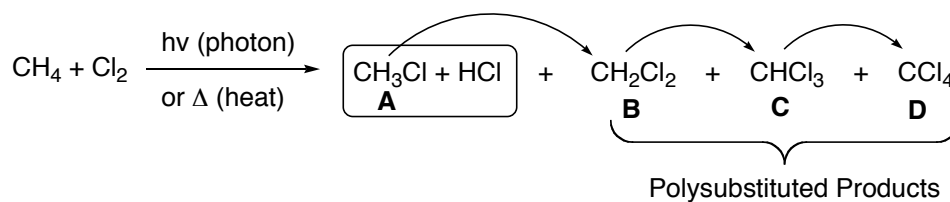


## Ch. 4 The Study of Chemical Reactions

### 4.1 Three Factors in Every Reaction:

1. Mechanism: what is the step-by-step pathway by which old bonds break and new bonds form?
2. Thermodynamics: what are the energy changes, both for the overall reaction and for individual steps in the reaction mechanism?
3. Kinetics: How fast does a reaction occur? How do changes in reactant structure, reaction solvent, or reaction temperature speed up or slow down a reaction?

### 4.2 The Chlorination of Methane: A Case Study



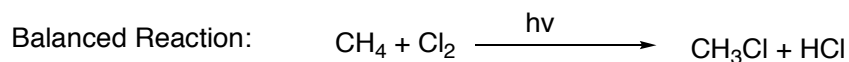
### Observations

-usually a mixture of products forms, including not only mono-chlorinated product **A**, but also polychlorinated products **B-D**.

1. Light (or heat) is required to initiate the reaction (energy required)
2. Blue light, absorbed by  $\text{Cl}_2$ , is most effective
3. High “quantum yield”: one photon can result in conversion of thousands of methane reactant molecules into product molecules
  - Q: if light energy is needed, why isn’t one photon needed for each reaction?

ANY MECHANISM MUST BE CONSISTENT WITH EXPERIMENTAL OBSERVATIONS

## 4.3 The Mechanism: Radical Chain Reaction

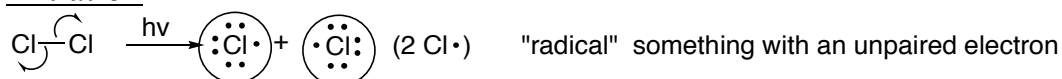


The mechanism must show all bonds broken and made:

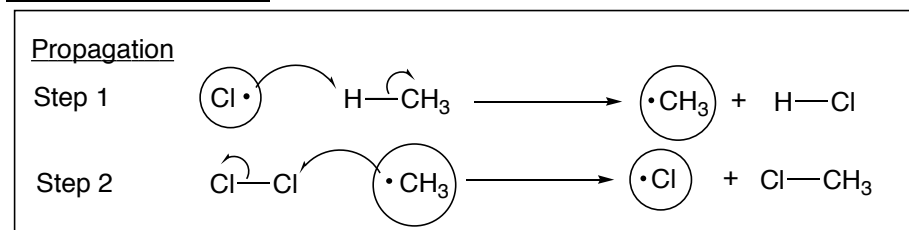
<u>Bonds Broken</u>	<u>Bonds Made</u>

## 3 Phases in Mechanism

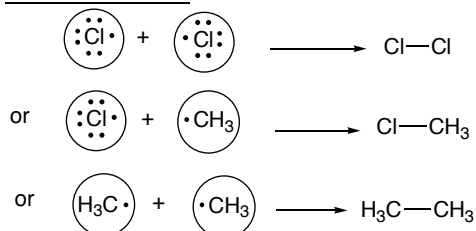
1. Initiation (gets it started)
2. **Propagation (keeps on going and going and going)**
3. Termination (what happens when it sometimes stops)

Initiation

- In a radical initiation step, two reactive radicals form from a nonradical precursor

PROPAGATION

- In each propagation step, one reactive radical reacts with a nonradical to produce a new reactive radical and a new nonradical.
- Since a reactive radical is reproduced in each step, you always have another reactive radical ready to keep the chain going.
- The chlorine radical produced in step two is the same as the chlorine radical that reacts in step 1.
- Thus you can sustain a repeating chain of step 1- step 2 -step 1- step 2 - step 1- step 2 - step 1- step 2 - step 1- step 2 - etc.
- -As long as there is a radical around, the chain will keep going
- The sum of the two propagation steps is the overall balanced reaction

Termination

Mechanism Notes:

1. “Radical”: Something with an unpaired electron.
  - Never satisfy octet rule → highly unstable and always highly reactive.
2. Initiation is needed to produce a highly reactive radical. But once you’ve got one, initiation is done.
3. **The main action is the propagation phase. Memorize how that works.**
4. The propagation phase involves a repeating chain of events (step 1 – step 2 – step 1 – step 2 etc.) **“Chain reaction”**
5. The overall reaction is the sum of the two propagation steps
  - When you sum the propagation steps, notice that the methyl radical cancels itself out (what’s formed in step one is erased in step 2) and the chlorine radical cancels itself out (what’s formed in step two is erased in step 1).
6. Like initiation, termination occurs only occasionally

## 7. Notice:

- Initiation: nonradical in → radicals out
- Each Propagation Step: radical + nonradical → nonradical + radical
- Any Termination Step: radical + radical → nonradical

## 4.4, 4.5 Free Energy, Enthalpy, Entropy

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

$\Delta G$ : Free Energy: favorable reactions have negative  $\Delta G$

$\Delta H$ : Enthalpy: heat lost or gained

- $\Delta H < 0$  exothermic       $\Delta H > 0$  endothermic

$\Delta S$ : Entropy: degree of randomness, disorder

In organic, enthalpy almost always dominates

**Exothermic → Favorable**

**Endothermic → Unfavorable**

If you can figure out whether a reaction will be exothermic or not, you can tell whether it is energetically favorable or not.

