- Actual pathway of reaction is called reaction mechanism
- Mechanism is only suggestive not conclusive
- Mechanism is based on available evidences

EVIDENCES

1. Nature of Products

2. Thermodynamics and Kinetic Requirements

3. Study of Intermediates
   - (i) Isolation of intermediates
   - (ii) Detection of intermediates
   - (iii) Trapping of Intermediates
   - (iv) Addition of Suspected intermediates

4. Stereochemical studies

5. Isotopic Studies
   - (i) Isotopic labelling
   - (ii) Isotopic effect
   - (iii) Isotopic scrambling

1. Nature of Products

- All major and minor products must be identified correctly
- A mechanism must account for all major and minor products of the reaction
- Any mechanism that failed to account for all products would be incorrect.
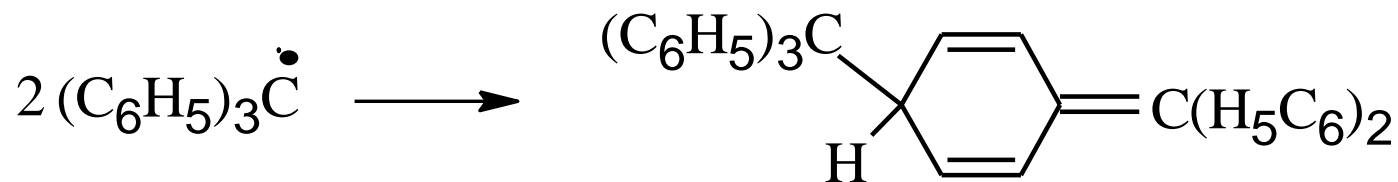
Example 1: Halogenation of Methane
- Small amount of ethane is also produced as minor product.
- A mechanism must account for the formation of ethane.

Example 2: Dimerization of triphenyl methyl free radical

$$2\,(C_6H_5)_3\overset{\bullet}{C} \longrightarrow (C_6H_5)_3C{-}C(H_5C_6)_3$$

NMR spectroscopy   Aromatic Protons: 30

$$2\,(C_6H_5)_3\overset{\bullet}{C} \longrightarrow$$

NMR spectroscopy   Aromatic Protons: 25
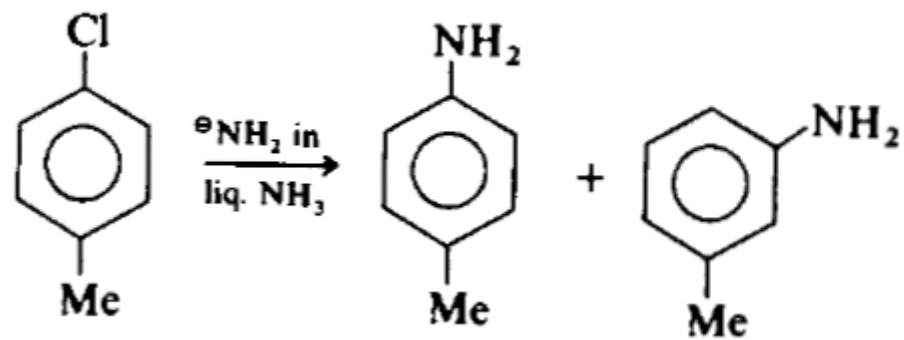   Olefinic Protons: 04
                                 Saturated Proton: 01

Example 3:

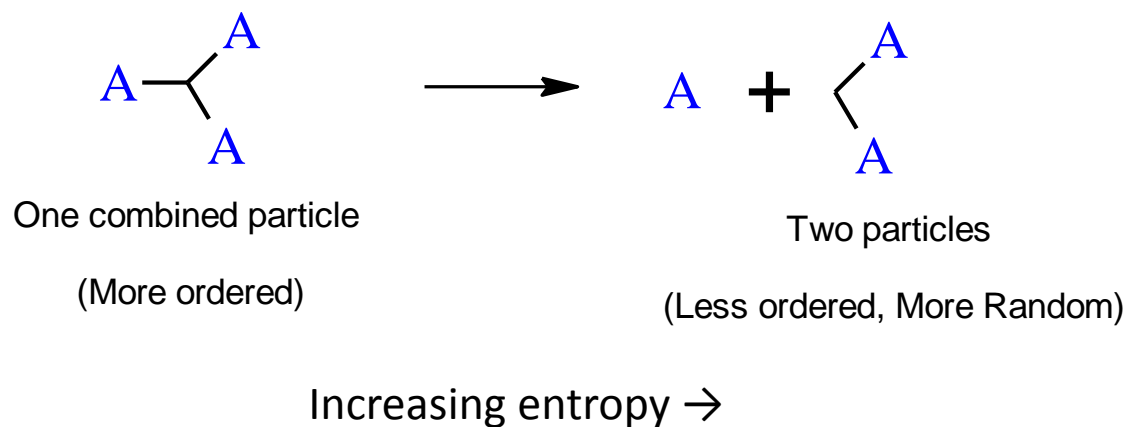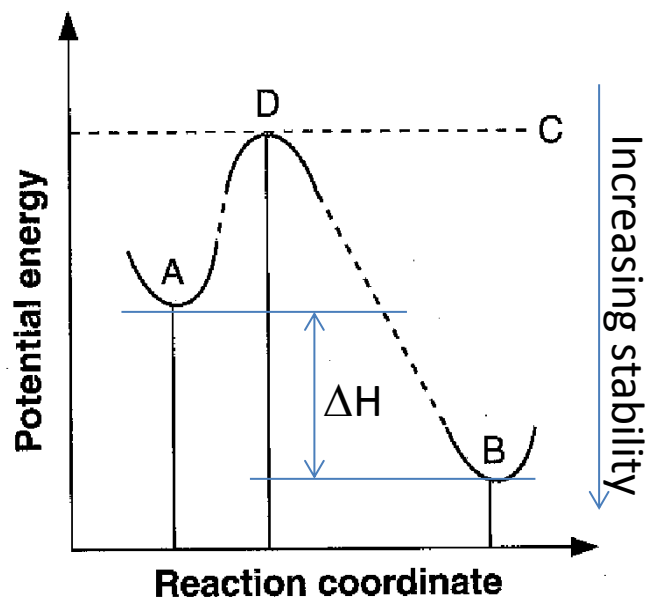# 2 (i) Thermodynamic Requirements

ENTHALPY (H), **ENTROPY (S) ,** **GIBBS FREE ENERGY (G)**

ENTHALPY CHANGE (∆H):

It is the difference in stability (bond strength) of the reactants and products
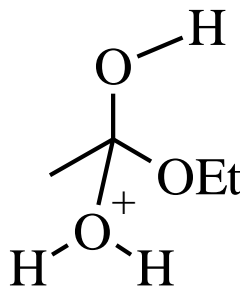
ENTROPY CHANGE (∆S):
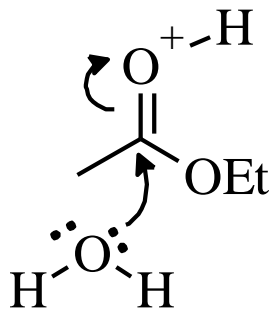
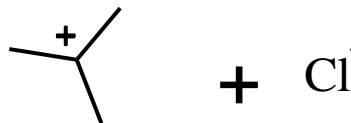*It is the difference between the disorder of the reactants and that of the products*

One combined particle

(More ordered)

Two particles
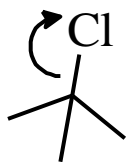
(Less ordered, More Random)

Increasing entropy →

Examples:

- ***Acid-Catalyzed hydrolysis of ethyl acetate in water*** $\Delta S^{\ddagger} = -26$ eu

- *Order increases*
- *Disorder decreases*
- *Entropy decreases*

- ***Hydrolysis of t-butyl chloride in water*** $\Delta S^{\ddagger} = +10$ eu

- *Order decreases*
- *Disorder increases*
- *Entropy increases*

Examples of Common Reactions and Representative $\Delta S^{\ddagger}$ Values

Entry	Reaction	ΔS of activation	Rate-determining/ rate-limiting step
1	Acid-catalyzed hydrolysis of ethyl acetate in water	−26 eu	
2	Acid-catalyzed ring opening of ethylene oxide in water	−6 eu	
3	Acid-catalyzed hydrolysis of α-methylglucopyranoside in water	+4.5 eu	
4	Displacement of iodide from methyliodide by pyridine	−31 eu	
5	Hydrolysis of t-butyl chloride in water	+10 eu	
6	A conjugate addition reaction	−17 eu	
7	Peroxide homolysis	+11 eu	

