

Stereospecificity and Stereoselectivity

Definitions from Stereochemistry of Organic Compounds (Eilel):

Stereoselectivity

- The preferential formation of one stereoisomer over another in a chemical reaction. If the stereoisomers are enantiomers, one speaks of enantioselectivity (quantified by ee); if they are diastereomers, one speaks of diastereoselectivity.

Stereospecific

- A reaction is termed stereospecific if, in such a reaction, starting materials differ only in their configuration are converted to stereoisomerically distinct products. According to this definition, a stereospecific process is necessarily stereoselective, but stereoselectivity does not necessarily imply stereospecificity.
- The term may be extended to a process involving a chiral catalyst, enzyme, or reagent when the configuration of the product of the reaction depends uniquely on the configuration of the catalyst or reagent., i.e. becomes reversed when a catalyst or reagent of opposite configuration is employed.

Definitions from Modern Physical Organic Chemistry (Anslyn and Dougherty):

Stereoselectivity

- A stereoselective reaction is one in which a single reactant can give two or more stereoisomeric products, and one or more of these products is preferred over the others – even if the preference is very small.

Stereospecific

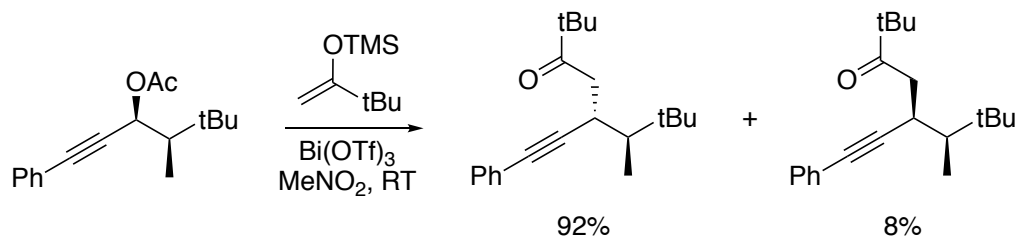
- In a stereospecific reaction, one stereoisomer of the reactant gives one stereoisomer of the product, while a different stereoisomer of the reactant gives a different stereoisomer of the product.

Steps:

1. Look at your reaction.
2. If multiple stereoisomeric products are possible, but one is produced in excess, the reaction is stereoselective.
3. Consider the stereochemical features of the reactants to determine stereospecificity or lack thereof.
 - If another stereoisomer of the reactant will give identical products in identical ratios, then the reaction is not stereospecific.
 - If a different stereoisomer of the reactant or reagent gives a stereoisomerically different product, then the reaction is stereospecific.

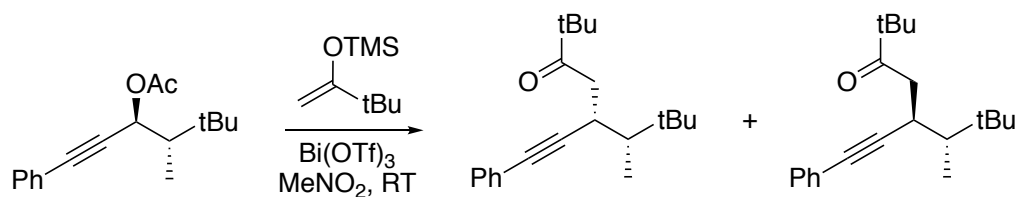
A Somewhat Tricky Example:

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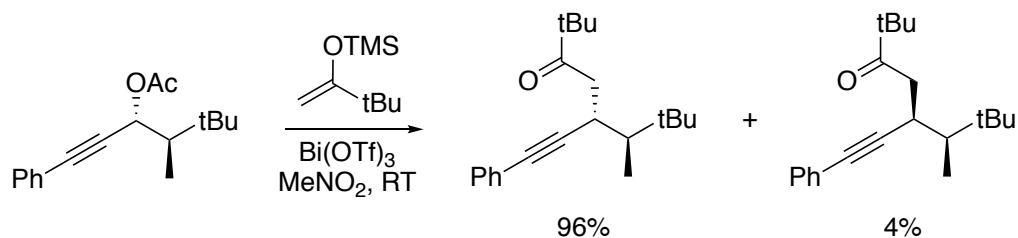


Reaction is **stereoselective** because one stereoisomer is produced in excess (**diastereoselective**)

You may be tempted to say it is also stereospecific because if another stereoisomer of the starting material were used, the reaction would give different stereoisomeric products.



But, because there is a stereoisomer of the original molecule that gives identical products in an "identical" ratio, the reaction is **not stereospecific**.



