

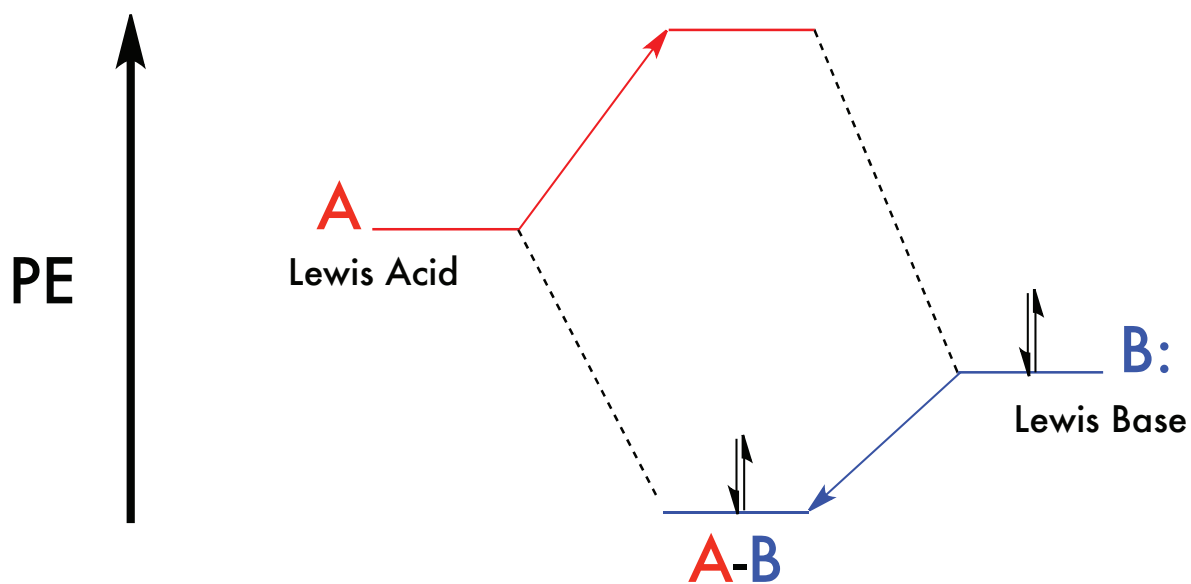
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Organic Chemistry

A learning approach based on
Lewis Acid-Base Theory.

VOLUME 1
VERSION 1.1



R.T. Patterson

Reactions and Mechanisms for Reactions

“Once we understand how molecules are formed, we can manipulate them.

If you can manipulate molecules, you can manipulate genes and matter,
you can synthesize new materials — the implications are just unbelievable.”

– Ahmed Zewail, 1999 Nobel Laureate in Chemistry, also known as the father of femtochemistry.

8-1-1. Introduction:

“We tend to think of Sisyphus as a tragic hero, condemned by the gods to shoulder his rock sweatily up the mountain, and again up the mountain, forever.

The truth is that Sisyphus is in love with the rock. He cherishes every roughness and every ounce of it. He talks to it, sings to it. It has become the mysterious Other. He even dreams of it as he sleepwalks upward. Life is unimaginable without it, looming always above him like a huge grey moon.

He doesn't realize that at any moment he is permitted to step aside,
let the rock hurtle to the bottom, and go home.

Tragedy is the inertial force of the mind.”

– Stephen Mitchell, “The myth of Sisyphus” from his marvelous collection of poems
“Parables and Portraits,” 1990

Ideas are important because they influence how we see the world around us. How we see the world, in turn, determines how we think about our world and, even more importantly, what we think of as possible to do in that world. As a result, this worldview is both a source of inspiration as well as a source of inertia that inhibits our consideration of new possibilities.

The goal in this chapter is to present and develop a rather simple model for interpreting chemical reactions that builds upon our understanding of molecular structure and bonding. This approach will provide a theory that is flexible enough to serve as a general framework for understanding both chemical reactions, and also reactivity.

Chemistry is defined as the breaking of old bonds and formation of new bonds. This definition was used back in Ch 5 without explanation to differentiate conformational energy changes from those chemical changes necessary to interconvert configurational isomers. This definition of a chemical reaction, combined with our model for molecular structure and bonding, provides a more nuanced picture of how chemical reactions transform reactant structures into product structures.

8-1-2. What will be presented:

1. A brief history of the concept of an activated state and the beginnings for an understanding of how reactants are transformed into products.

2. The relationship between bond breaking and new bond formation determines the energy changes for the conversion of R to P.
3. The Bell-Evans-Polanyi (BEP) postulate partitions a reaction into old bond breaking and new bond formation. This BEP model not only provides insight into the structure of a transition state (TS), and it also explains thermodynamic control of a reaction.
4. The Hammond postulate and how this idea relates the structural differences between early and late transition state structures to their activation energies.
5. Definitions for Kinetic vs thermodynamic control of chemical reactions and also how we distinguish between these effects.
6. The difference between elementary and complex chemical reactions.
7. What is an intermediate and what differentiates an intermediate from a transition state.
8. Types of carbon centered intermediates important to Organic Chemistry.

8-1-3. Arrhenius and his Activated State:

Before Arrhenius not much thought was given to the intimate details about how chemical reactions occur, in part, because the concept of an atom was still very much in its infancy.

In the period from about 1850 to about 1930 many chemists first noted and then explained some rather “strange” general characteristics of chemical reactions:

1. **Why don't all chemical reactions occur instantaneously?**
2. **Why do some reactions proceed at vastly different rates than other, similar reactions?**
3. **If one calculates the number of intermolecular collisions occurring between reactants at a given temperature, one notes that only a small fraction of these collisions lead to formation of products. In other words, the rate of reaction per unit time and volume is always less than the number of collisions occurring per unit time and volume. Why?**
4. **Why does an increase in reaction temperature have such a dramatic effect on the rate of a reaction (Rule of thumb: Reaction rate doubles for every 10° C increase in reaction temperature).**

Arrhenius' contribution to this rather specialized area of Physical Chemistry was to move beyond an empirical analysis of kinetics — e.g. determining reaction rates and rate laws — to provide what would become a more sweeping thermodynamically based interpretation for these rate laws.

Arrhenius confirmed an earlier observation that showed how a rate constant for a reaction changes as a function of temperature. Although he wasn't the first to undertake this kind of analysis, he was the

first to offer an interpretation that began to address those four “strange” features of chemical reactions just outlined above. I think that Arrhenius was, at this moment, exactly in the type of situation that the great scientist Louis Pasteur described when he said that: “Chance favors the prepared mind.” Here is how I think Arrhenius’ thoughts progressed from an empirical equation to a general model for chemical reactions. It begins with Van’t Hoff, who was a contemporary of Arrhenius. Van’t Hoff had recently reported how equilibrium constants change as a function of temperature:

Figure 8-1-1. Van’t Hoff equation relating the value of equilibrium constants to the difference in enthalpy between their A and B states:



$$\ln K_{\text{eq}} (\text{A-B}) = - \frac{\Delta H_{(\text{A-B})}}{RT} + \text{constant}$$

Arrhenius discovered that his rate constant for the pseudo rotation of glucose also had a temperature dependence for its rate of reaction that was similar in its form to that equation previously reported by Van’t Hoff:

Figure 8-1-2. Arrhenius equation relating the value of a rate constant to its activation energy (E_a):



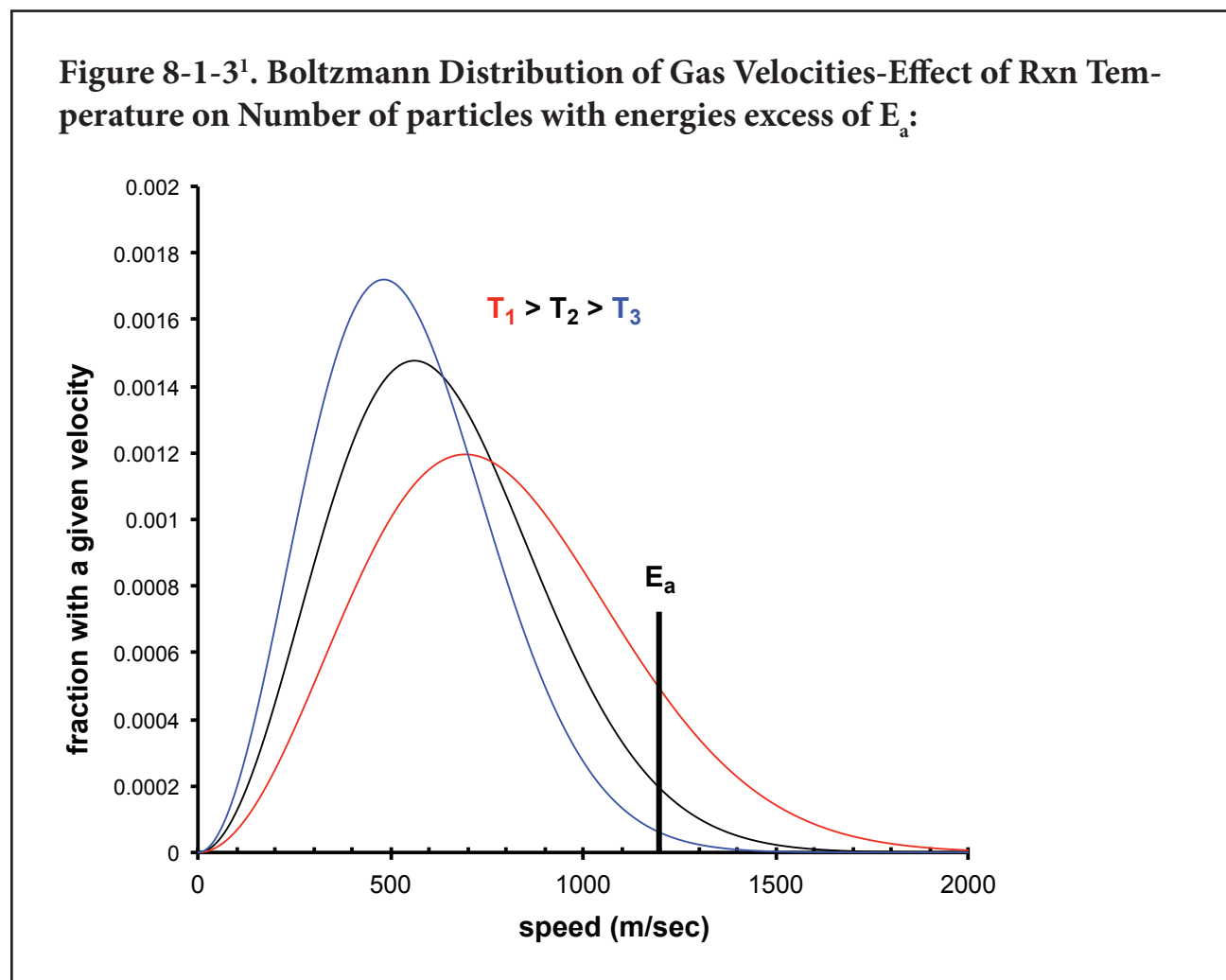
$$\ln k (\text{R-P}) = - \frac{E_a}{RT} + \text{constant}$$

E_a refers to the energy required to attain activated state for reaction to occur.

Arrhenius’ leap of faith probably went like this: If the Van’t Hoff equation describes temperature effects on an equilibrium process, it then follows that a similar equation for the temperature dependence of a rate constant for reaction necessarily implies that a chemical reaction also involves some kind of equilibrium process. For a chemical reaction, this equilibration had to be the rate limiting process for conversion of reactants into products because this “activated state” is higher in potential energy than the potential energy of either its reactants or products (i.e. $E_a > 0$). Thus Arrhenius postulated that for a chemical reaction to occur, reactant molecules must acquire enough activation energy (i.e. E_a) to pass through this “activated state” in order to be converted into products. An activated state is a **special thermodynamic state** that acts like a swinging door or portal connecting reactants to products. Thus a retro reaction of those products also must pass back through this same activated state to reform their reactants.

The idea of an activated state or transition state (TS) resolves most of the odd characteristics about chemical reactions that were noted at the start of this section. The reasons why chemical reactions don't occur instantaneously is that even reactive or labile reactant molecules must first absorb enough energy to attain an activated state before conversion into products. Different reactions and different reactants have different types of activated states (i.e. TS) with different potential energies. As a result, there is no reason why different reactants, even for related reactions, should react at identical rates. Finally, only a fraction of the molecules colliding will collide with enough energy, and also in a proper orientation to achieve an activated state that then can proceed on to products.

