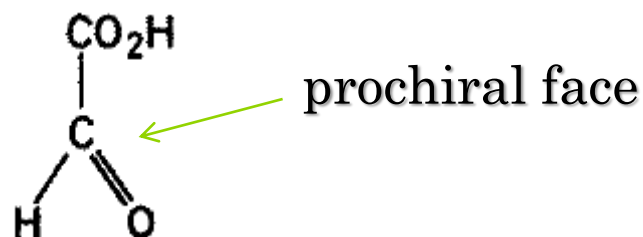
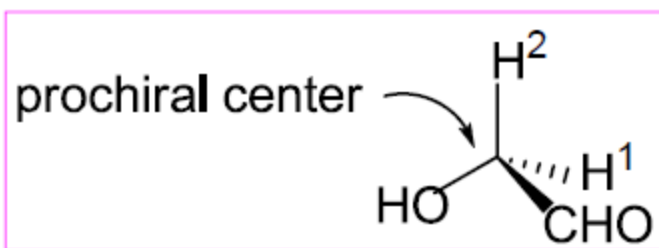


PROSTEREOMERISM

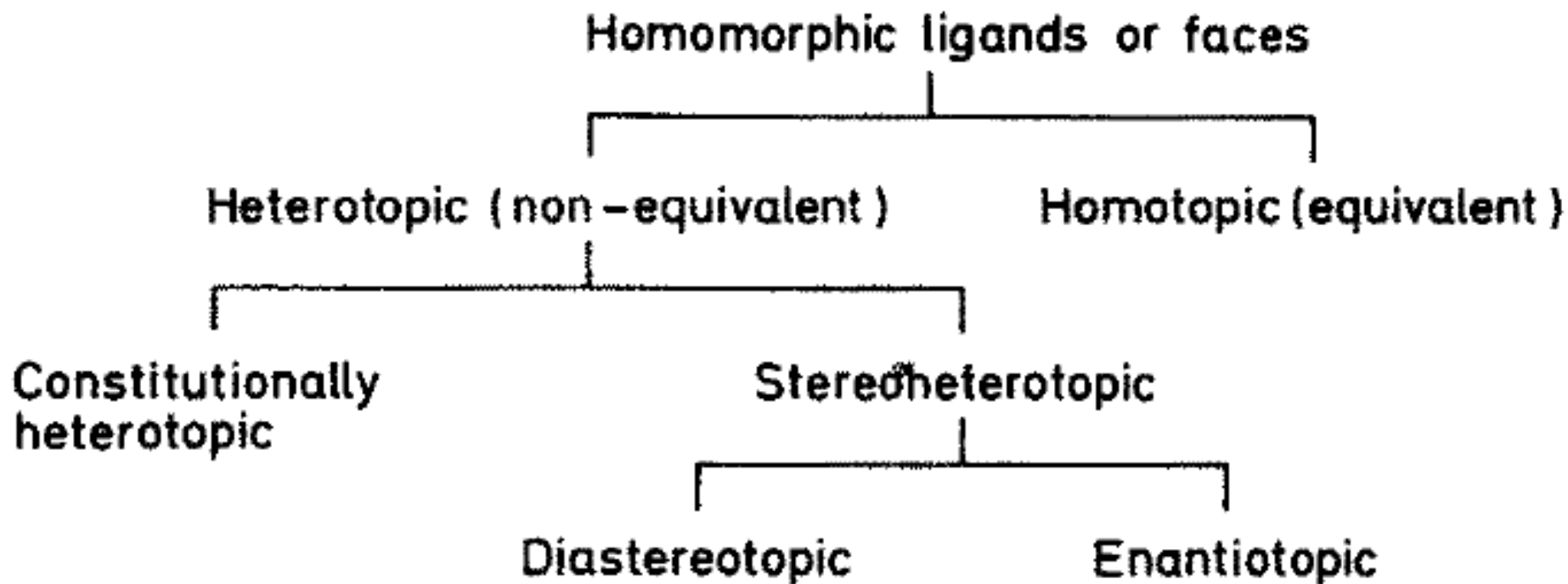


PROCHIRALITY

- The term **prochiral** is used for a compound or group that can be converted from achiral to chiral in a single step.
- To find the prochiral or prostereogenic center, the two similar atoms or groups (ligands) can be replaced by another ligand and the compound obtained is analysed.
- The replacement ligand must be different not only from the original one but also from all other ligands attached to the same atom.
- There are two criteria, a substitution criterion and a symmetry criterion. Similar criteria (addition or symmetry) serve to test the equivalency of faces.

