

SUBSTITUTION VERSUS ELIMINATION

1. Strong nucleophile and a methyl substrate: S_N2 reaction.
2. Strong nucleophile (base) and primary substrate (1°): An S_N2 reaction is most likely. Some E2 product might be obtained as well.
3. Strong nucleophile (base) and secondary substrate (2°): Both S_N2 and E2 reactions will occur and a mixture of substitution and elimination products is likely. Difficult to predict whether S_N2 or E2 will predominate.
4. Strong nucleophile (base) and tertiary substrate (3°): An E2 reaction. S_N2 does not occur since substrate is too sterically hindered.
5. Weak nucleophile (base) and methyl substrate: No reaction.
6. Weak nucleophile (base) and primary substrate (1°): No reaction. EXCEPTION: If the primary substrate can undergo a concerted process of ionization + rearrangement to give a more stable carbocation (as is the case with neopentyl substrates), then the outcome is a mixture of S_N1 and E1.
7. Weak nucleophile (base) and secondary substrate (2°): Both S_N1 and E1 will occur and a mixture of substitution and elimination products is likely.
8. Weak nucleophile (base) and tertiary substrate (3°): Both S_N1 and E1.

ONE GENERAL CONCLUSION: With strong nucleophiles (bases) the reactions occur via bimolecular mechanism: S_N2 or E2. With weak nucleophiles (bases) the reactions occur via monomolecular mechanism: S_N1 or E1.

9. Temperature of the reaction: Increase of temperature favors elimination. Reason: Elimination starts with two species (base and substrate) but produces three (the conjugate acid of the starting base, an alkene molecule and the leaving group). This increased number of molecules (or ions) causes an increase of entropy, i.e. a positive entropy change (ΔS). This in its turn increases the favorable contribution of the $T\Delta S$ -term in the overall Gibbs free energy change (because $\Delta G = \Delta H - T\Delta S$), making the Gibbs free energy change more negative.
10. Steric bulk of the nucleophile (base): In concerted reactions (S_N2 or E2) the nucleophile (base) participates in the rate-determining step. It has to approach closely the molecule and attack the electrophilic carbon center (then it is a nucleophile) or the proton at an adjacent carbon (then it is a base). Approaching closely the carbon center is more sensitive to changes of size. That is why the share (percentage) of elimination increases with an increasing size of the nucleophile (base).

STRONG NUCLEOPHILES: ^-OR , ^-OH , ^-CN , ^-SH , I^- , R_2NH , R_3N

WEAK NUCLEOPHILES: ROH , H_2O , F^-

MODERATE NUCLEOPHILES (of intermediate strength): Br^- , Cl^- , NH_3 , $RCOO^-$

GOOD LEAVING GROUPS: Cl , Br , I , $^+OH_2$, ^+O-R , $^+NR_3$

POOR LEAVING GROUPS: OH , OR , NR_2

POLAR PROTIC SOLVENTS: water, alcohols (CH_3OH , C_2H_5OH , etc.)

POLAR APROTIC SOLVENTS: acetone, acetonitrile, dimethylsulfoxide, dimethylformamide