- But, being energetically favorable still doesn’t prove it will happen very fast... That’s the kinetics issue, see later...

## 4.6 Bond Energies:

- **Exothermic reactions break weaker bonds and form stronger bonds**
- Exothermic steps (in a multistep reaction) also trade weaker for stronger
- Extensive tables of bond energies are available (Table 4.2) for when bonds break in half (to give two radicals)
- Often relative bond energies can be predicted by inspection

Bond Strength	Bond Energy (kcal/mol)	Molecule	Products	Radical Stability
		H—F →		
		H—Cl →		
		H—Br →		
		H—I →		

Skills:

- Given bond energies, be able to rank bond strengths
- Given bond energies, be able to rank radical stabilities
- Given known radical stabilities, be able to predict relative bond strengths
- **Memorize the stability pattern for the halogen radicals**
- **Memorize the bond strength pattern for H-X bonds**
- **Memorize: C-X bonds have the same pattern: iodide is the weakest**

H <sub>3</sub> C—F	H <sub>3</sub> C—Cl	H <sub>3</sub> C—Br	H <sub>3</sub> C—I
109	84	70	56

- Just as acidity reflects anion stability, bond energy values reflect radical stability

## Problems:

1. H<sub>3</sub>C—SeH bonds are weaker than H<sub>3</sub>C—OH bonds. Which is more stable, •SeH or •OH?
2. Which is stronger, CH<sub>3</sub>CH<sub>2</sub>—Cl or CH<sub>3</sub>CH<sub>2</sub>—Br?

Why are H-F and C-F bonds stronger than H-I and C-I bonds?**1. Electronegativity and radical stability: (Remember)**

- Radicals are short of octet rule → electron poor
- The more electronegative fluorine is least willing to be electron poor. As you go down the table, electronegativity decreases and it's less problematic to become radical

Problem: Rank the probable stability of the following radicals, 1 being most stable and 4 being least stable? (Use electronegativity to guide you...)

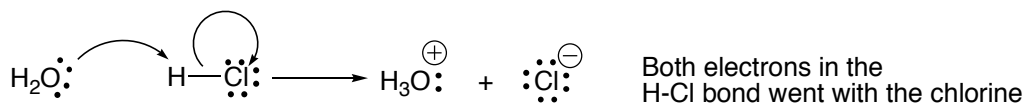
**2. Atomic size and orbital overlap:**

- Fluorine is small, and it's orbitals match up well size-wise with H and C resulting in strong overlap and strong bonds.
- Iodine is big, so it's orbitals don't match up well or overlap so well with H or C resulting in weak bonds.

Two Types of Bond Breaking:

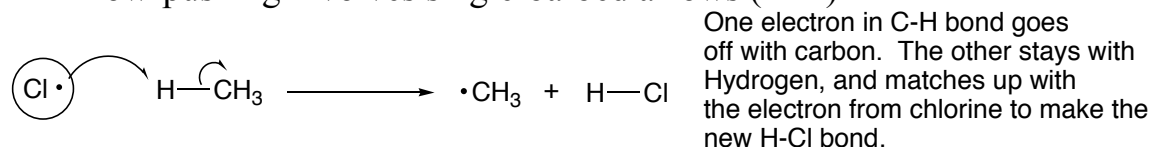
**Heterolysis:** one atom keeps both electrons (usual case)

- Ions are involved
- Arrow-pushing involves double-barbed arrows (↔)



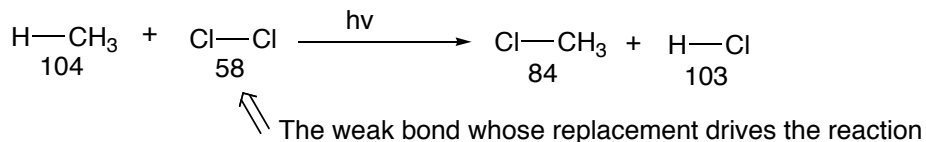
**Homolysis:** Bond breaks in half so that an electron goes with each atom (rare, but that's the type in this chapter)

- Radicals are involved
- Arrow-pushing involves single-barbed arrows (↷)



## 4.7 Calculating Energy Changes

$$\Delta H = (\text{bond energies of bonds broken}) - (\text{bond energies of bonds formed})$$

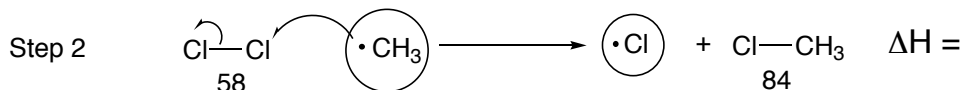
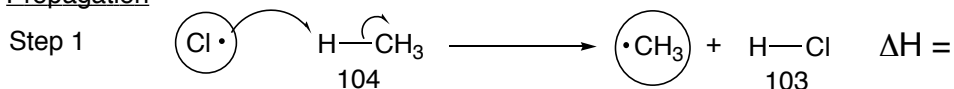


Q1: What is  $\Delta H$ :

Q2: Is the overall reaction energetically favorable?