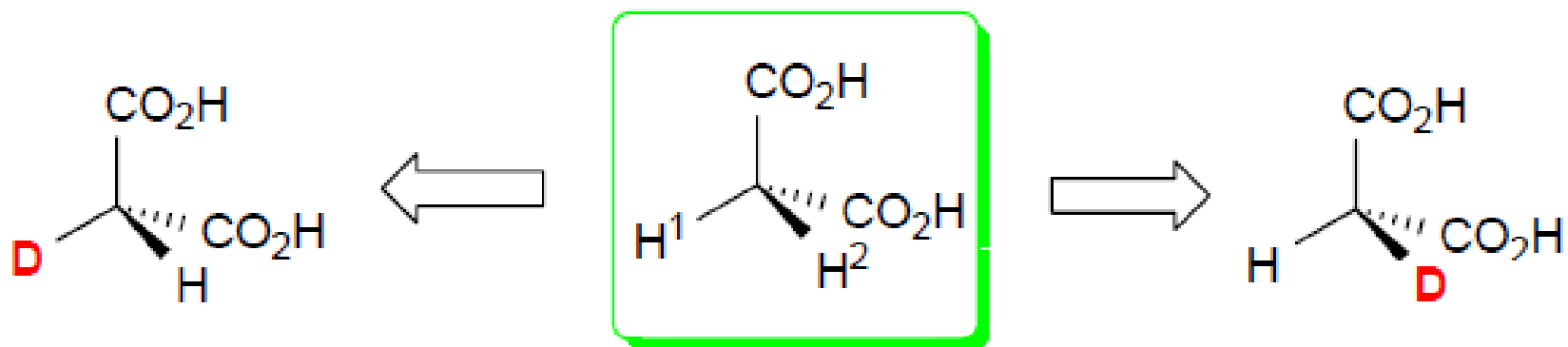


HOMOMORPHIC LIGANDS OR FACES



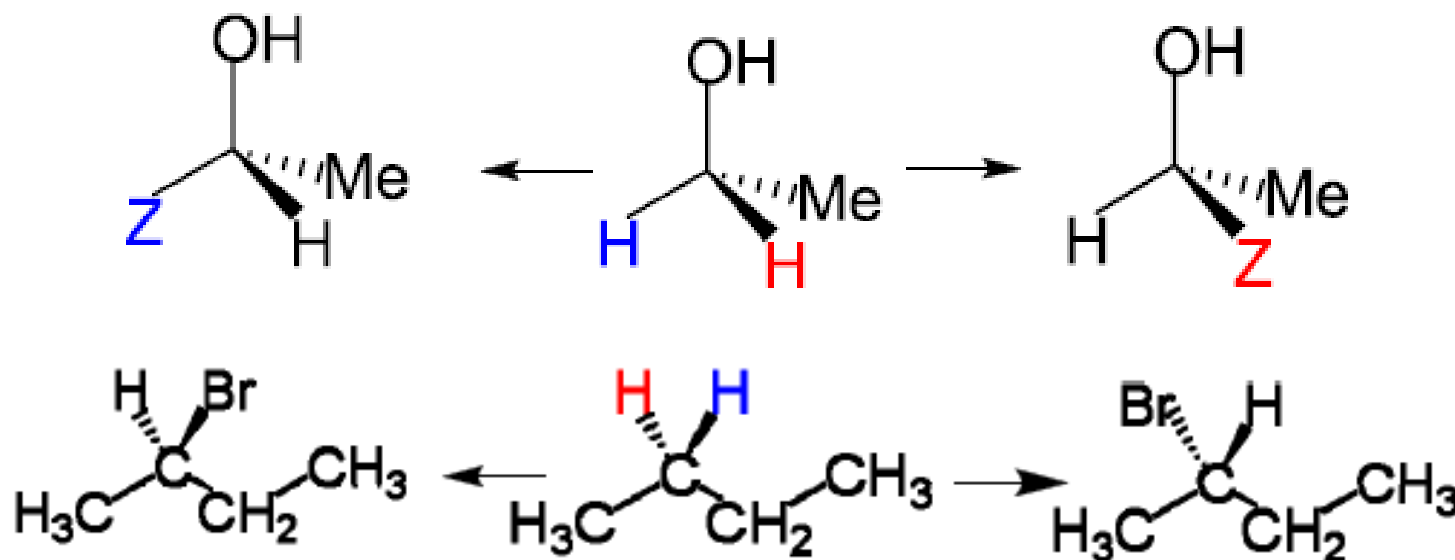
HOMOTOPIC LIGANDS

- Two groups A and B are **homotopic** if the molecule remains the same when the groups are interchanged with the remaining parts of the molecule fixed.
- Two homomorphic ligands are homotopic if replacement of first one and then the other by a different ligand leads to the same structure.
- Homotopic atoms have the same chemical shift in an NMR spectrum



ENANTIOTOPIC LIGANDS

- The stereochemical term **enantiotopic** refers to the relationship between two groups in a molecule which, if one or the other were replaced, would generate a chiral compound.
- The two possible compounds resulting from that replacement would be enantiomers.

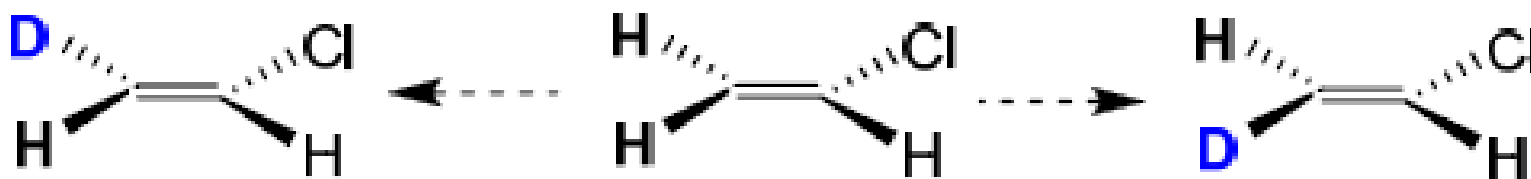
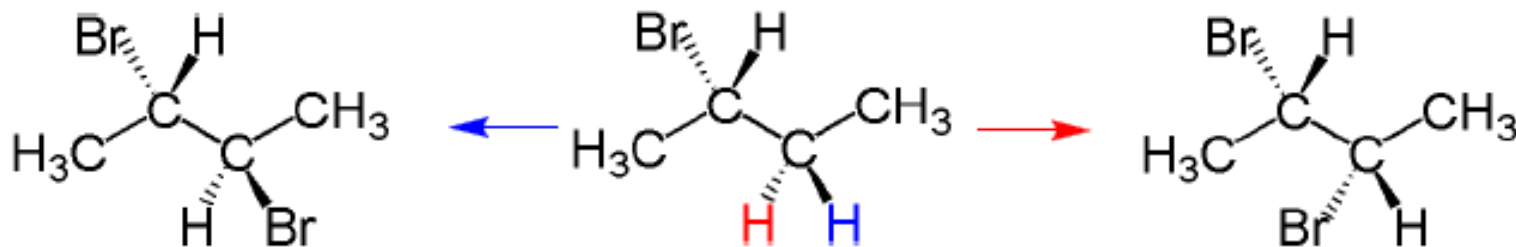


