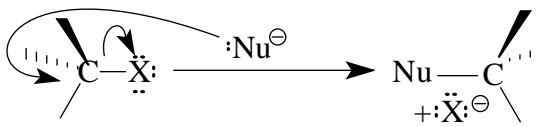
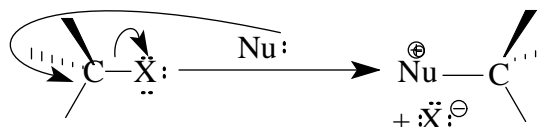
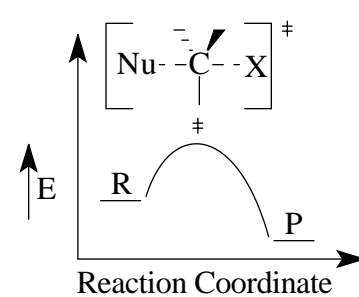
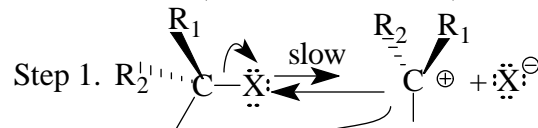
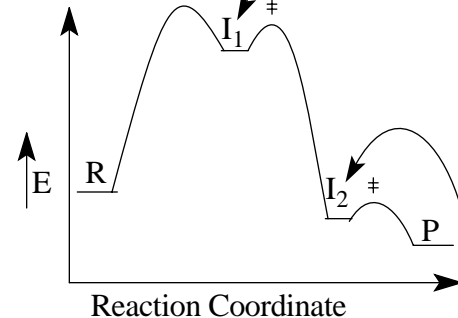
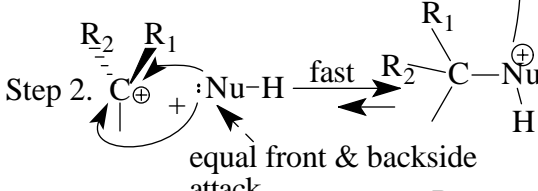
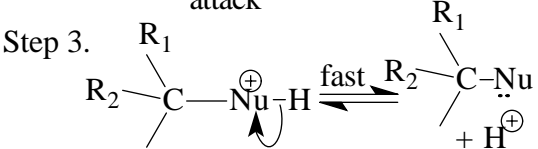


SUBSTITUTION REACTION CHARACTERISTICS	Chemistry 118A Workshop Jim Hollister, Doug Kent, Rolf Unterleitner Learning Skills Center; UC Davis
S_N2: Substitution Nucleophilic, Bimolecular: Characteristics	S_N1: Substitution Nucleophilic, Unimolecular: Characteristics
1) The 2 means Bimolecular (or 2 nd order) in the rate-determining (slow) step: rate = k [Nu: ⁻] [R-X] or rate = k [Nu:] [R-X] if the Nu is neutral.	1) The 1 means Unimolecular (or 1 st order) in the rate-determining (slow) step: rate = k [R-X]. The Nu is not in the rate law.
2) S _N 2 reactions are One Step and Concerted (<i>Concerted</i> means bond making and breaking at the same time):  <p>If the nucleophile is neutral;</p>  	2) Two (or Three) Steps: Step 1. Dissociation of halide from haloalkane. (I ₁ = Intermediate 1)   <p>Step 2. Nucleophilic Attack forms Intermediate 2 (I₂).</p>  <p>Step 3. Deprotonation step forms the Product.</p> 
3) There is a Transition State (TS) but no Intermediate (The symbol ‡ indicates a TS) (See above).	3) Has Intermediate Carbocation (sp ² carbon) and Transition States (See above).