In order to appreciate the dramatic effect of temperature on the rate of reaction, one need only consider a Maxwell-Boltzmann energy distribution for intermolecular collisions. Boltzmann's kinetic theory of gasses suggests that the energy distributions for such collisions should look something like those shown below. In Fig. 8-1-3 several molecular velocity profiles are shown for three different temperatures with $T_1 > T_2 > T_3$:

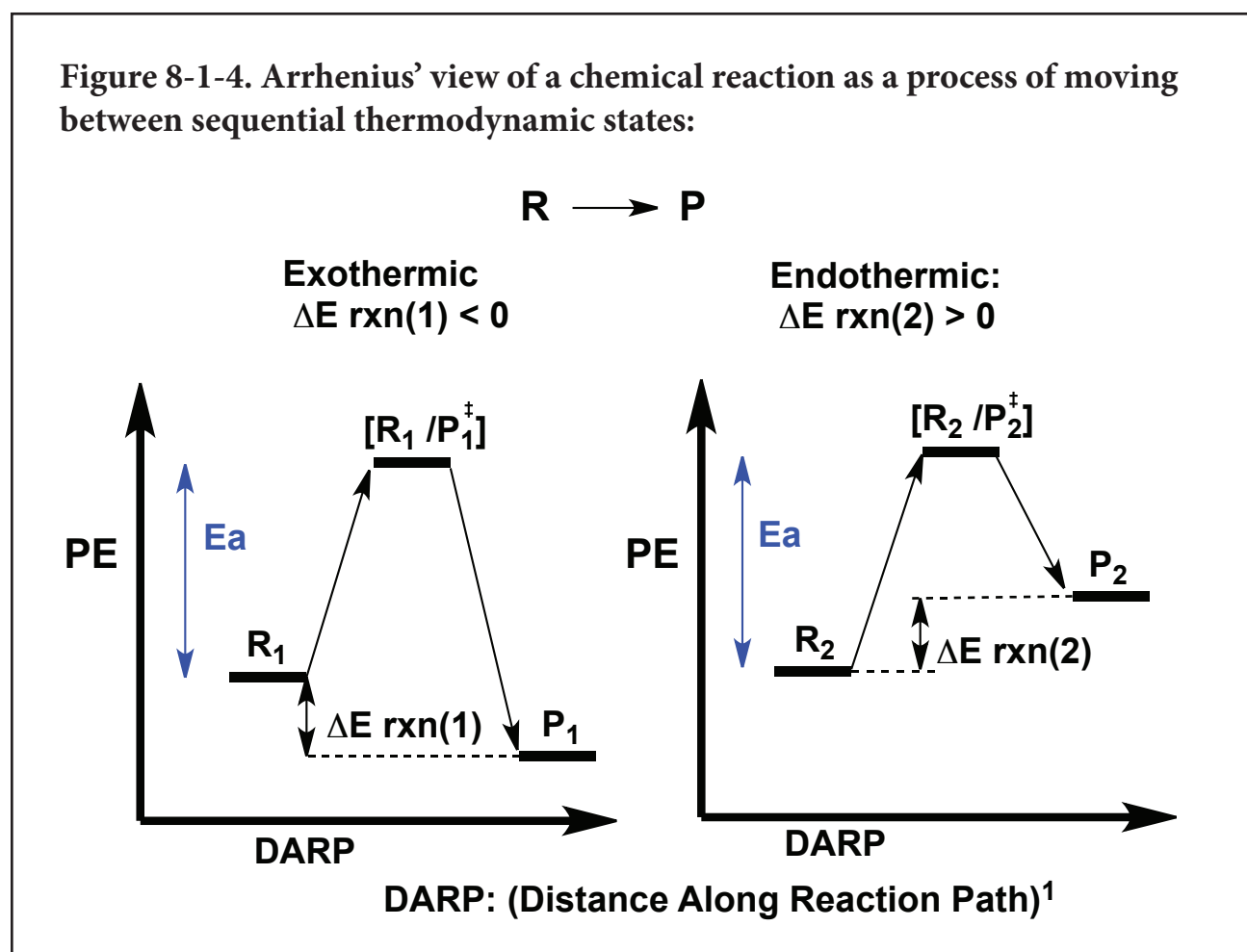


1) Graph is from F. Coleman, Chemistry Dept. Wellesley College: wcoleman@wellesley.edu See his Interactive Excel spread sheet for Boltzmann distribution of gas velocities- Copyright 2005 see file <http://academics.wellesley.edu/Chemistry/wfcspreadsheets.html>

As one can observe from Fig. 8-1-3, that only a fraction of the molecules within a given temperature have the necessary kinetic energy to attain a higher energy activated state (designated here as those collisions with an $E \geq E_a$). The reason that a rate for reaction increases so dramatically with temperature is that increasing a reaction temperature has a much larger effect on the number of high-energy collisions within a velocity distribution tail (i.e. $E \geq E_a$), than it does on the number of those collisions occurring with only an average kinetic energy (those collisions with velocities and energies around the centers for each of these velocity distribution curves). Notice that increasing a reaction temperature just from T_1 to T_2 dramatically increases the number of molecules colliding with energies in excess of E_a . It necessarily follows that if one doubles the number of collisions with energies in excess of E_a , then the rate of a reaction also should double with this increase in reaction temperature.

8-1-4. Is it reasonable to expect that a threshold energy or "activation" energy should be required for a reaction to occur?

A crude potential energy diagram based on the ideas presented by Arrhenius would look like that shown in Fig. 8-1-4 for either an endo- or exothermic reaction:



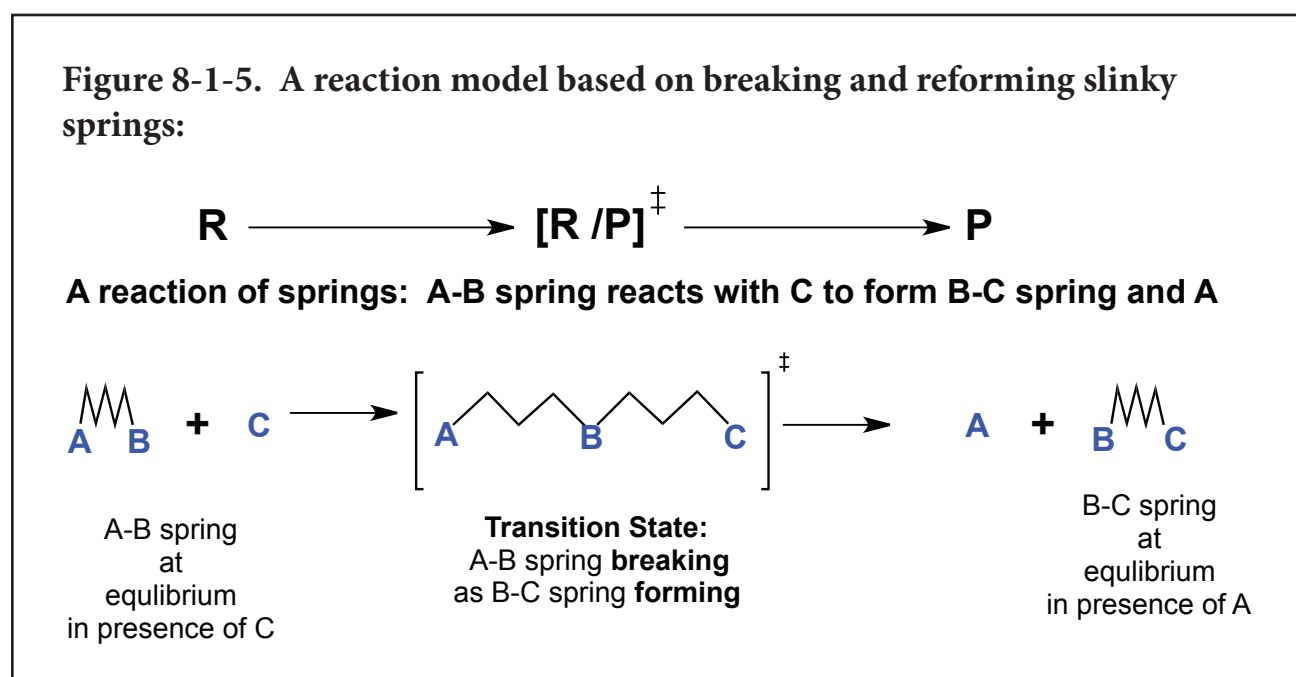
1) Distance along reaction path (DARP) refers to the changes in positions of the nuclei around a reacting bond that occur as a molecule distorts from its stable reactant structure (DARP = 0) through an activated state and on towards a stable product structure (DARP = 1)

If we build on this idea that chemical reactions involve breaking reactant bonds followed by formation of new product bonds, then it logically follows that breaking stable reactant bonds will require energy. Greater amounts of energy will be required to break stronger reactant bonds, which in turn, also will require an even larger activation energies (e.g. E_a) to achieve their activated states relative to that activation energy required to break weak bonds.

Greater BDE (R) \implies More energy to break \implies Increases E_a (R)

8-1-5: What is the shape of a PE pathway that connects bond breaking of reactants to an activated state and then to bond formation within the products?

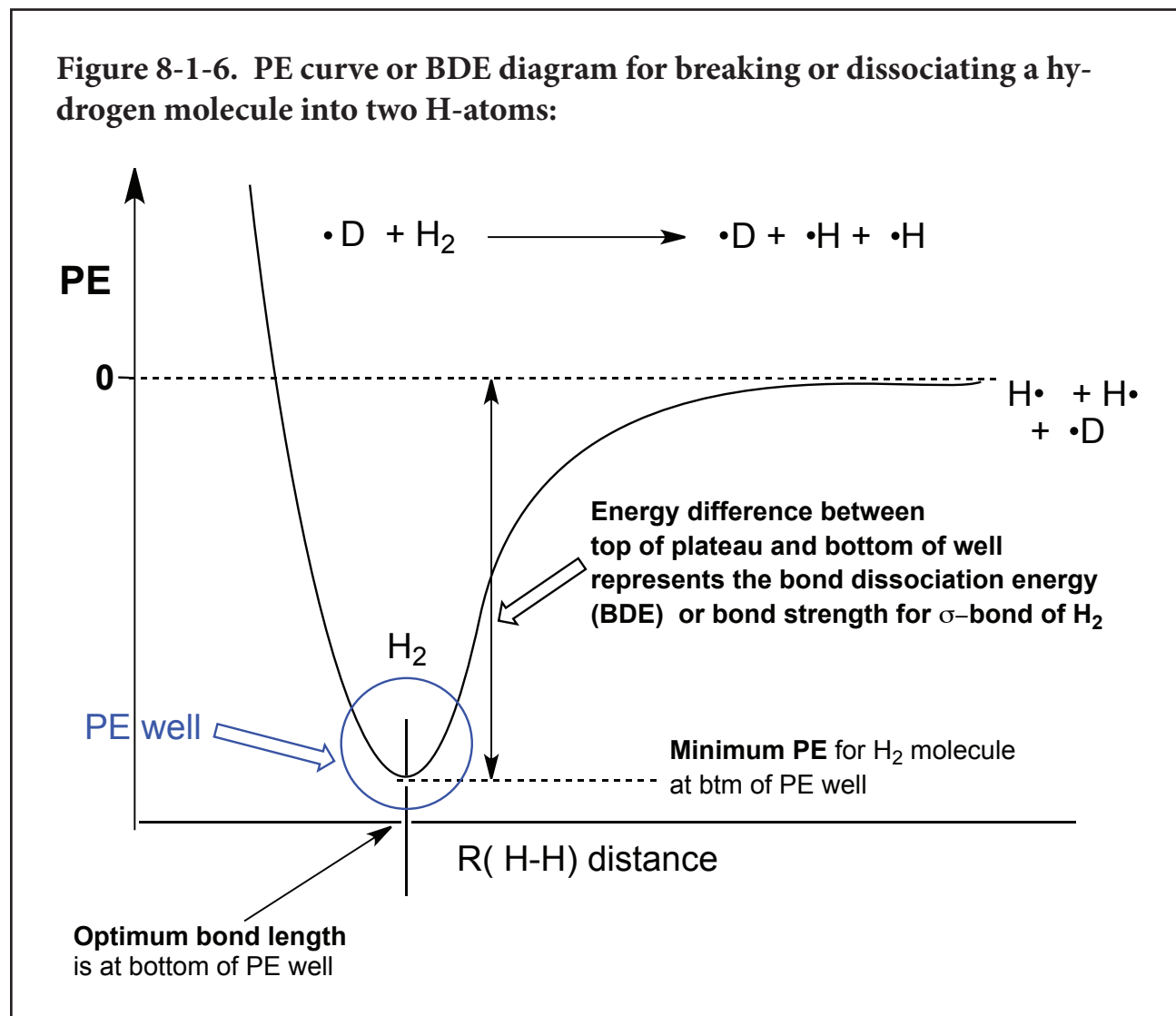
It might help in the development of a PE curve for reaction if this discussion begins with something physically familiar to the reader-like a Slinky. Now, consider a reaction as a conversion of atoms attached to the ends of a “slinky” spring like that shown in Fig. 8-1-5. For this “reaction” an old A-B slinky spring gets broken and a new B-C slinky spring is then formed:



For this slinky reaction to occur, the old slinky spring connecting A to B must be stretched until it breaks and a new B-C slinky must be formed. If we put these two processes (A-B breaking and B-C formation) into a diagram like shown in Fig. 8-1-4, then as this reaction proceeds, there will be a higher energy state in which A, B, and C together form some kind of a super connected slinky. As this A-B-C super slinky assembly moves through its stretched state, the B-C spring will continue to strengthen until the original A-B spring eventually is completely broken and the new B-C connected slinky spring finally achieves its optimum equilibrium structure. For this slinky reaction to be exothermic, the B-C spring formed will have to be stronger than the old A-B spring that was broken.

