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Subject	Chemistry
Paper No and Title	**5: Organic Chemistry-II (Reaction Mechanism-1)**
Module No and Title	**4, Intermediates, Transition states, Potential energy diagrams and Hammond's postulate**
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CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

TABLE OF CONTENTS

CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

1. Learning Outcomes

After studying this module, you shall be able to

- Identify various types of reactive intermediates
- Know the difference between transition state and intermediate
- Evaluate the stability of various transition states
- Analyse any type of reaction coordinate diagram
- Learn about Hammond postulate

2. Reactive Intermediates

Intermediate: It is a type of moiety formed in between the reaction, which represents a free energy minimum. For example figure 1 depicts carbocation intermediate formation during hydrolysis reaction of tert-butyl bromide.
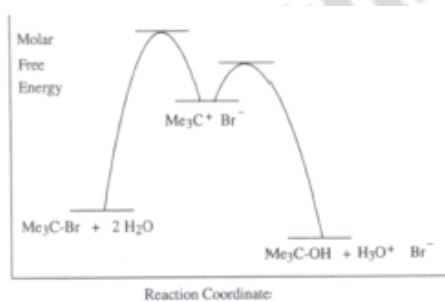

Fig 1: Reaction with an intermediate

The various types of reactive intermediates are **carbanion, carbocation, free radical, nitrene, carbene.**

Carbocations (Carbonium ions): The moieties in which a carbon atom bears a positive charge, is trivalent, sp^2 hybridized and has a planar structure (Figure 2).
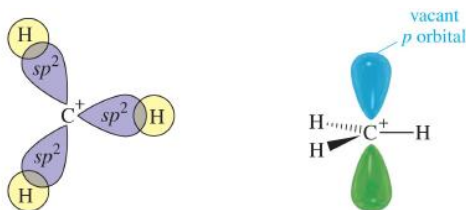
Fig. 2: Carbocation hybridization and structure

The more stable carbocation species have been prepared in solution phase and in some instances even as solid salts. Among simple alkyl carbocations, the stability order is tertiary > secondary > primary. There are many known examples of rearrangements of primary or secondary carbocations to tertiary, both in solution and in the gas phase. The most stable of the simple alkyl cations is the tert-butyl cation.

Carbanions: Carbanion contains a trivalent carbon that bears a negative charge, is sp^3 hybridized, tetrahedral, has one lone pair and is electron rich. Adhering to definition, each carbanion bears a pair of unshared electrons and is formally a base. The strength of the conjugate acid of a carbanion is a direct measure of its stability. The weaker the conjugate acid, the greater the base strength of the carbanion, and the lower the stability of the carbanion (Figure 3).
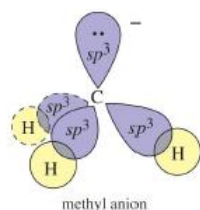

Fig. 3: Carbanion hybridization and structure

Free Radicals: Radicals are sp^2 hybridized, planar and neutral species with an odd electron in a perpendicular p orbital. As with carbocations and carbanions, simple alkyl radicals are very reactive and are usually transient species (Figure 4).
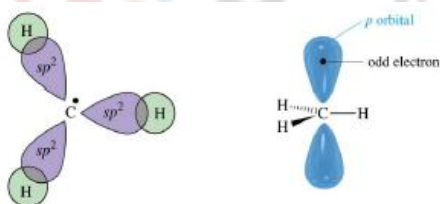

Fig. 4: Free radical structure and hybridization

Carbenes: These are uncharged reactive intermediates which have a divalent carbon atom. Carbenes are highly reactive species, and practically all have lifetimes considerably < 1 s. The parent species (CH_2) is usually known as methylene, although derivatives are more often named by the carbene nomenclature.

