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CHEMISTRY
PAPER No. 5: ORGANIC CHEMISTRY-II (REACTION MECHANISM-1)
MODULE No. 3: Thermodynamic and kinetic requirement of a reaction

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PAPER No. 5: ORGANIC CHEMISTRY-II (REACTION MECHANISM-1)

MODULE No. 3: Thermodynamic and kinetic requirement of a reaction

1. Learning Outcomes

After studying this module, you shall be able to

- Know what is thermodynamics and kinetics
- Learn difference between thermodynamics and kinetics of reaction
- Identify thermodynamics and kinetics controlled reactions
- Evaluate the energy profile diagram of a reaction

2. Introduction

During a chemical reaction the reactants are converted into products. The process can be described by its mechanism. Moreover, the energy changes taking place in each step can be shown using a reaction coordinate diagram. It depicts the transition state threshold which requires certain amount of activation energy. This is because the reactants are not reactive under certain conditions. The reactants must be supplied with enough activation energy to enable the reaction to proceed in the forward direction. The energy is supplied to the reactants by different energy sources (spark, heat, etc.). The rate of reaction (k) and the kinetic energy required for activation of reaction determines how fast any reaction reaches equilibrium.

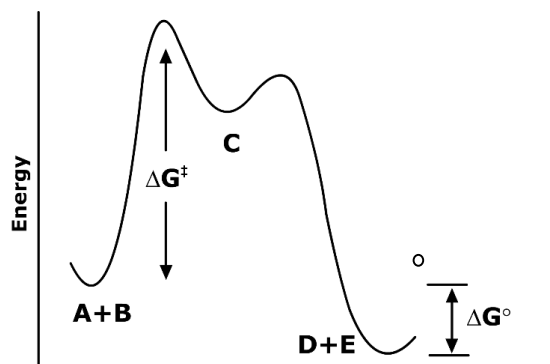
For a reaction:



$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]} = \frac{[D]^d [E]^e}{[A]^a [B]^b}$$

Rate of reaction = (number of collisions per unit time) x (fraction with sufficient energy) x (fraction with proper orientation)

The energy profile diagram for a reaction $A + B \longrightarrow D + E$ is shown in fig.1, here C is the intermediate formed:



Reaction Coordinate

Fig.1: Energy profile for reaction $A + B \rightarrow C \rightarrow D + E$

In figure 1,

$\Delta G^\circ = (\text{free energy of products}) - (\text{free energy of reactants})$

$\Delta G^\ddagger = (\text{free energy of transition state}) - (\text{free energy of reactants})$

Any quantity that refers to the transition state is represented by the doubledagger superscript (\ddagger)

ΔG° relates to equilibrium constant. The thermodynamic stability is indicated by ΔG° .

If ΔG° is **negative** the product is thermodynamically stable compared to reactant and the reaction is said to be **exergonic reaction**.

If ΔG° is **positive** the product is thermodynamically unstable compared to reactant and the reaction is said to be **endergonic reaction**.

The kinetic stability of a component is indicated by ΔG^\ddagger .

If ΔG^\ddagger is **large** the compound (here in fig. 1 the reactant) is kinetically stable because it does not undergo that reaction rapidly.

If ΔG^\ddagger is **small** the compound (here in fig. 1 the reactant) is kinetically unstable i.e, it undergoes the reaction rapidly.

For a reaction to take place spontaneously, the free energy of the products must be lower than the free energy of the reactants; that is, ΔG must be negative. The Gibbs standard free-energy (ΔG) change has an enthalpy component and an entropy component, which are related by the following equation:

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

The **enthalpy** term (ΔH) is the heat given off or the heat consumed during the course of a reaction. In a molecule or compound the atoms are held together by bonds. When new bonds are formed, heat is given off and when bonds are broken, heat is consumed. Thus, ΔH is a measure of the bond-making and bond-breaking processes that occur as reactants are converted into products.

Entropy (ΔS) is defined as the degree of disorder of a system.

Exothermic Reactions: If the bonds that are formed in a reaction are stronger than the bonds that are broken, more energy will be released as a result of bond formation than will be consumed in the bond-breaking process and ΔH will be negative. Therefore, **exothermic reaction** is a reaction with a negative ΔH (fig. 2). In exothermic reactions the products are more thermodynamically stable than the reactants. The equilibrium constant for the reaction will be large ($K > 1$) for exothermic reactions. This has no effect on the rate of the reaction. The rate depends on the activation energy (E_a).

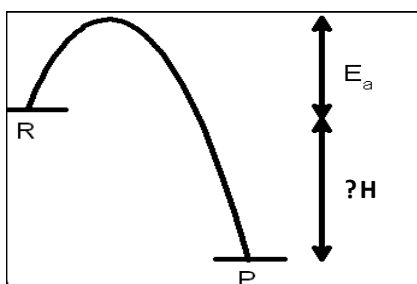


Fig. 2: Reaction profile for exothermic reaction

Endothermic Reactions: If the bonds that are formed are weaker than those that are broken, ΔH will be positive. Therefore, endothermic reaction is a reaction with a positive ΔH . In endothermic reactions the reactants are more thermodynamically stable than the products. The equilibrium constant for the reaction will be small ($K < 1$) for endothermic reactions because ΔH is positive (fig. 3). This has no effect on the rate of the reaction. The rate depends on the activation energy (E_a).

