

How to estimate relative acid strengths



How do you  
predict anion  
stability?

Compare the relative stabilities of the anions produced upon deprotonation → the more stable anion comes from the stronger acid

2 important principles for predicting anion stability

- 1) Negative charge ( $\ominus$ ) is neutralized by nuclear  $\oplus$  charge.
- 2) Delocalizing negative charge ( $\ominus$ ) over a larger area is better. → Golden Rule #5

## Rules for anion stability -

The anion is more stable when the negative charge ( $\ominus$ ) is:

a) On a more electronegative element (Principle 1)  
→ Periodic Table (across a single row)

b) On a larger atom (Principle 2)  
↓ Periodic Table (down a single column)

c) On an atom with more "s" character to its hybridization  
( $sp > sp^2 > sp^3$ )  
← anion stability

"s" orbitals are closer to the nucleus (Principle 1)

d) stabilized by resonance delocalization.  
(Principle 2)

e) Stabilized by the inductive effect  
(Principles 1 and 2)

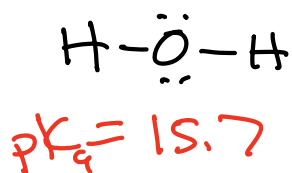
Operates  
through sigma  
bonds

nearby electronegative atoms attract  $\ominus$  charge and therefore spread the  $\ominus$  charge onto more atoms

# Examples

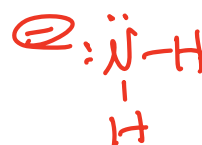
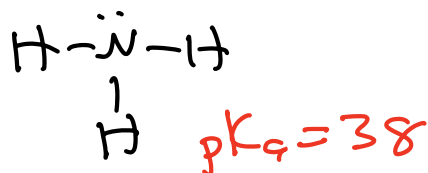
Rule a)

Ex.



more stable  
anion

O is more electronegative



Rule b)



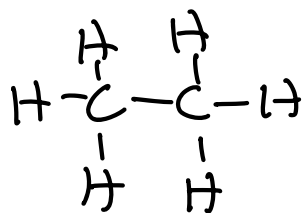
(Only compare atoms  
in same column of  
the Periodic Table)

|               |                    |                     |                     |                    |
|---------------|--------------------|---------------------|---------------------|--------------------|
| $\text{pK}_a$ | 3.5                | -7                  | -8                  | -9                 |
|               | H-F                | H-Cl                | H-Br                | H-I                |
|               | $\text{F}^\ominus$ | $\text{Cl}^\ominus$ | $\text{Br}^\ominus$ | $\text{I}^\ominus$ |

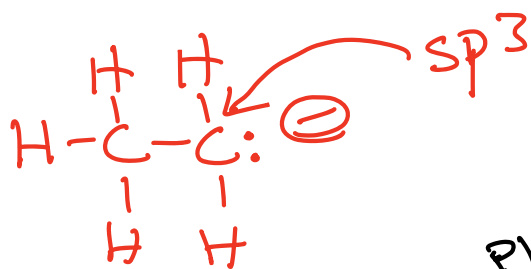
larger ion

acid strength

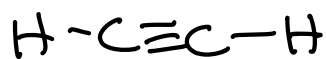
Rule c)



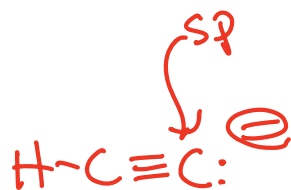
$$\text{p}K_{\text{a}} \cong 50$$



$$\text{sp}^3 \rightarrow 25\% \text{ s} \\ 75\% \text{ p}$$



$$\text{p}K_{\text{a}} = 25$$



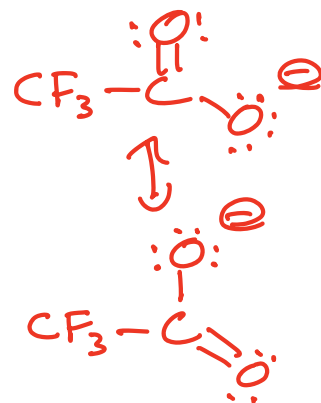
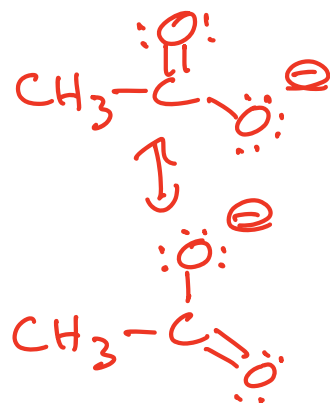
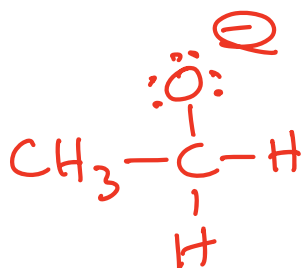
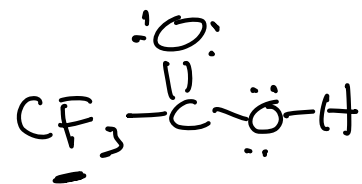
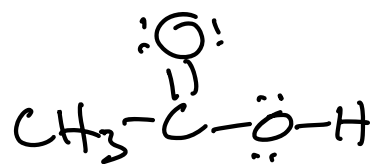
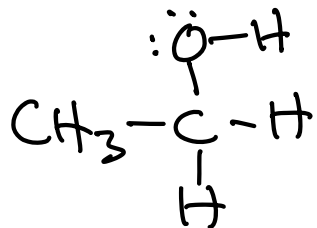
Places more  
 $\ominus$  closer  
to nucleus

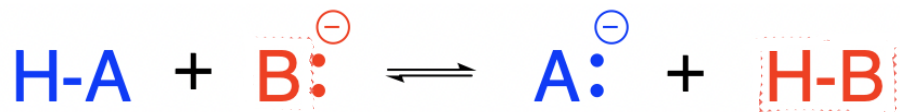
More "s"  $\rightarrow$

$$\text{sp} \rightarrow 50\% \text{ s} \\ 50\% \text{ p}$$

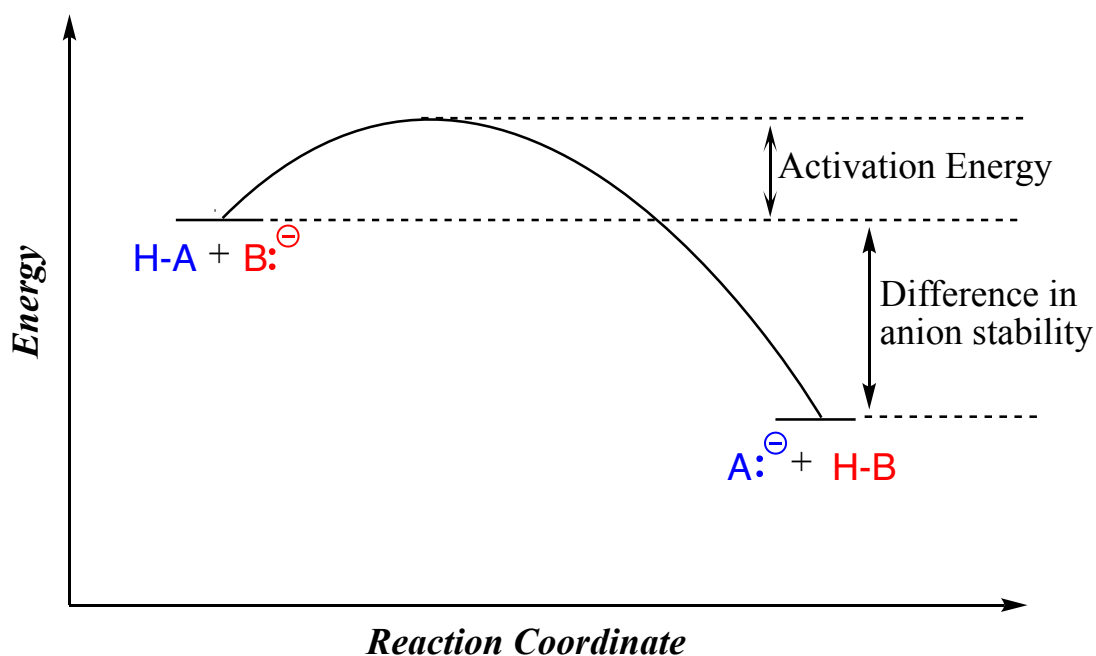
max stable anion

Reaks d) and e)



