

Reaction Mechanism: Structure and reactivity

Types of reactions:--

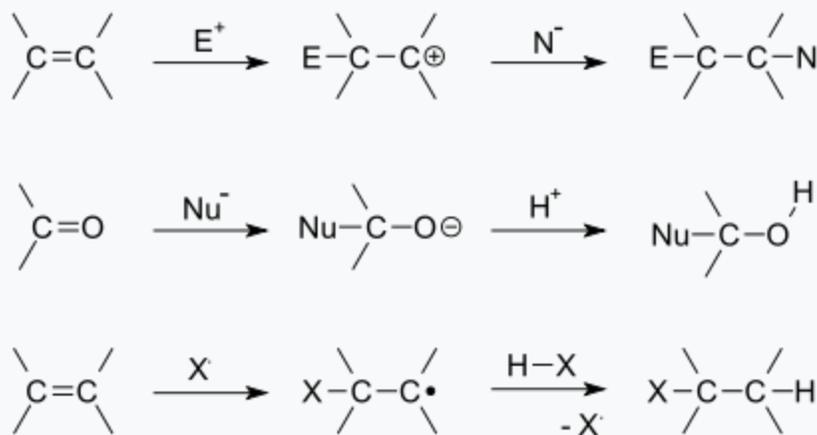
1. Addition reaction

An addition reaction, is simply termed as a reaction where two or more molecules combine to form a larger one (the adduct).

Addition reactions are limited to chemical compounds that have multiple bonds, such as molecules with carbon-carbon double bonds (alkenes), or with triple bonds (alkynes), and compounds that have rings, which are also considered points of unsaturation. Molecules containing carbon-hetero double bonds like carbonyl (C=O) groups, or imine (C=N) groups, can undergo addition, as they too have double-bond character.

An addition reaction is the reverse of an elimination reaction. For instance, the hydration of an alkene to an alcohol is reversed by dehydration.

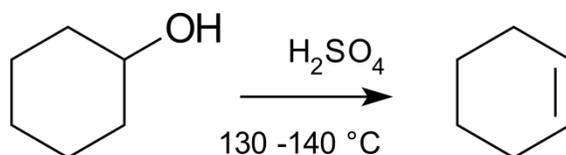
There are two main types of polar addition reactions: electrophilic addition and nucleophilic addition. Two non-polar addition reactions exist as well, called free-radical addition and cycloadditions. Addition reactions are also encountered in polymerizations and called addition polymerization.



General overview of addition reactions. Top to bottom: electrophilic addition to alkene, nucleophilic addition of nucleophile to carbonyl and free-radical addition of halide to alkene.

2. Elimination reaction

An elimination reaction is a type of reaction in which two substituents are removed from a molecule in either a one or two-step mechanism. The one-step mechanism is known as the **E2 reaction**, and the two-step mechanism is known as the **E1 reaction**. The numbers refer not to the number of steps in the mechanism, but rather to the kinetics of the reaction: E2 is bimolecular (second-order) while E1 is unimolecular (first-order). In cases where the molecule is able to stabilize an anion but possesses a poor leaving group, a third type of reaction, E1_{CB}, exists. Finally, the pyrolysis of xanthate and acetate esters proceed through an "internal" elimination mechanism, the E_i mechanism.



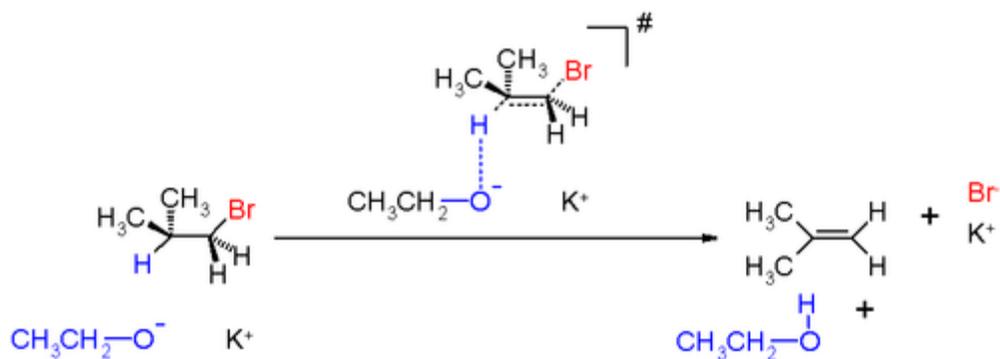
Elimination reaction of cyclohexanol to cyclohexene with sulfuric acid and heat