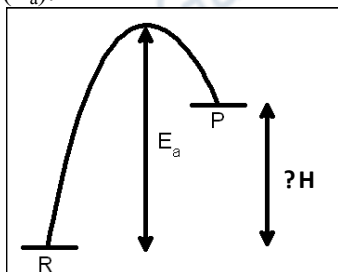


Fig. 3: Reaction profile for Endothermic reaction

There are certainly two factors which decides the outcome of a reaction, these are:

1. **Thermodynamic factor:** the relative stability of the products

2. **Kinetic factor:** the rate of product formation

3. Thermodynamics Overview

Thermodynamics is that branch of chemistry which describes the properties of a system at equilibrium. The more stable, a compound the greater is its concentration at equilibrium. Thus, if the products are more stable (have a lower free energy) than the reactants, there will be a higher concentration of products than reactants at equilibrium, and K_{eq} will be greater than 1. On the other hand, if the reactants are more stable than the products, there will be a higher concentration of reactants than products at equilibrium

$$K_{eq} < 1$$

$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]} = \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

Therefore, whether reactants or products are favored at equilibrium can be indicated either by the equilibrium constant K_{eq} or by the change in free energy ΔG°

Thermodynamics is only concerned with the final state of a system and the mechanism of transformation does not matter at all. The following comments help to clarify the meaning of this statement.

The thermodynamic quantity is the energy difference resulting from the free energy (ΔG) given off during a chemical reaction i.e., the stability of the products relative to the reactants. A thermodynamically controlled reaction involves higher temperatures and long reaction times to ensure that even the slower reactions have a chance to occur, and all the material is converted to the most stable compound.

All substances tend to be in the lowest energy state. So when a substance is at lower energy, it is more stable. Thermodynamic stability has to do with the relative energies of reactants and products and it is independent of the pathway.

One can think of thermodynamics as the energy stored within a reaction, a reactant, or a product.

With relation to Gibbs free energy ($\Delta G = \Delta H - T\Delta S$) thermodynamics is either:

(1) the energy released during a reaction, in which case ΔG will be negative and the reaction exothermic/spontaneous, or

(2) the energy consumed during a reaction, in which case ΔG will be positive and the reaction endothermic/nonspontaneous.

4. Kinetics Overview

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Kinetics is the study of the experimental measurement of macroscopic properties of a reaction mixture and how the concentration of product and reactants changes over time, i.e., reaction rate.

Kinetics describes the rates of reactions and how fast equilibrium is reached, it gives no information about conditions once the reaction reaches equilibrium. A kinetically controlled reaction involves lower temperatures and shorter reaction times, which ensures that only the fastest reaction has the chance to occur. The quantity related to kinetics is the rate constant (k). It is associated with the activation energy required for the reaction to move forward, that is, the reactivity of the reactants.

How fast the reaction occurs is independent of the type i.e. whether a given reaction is exergonic or endergonic. Kinetic stability has to do with the pathway between reactants and products. Kinetic stability is largely dependent on the activation energy for the reaction. The activation energy is determined by the chemical potential energy of the reaction intermediate(s). If the activation energy is high then at low temperatures the reaction will be slow. It can be made faster by increasing the temperature. If the activation energy is low then the reaction will be fast even at low temperatures. Such reactions do increase their rates with increasing temperature as well.

The smaller the E_a the faster is the reaction. Thus, anything that destabilizes the reactant or stabilizes the transition state will make the reaction go faster.

Some exergonic reactions can occur at room temperatures as their free energies of activation are small. In contrast, some exergonic reactions have free energies of activation that are so large that the reaction cannot take place without adding energy above that provided by the existing thermal conditions. Endergonic reactions can also have either small free energies of activation or large free energies of activation.

$$\Delta S^\ddagger = (\text{entropy of the transition state}) - (\text{entropy of the reactants})$$

$$\Delta H^\ddagger = (\text{enthalpy of the transition state}) - (\text{enthalpy of the reactants})$$

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$

The rate of a chemical reaction is the speed at which the reacting substances are used up or the speed at which the products are formed. The rate of a reaction depends on the following factors:

1. The number of collisions taking place between the reacting molecules in a given period of time. Greater the number of collisions, the faster will be the reaction.
2. The fraction of the collisions that occur with sufficient energy to overcome the energy barrier of the reacting molecules. Smaller the free energy of activation, more will be the collisions leading to product formation.
3. The fraction of the collisions occurring with proper orientation.

Rate of reaction = (number of collisions per unit time) x (fraction with sufficient energy) x (fraction with proper orientation)

Increasing the concentration of the reactants increases the rate of a reaction because it increases the number of collisions that occur in a given period of time. Increasing the temperature at which the reaction is carried out also increases the rate of a reaction because it increases both the frequency of collisions (molecules that are moving faster collide more frequently) and the number of collisions that have sufficient energy to get the reacting molecules over the energy barrier.

First order reaction

For the reaction: $A \longrightarrow B$

Rate $\propto [A]$

If the rate of a reaction is proportional to the concentration of only one reactant, it is called a first order reaction. The proportionality symbol can be replaced with an equals sign if using a proportionality constant k , which is called rate constant. The rate constant of a first order reaction is called a first-order rate constant.

Rate = $k [A]$

Second-order reaction:

$A + B \longrightarrow C + D$

A reaction whose rate depends on the concentrations of two reactants is called a second-order reaction.

Rate = $k [A] [B]$

5. Thermodynamics vs Kinetics

Thermodynamics is all about “if”

- if a process or a reaction can occur or not
- if a system is in stable or metastable equilibrium
- if sufficient driving force is present to enforce a favourable transformation

Kinetics is all about “how”

- how fast or slow a process can occur, i.e., determining the rate
- how transition from nonequilibrium to equilibrium systems, or between two equilibrium states occurs
- how to overcome the energy barrier to finish the transformation from the starting (reactant) state to the final (product) state.