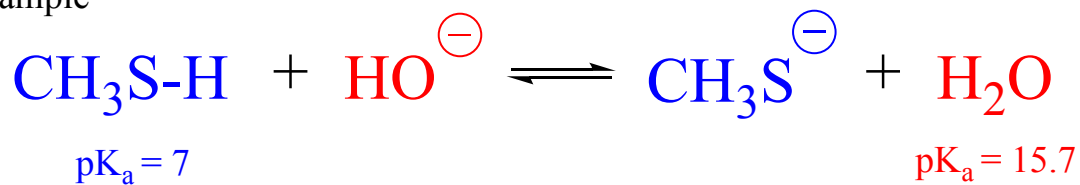


Assume  $\text{A:}^{\ominus}$  is more stable than  $\text{B:}^{\ominus}$



$$K_{\text{eq}} = 10^{(\text{pK}_{\text{a}} \text{H-B} - \text{pK}_{\text{a}} \text{H-A})}$$

Example



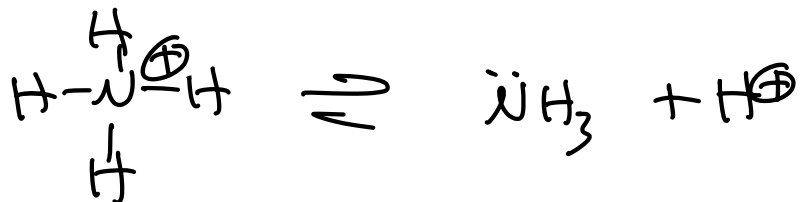
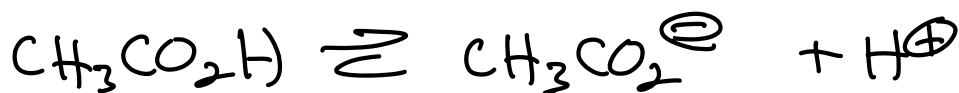
$$K_{\text{eq}} = 10^{(\quad - \quad)} = 10^{(\quad)}$$

New idea: How do  $pK_a$  and pH work together to determine predominant protonation states of acids?

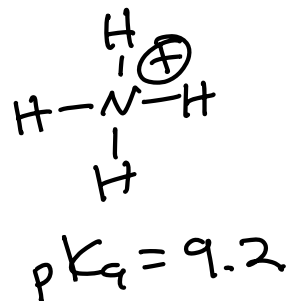
An acid is mostly \_\_\_\_\_ at a  
pH that is \_\_\_\_\_ its  $pK_a$

An acid is mostly \_\_\_\_\_ at a  
pH that is \_\_\_\_\_ its  $pK_a$

Examples:



Parent Acid  $\rightarrow$   $\text{CH}_3\text{CO}_2\text{H}$   
 $pK_a = 4.8$



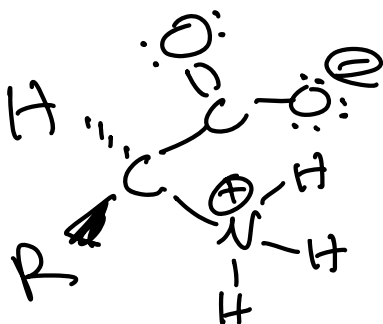
Forms Present  
at pH = 2.0

Forms Present  
at pH = 7.0

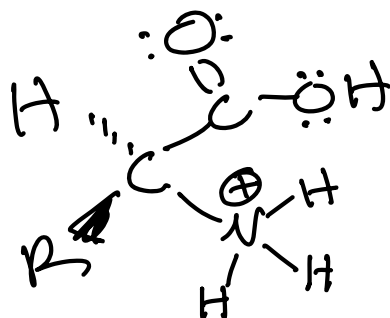
Forms Present  
at pH = 12.0

Application to important molecules  $\rightarrow$  amino acids  $\rightarrow$  same two groups we just saw

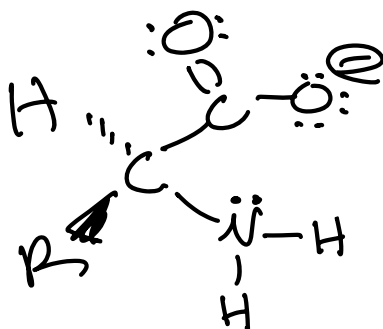
Form present  
at pH =



Form present  
at pH =



Form present  
at pH =



$\Rightarrow$  The and  
forms are NEVER both present  
at any pH  $\rightarrow$  Not possible!!

Why doesn't anyone get this right?



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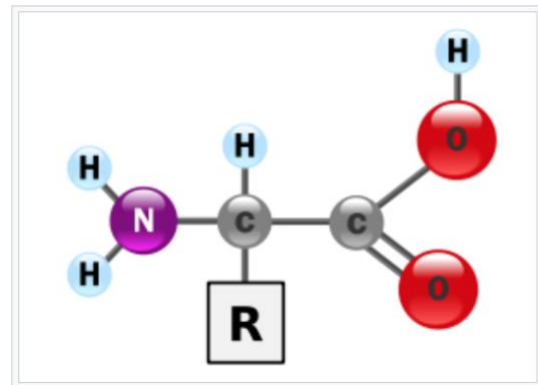
## Amino acid



From Wikipedia, the free encyclopedia

*This article is about the class of chemicals. For the structures and properties of the standard proteinogenic amino acids, see [Proteinogenic amino acid](#).*

**Amino acids** are [organic compounds](#) containing [amine](#) (-NH<sub>2</sub>) and [carboxyl](#) (-COOH) functional groups, along with a [side chain](#) (R group) specific to each amino acid.<sup>[1][2][3]</sup> The key [elements](#) of an amino acid are [carbon](#) (C), [hydrogen](#) (H), [oxygen](#) (O), and [nitrogen](#) (N), although other elements are



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Amino acid structure

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6.2.2 (a) Reactions of Amino Acids - ...