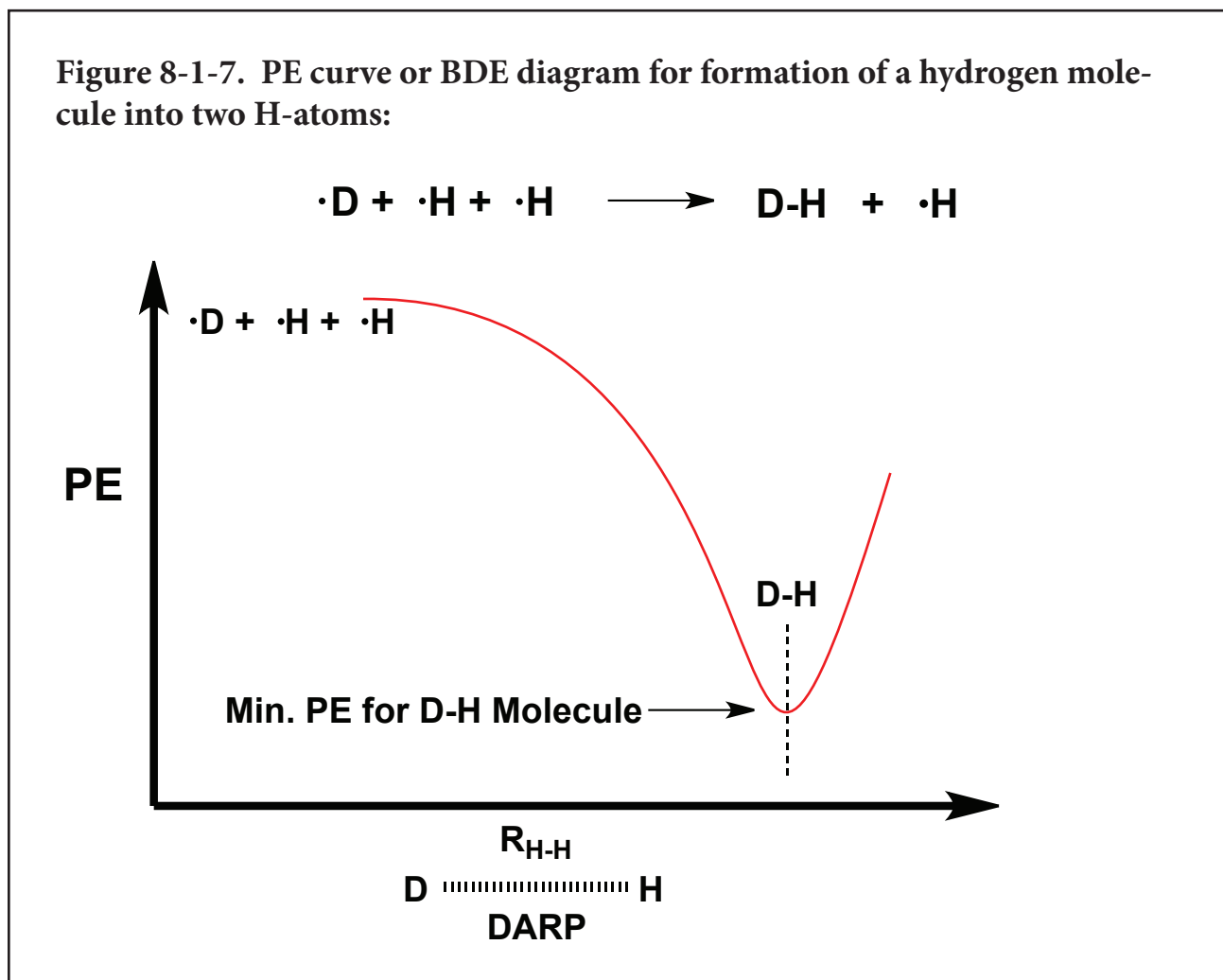
Thus it would seem logical that the PE for a reaction path should be related in its shape to the same type of PE curves already used to describe covalent bond formation between atoms. This BDE (bond dissociation energy) diagram is the same type of PE diagram that was used back in Ch 4 to describe those energy changes occurring as a hydrogen molecule is formed from its two isolated H-atoms.

For reaction of H_2 , the bond breaking starts from a stable H_2 molecule in its equilibrium structure at the bottom of its PE well and then pulls this molecule apart as is shown in Fig. 8-1-6. As an H-H bond length is stretched, the PE for that stretched H-H molecule steadily increases until the H-H bond is finally and completely broken to form two isolated and non-bonded H-atoms with zero PE:



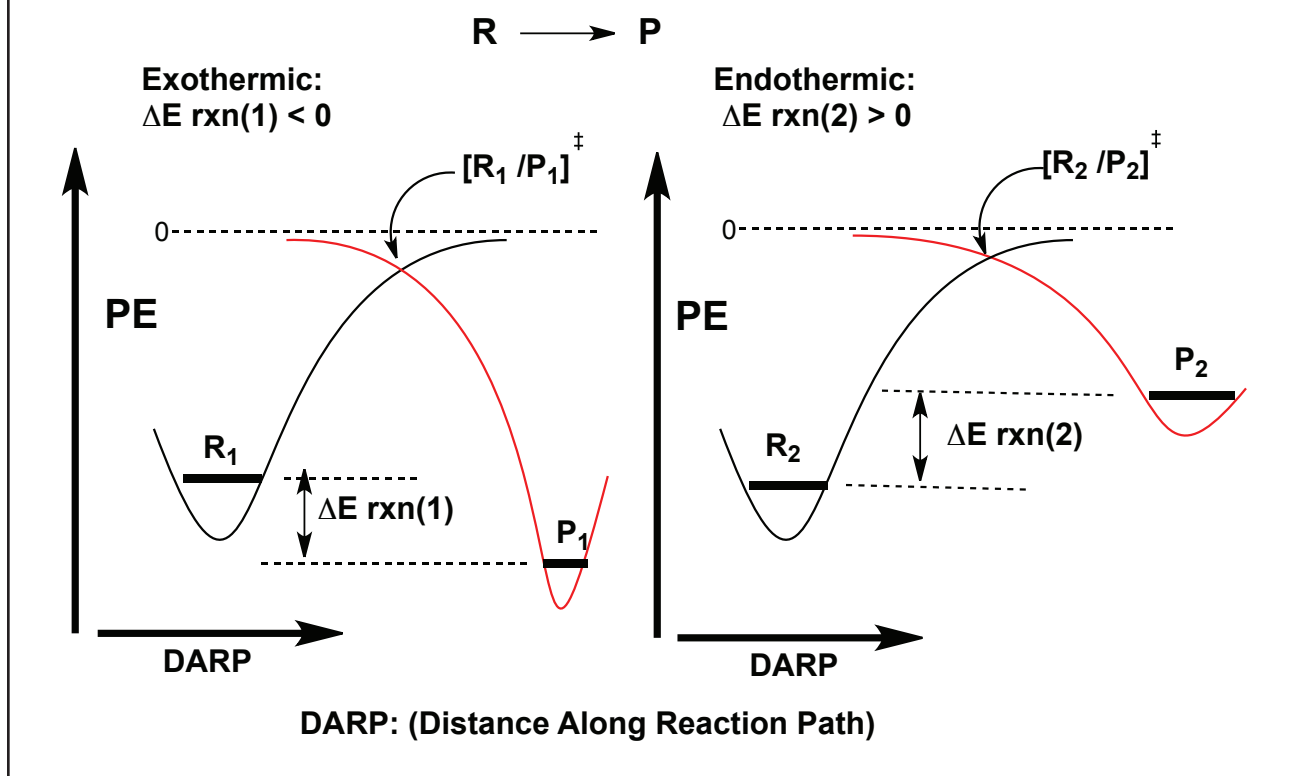
Notice that in Fig. 8-1-6, there is a parabolic shape to this PE curve around the equilibrium geometry for an H_2 molecule at the bottom of this H_2 PE well [i.e. around its equilibrium geometry, its PE has a Hook's law dependence, $PE = k (R_{H-H})^2$]. The deuterium atom does not contribute to the PE of this hydrogen molecule.

Flipping Fig. 8-1-6 around then can generate a similar PE diagram but now for formation of a deuterium-hydrogen molecule from its deuterium and hydrogen atoms that looks like the one shown in Fig. 8-1-7:



This BDE curve illustrates those energy changes resulting from new bond formation between the deuterium-hydrogen atoms as they combine to form a D-H molecule. The shape of the PE curve for this particular bond formation just happens to be the mirror image of that PE curve for the bond breaking of molecular hydrogen into its two H-atoms. By combining two such energy diagrams [one PE curve for bond breaking in reactants (R) and another PE curve for bond formation in products (P)] one then produces a new composite PE diagram (Fig. 8-1-8) that tracks bond energy changes occurring as a reaction proceeds from reactants (R) to products (P) [e.g. from $\cdot\text{D} + \text{H}_2$ to $\text{D-H} + \cdot\text{H}$]. It was Bell Evans and Polanyi who used this bond breaking and bond forming idea to explain several of the other general features of chemical reactions. As we'll see, the process used to assemble Fig. 8-1-8 is flexible enough to describe either exothermic or even endothermic reactions:

Figure 8-1-8. PE curves and BDE diagrams for both Exothermic and Endothermic Reactions:



For an exothermic reaction ($\Delta E_{\text{RXN1}} < 0$) the PE of the products (P) is lower than the PE of its reactants (R) of its reactants. The reverse will be true for an endothermic reaction ($\Delta E_{\text{RXN2}} > 0$).

Those points of intersection in each of these PE reaction diagrams in Fig. 8-1-8 represent activated states or transition states (TS) for either exothermic or endothermic conversions of R into P.

Several important observations flow naturally from this simple bond breaking-formation model for a chemical reaction:

1. The physical structure of an activated or transition state (i.e. TS) is bounded on one end of a PE diagram by its reactant structures (DARP = 0) and at the other end of this PE diagram by its product structures (DARP = 1). An activated state is **NOT** a random collection of atoms or molecular fragments. Instead, as we observe from these PE diagrams, activated or transition states are types of “metastable” molecules with definite structures.
2. It also follows that the principle source of an activation energy is the amount of energy required to distort or break reactant bonds as reactant structures move from their ground state or equilibrium reactant structures towards their activated or transition state structures (i.e. designated here on these PE diagrams as $[R/P]^{\ddagger}$).

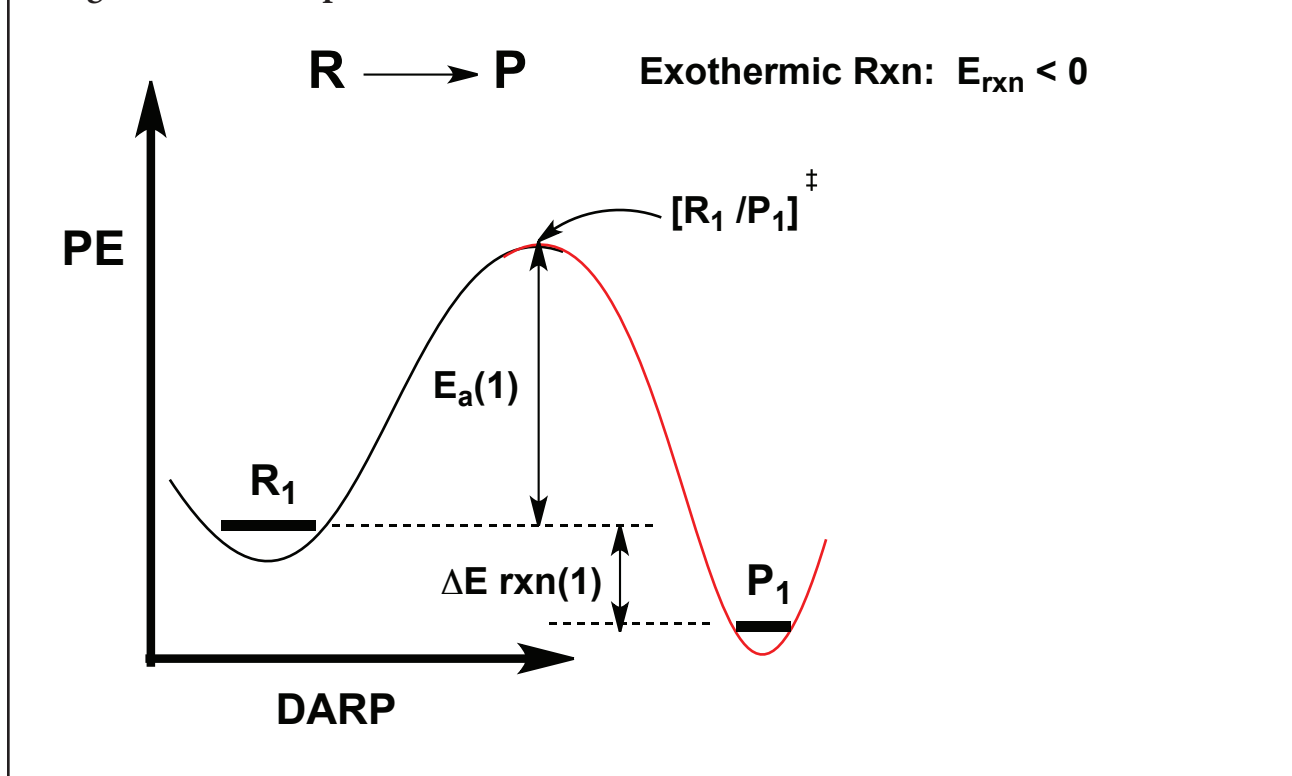
- It is not necessarily, nor is it required that one completely break a reactant bond prior to formation of a new product bond (i.e. E_a to attain a TS can be less than the BDE of the breaking bond). Notice from Fig. 8-1-8 that these points of intersection (i.e. where $[R/P]^\ddagger$) are below the PE plateaus where both reactant and product bonds are completely broken.
- An activated state now becomes a point on our reaction diagram (i.e. at state) that is simultaneously located on both of its reactant and product PE curves for their bond dissociations. At this point of intersection (i.e. at $[R/P]^\ddagger$), a TS structure is both distorted reactants (R^\ddagger) and also simultaneously distorted products (P^\ddagger). Perhaps a better way to view an activated state is to consider it as if it is a resonance structure consisting of distorted reactants and distorted products as its principle resonance hybrid structures — (all of its distorted R and distorted P atoms are in place, and it's just the electron density that flows or shifts between its R and P resonance hybrids) as a reaction proceeds along this reaction pathway from this state or point of intersection:



- The deeper the well on a PE curve for a bond, the more stable that bond (i.e. the stronger the bond or, alternatively, the greater its BDE and thus more energy will be required to break that bond). A subtler feature of these PE curves is that the deeper a PE well, the steeper are the slopes of its sides on a pathway that leads away from its equilibrium reactant geometry towards bond dissociation. Conversely, the shallower a PE well, the less stable its bond (i.e., the weaker this bond and, the smaller its BDE). A shallow PE well, also has a more gradual slope to the sides of its PE curve on a pathway that leads away from its equilibrium reactant geometry towards its bond dissociation.