ENANTIOTOPIC LIGANDS

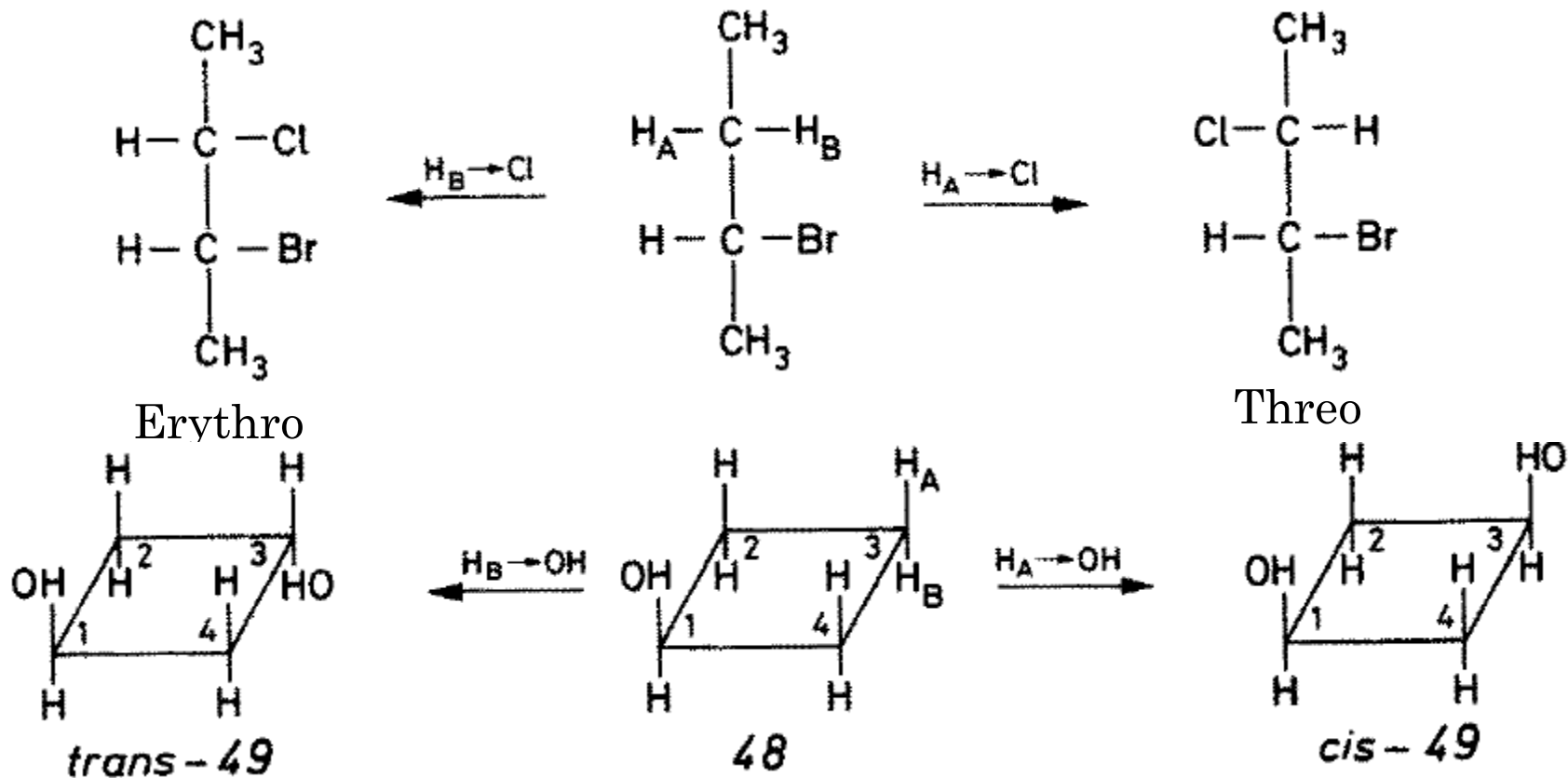
- In any molecule: **CX₂WY**, if neither W or Y is chiral, the X atoms or groups are always **enantiotopic**.
- Enantiotopic atoms or groups are equivalent in all chemical and physical respects **except toward a chiral reagent**.
- **Enantiotopic pairs** of NMR-active nuclei are also indistinguishable by NMR and produce a single signal.
- If two identical substituents are attached to an *sp*³-hybridized atom, the descriptors ***pro-R*** and ***pro-S*** are used to distinguish between the two.
- Replacing the *pro-R* substituent results in an *R* chirality center at the original *sp*³-hybridized atom, and *vice versa*.

DIASTEREOTOPIC LIGANDS

- Where two atoms or groups in a molecule are in such positions that replacing each of them in turn by a group Z gives rise to diastereomers, the atoms or groups are called **diastereotopic**.

