c. Nucleophilicity / Nucleophilicity
- looking at how fast a Lewis base displaces a LG. (Kinetics)

very good: \( \text{I}^- \), \( \text{HS}^- \), \( \text{CN}^- \)

Good: \( \text{Br}^- \), \( \text{OH}^- \) or \( \text{ON}_3^- \)

Fair: \( \text{NH}_3 \), \( \text{Cl}^- \), \( \text{Fe}^- \), \( \text{RCO}_2^- \)

Weak: \( \text{H}_2\text{O} \), \( \text{ROH} \)

Very Weak: \( \text{RCO}_2\text{H} \)

In general, anions are better nucleophiles than neutral molecules

*There is no direct connection between nucleophilicity and basicity.*
However:

1. So long as the nucleophilic atom is the same, the more basic one is better (anions > neutral)

   $\text{RO}^\ominus > \text{HO}^\ominus \gg \text{RCO}_2^\ominus > \text{ROH} > \text{H}_2\text{O}$

2. When going along a row on the periodic table, the more basic one is better.

   $\text{HO}^\ominus > \text{F}^\ominus \quad \text{NH}_3 > \text{H}_2\text{O}$

3. When going down a column on the periodic table, the connection doesn't work.

   $1^\ominus$ - least basic
   $7^\ominus$ - most nucleophilic

Also: polarizability is important. The more polarizable the $e^\prime$ cloud, the more the
bond is formed @ long distances +
the faster the ren.

Nucleophilicity: measured by relative rates
of ren - kinetic

Basicity (think pka): measured by the
position of an equilibrium - thermodynamics

d. Solvent effects
   polar vs nonpolar
     protic vs aprotic

   nonpolar: hexane, CCl₄
   polar protic: H₂O, CH₃OH, CH₃COOH
   polar aprotic: acetone, DMF, DMSO

protic - has a proton on an
  e'neg atom
  (can H-bond w/ itself)
DMF: Dimethyl formamide \( \text{CH}_3\text{-N}\text{-H} \)

DMSO: Dimethyl sulfoxide \( \text{CH}_3\text{-S}\text{-CH}_3 \)

Acetone: \( \text{CH}_3\text{-CH}_3 \)

SN1 runs go best in polar protic solvents.

(Solvolyis: solvent is the nucleophile)

Polar protic solvents can solvate anions and cations. Sometimes referred to as “ionizing” solvents—encourage ionization because stabilize both products.

Cations: Dipole-Dipole interactions.

\[
\begin{array}{c}
+ \\
+ \\
- \\
+ \\
\end{array}
\quad \Rightarrow 
\begin{array}{c}
+ \\
- \\
\end{array}
\quad \begin{array}{c}
\text{CH}_3\text{OH} \\
+ \\
- \\
+ \\
\end{array}
\]
anions: H-bonding

\( \text{CH}_3 - \text{H} \cdots \text{O} \cdots \text{H-OC}_2 \text{H}_3 \)

SN2 rens go better in polar aprotic solvents.

*Note - that doesn’t mean that they don’t work in polar protic solvents!

Why? Polar aprotic solvent will solvate the cation but not the anion. (No H-bonding) - whereas a polar protic solvent will effectively “blanket” the anion/nucleophile, a polar aprotic one doesn’t \( \Rightarrow \) a “naked nucleophile”.
Therefore the nucleophile has a much easier time getting at the LE in polar aprotic solvent.

**Note:** nucleophilicity changes in polar aprotic solvents.

In DMSO: \( F > Cl > Br > I \)

Usual combinations:

\[
\begin{align*}
  & CH_3OH / CH_3COONa \\
  & EtOH / EtOONa \\
  & HOH / HOOna
\end{align*}
\]
Summary:

<table>
<thead>
<tr>
<th></th>
<th>$\text{SN}_1$</th>
<th>$\text{SN}_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Substrate</strong></td>
<td>$3^0 &gt; 2^0 &gt;&gt; 1^0 &gt; \text{H}^+$ <em>cation stability</em></td>
<td>$\text{CH}_3 &gt; 1^0 &gt; 2^0 &gt;&gt; 3^0$ <em>stereics</em></td>
</tr>
<tr>
<td><strong>Nu</strong></td>
<td>weak (neutral molecules, can be solvent)</td>
<td>strong (amines, high concs. of $\text{Nu}$ preferred)</td>
</tr>
<tr>
<td><strong>Solvent</strong></td>
<td>polar protic</td>
<td>polar aprotic</td>
</tr>
<tr>
<td><strong>LG</strong></td>
<td>$I &gt; \text{Br} &gt; \text{Cl} &gt; \text{F}$</td>
<td>same</td>
</tr>
</tbody>
</table>

**SN$_1$**

- Br
- NaCN
- DMSO

**SN$_2$**

- Br
- CH$_3$OH
- H$_3$O$^+$
- HOCH$_3$
SN2 - used for functional group transformation.

\[ \text{Na}^+ \text{I} \xrightarrow{\text{acetone}} R-I \]  
* works because NaI is soluble in acetone but NaCl / NaBr aren't.

R-Br

\[ \xrightarrow{\text{OH}} \]  
R-OH

\[ \xrightarrow{\text{OR}} \]  
R-OR'

\[ \xrightarrow{\text{SH}} \]  
R-SH

\[ \xrightarrow{\text{CN}} \]  
R-CN

\[ \xrightarrow{\text{C=C-R'}} \]  
R-\equiv\text{C-R'}

\[ \xrightarrow{\text{N_3}} \]  
R-N_3

\[ \xrightarrow{\text{OR}} \]  
R-OR

\[ \text{* can't be done w/ 3° RX / aryl / vinylic} \]