

FACTORS AFFECTING THE RATE OF S_N2 REACTIONS

1. Strength of the nucleophile – there are three important trends:
 - 1) For similar species, the species with negative charge is always a stronger nucleophile than a neutral species.
 - 2) A more electronegative element holds more tightly its valence electrons, which makes it a weaker nucleophile. **Hence, from left to right within a row of the periodic table nucleophilic strength decreases.**
 - 3) Larger atoms are more *polarizable*, i.e. their electron clouds are more “flexible”, which makes the approach to substrate and the bonding an overall energetically easier process. **Hence, from top to bottom within a group in the periodic table the nucleophilic strength increases.** Also notice that in the same direction electronegativity decreases too, which contributes additionally towards an increased strength of the nucleophile.
2. Solvent effect on the nucleophile – there are three distinct cases:
 - 1) Polar protic solvents – usually have O – H or N – H bonds (capable of hydrogen bonding!!). Their effect is particularly adverse in the case of a negatively charged nucleophile (which is the most common case). The solvent forms loose hydrogen bonds with the nucleophile, reducing substantially the latter’s reactivity (You have to realize that in order for the nucleophile to react, it has to get rid of that solvent “coating”). This is particularly true for small, negatively charged nucleophiles, in which the negative charge is highly “concentrated” in a small amount of space. Larger anions have their charges more diffused and delocalized, which reduces the strength of interaction with the solvent. **Conclusion: Polar protic solvents tend to slow down substitution with negatively charged nucleophiles, particularly with smaller ones.**
 - 2) Polar aprotic solvents – they have highly polar bonds, but they are not O – H or N – H, and thus are incapable of interacting with negatively charged nucleophiles. But they do solvate strongly the positive counter-ion, producing essentially “free” anion nucleophiles, whose reactivity is even higher. **Conclusion: Polar aprotic solvents tend to accelerate substitution with negatively charged nucleophiles.**
 - 3) Nonpolar solvents – they do not have any unfavorable interactions with the nucleophile, but because of their nonpolar nature, majority of nucleophiles tend to be insoluble in them, and this constitutes the major obstacle.
3. Steric effect – because of the specific requirement in S_N2 reactions, that the nucleophile must closely approach the substrate in order for a reaction to occur, steric effects, resulting both from the structure of the nucleophile and the substrate, tend to play a very important role.
 - 1) Steric bulk of the nucleophile – for similar species (e.g. alkoxide anions) the rate of substitution diminishes with an increased size of the nucleophile.
 - 2) Steric effects in the substrate – the more substituted the carbon center is, the lower the rate of substitution. Reason: The TS is the most crowded species on the entire pathway from reactants to products. Therefore steric congestion will have a pronounced effect on the energy of the TS. For tertiary substrates its energy is considerably higher. Important exception: The so-called neopentyl type substrates. They are primary, but the alkyl substituent is particularly large, and has an even greater effect than three smaller alkyl groups.
4. Leaving group effect – as in the case of the nucleophile, there are three distinct trends:
 - 1) The more electronegative the leaving group is, the more it would polarize the carbon – leaving group bond, making the carbon atom more susceptible for an attack by a nucleophile. **Conclusion: From left to right within a row of the periodic table the leaving groups become better.**
 - 2) Stability of the leaving group – once it has left the substrate, it should be stable, i.e. a weak base. If it is a strong base (reactive) it would tend to re-connect with the carbon, driving constantly the equilibrium towards reactants. **Conclusion: The conjugate bases of strong acids are good leaving groups. The conjugate bases of weak acids**

are poor leaving groups. Practical trick: A poor leaving group can often be converted to a good leaving group by protonation since protonated species are much weaker bases.

- 3) Polarizability – very similar to the case of nucleophile. After all, we should realize that the departure of the leaving group is exactly like the entrance of the nucleophile, but in reverse order. **Conclusion: From top to bottom of the periodic table the leaving groups become better.**

TERMINOLOGY:

NUCLEOPHILE – a species (a molecule or an ion), which possesses and can donate an electron pair to an electrophilic carbon center

BASE – a species (a molecule or an ion), which possesses and can donate an electron pair to an electrophilic hydrogen center (we call it: which can abstract a proton)

ELECTROPHILE – a species (a molecule or an ion), which can accept a pair of electrons

LEAVING GROUP – the species (a molecule or an ion), which departs the substrate as a result of an attack by the nucleophile

BASICITY – the ability of a base to abstract a proton. It is defined by the equilibrium constant for the process of abstraction of proton

NUCLEOPHILICITY – the ability of the nucleophile to attack an electrophilic carbon center. It is defined by the rate constant of the reaction of attack of the nucleophile on the electrophilic carbon atom

POLAR PROTIC SOLVENT – a polar solvent that contains O – H and N – H bonds and is capable of making hydrogen bonds

POLAR APROTIC SOLVENT – a polar solvent that does not have O – H or N – H groups and is therefore incapable of making hydrogen bonds

STRONG NUCLEOPHILE – WEAK NUCLEOPHILE

GOOD LEAVING GROUP – POOR LEAVING GROUP (not bad leaving group)

HIGH ENERGY – LOW ENERGY (not big energy – small energy)