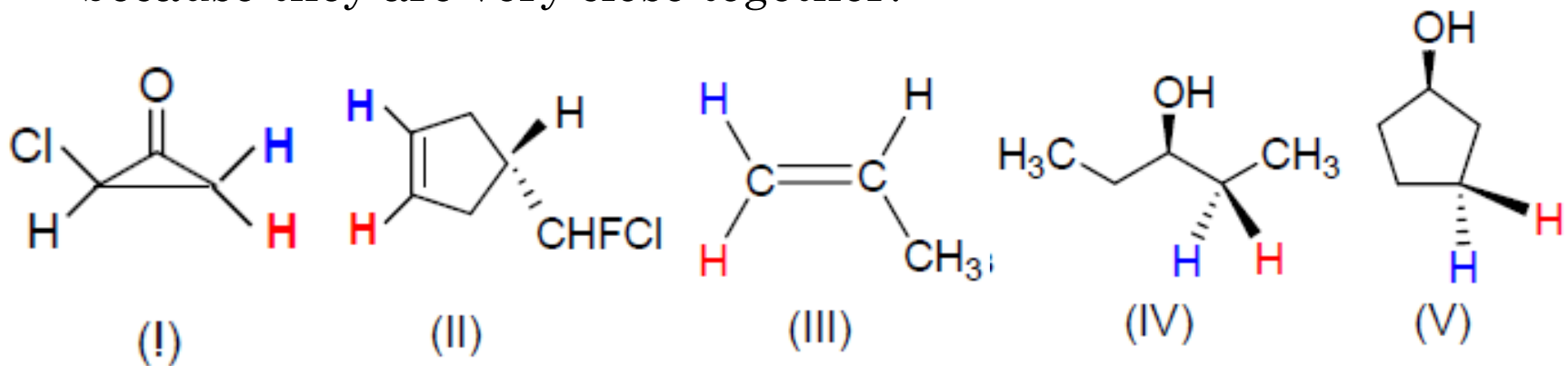


DIASTEREOTOPIC LIGANDS



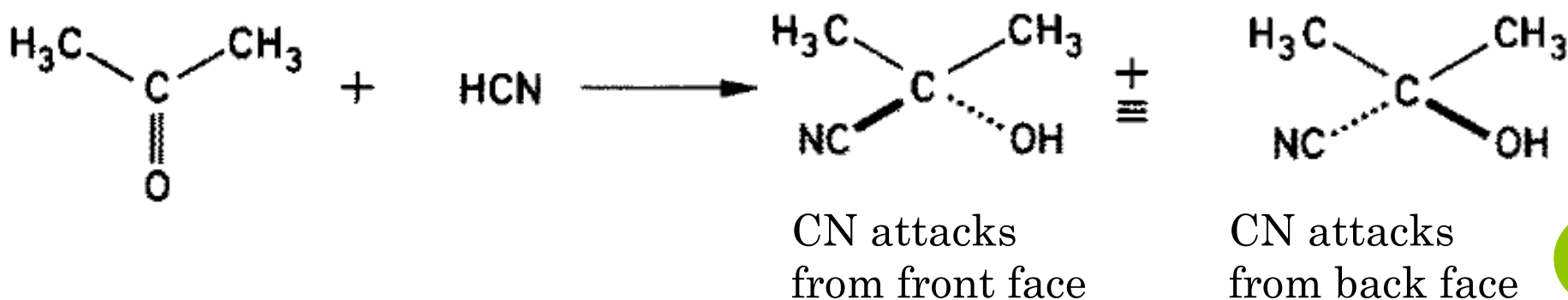
DIASTEREOTOPIC LIGANDS

- **X** atoms or groups in **CX₂WY** are diastereotopic if either W or Y is chiral (I).
- Diastereotopic groups need not be attached to the same atom (II).
- Furthermore, diastereotopic groups also arise in achiral molecules (III, IV, V).
- Diastereotopic atoms or groups are different in any environment, chiral or achiral.
- Diastereotopic hydrogens theoretically give different peaks and split each other, which are distinguishable in NMR, but this is merely because they are very close together.



HOMOTOPIC FACES

- Two corresponding faces of a molecule (usually but not invariably faces of a double bond) are homotopic when addition of the same reagent to either face gives the same product.
- For example, addition of HCN to acetone will give the same cyanohydrin, no matter to which face addition occurs.

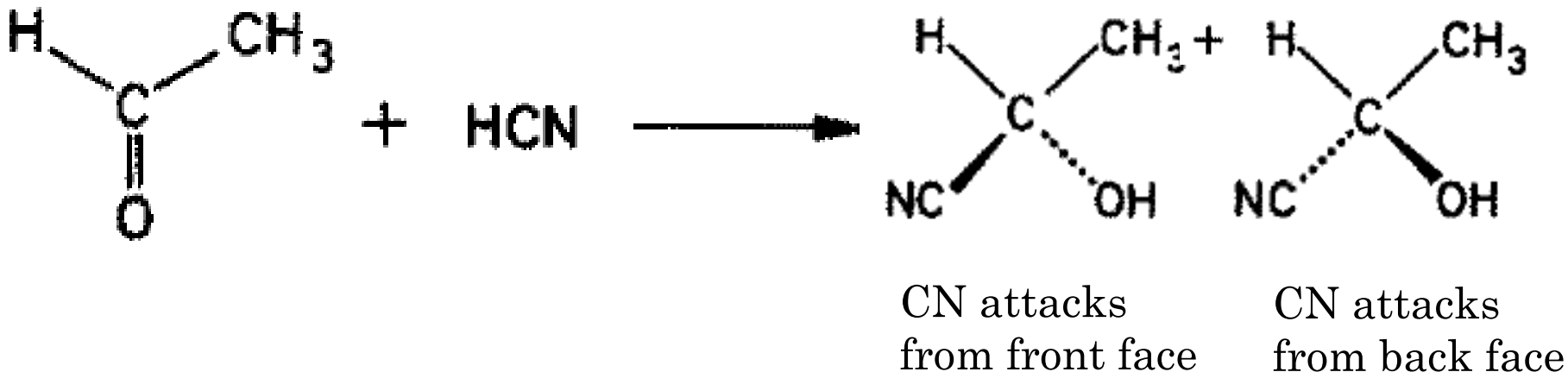


HETEROTOPIC FACES

- The sp^2 hybridized carbon bonded to three different groups will become chiral as the result of an addition reaction (which may also be a reduction) that results in formation of a bond between the sp^2 hybridized carbon and a fourth group that differs from the other three.
- The addition may result in the formation of enantiomers or diastereomers.
- Hence the two heterotopic faces can be either
 - Enantiotopic Face OR
 - Diastereotopic Face

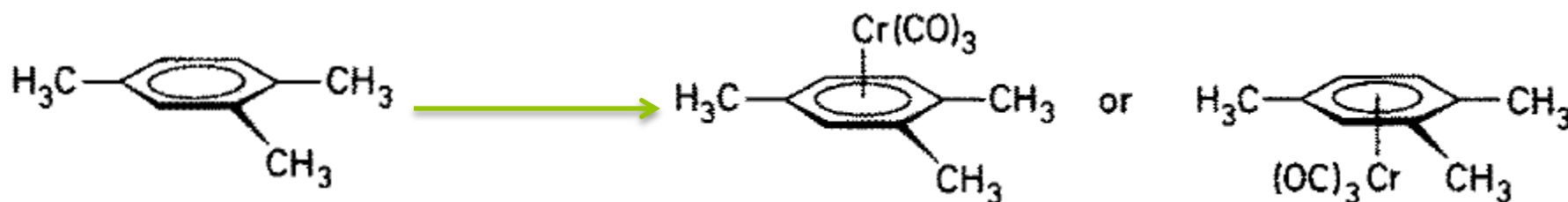
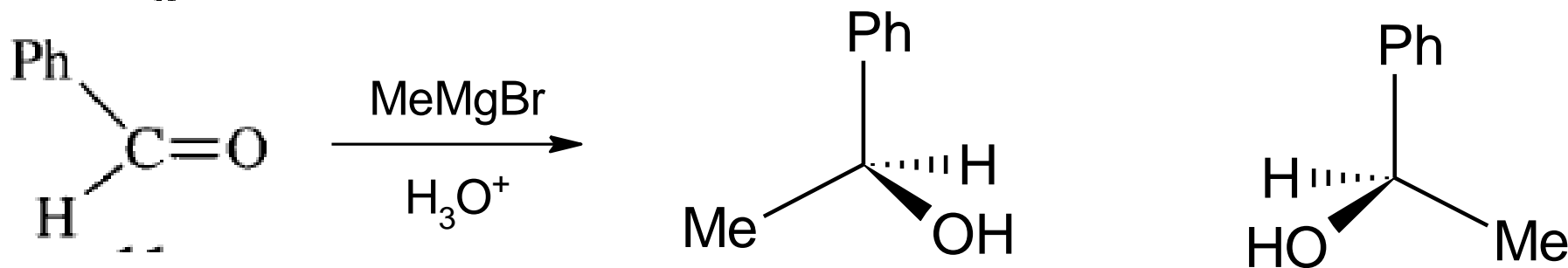
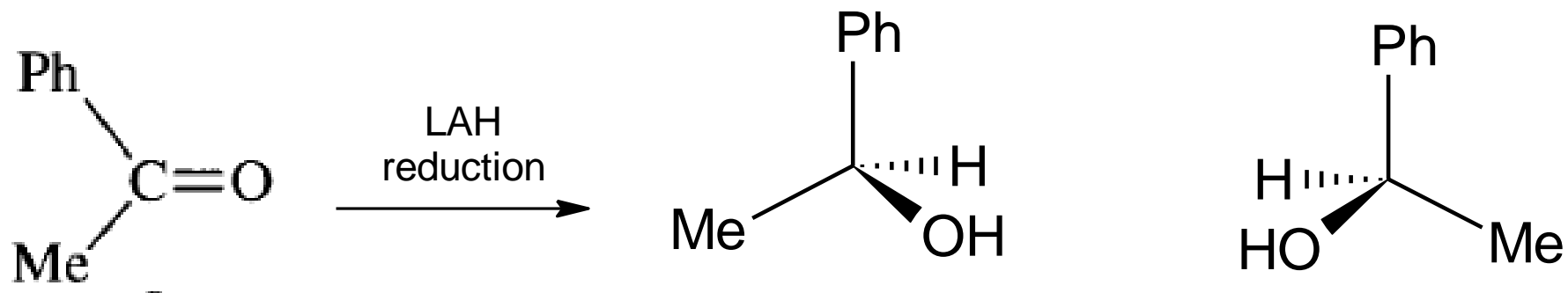
ENANTIOTOPIC FACES

