Recall: Nucleophilic Substitution or Elimination - potentially competing reaction pathways

\[
\text{ex: } \text{CH}_3\text{CH}_2\text{O}^-\text{Na}^+ + \text{H}_2\text{C}^-\text{CH}_2\text{CH}_3 \rightarrow \text{H}_3\text{C}^-\text{C}^-\text{H}_2\text{CH}_3 + \text{H}_2\text{C}^-\text{C}^=\text{CH}_2\text{CH}_3 \\
\text{(2°)} \quad \text{OCH}_2\text{CH}_3 + \text{Na}^+\text{Br}^- = \text{CH}_3\text{CH}_2\text{OH}
\]

A closer look... substitution...

\[
\text{CH}_3\text{CH}_2\text{O}^-\text{Na}^+ + \text{CH}_3\text{I} \rightarrow \text{CH}_3\text{CH}_2\text{OCH}_3 \\
\text{(+ NaI)}
\]

- can't eliminate
- no β H to pull off

Examine rates of reaction, varying concentrations of reactants. Allows us to formulate a rate law:

\[
\text{reaction rate} = k [\text{CH}_3\text{CH}_2\text{ONa}] [\text{CH}_3\text{I}]
\]

"rate constant"

Thus,
- reaction is 2nd order, overall (rate depends on conc. of 2 species)
- reaction is 1st order in \( \text{CH}_3\text{CH}_2\text{ONa} \) and also 1st order in \( \text{CH}_3\text{I} \) (1 molecular equivalent of each is involved in the rate-determining step)

Designation: \( \text{SN}_2 \)

2nd order, overall

nucleophilic

Interpretation of rate law: 1 molecule of each reactant is involved in the rate determining step or transition state.

Consistent with mechanistic hypothesis for the SN2 reaction:

\[
\text{CH}_3\text{CH}_2\text{O}^-\text{Na}^+ + \text{H}_2\text{C}^-\text{CH}_2\text{CH}_3 \rightarrow \left[ \text{CH}_3\text{CH}_2\text{O}^-\text{H} \right] \\
\text{(+ NaI)} \rightarrow \text{CH}_3\text{CH}_2\text{OCH}_3
\]
Recall: Analogy between nucleophilic substitution & Bronsted acid-base reactivity (Ch 3)

Consider rate differences:
\[ \text{CH}_3\text{CH}_2\text{O}^- + \text{H}_2\text{I} \rightarrow \text{CH}_3\text{CH}_2\text{O}^- + \text{H}_2\text{I} \]
\[ \text{CH}_3\text{CH}_2\text{O}^- + \text{H}_2\text{I} \rightarrow \text{CH}_3\text{CH}_2\text{I} \]

Steric Effects
- getting past 3 Hs to get to C is much more difficult than just getting to H or HI (useful calibration point)

Stereochemical analysis: requires a s.m. (in this, alkyl halide) w/ "steric chemical information"

\[ \text{(S)} \quad \text{NaBr} \quad \text{configuration has been inverted?} \]

"Backside attack" of nucleophile on electrophile
\[ \text{NECl} + \text{C} - \text{Br} \rightarrow \text{NECl} - \text{C} - \text{Br} \]

From molecular orbital considerations:
- putting e\(^-\) into \(\sigma^*\) orbital
- \(\sigma^*\) orbital empty
- \(\sigma^*\) orbital on C on 
- \(\sigma^*\) orbital on C
- putting e\(^-\) into \(\sigma^*\) weakens/breaks
- reaction starts by putting e\(^-\) into \(\sigma^*\), forming C-C bond while C-Br bond breaks
- only possible if backside attack occurs

Many factors can influence SN2 reactivity
- structure of electrophile (alkyl halide)
  \[ \Rightarrow \text{steric effects} \]
- nucleophilic reactivity
- solvent (solution of nucleophile - how does solvent interact w/ nucleophile?)
- leaving group (e.g. \(\text{Br}^\ominus\))
Submit a Single-sided Copy to the Office
DO NOT STAPLE

1) Alkyl halide structure (from Table 9.3) reaction:

\[
\begin{align*}
\text{S. M.} & \quad \text{reaction rate} \\
\text{CH}_3\text{Br} & \quad 145 \\
\text{CH}_3\text{CH}_2\text{Br} & \quad 1.0 \text{ point of comparison} \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{Br} & \quad 0.8 \\
\text{CH}_3\text{C} & \quad 0.008 \\
\text{CH}_3\text{C} & \quad \sim 0 \\
\text{CH}_3\text{C} & \quad \sim 0
\end{align*}
\]

* 3º alkyl halides do not react via an S_N2 mechanism!* 

Thus, in general for the S_N2 mechanism:
- methyl > 1º > 2º (3º unreactive)
- adding bulk away from substitution site usually not important

exception:
\[\begin{align*}
\text{CH}_3\text{Br} & \quad \text{very slow} \\
\text{"necophenyl bromide"}
\end{align*}\]