The two nonbonded electrons of a carbene can be either paired or unpaired. If they are paired, the species is spectrally a singlet, while, two unpaired electrons appear as a triplet (Figure 5).
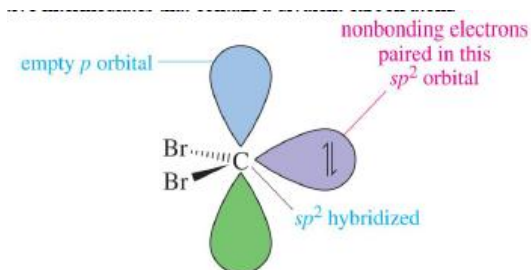
CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

Fig. 5: Carbene structure and hybridization

Nitrene: These are uncharged, electron-deficient species having a nitrogen atom with six electrons in its valence shell. These are analogous to carbene with respect to electronic structure (isoelectronic), methods of formation, detection and modes of reaction. Nitrenes are too reactive for isolation under ordinary conditions (Figure 6).
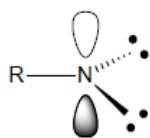

Fig. 6: Nitrene structure

3. **Transition State**

Transition state: The transition state (TS) is a configuration which possesses maximum potential energy which the reacting molecules should mandatorily pass through.

The TS is unstable and cannot be isolated. It is only a transient arrangement of atoms on the pathway from one intermediate to another. Transition state has high energy since old bonds starts breaking to form new bonds. The TS is represented by a double dagger symbol ($\ddagger$), as shown in figure 7. The free energy of the transition state is $\Delta G^{\ddagger}$. The difference in energy between the reactants and the transition state is called activation energy, Ea. A catalyst is a molecule which lowers the energy required to acquire the transition state.
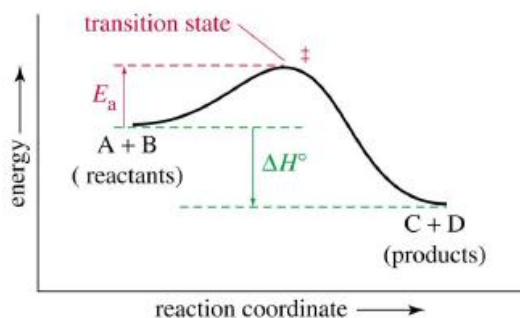
Fig.7: Reaction coordinate diagram showing TS

There may be more than one transition state for a reaction, generally for multi-step reactions. The local minima represent reactive intermediates and the local maxima are TSs (figure 8). The highest energy TS determines the overall reaction rate, and the step with highest energy TS is the rate determining step.
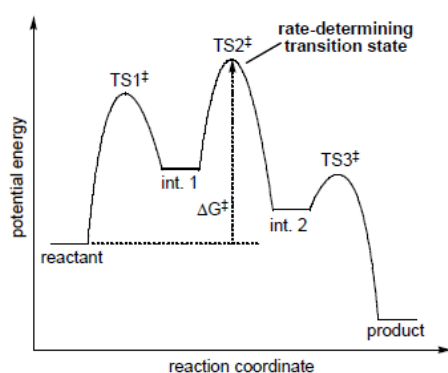

Fig. 8: Reaction coordinate diagram for multistep reaction showing TS and intermediate

Example of transition state:

(b) Addition of HCl to ethene

The C-C bond is double in the alkene (reactant structure). While addition of HCl to alkene, the TS must be intermediate between the single and the double bond. This is represented as a full line for the sigma bond and a dashed line for the partial pi bond. The new C-H bond made and the H-Cl bond in the TS is between no bond and a single bond, represented by a partial bond (Figure 9).
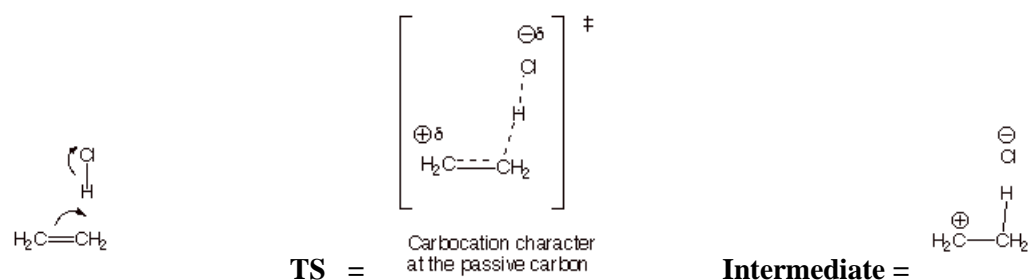
CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

