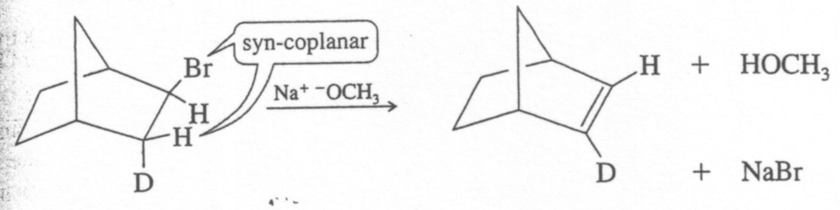
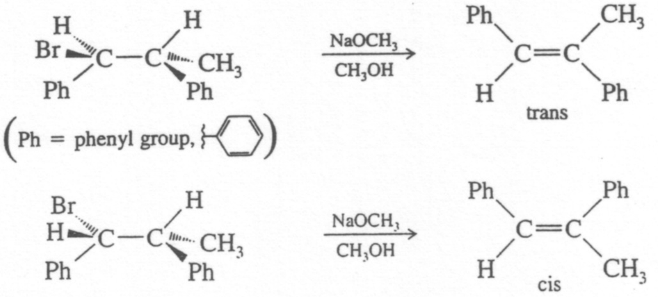


The E2 is a **stereospecific** reaction, because different stereoisomers of the starting material react to give different stereoisomers of the product. This stereospecificity results from the anti-coplanar transition state that is usually involved in the E2. We consider more of the implications of the anti-coplanar transition state in Chapter 7. For now, Problem 6-38 will give you an opportunity to build models and see how the stereochemistry of an E2 elimination converts different stereoisomers into different stereoisomers of the product.

PROBLEM 6-38

When the first compound shown below is treated with sodium methoxide, the only elimination product is the trans isomer. The second diastereomer (blue) gives only the cis product. Use your models and careful drawings of the transition states to explain these results.



PROBLEM-SOLVING HINT

Models are helpful whenever complex stereochemistry is involved.

6-21
Comparison of E1 and E2 Elimination Mechanisms

Let's summarize the major points to remember about the E1 and E2 reactions, concentrating on the factors that help us predict which of these mechanisms will operate under a given set of experimental conditions. Then we will organize these factors into a short table.

Effect of the Base The nature of the base is the single most important factor in determining whether an elimination will go by the E1 or E2 mechanism. If a strong base is present, the rate of the bimolecular reaction will be greater than the rate of ionization, and the E2 reaction will predominate (perhaps accompanied by the S_N2).

If no strong base is present, with a good solvent a unimolecular ionization is likely, followed by loss of a proton to a weak base such as the solvent. Under these conditions, the E1 reaction usually predominates (always accompanied by the S_N1).

E1:	Base strength is unimportant. (usually weak)
E2:	Strong bases are required.

Effect of the Solvent The slow step of the E1 reaction is the formation of two ions. Like the S_N1, the E1 reaction critically depends on polar ionizing solvents such as water and the alcohols.

In the E2 reaction, the transition state spreads out the negative charge of the base over the entire molecule. There is no more need for solvation in the E2 transition state than in the reactants. The E2 is therefore less sensitive to the solvent; in fact, some reagents are stronger bases in less polar solvents.

E1:	Good ionizing solvent required.
E2:	Solvent polarity is not so important.

Effect of the Substrate For both the E1 and the E2 reactions, the order of reactivity

E1, E2: 3° > 2° > 1° (1° usually will not go E1)

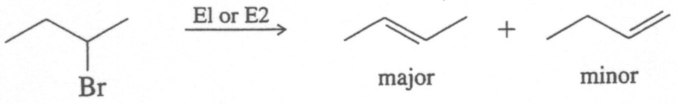
In the E1 reaction, the rate-limiting step is formation of a carbocation, and t reactivity order reflects the stability of carbocations. In the E2 reaction, the mc highly substituted halides generally form more highly substituted, more stab alkenes.