Notes:

- Compare the energies of the bonds broken versus the bonds made
- For an energetically **favorable** process, **weaker bonds are replaced by stronger bonds**
- With known bond energies, you can quantitatively calculate  $\Delta H$
- Even without bond energy numbers, a qualitative sense of bond strengths enables evaluation of whether or not a reaction makes sense energetically
- This type of analysis can be applied both to overall reactions, but also for individual steps in a multi-step reaction.

Propagation

Q1: Which step is better?

Q2: Which step is likely to be the rate-limiting step?

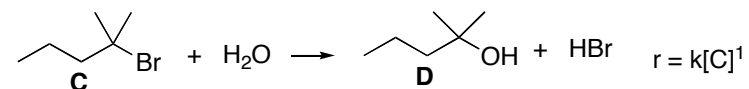
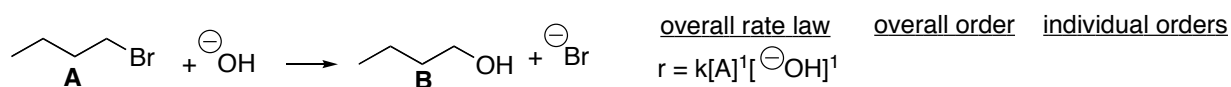
Q3: Note: Can you see what initiation would cost, and why a good chunk of energy is required to make it happen?

## 4.8 Kinetics, Reaction Rates, and Rate Laws

- Lots of reactions with seemingly favorable  $\Delta H$  energetics don't happen very fast or at all
- We're often really interested in reaction speed ("kinetics"). Not so simple!
- Rate Law: relationship between reactant concentrations and overall rate

General:  $\text{rate} = k[\text{A}]^x[\text{B}]^y$

- $k$  is rate constant: each reaction has its own unique rate constant.
- We will often be able to make qualitative predictions based on structural factors
- "x" and "y" are the "orders" of reactants A and B
- the "overall order" of a reaction =  $x + y$



- Different rate laws reflect different mechanisms
- Reactants that do not appear in a rate law do not appear in the mechanism until after the rate determining step
- The "k" values for the two reactions are **not** the same.
- Concentrations matter, for reactants that appear in the rate law
- Concentrations reflect not only how many moles of reactant are available, but also the amount of solvent.

Q1: If you use the same number of moles of reactants in reaction one, but you triple the volume of solvent, how will the rate change?

Q2: If you triple the volume of solvent for reaction two, again without changing the number of moles of reactants, how will its rate change?

#### 4.9 Activation Energies and Dependence of Rates on Temp

- So, if every reaction has it's own k value, what influences the “k” value?
- Arrhenius Equation:  $k = Ae^{-E_a/RT}$ 
  - A is a constant
  - $E_a$  or  $E_{act}$  is the “activation energy”
  - R is the ideal gas constant
  - T is the temperature
- Math: larger  $E_{act}/RT \rightarrow$  smaller k (and slower reaction)
- Math: smaller  $E_{act}/RT \rightarrow$  larger k (and faster reaction)

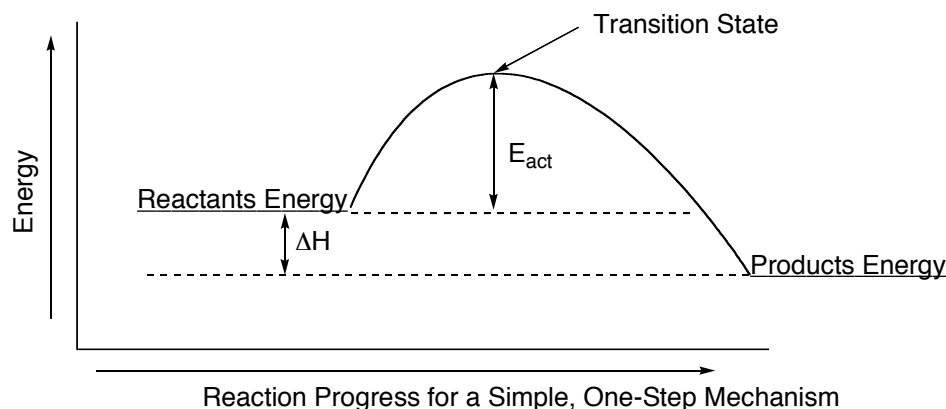
#### Practical Stuff

##### Temperature:

- Higher temp  $\rightarrow$  higher k  $\rightarrow$  faster reaction
- Lower temp  $\rightarrow$  smaller k  $\rightarrow$  slower reaction
- Crude guide: for every  $10^\circ$  rise in temp, the k value and reaction rate will double for an ordinary reaction. (This is super, super, super crude, though...)

