Nucleophilic Substitution Fundamentals

UCI Chem 51A
Dr. Link

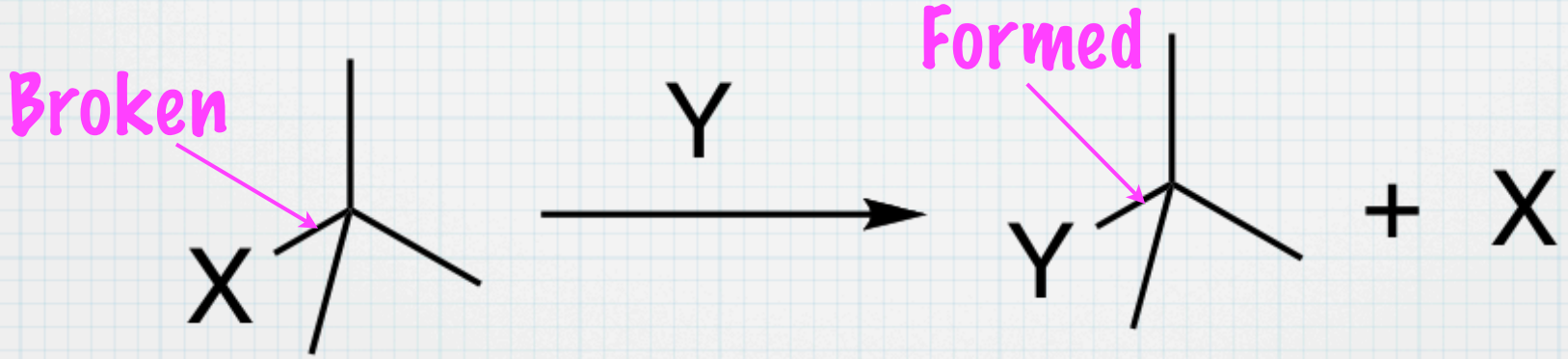
Goals

- 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
1σ

Formed
1σ



Four Main Factors

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

Electrophilic Carbon

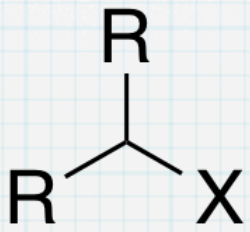
* sp^3 only for nucleophilic substitution
* Can be methyl, 1°, 2°, 3°, allylic, or benzylic

methyl

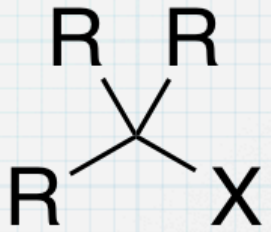
H_3C-X

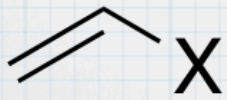
1°

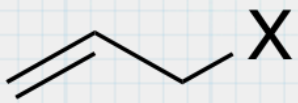
2°

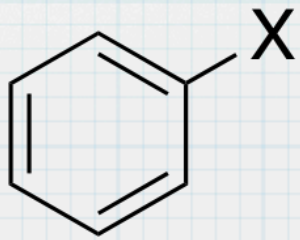


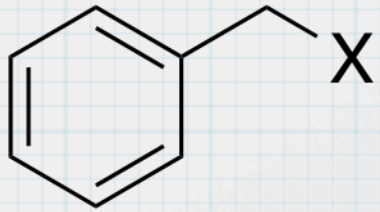
3°











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

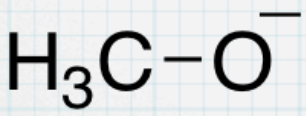
OH^- CH_3COO^-

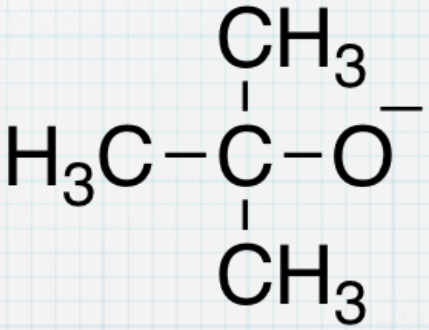
Same element? Charged > no charge

OH^- H_2O

Exception to Basicity/ Nucleophilicity Trends

Sterics: Size matters!





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

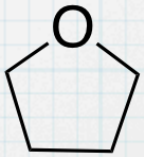
Polar Protic: solvents capable of hydrogen bonding

H_2O MeOH

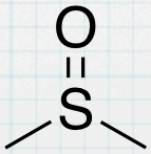
EtOH

Polar Aprotic: solvents not capable of hydrogen bonding

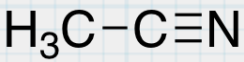
acetone



tetrahydrofuran (THF)



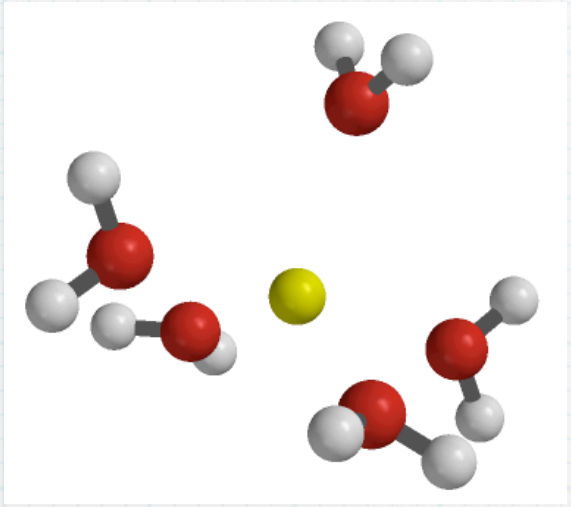
dimethyl sulfoxide (DMSO)



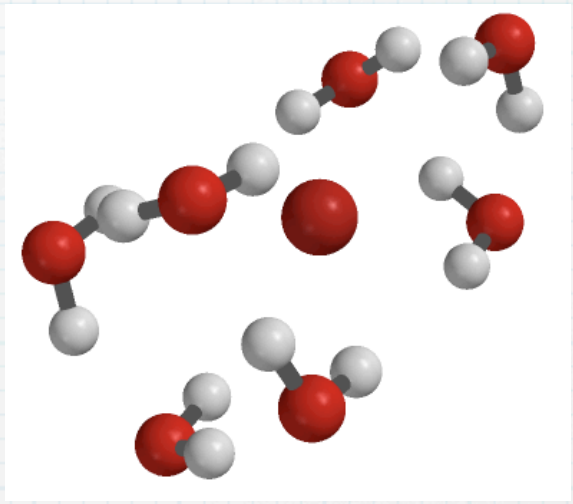
acetonitrile

Polar Protic Solvents & Nucleophilicity

* Nucleophilicity depends on solvent



Na^+ solvated

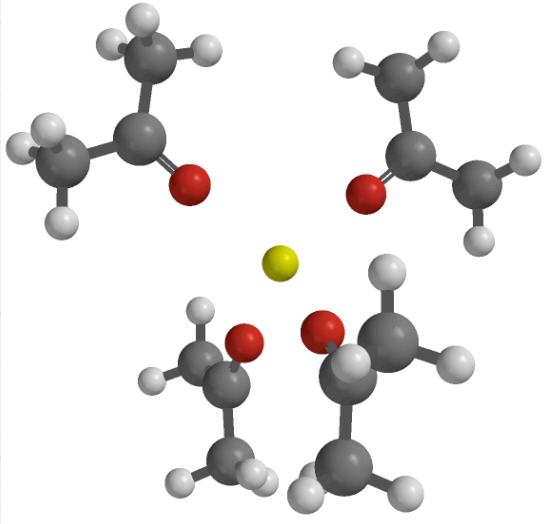


Br^- somewhat solvated

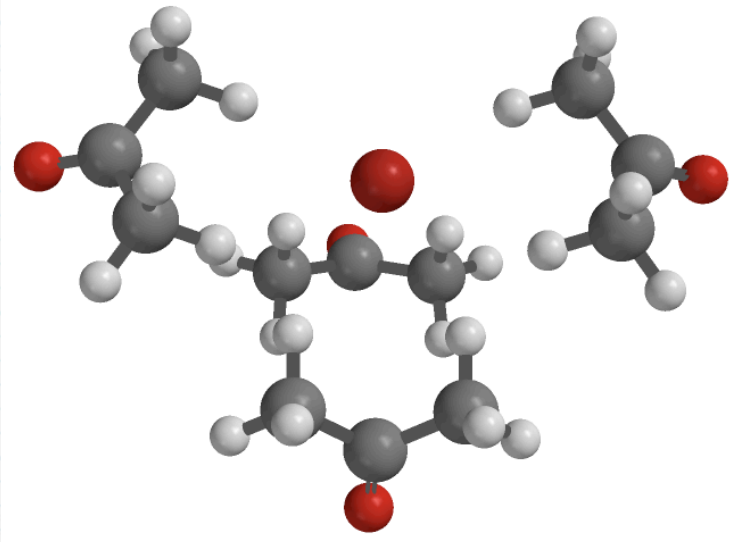
Smaller nucleophiles more tightly solvated = less nucleophilic

Polar Aprotic Solvents & Nucleophilicity

* Nucleophilicity depends on solvent



Na^+ solvated



Br^- not well solvated

Components Summary

- Electrophilic C = sp^3 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