- Two corresponding faces of a molecule (usually but not invariably faces of a double bond) are heterotopic when addition of the same reagent to either face gives the different product.
- If the addition give rise to enantiomers then it is called enantiotopic faces.
- For example, addition of HCN to acetaldehyde will give the different cyanohydrin, when added to different faces of sp² C-atom.

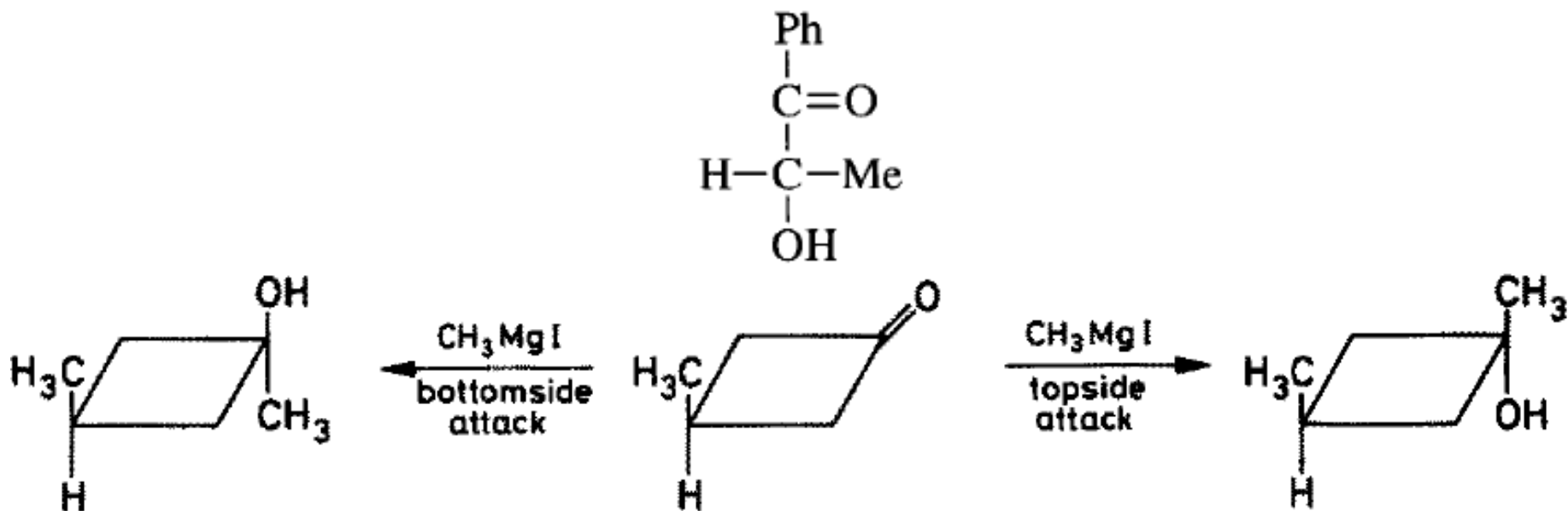
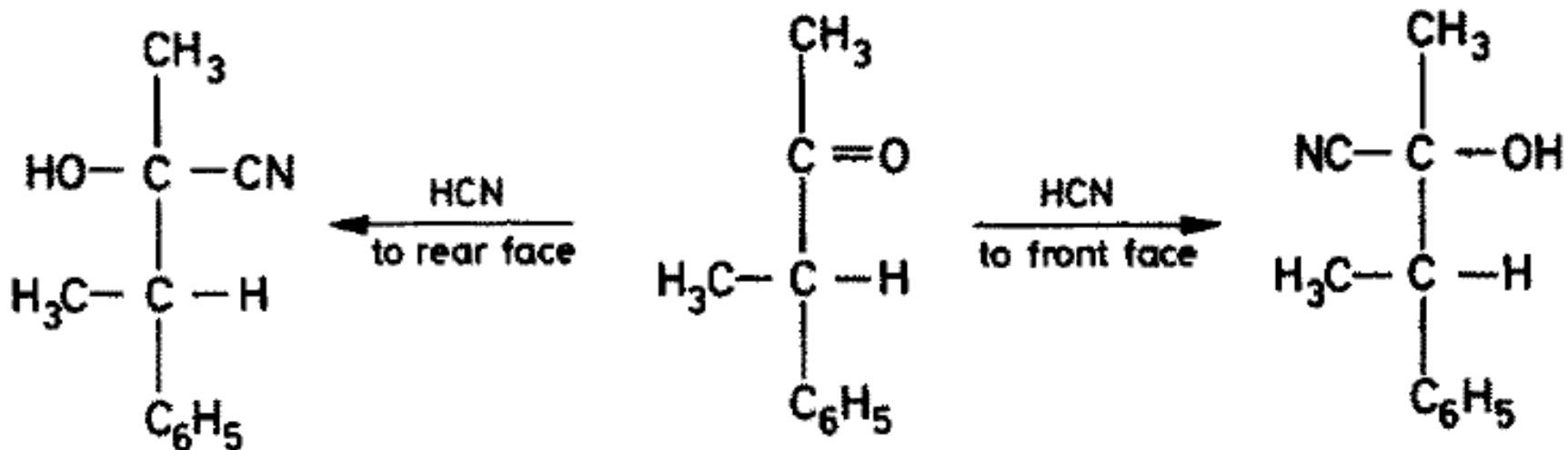


ENANTIOTOPIC FACES

- Substitution/Addition with a ligand which is not already present in the prostereogenic molecule.