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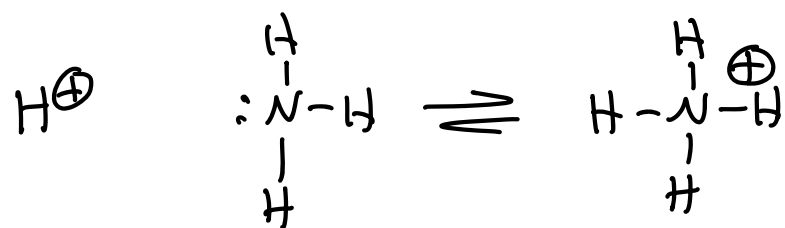
Image result for amino acid

[Visit](#) [Save](#) [View saved](#) [Share](#)

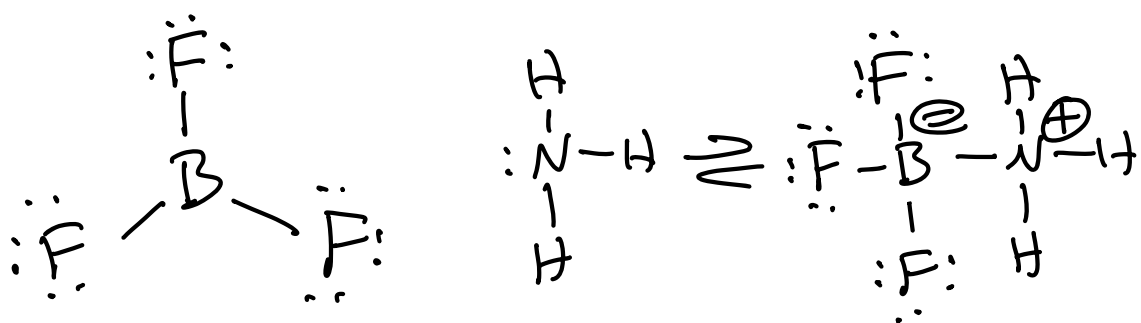
Related images:

Lewis Acid  $\rightarrow$

Lewis Base  $\rightarrow$

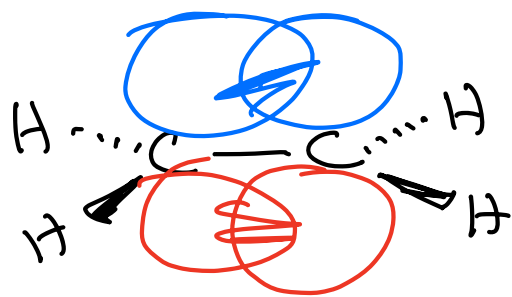


$\text{H}^{\oplus}$  can be thought of as a Lewis acid,  
but so can other species  $\rightarrow$  atoms with an  
incomplete valence shell  $\Rightarrow \text{B, Al, Zn, Fe}$





## Electronic Structure of Alkenes



$\pi$  bond  $\rightarrow$   
overlap of  
2p orbitals

## Consequences of $\pi$ bonds

- 1)  $\pi$  bonds cannot rotate
- 2) Electron density is

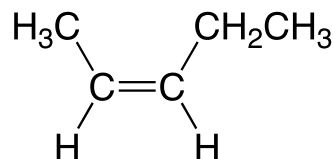
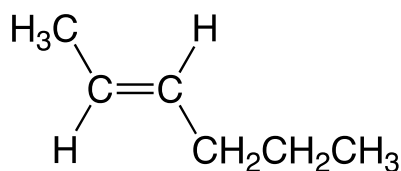
## Naming Alkenes

### General Directions:

1. Locate longest continuous chain.
2. Number the chain so the double bond gets the lowest possible number.
3. For the parent chain name, use “-ene” not “-ane” as suffix and place a number to indicate the location of the double bond before the main chain name.
4. Make the suffix “-adiene” , “-atriene”, etc. if multiple double bonds are present.

**cis/trans nomenclature** – older chemical nomenclature, but still used commonly in biochemistry – most useful when each  $sp^2$  atom of the double bond has an H atom.

1. Track the longest chain through the double bond
  - a. **cis** if whole main chain is on the same side of the double bond.
  - b. **trans** if chain emerges on opposite sides of the double bond.



## Naming Alkenes

General Directions:

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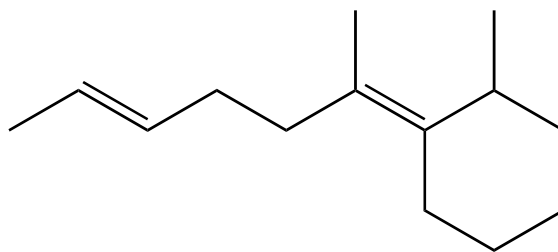
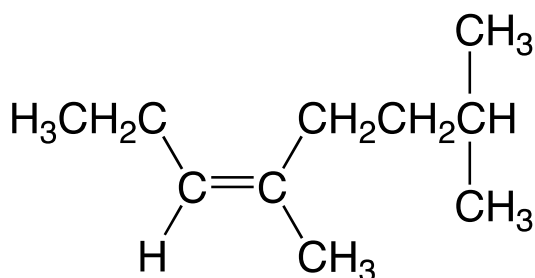
**E,Z nomenclature** - A general IUPAC nomenclature to names alkenes.



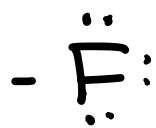
**Z** (zusammen) = same side, same side, same side

**E** (entgegen) = opposite side

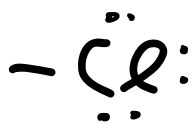
5. On each carbon of the double bond rank the two groups according to the Cahn, Ingold, Prelog priority rules (*R* vs. *S* rules).
6. If both of the highest-ranking groups are on the same side of the double bond it is **Z**.
7. If both of the highest-ranking groups are on opposite sides of the double bond it is **E**.



# Today's Special Bonus Feature: Halogen Nomenclature



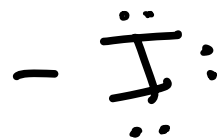
fluoro-



chloro-



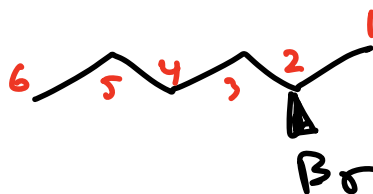
bromo-



iodo-



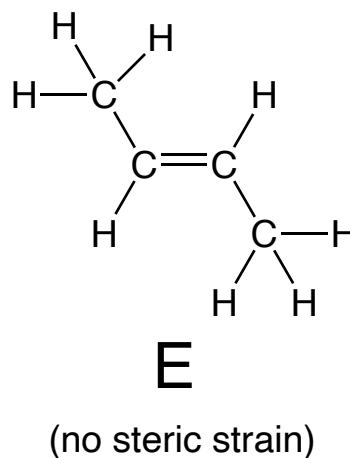
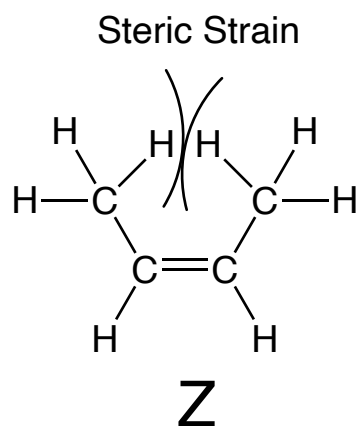
fluoromethyl  
group



(R)-2-bromohexane

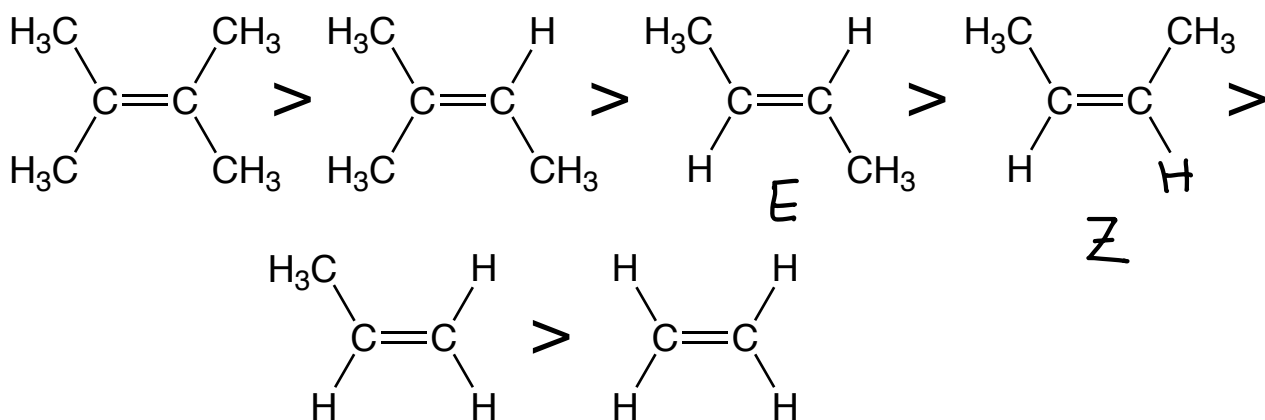
# Special Alkene Bonus: Important material you will need to know!