In order to combine these two PE curves: One “simply” adds a curve for R (bond breaking) to another curve for P (bond formation). This additive combination of these two PE curves “cleans up” our Fig. 8-1-8 and provides a more seamless PE curve that is identical to a traditional PE profile for a single step reaction that converts reactants (R) into products (P). The result of this process as it also appears in most texts is shown in Fig. 8-1-9:

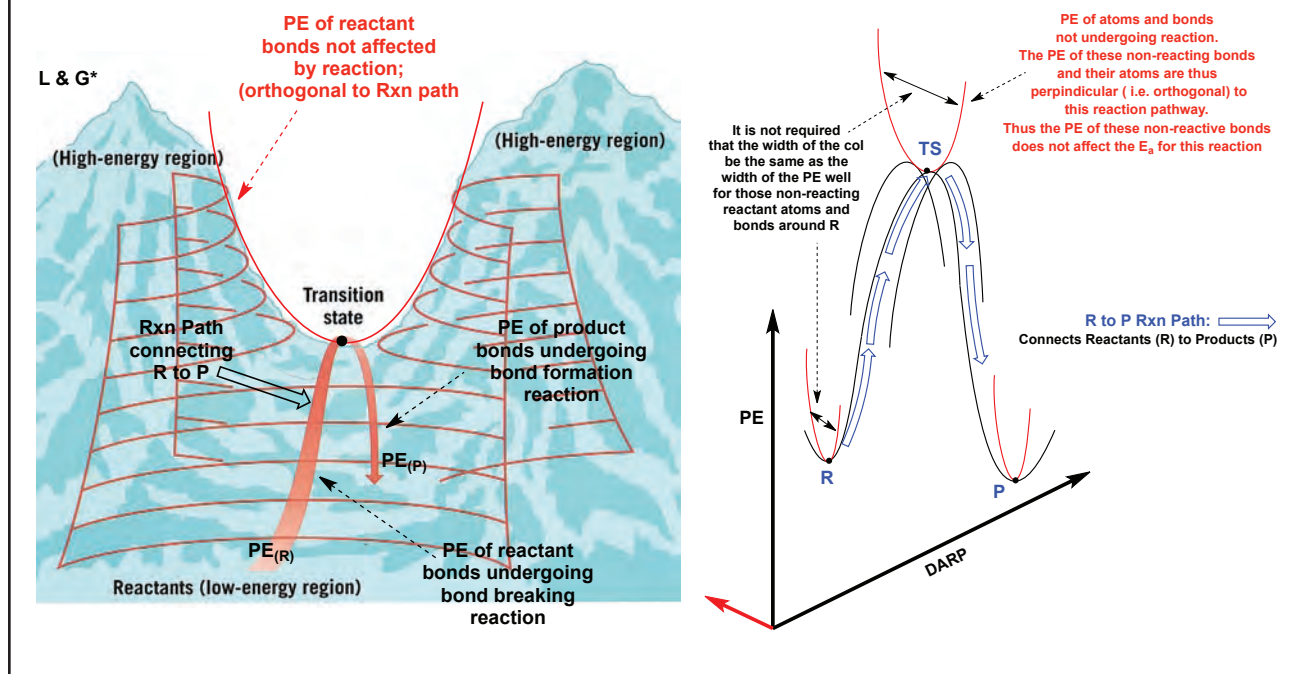
Figure 8-1-9. Completed PE curve for an Exothermic Reaction:



The final takeaway from this traditional PE curve (Fig. 8-1-9) for a single step reaction is that an activated state or transition state (TS) is the highest energy point on the lowest energy pathway connecting reactants (R) to products (P). Also, implied by this model is that a TS is like a kitchen door — it swings both ways. Thus the TS for a forward reaction to produce P also is the same TS for its reverse reaction that instead converts products (P) back into its reactants (R).

It may be helpful to conclude this section by offering one more physical analogy to help a reader visualize the general shape of energy changes around a transition state. In Fig. 8-1-10, a reaction is depicted as a journey that takes molecules from a reactant like valley, through a mountain pass or col (the activated state), and then down into a product like valley:

Figure 8-1-10. A reaction as a journey across a mountain pass connecting a reactant valley to a product valley:



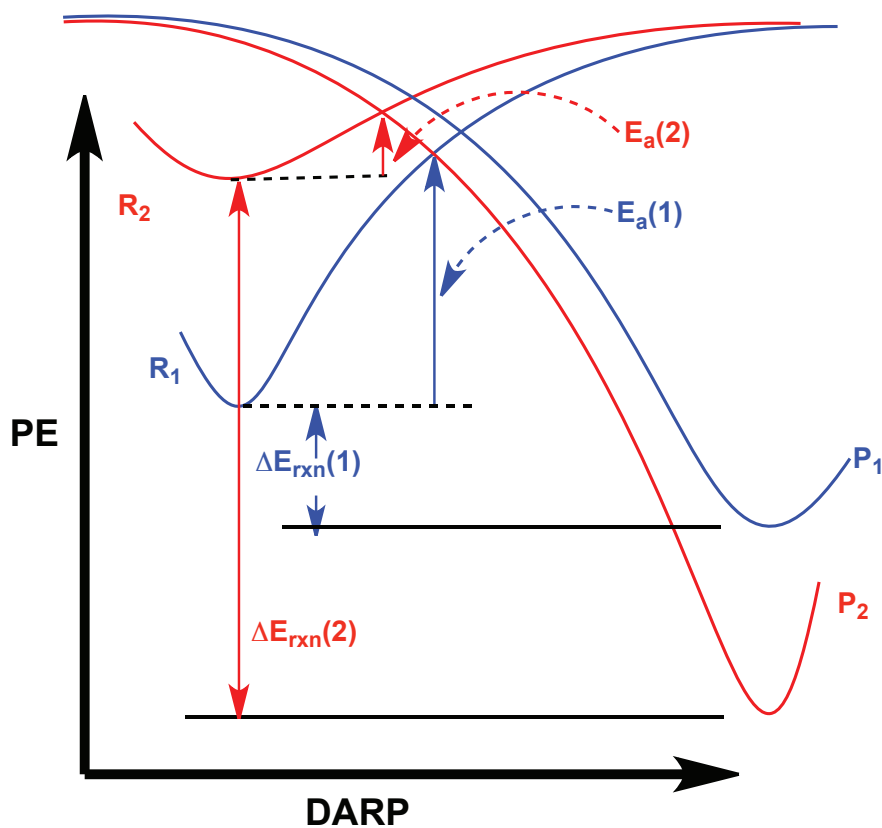
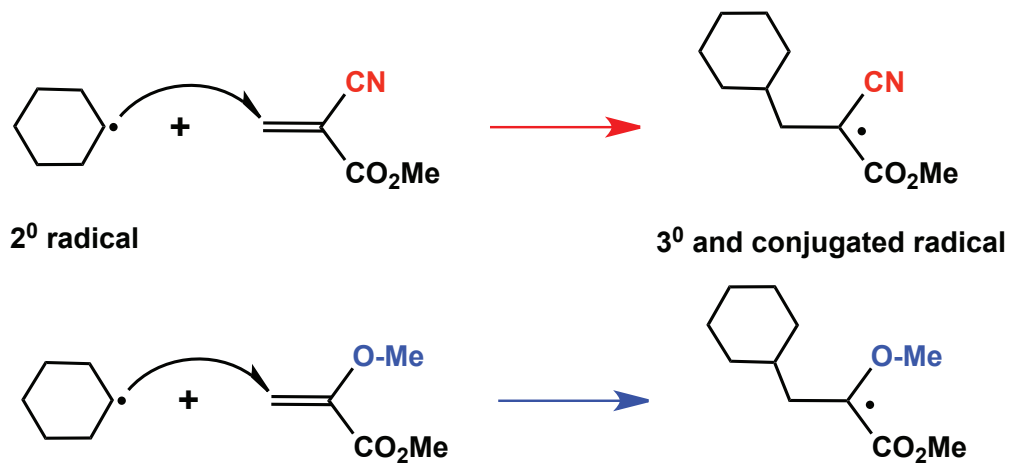
1) This particular image and analogy comes to us from J.E. Leffer and E. Grunwald: “Rates and Equilibria of Organic Reactions.”

Thus an activated or transition state is a “metastable” molecular structure that, in many ways, has numerous similarities to those structural descriptions also applied to “normal” or stable molecular structures in their equilibrium ground state geometries (all R and P bonds have positive PE curvatures or “curved up” parabolas for PE changes resulting from distortion away from their equilibrium geometries). The PE curve along a reaction path on either side of an activated state or TS connecting R to P has a negative curvature (i.e. has a “curved down” parabolic shape) around its TS. For those bonds not affected directly by this chemical reaction, one would expect them to remain close to those structural properties established for their equilibrium or ground state geometries. As a result, for an activated state, these non-reacting bonds also will possess “curved up” or positive PE curvatures around this activated state. Thus the PE contributed by these non-reacting bonds form the col walls that border the path through this mountain pass. These two features — height of reaction path and col width — affect both the E_a (black path) and reactant geometry around a TS. The PE of reactant bonds not directly affected by reaction (Red curves) determine whether a TS is a tight or loose assembly of reactant molecules or bonds (i.e. the entropy of this TS).

8-1-6. The relationship between the BEP and Hammond Postulates:

It has been observed that fast reactions not only have low activation energies, but they also often are exothermic reactions. Bell, Evans and Polanyi (BEP) explained this relationship between ΔE_{Rxn} and E_a using a BDE model just like the one we have just developed in this chapter.

Figure 8-1-11. Potential Energy curves for two related and exothermic reactions:



For many related reactions, such as those illustrated in Fig. 8-1-11, the more exothermic reactions also proceed faster than less exothermic or even endothermic reactions. These conditions are illustrated in Fig 8-1-11 for two radical addition reactions. In this example $E_a(2)$ for $R_2 \rightarrow P_2$ is less than $E_a(1)$ for $R_1 \rightarrow P_1$, (i.e. $E_a(2) < E_a(1)$). In this example, that reaction with a lower E_a (i.e. $R_2 \rightarrow P_2$) also proceeds at a faster rate than the rate of a reaction with a higher E_a (i.e. $R_1 \rightarrow P_1$): Thus $k_{Rxn2} > k_{Rxn1}$. One also observes, from Fig. 8-1-11, that product P_2 is more stable than P_1 and this makes reaction $R_2 \rightarrow P_2$ more exothermic than $R_1 \rightarrow P_1$, which also means that $\Delta E_{Rxn}(2) < \Delta E_{Rxn}(1)$. A direct relationship between E_a and ΔE_{Rxn} is possible because, for these reactions, a more stable product also lowers its E_a for reaction. For these types of reactions one then also can write a linear equation:

$$E_a = b + k(\Delta E_{Rxn}) ; \text{ where } b\text{-intercept, and } k\text{-slope are constants}$$

The BEP postulate or principle states that for a set of related chemical reactions, **the more stable product should be formed faster than a less stable product**. This relationship between heat of reaction and a rate of reaction is a necessary requirement for those reactions under thermodynamic control.

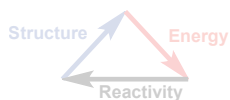
Later Hammond also observed from Fig. 8-1-11 that an activated or transition state (TS) with a low E_a also has a structure and bonding that more closely resembles its reactant structures than it resembles its product structures. Take a closer look at Fig. 8-1-11: Notice that the activated state for reaction ($R_2 \rightarrow P_2$) has a DARP that is **less than** the DARP required to achieve an activated state for reaction ($R_1 \rightarrow P_1$). The **smaller the DARP** required to attain a TS structure, the closer this TS is to its reactant structures and the easier it is to attain a TS for reaction:

$$\begin{aligned} & \text{If:} \\ & \quad E_a(2) < E_a(1) \\ & \text{then} \\ & \text{rate constant } k(2) > \text{rate constant } k(1) \\ & \text{and} \\ & \quad \text{DARP [TS(2)]} < \text{DARP [TS(1)]} \end{aligned}$$

Hammond generalized his conclusion by arguing that the amount of activation energy required for reaction is directly related to the amount of bond reorganization (i.e. structural distortion) required to attain an activated state or TS structure. This also means that reactant structures moving along a reaction path with small differences in their DARP also will have molecular structures that are similar to each other. Thus, early TS structures have lower activation energies (E_a 's) simply because they more closely resemble their reactant molecular structures than do those structures with late TS's:

TS₂ less distortion has a lower E_a < TS₁ with more distortion has a higher E_a

Thus the closer two structures are in their geometry and bonding, the smaller the amount of distortion required to convert one molecular structure into the other molecular structure. This is the reason for the smaller difference between their potential energies.



Hammond's Postulate is more than just an alternate statement of the BEP postulate because it is more general than the BEP principle. The BEP relationship between E_a and ΔE_{rxn} applies only to those reactions **under thermodynamic control**. Thermodynamic control requires a linkage between activation energy and product stability, or alternatively, its heat of reaction (i.e. ΔE_{rxn}). However, the Hammond postulate with its focus on TS structures and their relationship to reactant structures is applicable to all reactions. Hammond's postulate applies to all reactions, irrespective of whether they are under either thermodynamic or kinetic control. For those reactions under kinetic control, the less stable product is formed faster.

Hammond's Postulate:

“If two states, as for example, a transition state and an intermediate, occur consecutively during a reaction process and have nearly the same energy content, their interconversion will involve only a small reorganization of the molecular structures.”

– George S. Hammond

In other words, related structures that are close in energy also are close in their physical structures. Alternatively, the smaller the amount of distortion energy differences between two structures, the closer these two structures will be in their respective potential energy (i.e. PE) content.

