Teacher: DR. SUBHANKAR SARDAR
**Class :** Semester-2
Paper: C4T: Organic Chemistry
Topic : General Treatment of Reaction Mechanism II (Reaction Thermodynamics)

Comments: Read whole the notes thoroughly. This part is very important for final examination.

References:
1) Part-1: A Guide book of mechanism in Organic Chemistry by Peter Sykes
2) Few Important definations (https://chem.libretexts.org/Bookshelves/Organic_Chemistry/Map%3A_Organic_Chemistry_(Smith)/Chapter_16%3A_Conjugation%2C_Resonance%2C_and_Dienes/16.11%3A_Kinetic_Versus_Thermodynamic_Products)
3) Few youtube videos

Rearrangements may also proceed *via* intermediates that are essentially cations, anions, or radicals, though those involving carbocations, or other electron-deficient species, are by far the most common. They may involve a major rearrangement of the carbon skeleton of a compound, as during the conversion of 2,3-dimethylbutan-2,3-diol (pinacol, 42) into 2,2-dimethylbutan-3-one (pinacolone, 43, *cf.* p. 113):

$$Me_2C-CMe_2 \quad \xrightarrow{H^\oplus} \quad Me_3C-CMe$$
$$\underset{HO \quad OH}{|} \qquad \qquad \underset{O}{\overset{\|}{}}$$

(42)   (43)
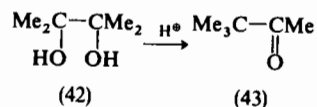
The actual rearrangement step in such reactions is often followed by a further displacement, addition or elimination, before a stable end-product is obtained.

2
Energetics, kinetics, and the investigation of mechanism

We have now listed a number of electronic and steric factors that can influence the reactivity of a compound in a given situation, and also the types of reagent that might be expected to attack particular centres in such a compound especially readily. We have as yet, however, had little to say directly about how these electronic and steric factors, varying from one structure to another, actually operate in energetic and kinetic terms to influence the course and rate of a reaction. These considerations are of major importance, not least for the light they might be expected to throw on the detailed pathway by which a reaction proceeds.

2.1 ENERGETICS OF REACTION

When we consider the conversion of starting materials into products, which constitutes an organic reaction, one of the things that we particularly want to know is '*how far* will the reaction go over towards products?' Systems tend to move towards their most stable state, so we might expect that the more stable the products are, compared with the starting materials, the further over in the former's favour any equilibrium between them might be expected to lie, i.e. the larger $\Delta_{stability}$ is in the diagram (Fig. 2.1) below, the greater the expected conversion into products:
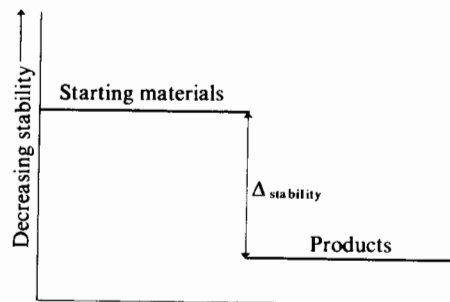
Fig. 2.1

However, it quickly becomes apparent that the simple energy change that occurs on going from starting materials to products, and that may readily be measured as the heat of reaction, ΔH^*, is not an adequate measure of the difference in stability between them, for there is often found to be no correlation between ΔH and the equilibrium constant for the reaction, K. Highly exothermic reactions are known with only small equilibrium constants (little conversion of starting materials into products), and some reactions with large equilibrium constants are known that are actually endothermic (enthalpy of products higher than that of starting materials): clearly some factor in addition to enthalpy must be concerned in the relative stability of chemical species.

That this should be so is a corollary of the Second Law of Thermodynamics which is concerned essentially with probabilities, and with the tendency for ordered systems to become disordered: a measure of the degree of disorder of a system being provided by its *entropy*, S. In seeking their most stable condition, systems tend towards *minimum* energy (actually enthalpy, H) and *maximum* entropy (disorder or randomness), a measure of their relative stability must thus embrace a compromise between H and S, and is provided by the *Gibb's free energy*, G, which is defined by,

$$G = H - TS$$

where T is the absolute temperature. The free energy change during a reaction, at a particular temperature, is thus given by,

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

* H is a measure of the heat content, or *enthalpy*, of a compound, and ΔH is preceded by a minus sign if the products have a lower heat content than the starting materials: when there is such a *decrease* in enthalpy the reaction is *exothermic*.

and it is found that the change in free energy in going from starting materials to products, $\Delta G^\ominus$ ($\Delta G^\ominus$ refers to the change under standard conditions: at unit activity; less exactly at unit, i.e. molar, concentration), is related to the equilibrium constant, K, for the change by the relation,

$$-\Delta G^\ominus = 2 \cdot 303 RT \log K$$

i.e. the larger the *decrease* in free energy (hence, *minus* $\Delta G^\ominus$) on going from starting materials to products, the larger the value of K, and the further over the equilibrium lies in favour of products. The position of minimum free energy thus corresponds to the attainment of equilibrium by starting materials/products. In a reaction for which there is *no* free energy change ($\Delta G^\ominus = 0$) $K = 1$, which corresponds to 50% conversion of starting materials into products. Increasing *positive* values of $\Delta G^\ominus$ imply rapidly *decreasing* fractional values of K (the relationship is a logarithmic one), corresponding to extremely little conversion into products, while increasing *negative* values of $\Delta G^\ominus$ imply correspondingly rapidly *increasing* values of K. Thus a $\Delta G^\ominus$ of -42 kJ (-10 kcal) mol^{-1} corresponds to an equilibrium constant of $\approx 10^7$, and essentially complete conversion into products. A knowledge of the standard free energies of starting materials and of products, which have been measured for a large number of organic compounds, thus enables us to predict the expected extent of the conversion of the former into the latter.