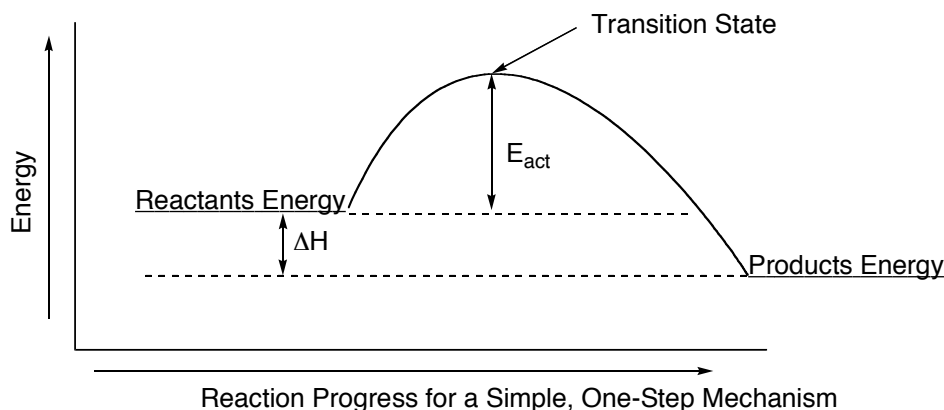
##### Activation Energy: the minimum energy needed for a reaction

- It's the minimum energy required to cross the energy barrier between reactants and products
- The height of the barrier influences reaction speed.
- Activation barriers explain why many exothermic, energy-favorable reactions don't actually occur at room temperature
- Temperature reflects the average kinetic energy of the molecules; but some are always above average.
- **An increase in temperature can strongly increase the reaction rate because a small temperature increase can substantially increase the population of molecules with  $E_{act}$  (see Figure 4.2 on p. 140 for a nice picture of this).**

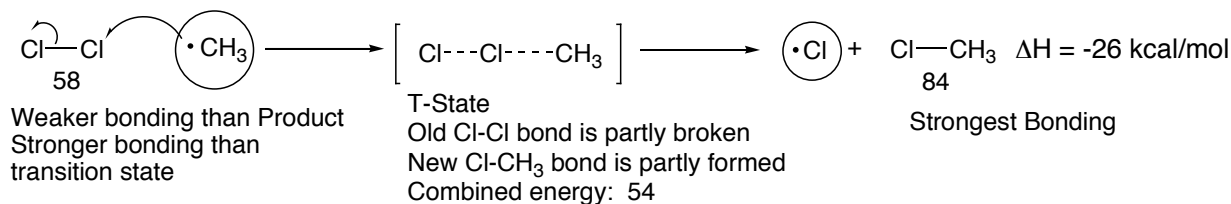




## 4.10 Transition States



- The transition state is the **highest, worst energy spot** on the road from reactants to products
- The height of the transition state dictates the magnitude of the activation barrier ( $E_{act}$ ). Thus the T-state has a huge impact on reaction rates.
- Why are T-states so much higher in energy than most products or reactants? And why do reaction with very favorable  $\Delta H$  often have fairly high T-states?
  - Because one full bond is better than two partial bonds. At the T-state, you are routinely at the transition between a breaking bond and a forming bond.



**Since rates are affected by  $E_{act}$ , and  $E_{act}$ 's are determined by Transition States,  $\rightarrow$  Transition states influence reactions rates.**

- Lower transition state  $\rightarrow$  faster reaction
- Higher transition state  $\rightarrow$  slower reaction

**Transition-State Stability/Reactivity Principle:** The more stable the transition state, the faster the reaction will be.

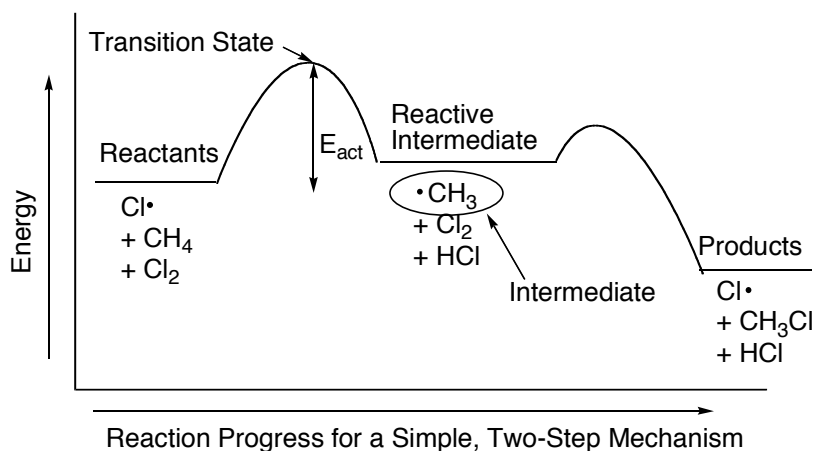
**Reactant Stability/Reactivity Principle:** The more stable the reactant, the slower it will react.

- A more stable reactant has lower starting energy. Therefore it has a larger  $E_{act}$  to get over the transition state.
- A less stable reactant has a higher starting energy, is closer to the T-state, and thus has a smaller energy barrier to cross.

