

6.18 Substitution versus Elimination

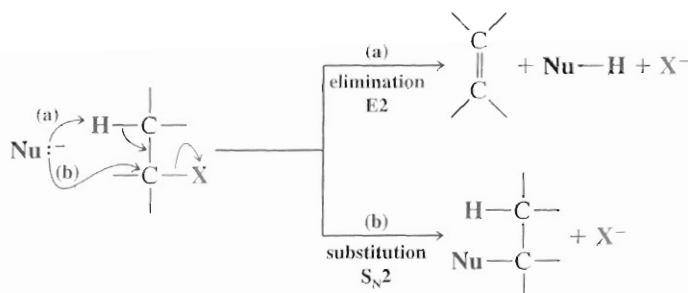
All nucleophiles are potential bases and all bases are potential nucleophiles. This is because the reactive part of both nucleophiles and bases is an unshared electron pair. It should not be surprising, then, that nucleophilic substitution reactions and elimination reactions often compete with each other.

6.18A S_N2 versus E2

S_N2 and E2 reactions are both favored by a high concentration of a strong nucleophile or base. When the nucleophile (base) attacks a β hydrogen atom, elimination occurs. When the nucleophile attacks the carbon atom bearing the leaving group, substitution results:

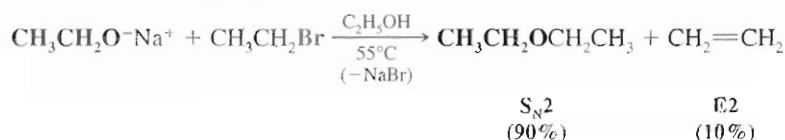
STUDY TIP

This section draws together the various factors that influence the competition between substitution and elimination.

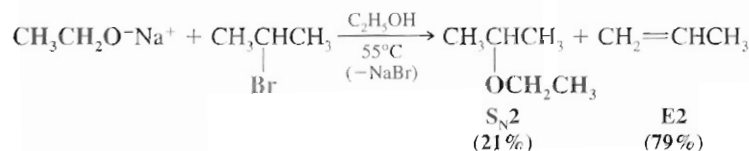


Consider the following examples with small (unhindered) nucleophiles and alkyl halides of different classes. Note the ratio of products formed in each case.

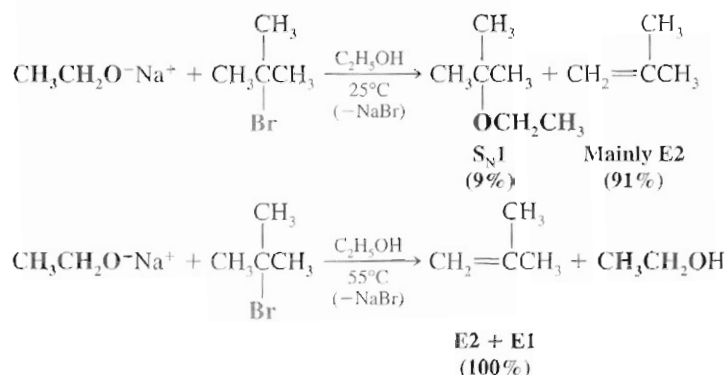
Primary Substrate When the substrate is a *primary* halide and the base is unhindered, like ethoxide ion, substitution is highly favored because the base can easily approach the carbon bearing the leaving group:



Secondary Substrate With *secondary* halides, however, a strong base favors elimination because steric hindrance in the substrate makes substitution more difficult:



Tertiary Substrate With *tertiary* halides, steric hindrance in the substrate is severe and an $\text{S}_{\text{N}}2$ reaction cannot take place. Elimination is highly favored, especially when the reaction is carried out at higher temperatures. Any substitution that occurs must take place through an $\text{S}_{\text{N}}1$ mechanism:

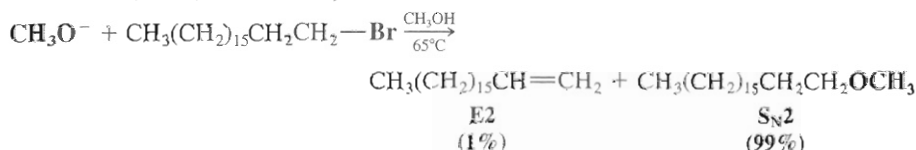


Temperature Increasing the reaction temperature favors elimination ($\text{E}1$ and $\text{E}2$) over substitution. Elimination reactions have greater free energies of activation than substitution reactions because more bonding changes occur during elimination. When higher temperature is used, the proportion of molecules able to surmount the energy of activation barrier for elimination increases more than the proportion of molecules able to undergo substitution, although the rate of both substitution and elimination will be increased. Furthermore, elimination reactions are entropically favored over substitution because the products of an elimination reaction are greater in number than the reactants. Additionally, because

