetric enantiomers (C_2, chiral) and a meso isomer (achiral)***

Diastereoisomers *cont.*

- ***Additional stereogenic centres add additional complexity***
  - *e.g.* 3 stereogenic centres → up to 2^3 (= 8) stereoisomers *etc.*

- ***As for enantiomers, the elements of chirality need not be stereogenic centres, they can be axes, helices etc. and combinations thereof. e.g.***

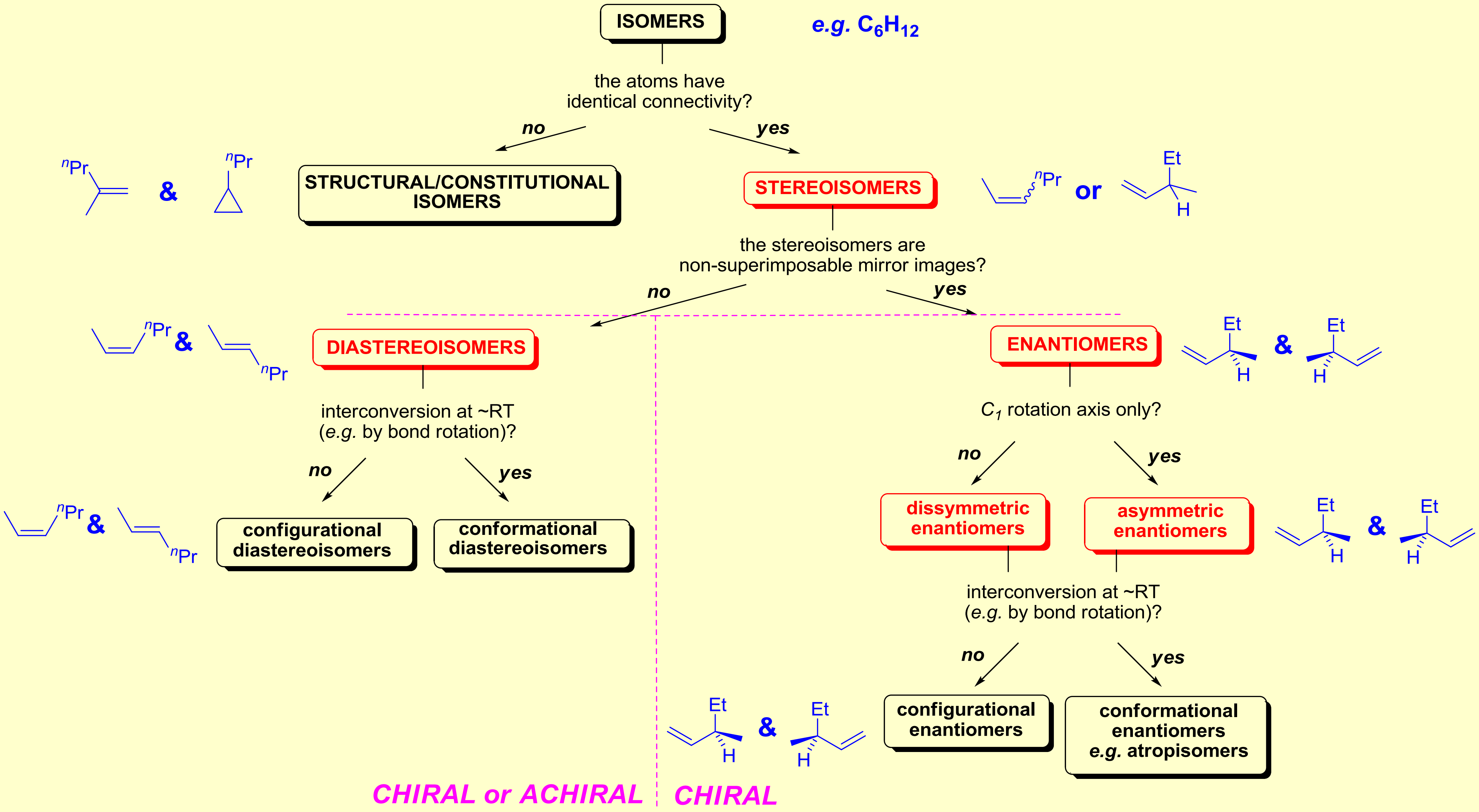


- ***The <u>maximum</u> number of stereoisomers is always 2^n, where n is the number of stereogenic elements (e.g. centres), but isomers may have improper rotation axes and will therefore be achiral (i.e. <u>meso</u>, as for 'case 2' above)***

- ***See later in the course for related stereochemical matters:***
  - Prochirality
  - Enantiotopic groups/substituents
  - Diastereotopic groups/substituents
  - *pro*-R and *pro*-S stereodescriptors
  - *Re* and *Si* faces of *e.g.* carbonyl groups

Isomers & stereoisomers - *definitions*

- ***Isomers*** are compounds with the same molecular formula; they are further classified as follows:



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