8-1-7. More on Competing Reaction Pathways: Thermodynamic vs Kinetic control:

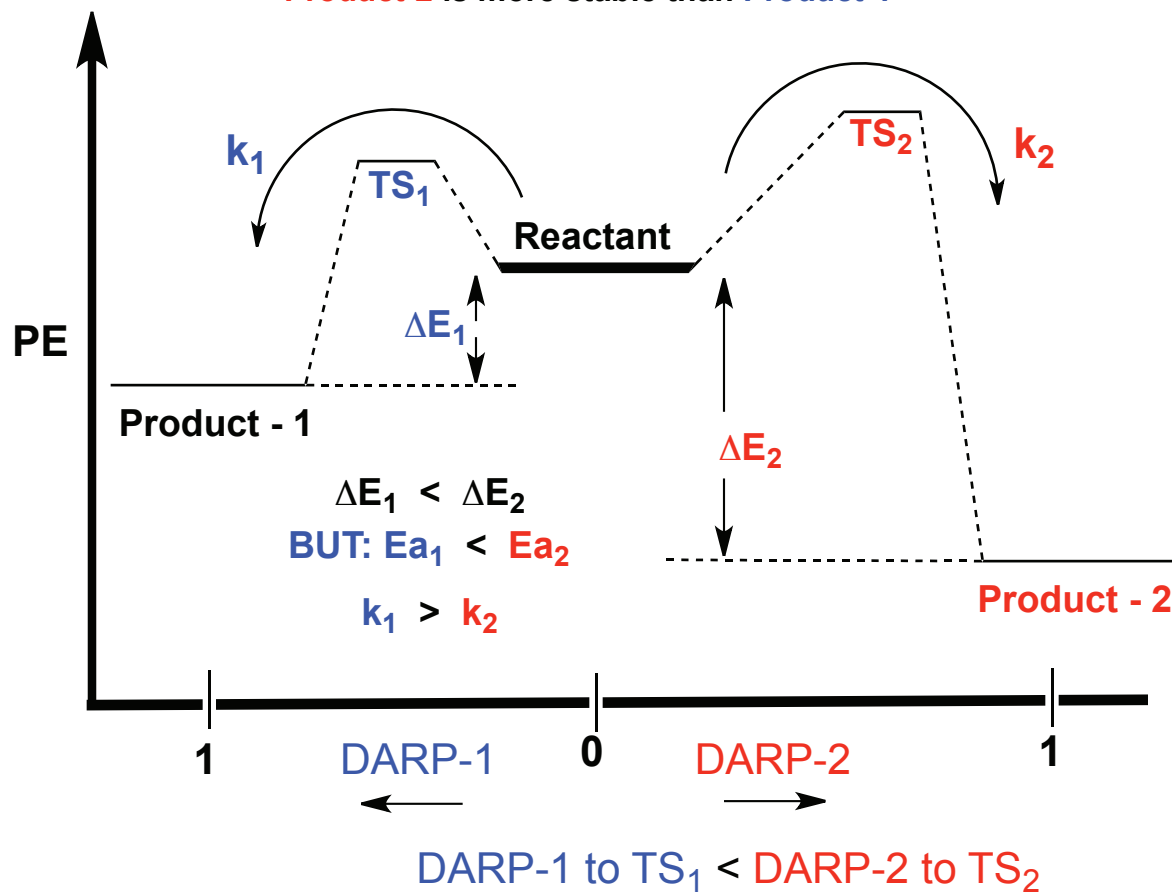
For thermodynamic control, more stable product(s) is/are formed faster (i.e. BEP) than their less stable products. However, for those reactions under kinetic control, it's the less stable product(s) that is/are formed faster than their more stable product(s).

Let's illustrate these competing types of reaction pathways using Fig. 8-1-12. In this PE diagram, a reactant can form two different products with the **same rate law**, but with different rate constants; i.e. $k_1 \neq k_2$:

Figure 8-1-12. Kinetic vs Thermodynamic Reaction Pathways:

Rate law Rxn 1 same as for Rxn 2
but
 $k_1(\text{Rxn 1})$ different from $k_2(\text{Rxn 1})$

Product-2 is more stable than Product-1



If this reaction as shown in Fig. 8-1-12 were to proceed so that a larger amount of the more stable product, (i.e. **Product-2**) is formed relative to **Product-1**, then this rxn **would be under thermodynamic control**. A thermodynamic product distribution occurs because the **rate of formation for the more stable Product-2 would be faster** than the rate of formation of the less stable **Product-1** (i.e. for thermo control: $k_2 > k_1$ because: $E_a(1) > E_a(2)$).

If Thermodynamic Control: Product distribution depends on relative stability of P-1 and P-2. For this example, thermodynamic control will provide a % yield of P-2 > % yield of P-1 because $k_2 > k_1$.

If instead, this reaction as is shown in Figure 8-1-12 proceeds such that a larger amount of the less stable product (i.e. Product-1) is formed faster than the more stable product (i.e. Product-2), then this rxn instead is under kinetic control. Kinetic control implies that rate constant for formation of less stable Product-1 is larger than the rate constant for formation of the more stable Product-2 (i.e. for kinetic control: $k_1 > k_2$ because: $E_a(1) < E_a(2)$).

For Kinetic control: Product distribution depends on the rate with which P-1 is formed and not on product stability. For this example of kinetic control, the rate of P-1 formation is faster than rate of formation of P-2 because $k_1 > k_2$. As a consequence of kinetic control, the % yield of P-1 > % yield of P-2.

Thermodynamic control typically is the norm for reactions (i.e. BEP control, lower E_a , and faster rate of formation for the more stable product). That said, one needs to appreciate that although reactions found to be under kinetic control tend to be less prevalent than the number of reactions under thermo control, many kinetically controlled reactions often are quite synthetically useful. Kinetic control also can be a source of cellular malfunction leading to disease in biological systems.

Q: Show how a reaction that produces Product-1, initially produced under kinetic control could be isomerized to produce a thermodynamically more stable Product-2?

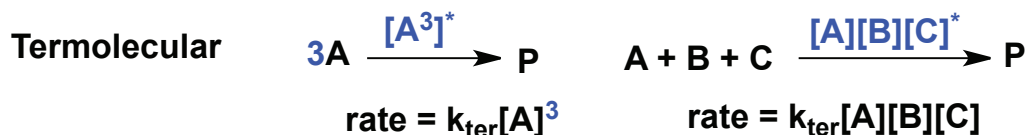
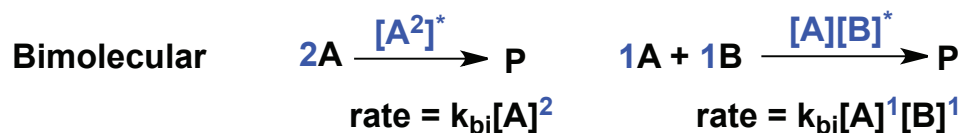
If the back reaction from Product-1 is fast enough to reversibly reform its reactants, which then can recombine to form Product-2, an indirect equilibrium exists between P-1 and P-2 and that equilibrium necessarily will eventually produce a larger yield of the more stable P-2. Alternatively, Product-1 might be in a direct equilibrium with Product-2. A direct equilibrium will convert P-1 and P-2 without requiring a reverse reaction back to their reactants. Either type of equilibrium will eventually produce a greater yield of Product-2.

8-1-8. Constructing Complex reactions from Elementary Reactions:

This activated or transition state (TS) approach described above also can be used to describe more complex reactions. So how does one extend this TS model to consider multistep reactions? The answer is to build complex reaction mechanisms up from their simple elementary reactions.

There are some special reactions for which the molecularity of a balanced reaction equation is identical to the molecularity of the rate law for its reaction (i.e. the molar composition of the TS is the same as the molar stoichiometry of the reactant side of its balanced equation). For an elementary reaction, all reactant molecules in a balanced equation come together in a single step to form a TS that then proceeds on to its product(s). Examples of important elementary reactions are collected in Fig. 8-1-13:

Figure 8-1-13. The Three Basic Types of Elementary Reactions, their equations and their rate laws:



Elementary reactions:

Composition of TS is same as composition in reactant side of equation for Rxn

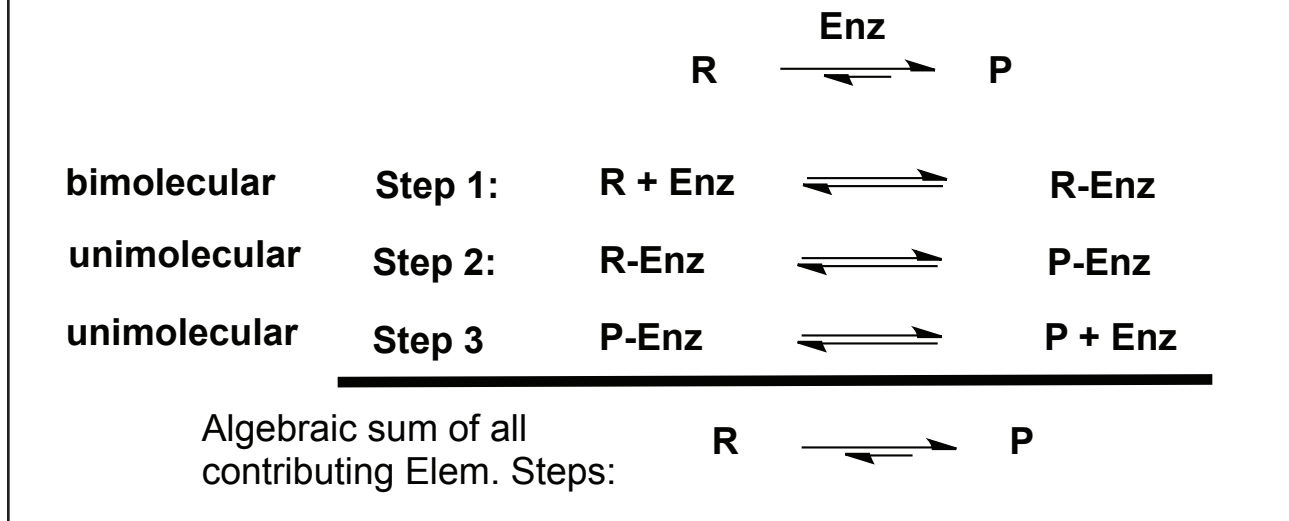
There are no other known examples of elementary reactions that are more complex than termolecular. True termolecular reactions, as one might have expected, are exceedingly rare because they require bringing three molecular structures together, simultaneously in a single collision with enough energy to form an activated or TS state.

Q: List at least one other reaction equation and its corresponding rate law that also could proceed by a Termolecular reaction mechanism not shown in Fig. 8-1-13:



Complex reaction mechanisms consist of a number of elementary reactions that occur in specific sequences. For example, consider Fischer's lock and key model for an enzymatically-catalyzed reaction as is shown in Fig. 8-1-14 below:

Figure 8-1-14. Fischer's Lock and key Mechanism Resolved into its Elementary Reaction Steps:



This enzyme (Enz) is a catalyst because it does not appear in the rate equation as a reagent (i.e. that Enz is not consumed as part of the transformation of R into P).

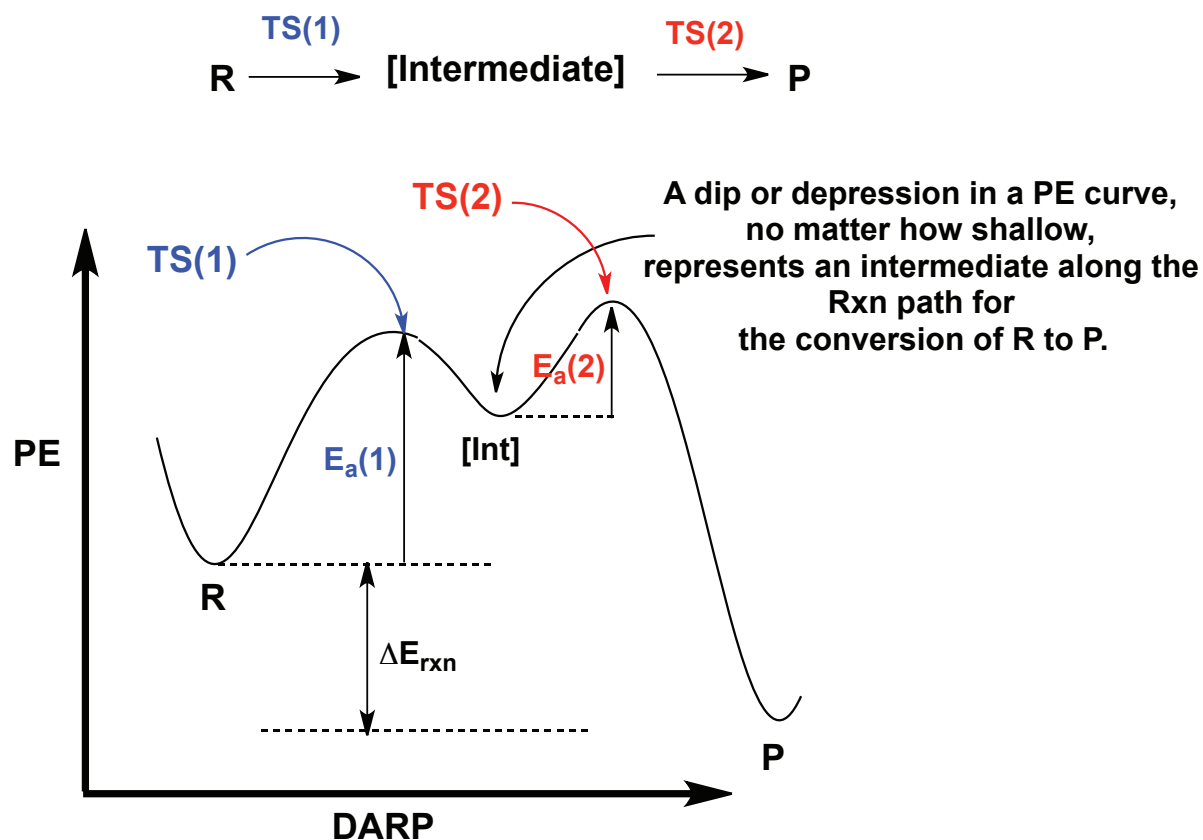
Fischer's lock and key mechanism requires that an enzyme first form a complex with a reactant (R-Enz). Then this complex undergoes a unimolecular reaction to form a product that, initially, remains bound to this enzyme (Enz-P). The final step in this mechanism occurs as this product-enzyme complex dissociates to produce free product and also regenerate free enzyme.

Q: Is an enzyme catalyzed reaction under thermodynamic or kinetic control? Explain your choice.