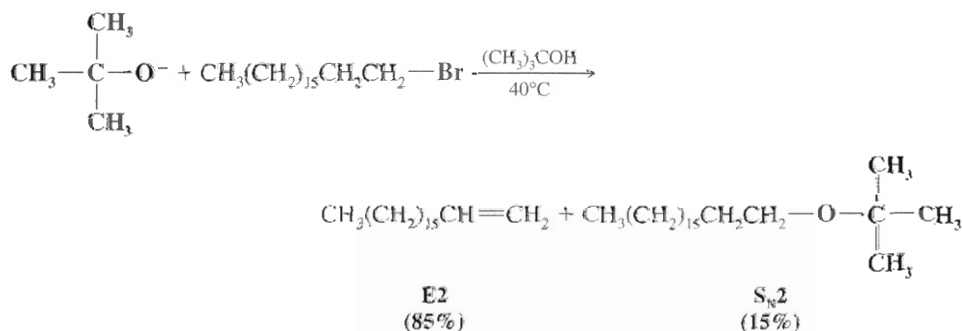
temperature is the coefficient of the entropy term in the Gibbs free-energy equation $\Delta G^\circ = \Delta H^\circ - T \Delta S^\circ$, an increase in temperature further enhances the entropy effect.

Size of the Base/Nucleophile Increasing the reaction temperature is one way of favorably influencing an elimination reaction of an alkyl halide. Another way is to use a **strong sterically hindered base** such as the *tert*-butoxide ion. The bulky methyl groups of the *tert*-butoxide ion inhibit its reacting by substitution, allowing elimination reactions to take precedence. We can see an example of this effect in the following two reactions. The relatively unhindered methoxide ion reacts with octadecyl bromide primarily by *substitution*, whereas the bulky *tert*-butoxide ion gives mainly *elimination*.

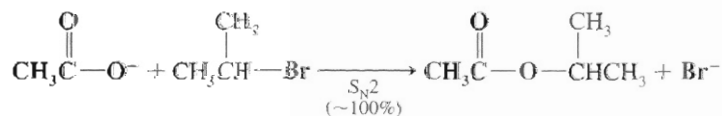
Unhindered (Small) Base/Nucleophile



Hindered Base/Nucleophile



Basicity and Polarizability Another factor that affects the relative rates of E2 and S_N2 reactions is the relative basicity and polarizability of the base/nucleophile. Use of a strong, slightly polarizable base such as amide ion (NH₂[−]) or alkoxide ion (especially a hindered one) tends to increase the likelihood of elimination (E2). Use of a weakly basic ion such as a chloride ion (Cl[−]) or an acetate ion (CH₃CO₂[−]) or a weakly basic and highly polarizable one such as Br[−], I[−], or RS[−] increases the likelihood of substitution (S_N2). Acetate ion, for example, reacts with isopropyl bromide almost exclusively by the S_N2 path:



The more strongly basic ethoxide ion (Section 6.15B) reacts with the same compound mainly by an E2 mechanism.

6.18B Tertiary Halides: S_N1 versus E1

Because E1 and S_N1 reactions proceed through the formation of a common intermediate, the two types respond in similar ways to factors affecting reactivities. E1 reactions are favored with substrates that can form stable carbocations (i.e., tertiary halides); they are also favored by the use of poor nucleophiles (weak bases) and they are generally favored by the use of polar solvents.

It is usually difficult to influence the relative partition between S_N1 and E1 products because the free energy of activation for either reaction proceeding from the carbocation (loss of a proton or combination with a molecule of the solvent) is very small.

In most unimolecular reactions the S_N1 reaction is favored over the E1 reaction, especially at lower temperatures. *In general, however, substitution reactions of tertiary halides do not find wide use as synthetic methods. Such halides undergo eliminations much too easily.*

Increasing the temperature of the reaction favors reaction by the E1 mechanism at the expense of the S_N1 mechanism. *If the elimination product is desired, however, it is more convenient to add a strong base and force an E2 reaction to take place instead.*

6.19 Overall Summary

The most important reaction pathways for the substitution and elimination reactions of simple alkyl halides are summarized in Table 6.7.

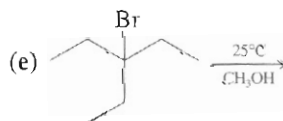
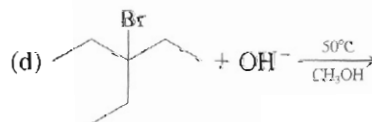
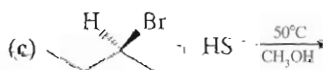
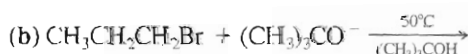
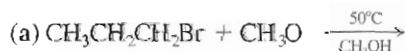
TABLE 6.7 Overall Summary of S_N1 , S_N2 , E1, and E2 Reactions

