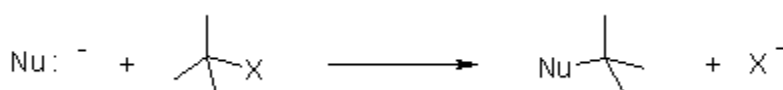


NUCLEOPHILIC SUBSTITUTION REACTIONS

DEFINITION:

Those reactions in which an atom or group of atoms in a molecule is substituted by a nucleophile are called nucleophilic substitution reactions. It is denoted by S_N where S stands for substitution and N for nucleophilic.

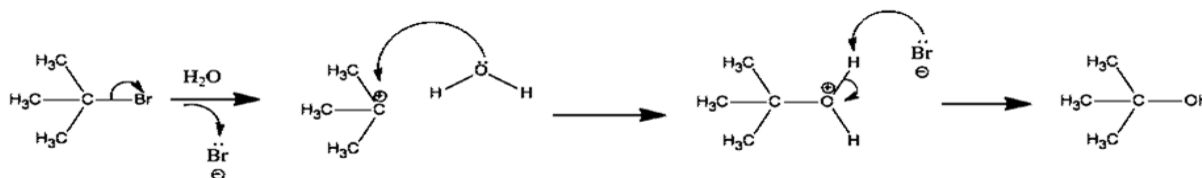
Aliphatic Nucleophilic Substitution (S_N1 S_N2)



Nucleophile *Substrate* *product* *leaving group*

Basically it is the reaction of an electron pair donor (the nucleophile, Nu) with an electron pair acceptor (the electrophile). A sp^3 hybridized electrophile must have a leaving group (X) in order for the reaction to take place.

The alkyl halides are good substrates for nucleophilic substitution reactions because the halide ion is a good leaving group and therefore can be readily substituted by a nucleophile. Since the alkyl group at which substitution takes place is generally aliphatic in nature, these reactions are commonly known as **aliphatic nucleophilic substitutions**. Sometimes, the solvent itself act as nucleophile; the reaction is then called *solvolysis*. Thus a reaction in which water is used as solvent and it also act as nucleophile, is called *hydrolysis*, while a reaction involving methanol as a solvent and also as a nucleophile, is known as *methanolysis*.



Types

There are two types of substitution reactions.

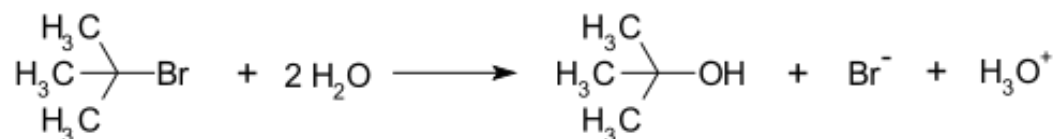
- 1) S_N1 reactions
- 2) S_N2 reactions

S_N1 Reaction:

The substitution nucleophilic unimolecular reactions are called S_N1 reactions. S_N1 reaction consists of two steps. The first step involves slow ionization of the substrate (alkyl halide) resulting in the formation of a carbocation that rapidly combines with the nucleophile to form the product in the second step. Mostly the solvent itself acts as nucleophile. The S_N1 reaction is generally called solvolysis.

Reaction Mechanism:

Hydrolysis of *tert*-butylbromide with water forming *tert*-butanol is an example of a reaction taking place with an S_N1 reaction mechanism.

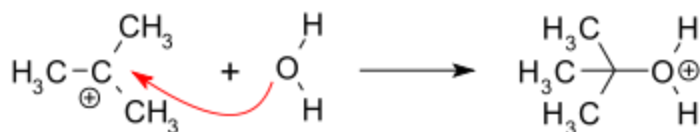


This S_N1 reaction takes place in three steps:

- Formation of a *tert*-butyl carbocation by separation of a leaving group (a bromide anion) from the carbon atom: this is a slow and reversible step



- Nucleophilic Attack: the carbocation reacts with the nucleophile (Nu). If the Nu is a neutral molecule (i.e. a solvent) a third step is required to complete the reaction. When the solvent is water, the intermediate is an oxonium ion. This reaction step is fast.



- Deprotonation: Removal of a proton on the protonated nucleophile by water acting as a base forming the alcohol and a hydronium ion. This reaction step is fast.



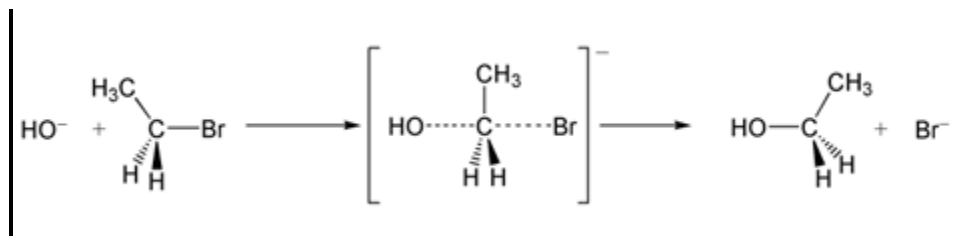
S_N2 Reaction:

The S_N2 reaction (also known as bimolecular nucleophilic substitution) is a type of nucleophilic substitution in which bond making and breaking occurs simultaneously. In S_N2 reaction a lone pair from a nucleophile attacks an electron deficient electrophilic carbon of alkyl halide and bonds to it, expelling another group called a leaving group. Thus the incoming group replaces the leaving group in one step. Since two reacting species are involved in the slow, rate-determining step of the reaction, this leads to the name bimolecular nucleophilic substitution, or S_N2. Among inorganic chemists, the S_N2 reaction is often known as the interchange mechanism.

Reaction mechanism:

The reaction most often occurs at an aliphatic sp³ carbon center with an electronegative stable leaving group attached to it - 'X' - frequently a halide atom. The breaking of the C-X bond and the formation of the new C-Nu bond occur simultaneously to form a transition state in which the carbon under nucleophilic attack is penta coordinate, and approximately sp² hybridised. The nucleophile attacks the carbon at 180° to the leaving group, since this provides the best overlap between the nucleophile's lone pair and the C-X σ* antibonding orbital. The leaving group is then pushed off the opposite side and the product is formed.

In an example of the S_N2 reaction, the attack of OH^- (the nucleophile) on a bromoethane (the electrophile) results in ethanol, with bromide ejected as the leaving group:



S_N2 reaction of bromoethane with hydroxide ion.

Primary alkyl halides follow S_N2 mechanism since it is not sterically hindered by bulky groups on the substrate. Therefore this mechanism usually occurs at an unhindered primary carbon centre.

Reactivity of S_N reactions:

We have considered two pathways i.e., S_N1 and S_N2 that are generally involved in the aliphatic nucleophilic substitution reactions. Which of these pathways is followed by a particular reaction, and at what rate, depends on the following factors

- 1) The substrate
- 2) The nucleophile
- 3) The leaving group
- 4) The solvent