Enzyme catalyzed reactions are under thermodynamic control because all of the elementary reactions in this mechanism are in equilibrium with each other. Catalyzed reactions do not alter the ΔE_{Rxn} or the thermodynamic stability of products. Catalysts just lower the activation energies for a reaction, and sometimes catalysts also can open up a new pathway between reactants and products. Remember that a catalyst for a forward reaction also is a catalyst for its reverse reaction.

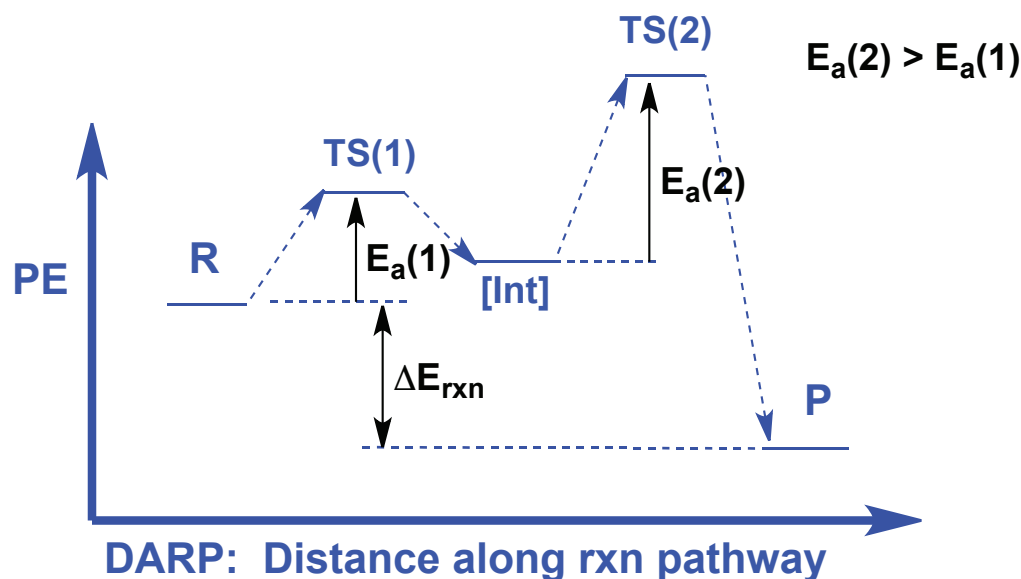
If a reaction occurs by a number of steps, then molecular products that intervene between initial reactants and final products are called *intermediates*. In a lock and key mechanism in Fig. 8-1-14, the complexes R-Enz and P-Enz are intermediates on this reaction path connecting R to P. Intermediates often possess higher potential energies than either their reactants or products, but such a difference in PE is not necessary nor is it required. What makes intermediates of special interest is that they are stable molecules that lie along a reaction path connecting reactants to products. Even though intermediates may have higher energies (i.e. PE), and possess relatively short lifetimes (i.e. be very reactive), they are just like any ordinary molecule and thus intermediates can, in principle, be isolated. Isolation is possible because intermediate structures exist at the bottom of their shallow PE wells and not like TS structures that, instead, lie on the cusps of their PE curves.

Figure 8-1-15. PE Profile for a Reaction Proceeding Through a Single Intermediate:



In Fig. 8-1-15, this PE curve has a first step $R \rightarrow [\text{Int}]$ that is rate determining because the activation energy for this first step is larger than the activation energy required for the second step for $[\text{Int}] \rightarrow P$, [i.e. $E_a(1) > E_a(2)$]. As a result of this difference between these two activation energies, the rate constants for $k_1(\text{step 1}) < k_2(\text{step 2})$. This slower rate for formation of $[\text{Int}]$, relative to its rate of decomposition, is what makes this first step for formation of this intermediate rate determining.

Q: Draw a PE profile for the reaction: $R \rightarrow [Int] \rightarrow P$ that also has a second step which is rate determining. Label all the parts of your curve that correspond to those labels shown above for Fig. 13.

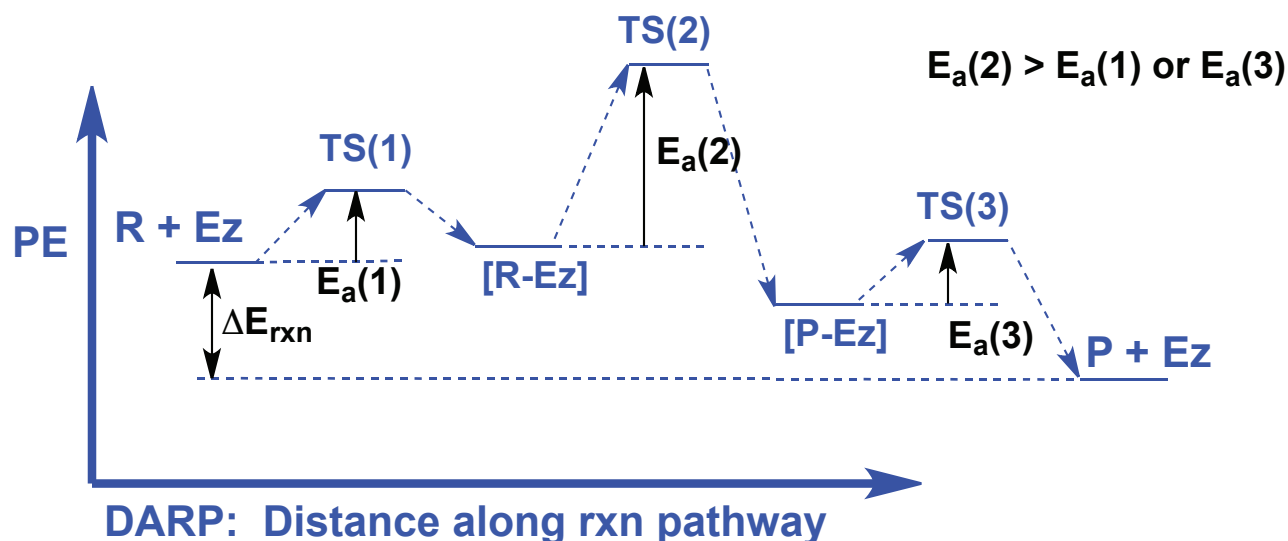


Q: How many intermediates are there in the lock and key mechanism for enzymatic catalyzed reaction shown above (Fig. 8-1-14)? How many TS structures? List them:

Two intermediates: R-Ez and P-Ez

Three TS: R to R-Ez, then R-Ez to P-Ez, and finally P-Ez to P + Ez

Q: Draw a PE profile for an enzyme catalyzed reaction that proceeds by a lock and key mechanism and assume that, in this mechanism, it's the conversion of R-Enz to P-ENZ which is rate determining.



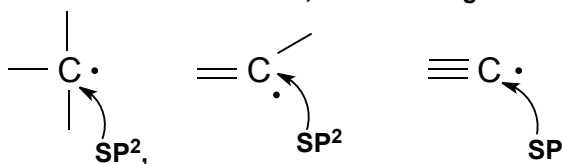
Q: What do you think will happen if either [R-Ez] or [P-Ez] is more stable than R or P?
The catalyzed reaction will shut down, because all the Ez will be “tied-up” or poisoned by either R or P. The end result would be that Ez will no longer be released in the presence of R or P.

8-1-9. The Four Classic Intermediates Observed in Organic Chemistry:

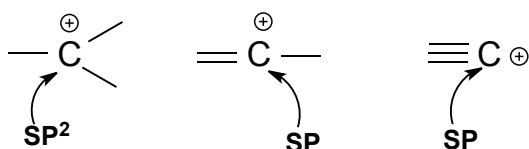
In Fig. 8-1-16 Lewis structures for various types of intermediates that can occur in the Organic Chemistry are shown. Each type of intermediate has its own electronic geometry, molecular shape, and pattern of reactions and reactivity.

Figure 8-1-16. Types of Intermediates found in Organic Chemistry:

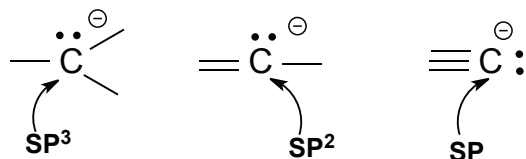
Radicals or Free Radicals; Formal Charge = 0 :



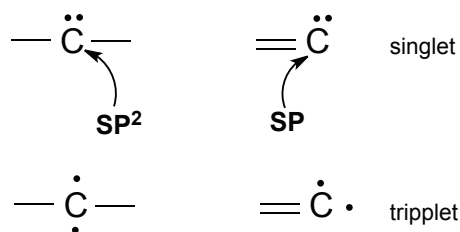
Carbonium ions or carbocations; Formal Charge = +1 :



Carbanion ions; Formal Charge = -1 :



Carbenes or divalent carbon; Formal Charge = 0 :



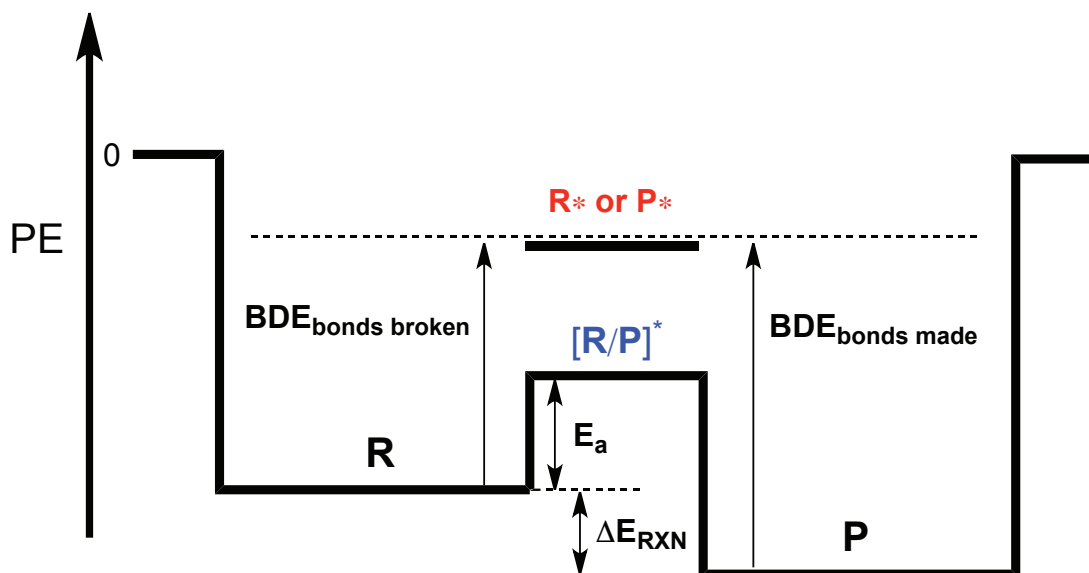
If electrons in a carbene occupy a single orbital, then that structure is identified as a singlet carbene because the spins of the electrons in that orbital are paired.
 If each electron is placed in its own separate orbital, then the electron spins are unpaired and this structure is identified as a triplet carbene.

Each of these types of intermediates will be discussed again and in more detail in subsequent chapters when we explore their methods of generation and their resulting chemistry.

8-1-10. Quick summary of Reaction Mechanics presented in this chapter:

1. Chemical reactions occur when reactants pass through an activated state, also known as a transition state, to form products. If a reverse reaction can be realized, then products will cross back through this same transition state to reform reactants.
2. The principle source of activation energy required for any reaction arises from the energy required to distort or even break reactant bonds. Energy gets released as a new product bond(s) get formed.
3. For a reaction to proceed, it is not necessary, nor is it required, that a reactant bond be completely broken before new product bonds can be formed:

Figure 8-1-17. A thermodynamic perspective of a chemical reaction:



R* represents an Intermediates created by completely breaking a bond in **R** before conversion to **P**. Intermediate **P*** represents the back or reverse reaction path-breaking a bond in **P** in order to regenerate **R**.

[R/P]* represents the activated state for the interconversion of **R** and **P**.

$$\Delta E_{rxn} = -BDE_{bonds\ made} + BDE_{bonds\ broken} = PE_{(prod)} - PE_{(react)}$$

BDE is defined as a positive number b/c it represents the energy required to **Break** a bond

4. Lower activation energies should occur when new bond formation occurs along with old bond breaking because, in such **concerted reactions**, the energy released by new bond formation helps to offset the energy required to break an old reactant bond. Such reactions are designated as concerted when bond breaking and bond formation occur together within a TS structure (e.g. as is shown in Fig. 8-1-17). The ultimate extreme form of a concerted reaction is a **synchronous** reaction for which bond breaking occurs **simultaneously and equally with new bond formation**. For example, an ideal TS for a synchronous reaction might consist of 50% old broken and 50% new forming bonds. However, even synchronous reactions will have both activation energies and TS structures.
5. A reaction is under thermodynamic control, if the more stable product also is formed fastest.
6. The Hammond postulate applies to reactions whether they are under thermodynamic or kinetic control. That TS with the least amount of changes in its bonding, relative to its reactants, will have a lower activation energy than a related TS structure which requires a greater amount of bonding distortion or reorganization.

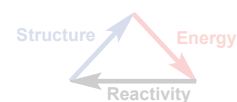
8-1-11. Conclusions:

This Chapter began with Arrhenius' "leap of faith" that postulated the intervention of an activated state between reactants and products in a chemical reaction and it ends with the stabilizing impact of new bond formation on the PE and structure of a TS. This BDE reaction model began a process of conceptualizing an activated or transition state within our current framework of molecular structure and bonding. An activated state can now be understood as a special type of pseudo or "metastable" molecule with a specific connectivity and structural geometry rather than just a black box containing a jumble of atoms or molecular fragments. Applying some rather basic knowledge about covalent bonding also enabled us to place limits on the structure of an activated state. An activated or TS lies on a bonding continuum limited at one end by reactant structures with $DARP = 0$, and at the other end by their product structures with $DARP = 1$. Combining these mechanical ideas, together with our model for covalent bonding, also provides both an additional layer of understanding, about the nature of concerted reactions, and also why it is that some similar reactions can proceed more rapidly than other related reactions.

