

Nucleophilic Substitution Bimolecular (S_N2)

Study Material for the classes on S_N1 and S_N2

✓ ***Chapter-Nucleophilic Substitution at Saturated Carbon***

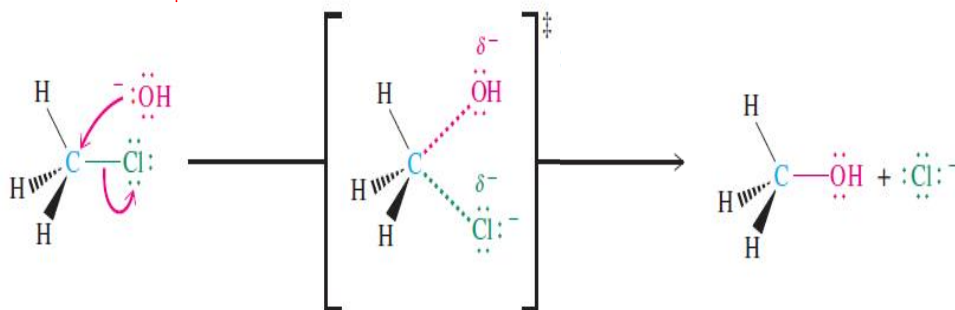
(Clayden Warren)

✓ ***I will also provide a classnote***

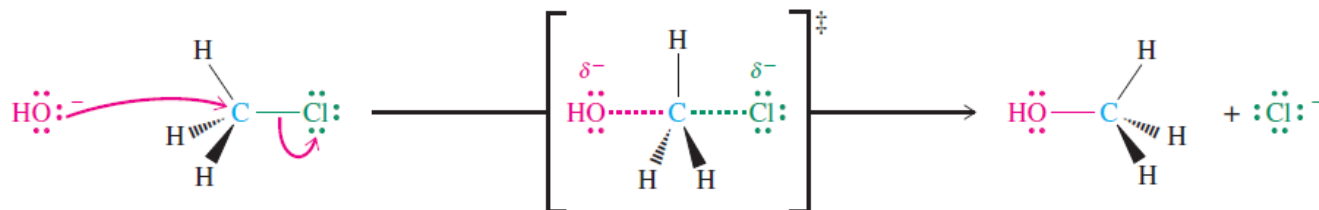
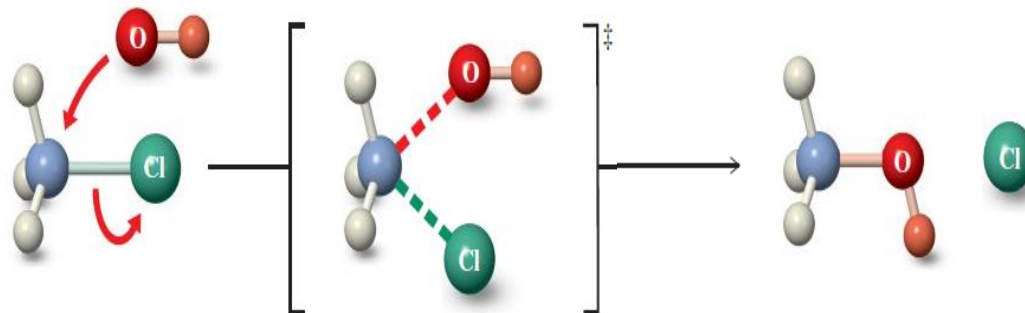


- ✓ *We are not going to look at every bonding and antibonding MOs in the reactants*
- ✓ First, we have to identify which bond is being formed and which one is being broken: *only they are the important ones*
- ✓ C-Cl bond breaks, C-O bond forms
- ✓ OH⁻ is the nucleophile here and CH₃Cl is the electrophile
- ✓ We have to identify the HOMO of OH⁻ and the LUMO of CH₃Cl
- ✓ The C-Cl bond breaking can be visualized as a pair of non-bonding electrons from the HOMO of OH⁻ are donated to the σ* of C-Cl bond and this will make the bond order of the C-Cl bond momentarily zero. Cl⁻ leaves and a new compound is formed having a C-O bond