The ΔH factor for the change can be equated with the difference in energies between the bonds in the starting materials and the bonds in the products, and an approximate value of ΔH for a reaction can often be predicted from tables of standard bond energies: which is hardly unexpected, as it is from ΔH data that the average bond energies were compiled in the first place!

The entropy factor cannot be explained quite so readily, but effectively it relates to the number of possible ways in which their total, aggregate energy may be shared out among an assembly of molecules; and also to the number of ways in which an individual molecule's quanta of energy may be shared out for translational, rotational, and vibrational purposes, of which the translational is likely to be by far the largest in magnitude. Thus for a reaction in which there is an *increase* in the number of molecular species on going from starting materials to products,

$$A \rightleftarrows B + C$$
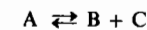
there is likely to be a sizeable *increase* in entropy because of the gain in translational freedom. The $-T\Delta S$ term may then be large enough to outweigh the $+\Delta H$ term of an endothermic reaction, thus leading to a negative value for ΔG, and an equilibrium that lies well over in favour of products. If the reaction is exothermic anyway (ΔH negative),

ΔG will of course be even more negative, and the equilibrium constant, K, correspondingly larger still. Where the number of participating species *decreases* on going from starting materials to products there is likely to be a *decrease* in entropy (ΔS negative); hence,

$$A + B \rightleftharpoons C \qquad \Delta G = \Delta H - (-)T\Delta S$$

and unless the reaction is sufficiently exothermic (ΔH negative and large enough) to counterbalance this, ΔG will be positive, and the equilibrium thus well over in favour of starting materials.

Cyclisation reactions may also be attended by a decrease in entropy,

$$CH_3(CH_2)_3CH{=}CH_2 \rightleftharpoons$$
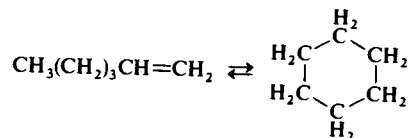
for though there is no necessary change in translational entropy, a constraint is imposed on rotation about the carbon–carbon single bonds: this is essentially free in the open chain starting material, but is greatly restricted in the cyclic product. This rotational entropy term is, however, smaller in size than the translational entropy term involved in reactions where the number of participating species decreases on forming products—a fact that is reflected in the preference for *intra*- rather than *inter*-molecular hydrogen bonding in 1,2-diols:

intra-molecular   *inter*-molecular
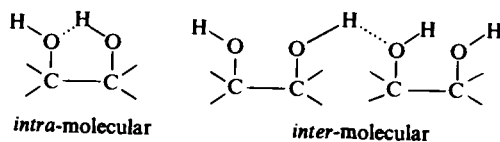
It should not be overlooked that the entropy term involves temperature ($T\Delta S$) while the enthalpy (ΔH) term does not, and their relative contributions to the free energy change may be markedly different for the same reaction carried out at widely differing temperatures.

2.2 KINETICS OF REACTION

Though a negative value for $\Delta G^{\ominus}$ is a necessary condition for a reaction to take place at all under a given set of conditions, further information is still needed as the $-\Delta G^{\ominus}$ value tells us nothing about *how fast* the starting materials are converted into products. Thus for the oxidation of cellulose,
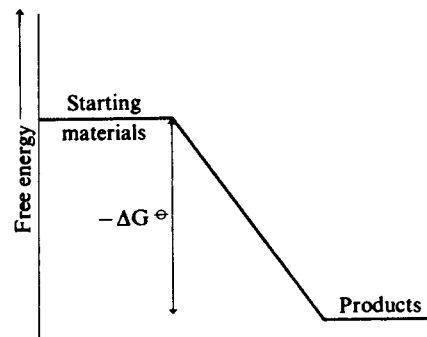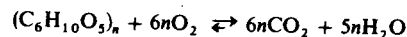
$$(C_6H_{10}O_5)_n + 6nO_2 \rightleftharpoons 6nCO_2 + 5nH_2O$$

Fig. 2.2

$\Delta G^{\ominus}$ is negative and large in magnitude, so that the equilibrium lies essentially completely over in favour of CO_2 and H_2O; but a newspaper (very largely cellulose) can be read in the air (or even in an oxygen tent!) for long periods of time without it noticeably fading away to gaseous products: the *rate* of the conversion is extremely slow under these conditions despite the very large $-\Delta G^{\ominus}$, though it is, of course, speeded up at higher temperatures. The conversion of starting materials into products, despite a negative $\Delta G^{\ominus}$, is rarely if ever a mere run down-hill (Fig. 2.2), there is generally a barrier to be overcome *en route* (Fig. 2.3):
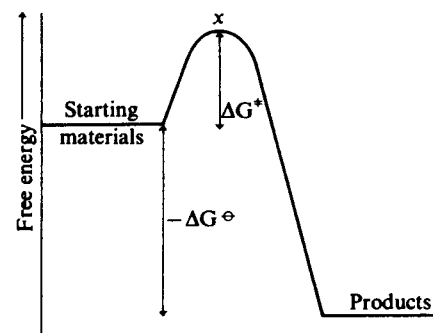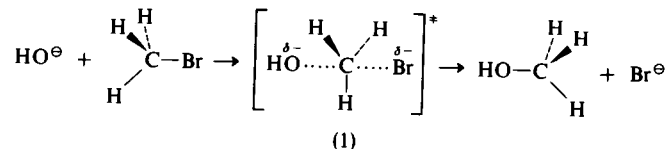