8-1-12. What you should know and be able to do:

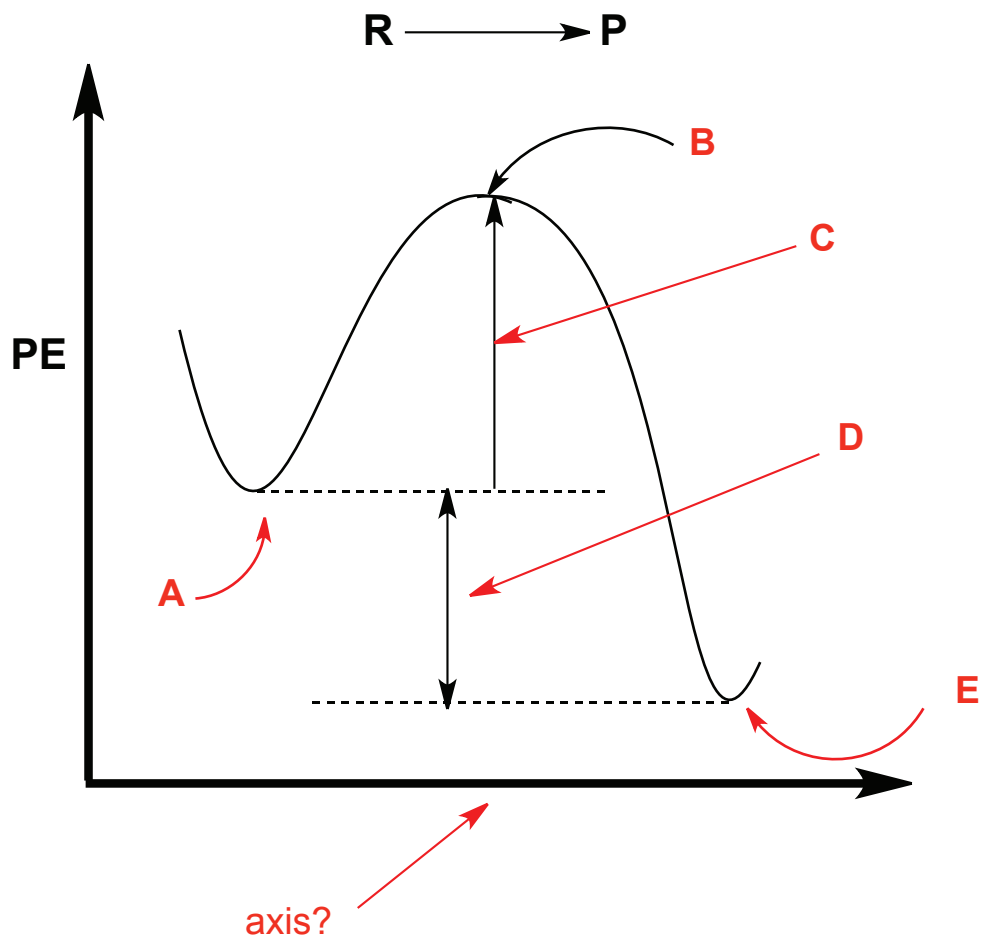
1. You should be able to name and explain the four "strange" features of a chemical reaction.
2. You should be able to sketch out a PE curve or diagram for a reaction mechanism using the BDE data for reactants, products, and any necessary intermediates.
3. Identify and label those components that characterize a PE curve or diagram for a reaction: (e.g. R, P, E_{rxn} , E_a , and intermediates).
4. Explain the difference between an intermediate and transition state, and where these structures will be located on a PE diagram for a chemical reaction.

5. Understand the linkage between product stability, E_{rxn} and E_{a} necessary for thermodynamic control. Also understand what is necessary for required for kinetic control.
6. Use the Hammond postulate to explain how a kinetically controlled reaction can have a lower activation energy than a thermodynamically controlled reaction.
7. Know how to determine, from available experimental data, whether a particular reaction is under thermodynamic or kinetic control.
8. Name and identify the three types of elementary reactions and also state what is required for a reaction to be characterized as an elementary reaction.
9. Be able to move between a complex reaction mechanism and a PE curve that describes that reaction mechanism.
10. Define a rate-determining step in a complex reaction mechanism, and also be able to locate that step from a PE diagram for a particular reaction.



8-1-13. Problems:

1. Label the various designated components on this PE diagram for the conversion of R to P:



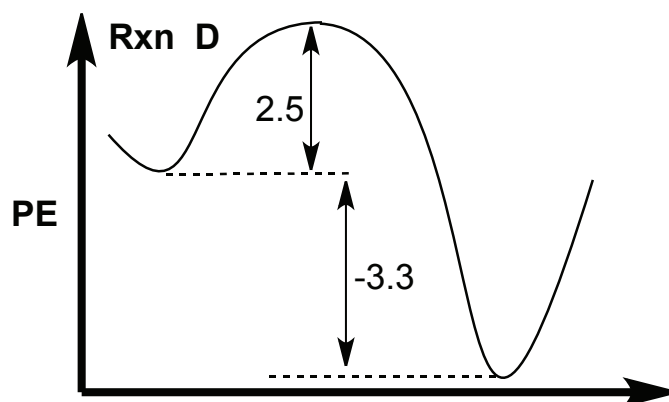
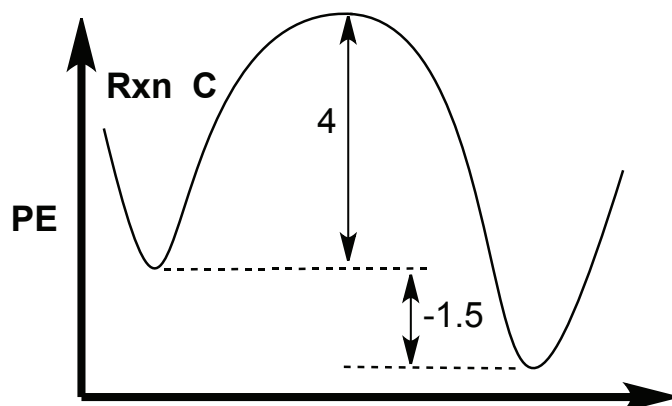
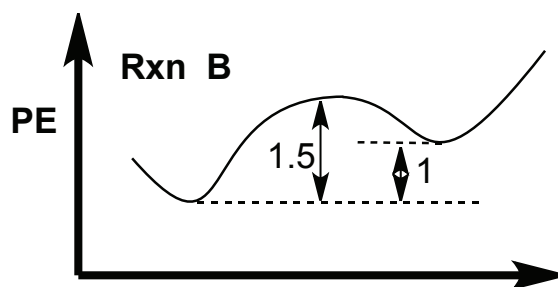
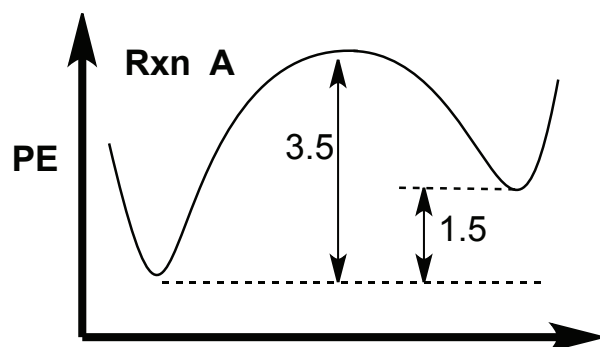
b) Is there an intermediate in this reaction? Explain your reasoning.

c) Is this an exothermic, thermoneutral or endothermic reaction? Explain your reasoning

2. If stronger bonds are formed and weaker bonds are broken in a chemical reaction, then such a reaction is likely to be _____ (if necessary refer back to PE diagram used in Q1):

- a) Exothermic
- b) Thermoneutral
- c) Endothermic
- d) At equilibrium

3. Select your answers to Q3 from the four different PE Diagrams shown below:



Answer the following questions about these PE curves and also assume that each of these reactions is under thermodynamic control. Also please explain the reasoning for your choices.

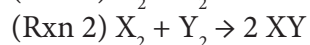
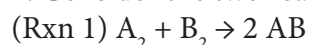
a) Which PE curve should have the fastest forward reaction?

b) Which is the most endothermic forward reaction?

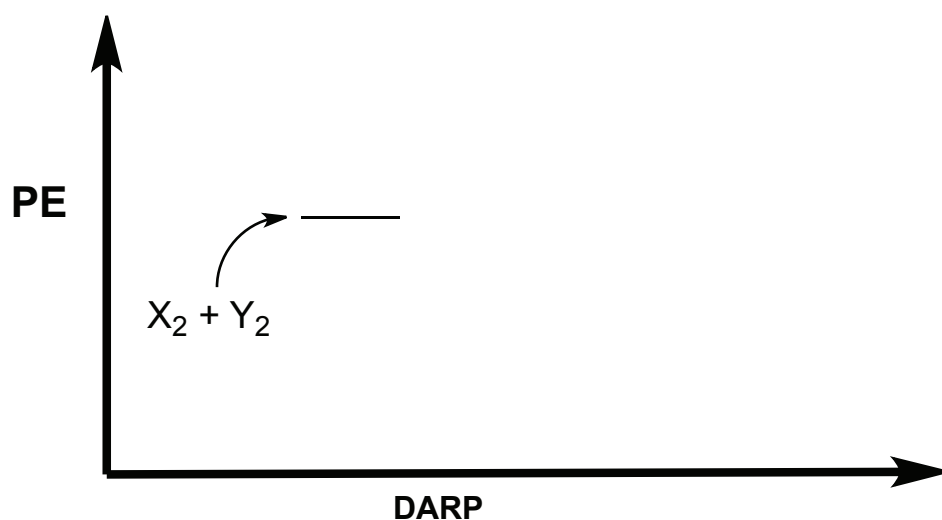
c) Which is the most exothermic reaction?

d) Which reverse or back reaction should be fastest?

4. Consider the two reactions shown below:



A partial potential energy diagram is started for helping to start the PE curve for Rxn II is shown below. Complete the PE curves for these two Rxns using information based on the following observations:

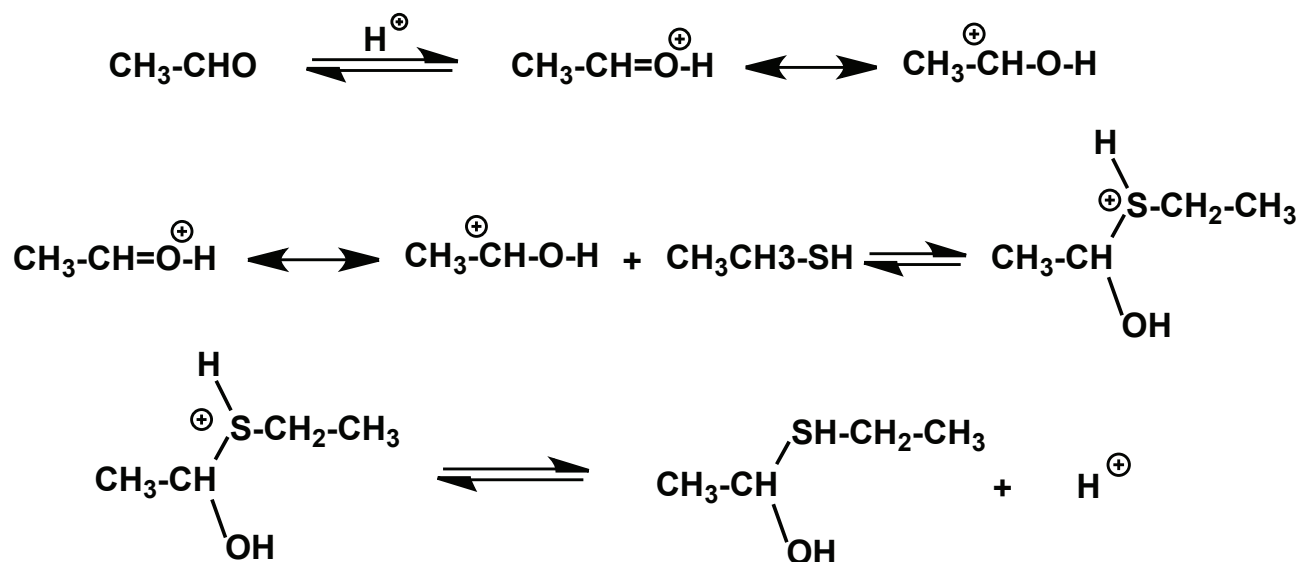


Facts about reaction (I and II): These reactions are similar and both reactions are exothermic but reaction I is more exothermic than reaction II and, the activation energy of reaction I ($A_2 + B_2$) is less than the E_a for reaction II.

a) With all of this information outlined above complete the potential energy diagram for reaction II on the graph above.

b) Are these reactions under thermodynamic control?