For a reaction irreversible under mild conditions and reversible under vigorous conditions at a certain temperature one product changes to another. At this particular temperature there is change between a kinetic and a thermodynamic product.

Thermodynamics	Kinetics
talks about how stable a material (or system) is in one state	considers how quickly or slowly a change can occur
tells that a reaction should go if the products are more stable (have a lower free energy) than the reactants i.e, the reaction has a negative free energy change.	tells how fast the reaction will go, it doesn't tell anything about the final state.
the most stable state of a thermodynamic reaction is that of being in the state of products, because the reaction will happen spontaneously, without the need for energy to be added to make the reaction go forward.	the most stable states of a kinetic reaction are those of the reactants, in which an input of energy will be required to move the reaction from a state of stability, to that of reacting and converting itself to products.
Thermodynamics is related to stability.	Kinetics is related to reactivity.
At high temperature, the reaction is under thermodynamic control (equilibrium, reversible conditions) and the major product is the more stable system.	At low temperature, the reaction is under kinetic control (rate, irreversible conditions) and the major product is that from fastest reaction.
The thermodynamic product is the most stable product.	The kinetic product is the product that is formed most rapidly
The thermodynamic product predominates when the reaction is reversible (thermodynamic control)	The kinetic product predominates when the reaction is irreversible (kinetic control)

Figure 2 shows the conditions under which a kinetic or thermodynamic product is preferred. Here R is the reactant and A or B are products formed under different conditions. Figure 2 shows that if activation energy is less kinetic product will form predominantly.

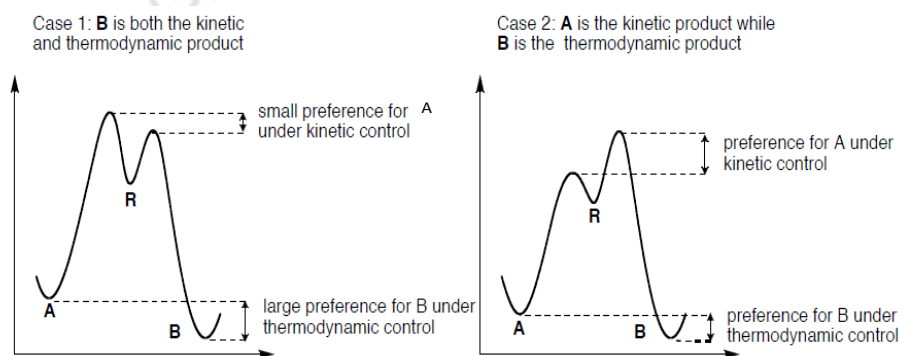


Fig. 4: Energy profile for a thermodynamic and kinetic product

The other way to determine whether a reaction yields kinetic or thermodynamic product is through temperature.

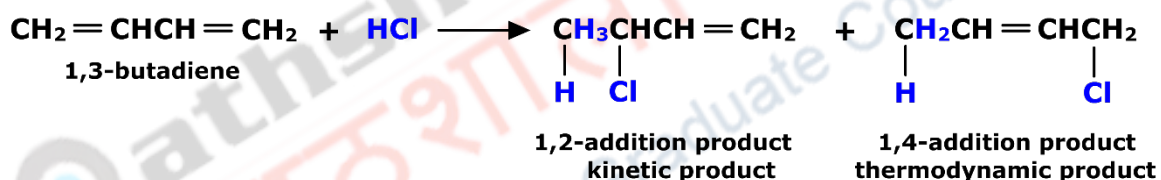
lower temps \implies irreversible reaction \implies *kinetic product*

higher temps \implies reversible reaction \implies *thermodynamic product*

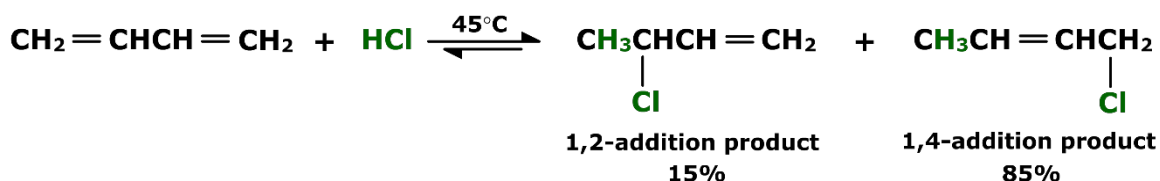
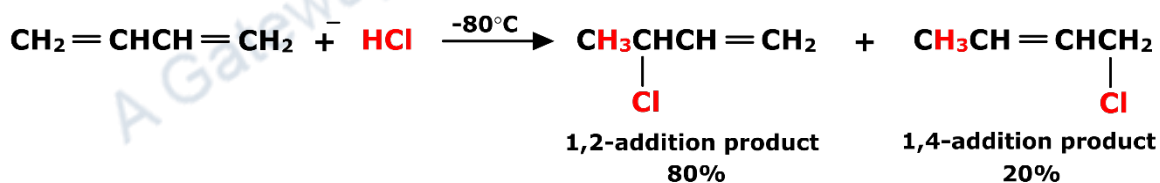
6. Selected Examples of thermodynamically and kinetically controlled reactions

6.1 Addition of HCl to conjugated dienes

The addition of HCl to 1,3-butadiene can give two products one is 1,2- and another is 1,4-addition product. The amount of each will depend upon the reaction conditions. The 1,2- product is called kinetic product and 1,4- is thermodynamic product.