Fig. 9 Addition of HCl to ethene

(b) Abstraction of hydrogen atoms from an alkane by bromine

The hydrogen atoms abstracted from an alkane by bromine atoms has a TS with radical character (Figure 10).
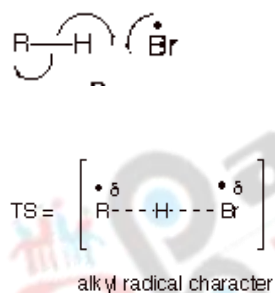

Fig. 10: Abstraction of H atom from an alkane by bromine

(c) Hydroboration

Although, the TS for addition of borane to an alkene has reactant and product character, the TS has some additional characters which are not present in either the reactant or the product. As a result, there is carbocation character at the carbon to which the hydrogen attached (Figure 11).
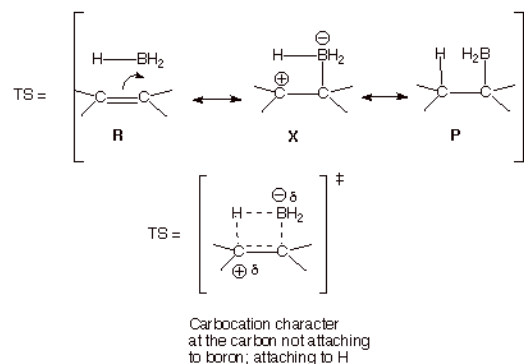
Fig. 11: Hydroboration reaction mechanism

(d) E2 Elimination reaction

E2 elimination reactions have predominant alkene (Product-like) character in the TS, there is also a significant carbanion character present at the beta carbon in the TS. Moreover, in some instances it becomes the dominant character and certain elimination reactions prefer to yield the thermodynamically less stable alkene (Figure 12).
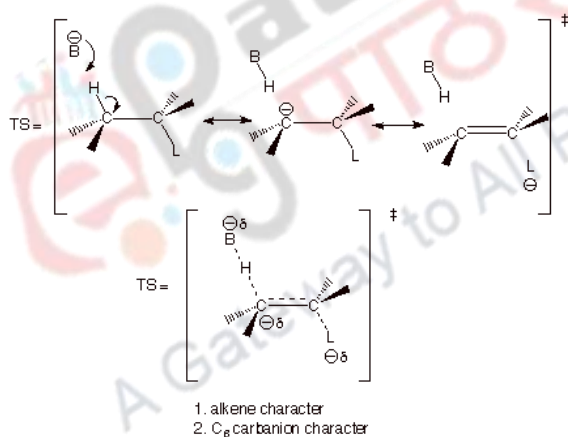

Fig. 12: E2 reaction mechanism

(e) Reaction of an unsymmetrical alkene, with unsymmetrical reagent

The reaction of isobutene with hydrogen chloride could generate either one or both of two products, i.e., tert-butyl chloride or isobutyl chloride.

The outcome of the competition between two distinct transition states determines the product in this case. One of the TS possesses tertiary carbocation character, and the other TS has primary

carbocation character. Since tertiary carbocation character is favoured more than the primary carbocation character, the TS for the formation of *tert*-butyl chloride is preferred. Thus, one of the products (tert-butyl chloride) is obtained with a very high selectivity (Figure 13).
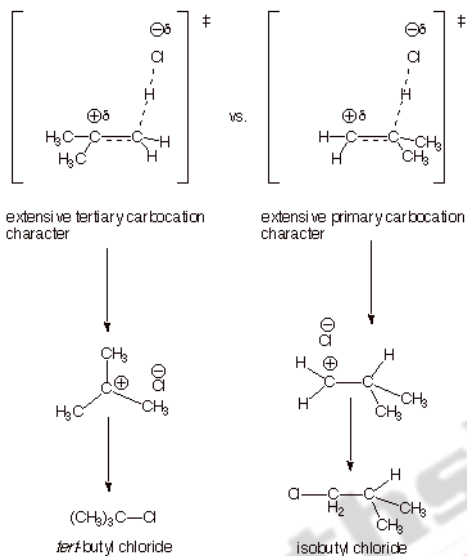