Fig. 2.3

2.2.1   Reaction rate and free energy of activation

The position x in the *energy profile* above (Fig. 2.3) corresponds to the least stable configuration through which the starting materials pass during their conversion into products, and is generally referred

to as an *activated complex* or *transition state*. It should be emphasised that this is merely a highly unstable state that is passed through in a dynamic process, and not a discrete molecular species, an intermediate, that can actually be detected or even isolated (*cf.* p. 49). An example is (1) in the alkaline hydrolysis of bromomethane, in which the HO—C bond is being formed at the same time as the C—Br bond is being broken,

$$HO^{\ominus} + \underset{H}{\overset{H\ \ H}{\diagdown}}C{-}Br \rightarrow \left[HO\cdots\underset{H}{\overset{H\quad H}{C}}\cdots Br \right]^{\pm} \rightarrow HO{-}\underset{H}{\overset{H\ H}{C}} + Br^{\ominus}$$

(1)

and the three hydrogen atoms attached to carbon are passing through a configuration in which they all lie in one plane (at right-angles to the plane of the paper). This reaction is discussed in detail below (p. 77).

The height of the barrier in (Fig. 2.3), $\Delta G^{\pm}$, is called the *free energy of activation* for the reaction (the higher it is the slower the reaction), and can be considered as being made up of enthalpy ($\Delta H^{\pm}$) and entropy ($T\Delta S^{\pm}$) terms:

$$\Delta G^{\pm} = \Delta H^{\pm} - T\Delta S^{\pm}$$

$\Delta H^{\pm}$ (the *enthalpy of activation*) corresponds to the energy necessary to effect the stretching or even breaking of bonds that is an essential prerequisite for reaction to take place (e.g. stretching of the C—Br bond in 1). Thus reacting molecules must bring with them to any collision a certain minimum threshold of energy for reaction to be possible (often called simply the *activation energy*, E_{act}, but related to $\Delta H^{\pm}$); the well-known increase in the rate of a reaction as the temperature is raised is, indeed, due to the growing proportion of molecules with an energy above this minimum as the temperature rises.

The magnitude of E_{act} for a reaction may be calculated from values of k, the rate constant (*cf.* p. 39), determined experimentally at two different temperatures, T_1 and T_2, using the Arrhenius expression which relates k to T, the absolute temperature:

$$k = Ae^{-E/RT} \quad \text{or} \quad \log_{10} k = -\frac{E_{act}}{2\cdot303RT} + \log_{10} A$$

Where R is the gas constant ($8\cdot32$ joules mol^{-1} deg^{-1}), and A is a constant for the reaction—independent of temperature—that is related to the proportion of the total number of collisions between reactant molecules that result in successful conversion into products. The value

* The symbol $\pm$ will often be applied to a structure to indicate that it is intended as an attempted representation of a transition state (T.S.).

of E_{act} may then be obtained graphically by plotting values of $\log_{10} k$ against 1/T, or by conversion of the above equation into,

$$\log_{10} k_1/k_2 = -\frac{E_{act}}{2\cdot303R}\left[\frac{1}{T_1} - \frac{1}{T_2} \right]$$

and subsequent calculation.

The $\Delta S^{\pm}$ term (the *entropy of activation*) again relates to randomness. It is a measure of the change in degree of organisation, or ordering, of both the reacting molecules themselves and of the distribution of energy within them, on going from starting materials to the transition state; $\Delta S^{\pm}$ is related to the A factor in the Arrhenius equation above. If formation of the transition state requires the imposition of a high degree of organisation in the way the reactant molecules must approach each other, and also of the concentration of their energy in particular linkages so as to allow of their ultimate breakage, then the attainment of the transition state is attended by a sizeable decrease in entropy (randomness), and the probability of its formation is correspondingly decreased.

2.2.2   Kinetics and the rate-limiting step

Experimentally, the measurement of reaction rates consists in investigating the rate at which starting materials disappear and/or products appear at a particular (constant) temperature, and seeking to relate this to the concentration of one, or all, of the reactants. The reaction may be monitored by a variety of methods, e.g. directly by the removal of aliquots followed by their titrimetric determination, or indirectly by observation of colorimetric, conductimetric, spectroscopic, etc., changes. Whatever method is used the crucial step normally involves matching the crude kinetic data against variable possible functions of concentration, either graphically or by calculation, until a reasonable fit is obtained. Thus for the reaction,

$$CH_3Br + {}^{\ominus}OH \rightarrow CH_3OH + Br^{\ominus}$$
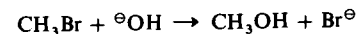
it comes as no surprise to find a rate equation,

$$\text{Rate} = k[CH_3Br][{}^{\ominus}OH]$$

where k is known as the *rate constant* for the reaction. The reaction is said to be *second order* overall; *first order* with respect to CH_3Br, and *first order* with respect to ${}^{\ominus}OH$.

