VIVEKANANDA COLLEGE THAKURPUKUR KOLKATA-700063

NAAC ACCREDITED ‘A’ GRADE

Topic : Enzyme Catalysis

Course Title : Enzymes

Paper : CC4

Unit : 1

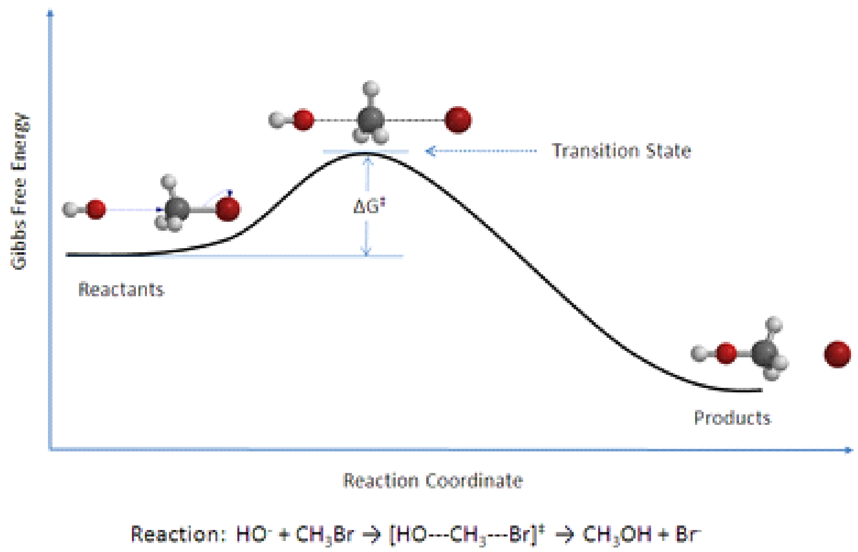
Semester : 2

Name of the Teacher : Dr. Kakali Roy

Name of the Department : Biochemistry

Transition state theory

Transition state theory (TST) explains the reaction rates of elementary chemical reactions. The theory assumes a special type of chemical equilibrium between reactants and activated transition state complexes.



The transition state of a chemical reaction is a particular configuration along the reaction coordinate. It is defined as the state corresponding to the highest potential energy along this reaction coordinate.

Transition State Theory postulates that a hypothetical transition state occurs after the state in which chemicals exist as reactants, but before the state in which they exist as products. activated complex A higher-energy species that is formed during the transition state of a chemical reaction.

How does an enzyme affect the transition state of a reaction ?

Enzymes are usually proteins that act like catalysts. The enzyme's ability to make the reaction faster depends on the fact that it stabilizes the transition state. Enzymes decreases activation energy by shaping its active site such that it fits the transition state even better than the substrate.

The transition state is a high-energy state, and some amount of energy – the activation energy – must be added in order for the molecule reach it. Because the transition state is unstable, reactant molecules don't stay there long, but quickly proceed to the next step of the chemical reaction.

The **basic ideas behind transition state theory** are as follows:

- Rates of reaction can be studied by examining activated complexes near the saddle point of a potential energy surface. The details of how these complexes are formed are not important. The saddle point itself is called the transition state.

- The activated complexes are in a special equilibrium (quasi-equilibrium) with the reactant molecules.
- The activated complexes can convert into products, and kinetic theory can be used to calculate the rate of this conversion.

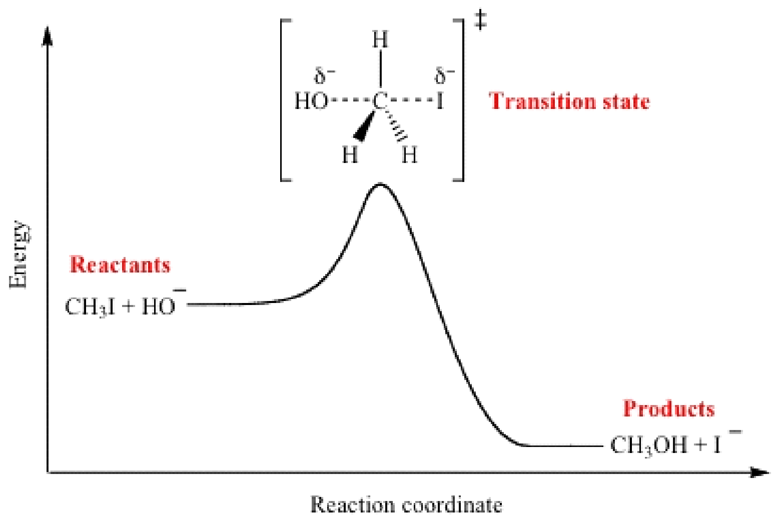
If the rate constant for a reaction is known, TST can be used successfully to calculate the standard enthalpy of activation, the standard entropy of activation, and the standard Gibbs energy of activation.