<p>4) Backside Attack- get Inversion (and, if the electrophilic carbon is chiral, usually get a change in absolute configuration, as from R to S, but not necessarily, because it depends on the priorities of the attaching nucleophile and the leaving group relative to the other groups attached to the chiral carbon.)</p>	<p>4) Equal Front and Backside Attack; not stereospecific; if start with chiral carbon, get racemic mixture.</p>
<p>5) Enhanced by aprotic polar solvents which make the nucleophile unhindered, or "naked."</p>	<p>5) Enhanced by protic, polar solvents, as H₂O, R-O-H, and small carboxylic acids, which stabilize the carbocation by H bonding.</p>
<p>6) Sensitive to steric hindrance.</p>	<p>6) Solvolysis: Solvents as H₂O, R-O-H, and small carboxylic acids, can act as nucleophiles.</p>
<p>7) Occurs in methyl > 1° > 2° haloalkanes substrates. Reacts best in order indicated.</p>	<p>7) Occurs best in 3° haloalkanes substrates and slowly in 2° haloalkanes.</p>

Four Factors For Finding Products of Sn1, Sn2, E1 & E2

1) Substrate

Steric Hindrance: The more groups around the reactive center (the C with the leaving group), the harder it is to get to, therefore the less reactive via S_N2 .

Order of Steric hindrance; methyl < 1° < 2° < 3°
Order of reactivity via S_N2 ; methyl > 1° > 2° > 3°

Carbocation stability: The more alkane groups around a reactive center (the C with the leaving group), the more stable it will be.

Order of stability of carbocations; 3° > 2° > 1° > methyl
Order of reactivity via S_N1 ; 3° > 2° > 1° > methyl

2) Nucleophile

A) 3 Trends

1) nucleophilicity (and basicity) increase with incr. neg. charge.

e.g. $\text{OH}^- > \text{H}_2\text{O}$; $\text{NH}_2^- > \text{NH}_3$; $\text{SH}^- > \text{SH}_2$; $\text{Cl}^- > \text{HCl}$

2) Nucleophilicity (and basicity) decr. within a period from left to right

e.g. $\text{NH}_3 > \text{H}_2\text{O} > \text{FH}$; $\text{CH}_3^- > \text{NH}_2^- > \text{OH}^- > \text{F}^-$ (note: no CH_4 in the first group because if you don't have any lone pairs, it isn't nucleophilic or basic).

3) Nucleophilicity incr., but basicity decr., as you go down the periodic table within a group e.g. $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$; $\text{H}_2\text{Se} > \text{H}_2\text{S} > \text{H}_2\text{O}, \text{HSe}^- > \text{HS}^- > \text{OH}^-$ (trend 3 due to polarizability: bigger p orbitals can reach out better than smaller ones, 4p is bigger than 3p)* in protic solvents, due in large part to solvation.

In aprotic solvents the trend for halogens is the same as basicity $\text{F}^- > \text{Cl}^- > \text{Br}^- > \text{I}^-$.

B) General Rules

1) Strong bases are usually good nucleophiles (trends 1 and 2 above), but always look out for E2 with all strong base nuc.'s especially with "bulky ones" like $\text{OC}(\text{CH}_3)_3$.

2) Weak bases can be good nuc.'s if they have big p orbitals (trend 3 above)

3) Leaving Group

The more stable it is by itself, the better it is as a leaving group

1) Weak bases are good leaving groups (strong bases are bad)

2) Halogens: $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$ (F^- is a poor leaving group)
weakest base, best leaving group

3) Strong bases (OH^- , RO^-) can be made into a good leaving groups (H_2O , ROH) by adding a strong acid.

4) If the negative charge can be delocalized, the ion will be more stable, therefore, it will be a better leaving group (RSO_3^- ; $\text{CH}_3\text{-C}_6\text{H}_4\text{-SO}_3^-$)

4) Solvent

Polar like polar: If you have a polar, or a charged species or intermediate, then you need a polar solvent which will help stabilize these species.

Polar protic (have H-bonding) (H_2O , ROH ...): Lowers the reactivity of the nuc. because of H-bonding to nuc., so it is bad for S_N2 . Stabilizes carbocation intermediates, so it is good for S_N1 .

Polar aprotic (have NO H-bonding) (acetone, DMSO, HMPA...): Leaves nucleophiles naked and ready to react, also helps to stabilize reactants so it is good for S_N2 .

S_n2 substitution rxnsFactors favoring S_n2

- 1) **Substrate:** methyl > 1° > 2° (never 3°)
Can't have things in the way or the nucleophile won't make it in.
- 2) **Good nucleophile needed** Nuc. has to go after the reactive center or no rxn.
- 3) The substrate needs to have a **good leaving group**. Good LG's are very weak bases which can accommodate their negative charge by high electronegativity &/or delocalization.
- 4) **Best with aprotic polar solvents**
They leave the nuc. free to react, and help to stabilize the polar species.