E2 Reaction:

E2 stands for bimolecular elimination which reaction involves a one-step mechanism in which *carbon-hydrogen* and *carbon-halogen* bonds break to form a double bond (*C=C Pi bond*).

The characteristics of the reaction are as follows:

- E2 is a single step elimination, with a single transition state.
- It is typically undergone by primary substituted alkyl halides, but is possible with some secondary alkyl halides and other compounds.
- The reaction rate is second order, because it's influenced by both the alkyl halide and the base (bimolecular).
- Because the E2 mechanism results in the formation of a pi bond, the two leaving groups (often a hydrogen and a halogen) need to be antiperiplanar due to which transition state has staggered conformation with lower energy .
- E2 typically uses a strong base. It must be strong enough to remove a weakly acidic hydrogen.
- In order for the pi bond to be created, the hybridization of carbons needs to be lowered from sp^3 to sp^2 .
- E2 competes with the S_N2 reaction mechanism if the base can also act as a nucleophile (true for many common bases).



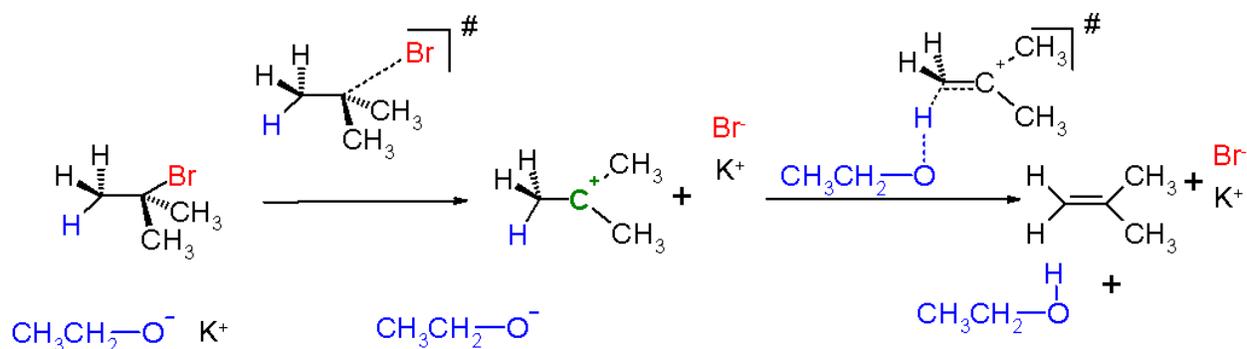
An example of this type of reaction is the reaction of isobutyl bromide with potassium ethoxide in ethanol. The reaction products are isobutylene, ethanol and potassium bromide.

E1 Reaction:

E1 stands for unimolecular elimination and it is a two-step process of elimination which involves *ionization* of the carbon-halogen bond breaks to give a carbocation intermediate *and deprotonation*.

The characteristics of the reaction are as follows:

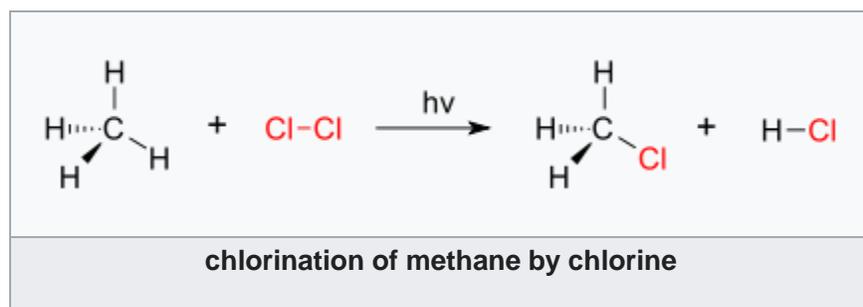
- E1 typically takes place with tertiary alkyl halides, but is possible with some secondary alkyl halides.
- The reaction rate is influenced only by the concentration of the alkyl halide because carbocation formation is the slowest step, as known as the rate-determining step. Therefore, first-order kinetics apply (unimolecular).
- The reaction usually occurs in the complete absence of a base or the presence of only a weak base (acidic conditions and high temperature).
- E1 reactions are in competition with S_N1 reactions because they share a common carbocationic intermediate.