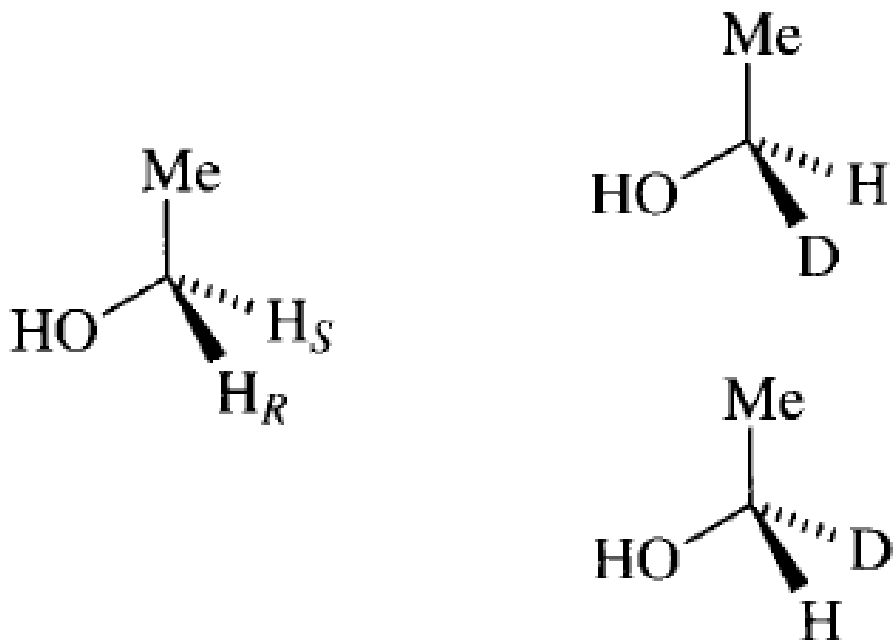


DIASTEREOTOPIC FACES



CONFIGURATIONAL DESCRIPTOR R-S FOR PROCHIRAL CENTER

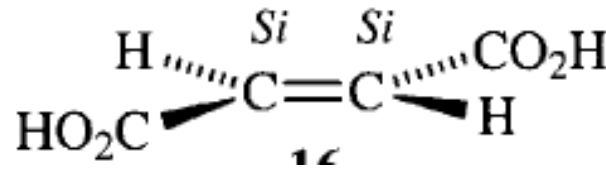
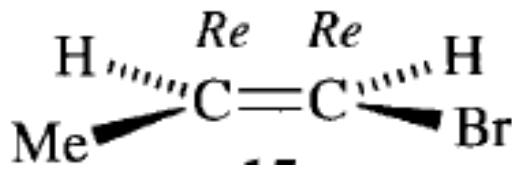
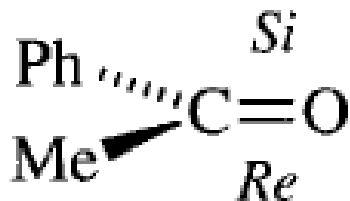
- In a molecule like ethanol, when H_R is replaced by D gives a molecule with R configuration, then hydrogen is called as **pro-R**
- Similarly, when H_S is replaced by D gives a molecule with S configuration, then hydrogen is called as **pro-S**.



CONFIGURATIONAL DESCRIPTOR R-S

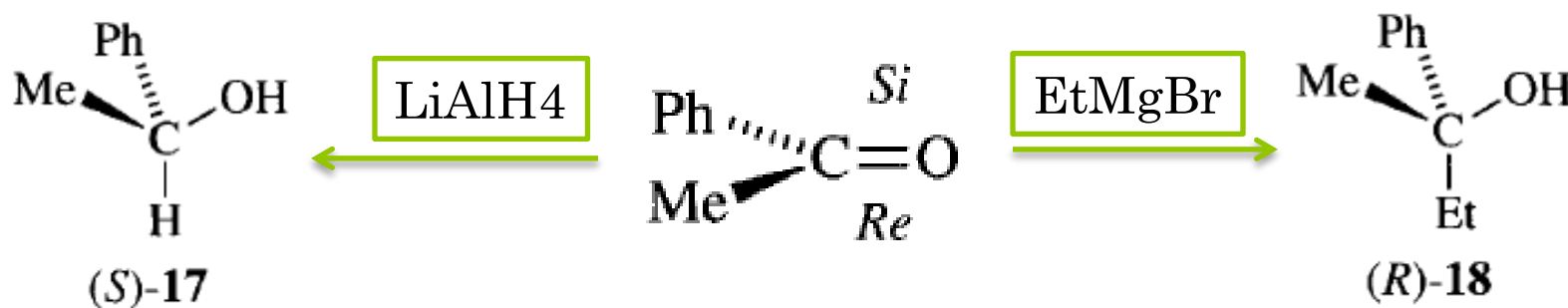
PROCHIRAL FACE

- Consider the case of phenylethanone, re-drawn in the CIP sequencing of substituents is $0 > \text{Ph} > \text{Me}$.
- One looks down on the carbonyl group from the top face, and since the priorities decrease in an anticlockwise sense, this face is described as *Si* (the first two letters of *sinister*).
- Looking at the carbonyl carbon from the bottom face, the substituent priorities decrease in a clockwise sense, and so the lower face, as drawn, of the carbonyl carbon is described as *Re* (the first two letters of *rectus*).