Mechanism: Backside attack. In the transition state, the nucleophile is coming in as the leaving group is coming off. Inversion changes R/S configurations most of the time.

E2 Elimination rxns

Factors favoring E2

- 1) **Nucleophile** □ strong bases The nuc. acts like what it is, a strong base. It tears a □-H off a □-carbon, which is next to the carbon with the leaving group on the substrate (called the □-carbon).
- 2) **Needs a good leaving group** in anti-position to a neighboring □-hydrogen. When the □-H is being removed, the leaving group needs to be free to come off. A double bond forms.
- 3) **Solvent** is often the conjugate acid of basic nuc., as NaOH in H₂O (but could also be in CH₃OH), CH₃CH₂O⁻K⁺ in CH₃CH₂OH, etc. (Strong bases are looking for H's. You need the base to remove the H's from the substrate and not the solvent).
- 4) **Substrate** not as important, but they should not be methyl and 1° unbranched (which with small, strong bases will favor S_n2 product). Needs a leaving group, which is anti to the □-H being removed.

Mechanism: Anti-elimination. Base removes a □-H 180° to leaving group on neighboring carbon.

S_n1 substitution rxnsFactors favoring S_n1

- 1) **Substrate:** 3° > 2° (never 1° and methyl) More alkyl groups help to stabilize the carbocation intermediate.
- 2) The substrate needs to have a **good leaving group (LG)**. To fall off and leave a carbocation behind, the LG has to be stable on its own. Good LG's are very weak bases which can accommodate their negative charge by high electronegativity &/or delocalization [as I⁻, or RSO₄⁻ (sulfates) or RSO₃⁻ (.sulfonates)]
- 3) Works with **poor nucleophiles** as H₂O or ROH). Once the carbocation is formed in the rate determining step, it is very, very reactive; anything with a lone pair will do.
- 4) **Best with aprotic polar solvents.** The carbocation is a charged (+1) species, so polar solvents help stabilize it (H-bonds).

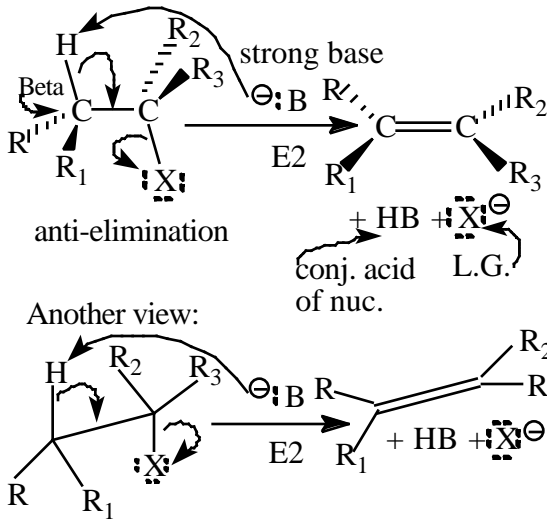
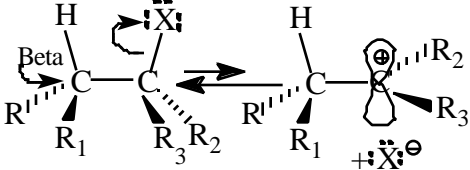
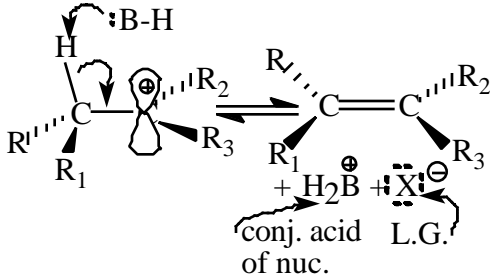
Mechanism: Carbocation intermediate. You get a mixture of both R and S. Beware of rearrangements.

E1 Elimination rxns

Factors favoring E1

- 1) **Substrate** 3° > 2° (never 1° and methyl) More alkyl groups help to stabilize the carbocation intermediate.
- 2) The substrate needs to have a **good leaving group (LG)**. To fall off and leave a carbocation behind, the LG has to be stable on its own (needs to accommodate its negative charge by high electronegativity &/or delocalization [as I⁻, or RSO₄⁻, or RSO₃⁻ (sulfonates)])
- 3) **Best with aprotic polar solvents** As with S_n1, the carbocation is a charged (+1) species; polar solvents help stabilize it.
- 4) **Poor nucleophiles** as H₂O or ROH.

Mechanism: Carbocation intermediate. The product that comes from the most substituted (most alkyl groups around it) carbocation is usually the major product. Beware of rearrangements too.

<p>ELIMINATION REACTIONS FORM ALKENES.</p> <p>THEY ARE FAVORED BY STERICALLY HINDERED MOLECULES, EITHER HALOALKANES, NUCLEOPHILES, OR BOTH.</p>	<p>Chemistry 118A Workshop</p> <p>Jim Hollister, Doug Kent, Rolf Unterleitner Learning Skills Center; UC Davis</p>
<p>E2: Elimination, Bimolecular: Characteristics</p>	<p>E1: Elimination, Unimolecular: Characteristics</p>
<p>1) The 2 means Bimolecular (or 2nd order) in the rate-determining (slow) step: rate = k [Nu:-] [R-X] or rate = k [Nu:] [R-X] if the Nu is neutral.</p>	<p>1) The 1 means Unimolecular (or 1st order) in the rate-determining (slow) step: rate = k [R-X]. The Nu is not in the rate law.</p>
<p>2) E2 reactions are One Step Concerted Acid/Base reaction with elimination of the LG: (Acid/Base reactions happen faster than nucleophilic/electrophilic reactions.) Alkene forms.</p>  <p>The diagram shows two views of the E2 mechanism. In the first, a strong base (B:) attacks a beta-hydrogen (H) on a carbon atom bonded to a leaving group (X). Simultaneously, the C-H bond electrons move to form a C=C double bond, and the C-X bond breaks, releasing the leaving group (X-). The products are an alkene, a conjugate acid (HB), and the leaving group (X-). The transition state is shown with partial bonds and partial negative charge on the base. The second view shows the same reaction from a different perspective, emphasizing the anti-periplanar arrangement of the H and X groups.</p> <p>anti-elimination</p> <p>Another view:</p>	<p>2) E1 reactions are Two Steps: Alkene forms.</p> <p>Step 1. Dissociation of halide</p>  <p>The diagram shows a haloalkane dissociating into a carbocation intermediate and a halide ion (X-). The carbocation is shown with a positive charge on the carbon atom and a p-orbital lobe.</p> <p>Step 2. Acid/Base Reaction. A poor nuc. acts as a base to remove the acidic H. Alkene forms.</p>  <p>The diagram shows a base (B-H) removing a beta-hydrogen from the carbocation intermediate. The electrons from the C-H bond move to form a C=C double bond, and the C-X bond breaks, releasing the leaving group (X-). The products are an alkene, a conjugate acid (H2B+), and the leaving group (X-).</p>
<p>3) Concerted Mechanism-No Intermediate</p>	<p>3) Carbocation Intermediate</p>
<p>4) Anti-Elimination: The base takes the H of the TS which is in anti-conformation (180°) to the Leaving Group (LG). (The carbon with the LG on it is called the carbon and the carbon(s) with the acidic H on it is called the carbon.).</p>	<p>4) The H is removed from the Carbocation Intermediate in the second step (the LG left when the intermediate was formed by dissociation in the first step. Therefore, the LG and the acidic H are not in anti-conformation.)</p>

<p>5) Enhanced by sterically hindered, strongly basic nucleophiles as LDA or tert-butoxide.</p>	<p>5) E1 product usually seen as a minor product along with a major S_N1 product; the solvent, usually H₂O or an R-O-H, acts as a base to deprotonate the carbocation. (E1 can be a minor product with a major E2 also, but do not worry about this.)</p>
<p>6) Can have more than one type of alkene product if the haloalkane has more than one different type of carbon with H's on them. (Chapter 11 in Vollhardt and Schore)</p>	<p>6) Same as E2.</p>
<p>7) Occurs with 2° and 3° haloalkanes and 1° haloalkanes branched near the α carbon.</p>	<p>7) Best with 3° haloalkanes.</p>