3. Substitutions Reactions

Substitution reaction is a chemical reaction during which one functional group in a chemical compound is replaced by another functional group

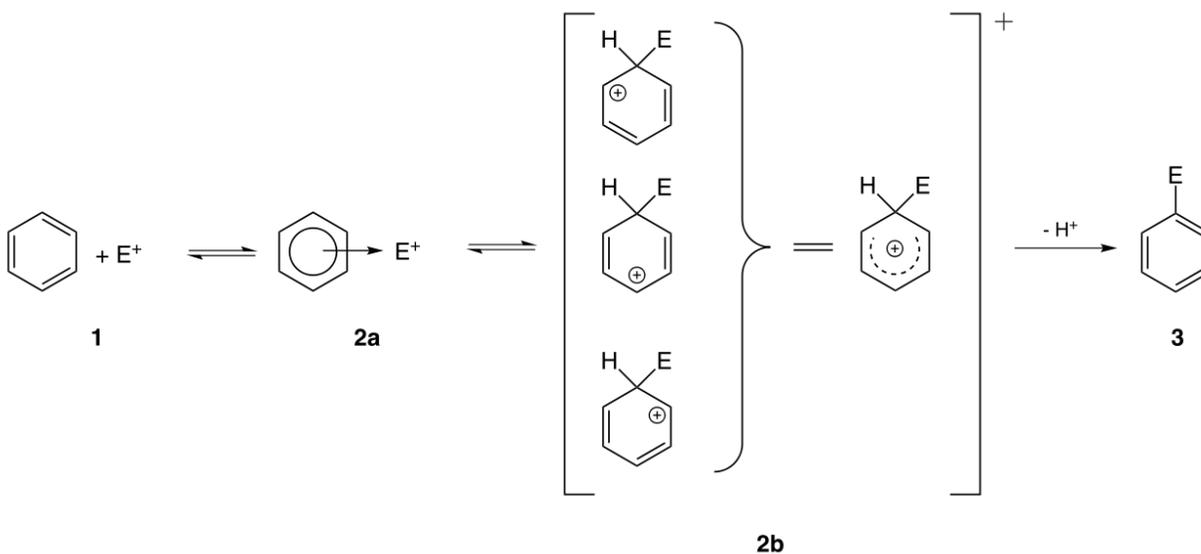
A good example of a substitution reaction is halogenation. When chlorine gas (Cl_2) is irradiated, some of the molecules are split into two chlorine radicals. One of them breaks a C–H covalent bond in CH_4 and grabs the hydrogen atom to form the electrically neutral HCl . The other radical reforms a covalent bond with the $\text{CH}_3\cdot$ to form CH_3Cl (methyl chloride).



Substitutions reactions are classified broadly into two types:

Electrophilic substitutions and Nucleophilic substitutions

Electrophilic substitutions:- Common example of this category is the aromatic electrophilic substitutions.



Electrophilic aromatic substitution

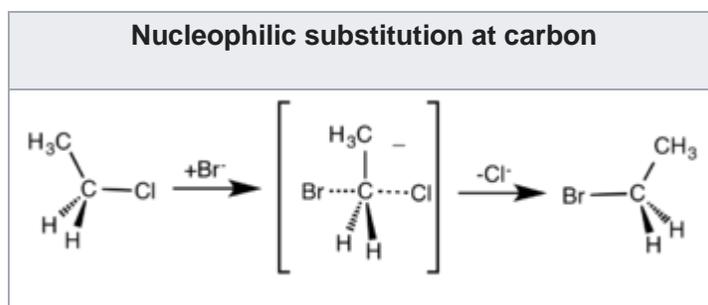
Nucleophilic substitution

Nucleophilic substitution is a fundamental class of reactions in which a leaving group is replaced by an electron rich compound(nucleophile).