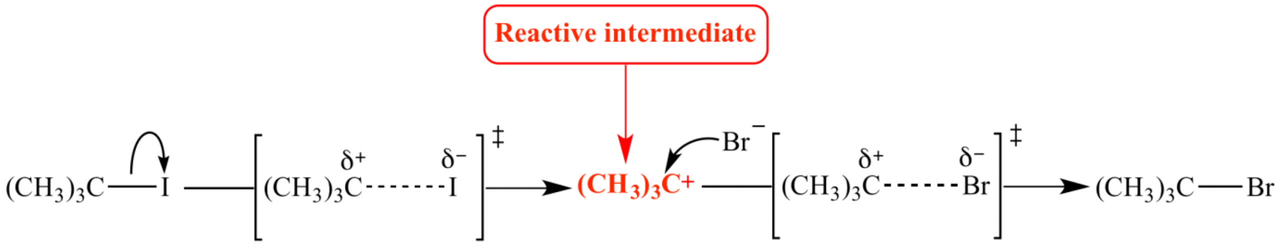
Postulates of Transition State Theory

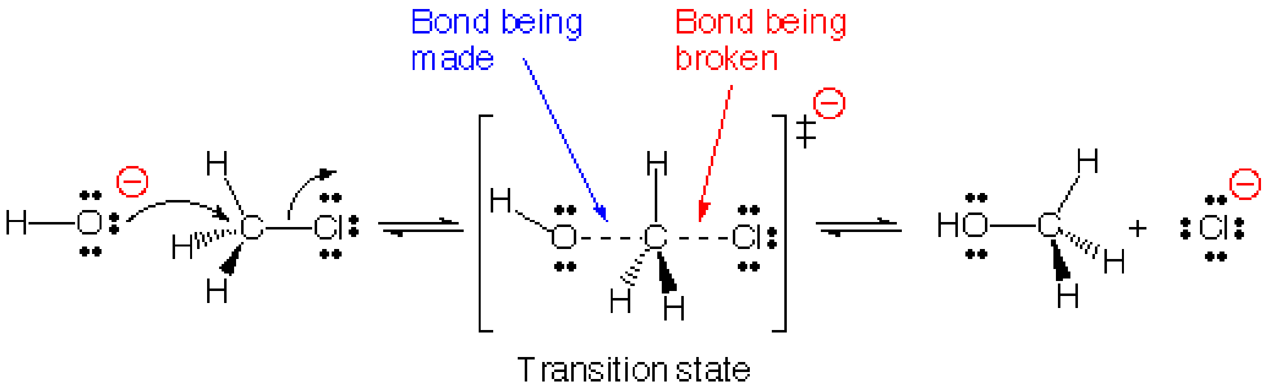
According to transition state theory, between the state in which molecules exist as reactants and the state in which they exist as products, there is an intermediate state known as the transition state. The species that forms during the transition state is a higher-energy species known as the activated complex. TST postulates three major factors that determine whether or not a reaction will occur. These factors are:

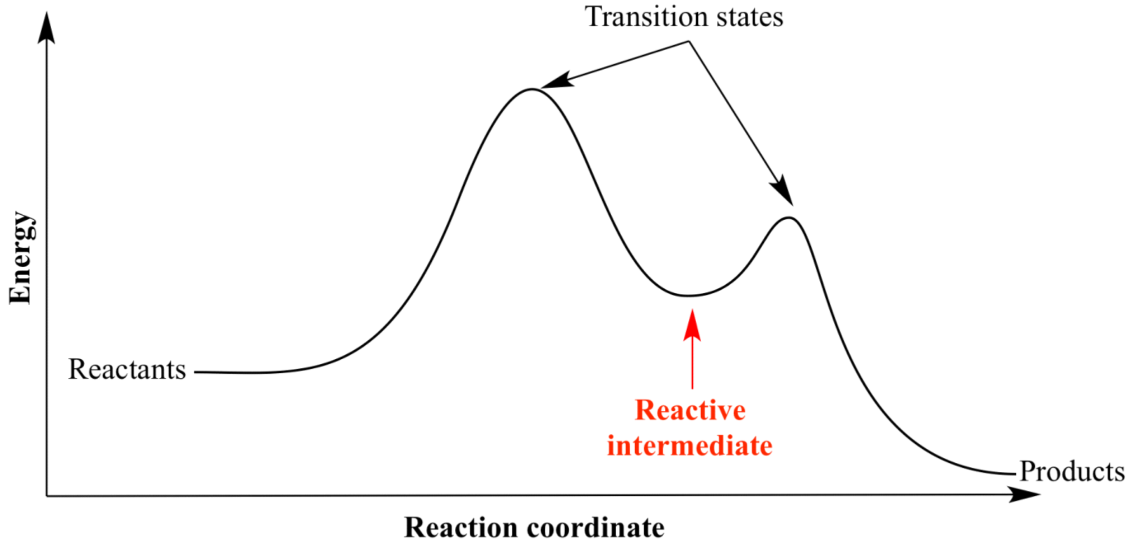
- The concentration of the activated complex.
- The rate at which the activated complex breaks apart.
- The mechanism by which the activated complex breaks apart; it can either be converted into products, or it can "revert" back to reactants.

