

Asymmetric Induction

If a reaction is carried out using a chiral or optically active reagent, only one of the enantiomer or an excess of one enantiomer can be formed. This introduction of chirality or asymmetry is called asymmetric induction. In other words asymmetric induction converts a achiral reactant to a chiral product having an excess of one of the enantiomers with the help of a chiral reagent or a chiral catalyst. This principle can be used for resolving racemic mixtures into *d*-or-*l*-forms.

Asymmetric induction (also enantio induction) in stereochemistry describes the preferential formation in a chemical reaction of one enantiomer or diastereoisomer over the other as a result of the influence of a chiral feature present in the substrate, reagent catalyst or environment. Asymmetric induction is a key element in asymmetric synthesis. Several types of induction exist.

Internal asymmetric induction makes use of a chiral centre bound to the reactive centre through a covalent bond and remains so during the reaction. The starting material is often derived from chiral pool synthesis. In **relayed asymmetric induction** the chiral information is introduced in a separate step and removed again in a separate chemical reaction. Special synthons are called **chiral auxiliaries**. In **external asymmetric induction** chiral information is introduced in the transition state through a catalyst of chiral ligand. This method of asymmetric synthesis is economically most desirable.

Carbonyl 1, 2 asymmetric induction

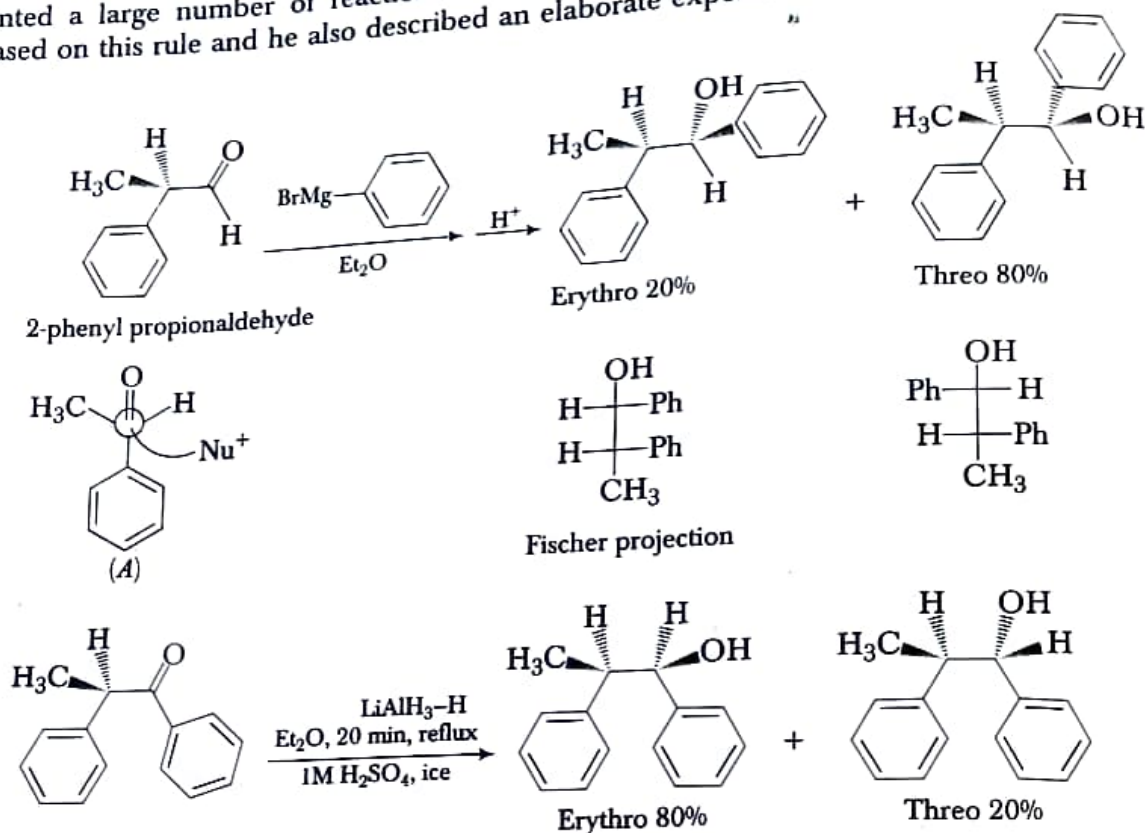
Several models exist to describe chiral induction at carbonyl carbons during nucleophilic additions. These models are based on a combination of steric and electronic considerations and are often in conflict with each other. Models have been devised by Cram (1952), Cornforth (1959), Felkin (1969) and others.

The **Cram's rule of asymmetric induction** developed by **Donald J. Cram** (1952) is an early concept relating to the prediction of stereochemistry in certain acyclic system. In full the rule is :

In certain non-catalytic reactions that diastereomer will predominate, which could be formed by the approach of the entering group from the least hindered side when the rotational conformation of the C—C bond is such that the double bond is flanked by the two least bulky groups attached to the adjacent asymmetric centre.

The rule indicates that the presence of an asymmetric centre in a molecule induces the formation of an asymmetric centre adjacent to it based on steric hindrance.

Cram presented a large number of reactions for which the conformation of the reaction products could be explained based on this rule and he also described an elaborate experiment making his case.



The experiments involved two reactions. In first experiment 2-phenylpropionaldehyde (racemic but (*R*)-enantiomer shown) was reacted with the Grignard reagent of bromobenzene to 1, 2-diphenyl-1-propanol as a mixture of diastereomers, predominantly the **threo isomer** (see for explanation the Fischer projection).

The preference for the formation of the threo isomer can be explained by the rule stated above by having the active nucleophilic in this reaction attacking the carbonyl group from the least hindered side (see Newman projection A) when the carbonyl is positioned in a staggered formation with the methyl group and the hydrogen atom, which are the two smallest substituents creating a minimum of steric hindrance, in a *gauche* orientation and phenyl as the most bulky group in the *anti*-conformation.

The second reaction is the organic reduction of 1, 2-diphenyl-1-propanone with lithium aluminium hydride, which results in the same reaction product as above but now with preference for the erythro isomer. Now, a hydride anion (H^-) is the nucleophile attacking from the least hindered side (imagine hydrogen entering from the paper plane).