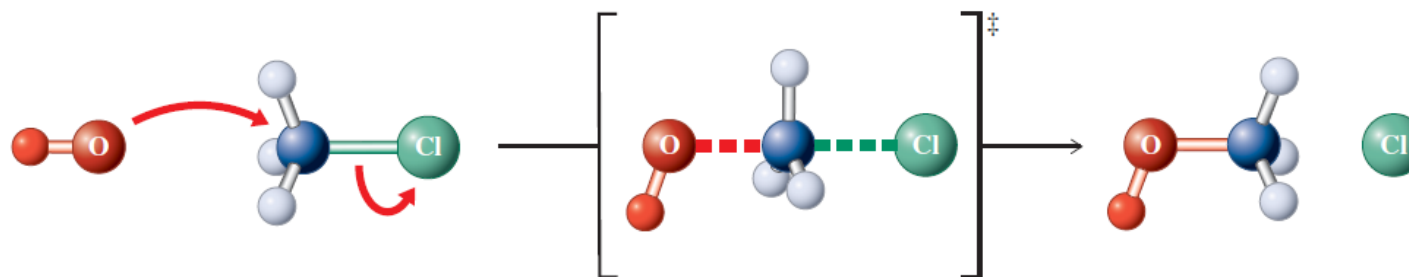
Approach of the Nucleophile



Front-side Displacement

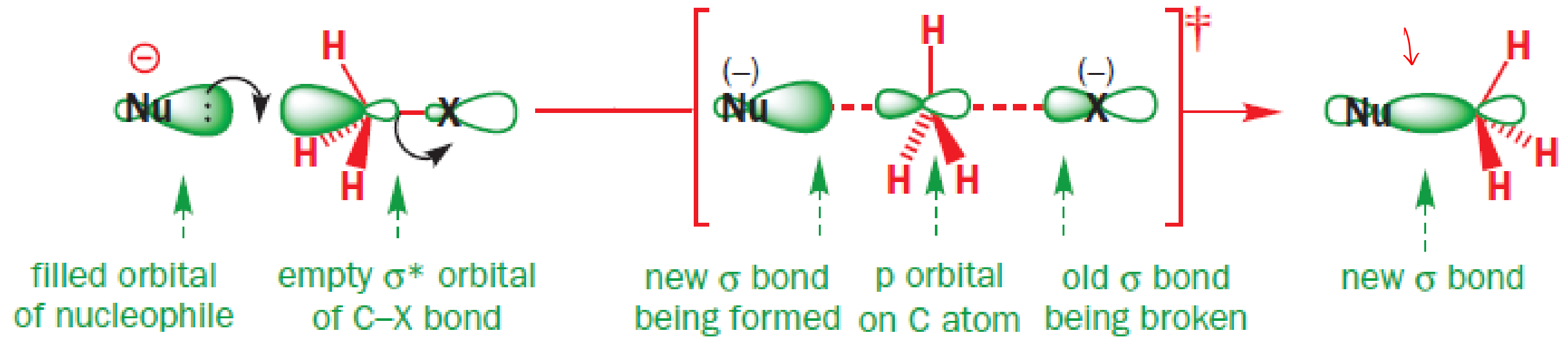


Back-side Displacement



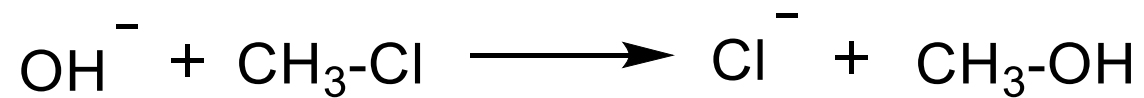
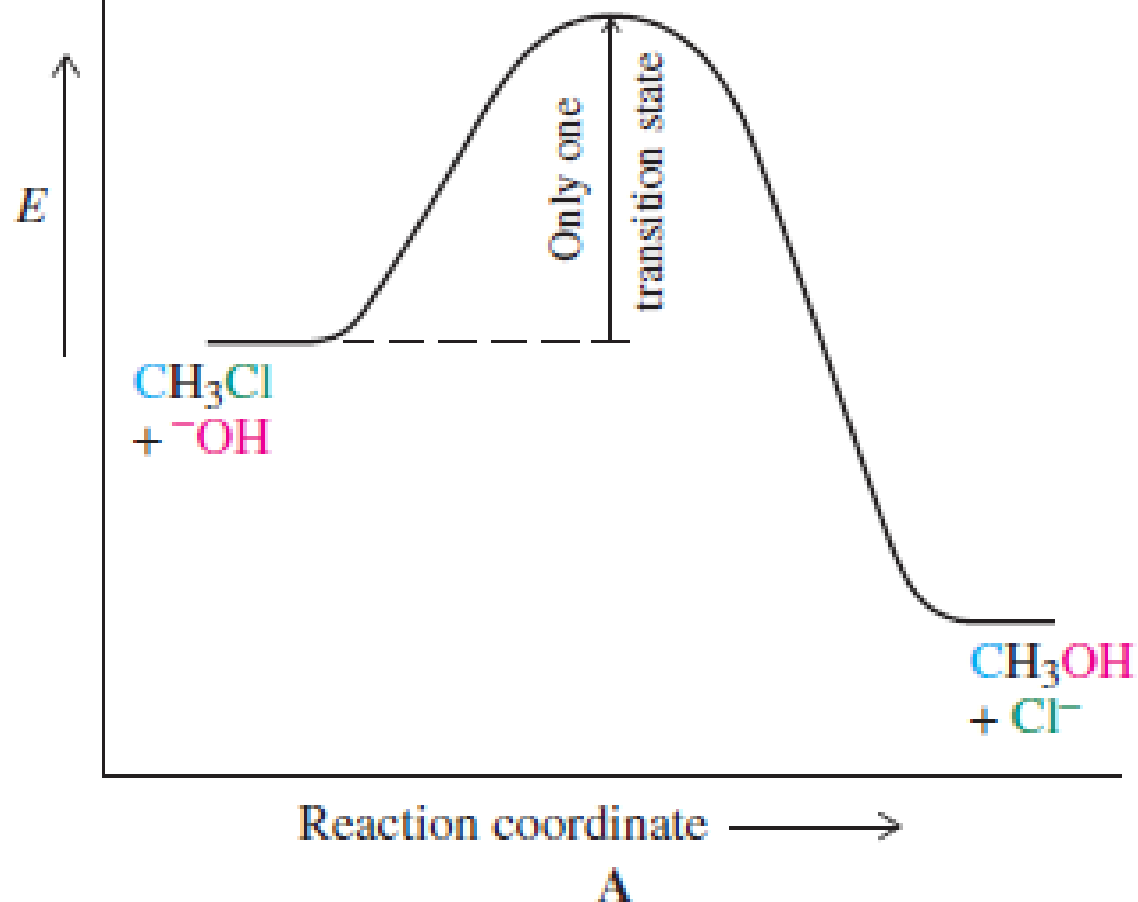
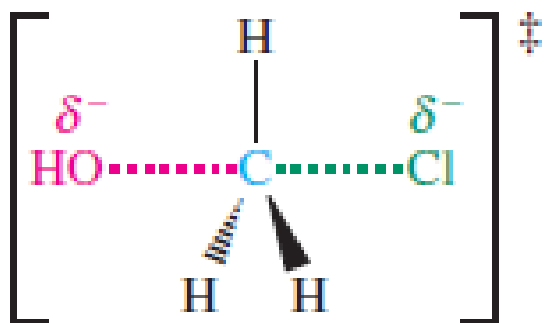
Molecular Orbitals Support Back-side Approach

- The nucleophile attacks the σ^* orbital of the C-X bond



ΔE (interaction energy) : Σ sterics $- \Sigma$ orbital overlap / $(E_{LUMO} - E_{HOMO}) + \Sigma$ charge interaction

S_N2 : One Step

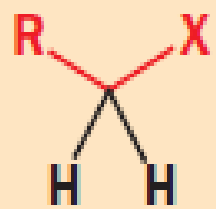
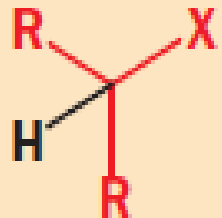
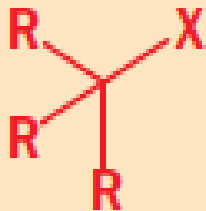


$$\text{Rate} = k [\text{RX}] [\text{Nu}]$$

The reaction rate will depend on the following four factors:

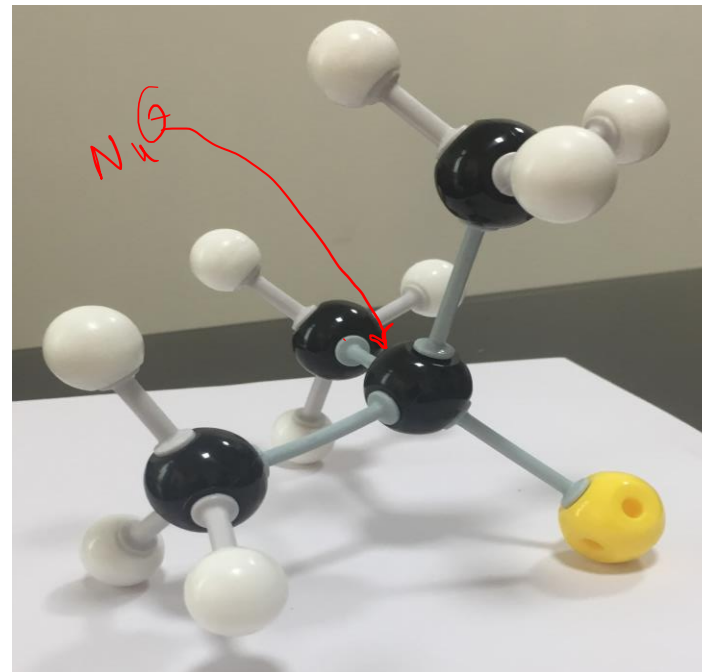
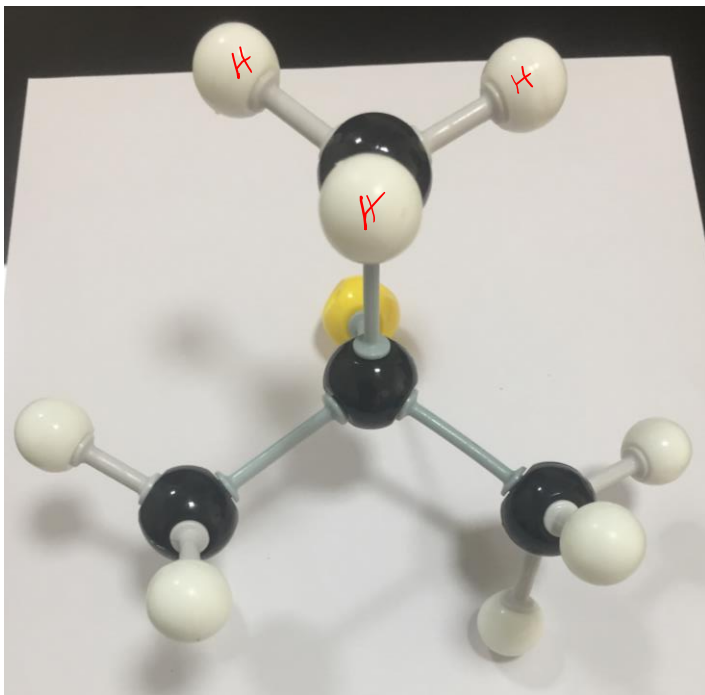
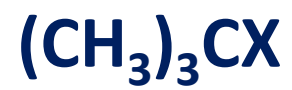
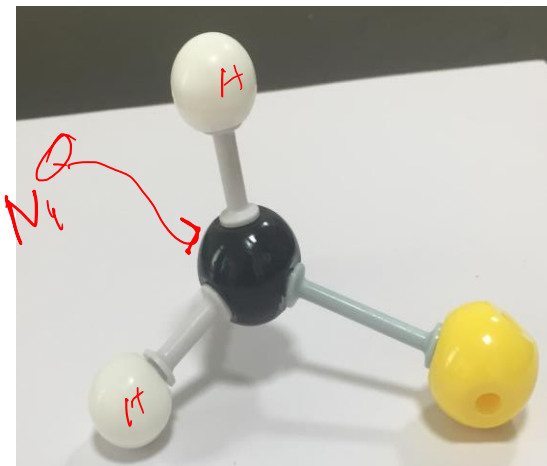
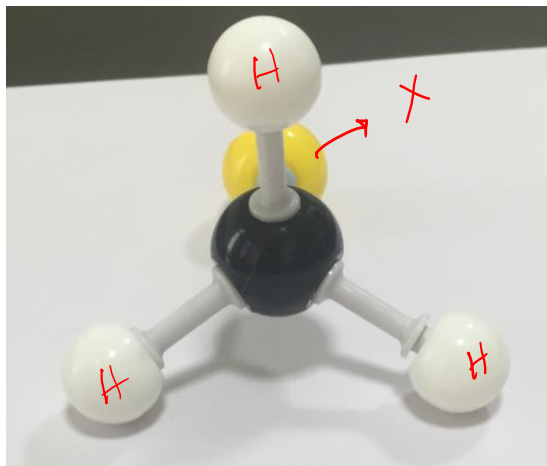
1. Structure of alkyl halide
2. Nature of nucleophile
3. Nature of leaving group
4. Solvent