5. Consider the reaction mechanism shown below:



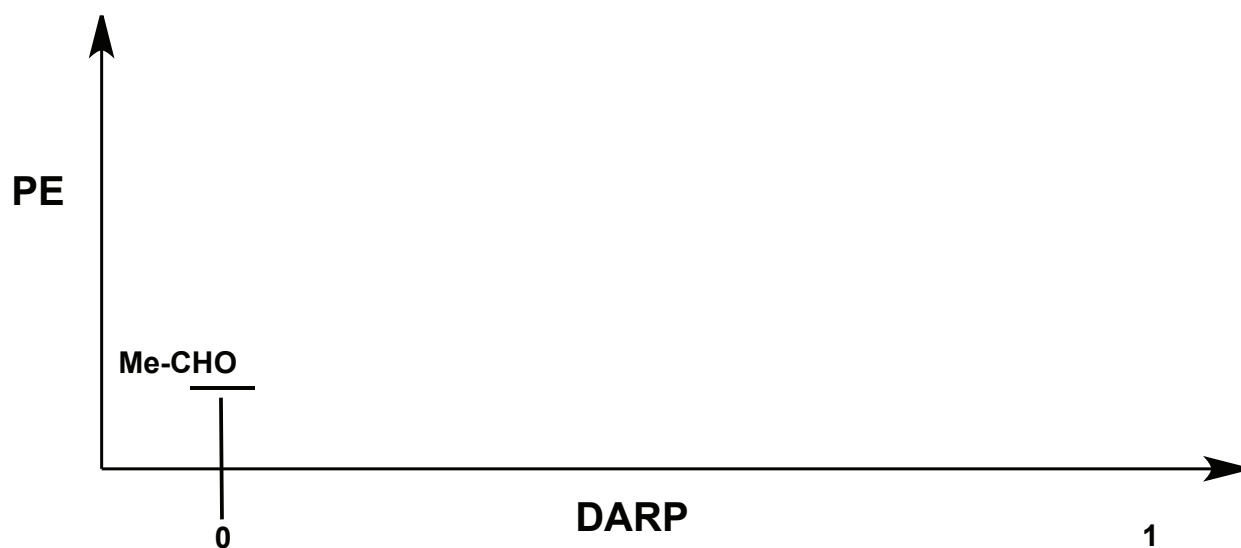
Answer the following questions:

a) How many steps in this mechanism?

b) How many transition states?

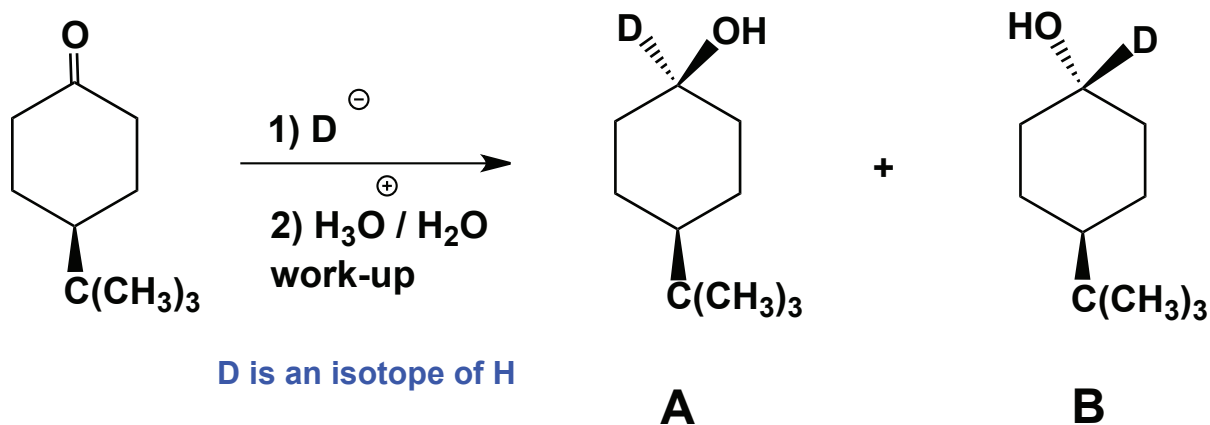
c) How many intermediates?

d) Let each intermediate and the product in this mechanism be slightly more endothermic than those in a previous step and also let the first step be rate determining. Complete a PE diagram for this reaction and label its components.



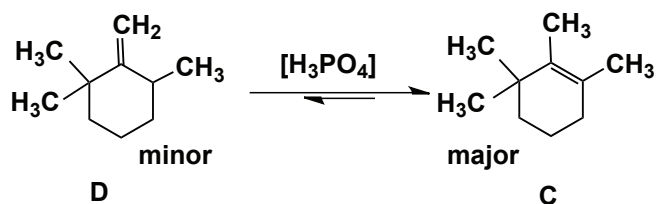
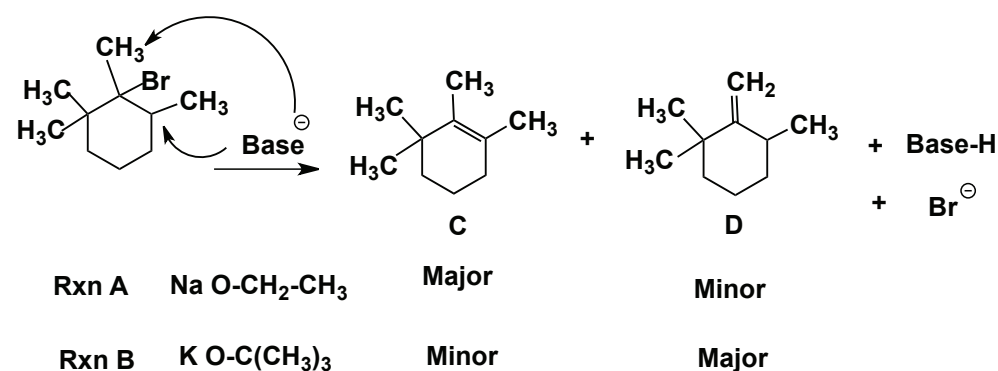
e) If the reaction coordinate or DARP is 0 at the reactants, indicate where on your PE plot the value of DARP for this reaction is equal to 1.

6. Use your knowledge about the conformation of cyclohexane derivatives to answer the questions about the following reaction:



Many hydride reagents selectively produce a kinetic product, while other reagents produce a thermodynamic product. Which product (A or B) is the kinetic product, and why is it the kinetic product?

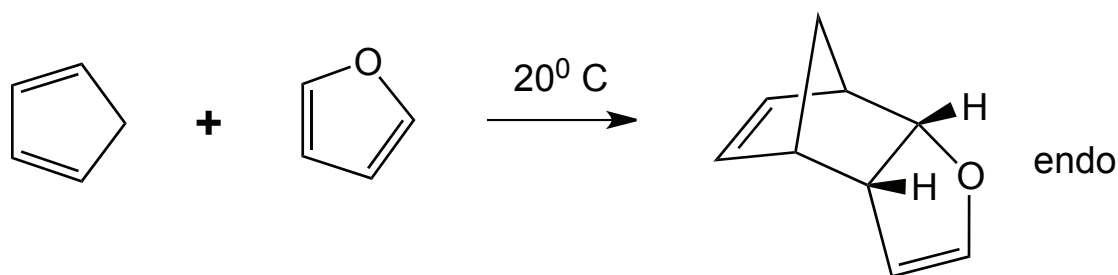
7. Consider the two elimination reactions below (this elimination reaction removes H and Br from the reactant):



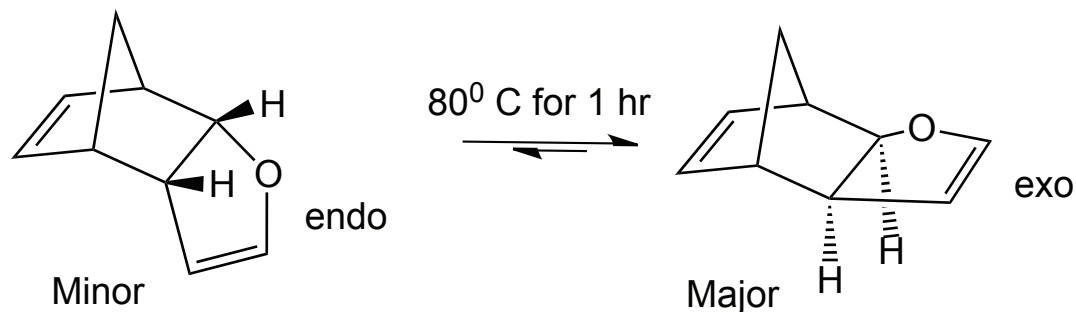
7.

a) Major refers to the major isomer produced. The major isomer is produced in the greatest % yield in an isomeric mixture of products. Minor is a minor isomeric product produced in a lower % yield in a mixture of isomeric products. Which reaction is under thermodynamic control? Explain why.

8. You do the following cycloaddition reaction at room temperature (20°C):



On warming this endo product to 80°C for an extended period of time produces a mixture of both endo and exo adducts:



This same product mixture will be obtained if the cycloaddition reaction temperature is raised from 20°C to 80°C .

Reaction Tempt.	Endo	Exo
20°C	100%	-
80°C	10%	90%

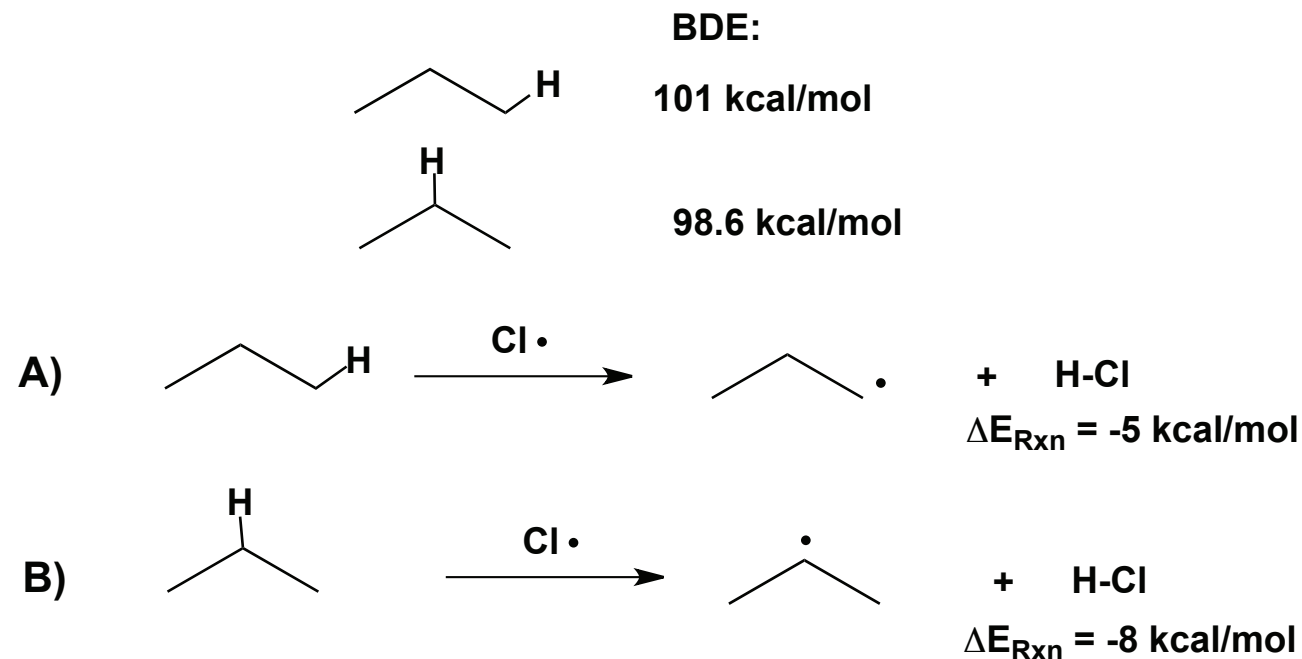
a) Which of these two cycloaddition reaction temperatures (20°C or 80°C) leads to kinetic control? Which reaction temperature leads to thermodynamic control? How did you decide this?

b) Is it ever possible to produce a kinetic product if the reaction or its products undergo an at equilibration at the reaction temperature?

c) Draw a pair of PE curves (like that used in Fig. 8-1-12) that illustrates these results for the reaction kinetic vs thermodynamic reaction described in Q8. Be sure to also include the relative positions of these two endo and exo TS structures: (Hint: Start with same pair of reactants, apply Hammond postulate and decide which TS has the lower energy? And then consider which product (endo or exo) is more stable, then just connect up your curves through these points.)

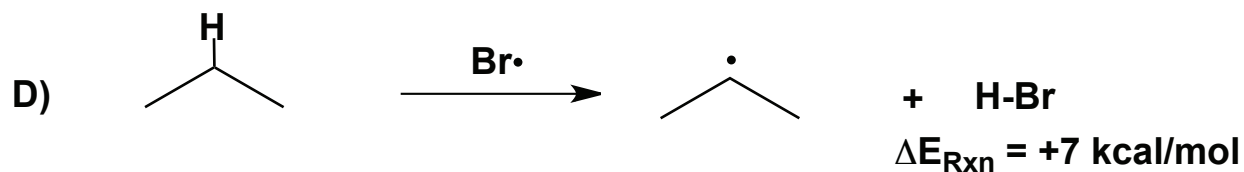
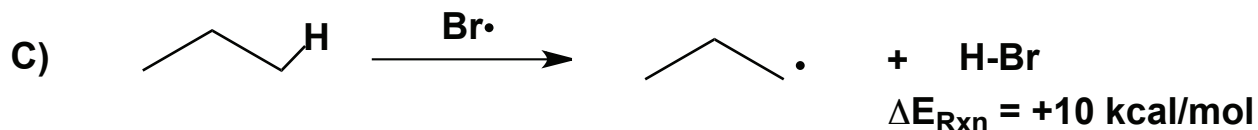
9.

a) Consider the BDE data and then the following pairs of similar hydrogen abstraction reactions:



Both of these reactions are under thermodynamic control. If BDE is approximately equal to the E_a for these reactions, and if the rate of Rxn B is 4.5 times faster than for Rxn A, then what can you say about TS(A) relative to TS(B)? What about E_a (A) relative to E_a (B)? What about the relative positions (earlier vs later) for TS(A) relative to TS(B)?

b) Consider the following pair of similar hydrogen abstraction reactions:



Information you'll need to answer questions: Both of these reactions are under thermodynamic control. The rate of Rxn D is 97 times faster than Rxn C. What can you say about the TS(C) relative to TS(D)? What about E_a (C) relative to E_a (D), and relative positions (earlier vs later) of TS(C) relative to TS(D)?

c) Based on your answers to parts 9a and 9b, use your answers to make a pair of PE reaction profiles (e.g. like Fig.8-1-12) that compares and contrasts TS(B) with that expected for TS(D):

10. Look at the reactants and products for the following reactions. Then circle each of the bond(s) or non-bonding electrons involved in the “bond breaking” for those particular reactions listed below:

