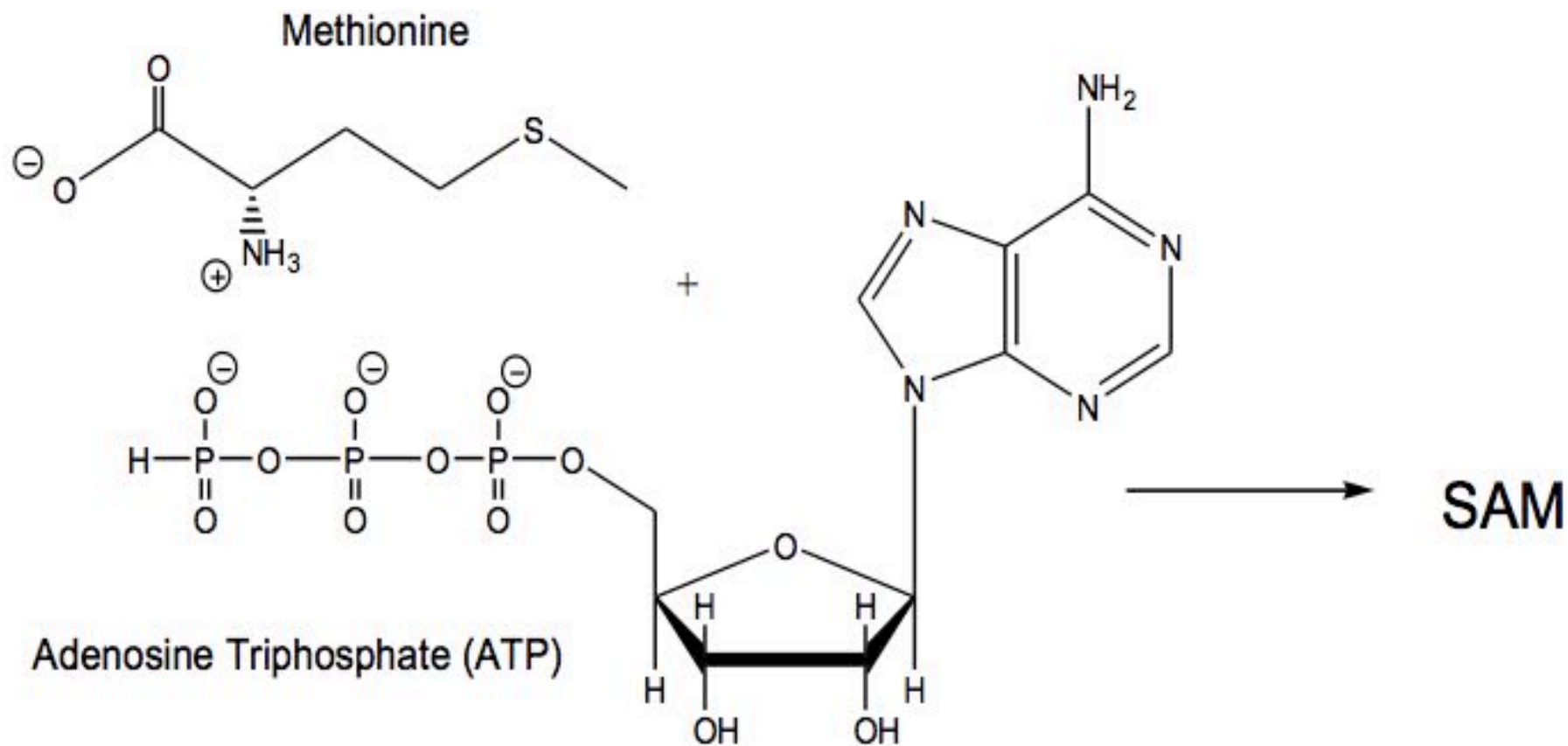


Objective 8

intro to Reactivity 2: identify polar bonds ($\delta +$ and $\delta -$), nucleophiles (Lewis base, electron pair donor), electrophiles (Lewis acid, electron pair acceptor). Use curved arrows to predict product. Identify common bond breaking and making processes.

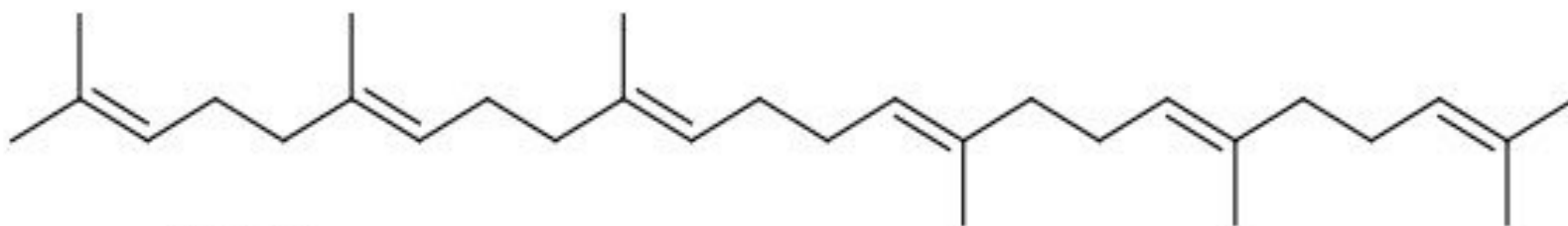
Chem 12A Objectives

Predict the product of a reaction.

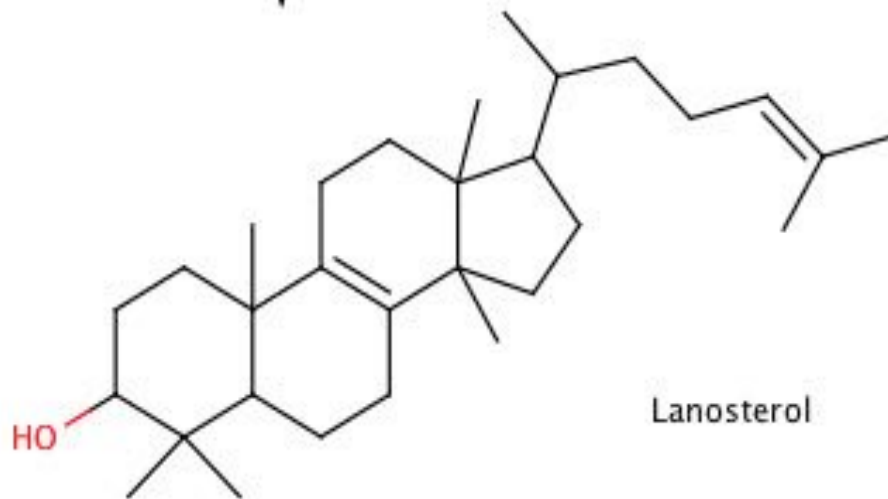


Chem 12A Objective

Explain how reactants form products with a mechanism.

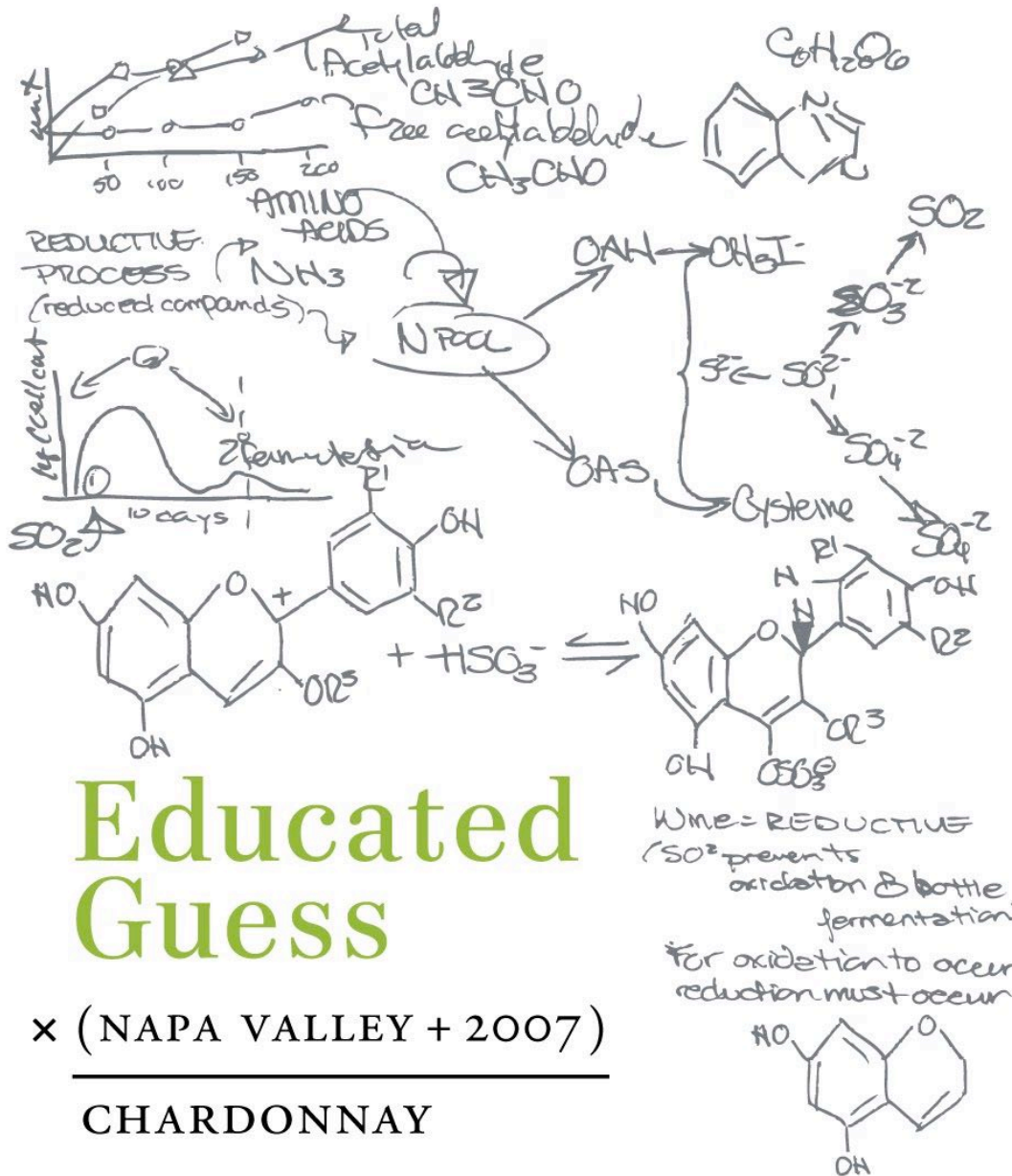


Squalene



Lanosterol

Precursor to cholesterol



http://www.rootsrundeep.com/educated_guess.html

Roots Run Deep Winery

“Our label was designed to tell the story of how you can make an educated guess in winemaking, not to give you nightmares about your high school chemistry class. It shows you actual winemaking formulas that are either induced or naturally occur during a specific winemaking process.”

Educated Guess

× (NAPA VALLEY + 2007)

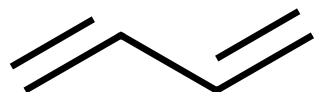
CHARDONNAY

Chem 12A Objective

How is an unsaturated fat made saturated?

How do you synthesize an organic compound?

E.g., How would you synthesize 1,3-butadiene (precursor to rubber) from acetylene?



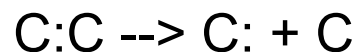
from



Organic Reactions are classified as **Polar**, Radical, or Pericyclic.

1. **Polar** reactions – nucleophile (Lewis base) reacts with an electrophile (Lewis acid).

- heterolytic bond breaking and making



Use “Curved Arrows” From Nu:- to E⁺ to Show Bonds Forming and Breaking (electron pairs move in the same direction)

• **Most organic reactions are polar reactions and equilibrium reactions.**

• Polar reaction: ID nucleophile and electrophile - see structure.

• Best Nu:- reacts with best E⁺.

2. Radical reactions - light (usually UV) is used to break chemical bonds

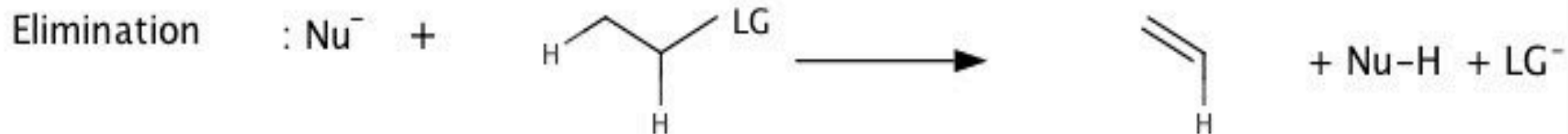
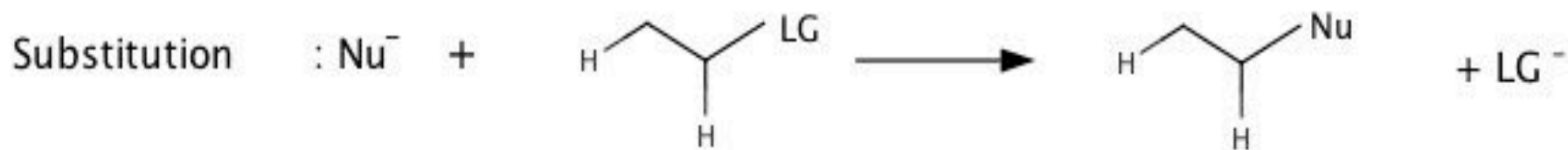
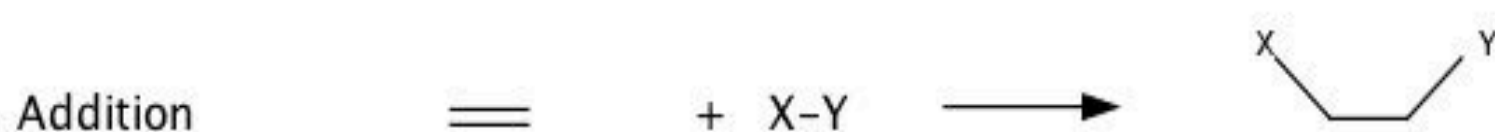
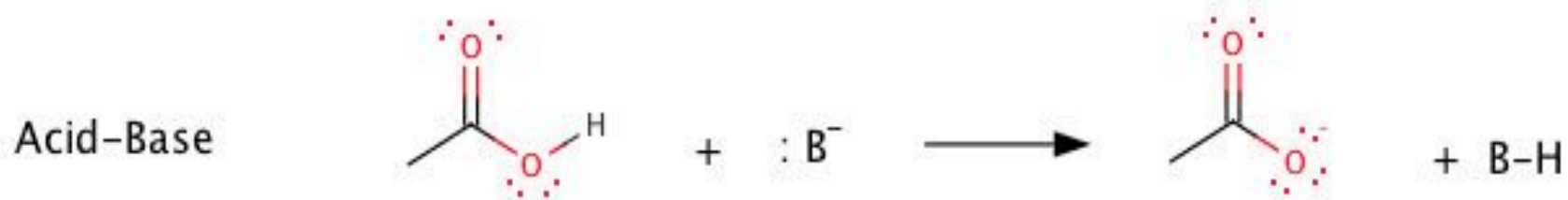
- homolytic bond breaking and making



Curved arrows: one electron moves in opposite directions

3. pericyclic reactions - several pairs of electrons breaking/forming bonds in concert

4 Types of Organic Polar Reactions



Identify the Nu:⁻ and E⁺ in each reaction.

Structural Features (functional groups) give you information about how organic compounds react.

- a. Identify the most reactive nucleophile and electrophile to predict the most probable reaction partners.
- b. Rank the relative reactivity of the common Nu:⁻ and E⁺ (best to worst) by type and within each type. See Table 1 on Reactivity Principles and Trends (Course Info Handout, p. 5)
- c. Draw a “curved arrow” from the nucleophile to the electrophile using a **known** bond breaking/making process. See Table 2 on Reactivity Principles and Trends
- d. Many Organic Reactions occur at **alpha** carbon or **H bonded to beta** carbon.