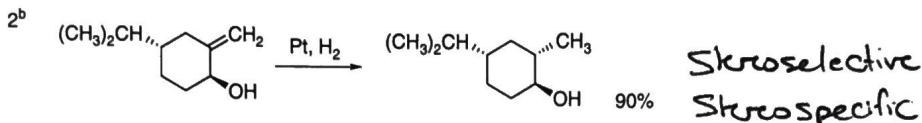
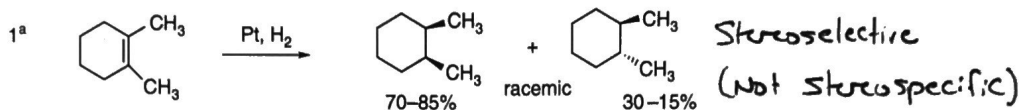
Scheme 2.6. Examples of Stereoselective Reactions

A. Catalytic Hydrogenation. (See section 2.4.1.1)

SECTION 2.4

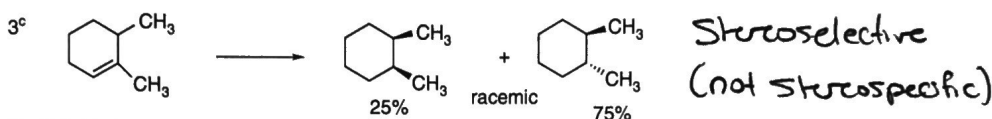
Unfunctionalized alkene usually reacts by preferential *syn* delivery of hydrogen from the less hindered face of the double bond. The degree of stereoselectivity is dependent on the reactant structure, catalysts and reaction conditions. Donor functional groups, particularly hydroxy and amino can be *syn* directive.

Stereoselective and Stereospecific Reactions



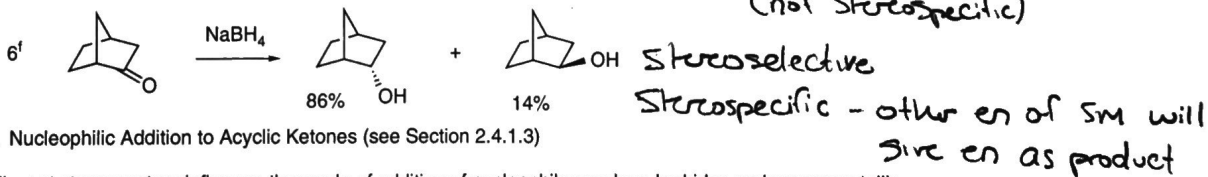
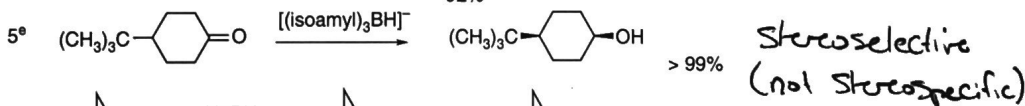
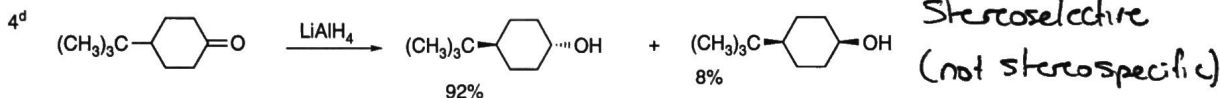
(The same article also sites other examples with low stereoselectivity.)

A representative exception.



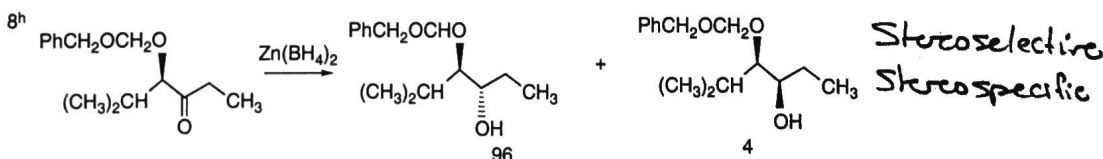
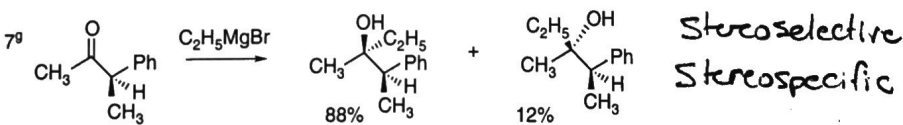
B. Hydride Reduction of Cyclic Ketones (see Section 2.4.1.2)

Unhindered cyclohexanones normally react with NaBH₄ and LiAlH₄ by preferential reagent approach from the axial direction forming mainly the equatorial alcohol. The presence of axial substituents or use of more sterically demanding reagents, such as alkylborohydrides leads to selective equatorial approach and formation of axial alcohols. Bicyclic ketones are generally reduced by hydride approach from the less hindered face of the carbonyl group.



C. Nucleophilic Addition to Acyclic Ketones (see Section 2.4.1.3)

Adjacent stereocenters influence the mode of addition of nucleophiles such as hydrides and organometallic reagents to acyclic ketones. The Felkin-Ahn transition state provides a predictive model that is general when steric effects are dominant. Other factors must be considered when polar or chelating substituents are present.



(Continued)