Alkene stability part 1: Z (cis) groups larger than H atoms will crunch into each other causing steric strain.



Alkene stability part 2: For reasons we are not able to tell you, more substituted alkenes have more stable (stronger) pi bonds than alkenes with more H atoms on their  $sp^2$ -hybridized C atoms (despite there being steric strain present in the most substituted alkenes).

## Strongest Pi Bond

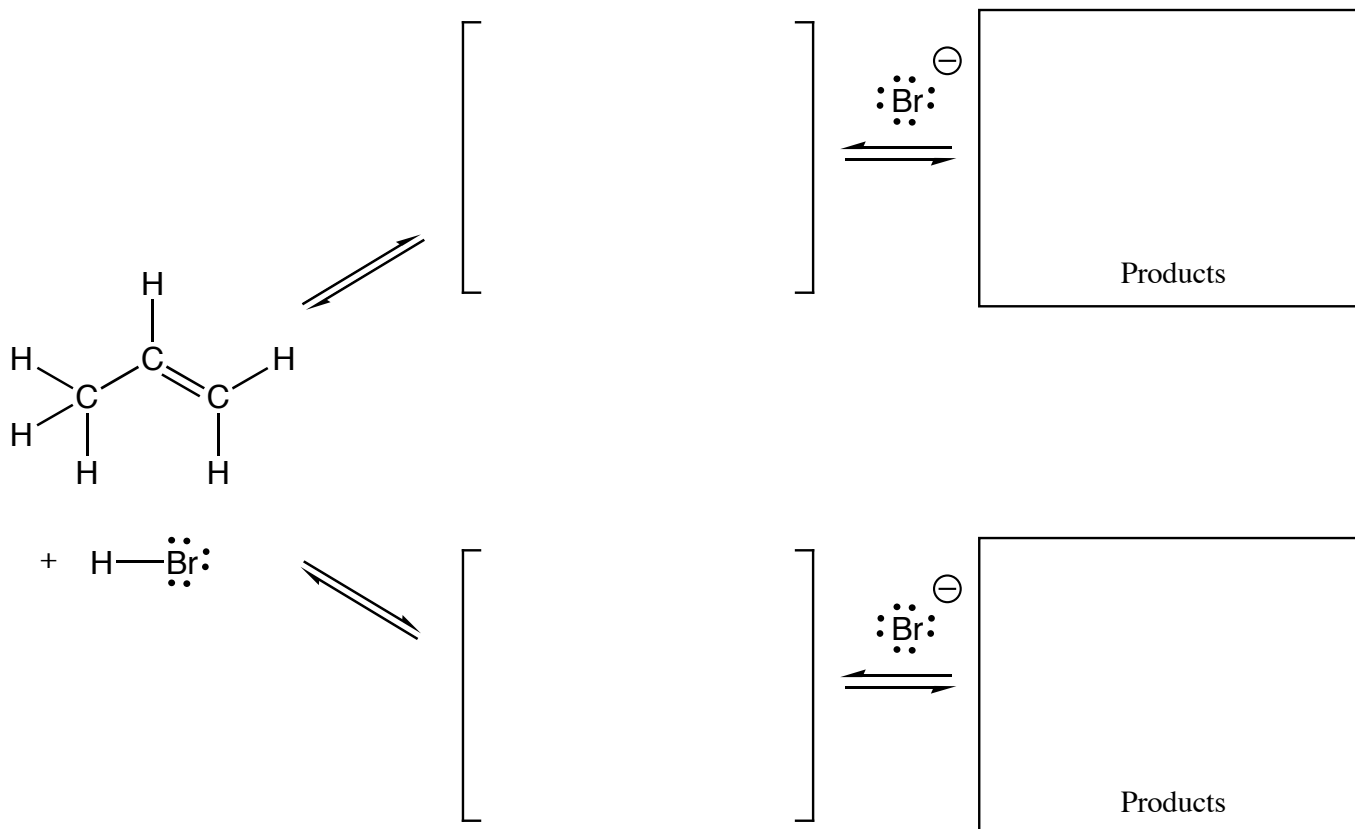


**Weakest Pi Bond**



***Time Capsule:  
Zaitsev's rule follows  
this trend!!***

## Addition of H-X to an Alkene

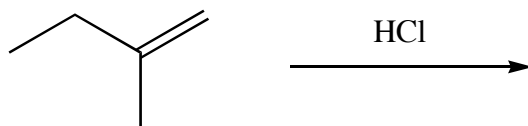


Summary:

Regiochemistry:

Stereochemistry:

Example:



For a reaction to take place, you need both:

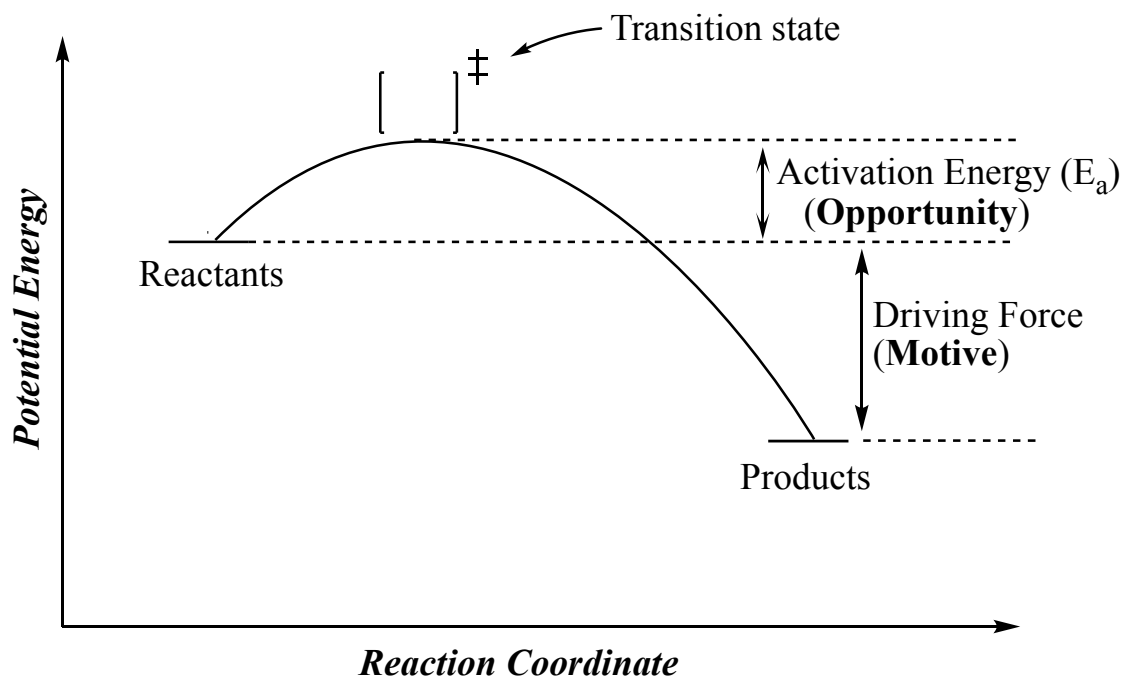
Motive  $\rightarrow$  thermodynamic driving force