Fig. 13: Reaction of isobutene with HCl

(f) S_N2 reaction between hydroxide and chloromethane

The S_N2 reaction involves a collision between *two* molecules and the reaction proceeds via a transition state as shown. (Figure 14)
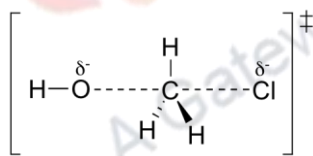

Fig. 14: Collision between two molecules

4. Potential Energy Diagram

Potential energy diagrams depict the potential energies of the reactants and products for a chemical reaction and how this energy changes during a reaction. The potential energy measures the energy stored within the bonds and phases of the reactants and the products. This potential energy is a part of the internal energy. In chemical reactions, the internal energy represents the total energy of the system and is often called enthalpy. During a chemical reaction the enthalpy or heat content of the reactants changes into the enthalpy or heat content of the products. (Figure 15)
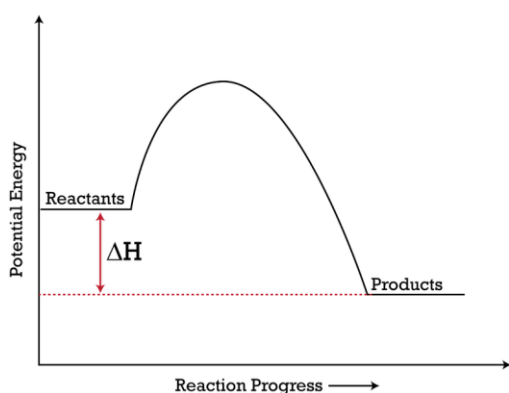

Fig. 15: Potential energy diagram of a reaction

Reaction Coordinate: The reaction coordinate, represents the extent to which the coordinates such as bond lengths, angles, and dihedral angles of the reactants gets converted to those of the products during the progress of a reaction. The reaction coordinate (the x-axis in an energy diagram) is a parameter used to describe the progress of the reaction. This axis could be time, a structural parameter or bond dissociation.

The Reaction Energy Profiles help to explain the concepts of Ea and TS. The vertical axis represents the total potential energy, and the horizontal axis represents the reaction co-ordinate, which depicts the progress of the reaction, with reactants placed on the left and products placed on the right. $\Delta H°$ is the difference in energy between the reactants and the products.

The figure 16 for reaction potential energy diagrams for irreversible exothermic and endothermic reactions shows a large ΔH value. While figure 17 for reaction potential energy diagrams for reversible exothermic and endothermic reactions shows a small ΔH value.

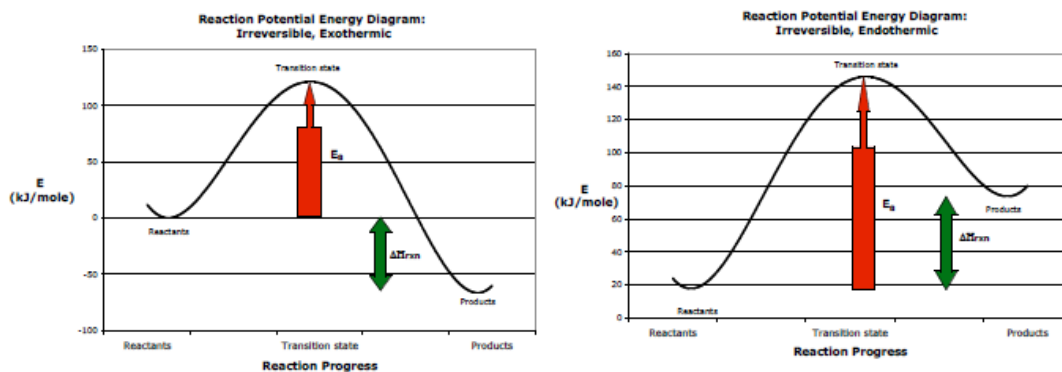| CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