Organic Reactions Involve
Converting One Functional Group to Another

Most organic reactions are **Polar Reactions**

Polar = look for (+) and (-) poles in molecule
Electrophiles **Nucleophiles**

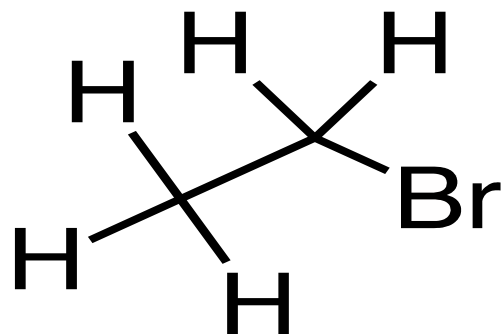
(+) pole	(-) pole
Electron Sink	Electron Source
<i>Electrophile</i>	<i>Nucleophile</i>
(+) charge	(-) charge
Acid (Lewis)	Base (Lewis)
Electron deficient species	Lone pair
Less EN atom in polar bond	π bond

Reactivity Principles and Trends

Table 1. Nucleophile (Electron Sources) and Electrophile (Electron Sinks) Classification

Nucleophile Type	Example		Electrophile Type	Example
Organometallics (see carbanions)	alkyl lithium (CH_3^-)	Best	Electron deficient species	carbocations, CH_3^+ , BF_3
Group I hydrides (H^-)	NaH		Acids	HCl
Complex metal hydrides	NaBH_4		Single bonds between heteroatoms	C-O (C is the E^+)
Active metals	Li metal		Leaving groups on sp^3 carbons	CH_3I (I is the leaving group)
Lone pair nucleophiles, bases (see pK_a table)	ROH, RNH_2 , OH		Carboxyl derivatives (sp^2 -bound L)	acyl halides, anhydrides, esters
Allylic sources	enolates, enamines		Heteroatom-carbon multiple bonds	aldehydes, ketones, nitriles, CO_2
Simple pi bonds	alkenes, alkynes, dienes		Conjugate acceptors	enones, acrylates
Aromatic rings	benzene	Worst	redox-active metals	CrO_3

Electronegativity tells us _____.

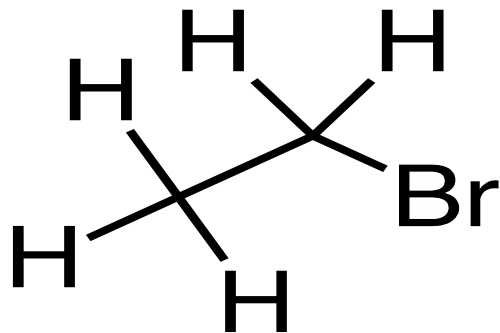


Identify the polar bond(s).

For each polar bond, show the atom with the partial positive charge (δ^+) and the atom with the partial negative charge (δ^-).

What *type of electrophile* is the δ^+ atom?

Electronegativity tells us about **bond polarity**.



Intro to Reactivity and Structural Features:

An anion (**nucleophile**) can react with the:

1. carbon bonded to the Br (this C is called the **alpha** C and is an **electrophile** and is involved in **substitution** reactions),
2. H bonded to the carbon adjacent to the C bonded to Br (this C is called the **beta** carbon and is an **electrophile** and is involved in **elimination** reactions).

Explain using bond polarity.

Polar Reactions Involve Nucleophiles and Electrophiles

Fill in the table below.

Which functional group is the best Nu:-? E+?

Which reactant is the best Nu:-? E+?

Chem 12A Functional Groups and Reactants

Functional Group/ Structural Feature	Nu:- or E+? Type?	Reactant	Nu:- or E+? Type?
Alkane	See radical rxns	OH ⁻	
Alkene/pi bond		H ₂ O	
Alkyne/pi bond		HX	
Alcohol/acidic H, basic O, alpha C		X ⁻	
Alkyl Halide/alpha C, H on beta C		X ₂	
		CH ₃ O ⁻	

Hint: see Table 1 on Reactivity Principles and Trends

Explain or Predict the Major and Minor Reaction Products With a ***Reaction Mechanism***

Experiment --> Rate law --> Reaction mechanism

Reaction mechanism: sequence by which bonds break and form going from reactants to intermediates to products.

Rate determining step: slowest step in mechanism

Stability of intermediate or product helps you determine product distribution.

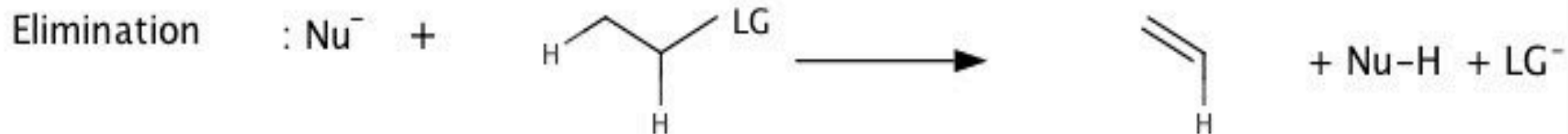
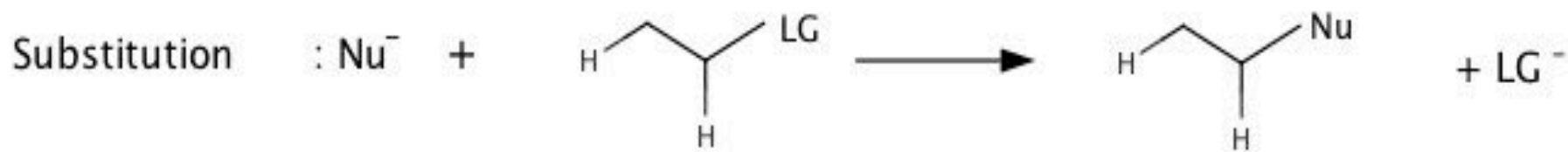
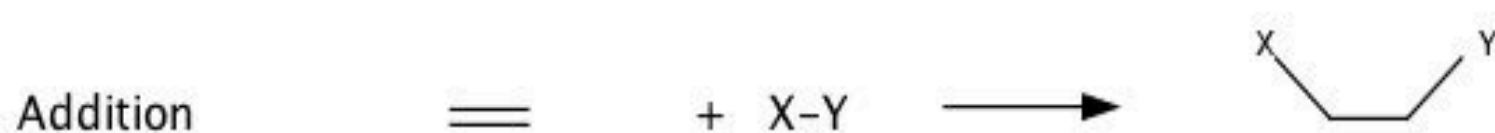
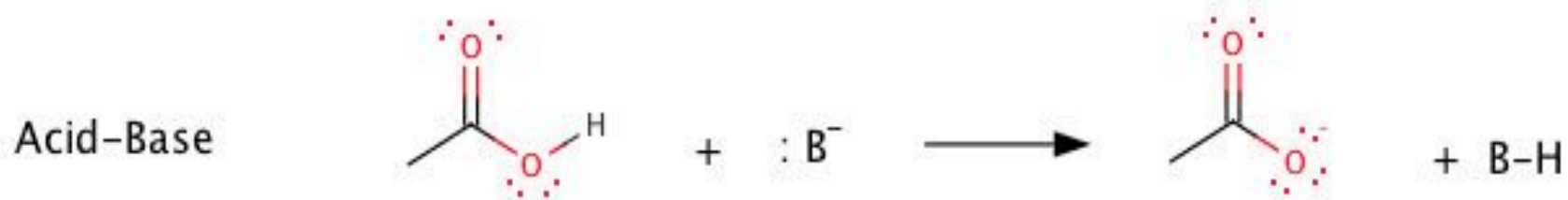
Use “curved arrows” to show bonds breaking and forming in each elemental step.

For polar reactions:

Nu:⁻ reacts with E⁺

Draw curved arrow from Nu:⁻ to E⁺

4 Types of Organic Polar Reactions



Identify the Nu:⁻ and E⁺ in each reaction.