According to collision theory, a successful collision is one in which molecules collide with enough energy and with proper orientation, so that reaction will occur. However, according to transition state theory, a successful collision will not necessarily lead to product formation, but only to the formation of the activated complex. Once the activated complex is formed, it can then continue its transformation into products, or it can revert back to reactants.




Reactive intermediate
$(CH_3)_3C$—I
$[(CH_3)_3C^{\delta+}$------$I^{\delta-}]^{\ddagger}$
$(CH_3)_3C^{+}$
Br^{-}
$[(CH_3)_3C^{\delta+}$------$Br^{\delta-}]^{\ddagger}$
$(CH_3)_3C$—Br


Bond being made
Bond being broken
Transition state

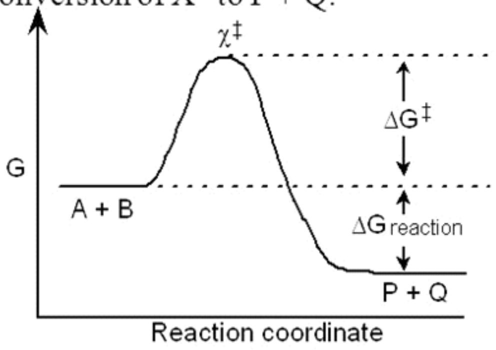

Transition states
Energy
Reactants
Reactive intermediate
Products
Reaction coordinate

I. Transition state theory

Consider the reaction $A + B \rightarrow P + Q$

$$A + B \underset{}{\overset{K^{\ddagger}}{\rightleftharpoons}} X^{\ddagger} \overset{k'}{\rightarrow} P + Q$$

where $A + B$ react through transition state, $X^{\ddagger}$, to form products $P + Q$. $K^{\ddagger}$ is the equilibrium constant between $A + B$ and $X^{\ddagger}$ and k' is the rate constant for conversion of $X^{\ddagger}$ to $P + Q$.

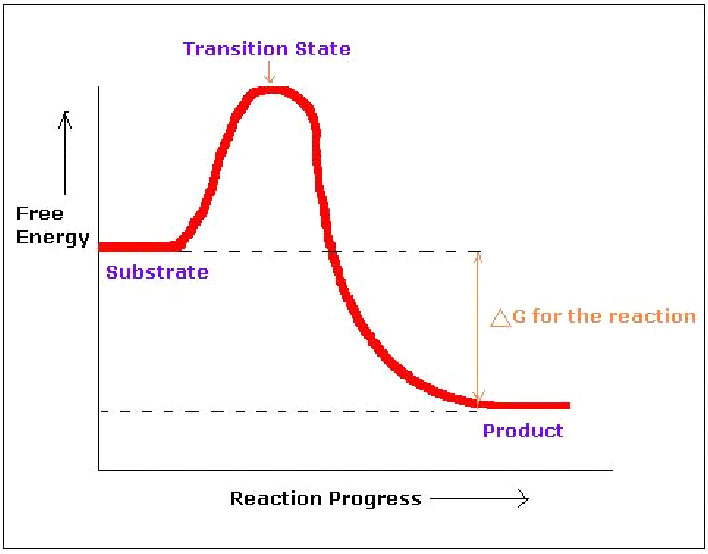


The minimum energy pathway of the reaction is shown in the reaction coordinate, or transition state diagram, at left. Chemical conversion of A + B to P + Q proceeds through a transition state $X^{\ddagger}$ which is the least stable (least probable, highest free energy) species along the pathway. Molecules that achieve the activation energy, $\Delta G^{\ddagger}$, can go on to react while molecules that fail to achieve the transition state fall back to the ground state.

The transition state, $X^{\ddagger}$, is metastable. (Unlike a reaction intermediate, the transition state has only a transient existence, like a pebble balanced on a pin. By definition, a transition state cannot be isolated.) The transition state can be thought of as sharing some features of the reactants and some features of the products. That is, some bonds in the substrate are on their way to being broken and some bonds in the product are partially formed.

The transition state is the transitory of molecular structure in which the molecule is no longer a substrate but not yet a product. All chemical reactions must go through the transition state to form a product from a substrate molecule. The transition state is the state corresponding to the highest energy along the reaction coordinate. It has more free energy in comparison to the substrate or product; thus, it is the least stable state. The specific form of the transition state depends on the mechanisms of the particular reaction.