1) Make stronger bonds

2) Formation of a

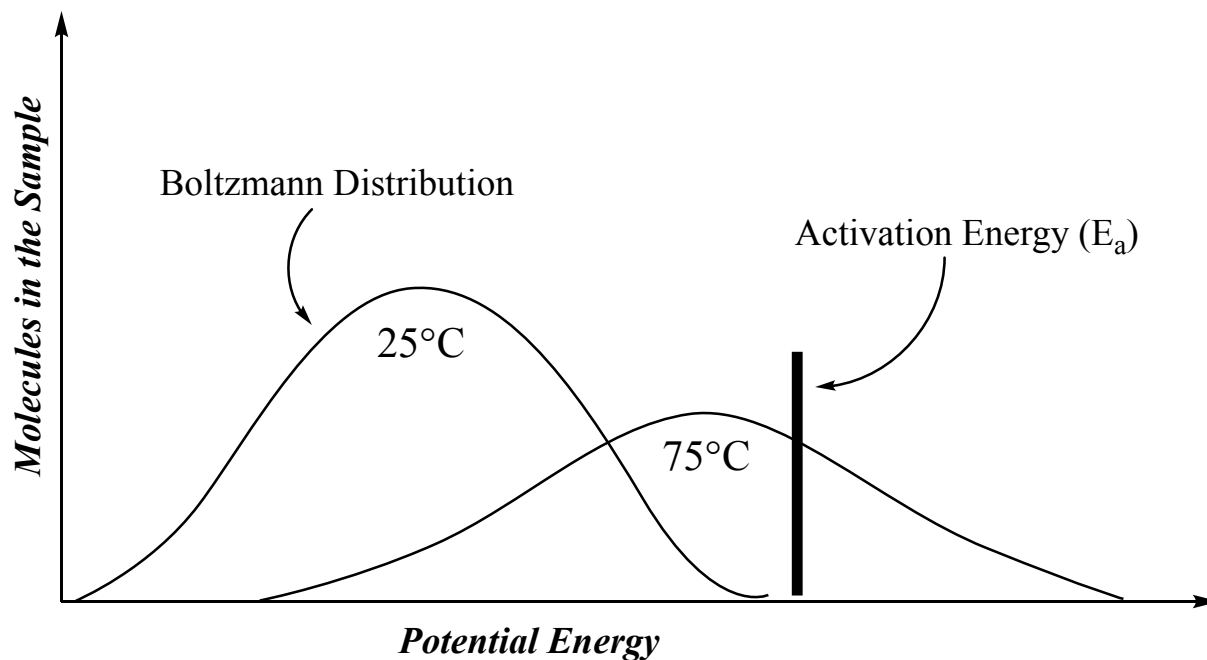
3) Entropy  $\rightarrow$

Opportunity  $\rightarrow$  reasonable mechanism



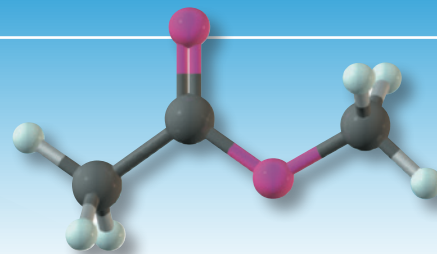
$$k = \text{reaction rate} = Ae^{-E_a/RT}$$

Increasing Temperature  $\rightarrow$



# Appendix 3

## Bond Dissociation Enthalpies



Bond dissociation enthalpy (BDE) is defined as the amount of energy required to break a bond homolytically into two radicals in the gas phase at 25°C.



| Bond                                                                 | $\Delta H^0$ | Bond                                              | $\Delta H^0$ | Bond                                              | $\Delta H^0$ |
|----------------------------------------------------------------------|--------------|---------------------------------------------------|--------------|---------------------------------------------------|--------------|
| <b>H—H bonds</b>                                                     |              | <b>C—C multiple bonds</b>                         |              | <b>C—Br bonds</b>                                 |              |
| H—H                                                                  | 435 (104)    | CH <sub>2</sub> =CH <sub>2</sub>                  | 727 (174)    | CH <sub>3</sub> —Br                               | 301 (72)     |
| D—D                                                                  | 444 (106)    | HC≡CH                                             | 966 (231)    | C <sub>2</sub> H <sub>5</sub> —Br                 | 301 (72)     |
|                                                                      |              |                                                   |              | (CH <sub>3</sub> ) <sub>2</sub> CH—Br             | 309 (74)     |
| <b>X—X bonds</b>                                                     |              | <b>C—H bonds</b>                                  |              | (CH <sub>3</sub> ) <sub>3</sub> C—Br              | 305 (73)     |
| F—F                                                                  | 159 (38)     | CH <sub>3</sub> —H                                | 439 (105)    | CH <sub>2</sub> =CHCH <sub>2</sub> —Br            | 247 (59)     |
| Cl—Cl                                                                | 247 (59)     | C <sub>2</sub> H <sub>5</sub> —H                  | 422 (101)    | C <sub>6</sub> H <sub>5</sub> —Br                 | 351 (84)     |
| Br—Br                                                                | 192 (46)     | (CH <sub>3</sub> ) <sub>2</sub> CH—H              | 414 (99)     | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> —Br | 263 (63)     |
| I—I                                                                  | 151 (36)     | (CH <sub>3</sub> ) <sub>3</sub> C—H               | 405 (97)     |                                                   |              |
|                                                                      |              | CH <sub>2</sub> =CH—H                             | 464 (111)    | <b>C—I bonds</b>                                  |              |
| <b>H—X bonds</b>                                                     |              | CH <sub>2</sub> =CHCH <sub>2</sub> —H             | 372 (89)     | CH <sub>3</sub> —I                                | 242 (58)     |
| H—F                                                                  | 568 (136)    | C <sub>6</sub> H <sub>5</sub> —H                  | 472 (113)    | C <sub>2</sub> H <sub>5</sub> —I                  | 238 (57)     |
| H—Cl                                                                 | 431 (103)    | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> —H  | 376 (90)     | (CH <sub>3</sub> ) <sub>2</sub> CH—I              | 238 (57)     |
| H—Br                                                                 | 368 (88)     | HC≡C—H                                            | 556 (133)    | (CH <sub>3</sub> ) <sub>3</sub> C—I               | 234 (56)     |
| H—I                                                                  | 297 (71)     |                                                   |              | CH <sub>2</sub> =CHCH <sub>2</sub> —I             | 192 (46)     |
|                                                                      |              | <b>C—F bonds</b>                                  |              | C <sub>6</sub> H <sub>5</sub> —I                  | 280 (67)     |
| <b>O—H bonds</b>                                                     |              | CH <sub>3</sub> —F                                | 481 (115)    | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> —I  | 213 (51)     |
| HO—H                                                                 | 497 (119)    | C <sub>2</sub> H <sub>5</sub> —F                  | 472 (113)    |                                                   |              |
| CH <sub>3</sub> O—H                                                  | 439 (105)    | (CH <sub>3</sub> ) <sub>2</sub> CH—F              | 464 (111)    | <b>C—N single bonds</b>                           |              |
| C <sub>6</sub> H <sub>5</sub> O—H                                    | 376 (90)     | C <sub>6</sub> H <sub>5</sub> —F                  | 531 (127)    | CH <sub>3</sub> —NH <sub>2</sub>                  | 355 (85)     |
|                                                                      |              |                                                   |              | C <sub>6</sub> H <sub>5</sub> —NH <sub>2</sub>    | 435 (104)    |
| <b>O—O bonds</b>                                                     |              | <b>C—Cl bonds</b>                                 |              |                                                   |              |
| HO—OH                                                                | 213 (51)     | CH <sub>3</sub> —Cl                               | 351 (84)     | <b>C—O single bonds</b>                           |              |
| CH <sub>3</sub> O—OCH <sub>3</sub>                                   | 159 (38)     | C <sub>2</sub> H <sub>5</sub> —Cl                 | 355 (85)     | CH <sub>3</sub> —OH                               | 385 (92)     |
| (CH <sub>3</sub> ) <sub>3</sub> CO—OC(CH <sub>3</sub> ) <sub>3</sub> | 159 (38)     | (CH <sub>3</sub> ) <sub>2</sub> CH—Cl             | 355 (85)     | C <sub>6</sub> H <sub>5</sub> —OH                 | 468 (112)    |
|                                                                      |              | (CH <sub>3</sub> ) <sub>3</sub> C—Cl              | 355 (85)     |                                                   |              |
| <b>C—C single bonds</b>                                              |              | CH <sub>2</sub> =CHCH <sub>2</sub> —Cl            | 288 (69)     |                                                   |              |
| CH <sub>3</sub> —CH <sub>3</sub>                                     | 378 (90)     | C <sub>6</sub> H <sub>5</sub> —Cl                 | 405 (97)     |                                                   |              |
| C <sub>2</sub> H <sub>5</sub> —CH <sub>3</sub>                       | 372 (89)     | C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> —Cl | 309 (74)     |                                                   |              |
| CH <sub>2</sub> =CH—CH <sub>3</sub>                                  | 422 (101)    |                                                   |              |                                                   |              |
| CH <sub>2</sub> =CHCH <sub>2</sub> —CH <sub>3</sub>                  | 322 (77)     |                                                   |              |                                                   |              |
| C <sub>6</sub> H <sub>5</sub> —CH <sub>3</sub>                       | 435 (104)    |                                                   |              |                                                   |              |
| C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> —CH <sub>3</sub>       | 326 (78)     |                                                   |              |                                                   |              |