Such coincidence of stoichiometry and rate law is fairly uncommon, the former is commonly no guide at all to the latter, which can only be obtained by experiment. Thus for the base catalysed bromination

of propanone,

$$CH_3COCH_3 + Br_2 \xrightarrow{\ominus OH} CH_3COCH_2Br + HBr$$
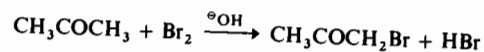
we find the rate equation,

$$\text{Rate} = k[CH_3COCH_3][\ominus OH]$$

i.e. bromine does not appear, though $[\ominus OH]$ does (*cf.* p. 295). Clearly bromine must be involved at some stage in the overall reaction as it is incorporated into the final product, but it patently cannot be involved in the step whose rate we are actually measuring. The overall reaction must thus involve at least two steps: one in which bromine is not involved (whose rate we are measuring), and one in which it is. In fact, very few organic reactions are one-step processes as depicted in Fig. 2.3. This is obvious enough in an extreme example such as the formation of hexamine,

$$6CH_2O + 4NH_3 \rightarrow C_6H_6N_4 + 6H_2O$$
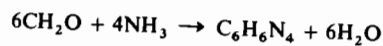
where the chance of the <u>simultaneous</u> collision of *six* molecules of CH_2O and *four* of NH_3 <u>in a *ten*-body</u> collision is effectively non-existent. But even where the stoichiometry is less extreme, reactions are normally composite, consisting of a number of successive steps (often two-body collisions) of which we are actually measuring the slowest, and thus *rate-limiting*, one—the kinetic 'bottleneck' on the production line converting starting materials into products:
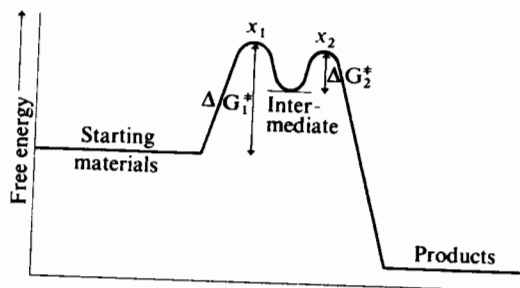

Fig. 2.4

In Fig. 2.4 starting materials are being converted *via* transition state x_1 into an intermediate, which then decomposes into products *via* a second transition state x_2. As depicted above the formation of the intermediate *via* x_1, is the more energy-demanding ($\Delta G_1^{\ddagger} > \Delta G_2^{\ddagger}$)

of the two steps, and hence will be the slower, i.e. the step whose rate our kinetic experiments will actually be measuring. It is followed by a fast (less energy-demanding), non rate-limiting conversion of the intermediate into products. The above bromination of propanone, can, under certain conditions, be said to follow an idealised pattern corresponding to Fig. 2.4, in which slow, rate-limiting removal of proton by base results in the formation of the carbanion intermediate (2), which then undergoes rapid, non rate-limiting attack by Br_2 to yield bromopropanone and bromide ion as the products:
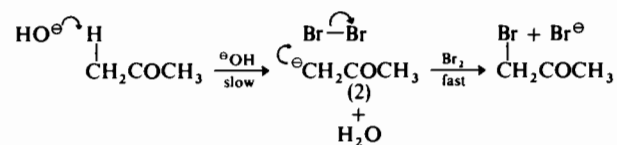
It should be emphasised that though this explanation is a reasonable deduction from the experimentally established rate equation, the latter cannot be claimed to *prove* the former. Our experimentally determined rate equation will give us information about the species that are involved up to and including the rate-limiting step of a reaction: the rate equation does indeed specify the *composition* but not, other than by inference, the *structure* of the transition state for the rate-limiting step. It gives no direct information about intermediates nor, except by default as it were, about the species that are involved in rapid, non rate-limiting processes beyond this rate-limiting step.

In considering the effect that a change of conditions, e.g. of solvent or in the structure of the starting material, might be expected to have on the rate of a reaction, we need to know what effect such changes will have on the stability (free energy level) of the transition state: any factors which serve to stabilise it will lead to its more rapid formation, and the opposite will also apply. It is seldom possible to obtain such detailed information about these high-energy transition states: the best we can commonly do is to take the relevant intermediates as models for them, and see what effect such changes might be expected to have on these. Such a model is not unreasonable; the transiently formed intermediate in Fig. 2.4 closely resembles, in terms of free energy level, the transition state that precedes it, and might be expected to resemble it in structure as well. Certainly such an intermediate is normally likely to be a better model for the transition state than the starting material would be. Thus σ complexes (Wheland intermediates) in aromatic electrophilic substitutions are used as models for the transition states that are their immediate precursors (p. 151).

The effect of a catalyst is to increase the rate at which a reaction will take place; this is done by making available an alternative path of less energetic demand, often through the formation of a new, and more
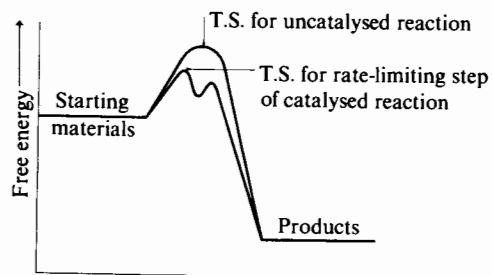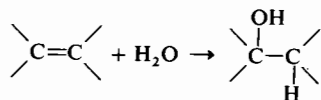
stable (lower energy), intermediate:

Fig. 2.5

Thus the rate of hydration of an alkene, directly with water,

is often extremely slow, but it can be greatly speeded up by the presence of an acid catalyst, which effects initial protonation of the alkene to a carbocationic intermediate. This is then followed by easy and rapid attack on the now positively charged carbocation by a water molecule acting as a nucleophile, and finally by liberation of a proton which is able to function again as a catalyst (p. 187):
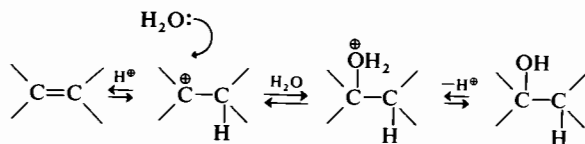
The details of acid/base catalysis are discussed subsequently (p. 74).

2.2.3 Kinetic versus thermodynamic control

Where a starting material may be converted into two or more alternative products, e.g. in electrophilic attack on an aromatic species that already carries a substituent (p. 150), the proportions in which the alternative products are formed are often determined by their relative rate of formation: the faster a product is formed the more of it there will be in the final product mixture; this is known as *kinetic control*. This is not always what is observed however, for if one or more of the

alternative reactions is reversible, or if the products are readily interconvertible directly under the conditions of the reaction, the composition of the final product mixture may be dictated not by the relative rates of formation of the different products, but by their relative thermodynamic stabilities in the reaction system: we are then seeing *thermodynamic* or *equilibrium control*. Thus the nitration of methylbenzene is found to be kinetically controlled, whereas the Friedel–Crafts alkylation of the same species is often thermodynamically controlled (p. 163). The form of control that operates may also be influenced by the reaction condition, thus the sulphonation of naphthalene with concentrated H_2SO_4 at 80° is essentially kinetically controlled, whereas at 160° it is thermodynamically controlled (p. 164).

2.3 INVESTIGATION OF REACTION MECHANISMS

It is seldom, if ever, possible to provide complete and entire information, structural, energetic, and stereochemical, about the pathway that is traversed by any chemical reaction: no reaction mechanism can ever be proved to be correct! Sufficient data can nevertheless usually be gathered to show that one or more theoretically possible mechanisms are just not compatible with the experimental results, and/or to demonstrate that of several remaining alternatives one is a good deal more likely than the others.

2.3.1 The nature of the products

Perhaps the most fundamental information about a reaction is provided by establishing the structure of the products that are formed during its course, and relating this information to the structure of the starting material. Where, as is often the case with organic reactions, more than one product is obtained then it is usually an advantage to know also the relative proportions in which the products are obtained, e.g. in establishing, among other things, whether kinetic or thermodynamic control is operating (*cf.* p. 42). In the past this had to be done laboriously—and often imprecisely—by manual isolation of the products, but may now often be achieved more easily, and precisely, by sophisticated chromatographic methods or, indirectly, by suitable spectroscopic ones.

The importance of establishing the correct structure of the reaction product is best illustrated by the confusion that can result when this has been assumed, wrongly, as self-evident, or established erroneously. Thus the yellow triphenylmethyl radical (3, *cf.* p. 300), obtained from the action of silver on triphenylmethyl chloride in 1900, readily forms a colourless dimer (m.w. = 486) which was—reasonably enough—assumed to be hexaphenylethane (4) with *thirty* 'aromatic'

<u>Few Important things demonstration:</u>

The **kinetically controlled product** is the product associated with the lowest energy barrier to its formation. The **thermodynamically controlled product** is the most stable product with the lowest energy, irrespective of any intervening barrier (If the barrier to its formation is the lowest, the thermodynamic product may be the kinetic product as well). I have attached a sketch of an idealised reaction pathway highlighting these points.

Running your reaction at the lowest temperature possible (where it still proceeds) will tend to favour the kinetic product, as the starting materials will only just have enough energy to cross the lowest barrier to the corresponding kinetic product.

Conversely, running your reaction at a high temperature will tend to favour the thermodynamic product (provided that you don't simply decompose your starting materials, though strictly speaking this 'decomposition' would just be a particularly low energy thermodynamic product). This is because at 'high temperatures' the starting materials will all have enough energy to overcome any barrier en route to their lowest energy configuration.
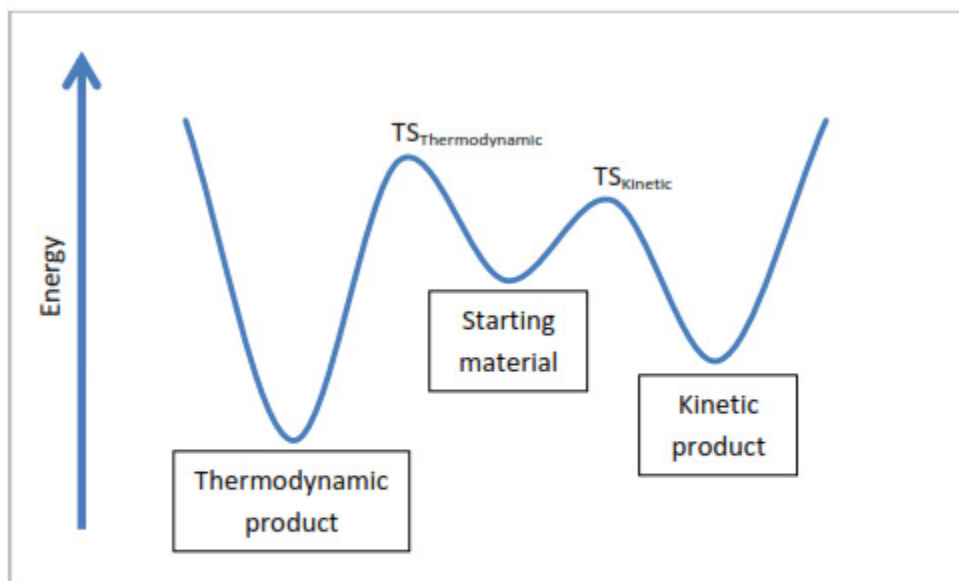
$TS_{Thermodynamic}$ - the Transition State barrier associated with the Thermodynamic Product

$TS_{Kinetic}$ - the Transition State barrier associated with the Kinetic Product

For details of Kinetic vs Thermodynamic Controlled reactions and corresponding products, see the video in the link: https://www.youtube.com/watch?v=6J-XsgLBhho

The **kinetic isotope effect** (KIE) is a phenomenon associated with isotopically substituted molecules exhibiting different reaction rates. Isotope effects such as KIEs are invaluable tools in both physical and biological sciences and are used to aid in the understanding of reaction kinetics, mechanisms, and solvent effects.