At low temperature -80 or 0 °C the kinetic product is obtained as major due to low E_a . While at high temperature 40 - 45 °C the thermodynamic product is major, due to greater stability. The 1,4-addition product is more stable as greater the number of alkyl groups attached to a sp^2 carbon more stable it is (more substituted alkene). But, 1,2-addition product is formed faster, as the transition state for formation of 1,2-product is more stable (fig. 5).



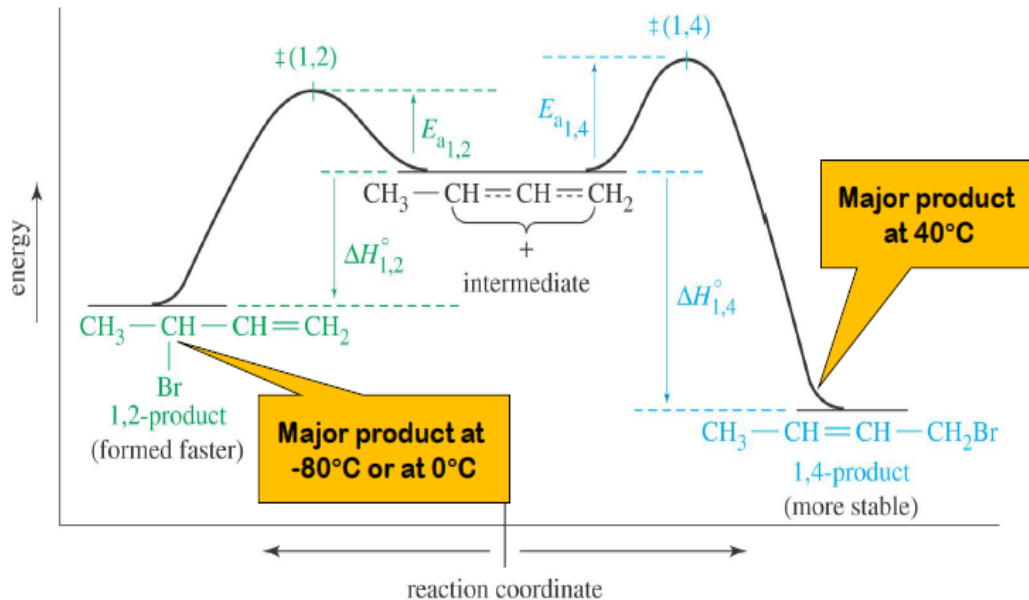
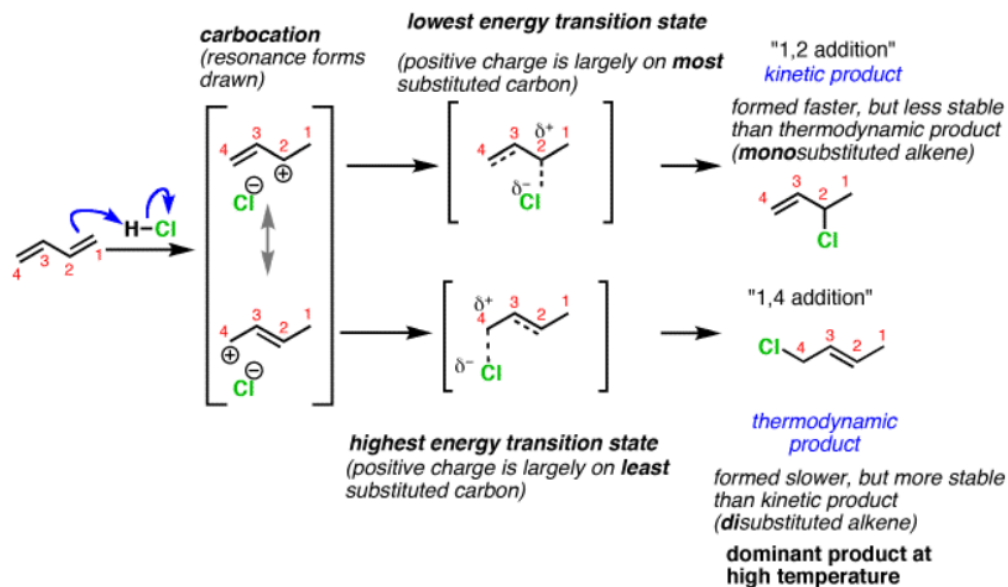
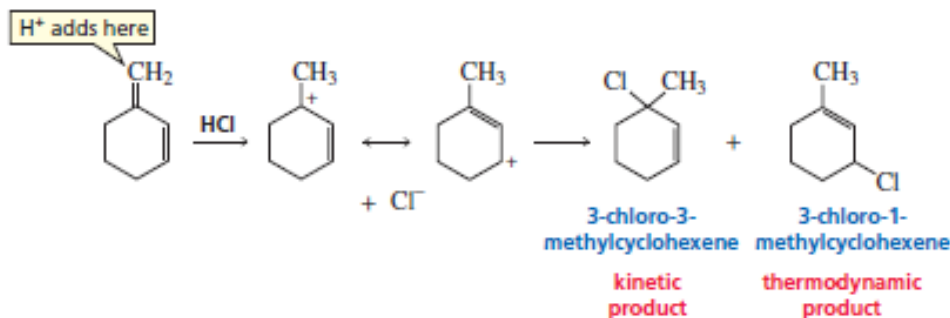


Fig.5: Reaction coordinate diagram for addition of HBr to 1,3-butadiene { $\ddagger(1,2)$ represents transition state for 1,2-addition; $\ddagger(1,4)$ represents transition state for 1,4-addition}

The transition state for 1,4-addition has positive charge is on less substituted carbon, therefore its activation energy is large and formed slowly. Whereas, the transition state for 1,2-addition has positive charge on more substituted carbon, and has lesser activation energy thus formed faster.