**Product Stability/Reactivity Principle:** The more stable the product, the faster the reaction.

- A more stable product has lower energy. Often the T-state is stabilized/lowered by the same factors that may stabilize the products.

## 4.11 Rates of Multistep Reactions



- Most reactions involve 2 or more steps with one or more “intermediates” ( $\bullet\text{CH}_3$  is the key intermediate in the reaction above)
- An “**intermediate**” is something that forms temporarily, but then rapidly converts into something else. Normally the intermediate is highly reactive and has a very short lifetime. A significant population of intermediate never accumulates.
- The **transition state** for the overall reaction is still the **highest, worst energy spot** on the road from reactants to products
- There is only one transition state for the overall process, no matter how many steps
- The step that goes through the transition state will be the **slowest step** and is often referred to as **the rate-determining step** or the **slow step**.

**Practical: To handle rates, identify and only think about the slowest step!!!**

**Practical: The rate determining step will **always** be the step leading to the worst, least stable intermediate. ( $\bullet\text{CH}_3 < \bullet\text{Cl}$ )**

- Therefore the ability to recognize stability patterns for reactive intermediate radicals, cations, and anions is super useful

**Product Stability/Reactivity Principle:** The more stable the product, the faster the reaction.

- In multistep reactions, **the product that matters kinetically is the product of the rate-determining step. Which is often a reactive intermediate.**
- In order to apply the product stability/reactivity principle in multistep reactions, you’ll need to:
  - Know the mechanism. (What is the rate determining step? And what kind of reactive intermediate is produced in that rate-determining step?)
  - Know how structural factors impact the relative stabilities of reactive intermediates. (For example, is a  $3^\circ$  radical better or worse than a  $1^\circ$  radical?)

**Reactant Stability/Reactivity Principle:** If a reactive intermediate is a reactant in a rate-determining step (rare, but this chapter), knowing stability patterns will help predict speeds.

## 4.12 Dependence of Halogenation Rates on Halogen

General reaction:  $\text{CH}_4 + \text{X}_2 \rightarrow \text{CH}_3\text{X} + \text{HX}$

Rate determining step:  $\text{CH}_4 + \cdot\text{X} \rightarrow \cdot\text{CH}_3 + \text{HX}$

<u>Halogen</u>	<u>Rate Determining Step</u>	$E_{\text{act}}$ (kcal/mol)	$\cdot\text{X}$ <u>Stability</u>	$\cdot\text{X}$ <u>Reactivity</u>
$\text{F}_2$	$\text{CH}_4 + \cdot\text{F} \rightarrow \cdot\text{CH}_3 + \text{HF}$	1		
$\text{Cl}_2$	$\text{CH}_4 + \cdot\text{Cl} \rightarrow \cdot\text{CH}_3 + \text{HCl}$	4		
$\text{Br}_2$	$\text{CH}_4 + \cdot\text{Br} \rightarrow \cdot\text{CH}_3 + \text{HBr}$	18		
$\text{I}_2$	$\text{CH}_4 + \cdot\text{I} \rightarrow \cdot\text{CH}_3 + \text{HI}$	34		

- Iodine is not reactive enough; fluorine is actually too dangerous to use

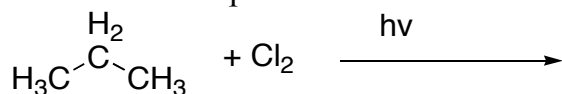
**Reactant Stability/Reactivity Principle:** The more stable the reactant, the slower it will react.

- The halogen radicals are reactants in the rate determining step.

## 4.13,14 Selective Halogenations of Higher Alkanes (Higher than Methane)

This is where most of the real problems will come from

## A. Chlorination of Propane

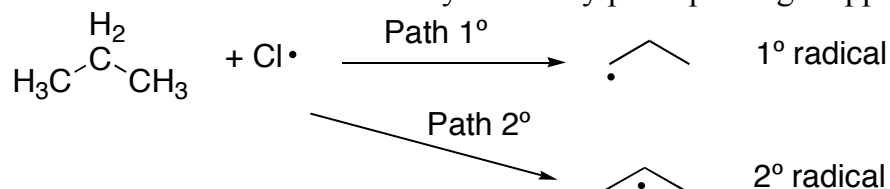


Notes

Reactivity ratio:

Why are 2° C-H's more reactive than 1° C-H's?

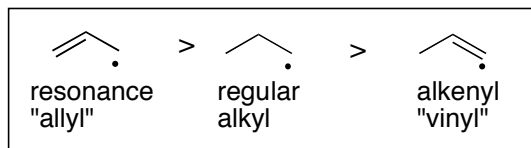
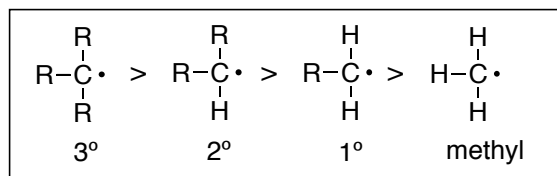
- Think rate determining step
- Think whether some stability/reactivity principle might apply



Path 2° is faster than path 1° because path 2° produces a more stable radical product. The path 2° transition-state is stabilized as a result. Product stability/reactivity principle.