S_N2 reactions

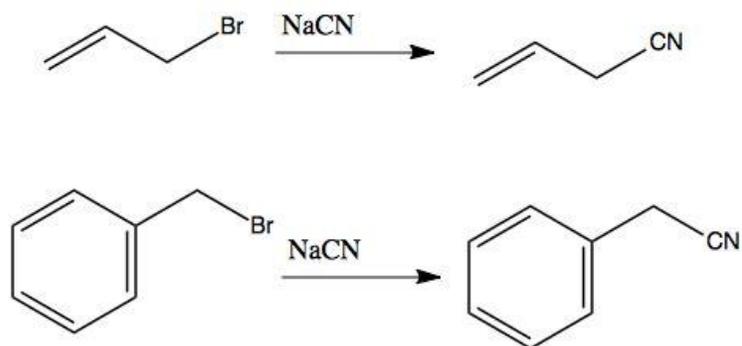
Hughes and Sir Christopher Ingold studied nucleophilic substitution reactions of alkyl halides and related compounds and they proposed two main mechanisms are the S_N1 reaction and the S_N2 reaction. S stands for chemical substitution, N stands for nucleophilic, and the number represents the kinetic order of the reaction.

In the S_N2 reaction, the addition of the nucleophile and the elimination of leaving group take place simultaneously (i.e. concerted reaction). S_N2 occurs where the central carbon atom is easily accessible to the nucleophile.



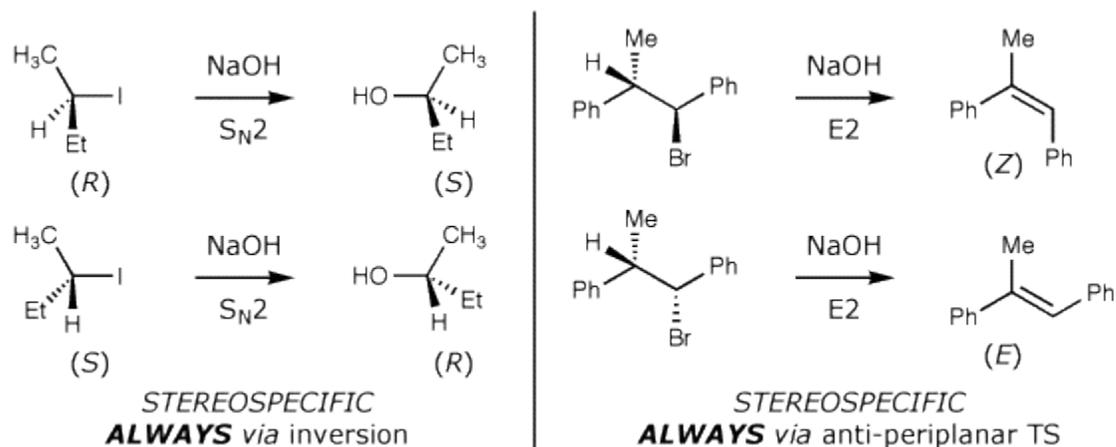
In S_N2 reactions, there are a few conditions that affect the rate of the reaction. First of all, the 2 in S_N2 implies that there are two concentrations of substances that affect the rate of reaction: substrate and nucleophile. The rate equation for this reaction would be $\text{Rate} = k[\text{Sub}][\text{Nuc}]$. For a S_N2 reaction, an aprotic solvent is best, such as acetone, DMF, or DMSO.

Since this reaction occurs in one step, steric effects drive the reaction speed. In the intermediate step, the nucleophile is 180 degrees from the leaving group and the stereochemistry is inverted as the nucleophile bonds to make the product. Also, because the intermediate is partially bonded to the nucleophile and leaving group, there is no time for the substrate to rearrange itself: the nucleophile will bond to the same carbon that the leaving group was attached to. A final factor that affects reaction rate is nucleophilicity; the nucleophile must attack an atom other than a hydrogen.