Kinetics The rate of the E1 reaction is proportional to the concentration of the all halide [RX] but not to the concentration of the base. It follows a first-order rate equati

The rate of the E2 reaction is proportional to the concentrations of both the all halide [RX] and the base $[B:^-]$. It follows a second-order rate equation.

$$\text{E1 rate} = k_r[\text{RX}]$$
$$\text{E2 rate} = k_r[\text{RX}][\text{B}:^-]$$

Orientation of Elimination In most E1 and E2 eliminations with two or more p sible products, the product with the most highly substituted double bond (the most s ble product) predominates. This principle is called the **Saytzeff rule**, and the m highly substituted product is called the **Saytzeff product**.



E1, E2: Usually Saytzeff orientation.

Stereochemistry The E1 reaction begins with an ionization to give a flat carbc tion. No particular geometry is required.

The E2 reaction takes place through a concerted mechanism that requires a co nar arrangement of the bonds to the atoms being eliminated. The transition state is u ally anti-coplanar, although it may be syn-coplanar in rigid systems.

E1: No particular geometry required for the slow step.
E2: Coplanar arrangement (usually anti) required for the transition st

Rearrangements The E1 reaction involves a carbocation intermediate. This ir mediate can rearrange, usually by the shift of a hydride or an alkyl group, to gi more stable carbocation.

The E2 reaction takes place in one step with no intermediates. No rearrangen is possible in the E2 reaction.

E1: Rearrangements are common.
E2: No rearrangements.

SUMMARY Elimination Reactions

	E1	*E2*
promoting factors		
base	weak bases work	strong base required
solvent	good ionizing solvent	wide variety of solvents
substrate	3° > 2°	3° > 2° > 1°
leaving group	good one required	good one required
characteristics		
kinetics	first order, k_r[RX]	second order, $k_r[\text{RX}][\text{B}:^-]$
orientation	most highly substituted alkene	most highly substituted alkene
stereochemistry	no special geometry	coplanar transition state required
rearrangements	common	impossible

PROBLEM-SOLVING STRATEGY
Predicting Substitutions and Eliminations

Given a set of reagents and solvents, how can we predict what products will result and which mechanisms will be involved? Should you memorize all this theory about substitutions and eliminations? Students sometimes feel overwhelmed at this point.

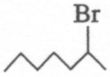
Memorizing is not the best way to approach this material because it is too much and there are too many factors. Besides, the real world with its real reagents and solvents is not as clean as our equations on paper. Most nucleophiles are also basic, and most bases are also nucleophilic. Most solvents can solvate ions or react as nucleophiles, or both. We will review the most important factors that determine the reaction pathway, organized in a sequence that allows you to predict as much as can be predicted.

The first principle you must understand is that *we cannot always predict one unique product or one unique mechanism*. Often, the best we can do is to eliminate some of the possibilities and make some good predictions. Remembering this limitation, here are some general guidelines:

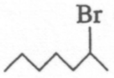
1. **The strength of the base or nucleophile determines the order of the reaction.**
If a strong nucleophile (or base) is present, it will force second-order kinetics: either S_N2 or E2. A strong nucleophile attacks the electrophilic carbon atom or abstracts a proton faster than the molecule can ionize for first-order reactions.

If no strong base or nucleophile is present, the fastest reaction will probably be a first-order reaction, either S_N1 or E1. Addition of silver salts to the reaction can force some kind of ionization.

This is the most important of these guidelines. Consider the following examples:



$\xrightarrow[\text{heat}]{CH_3OH}$ S_N1 and E1

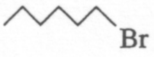


$\xrightarrow[CH_3OH]{NaOCH_3}$ S_N2 and E2

$(CH_3)_3C—Br \xrightarrow[CH_3OH]{NaOCH_3}$ E2 (no S_N2 on 3° carbon)

2. **Primary halides usually undergo the S_N2 reaction, occasionally the E2 reaction.**
Primary halides rarely undergo first-order reactions, since primary carbocations are rarely formed. With good nucleophiles, S_N2 substitution is usually observed. With a strong base, E2 elimination may also be observed.

Sometimes silver salts or high temperatures are used to force a primary halide to ionize, usually with rearrangement to give a more stable carbocation. In such a case, the rearranged S_N1 and E1 products may be observed.



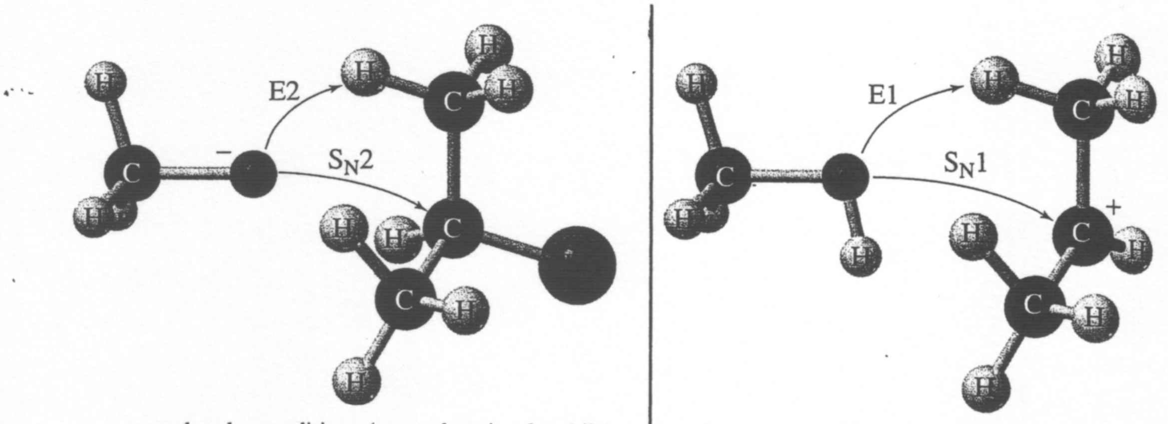
$\xrightarrow[CH_3OH]{NaOCH_3}$ S_N2 (and possibly E2)

$\xrightarrow[CH_3OH]{AgNO_3\text{, heat}}$ S_N1 and E1 (both with rearrangement)

3. **Tertiary halides usually undergo the E2 reaction (strong base) or a mixture of S_N1 and E1 (weak base).**
Tertiary halides cannot undergo the S_N2 reaction. A strong base forces second-order kinetics, resulting in elimination by the E2 mechanism. In the absence of a strong base, tertiary halides react by first-order processes, usually a mixture of S_N1 and E1. The specific reaction conditions determine the ratio of substitution to elimination.

$(CH_3)_3C—Br \xrightarrow[CH_3OH]{NaOCH_3}$ E2 (no S_N2 on 3° carbon)

$(CH_3)_3C—Br \xrightarrow[\text{heat}]{CH_3OH}$ S_N1 and E1

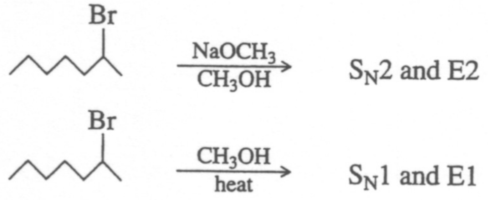


second-order conditions (strong base/nucleophile)

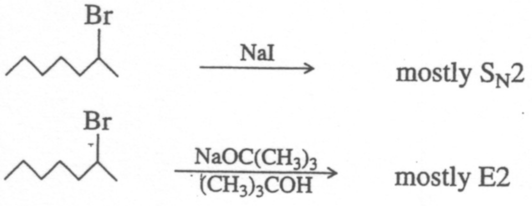
first-order conditions (weak base/nucleophile)

▲ Figure 6-14
Under second-order conditions (strong base/nucleophile), a secondary alkyl halide might undergo either substitution (S_N2) or elimination (E2). Under first-order conditions (weak base/nucleophile), S_N1 and E1 are possible.

4. **The reactions of secondary halides are the most difficult to predict.** With a strong base, either the S_N2 or the E2 reaction is possible. With a weak base and a good ionizing solvent, either the S_N1 or the E1 reaction is possible. Mixtures of products are common. Figure 6-14 shows these possibilities with a secondary halide under second-order and first-order conditions.



5. **Some bases favor substitution or elimination.** To promote elimination, the base should readily abstract a proton, but not readily attack a carbon atom. A bulky strong base, such as *t*-butoxide [$^{-}OC(CH_3)_3$], enhances elimination. To promote substitution, we need a good nucleophile with limited basicity: a highly polarizable species that is the conjugate base of a strong acid. Bromide (Br^-) and iodide (I^-) are examples of good nucleophiles that are weak bases and favor substitution.



PROBLEM 6-39

Give the structures of the products expected from the indicated mechanisms in the examples shown above.