**Organic Chemistry is the study of carbon-containing molecules.**

**This class has two points.**

***The first point of the class is to understand the organic chemistry of living systems. We will teach you how to think about and understand the most amazing things on the planet!!***

Water is essential for life, you will learn why water has such special properties. 8/24/26

You will learn the secret structural reason proteins, the most important molecular machines in our bodies, can support the chemistry of life. 9/9/26

You will learn why when you take Advil for pain, exactly half of what you take works, and the other half does nothing.

You will learn how toothpaste works. 9/21/26

You will learn how a single chlorofluorocarbon refrigerant molecule released into the atmosphere can destroy many, many ozone molecules, leading to an enlargement of the ozone hole.

You will learn how medicines like Benadryl, Seldane, and Lipitor work.

You will learn how Naloxone is an antidote for an opioid overdose.

You will learn why Magic Johnson is still alive, decades after contracting HIV.

You will learn how MRI scans work.

***The second point of organic chemistry is the synthesis of complex molecules from simpler ones by making and breaking specific bonds.***

You will learn how to understand movies of reaction mechanisms like alkene hydration.

You will learn reactions that once begun, will continue reacting such that each product molecule created starts a new reaction until all the starting material is used up.

You will learn reactions that can make antifreeze from vodka.

You will learn a reaction that can make nail polish remover from rubbing alcohol.

You will learn how to look at a molecule and accurately predict which atoms will react to make new bonds, and which bonds will break during reactions.

You will learn how to analyze a complex molecule's structure so that you can predict ways to make it via multiple reactions starting with less complex starting molecules.

Mechanisms → movement of electrons and atoms in chemical reactions

1) Arrows in reaction mechanisms

2) Arrows in reaction mechanisms

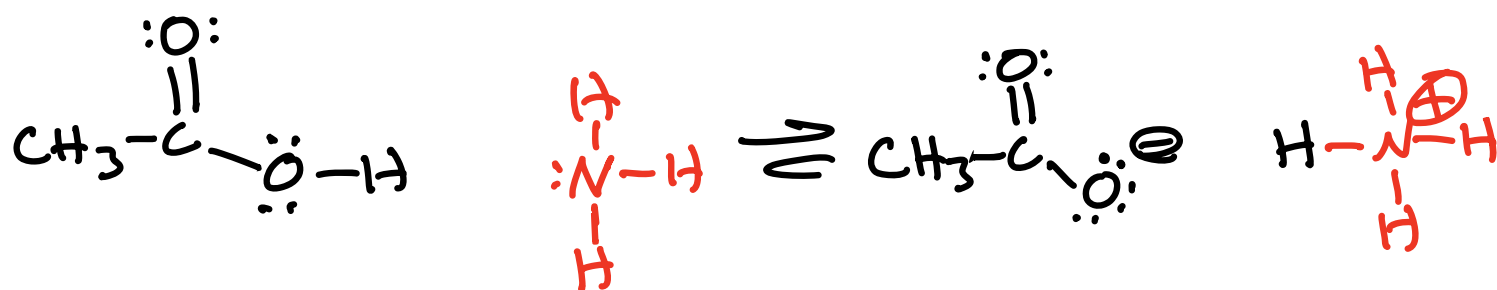
3) Arrows start at an

electron 

and end at an

electron 

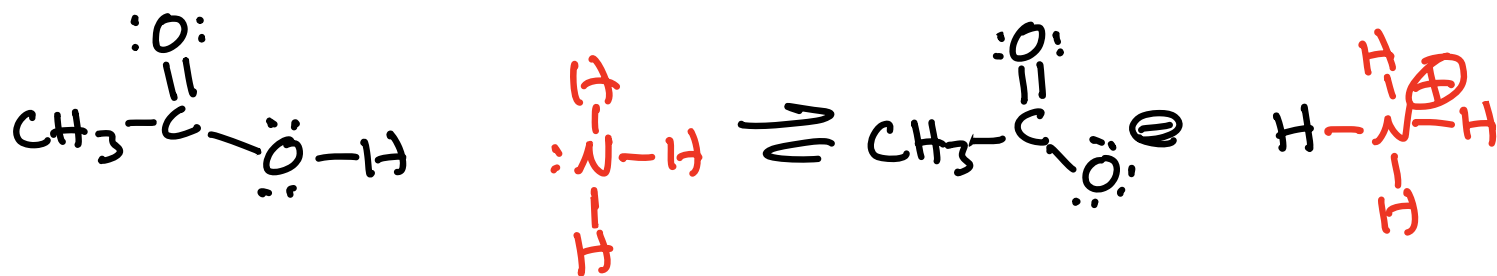
4) Breaking a bond will occur



a)  $\rightarrow$  lone pair on N atom

b)  $\rightarrow$  OH sigma bond breaks

Mistake to avoid  $\rightarrow$  moving an atom  
with an arrow



WRONG!!  $\rightarrow$

Nucleophile  $\rightarrow$  electron rich species

$\downarrow$   
analogous to  
a

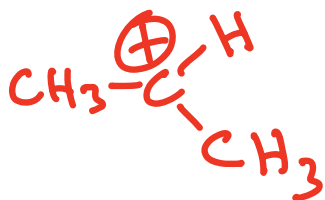
Ex.



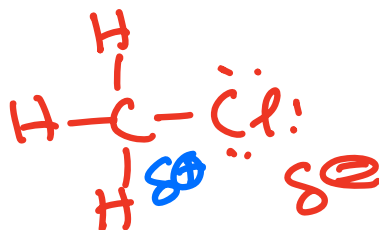
Electrophile  $\rightarrow$  electron deficient species

$\downarrow$   
analogous to

Ex. Full  $\oplus$



Partial  $\oplus$



Weak bond



# The 4 Most Important Mechanistic Elements

The following are expressed from the point of view of the carbon-containing molecule taking part in a reaction

- 1) **Make a bond** between a nucleophile and electrophile.  
⇒ A nucleophile and electrophile are both present
- 2) **Break a bond** to give stable molecules or ions.  
⇒ None of the other possibilities are likely
- 3) **Add a proton**  
⇒ Acid is present
- 4) **Take a proton away**  
⇒ Base is present

Notice →

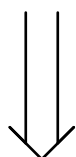
# Mechanism Summary

The following questions and mechanistic elements are described from the point of view of the carbon-containing reagent, written in the form of a flowchart.

Is there a strong acid present or is the carbon-containing reagent a strong base?

**YES**  
⇒

**Add a proton**

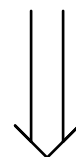


**NO**

Is there a strong base present or is the carbon-containing reagent a strong acid?

**YES**  
⇒

**Take a proton away**

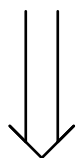


**NO**

Are there a nucleophile and electrophile present?

**YES**  
⇒

**Make a bond**

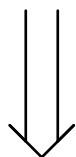


**NO**

Can a bond be broken to create stable molecules or ions?

**YES**  
⇒

**Break a bond**



**NO**

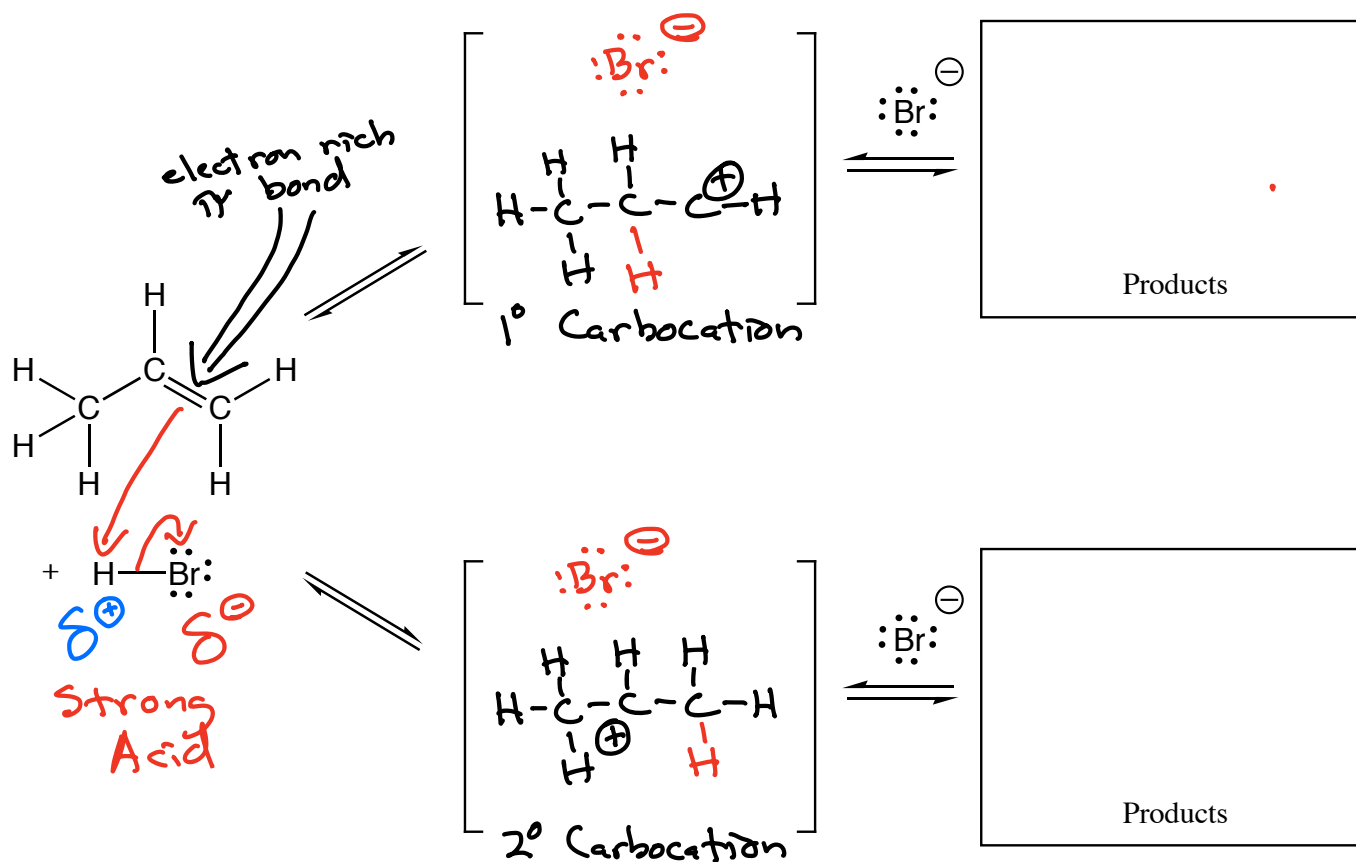
Think about alternative mechanistic elements







## Addition of H-X to an Alkene

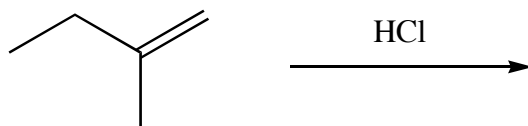


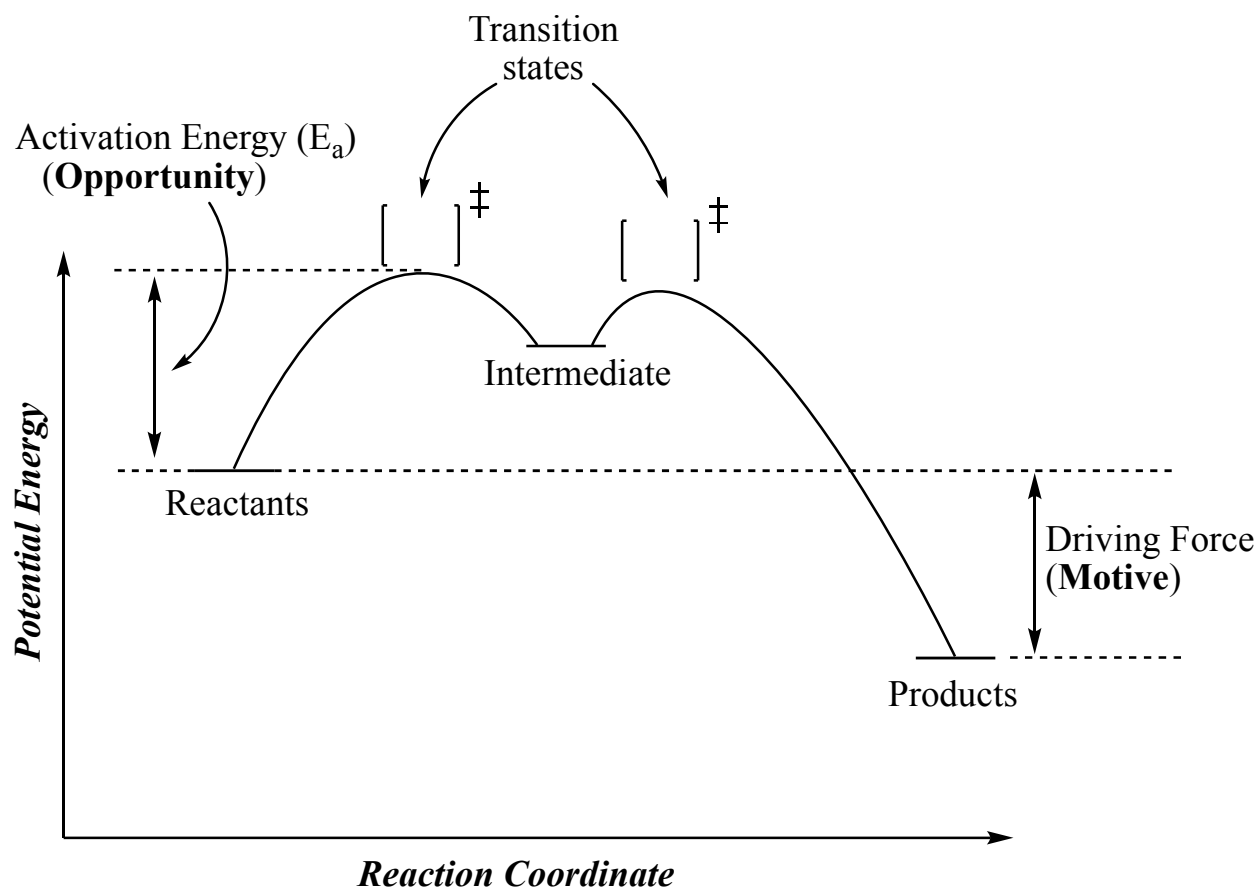
Summary:

Regiochemistry:

Stereochemistry:

Example:

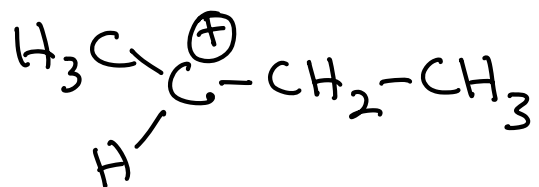




During reactions we often encounter intermediates →

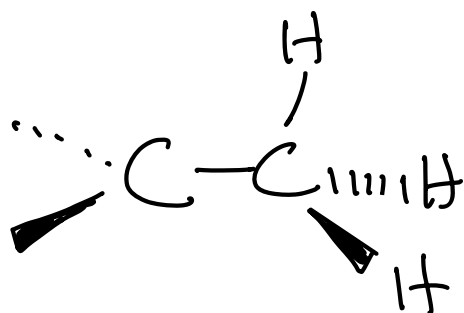
When alkenes react with  $H-X \rightarrow$

Carbocations  $\rightarrow$



Alkyl groups stabilize carbocations by  
2 different mechanisms

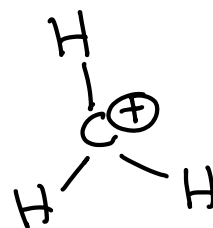
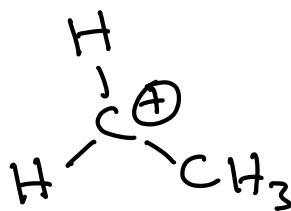
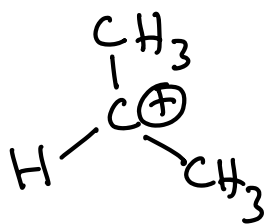
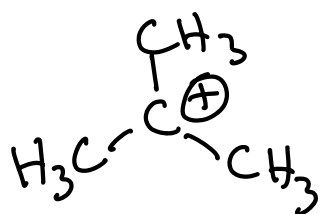
1) Hyperconjugation  $\rightarrow$



Some electron  
density of the  
C-H  $\sigma$  bond

## 2) Inductive effect $\rightarrow$

Carbocation stability  $\rightarrow$

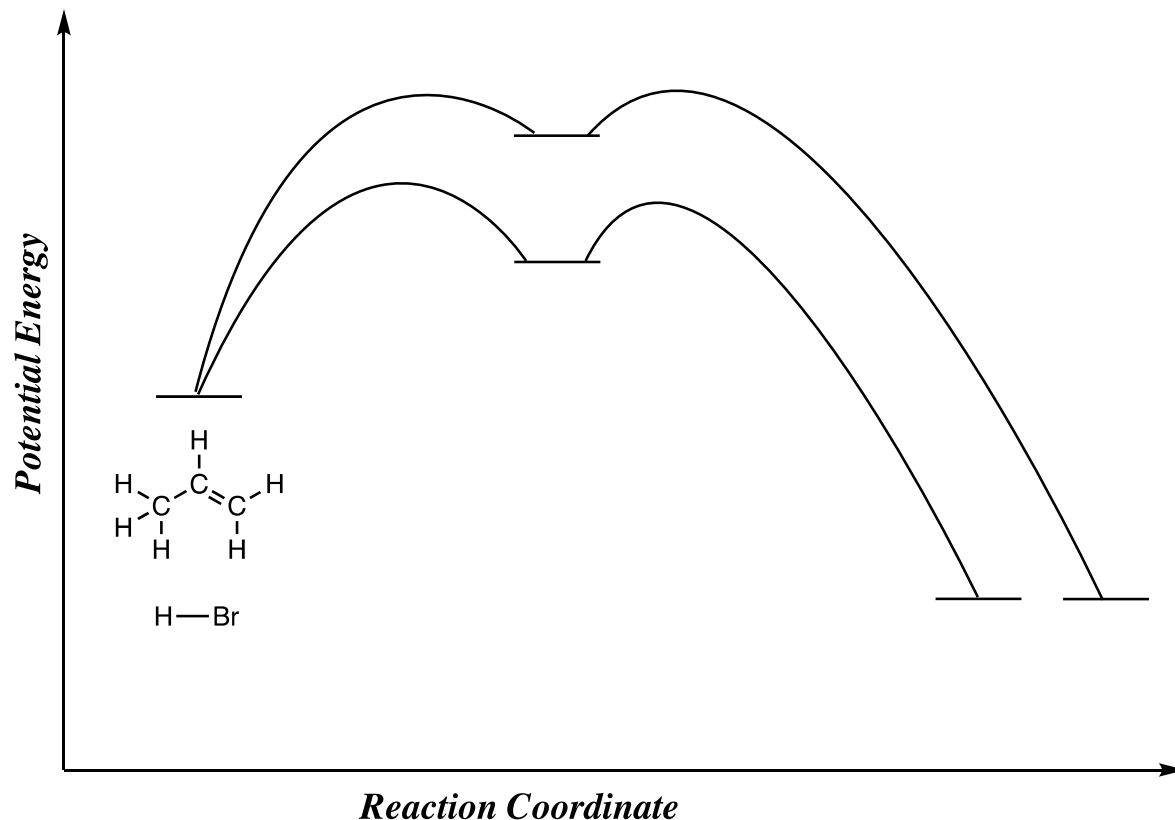


$\leftarrow$

$\leftarrow$

$\leftarrow$

Markovnikov's Rule  $\rightarrow$  For alkene reactions involving a carbocation intermediate the nucleophile (ex.  $:\ddot{\text{Br}}:^{\ominus}$ ) will make a bond to the more substituted C atom  $\rightarrow$



Creation of CCC(Br)C has a lower energy barrier and it forms faster  $\rightarrow$  we get more product