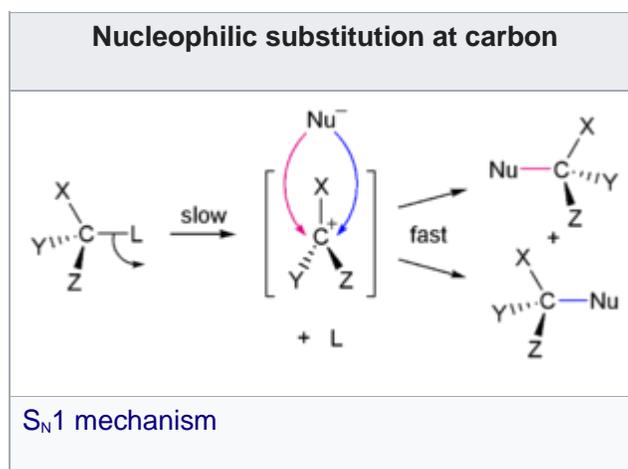
SN2 Reaction

SN2 reactions are always stereospecific in nature



S_N1 reactions

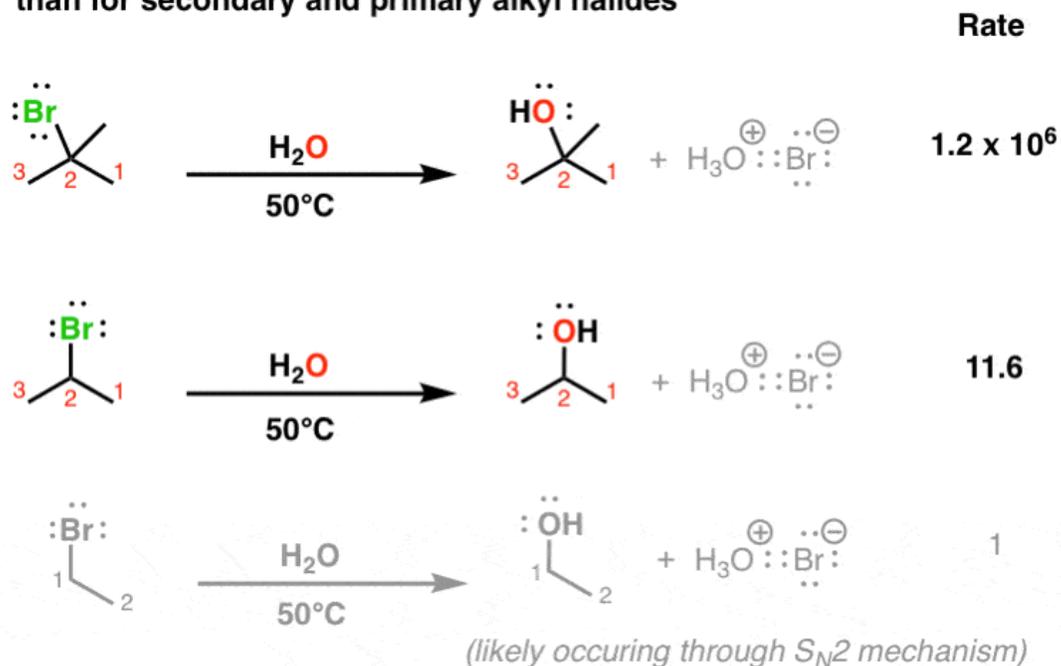
S_N1 reaction involves two steps and it is preferable when the central carbon atom of the substrate is surrounded by bulky groups, because such groups interfere sterically with the S_N2 reaction and because a highly substituted carbon forms a stable carbocation.



