Goals

- After this lesson you should be able to
  - Identify the four main factors affecting substitution reactions
  - Identify an electrophilic carbon capable of participating in substitution reactions
  - Rank leaving group abilities
  - Rank nucleophilicities
  - Explain solvent effects on nucleophilicity
  - Predict possible pathways for substitution reactions
Nucleophilic Substitution Reactions

Broken $1\sigma$

Formed $1\sigma$

$X \rightarrow Y + X$
Four Main Factors

- Electrophilic Carbon (R)
- Leaving Group
- Nucleophile
- Solvent
Electrophilic Carbon

* $sp^3$ only for nucleophilic substitution
* Can be methyl, $1^\circ$, $2^\circ$, $3^\circ$, allylic, or benzylic

- Methyl: $H_3C-X$
- $1^\circ$: $R \text{C}_2 \text{H}_5 X$
- $2^\circ$: $R \text{C}_3 \text{H}_7 X$
- $3^\circ$: $R \text{C}_4 \text{H}_{9} X$

- Allylic: $\text{CH} = \text{CH}_2 X$
- Benzylic: $\text{C}_6 \text{H}_5 \text{CH}_2 X$
The Leaving Group

* For now, halogens
* In later classes, others too

Good LGs

Bad LGs
## The Nucleophile

* Nucleophiles attack electrophiles!

In general, strong base = strong nucleophile

### Same element? Stronger base = stronger nucleophile

<table>
<thead>
<tr>
<th>OH(^{-})</th>
<th>CH(_3)COO(^{-})</th>
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### Same element? Charged > no charge

| OH\(^{-}\)      | OH\(^{-}\)  | H\(_2\)O |
Exception to Basicity/Nucleophilicity Trends

Sterics: Size matters!

\[ \text{H}_3\text{C-O}^- \quad \text{CH}_3 \quad \text{H}_3\text{C-C-O}^- \quad \text{CH}_3 \]
Caution Comparing Nucleophile vs. Base!

* Comparing nucleophilicity vs basicity...BE CAREFUL!!!

* **Basicity** = measure of equilibrium (thermodynamics)

* **Nucleophilicity** = measure of reaction rate (kinetics)

Basicity & nucleophilicity often parallel, but are measures of different properties!
## Solvent Effects: Types of Solvents

**Polar Protic:** solvents capable of hydrogen bonding
- $\text{H}_2\text{O}$
- $\text{MeOH}$
- $\text{EtOH}$

**Polar Aprotic:** solvents not capable of hydrogen bonding
- Acetone
- Tetrahydrofuran (THF)
- Dimethyl sulfoxide (DMSO)
- Acetonitrile

$\text{H}_3\text{C}-\text{C}≡\text{N}$
Polar Protic Solvents & Nucleophilicity

* Nucleophilicity depends on solvent

Na⁺ solvated

Br⁻ somewhat solvated

Smaller nucleophiles more tightly solvated = less nucleophilic
Polar Aprotic Solvents & Nucleophilicity

* Nucleophilicity depends on solvent

Na⁺ solvated

Br⁻ not well solvated
Components Summary

* Electrophilic C = sp³ only
* LG: Weaker base = better LG
* Nu: Stronger base = stronger Nu*
  * Exceptions: sterics, polar protic solvents
How Does Nucleophilic Substitution Happen?

All at once:

Break, then form:

Form, then break:
Wrapping Up

* Practice identifying compounds containing electrophilic carbons for substitution reactions

* Practice differentiating between good and poor leaving groups

* Practice comparing nucleophilicities of different species