B. Free Radical Stability Pattern:  $3^\circ > 2^\circ > 1^\circ > \text{methyl}$

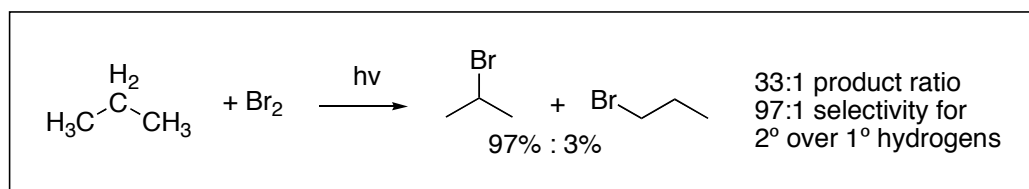
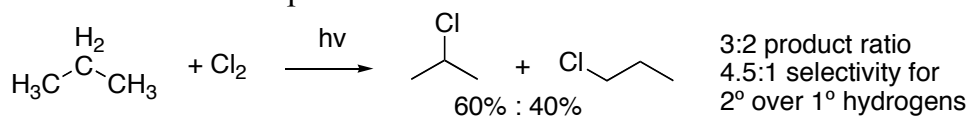
Memorize!



Resonance helps a lot (“**Allylic**”)  
 Being on an alkene is bad (“**Vinyl**”)

Bond Energy	87	91	95	98	104	111
Class	Allylic	3°	2°	1°	Methyl	vinyl

### C. Bromination of Propane



### Notes

Bromine is **way** more selective than chlorine

Practical: to do a selective halogenation, use bromine rather than chlorine

Just as 2° > 1°, so allylic > 3° > 2° > 1° > methyl > vinyl

### D. Why bromination is so much more selective than chlorination:

**Reactant Stability/Reactivity/Selectivity Principle:** Often a reaction can proceed to give either of two products, of unequal stability. The pathway leading to the more stable product will be preferred. However, the selectivity between formation of the more stable and less stable product will vary depending on the stability of the reactant. The more stable the reactant, the less reactive it will be and the more selective it will be. (The concept here is that a more stable reactant is less desperate to react, and is more choosy, better able to select the best possible pathway without using a less favorable pathway that would result in a less stable product. A more sophisticated picture is that a more stable reactant will have larger activation barriers to cross; it has a hard enough time crossing even the lowest transition state leading to the best possible product, and is much less likely to have the surplus energy required to cross the high transition state leading to the less stable product.)

### Application to the Propane Halogenation Situation:

- Br• is more stable than Cl•,

- Therefore  $\text{Br}\cdot$  is more selective and choosy to make the better  $2^\circ$  radical (leading to 2-bromopropane) rather than the less stable  $1^\circ$  radical (leading to 1-bromopropane).
- $\text{Cl}\cdot$  is less stable, and really wants to react. So it doesn't wait around for a weak  $2^\circ$  hydrogen; it often settles for a stronger  $1^\circ$  hydrogen even though it gives an inferior  $1^\circ$  radical product (in the rate determining step)
- “Beggars can't be choosers”: the less stable, more reactive  $\text{Cl}\cdot$  is the “beggar” than can't be as choosy as the more stable, less reactive  $\text{Br}\cdot$

<ul style="list-style-type: none"> <li>• Endothermic</li> <li>• Late transition states</li> <li>• T-states resemble product(s)</li> <li>• The energy gap between alternate T-states is almost as large as the energy gap between alternate products.</li> <li>• The strong energy difference between the two T-states results in high selectivity</li> </ul>	<ul style="list-style-type: none"> <li>• Exothermic</li> <li>• Early transition states</li> <li>• T-states resemble reactant</li> <li>• The energy gap between alternate T-states isn't nearly as large as the energy gap between alternate products.</li> <li>• The limited energy difference between the two T-states results in limited selectivity</li> </ul>

#### E. Hammond Postulate:

- For an exothermic step, the T-state is “early” and much resembles reactants
- For an endothermic step, the T-state is “late” and much resembles products

#### Who Cares?

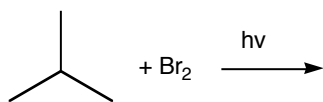
- Transition-states are important! The Hammond postulate helps us to understand what the structure of the transition state is like.
- For most multi-step reactions, the transition-states are late and product-like.
- **For late, product-like transition states, assume that any structural factor that stabilizes the product (of the rate-determining step) will also stabilize the transition state and increase the reaction rate. (This is the basis of the product stability/reactivity principle.)**
- KEY: Remember that you must always be thinking about the products of the rate-determining step, which will routinely be a reactive intermediate that does not appear as a product in the balanced reaction.