The rate equation for this would be $\text{Rate} = k[\text{Sub}]$. Since the rate of a reaction is only determined by its slowest step, the rate at which the leaving group "leaves" determines the speed of the reaction. This means that the

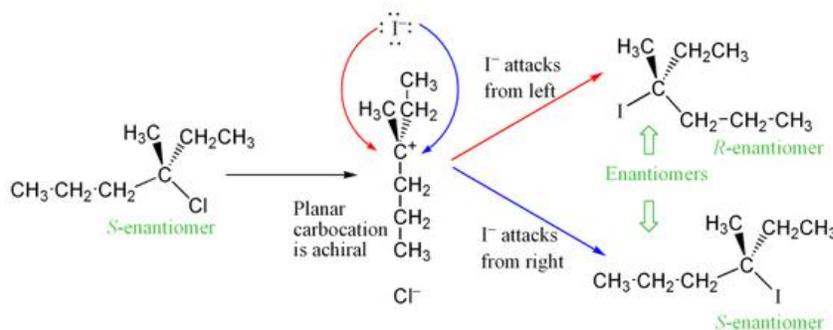
better the leaving group, the faster the reaction rate. A general rule for what makes a good leaving group is the weaker the conjugate base, the better the leaving group.

The reaction rate is dramatically higher for tertiary alkyl halides than for secondary and primary alkyl halides

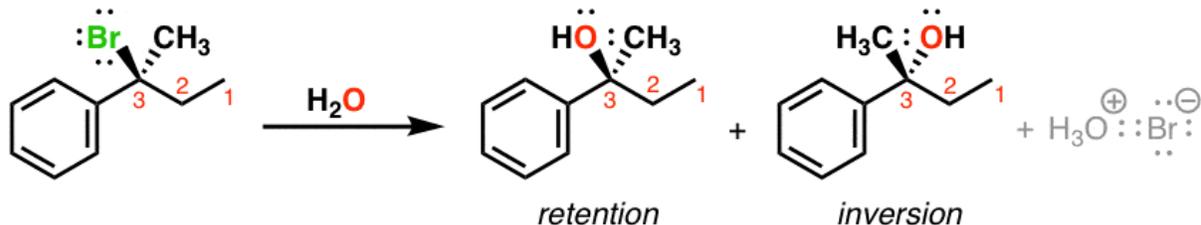


From "March's Advanced Organic Chemistry", 5th Ed. p. 431

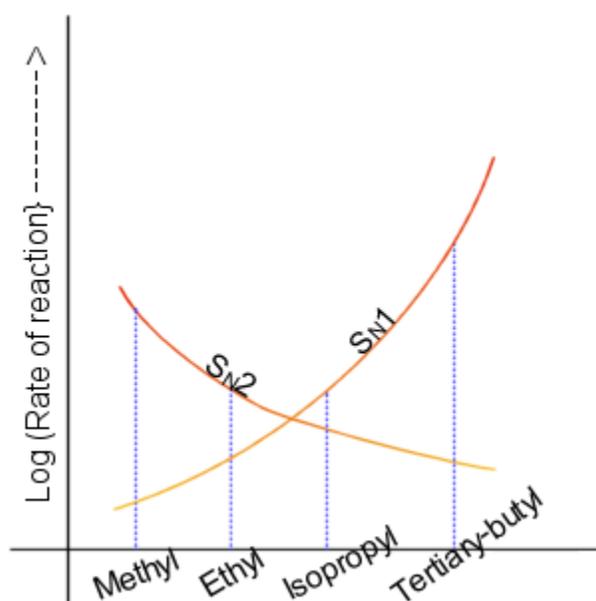
S_N1 is also stereospecific in nature



Substitution occurs with a mixture of retention and inversion at a stereocenter



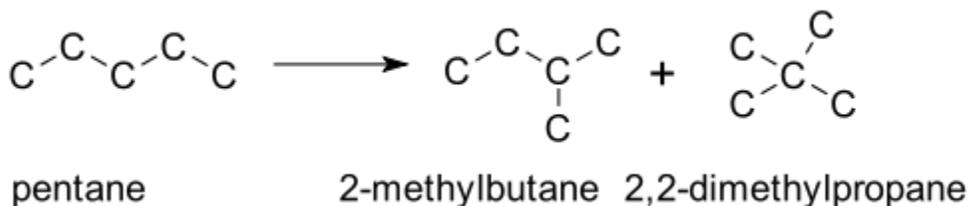
A graph showing the relative reactivities of the different alkyl halides towards $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ reactions



