Nucleophilic Substitution Reactions - SN2 Reaction:

- **Reaction is:**
  - Stereospecific (Walden Inversion of configuration)
  - Concerted - all bonds form and break at same time
  - Bimolecular - rate depends on concentration of both nucleophile and substrate

- **Substrate:**
  - Best if primary (one substituent on carbon bearing leaving group)
  - works if secondary, fails if tertiary

- **Nucleophile:**
  - Best if more reactive (i.e. more anionic or more basic)

- **Leaving Group:** Best if more stable (i.e. can support negative charge well):
  - TsO- (very good) > I- > Br- > Cl- > F- (poor)
  - RF, ROH, ROR, RNH2 are NEVER Substrates for SN2 reactions
  - Leaving Groups on double-bonded carbons are never replaced by SN2 reactions

- **Solvent:** Polar Aprotic (i.e. no OH) is best.
  - For example dimethylsulfoxide (CH3SOCH3), dimethylformamide (HCON(CH3)2), acetonitrile (CH3CN).
  - Protic solvents (e.g. H2O or ROH) deactivate nucleophile by hydrogen bonding but can be used in some case
Nucleophilic Substitution Reactions – SN1 Reaction:

- **Reaction is:**
  - Non-stereospecific (attack by nucleophile occurs from both sides)
  - Non-concerted - has carbocation intermediate
  - Unimolecular - rate depends on concentration of only the substrate

- **Substrate:**
  - Best if tertiary or conjugated (benzylic or allylic) carbocation can be formed as leaving group departs
  - Never primary

- **Nucleophile:**
  - Best if more reactive (i.e. more anionic or more basic)

- **Leaving Group:**
  - Same as SN2
  - Best if more stable (i.e. can support negative charge well)
  - Examples: TsO- (very good) > I- > Br- > Cl- > F- (poor)
  - However, tertiary or allylic ROH or ROR' can be reactive under strongly acidic conditions to replace OH or OR

- **Solvent:**
  - Same as SN2
  - Polar Aprotic (i.e. no OH) is best
  - Examples: dimethylsulfoxide (CH₃SCH₃), dimethylformamide (HCON(CH₃)₂), acetonitrile (CH₃CN).
  - Protic solvents (e.g. H₂O or ROH) deactivate but can be used in some cases
Elimination Reactions - E2 Reaction:

- Reaction is:
  - Stereospecific (Anti-periplanar geometry preferred, Syn-periplanar geometry possible)
  - Concerted - all bonds form and break at the same time
  - Bimolecular - rate depends on concentration of both base and substrate
  - Favoured by strong bases

Elimination Reactions – E1 Reaction:

- Reaction is:
  - Non-stereospecific- follows Zaitsev (Saytseff) Rule
  - Non-concerted - has carbocation intermediate - favoured for tertiary leaving groups
  - Unimolecular - rate depends on concentration of only the substrate
  - Does NOT occur with primary alkyl halides (leaving groups)
  - Strong acid can promote loss of OH as H₂O or OR as HOR if tertiary or conjugated carbocation can be formed