✓ The rate of S_N2 reaction is critically dependent on the nature of alkyl halide

structure	$\text{Me}-\text{X}$			
type	methyl	primary	secondary	tertiary
S_N2 reaction?	good	good	yes	no

ΔE (interaction energy) : $\Sigma \text{ sterics} - \Sigma \text{ orbital overlap} / (E_{\text{LUMO}} - E_{\text{HOMO}}) + \Sigma \text{ charge interaction}$

Steric Factors in S_N2 Reactions

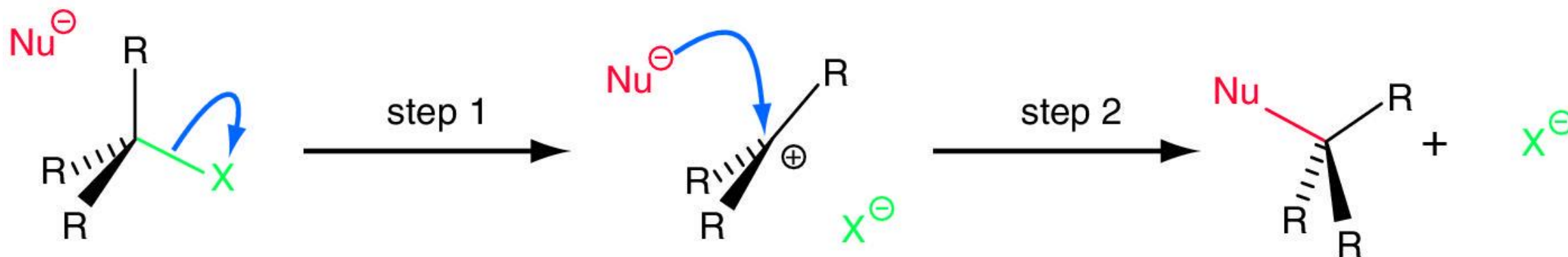


Nucleophilic Substitution Unimolecular (S_N1)



(t-Alkyl halide)

S_N1 : Nucleophilic Substitution Unimolecular

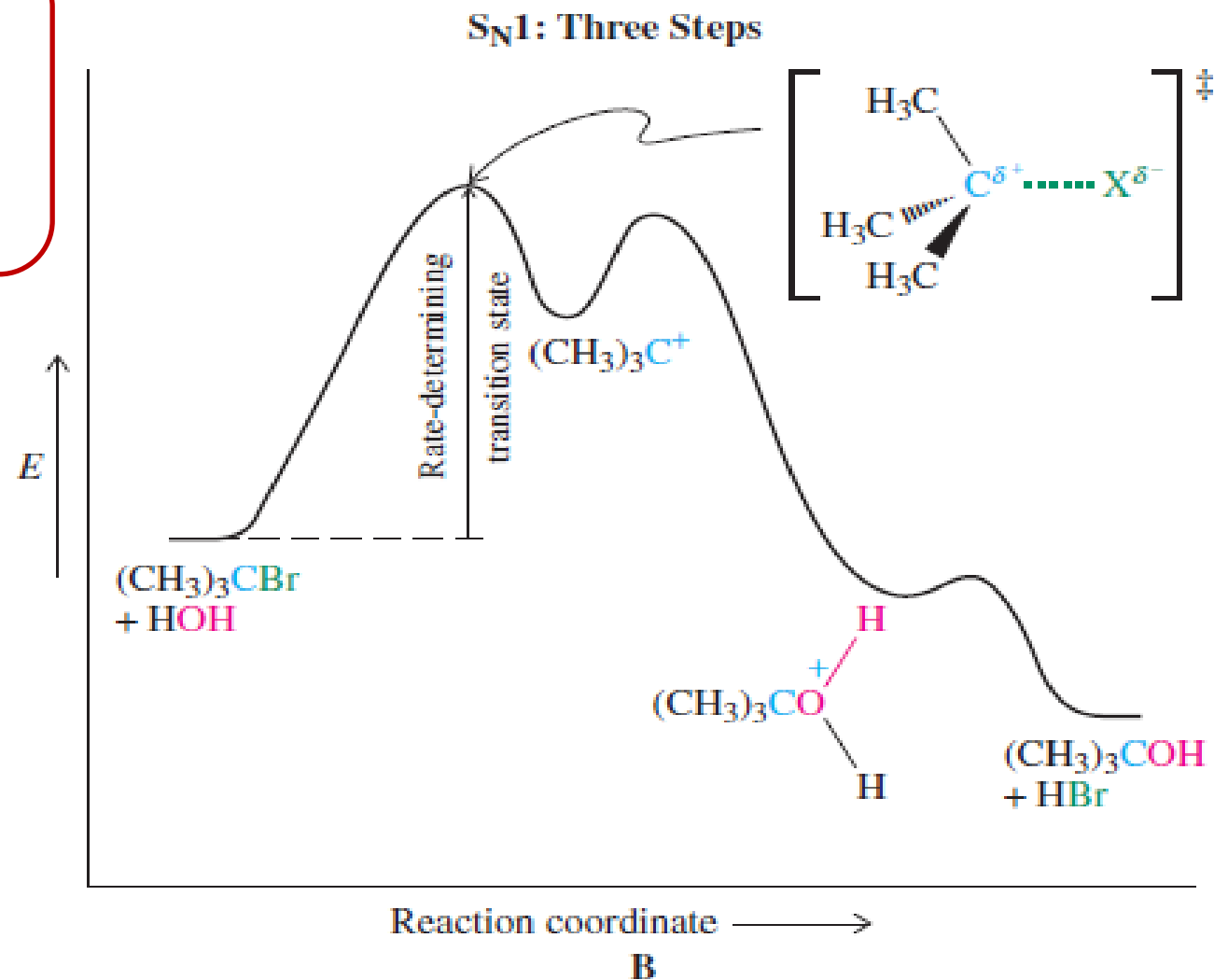


- The leaving group departs early; a carbocation is formed as the intermediate
- **Step 1** is slow and the rate determining step (rds)

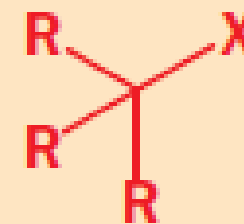
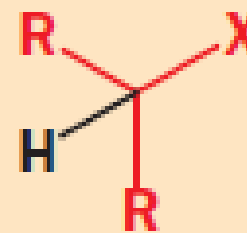
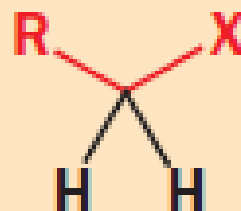


$$\text{Rate} = k [\text{RX}]$$

- ✓ When solvent is the nucleophile, it is called solvolysis
- ✓ Protonation/deprotonation steps are typically fast; small activation energy



structure



type

methyl

primary

secondary

tertiary

S_N1 reaction?

no

no

yes

good

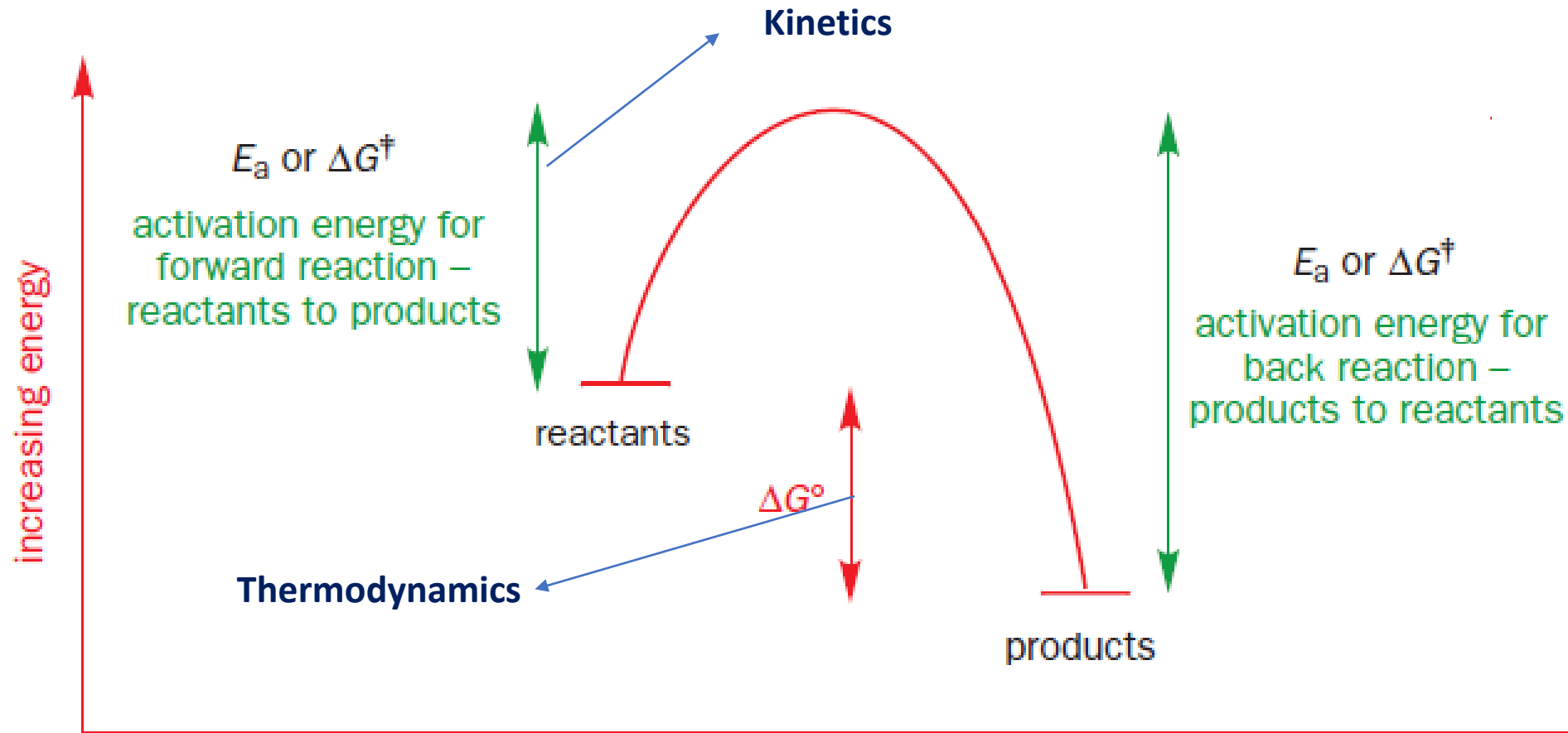
S_N2 reaction?

good

good

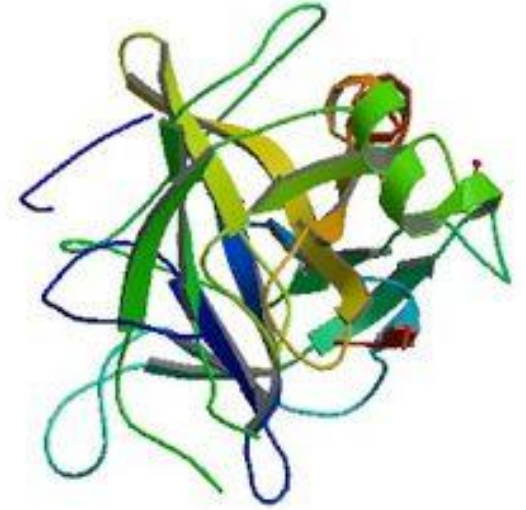
yes

no



- ✓ The lower the value of E_a , the faster the reaction: **Kinetically favourable**
- ✓ Higher negative value of ΔG : **Thermodynamically favourable**

- ✓ Chymotrypsin is a digestive enzyme present in pancreatic juice
- ✓ It helps in hydrolysing peptide bonds
- ✓ These reactions are thermodynamically favorable, *but occurs extremely slowly in the absence of a catalyst*



Chymotrypsin



$$\text{Rate} = k [\text{RX}]$$

- ✓ It is true that a t-butyl carbocation is more stable than methyl or primary carbocations
- ✓ At the same time, the activation energy of its formation (E_a) is smaller than methyl/primary: *Important for S_N1 reactions*