Table 2. Known Bond Breaking and Making Processes

(Course Info Handout, p. 5)

Polar Reactions:

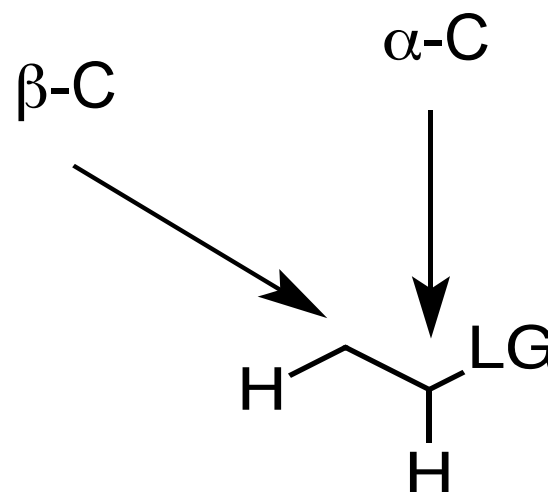
1. Proton transfer

2. Ionization of a leaving group

3. Nucleophilic attack on:

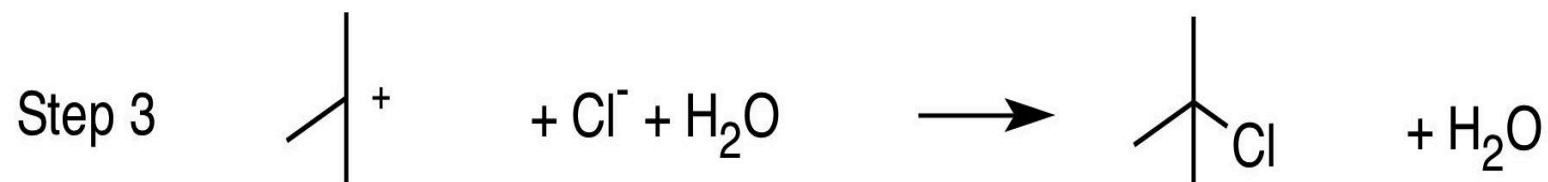
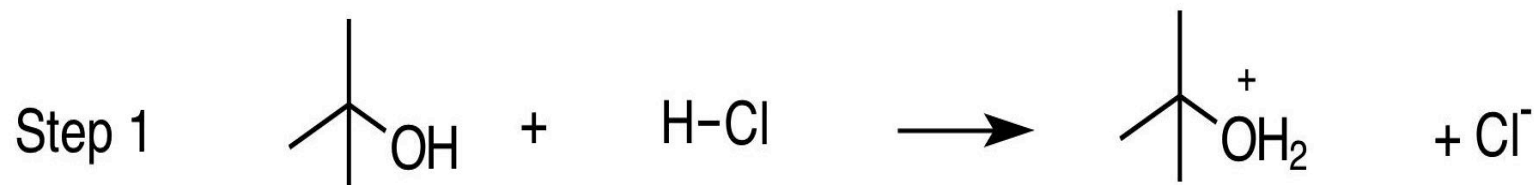
- Electron deficient species, e.g., C^+
- C bonded to leaving group (α -C)
- H bonded to β C (C adjacent to C bonded to leaving group)
- A polarized multiple bond, e.g., $C=O$

LG = Leaving Group



4. 1,2 rearrangement of a carbocation

Identify the bond making/breaking process in each step.
Use curved arrows to show bonds breaking/forming.

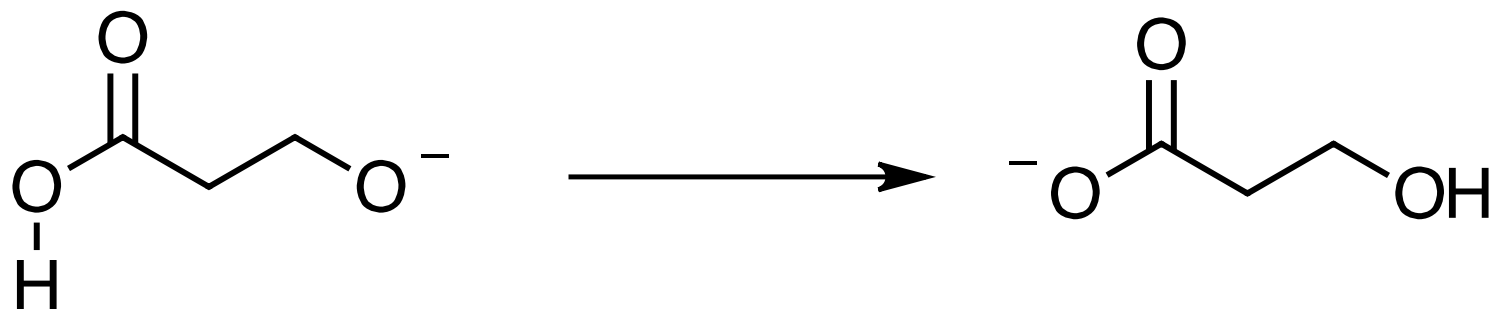


Choices: Proton transfer, ionization of LG, nucleophilic attack

Identify the bond making/breaking process in each step.

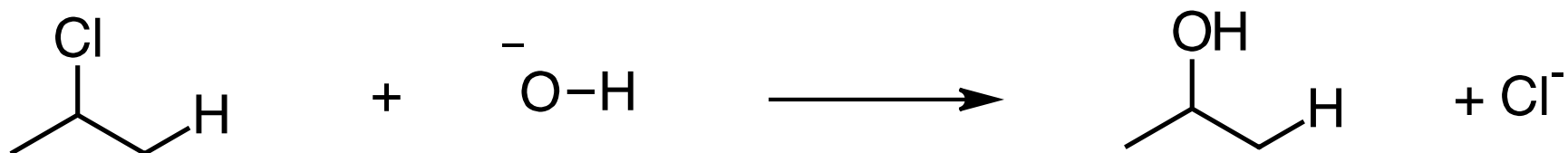
Use curved arrows to show bonds breaking/forming.

More Practice Problems: Klein, Ch. 6.30



Choices: Proton transfer, ionization of LG, nucleophilic attack

Use curved arrows to show how each product is produced.



The bond breaking/making process is a **nucleophilic attack**.

What **type** of nucleophilic attack is this?

- Electron deficient species, e.g., C⁺
- C bonded to leaving group (α -C)
- H bonded to β C (C adjacent to C bonded to leaving group)
- A polarized multiple bond, e.g., C=O

What is the reaction type?

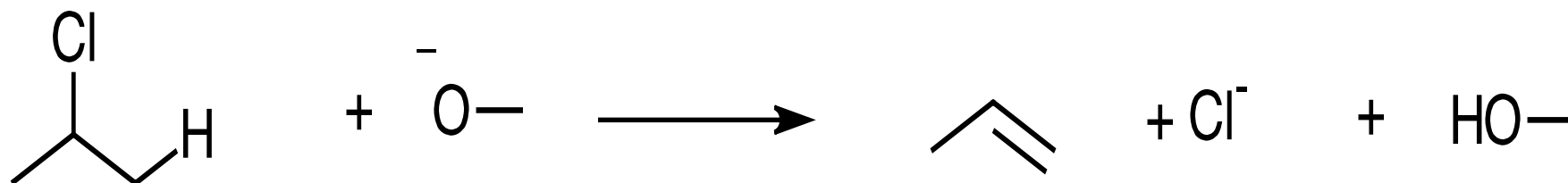
Acid-base

Elimination

substitution

addition

Use curved arrows to show how each product is produced.



The bond breaking/making process is a **nucleophilic attack**.

What **type** of nucleophilic attack is this?

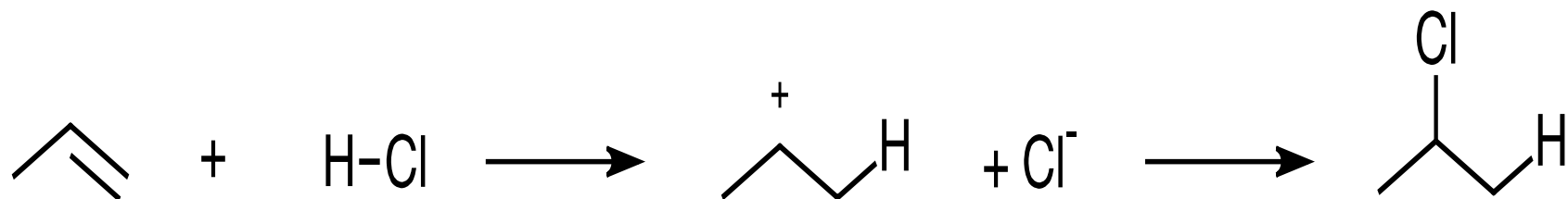
- Electron deficient species, e.g., C⁺
- C bonded to leaving group (α -C)
- H bonded to β C (C adjacent to C bonded to leaving group)
- A polarized multiple bond, e.g., C=O

What is the reaction type?

Acid-base
Elimination

substitution
addition

Use curved arrows to show how each product is produced.



This reaction is an **addition** reaction.

What is the bond breaking/making process in the 1st step?

In the 2nd step, the bond breaking/making process is a

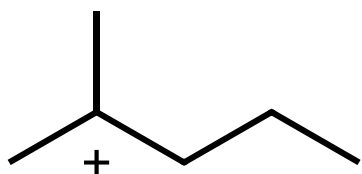
nucleophilic attack.

What **type** of nucleophilic attack is this?

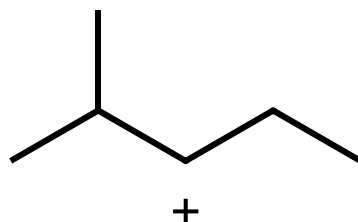
- Electron deficient species, e.g., C⁺
- C bonded to leaving group (α -C)
- H bonded to β C (C adjacent to C bonded to leaving group)
- A polarized multiple bond, e.g., C=O

Objective: Identify 3° or 2° or 1° Carbocations.
Rank Carbocations by stability: 3° > 2° > 1°

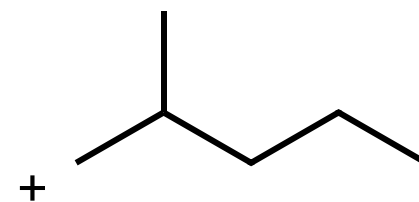
Classify the following carbocations as 3° or 2° or 1°.
Which carbocation is the most stable? Least stable?



A



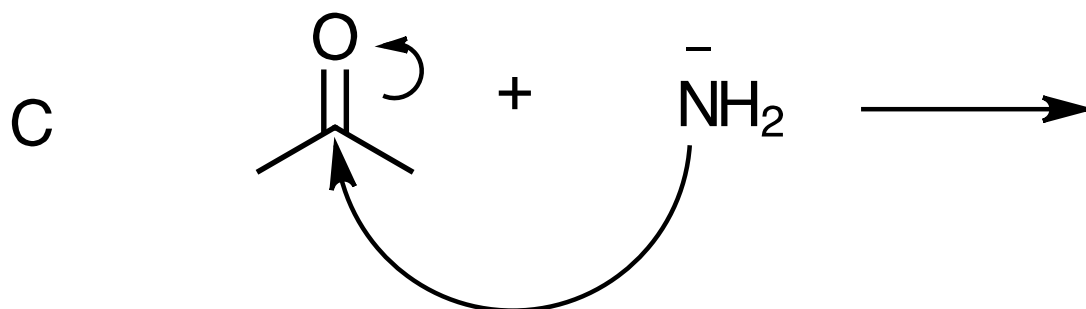
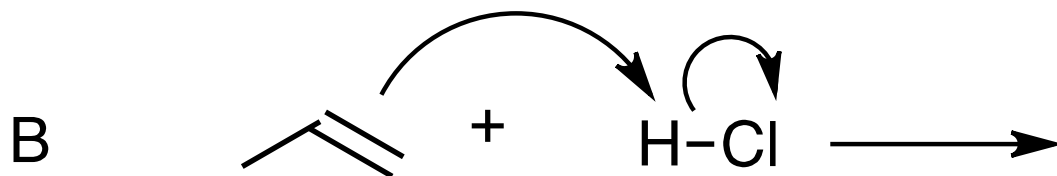
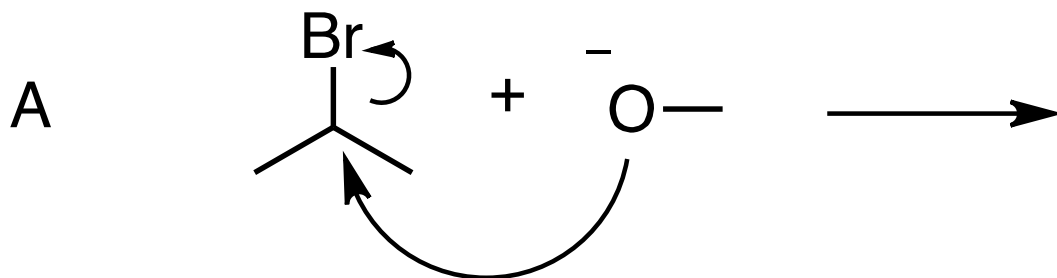
B



C

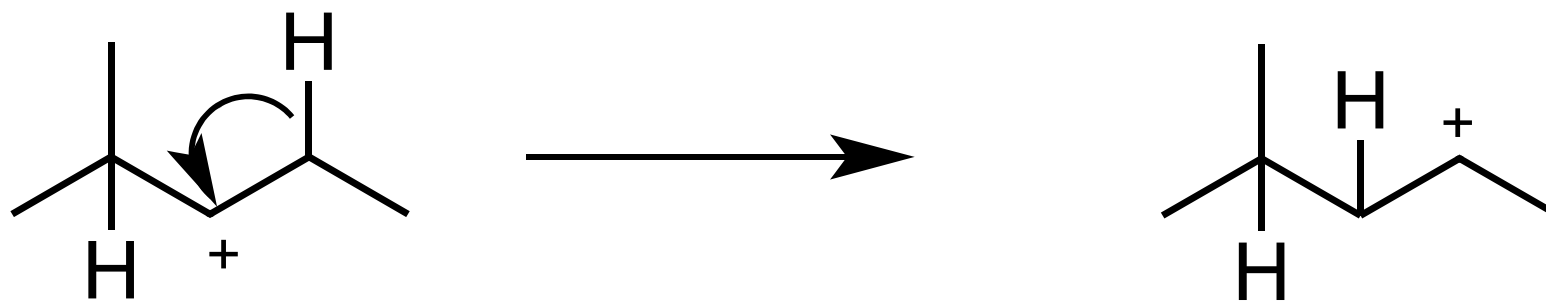
Objective: Identify how a Carbocation forms.
Identify how a Carbanion forms.

Which reaction forms a **Carbocation**?



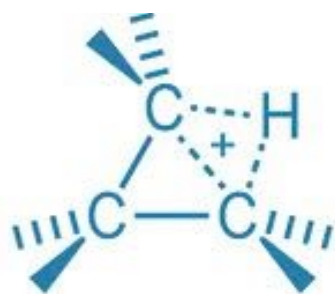
Hint: ID Nu^- and E^+ and reaction type.

1,2 rearrangement: If you see a 2° or 1° carbocation, see if a more stable C⁺ can form via hydride shift or alkyl shift on adjacent carbon.

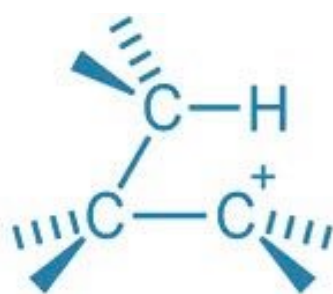


*Does this hydride (H⁻) shift make a more stable carbocation?
If not, show a rearrangement that makes a more stable C⁺.*

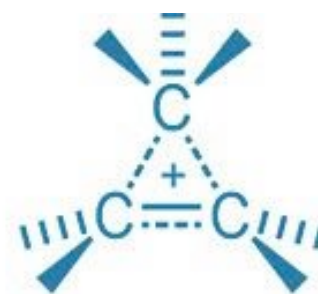
2/15/16, CEN, p. 23 Carbocation Rearrangement Mechanism:
Rearrangement proceeds through a protonated *mesomeric*
cyclopropane intermediate (through computer simulations)



Edge-protonated



Mesomeric

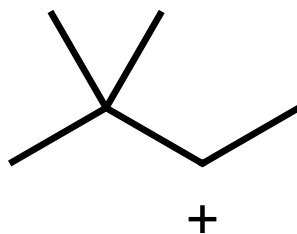
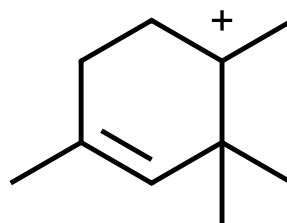
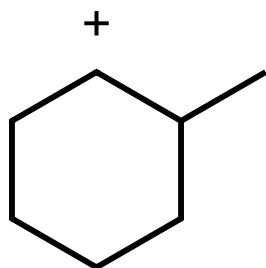


Corner-protonated

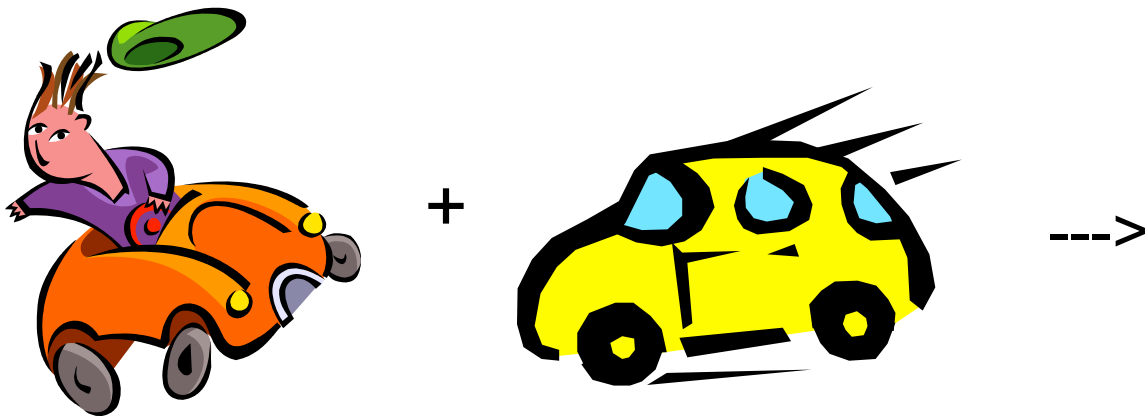
Proposed cyclopropane intermediates

<http://cen.acs.org/articles/94/i7/Chemists-Confirm-Identity-Pivotal-Intermediate.html>

Which compound(s) will undergo a rearrangement? Use curved arrows to show the rearrangement.
(Klein, 6.18 a, c, and f)



See **Reactivity Principles and Trends** (Course Info Handout, p. 5)
A Chemical Reaction Occurs When *Reactants Collide* with _____ and _____ for Bonds to Break or Form



Unstable, high energy substances

**More reactive
Or
Less reactive?**

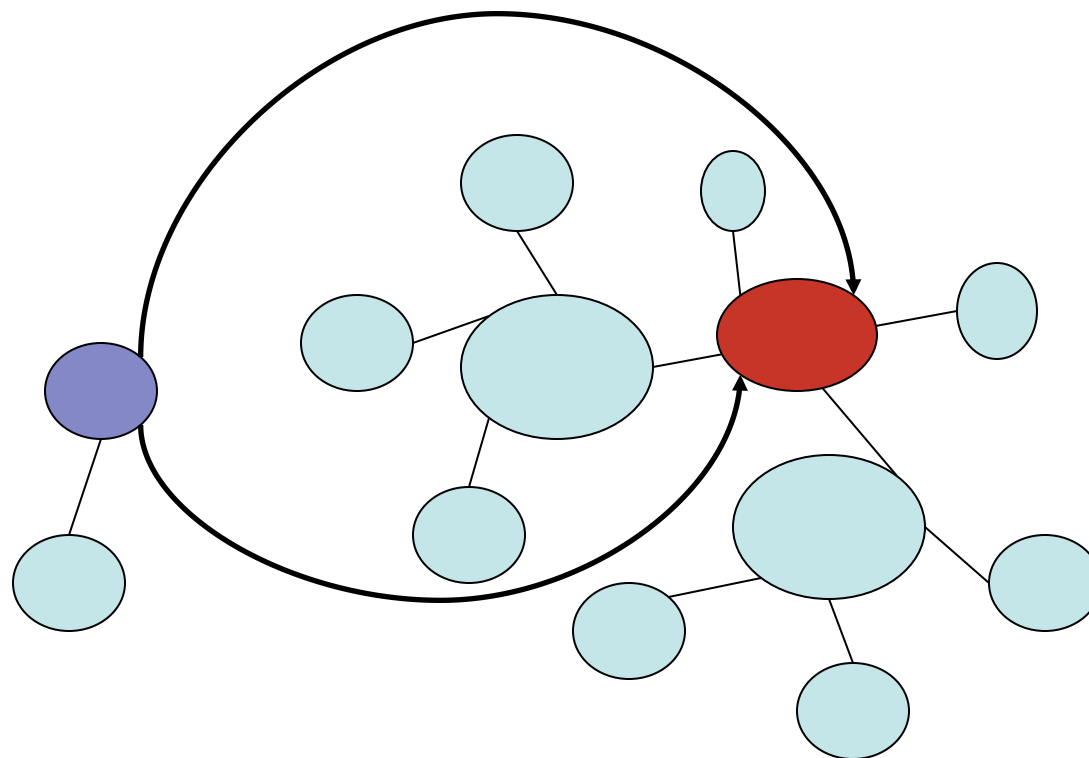


Stable, low energy substances

A **Reaction** Occurs When **Reactants Collide** with **Sufficient Energy** and **Correct Orientation** for Bonds to Break or Form

Sufficient Energy:

high T or low T?



Correct Orientation:

Which path does blue take to red?
The “right” atoms in each reactant have to collide together. Alignment and access.

To Break a Bond _____ Energy
When a Bond Forms, Energy is _____

Teflon: A C-F bond is strong and is hard to break.
A lot of energy is _____ when a C-F bond is formed.

Dynamite and TNT: A N-O is weak and is easy to break.
A _____ of energy is _____ when a N-O bond is formed.

To Break a Bond **REQUIRES** Energy
When a Bond Forms, Energy is **RELEASED**

Teflon: A C-F bond is strong and is hard to break.

A lot of energy is **RELEASED** when a C-F bond is formed.

Dynamite and TNT: A N-O is weak and is easy to break.

A **LITTLE BIT** of energy is **RELEASED** when a N-O bond is formed.

Bond	ΔH , kcal/mole	Bond	ΔH , kcal/mole
C-F	116	C-H	109
C-Cl	81	N-H	101
C-Br	68	O-H	96
C-I	51	C-O	94
		N-O	48

Organic Chemists talk about “activating a C-H bond.” What does that mean?

General Reaction Principles are useful on paper (lecture) and in lab

(i) ***Thermodynamics***

2 driving forces: enthalpy and entropy

What does structure tell you about stability?

Strong bonds don't react (see Teflon with strong C-F bonds);

Weak bonds do react (see weak N-O bonds in TNT).

Bond dissociation energies can be used to estimate ΔH_{rxn} ("bonds broken minus bonds made") and give relative stabilities of reactants and products.

(ii) ***Reaction rates***

3 factors: Temperature, concentration, and catalyst

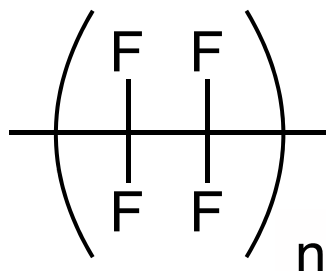
What does structure tell you about reaction rate? Accessibility of reactant to reaction site.

(iii) ***Equilibrium*** (reversible reactions)

LeChatelier's principle: stressing a reaction shifts the reaction in a direction that relieves the stress.

Stress: concentration, temperature, pressure (gases)

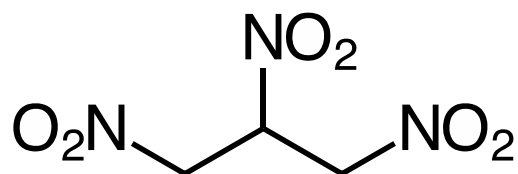
Teflon is stable and unreactive because of strong C-F bonds



<http://en.wikipedia.org/wiki/Polytetrafluoroethylene#Properties>

Properties: high m.p. (327°C)
Non-polar and Insolubility
High thermal stability
Low coefficient of friction
Low dielectric constant
Excellent weatherability
Flame resistant
Excellent toughness

Nitroglycerin is unstable and reactive because of weak N-O bonds.



nitroglycerin

Colorless liquid

$\Delta H_{\text{combustion}} = -1.53 \text{ MJ/mole}$

Shock sensitivity = high

Friction sensitivity = high

Explosive velocity = 7700 m/sec

Since the 1860s, nitroglycerin has been used as an active ingredient in the manufacture of explosives, mostly dynamite. Nitroglycerin is also used medically as a vasodilator to treat heart conditions, such as angina and chronic heart failure

<http://en.wikipedia.org/wiki/Nitroglycerin>

Bond Strength Determines Reactivity.

What makes a bond strong or weak? What does d tell you?

Bond	d , pm	ΔH , kcal/ mole	Bond	d , pm	ΔH , kcal/ mole	Bond	d , pm	ΔH , kcal/ mole
C-H	109	99	C-C	154	83	C-O	143	94
O-H	96	88	C=C	134	146	C=O	120	177
N-H	101	101	C \equiv C	120	201	C \equiv O	113	256
H-F	92	136	C-F	135	116	C-N	147	73
H-Cl	127	103	C-Cl	177	81	C=N	129	147
H-Br	141	87.5	C-Br	194	68	C \equiv N	116	212
H-I	161	71	C-I	214	51	N-O	140	48
						N=O	121	145

Note: Average bond energies. Some bonds show considerable variability.

Table 1. Molecular Bond Dissociation Energies for $\text{RH} \rightarrow \text{R} + \text{H}$: Experimental Bond Enthalpies and Radical Heats of Formation at 298 K

	DH_{298} (kcal mol ⁻¹)	$\Delta_f H_{298}(\text{R})$ (kcal mol ⁻¹)	ref		DH_{298} (kcal mol ⁻¹)	$\Delta_f H_{298}(\text{R})$ (kcal mol ⁻¹)	ref
Inorganics							
H ₂	104.206 ± 0.003	52.103 ± 0.003	4	OH ⁻ → O ⁻ + H	110.21 ± 0.07	-33.23 ± 0.07	34
HF	136.25 ± 0.01	18.83 ± 0.17	6	OH ⁺ → O + H ⁺	115.2 ± 0.1	59.55 ± 0.02	34
HCl	103.15 ± 0.03	29.03 ± 0.04	9	H ₂ S	91.2 ± 0.1	34.2 ± 0.2	6
HBr	87.54 ± 0.05	28.62 ± 0.06	9	SH	84.1 ± 0.2	66.2 ± 0.3	6
HI	71.32 ± 0.06	26.04 ± 0.08	9	H-NO	49.5 ± 0.7	21.8 ± 0.1	4
H-CN	126.3 ± 0.2	105.0 ± 0.7	6	H-ONO (trans)	79.1 ± 0.2	8.2 ± 0.1	4
NH ₃	107.6 ± 0.1	44.5 ± 0.1	6	H-ONO ₂	101.7 ± 0.4	17.6 ± 0.3	35
H ₂ O	118.82 ± 0.07	8.86 ± 0.07	34	SiH ₄	91.7 ± 0.5	47.9 ± 0.6	9
OH	101.76 ± 0.07	59.55 ± 0.02	34	GeH ₄	83 ± 2	53 ± 2	9
Hydrocarbons							
CH ₄	104.99 ± 0.03	35.05 ± 0.07	31	CH ₂ CH-H	110.7 ± 0.6	71.1 ± 0.7	6
CH ₃	110.4 ± 0.2	93.3 ± 0.2	31	HCC-H	133.32 ± 0.07	135.6 ± 0.2	36
CH ₂	101.3 ± 0.3	142.5 ± 0.2	9	C ₆ H ₅ -H	112.9 ± 0.5	80.5 ± 0.5	6
CH	80.9 ± 0.2	171.3 ± 0.1	9	C ₆ H ₅ → <i>o</i> -C ₆ H ₄ + H	78 ± 3	106 ± 3	37
CH ₃ CH ₂ -H	101.1 ± 0.4	29.0 ± 0.4	10	C ₆ H ₅ → <i>m</i> -C ₆ H ₄ + H	94 ± 3	122 ± 3	37
(CH ₃) ₂ CH-H	98.6 ± 0.4	21.5 ± 0.4	10	C ₆ H ₅ → <i>p</i> -C ₆ H ₄ + H	109 ± 3	138 ± 3	37
CH ₃ CH ₂ (CH ₃)CH-H	98.2 ± 0.5	16.1 ± 0.5	10	CH ₂ CHCH ₂ -H	88.8 ± 0.4	41.4 ± 0.4	38
(CH ₃) ₃ C-H	96.5 ± 0.4	12.3 ± 0.4	10	C ₆ H ₅ CH ₂ -H	89.8 ± 0.6	49.7 ± 0.6	38
Alcohols							
H-CH ₂ OH	96.1 ± 0.2	-4.08 ± 0.2	16	CH ₃ CH ₂ O-H	104.7 ± 0.8	-3.6 ± 0.8	6
CH ₃ O-H	104.6 ± 0.7	4.3 ± 0.7	6	(CH ₃) ₂ CHO-H	105.7 ± 0.7	-11.5 ± 0.7	6
CH ₃ S-H	87.4 ± 0.5	29.8 ± 0.4	39,40	(CH ₃) ₃ CO-H	106.3 ± 0.7	-20.5 ± 0.7	6
H-CH ₂ SH	94 ± 2	36 ± 2	39, 40	C ₆ H ₅ O-H	90 ± 3	-58 ± 3	41
Peroxides							
HOO-H	87.8 ± 0.5	3.2 ± 0.5	14	CH ₃ CH ₂ OO-H	85 ± 2	-6.8 ± 2.3	42
CH ₃ OO-H	88 ± 1	4.8 ± 1.2	42	(CH ₃) ₃ COO-H	84 ± 2	-25.2 ± 2.3	42
Carbonyls							
H-CHO	88.144 ± 0.008	10.1 ± 0.1	6	H-COOH is ≥	96 ± 1	-46.5 ± 0.7	45
CH ₃ C(O)-H	89.4 ± 0.3	-2.4 ± 0.3	43	CH ₃ COO-H	112 ± 3	-43 ± 3	44
H-CH ₂ CHO	94 ± 2	2.5 ± 2.2	9	C ₆ H ₅ COO-H	111 ± 4	-12 ± 4	44
HCOO-H	112 ± 3	-30 ± 3	44				

Reference: <http://www.colorado.edu/chem/ellison/research/resThermo.html>

Bigger Orbital Overlap Means Stronger Bond

- A _____ (stronger or weaker) bond will have _____ (more or less) s character in the bonding orbital.
- In general, a weak bond is _____ (more or less) reactive than a strong bond.
- A C-C single bond is unreactive.
- The π bond in a C-C double bond or triple bond is reactive.

RESONANCE STABILIZATION

RESONANCE STABILIZATION

RESONANCE STABILIZATION

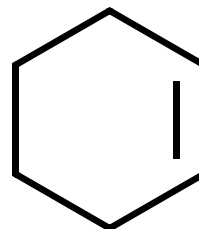
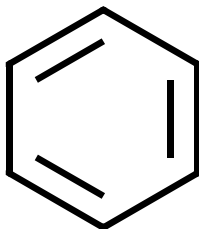
It is better to be spread out than concentrated.



<http://www.homocon.com/archives/2006/12/>



<http://danceswithfat.wordpress.com/2011/05/25/taking-up-space/crowded-subway/>



Which compound is more stable? Why?

General Reaction Principles are useful on paper (lecture) and in lab

(i) ***Thermodynamics***

2 driving forces: enthalpy and entropy

What does structure tell you about stability?

(ii) ***Reaction rates***

3 factors: Temperature, concentration, and catalyst

What does structure tell you about reaction rate? Accessibility of reactant to reaction site.

Which process occurs fastest? The fastest reactions produce the major product. E.g., proton transfer is very fast - often the first step in a reaction mechanism.

But with weak organic acids and bases, proton transfer is slow enough to allow nucleophilic attack.

(iii) ***Equilibrium*** (reversible reactions)

LeChatelier's principle: stressing a reaction shifts the reaction in a direction that relieves the stress.

Stress: concentration, temperature, pressure (gases)

Fill in the blanks:

A catalyst is used to _____ the reaction rate.

A catalyst _____ the activation energy of a reaction.

A catalyst _____ the equilibrium constant.

A catalyst _____ the reaction mechanism.

Increase

Raises

Changes

Decrease

Lowers

Does not change

Kinetics:

The rate law of a reaction is determined by Experiment



What information does x and y tell us?

The rate law tells us the number of each reactant in the rate determining step in a Reaction Mechanism.

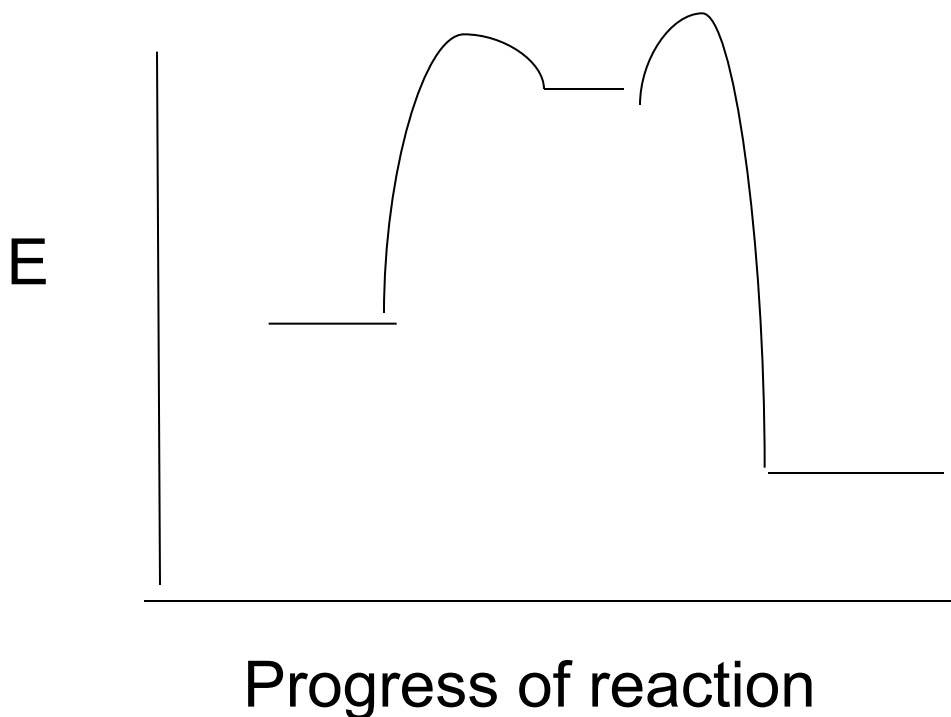
What is a Reaction Mechanism?

We can use a Reaction Mechanism to:

- explain product distribution.
- help us predict a product of a reaction.

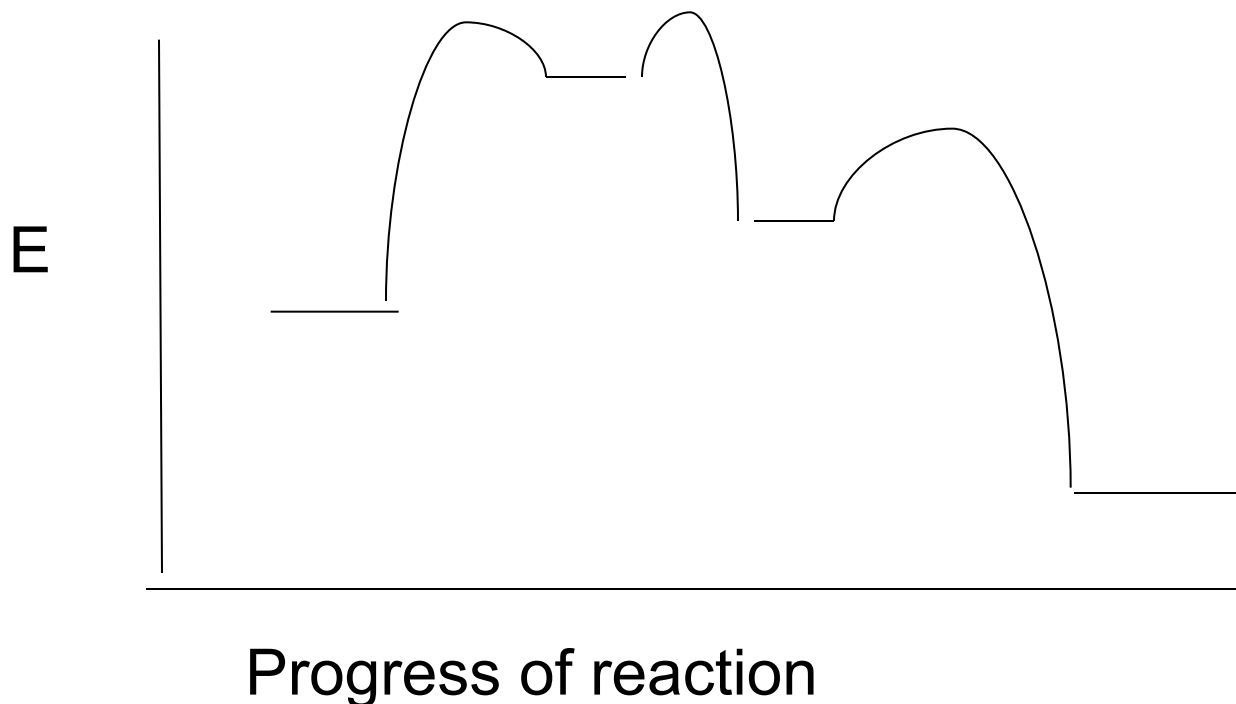
The rate determining step is the _____ step of a mechanism.

**A Reaction Energy Diagram tells you about
THERMO and KINETICS**



Label the following: reactants, products, intermediate, ΔH , E_a
Where is the thermo in this diagram?
Where is the kinetics in this diagram?

A Reaction Energy Diagram tells us about a Mechanism



How many steps in this mechanism?

Which step is the rate determining step?

If a catalyst is used, does the mechanism change?

Thermo: The stability of intermediates, such as 1^o, 2^o, 3^o carbocation, anions, radicals, can be used to choose between reasonable alternatives, e.g., Markovnikov's rule. (see Reactivity Principles and Trends)

General Reaction Principles are useful on paper (lecture) and in lab

(i) **Thermodynamics**

2 driving forces: enthalpy and entropy

What does structure tell you about stability?

(ii) **Reaction rates**

3 factors: Temperature, concentration, and catalyst

What does structure tell you about reaction rate? Accessibility of reactant to reaction site.

(iii) **Equilibrium** (reversible reactions)

LeChatelier's principle: stressing a reaction shifts the reaction in a direction that relieves the stress.

Stress: concentration, temperature, pressure (gases)

E.g., organic acid-base (proton transfer) reactions are equilibrium reactions and tend to form the weaker acid/base.

See pK_a tables.

Most organic reactions are exothermic and equilibrium reactions.

In the Organic Chemistry Lab, you synthesize compounds:



You choose the Reaction Conditions:

Temperature, time, limiting reactant, excess reactant, ...

What reaction conditions would you choose to maximize product yield and minimize reaction time?

Back to the Lab - Reaction conditions:

- High temperature or low temperature?
- What solvent to use if you reflux?
- Which reactant should be the excess reactant?
- How much excess reactant should you use?
- You can distill rather than reflux. Why would you want to distill your reaction mixture?
- Should you use a catalyst?