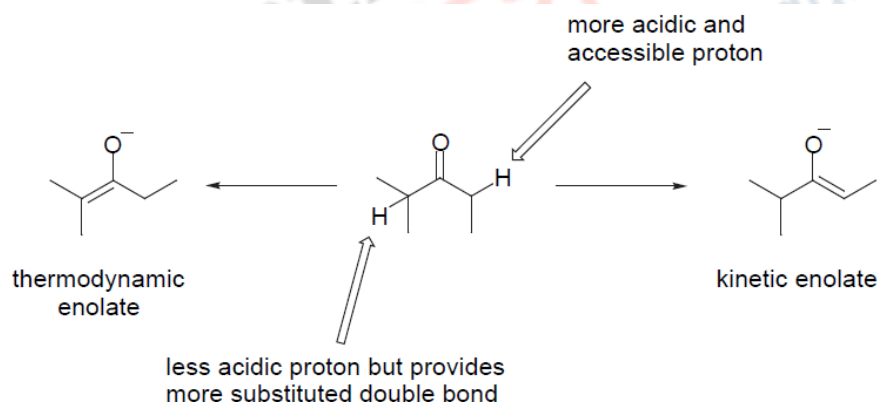


Another example of kinetic and thermodynamic product formation is addition to 3-methylcyclohexene. When HCl add to 3-methylenecyclohex-1-ene the kinetic product is 3-chloro-3-methylcyclohexene and thermodynamic product is 3-chloro-1-methylcyclohexene.

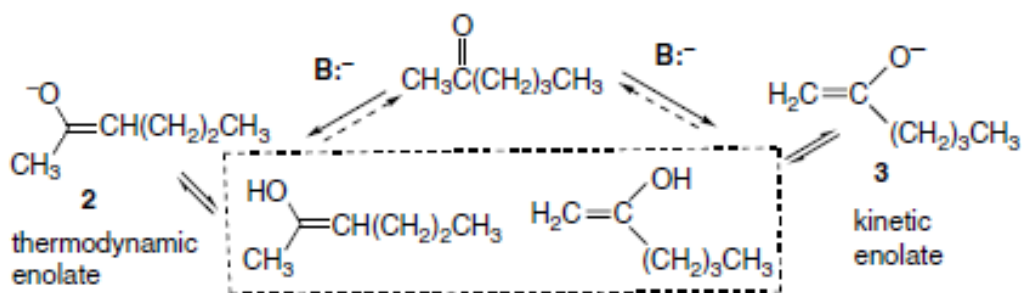


6.2 The selective formation of enolates

Alkylation of unsymmetrical ketones gives two different products because either of the α -carbons can be alkylated. As the reaction proceeds via formation of enolate in basic medium and most ketone can give rise to more than one enolate depending upon the reaction conditions.



For example, in the case of 2-hexanone if a strong and sterically hindered base (lithium diisopropylamide) and aprotic solvent is used the kinetic enolate is major product. However, with protic solvent or weak base thermodynamic enolate is predominant.

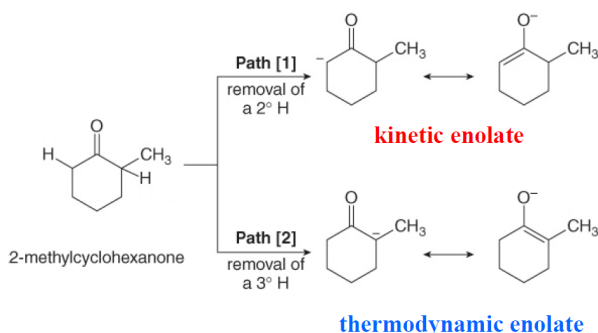


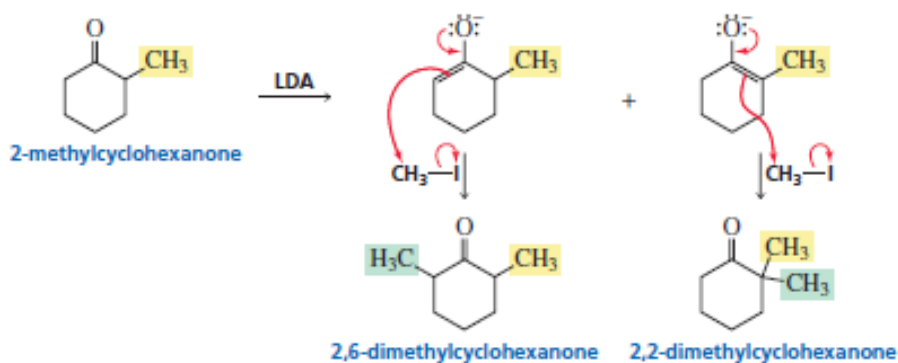
The formation of different types of enolates can be explained as follows. In 2-hexanone, the α -hydrogen of methyl groups are less sterically hindered than the α -hydrogen of butyl group. Thus removal of proton from methyl hydrogen is faster than removal of proton from butyl. In presence of strong base enolate will not be converted back to ketone as the enolate is a weak base to regain proton. With weaker base and protic solvent protons can be transferred reversibly between isomeric enolates and the base. Under these conditions the more stable enolate will be major as they are in equilibrium with each other. The more substituted enolate is more stable.

Another, example is the methylation of 2-methylcyclohexanone with one equivalent of methyl iodide it forms both 2,6-dimethylcyclohexanone and 2,2-dimethylcyclohexanone. The relative amounts of the two products depend on the reaction conditions (fig. 6).