- # Energy Diagram

GIBBS FREE ENERGY (G):

*The **energy** associated with a chemical reaction that can be used to do work*

*The **free energy** of a system is the enthalpy (H) minus the product of the temperature (Kelvin) and the entropy (S) of the system*

i.e. $G = H - TS$

For a change in system at constant temperature it can be written as

$\Delta G = \Delta H - T\Delta S$
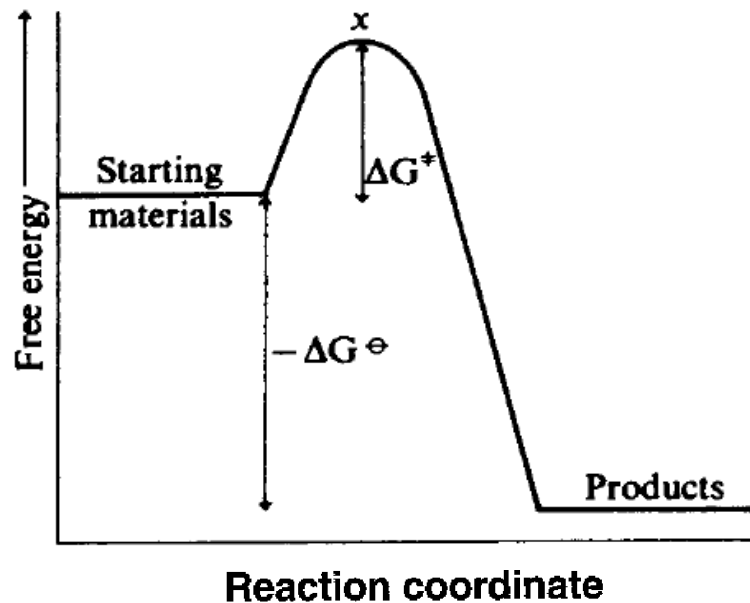
where

ΔG = Gibb's Free Energy Change ΔH = Enthalpy Change ΔS = Entropy Change

Free Energy of Activation (ΔG^*)
Enthalpy of Activation (ΔH^*)
Entropy of Activation (ΔS^*)

Free Energy and Equilibrium

$$\Delta G° = \Delta H° - T\Delta S° \qquad\qquad \Delta G° = -RT \ln K_{eq}$$

The sign of $\Delta G°$ tells us whether products or reactants are favoured at equilibrium

$$K_{eq} = \frac{[\text{hydrate}]_{eq}}{[\text{aldehyde}]_{eq}} = 0.5 \text{ at } 25°C$$

$$\Delta G° = -RT \ln K_{eq} = -8.315 \times 298 \times \ln(0.5) = +1.7 \text{ kJ mol}^{-1}$$

$\Delta G°$ tells us about the position of equilibrium

- If $\Delta G°$ for a reaction is *negative*, the *products* will be favoured at equilibrium
- If $\Delta G°$ for a reaction is *positive*, the *reactants* will be favoured at equilibrium
- If $\Delta G°$ for a reaction is *zero*, the equilibrium constant for the reaction will be 1

ΔG°, kJ mol^{-1}	K_{eq}	% of more stable state at equilibrium
0	1.0	50
1	1.5	60
2	2.2	69
3	3.5	77
4	5.0	83
5	7.5	88
10	57	98
15	430	99.8
20	3 200	99.97