Fig 16: Reaction potential energy diagrams for irreversible exothermic and endothermic reactions
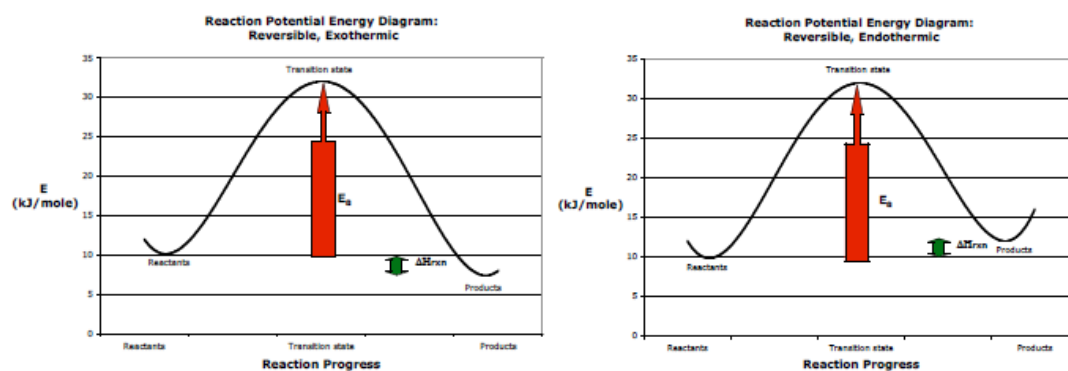

Fig 17: Reaction potential energy diagrams for reversible exothermic and endothermic reactions

5. Hammond Postulate

The relationship of the transition state structure to the structure of reactants, intermediates, or products is postulated by Hammond in his statement known as **Hammond's postulate.**

It states: "If two states, as, for example, a transition state and an unstable intermediate, occur consecutively during a reaction process and have nearly the same energy content, their interconversion will involve only a small reorganization of molecular structure." In other words, **the TS is more similar in structure to the species to which it is more similar in energy**.

Because the rates of chemical reactions are controlled by $\Delta G^{\ddagger}$, information regarding the structure of TS is crucial to understanding reaction mechanisms. On the contrary, TSs have only transitory

existence, thus, it is not possible to make experimental measurements that provide direct information about their structure.

Considering an exergonic reaction, the TS appears more similar in energy to the reactant as compared to product. Therefore, the structure of the TS will resemble the structure of the reactant more than that of the product.

In an endergonic reaction, the TS is more similar in energy to the product, so the structure of the TS will more closely resemble the structure of the product. Only when reactant as well as the product have identical energies would we expect the structure of the TS to be exactly halfway between the structures of the reactant and the product.

Sometime the terms "early" or "late" TS are used. An "**early TS**" is reactant-like, whereas a **"late TS"** is intermediate- (or product-) like (figure 18).

In an endothermic reaction, the T.S. is closer to the products in energy and in structure. (**Late TS**)

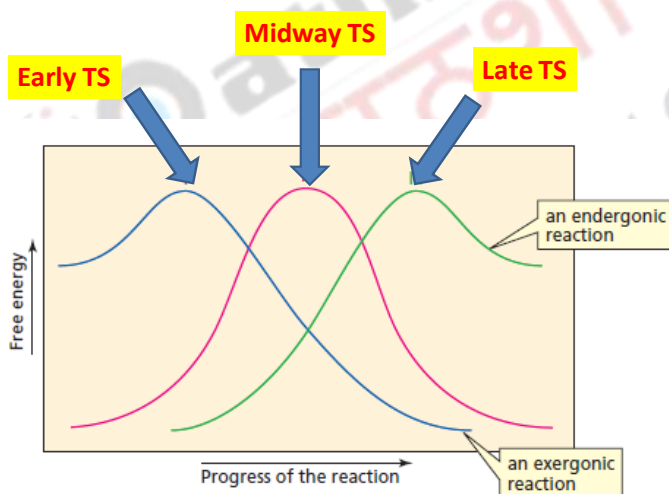In an exothermic reaction, the T.S. is closer to the reactants in energy and structure. (**Early TS**)