The enolate leading to 2,6-dimethylcyclohexanone is the kinetic enolate because the α -hydrogen that is removed to make this enolate is more accessible (particularly if a hindered base like LDA is used) and slightly more acidic. So 2,6-dimethylcyclohexanone is formed faster and is the major product if the reaction is carried out at -78°C .

The enolate leading to 2,2-dimethylcyclohexanone is the thermodynamic enolate because it has the more substituted double bond, making it the more stable enolate. Therefore, 2,2-dimethylcyclohexanone is the major product if the reaction is carried out under conditions that cause enolate formation to be reversible and if a less hindered base (KH) is used.





Low temperature favors kinetic enolate as the system can not equilibrate to form the more stable thermodynamic enolate. At high temperature the more stable thermodynamic enolate is formed predominantly.

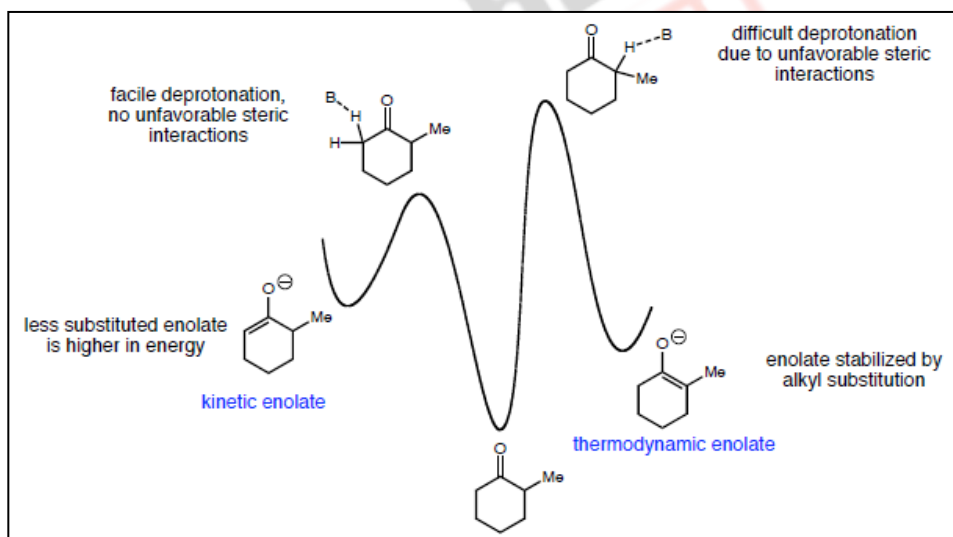
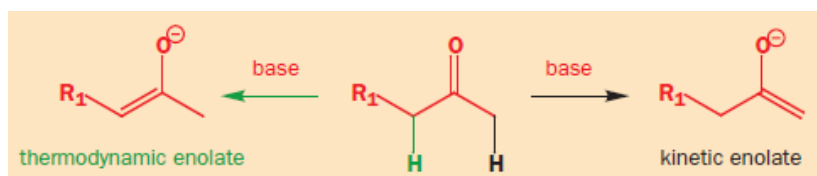


Fig.6: Reaction coordinate diagram for enolate formation

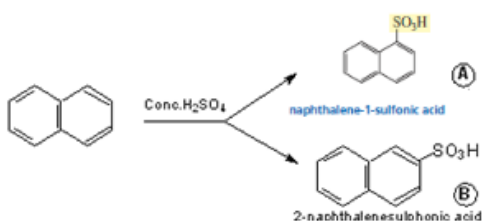
The regioselective formation of enolates to give kinetic or thermodynamic product can be differentiated as follows:



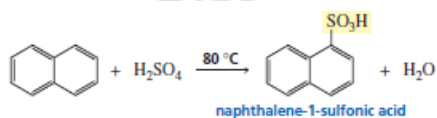
Thermodynamic enolate	Kinetic enolate
more substituted	less substituted
more stable	less stable
favoured by excess ketone	favoured by strong and hindered base
high temperature	low temperature
long reaction time	short reaction time
favoured by protic solvents <i>e.g.</i> ROH (which have slightly more acidic protons than the enolate and favour formation of the enol allowing tautomerisation to the ketone)	favoured by aprotic solvents <i>e.g.</i> THF, Et ₂ O (as there is no acidic proton to encourage the reverse reaction)
favoured by weaker bases which provide a relatively strong conjugate acid	favoured by strong bases <i>e.g.</i> LDA (which generate a weak conjugate acid (<i>e.g.</i> <i>i</i> -Pr ₂ NH))

6.3 Sulphonation of naphthalene

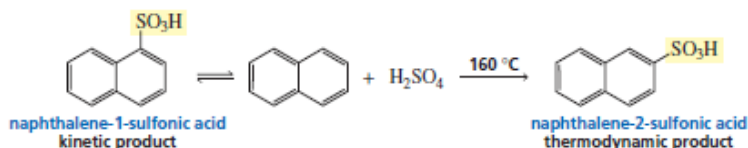
Naphthalene on sulphonation with conc. sulphuric acid yields 1-naphthalene sulphonic acid and 2-naphthalene sulphonic acid under different conditions.



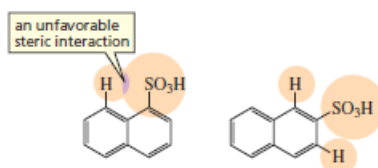
If sulphonation of naphthalene is carried out at 80 °C i.e., under irreversible conditions the kinetic product (1-substituted) is formed.



However, under reversible conditions, at 160 °C the thermodynamic product (2-substituted) is formed.



The kinetic product is easier to form because the carbocation leading to its formation is more stable. The 2-substituted product is more stable and formed at high temperature, because there is a bulky sulphonic group at 2-position is sterically less hindered. Whereas, in the kinetic product (1-substituted) the sulphonic group is close to hydrogen at 8-position.

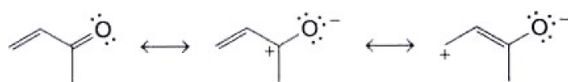


6.4 Addition of HCN to α,β -unsaturated carbonyl compounds

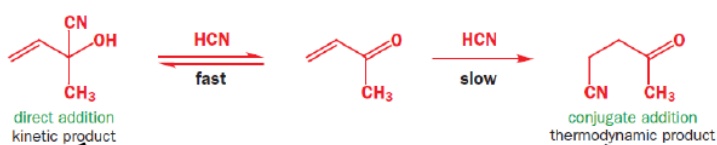
There are two electrophilic centres in α,β -unsaturated carbonyl system i.e

- The carbonyl carbon and
- The terminal carbon of the unsaturated system.

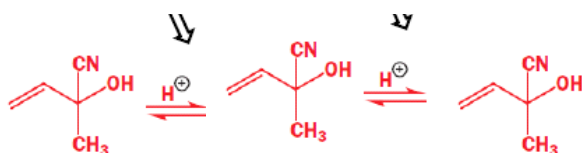
The nucleophile may attack to give either 1,2- or 1,4- addition products.



When HCN is added to α,β -unsaturated carbonyl compounds the cyanohydrin (direct addition) is obtained fast and it is kinetic product. While the β -cyano carbonyl compound (conjugate addition) is obtained in a slow reaction and it is the thermodynamic product.



The mechanism of direct addition is as follows:



The mechanism of conjugate addition is as follows:

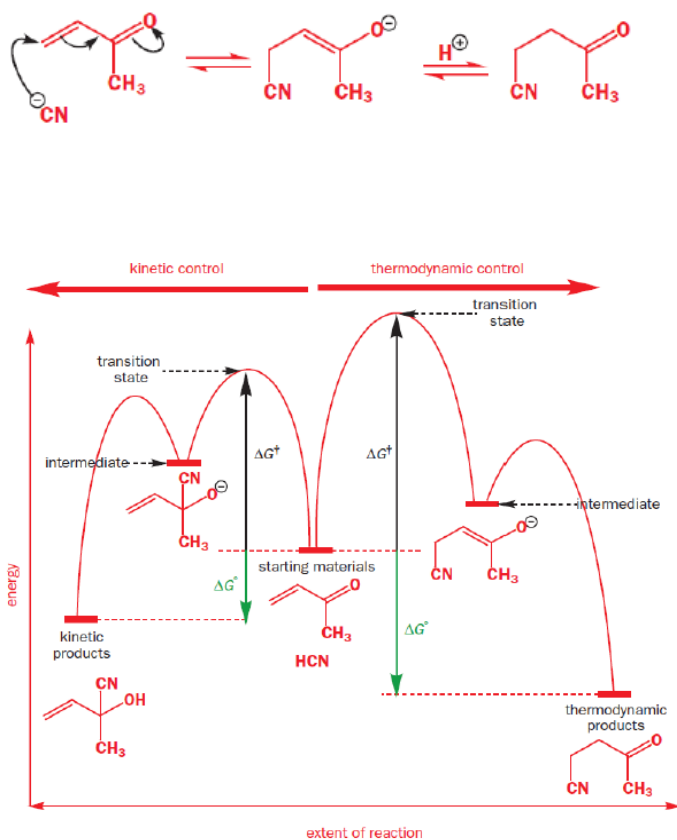
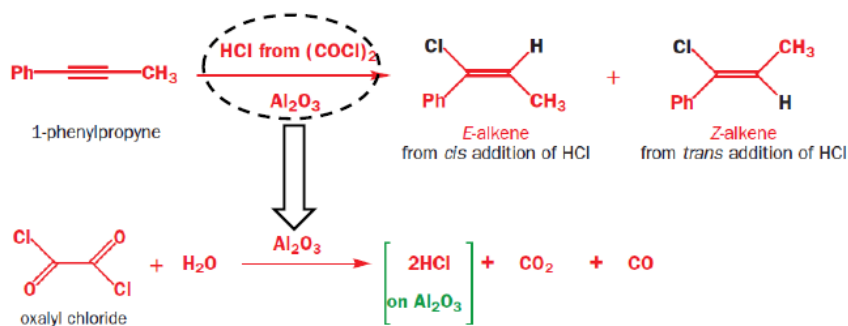


Fig.7: Reaction coordinate diagram for addition of HCN

6.5 Isomerization of alkenes

When HCl is added to alkynes it gets converted to an alkene. The E-alkene is formed faster and is known as the kinetic product; the Z-alkene is more stable and is known as the thermodynamic product. The HCl used for the reaction can be generated using oxaloyl chloride in alumina.



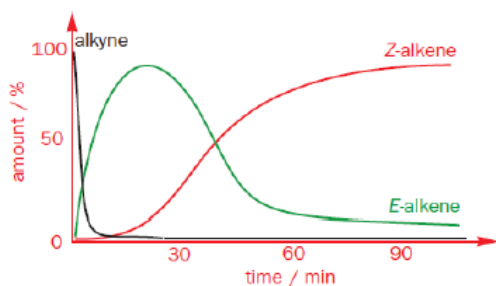


Fig.8: Progress of reaction for formation of Z or E alkene

The E-alkene is formed through addition of the adsorbed HCl on the alumina surface. It gets isomerized to the more stable Z-alkene. The reverse is not possible as the activation energy for conversion of Z back to E alkene is very high.