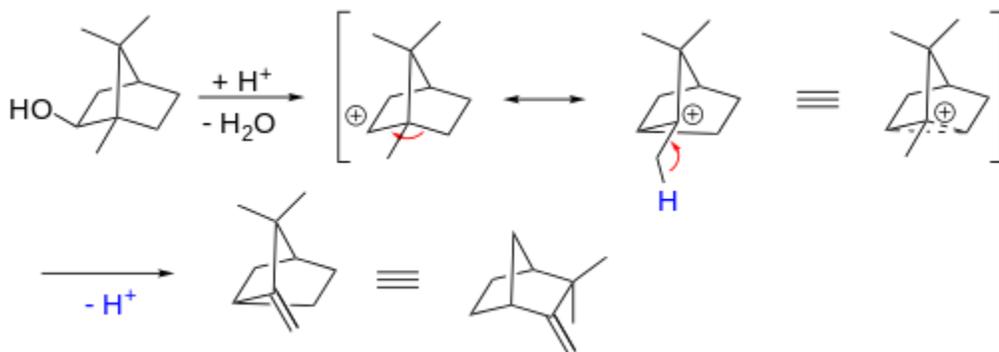
4. Rearrangement reaction

A rearrangement reaction is a broad class of organic reactions where the carbon skeleton of a molecule is rearranged to give a structural isomer of the original molecule. Often a substituent moves from one atom to another atom in the same molecule.

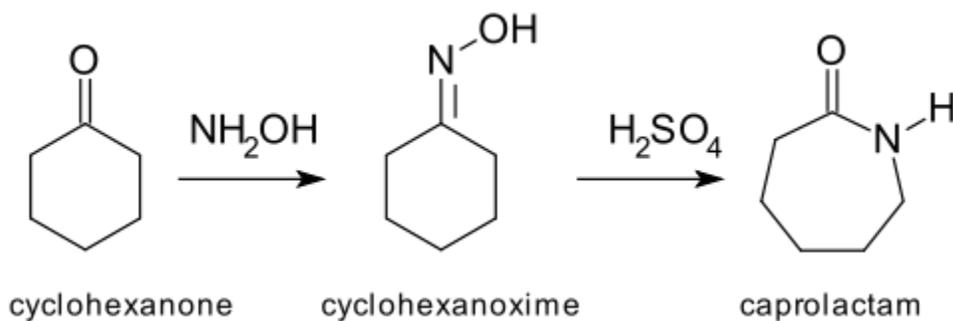
Isomerisation of n-butane to isobutane and pentane to isopentane



Common examples are the Wagner-Meerwein rearrangement:



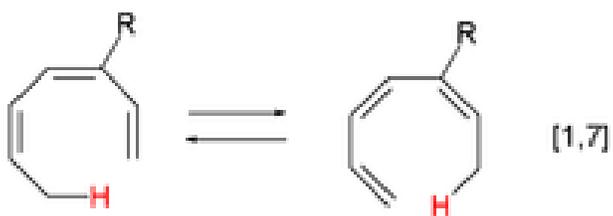
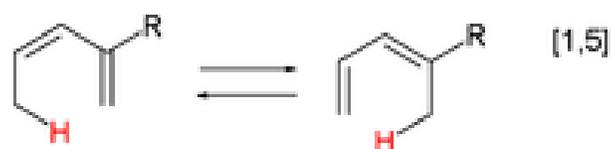
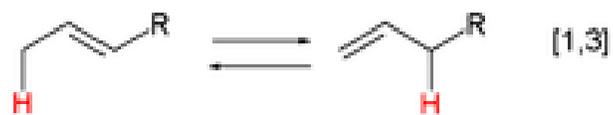
Beckmann rearrangement, which is relevant to the production of certain nylons:



Pericyclic reaction

A pericyclic reaction is a type of rearrangement reaction with multiple carbon-carbon bond making and breaking wherein the transition state of

the molecule has a cyclic geometry, and the reaction progresses in a concerted fashion.



Claisen rearrangement:

