

## Alkyl Halides

**Reading:** Wade chapter 6, sections 6-13- 6-21

**Study Problems:** 6-45, 6-49, 6-51, 6-52, 6-60, 6-61, 6-66

### **Key Concepts and Skills:**

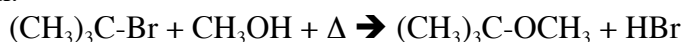
- Predict the products of SN1, E2, and E1 reactions, including stereochemistry
- Draw mechanisms and energy profiles of SN1, E1, and E2 reactions.
- Predict the predominance of substitution or elimination; use the Saytzeff rule to predict major and minor elimination products.

### **Lecture Topics:**

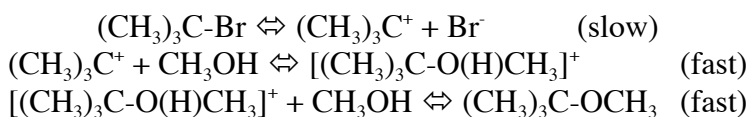
#### **I. SN1 reaction**

##### **Unimolecular Nucleophilic Substitution SN1**

Also referred to as a solvolysis reaction, is a first-order process in which the rate does not depend on the concentration of the nucleophile. The reaction takes place under non-basic conditions (frequently performed under acidic conditions). The SN1 reaction is a multistep process, the rate-determining step of which is ionization of the alkyl halide to form a carbocation.



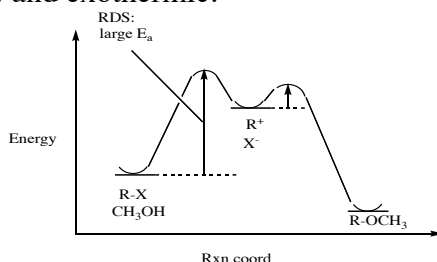
Mechanism:



Because of the formation of an **intermediate** carbocation, the rate of the SN1 reaction is proportional to the halide substitution:  $3^\circ > 2^\circ > 1^\circ > \text{CH}_3\text{X}$ , since tertiary carbocations are more stable than secondary, which are more stable than primary. The kinetics of this reaction are first order:  $\text{rate} = k[(\text{CH}_3)_3\text{C-Br}]$

Note that the nucleophile is not involved in the rate-determining step

The ionization step is highly endothermic and slow (large  $E_a$ ), whereas reaction of the carbocation is fast (low  $E_a$ ) and exothermic:



Since the RDS is endothermic, the transition state for the RDS resembles the intermediate carbocation in both structure and energy, thus the rates of SN1 reactions depends strongly on intermediate carbocation stability. Resonance stabilization (as available when allylic halides ionize to form allylic cations) also promotes the SN1 reaction.

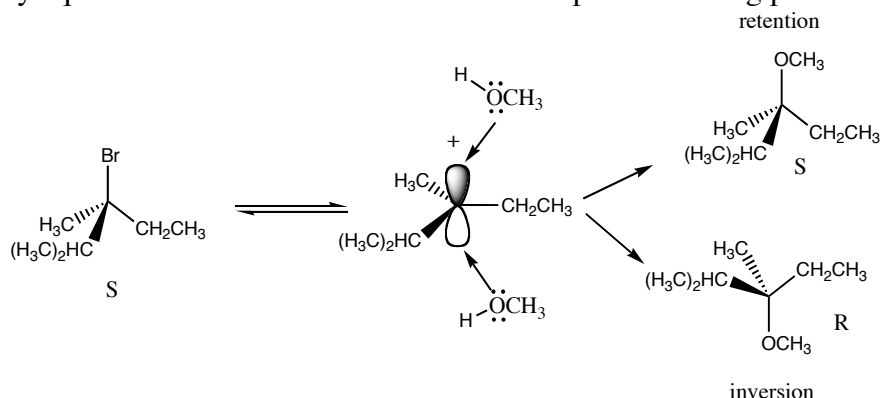
#### **II. Effect of solvent, leaving group on the rate of the SN1 reaction**

- As for SN2 reactions, the leaving group must be highly polarizable and a weak base; it must be able to stabilize a negative charge

- The solvent for SN1 reactions must be polar and have a high dielectric constant so as to assist ionization (water, CH<sub>3</sub>OH, CH<sub>3</sub>CH<sub>2</sub>OH). Hydrogen-bonding solvents can strongly stabilize both the intermediate carbocation and the halide leaving group

### III. Stereochemistry of the SN1 reaction

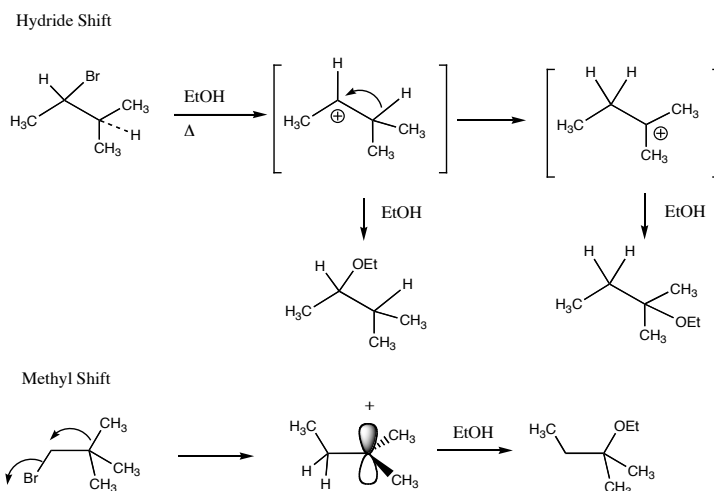
- Note that the intermediate carbocation is planar, and attack by nucleophiles can occur from either face of that carbocation. As a result, we might expect racemization to occur, with roughly equal amounts of retention and inversion products being produced:



In practice, generally more inversion products than retention products are obtained because the exiting leaving group blocks one face of the carbocation as a tight ion pair.

### IV. Rearrangements of Carbocations

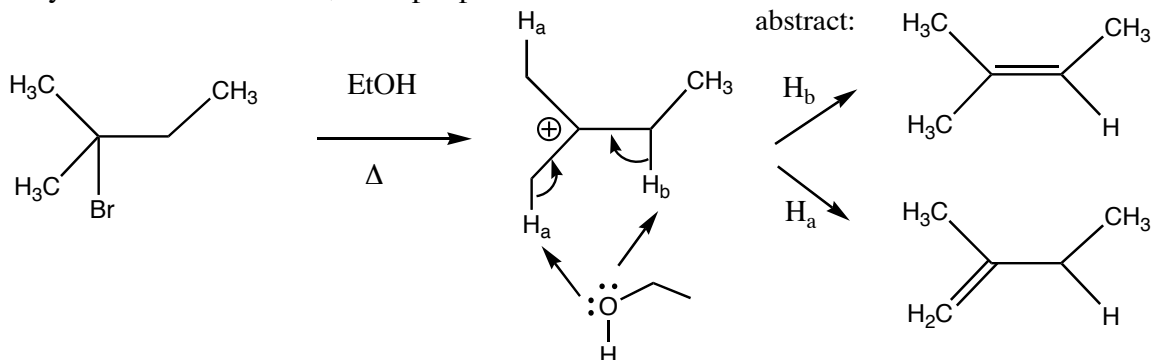
- Carbocation intermediates may undergo rearrangements to form more stable carbocations: two possibilities are hydride shift and methyl shift. Usually the driving force for these processes is the formation of a more stable 3° carbocation intermediate.



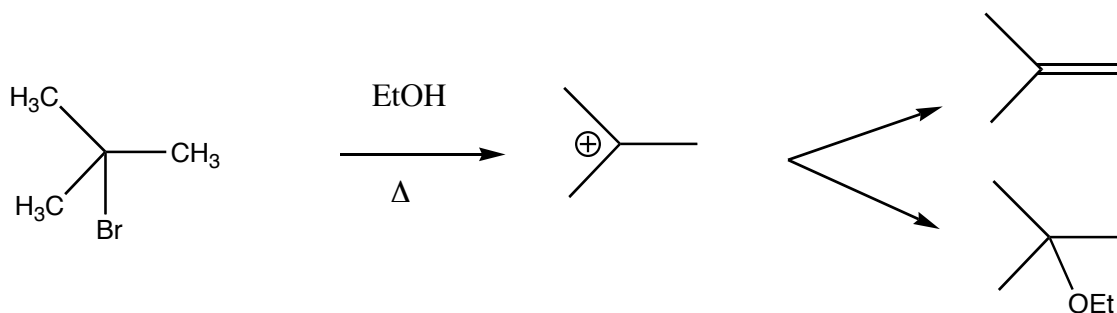
### V. Elimination reactions and the Synthesis of Alkenes

E1 is a unimolecular elimination reaction and E2 is bimolecular elimination reaction; in both cases the elements of H-X are removed from an alkyl halide and a new pi bond is formed in their place.

•The E1 reaction has the same slow step as the SN1 reaction → a rate-limiting ionization step to produce an intermediate carbocation. Thus, the rates of E1 reactions parallel carbocation stability orders:  $3^\circ > 2^\circ > 1^\circ$ . The fast second step is proton abstraction from an adjacent carbon atom. Again, first-order conditions assumes non-basic conditions. In unsymmetrical substrates, multiple products can be formed:



• Frequently competitive E1 and SN1 reactions (under first-order conditions) may be observed, that is, both substitution and elimination products may be formed in a given reaction.



•In summary, carbocations are formed under neutral, non-basic conditions  
 -they can react with a nucleophile to form a substitution product  
 -they can lose a proton to form an elimination product  
 -they can rearrange to a more stable carbocation before undergoing substitution or elimination.

## VI. E2 elimination reaction

Like the SN2 reaction, occurs best under basic conditions. It is a second-order process requiring a strong base.

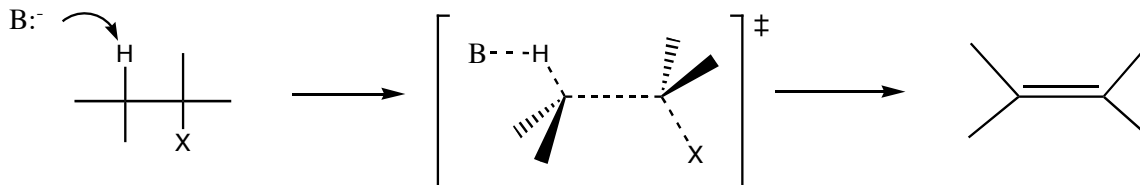


$$\text{rate} = k [(\text{CH}_3)_3\text{C-Br}] [\text{CH}_3\text{O}^-]$$

•Under basic conditions, proton abstraction is faster than ionization to form the carbocation.

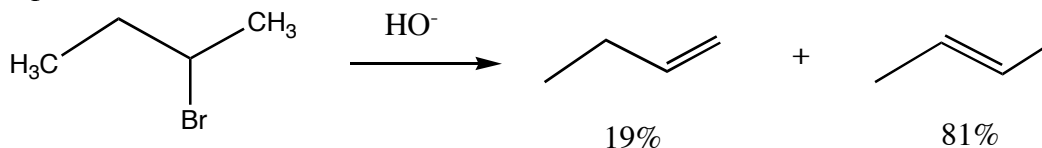
- SN2 reaction is blocked by steric hindrance, since the best alkyl halide substrates for E2 are  $3^\circ > 2^\circ > 1^\circ$ .

- E2 reaction is a single-step mechanism with no intermediates:

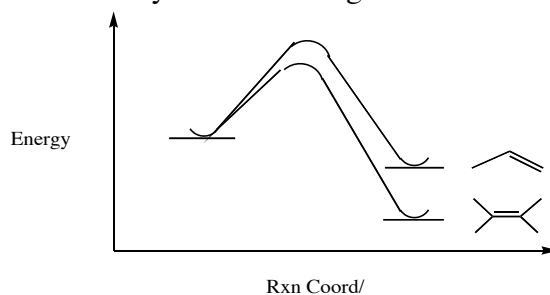


- Mixtures of products may result when more than one kind of proton is available for abstraction by base. To predict which alkene will predominate, when mixtures are possible, we use the **Saytzeff rule**: *in elimination reactions, the most highly substituted alkene predominates*. The reason for this is that more highly substituted alkenes are more stable:  $R_2C=CR_2 > R_2C=CHR > RHC=CRH$  (and  $R_2C=CH_2$ )  $> H_2C=CH_2$

Example:

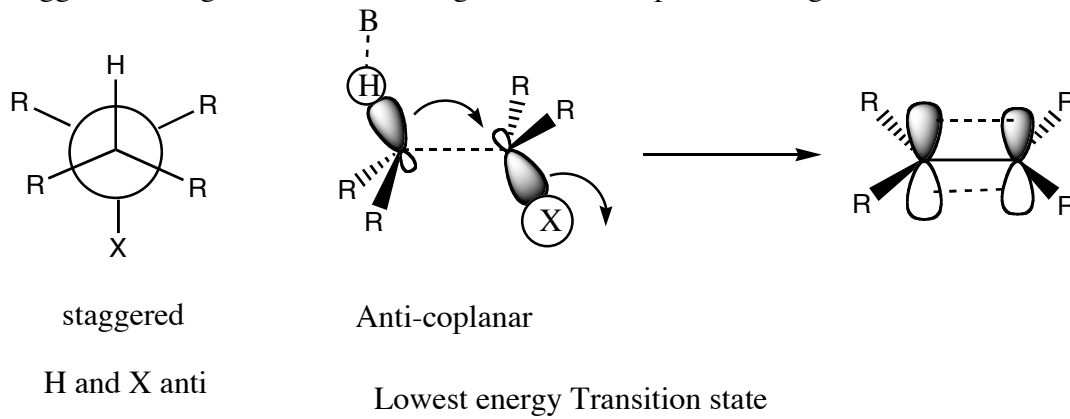


- The reactivity order of alkyl halides toward E2 elimination is the same as for E1 eliminations, since product stability effects the degree of exothermicity.

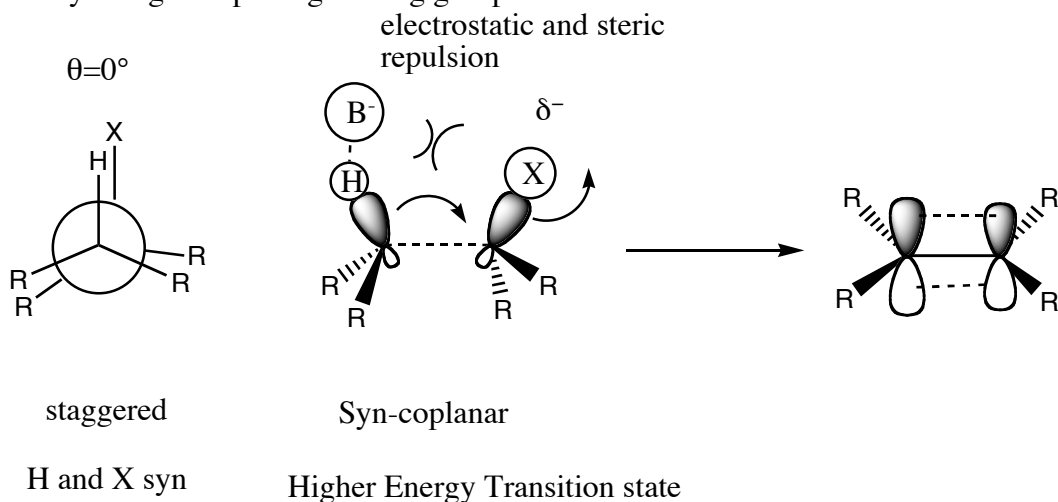


### Stereochemistry of E2 eliminations:

- A coplanar arrangement of orbitals is required in the transition state for the rate-limiting step: the C-H and C-X bonds must be either **syn-coplanar** or **anti-coplanar**. The staggered arrangement of H and X gives the anticoplanar arrangement:

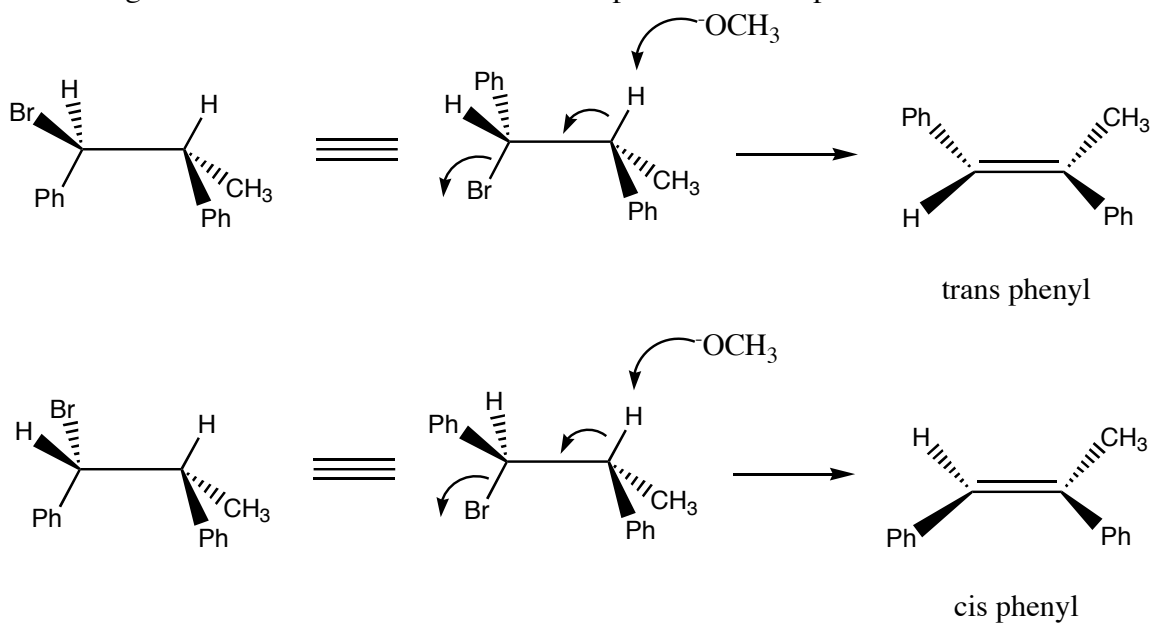


•The Syn-coplanar arrangement of orbitals in the transition state for E2 elimination is higher in energy than the anti-coplanar arrangement because of both steric and electrostatic repulsion between the negatively charged incoming base and the partially negatively charged departing leaving group.



high energy conformer

•The E2 reaction is stereospecific, just like the SN2 reaction: different stereoisomers of reactants give rise to different stereoisomers of products. Examples:



## Summary of Reactivity

	Basic conditions		Neutral/acidic conditions	
	<b>SN2</b>	<b>E2</b>	<b>SN1</b>	<b>E1</b>
Alkyl halide Reactivity	MeX>1°> 2°>3°	3°>2°>1°	3°>2°>1°	3°>2°>1°
Order	bimolecular	bimolecular	unimolecular	unimolecular
Stereochem.	Stereospecific Specific geometry required in T.S.	stereospecific	racemization common rearrangements common No geometry required	
Nu	strong nucleophile Required	strong base required	weak nucleophile ok	
Solvent:	polar aprotic	polar aprotic	good ionizing solvent Polar protic solvents best	

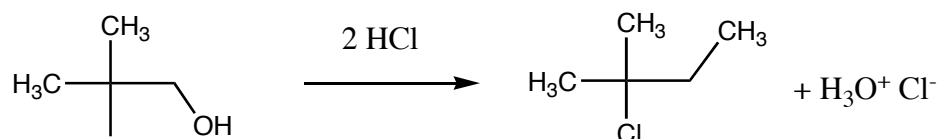
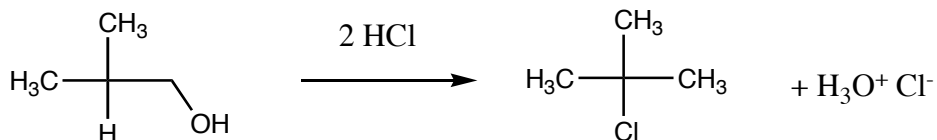
**3° halides** will never undergo SN2 reactions; they can undergo E1, SN1, or E2 reactions. Under basic conditions, the reaction will be E2. Under neutral/acidic conditions, E1 or SN1 reactions can take place.

**1° halides** rarely undergo SN1 or E1 reactions; the SN2 reaction is most common under basic conditions. E2 reaction will occur if a bulky base is employed

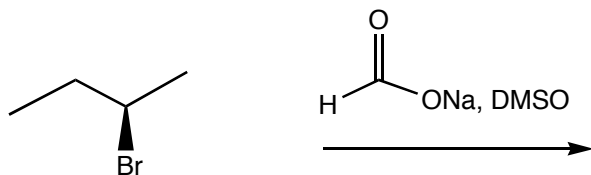
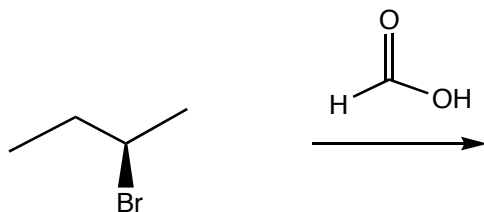
**2° halides** can undergo all types of substitution/elimination reactions; which predominates depends on conditions. Under basic conditions, SN2 reactions can occur when a good leaving group (I) is employed along with an unhindered strong nucleophile. Otherwise, E2 elimination is observed with 2° halides. Both SN1 and E1 reactions are possible under neutral/acidic conditions, and frequently mixtures of substitution and elimination products are obtained

Additional Problems for practice:

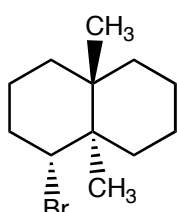
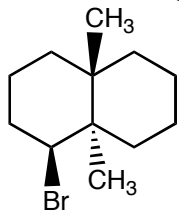
1. Draw a mechanism for each of the following reactions:



2. Two substitution reactions are shown below. Predicts the comparative stereochemical results of these two reactions:



3. One of the following molecules undergoes E2 reaction with  $\text{NaOCH}_3$  considerably faster than the other. Identify which is which and explain. Draw the product. Hint: draw the chair form of each.



4. Draw a mechanism and a qualitative potential energy diagram for the following reaction. Indicate the locations of the rate-determining and the product-determining transition states. Explain the ratio of alkenes observed.