Fig 18: Reaction coordinate diagram showing early and late transition states

Examples of reactions involving TS

(a) **Electrophilic aromatic substitution**

In electrophilic aromatic substitution TS structure is discussed in terms of a reaction intermediate. Examples are bromination, chlorination, nitration or sulphonation of benzene, methoxybenzene (anisole), nitrobenzene etc. (Figure 19)
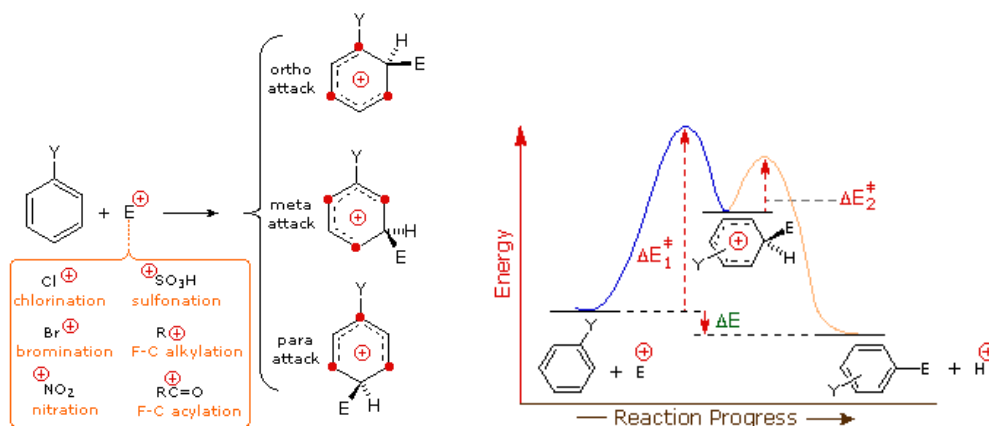
Fig. 19: Electrophilic aromatic substitution and its PE diagram

(b) Formation of tert-butyl cation

The tert-butyl cation is formed faster than the isobutyl cation when 2-methylpropene reacts with HCl. Because the formation of a carbocation is an endergonic reaction, the structure of the TS will resemble the structure of the carbocation product. This means that the TS will have a significant amount of positive charge on a carbon. The *tert*-butyl cation (a tertiary carbocation) is more stable than the isobutyl cation (a primary carbocation). (Figure 20)
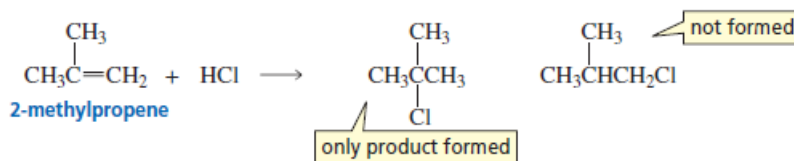

Fig. 20: *tert.* butyl cation and its favoured formation

The factors that stabilize the positively charged carbocation product stabilize the partially positive charged TS.

Therefore, the TS forming the *tert*-butyl cation is more stable than the TS leading to the isobutyl cation. Because the amount of positive charge in the TS is not as large as the amount of positive charge in the present in the carbocation product, the difference in the stabilities of the two TSs is not as great as the difference in the stabilities of the two carbocation products. (Figure 21)
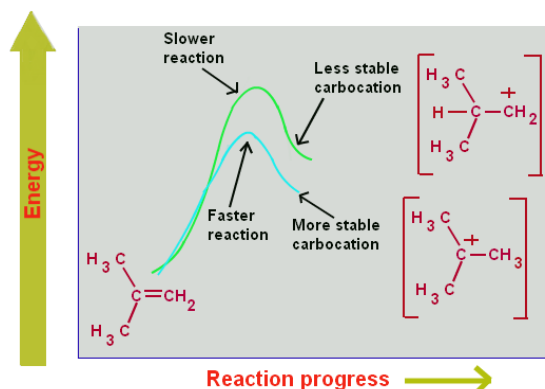
CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

Fig. 21: PE diagram for the formation of *tert.* butyl cation

(c) Electrophilic addition reaction for an alkyne

Why is the TS for the first step of an electrophilic addition reaction for an alkyne less stable than that for an alkene?

The Hammond postulate predicts that the structure of the TS will resemble the structure of the intermediate. The intermediate formed when a proton adds to an alkyne is a vinylic proton. In the second step of the reaction, the positively charged carbocation intermediate reacts rapidly with the negatively charged chloride ion.

Thus alkynes, like alkenes, undergo electrophilic addition reactions. The same electrophilic reagents that add to alkenes also add to alkynes and that again like alkenes electrophilic addition to a *terminal* alkyne is regioselective. When an electrophile adds to a terminal alkyne, it adds to the *sp* carbon that is bonded to the hydrogen. The addition reactions of alkynes, however, have a feature that alkenes do not have. Because the product of the addition of an electrophilic reagent to an alkyne is an alkene, a second electrophilic addition reaction can occur.

An alkyne is less reactive than an alkene. This might at first seem surprising because an alkyne is less stable than an alkene. However, reactivity depends on $\Delta G^{\ddagger}$ which in turn depends on the stability of the reactant and the stability of the TS. For an alkyne to be both less stable and less reactive than an alkene, two conditions must hold: The TS for the first step (the rate-limiting step) of an electrophilic addition reaction for an alkyne must be less stable than the TS for the first step of an electrophilic addition reaction for an alkene, and the difference in the stabilities of the TSs must be greater than the difference in the stabilities of the reactants so that $\Delta G^{\ddagger}$ alkyne > $\Delta G^{\ddagger}$ alkene.

(d) The hydrogen abstraction for bromine is endothermic, but exothermic for chlorine.

CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

The hydrogen abstraction for bromine is endothermic, as the TS is close in energy to products. But hydrogen abstraction for chlorine is exothermic, as the TS is close in energy to reactant.

Hydrogen abstraction for chlorination is exothermic, because the TS resembles the alkane and a chlorine atom. There is little radical character on carbon in the TS. Regioselectivity is only slightly influenced by radical stability.

However, in bromination of alkanes, the abstraction of hydrogen is an endothermic step and TS shows resemblance with an alkyl radical and HBr, therefore carbon atom in transition stat TS e has significant radical character. Compare to chlorination, the activation energy of bromination is much more so reaction becomes more selective. (Figure 22)
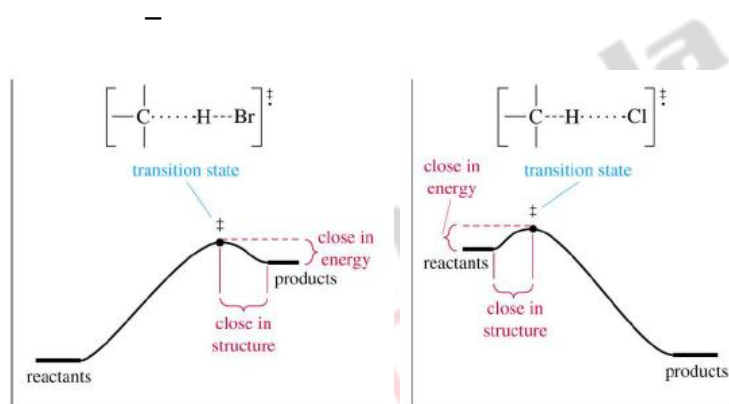

Fig. 22: Comparison of chlorination and bromination of alkanes

The TS's forming for the 1° and 2° radicals for the endothermic bromination have a larger energy difference (9 kJ) than those forming for the exothermic chlorination (4 kJ). However, the energy difference of the 1° and 2° products formed in chlorination and bromination is the same (13 kJ). (Figure 23)
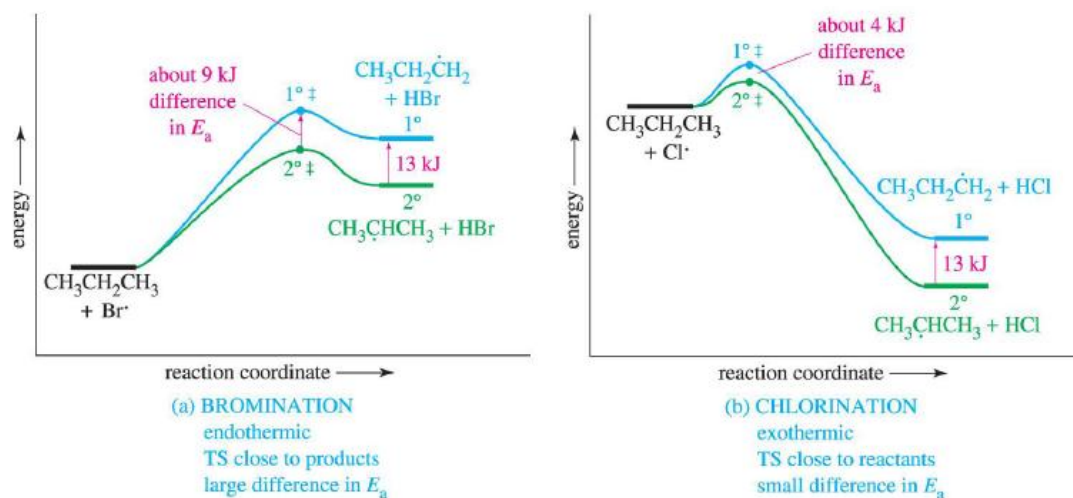
Fig. 23: Transition states in chlorination and bromination reactions

Any change that helps to stabilize the products relative to the reactants shifts the TS toward the reactants. For example, the TS for the carbocation intermediate is moves towards the reactants as the intermediate species becomes more stabilized (1°, 2° and 3°). (Figure 24)
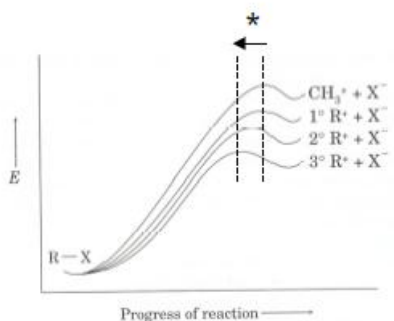

Fig. 24: Depiction of transition states for the carbocation intermediate

Some Applications of Hammond Postulate are:

- Easily explain the relationship between the rate of a reaction and the stability of the products.
- Applicable on electrophilic addition reactions which proceed through the formation of carbocation which formed by protonation of an alkene is an endergonic step.

CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate

- Explain the selectivity of product formation during bromination and chlorination of alkanes.
- Useful in rationalizing the S_N1 mechanism of alkyl halides which proceeds through the formation of carbocation as an intermediate.

Limitations of Hammond Postulate:

- The Hammond postulate makes a connection between rate (kinetics) and equilibrium (thermodynamics) that has no theoretical basis.
- Use of the Hammond postulate is based primarily on enthalpy considerations and neglects the effects that activation entropies can have on reaction rates.
- The Bronsted Catalysis Law (an empirical linear free energy relationship) *is valid* within carefully chosen groups of acids or bases.

6. Summary

- An intermediate is a species formed in a stepwise reaction, which represents a free energy minimum.
- The various types of reactive intermediates are carbocation, carbanion, free radical, carbene, nitrene.
- The TS is a configuration of maximum potential energy which the reacting molecules must pass through.
- The TS cannot be isolated, is unstable, and it is only a transient arrangement of atoms on the pathway from one intermediate to another.
- The reaction coordinate, represents the extent to which the coordinates such as bond lengths, angles, and dihedral angles of the reactants gets converted to those of the products during the progress of a reaction.
- Reaction path diagram of a reaction is a two dimensional slice of a multidimensional energy surface.
- According to Hammond's postulate the TS is more similar in structure to the species to which it is more similar in energy.
- In an endothermic reaction, the T.S. is closer to the products in energy and in structure. (Late TS)
- In an exothermic reaction, the T.S. is closer to the reactants in energy and structure. (Early TS)

CHEMISTRY	PAPER : 5 ,Organic Chemistry- II (Reaction Mechanism-1)
	MODULE :4 , Intermediates, Transition states, Potential energy diagrams and Hammond's postulate