For details of Kinetic Isotopic effect, see the video in the link: https://www.youtube.com/watch?v=1gU2aluprdg

14.3 Kinetic vs. Thermodynamic Control of Reactions

Objectives

After completing this section, you should be able to

1. explain the difference between thermodynamic and kinetic control of a chemical reaction; for example, the reaction of a conjugated diene with one equivalent of hydrogen halide.
2. draw a reaction energy diagram for a reaction which can result in both a thermodynamically controlled product and a kinetically controlled product.
3. explain how reaction conditions can determine the product ratio in a reaction in which there is competition between thermodynamic and kinetic control.

Key Terms

Make certain that you can define, and use in context, the key terms below.

- kinetic control
- thermodynamic control

Like nonconjugated dienes, conjugated dienes are subject to attack by electrophiles. In fact, conjugated electrophiles experience relatively greater kinetic reactivity when reacted with electrophiles than nonconjugated dienes do. Upon electrophilic addition, the conjugated diene forms a mixture of two products—the kinetic product and the thermodynamic product—whose ratio is determined by the conditions of reaction. A reaction yielding more thermodynamic product is under thermodynamic control, and likewise, a reaction that yields more kinetic product is under kinetic control.

The reaction of one equivalent of hydrogen bromide with 1,3-butadiene gives different products at under different conditions and is a classic example of the concept of *thermodynamic* versus *kinetic* control of a reaction
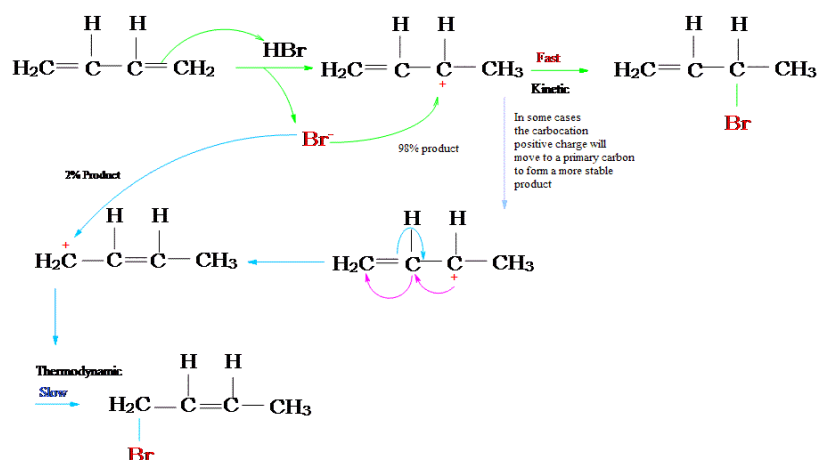
Take a look at this energy profile diagram in Figure 1. In this scenario, the starting material A can react to form either B (to the left) or C (to the right). The formation of the product C involves evolution over barriers (assuming a two step process) with *lower activation energies*, which means that it will form faster (ignoring the pre-exponential constant effects).
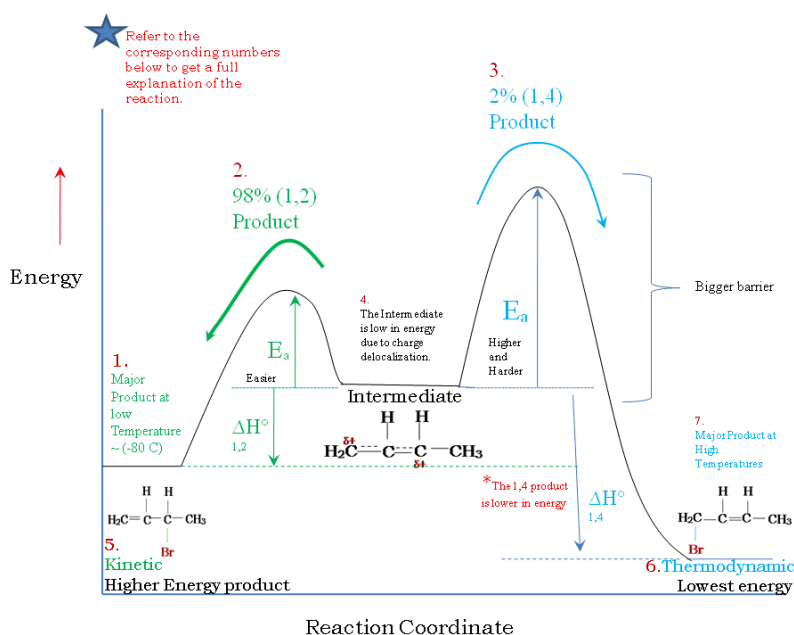
Figure 1: *Energy profile diagram for $A \rightarrow B$ (left) and $A \rightarrow C$ (rght). The horizontal axis is a reaction coordinate, and the vertical axis represents Gibbs energy. I_B and I_C are intermediates in the two reactions and T_{B1}, T_{B2}, T_{C1}, and T_{C2} are transitions states.*

If we keep the temperature sufficiently *low*, the molecules of C, which are inevitably formed faster, will probably not have enough energy to overcome the reverse activation barrier (i.e., $C \rightarrow A$) to regenerate A (Table 1). The forward reactions $A \longrightarrow B$ and $A \longrightarrow C$ are, under such conditions, effectively irreversible. Since the formation of C is faster, it will predominate, and the major product formed will be C. This is known as *kinetic control* and C is the *kinetic product*.