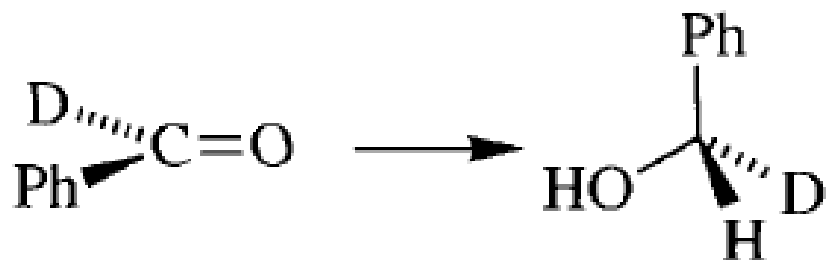
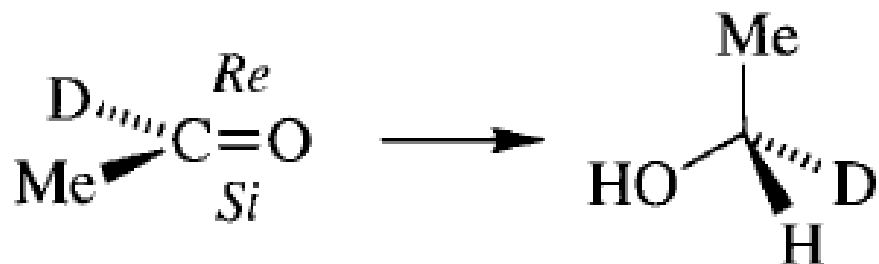


CONFIGURATIONAL DESCRIPTOR R-S FOR PROCHIRAL FACE

- Attack by LiAlH_4 , at the *Re* face will produce one enantiomer, and attack at the *Si* face will produce the other.
- There is no correlation between the configuration of the carbonyl face and that of the tetrahedral product after addition of a reagent.
- It all depends on the priority rating of the added reagent with respect to the groups in the original carbonyl compound.
- E.g. addition of LiAlH_4 to *Re* face produce (S) isomer whereas addition of EtMgBr to *Re* face produce (R) isomer.



CONFIGURATIONAL DESCRIPTOR R-S FOR PROCHIRAL FACE



PROCHIRALITY: SYMMETRY CRITERION

○ HOMOTOPIC LIGANDS

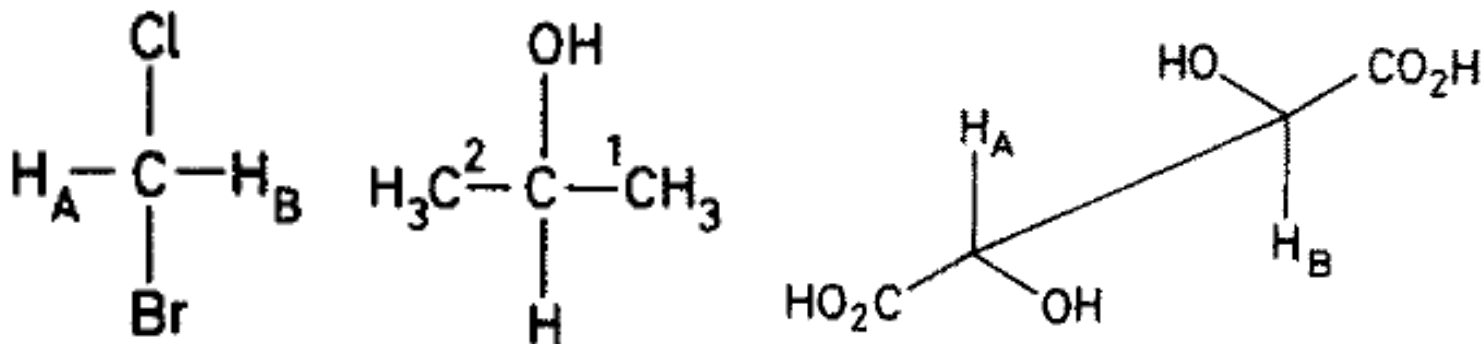
- Ligands are homotopic if they can interchange places through operation of a C_n symmetry axis.
- Thus the chlorine atoms in methylene chloride (symmetry point group C_{2v}) are homotopic since they exchange places through a 180° turn around the C_2 axis.
- Faces of double bonds are similarly homotopic when they can be interchanged by operation of a symmetry axis.

PROCHIRALITY: SYMMETRY CRITERION

○ HETEROTOPIC LIGANDS:

• ENANTIOTOPIC LIGANDS

- Enantiotopic ligands and faces are not interchangeable by operation of a symmetry element of the first kind (C , simple axis of symmetry)
- But must be interchangeable by operation of a symmetry element of the second kind (σ , plane of symmetry; i , center of symmetry or S , alternating axis of symmetry).

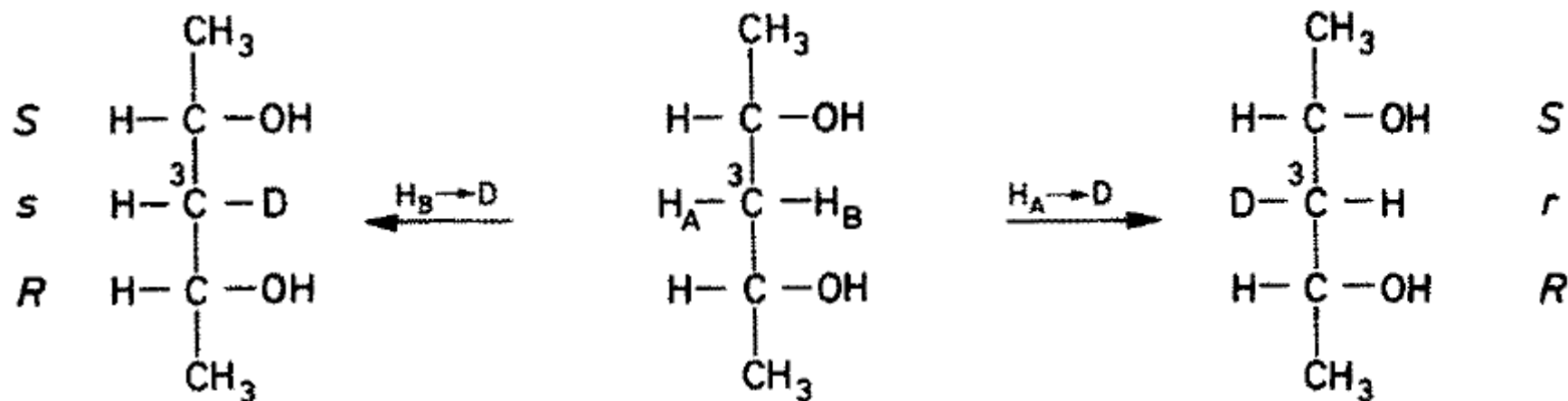


PROCHIRALITY: SYMMETRY CRITERION

- **HETEROTOPIC LIGANDS:**
 - **DIASTEREOTOPIC LIGANDS**
- The symmetry criteria of diastereotopic ligands or faces are simple:
- Such ligands or faces must be related neither by a symmetry element of the first kind (axis) nor by one of the second kind (plane, center, alternating axis).