## Alkane Brominations:

Skills:

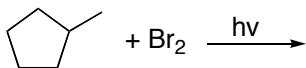
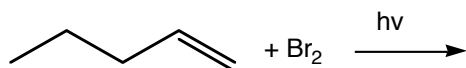
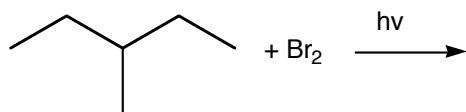
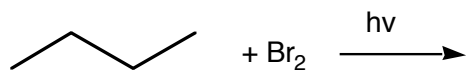
1. Identify all possible monosubstituted products
2. Identify the Major Product
  - Consider all possible radicals. The carbon that gives the most stable radical will be the carbon that gets brominated preferentially.
  - This is true because the rate determining step is the step in which a hydrogen is abstracted and a carbon radical is formed.
  - Thus, according to the product stability/reactivity principle, the pathway leading via the best carbon radical is the preferred path.
3. Write the mechanism for chain propagation (with detailed arrows)

1. Do all three things for:



Mechanism

2. Identify the Major Product for each of the following:



## 4.16 Reactive Intermediates: Stability Patterns

- Shortlived, unstable, highly reactive intermediates
- Normally lack normal bonding

These are tremendously important:

1. They will be the **least stable intermediate** in any multistep mechanism
2. When formed, they are **products of the rate-determining step**
3. **Factors that stabilize them will speed up reaction rates**

**Thus it is very important to know their stability patterns!**

Class	Structure	Stability Pattern		
Carbocations	$\begin{array}{c}   \\ -\text{C}^{\oplus} \\   \end{array}$	Allylic > 3° > 2° > 1° > methyl > alkenyl (vinyl, aryl)	Electron Poor	Electrophilic/Acidic
Carbon Radicals	$\begin{array}{c}   \\ -\text{C}^{\cdot} \\   \end{array}$	Allylic > 3° > 2° > 1° > methyl > alkenyl (vinyl, aryl)	Electron Poor	Electrophilic/Acidic
Carbanions	$\begin{array}{c}   \\ -\text{C}^{\ominus} \\   \end{array}$	Allylic > alkenyl (vinyl, aryl) > methyl > 1° > 2° > 3°	Electron Rich	Nucleophilic/Basic

Notes

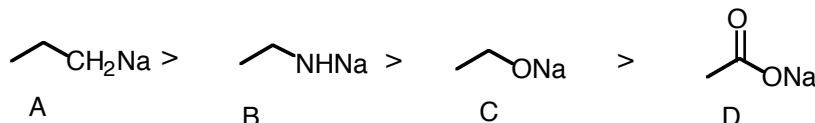
1. Both carbocations and radicals have the same pattern. So you don't need to memorize them twice!
2. Carbanions are almost exactly the reverse, except that being allylic is ideal for both.
3. All benefit from resonance (allylic).
4. Cations and radicals both fall short of octet rule. As a result, they are both electron deficient. Carbanions, by contrast, are electron rich.
5. Alkyl substituents are electron donors. As a result, they are good for electron deficient cations and radicals (3° > 2° > 1° > methyl) but bad for carbanions.
6. Alkenyl (vinyl or aryl) carbons are inherently a bit electron poor. This is excellent for carbanions, but terrible for cations or radicals.

## Stability/Reactivity/Selectivity Principles

1. **Reactant Stability/Reactivity:** The more stable the reactant, the less reactive it will be. In terms of rates, this means that the more stable the reactant, the slower it will react. (The concept here is that the more stable the reactant, the more content it is to stay as is, and the less motivated it is to react and change into something different)

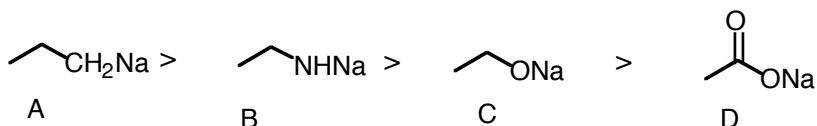
**Key note:** Often the “reactant” that’s relevant in this context will not be the original reactant of the reaction, but will be the “reactant” involved in the rate determining step.

- **Basicity**



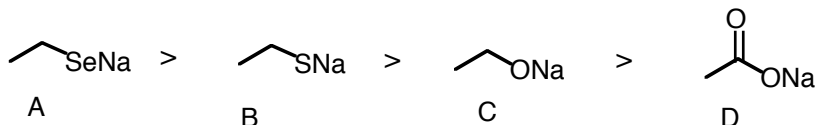
Why: As anion stability increases from A to D, the reactivity decreases

- **Nucleophilicity**



Why: As anion stability increases from A to D, the reactivity decreases

- **Nucleophilicity**



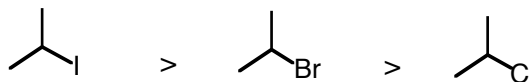
Why: As anion stability increases from A to D, the reactivity decreases

- **Reactivity toward alkanes via radical halogenation**



Why: Chlorine is more reactive than bromine because chlorine radical is less stable than bromine radical.

- **Electrophilicity (Reactivity in S<sub>N</sub>2, S<sub>N</sub>1, E2, E1 Reactions)**



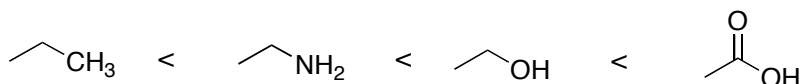
Why: As carbon-halogen bond stability increases, the reactivity decreases



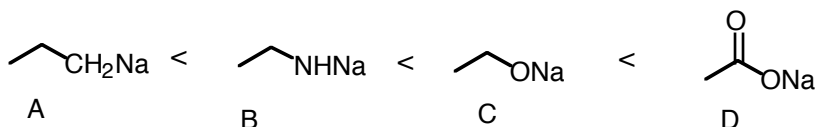
2. **Product Stability/Reactivity:** The more stable the product, the more favorable its formation will be. In terms of rates, this means that the more stable the product, the faster the reaction. (The concept here is that the more stable the product, the more favorable it will be to make that product.)