At elevated temperatures, C is still going to be the product that is formed *faster*. However, it also means that all the reactions will be reversible. This means that molecules of C can revert back to A. Since the system is no longer limited by temperature, the system will minimize its Gibbs free energy, which is the thermodynamic

criterion for chemical equilibrium. This means that, as the most thermodynamically stable molecule, B will be predominantly formed.[2] The reaction is said to be under *thermodynamic control* and B is the *thermodynamic product*.

Table 1: *Conjugated Diense: Kinetic vs. Thermodynamic Conditions*

| Temperature	Kinetic or Thermodynamically Controlled	Speed of Reaction	1,2-adduct : 1,4-adduct Rati...
-15 °C	Kinetic	Fast	70:30
0 °C	Kinetic	Fast	60:40
40 °C	Thermodynamic	Slow	15:85
60 °C	Thermodynamic	Slow	10:90

> *A simple definition is that the kinetic product is the product that is formed faster, and the thermodynamic product is the product that is more stable. This is precisely what is happening here. The kinetic product is 3-bromobut-1-ene, and the thermodynamic product is 1-bromobut-2-ene (specifically, the trans isomer).*

### A Warning: Not every reaction has different thermodynamic and kinetic products!

Note that not every reaction has an energy profile diagram like Figure 1, and not every reaction has different thermodynamic and kinetic products! If the transition states leading to the formation of C (e.g., T_{C1}, and T_{C2}) were to be higher in energy than that leading to B (e.g., T_{B1}, and T_{B2}), then B would simultaneously be both the thermodynamic and kinetic product. There are plenty of reactions in which the more stable product (*thermodynamic*) is also formed faster (*kinetic*).

The Reaction Mechanism

The first step is the protonation of one of the C=C double bonds. In butadiene (**1**), both double bonds are the same, so it does not matter which one is protonated. The protonation occurs regioselectively to give the more stable carbocation (i.e., $I_B=I_C$ in Figure 11):
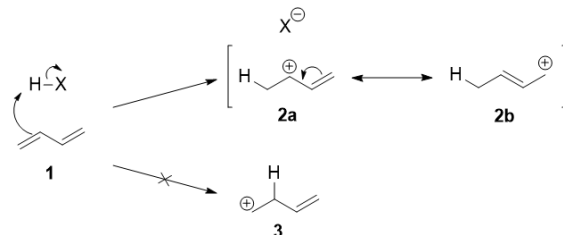
The more stable cation is not only secondary, but also *allylic*, and therefore enjoys stabilization via resonance (or conjugation). This is depicted in the resonance forms **2a** and **2b** above. This allylic carbocation, more properly denoted as the resonance hybrid **2**, has two carbons which have significant positive charge, and the bromide ion (here denoted as X^-) can attack either carbon. Attacking the central carbon, adjacent to the site of protonation, leads to the kinetic product **3** (called the 1,2-adduct); attacking the terminal carbon, distant from the site of protonation, leads to the thermodynamic product **4** (called the 1,4-adduct).
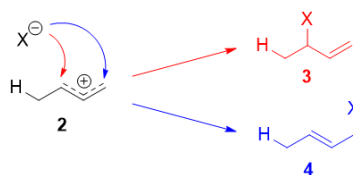

A Common Mistake: Resonance Structures do not Independently Exist

There are some people who write that **3** results from attack of X^- on resonance form **2a**, and **4** from attack of X^- on resonance form **2b**. ***This is not correct!*** Resonance forms do not separately exist, and they are not distinct species that rapidly interconvert. As such, one cannot speak of *one single resonance form* undergoing a reaction.

Now, why **4** is the thermodynamic product, and why **3** is the kinetic product for this reaction?

The thermodynamic product: *trans*-1-bromobut-2-ene

It is perhaps simple enough to see why **4** is more stable than **3**. It has an internal, disubstituted double bond, and we know that as a general rule of thumb, the thermodynamic stability of an alkene increases with increasing substitution. So, compared to the terminal, monosubstituted alkene **3**, **4** is more stable.
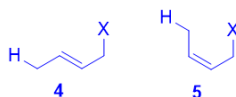
Both the *trans* isomer **4** as well as the *cis* isomer **5** can be formed via attack of the nucleophile at the terminal carbon, and both are disubstituted alkenes. However, the *trans* isomer **4** is more stable than the *cis* isomer **5**, because there is less steric repulsion between the two substituents on the double bond. As such, **4** is the thermodynamic product.

### The kinetic product: 3-bromobut-1-ene

Several explanations may be proposed to explain the nature of the kinetic product.

The worst possible argument argues that the resonance form **2a**, being an allylic *secondary* carbocation, is more stable than resonance form **2b**, which is an allylic *primary* carbocation. Therefore, resonance form **2a** exists in greater relative proportion (i.e., more molecules will look like **2a** than **2b**), and the nucleophile preferentially reacts with this specific carbocation, leading to the formation of **3**. However, this is incorrect, since individual resonance forms do not exist. Moreover, such an argument suggests that we are looking for the more stable *intermediate* (I_B or I_C in Figure 1). In fact, we should be looking for the more stable *transition states* (T_{B1}, T_{B2}, T_{C1}, and T_{C2} in Figure 1). The carbocation is an *intermediate*, and not a *transition state*.

The most common argument is since resonance form **2a** is more stable than **2b**, is that it contributes more towards the *resonance hybrid* **2**. As such, the positive charge on the internal carbon is greater than the positive charge on the terminal carbon. The nucleophile, being negatively charged, is more strongly attracted to the more positively charged or more electrophilic carbon, and therefore attack there occurs faster (the transition state being stabilized by greater electrostatic interactions). That's actually a very sensible explanation; with only the data that has been presented so far, we would not be able to disprove it, and it was indeed the accepted answer for quite a while.