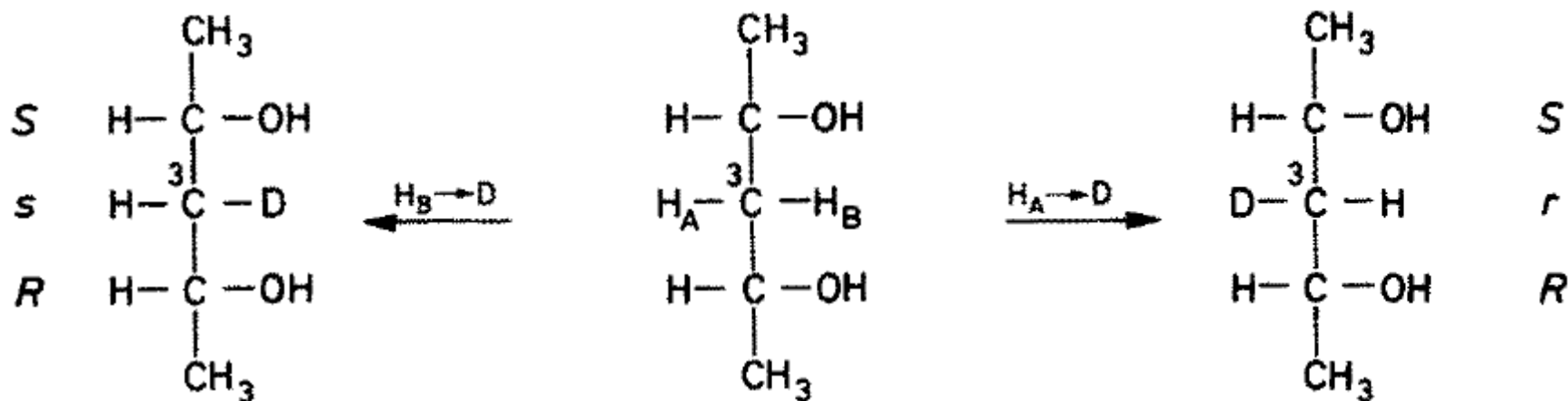
PRO-PSEUDOASYMMETRIC CENTER

- In *meso-2,4-pentanediol* the products of replacement of H_A and H_B are diastereomeric meso forms in which C(3) is pseudoasymmetric.
- C(3) in the *meso-2,4-pentanediol* molecule is called pro-pseudoasymmetric; H_A and H_B are diastereotopic.



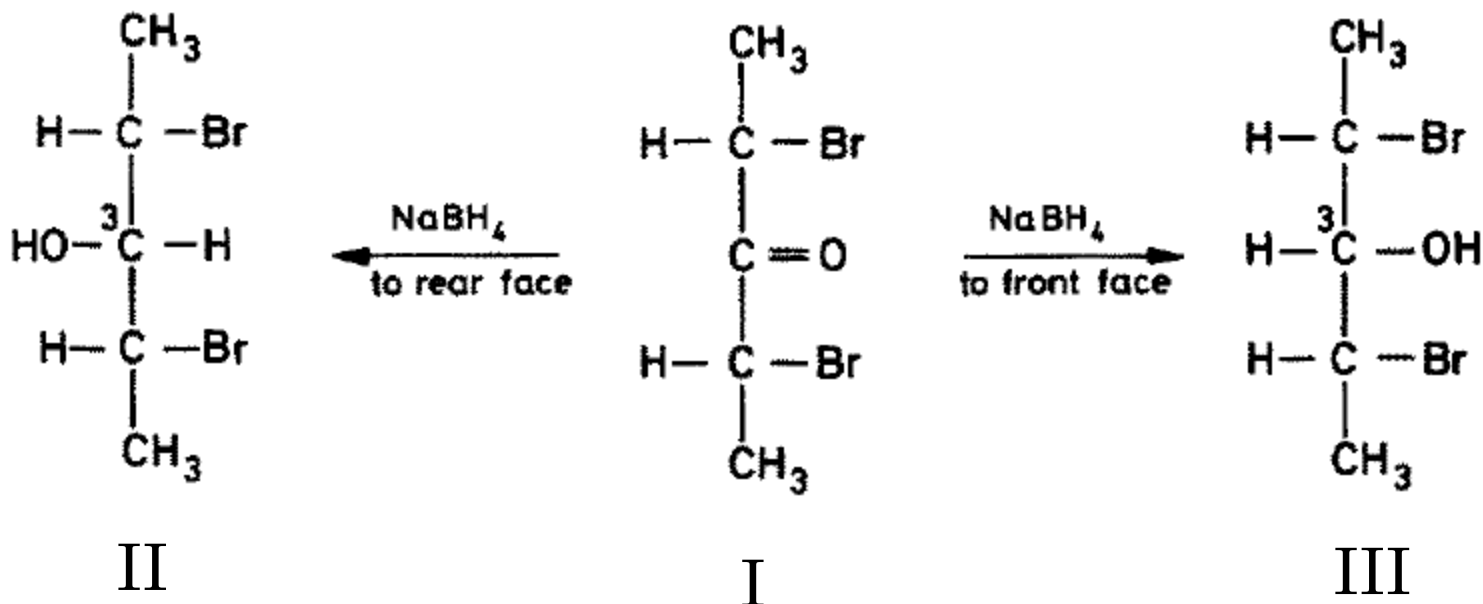
CONFIGURATIONAL DESCRIPTOR

- In pro-pseudoasymmetric center the substitution gives rise to a pseudoasymmetric center which, in the compound of the left is *s*, in the compound on the right *r*.
- Hence H_A is called *pro-r* and H_B - *pro-s*



PRO-PSEUDOASYMMETRIC CENTER

- The C = O group in I is pro-pseudoasymmetric, since C(3) in II & III is a pseudoasymmetric center.



PROCHIRAL AXIS AND PLANE