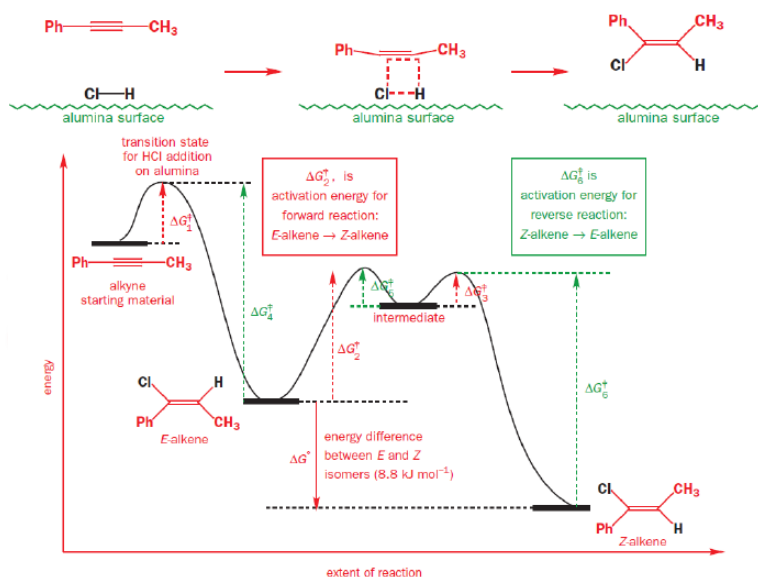
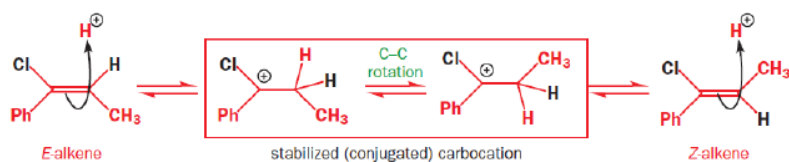


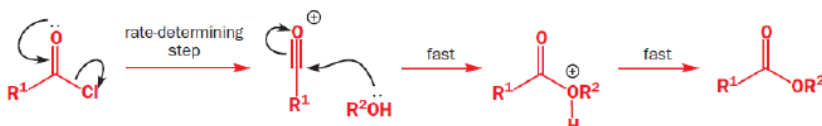
Fig.9 Reaction coordinate diagram for formation of Z or E alkene

The mechanism for the isomerisation of E into Z is shown below. It involves formation of a carbocation and breaking of the pi-bond on alkene. The single bond undergoes rotation and further elimination leads to the formation of Z-alkene.



6.6 Esterification of acid chlorides

The conversion of acid chloride to ester in acidic medium proceed via nucleophilic attack of alcohol on the carbonyl carbon.



Kinetics gives an insight into the mechanism of a reaction. Rate depends on the concentration of acid chloride, thus it is a Unimolecular reaction.

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

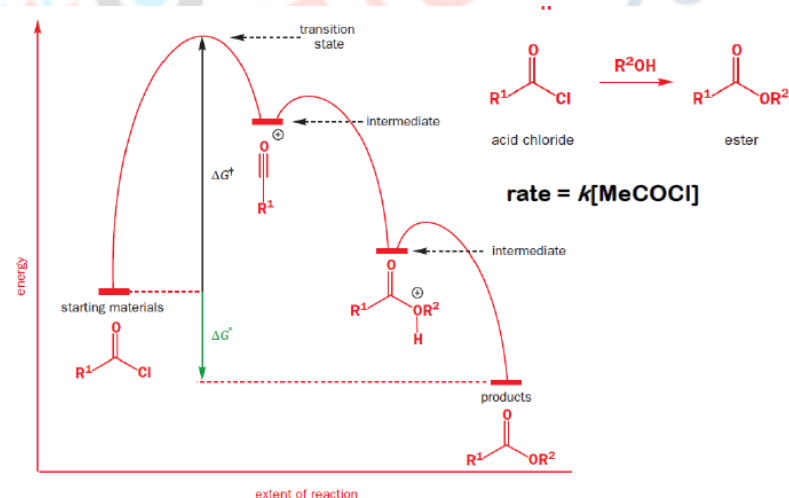


Fig.10: Reaction coordinate diagram for esterification of acid chlorides

5. Summary

- Thermodynamics is only concerned with the final state of a system and the mechanism of transformation does not matter at all.
- Kinetics describes the rates of reactions and how fast equilibrium is reached, it gives no information about conditions once the reaction equilibrates.
- Thermodynamic stability determines the equilibrium constant (K) and kinetic stability determines the rate constant (k).
- If ΔG^\ddagger is large the compound is kinetically stable.
- If ΔG° is negative the product is thermodynamically stable compared to reactant and the reaction is said to be exergonic reaction.
- If ΔG° is positive the product is thermodynamically unstable compared to reactant and the reaction is said to be endergonic reaction.
- During addition of HCl to 1,3-butadiene the 1,2- product is kinetic product and 1,4- is thermodynamic product.
- Low temperature favors kinetic enolate and at high temperature the more stable thermodynamic enolate is formed.
- Sulphonation of naphthalene at 80 °C gives kinetic product (1-substituted) but at 160 °C the thermodynamic product (2-substituted) is formed.
- When HCN is added to α,β -unsaturated carbonyl compounds the cyanohydrin (direct addition) is kinetic product. While the β -cyano carbonyl compound (conjugate addition) is the thermodynamic product.