Experimental Results

In 1979, Nordlander *et al.* carried out a similar investigation on the addition of $\ce{DCl}$ to a different substrate, 1,3-pentadiene.[7] This experiment was ingenious, because it was designed to proceed via an almost symmetrical intermediate:
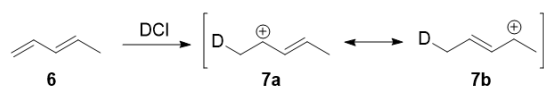
Resonance forms **7a** and **7b** are both allylic and secondary. There is a very minor difference in their stabilities arising from the different hyperconjugative ability of C−D *vs* C−H bonds, but in any case, it is not very large. Therefore, if we adopt the explanation in the previous section, one would expect there not to be any major *kinetic* pathway, and both 1,2- and 1,4-addition products (**8** and **9**) would theoretically be formed roughly equally.
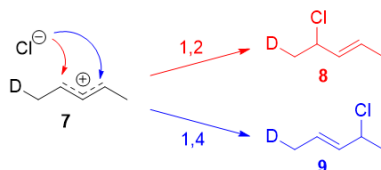
Instead, it was found that the 1,2-addition product was favored over the 1,4-addition product. For example, at $-78\,^{\circ}\mathrm{C}$ in the absence of solvent, there was a roughly $75:25$ ratio of 1,2- to 1,4-addition products. Clearly, there is a factor that favors 1,2-addition that does not depend on the electrophilicity of the carbon being attacked! The authors attributed this effect to an *ion pair* mechanism. This means that, after the double bond is protonated (deuterated in this case), the chloride counterion remains in close proximity to the carbocation generated. Immediately following dissociation of DCl, the chloride ion is going to be much closer to C−2 than it is to C−4, and therefore attack at C−2 is much faster. In fact, normal electrophilic addition of HX to conjugated alkenes in polar solvents can also proceed via similar ion pair mechanisms. This is reflected by the greater proportion of *syn* addition products to such substrates.[11]

> *The mechanism that favors 1,2-addition clearly does not depend on the electrophilicity of the carbon being attacked.*

This ion pair mechanism is a pre-exponential constant effects that is attributed to the proximity and frequency of collision rather than a activation barrier effect.

Conclusion

The reactivity of conjugated dienes (hydrocarbons that contain two double bonds) varies depending on the location of double bonds and temperature of the reaction.These reactions can produce both thermodynamic and kinetic products. Isolated double bonds provide dienes with less stability thermodynamically than conjugated dienes. However, they are more reactive kinetically in the presence of electrophiles and other reagents. This is a result of Markovnikov addition to one of the double bonds. A carbocation is formed after a double bond is opened. This carbocation has two resonance structures and addition can occur at either of the positive carbons.

References

1. Smith, M. B. *March's Advanced Organic Chemistry*, 7th ed., p 272
2. This does not mean that *all* of A will be converted to B; the reaction is still an *equilibrium*, and equilibria always go forward and backward. In general, the minimum system Gibbs free energy (G_{syst}) will occur at a certain proportion of A, B, and C. However, since B has the lowest Gibbs free energy, it will be formed in a greater proportion than C.
3. http://www.ochempal.org/index.php/alphabetical/a-b/14-addition/
4. *J. Am. Chem. Soc.* **1979,** 101 (5), 1288–1289
5. Because of the larger reduced mass and lower zero-point energy, a $\ce{C-D}$ bond is stronger and therefore less willing to donate electron density into an adjacent empty p orbital. This is the origin of some secondary kinetic isotope effects; in our case, it means that **7a** is marginally less stable than **7b**.
6. *J. Am. Chem. Soc.* **1969,** 91 (14), 3865–3869
7. Addition of HX to butadiene in the gas phase gives approximately a $1:1$ ratio of 1,2- to 1,4-addition product, suggesting that an ion pair mechanism (which would favor the 1,2-addition product) does not operate: *J. Org. Chem.,* **1991,** 56 (2), 595–601

Practice Problems

1. Write out the products of 1,2 addition and 1,4- addition of a) HBr and Br. b) DBr to 1,3-cyclo-hexadiene. What is unusual about the products of 1,2- and 1,4- addition of HX to unsubstituted cyclic 1,3-dienes?
2. Is the 1,2-addition product formed more rapidly at higher temperatures, even though it is the 1,4-addition product that predominates under these conditions?
3. Why is the 1,4-addition product the thermodynamically more stable product?
4. Out of the following radical cations which one is not a reasonable resonance structure?
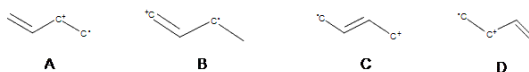
5. Addition of 1 equivalent of Bromine to 2,4-hexadiene at 0 degrees C gives 4,5-dibromo-2-hexene plus an isomer. Which of the following is that isomer:

a. 5,5-dibromo-2-hexene
b. 2,5-dibromo-3-hexene
c. 2,2-dibromo-3-hexene
d. 2,3-dibromo-4-hexene

6. Which of the following will be the kinetically favored product from the depicted reaction?
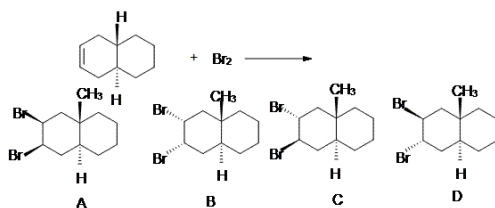
7. Addition of HBr to 2,3-dimethyl-1,3-cyclohexadiene may occur in the absence or presence of peroxides. In each case two isomeric $C_8H_{13}Br$ products are obtained. Which of the following is a common product from both reactions?