**Key note:** Often the “product” that’s relevant in this context will not be the final product of the reaction, but will be the “product” of the rate determining step.

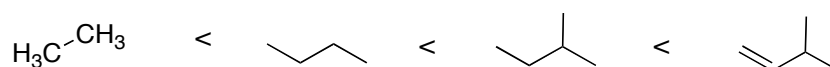
- Acidity



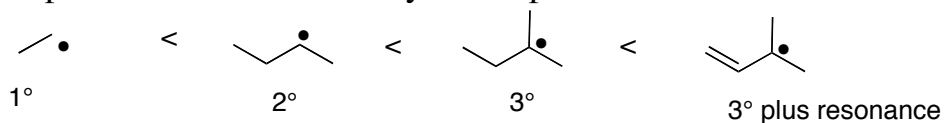
Why: Because as the stability of the anion products increases from A to D, the reactivity of the parent acids increase



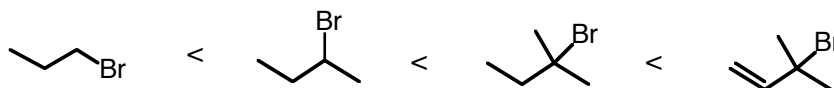
- Reactivity of alkanes toward radical halogenation



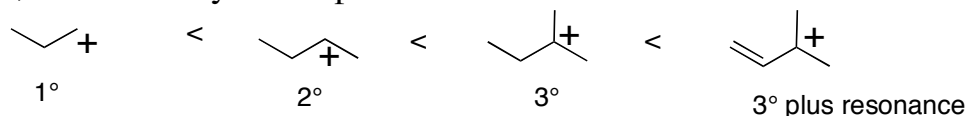
Why: Because as the stability of the radical produced during the rate-determining-step increases, the reactivity of the parent alkane increases



- S<sub>N</sub>1, E1 Reactivity

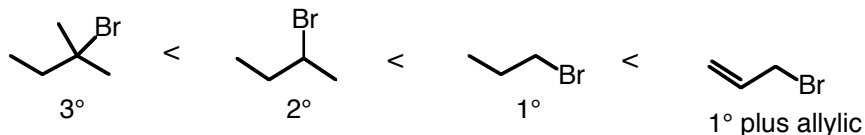


Why: Because as the stability of the cation produced in the rate-determining step increases, the reactivity of the parent halide increases as well



3. **Transition-State Stability/Reactivity:** The more stable the transition state, the faster the reaction will be. (The concept here is that the lower the transition state, the more easily it will be crossed.)

- **S<sub>N</sub>2 Reactivity**

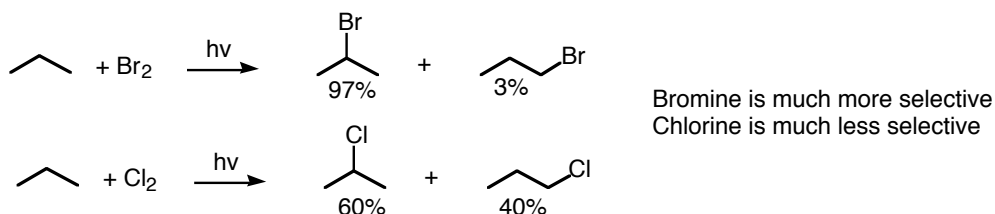


Why: The pattern reflects the relative stability of the transition states. In the case of 3° versus 2° versus 1°, the issue is steric congestion in the transition state. The transition states for the more highly substituted halides are destabilized. In the case of allylic halides, the transition state is stabilized for orbital reasons, not steric reasons.

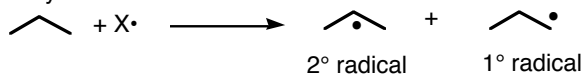
4. **Reactant Stability/Reactivity/Selectivity:** Often a reaction can proceed to give either of two products, of unequal stability. The pathway leading to the more stable product will be preferred. However, the selectivity between formation of the more stable and less stable product will vary depending on the stability of the reactant. The more stable the reactant, the less reactive it will be and the more selective it will be. (The concept here is that a more stable reactant is less desperate to react, and is more choosy, better able to select the best possible pathway without using a less favorable pathway that would result in a less stable product. A more sophisticated picture is that a more stable reactant will have larger activation barriers to cross; it has a hard enough time crossing even the lowest transition state leading to the best possible product, and is much less likely to have the surplus energy required to cross the high transition state leading to the less stable product.)

**Key note:** The “reactant” and “products” involved are those for the rate-determining step.

- **Selectivity in the reaction of bromine versus chlorine with alkanes via radical halogenation**



Why?



Formation of the secondary radical is more favorable than formation of the primary radical, in the rate determining step. Bromine radical, being less reactive, is more selective for the 2° radical. Cl•, being less stable and more reactive, is less choosy and less selective.