In the equation $S \rightarrow X \rightarrow P$, X is the transition state, which is located at the peak of the curve on the Gibbs free energy graph.



Application to Enzymes

The enzyme's ability to make the reaction faster depends on the fact that it stabilizes the transition state. The transition state's energy or, in terms of a reaction, the activation energy is the minimum energy that is needed to break certain bonds of the reactants so as to turn them into products. Enzymes decreases activation energy by shaping its active site such that it fits the transition state even better than the substrate. When the substrate binds, the enzyme may stretch or distort a key bond and weaken it so that less activation energy is needed to break the bond at the start of the reaction. In many cases, the transition state of a reaction has a different geometry at the key atom (for instance, tetrahedral instead of trigonal planar). By optimizing binding of a tetrahedral atom, the substrate is helped on its way to the transition state and therefore lowers the activation energy, allowing more molecules to be able to turn into products in a given period of time. The enzyme stabilizes the transition state through various ways. Some ways an enzyme stabilizes is to have an environment that is the opposite charge of the transition state, providing a different pathway, and making it easier for the reactants to be in the right orientation for reaction.

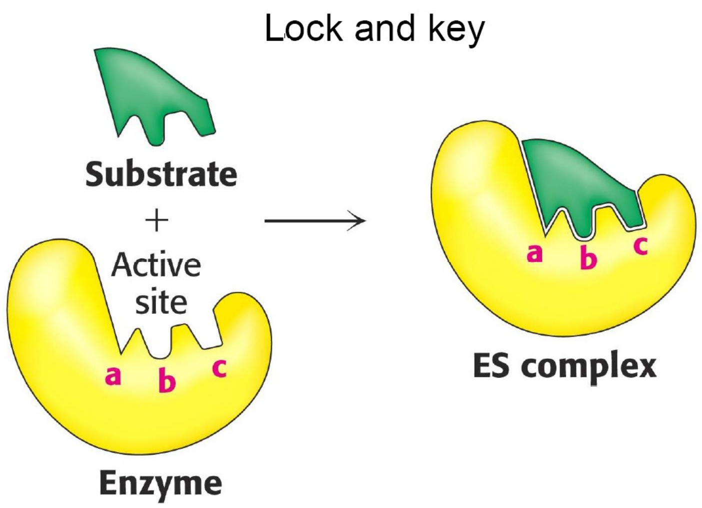
Transition state analogue

Transition state analogues are chemical compounds with a chemical structure that resembles the transition state of a substrate molecule in an enzyme-catalyzed chemical reaction. Transition state analogs can be used as inhibitors in enzyme-catalyzed reactions by blocking the active site of the enzyme. Theory suggests that enzyme inhibitors which resembled the transition state structure would bind more tightly to the enzyme than the actual substrate, thus do not undergo a catalytic reaction.

Theories of active site-substrate interaction

Fischer theory (lock and key model)

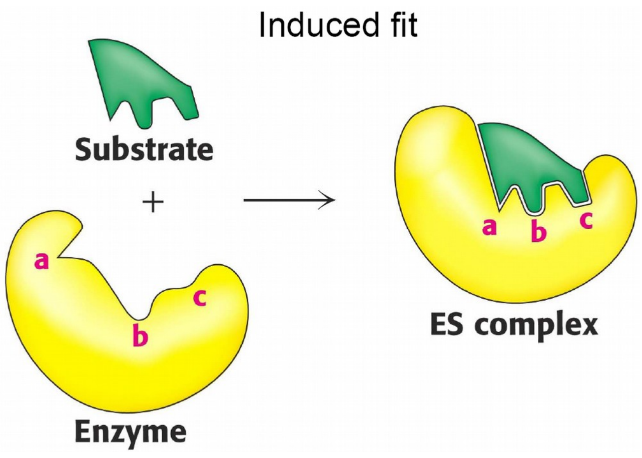
The enzyme active site (**lock**) is able to accept only a specific type of substrate (**key**)



According to this model a substrate binds with its enzyme at its active site which is rigid, pre shaped template to the complementary structure of the substrate.

Koshland theory (induced-fit model)

The process of substrate binding induces specific conformational changes in the the active site region



According to this model, the active site of the enzyme is flexible and when an enzyme binds with a substrate, the substrate induces a conformational change in the enzyme. This aligns amino acid residues in the enzymes in the correct spatial orientation for proper binding of the substrate. Thus the active site does not possess a rigid, pre formed structure on the enzyme but substrate can induce some change in it so that it can fit properly.

References :

1. Voet D, Voet JG (2011), Biochemistry (4th ed.), New York : Wiley
2. www.google.com