- *Ionization of acetic acid in water at 25°C*

$\Delta H° = -0.5$ kJ $\quad\quad \Delta S° = -92$ kJ $\quad\quad T\Delta S° = -27.6$ kJ $\quad\quad \Delta G° = 27.2$ kJ
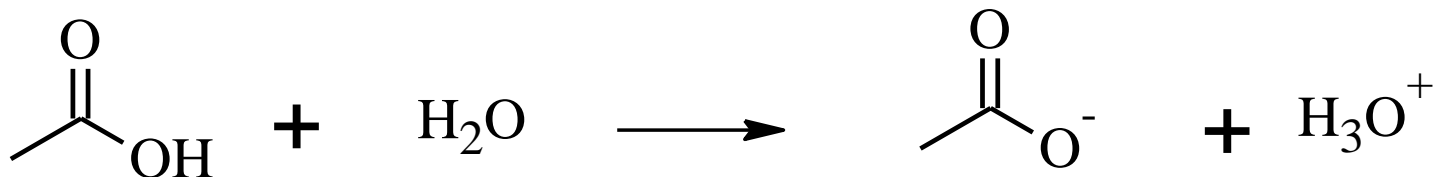
- *Ionization of formic acid in water at 25°C*

$\Delta H° = -0.3$ kJ $\quad\quad \Delta S° = -74$ kJ $\quad\quad T\Delta S° = -21.3$ kJ $\quad\quad \Delta G° = 21$ kJ
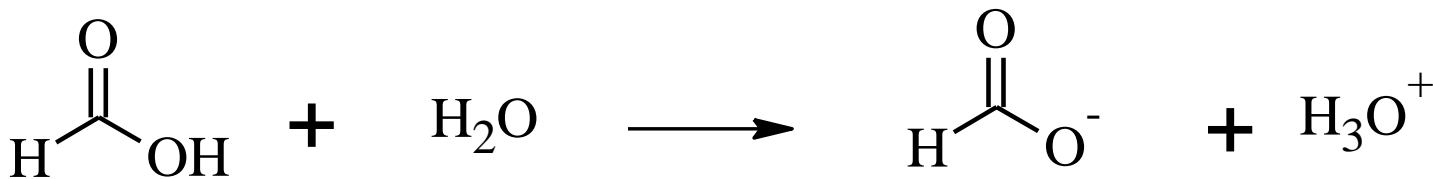
Thermodynamics for the organic chemist

- The free energy change $\Delta G°$ in a reaction is proportional to $\ln K$ (that is, $\Delta G° = -RT \ln K$)
- $\Delta G°$ and K are made up of enthalpy and entropy terms (that is, $\Delta G° = \Delta H° - T\Delta S°$)
- The enthalpy change $\Delta H°$ is the difference in stability (bond strength) of the reagents and products
- The entropy change $\Delta S°$ is the difference between the disorder of the reagents and that of the products
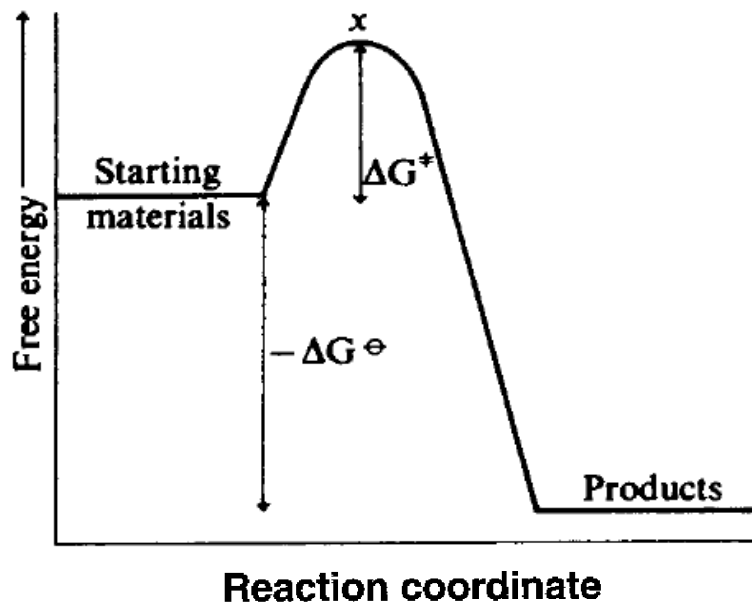
Free Energy of Reaction (ΔG)
Enthalpy of Reaction (ΔH)
Entropy of Reaction (ΔS)

Free Energy of Activation (ΔG^*) or $\Delta G^{\ddagger}$
Enthalpy of Activation (ΔH^*) or $\Delta H^{\ddagger}$
Entropy of Activation (ΔS^*) or or $\Delta S^{\ddagger}$