	$\begin{array}{c} \text{H} \\ \\ \text{R}-\text{C}-\text{X} \\ \\ \text{H} \end{array}$	$\begin{array}{c} \text{R} \\ \\ \text{R}-\text{C}-\text{X} \\ \\ \text{H} \end{array}$	$\begin{array}{c} \text{R} \\ \\ \text{R}-\text{C}-\text{X} \\ \\ \text{R} \end{array}$
	1°	2°	3°
	Bimolecular (S_N2 /E2) Reactions Only		S_N1 /E1 or E2
CH ₃ X			
Methyl			
Gives S_N2 reactions	Gives mainly S_N2 except with a hindered strong base [e.g., $(\text{CH}_3)_3\text{CO}^-$] and then gives mainly E2.	Gives mainly S_N2 with weak bases (e.g., I^- , CN^- , RCO_2^-) and mainly E2 with strong bases (e.g., RO^-).	No S_N2 reaction. In solvolysis gives S_N1 /E1, and at lower temperatures S_N1 is favored. When a strong base (e.g., RO^-) is used, E2 predominates.

Let us examine several sample exercises that will illustrate how the information in Table 6.7 can be used.

Study Problem

Give the product (or products) that you would expect to be formed in each of the following reactions. In each case give the mechanism (S_N1 , S_N2 , E1, or E2) by which the product is formed and predict the relative amount of each (i.e., would the product be the only product, the major product, or a minor product?).

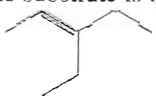


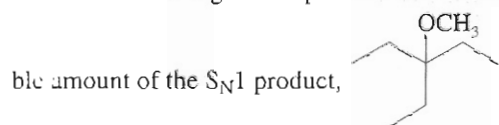
STRATEGY AND ANSWER

- (a) The substrate is a 1° halide. The base/nucleophile is CH_3O^- , a strong base (but not a hindered one) and a good nucleophile. According to Table 6.7, we should expect an S_N2 reaction mainly, and the major product should be $\text{CH}_3\text{CH}_2\text{CH}_2\text{OCH}_3$. A minor product might be $\text{CH}_3\text{CH}=\text{CH}_2$ by an E2 pathway.

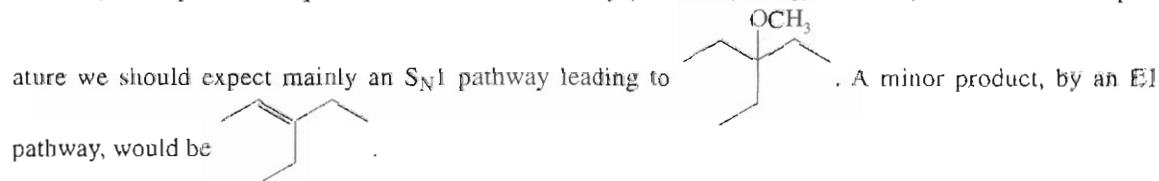
- (b) Again the substrate is a 1° halide, but the base/nucleophile, $(\text{CH}_3)_3\text{CO}^-$, is a strong hindered base. We should expect, therefore, the major product to be $\text{CH}_3\text{CH}=\text{CH}_2$ by an E2 pathway and a minor product to be $\text{CH}_3\text{CH}_2\text{CH}_2\text{OC}(\text{CH}_3)_3$ by an $\text{S}_\text{N}2$ pathway.
- (c) The reactant is (*S*)-2-bromobutane, a 2° halide and one in which the leaving group is attached to a chirality center. The base/nucleophile is HS^- , a strong nucleophile but a weak base. We should expect mainly an $\text{S}_\text{N}2$ reaction, causing an inversion of configuration at the chirality center and producing the (*R*) stereoisomer:

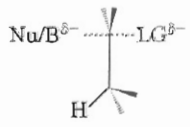



- (d) The base/nucleophile is OH^- , a strong base and a strong nucleophile. However, the substrate is a 3° halide; therefore, we should not expect an $\text{S}_\text{N}2$ reaction. The major product should be  via an E2 reaction. At this higher temperature and in the presence of a strong base, we should not expect an apprecia-



- (e) This is solvolysis; the only base/nucleophile is the solvent, CH_3OH , which is a weak base (therefore, no E2 reaction) and a poor nucleophile. The substrate is tertiary (therefore, no $\text{S}_\text{N}2$ reaction). At this lower temper-



Summary and Review Tools	
Mechanism Review: Substitution versus Elimination	
$\text{S}_\text{N}2$	$\text{S}_\text{N}1$ and E1
Primary substrate Back side attack of Nu: with respect to LG Strong/polarizable unhindered nucleophile	Tertiary substrate Carbocation intermediate Weak nucleophile/base (e.g., solvent)
Bimolecular in rate-determining step Concerted bond forming/bond breaking Inversion of stereochemistry Favored by polar aprotic solvent	Unimolecular in rate-determining step Racemization if $\text{S}_\text{N}1$ Removal of β -hydrogen if E1 Protic solvent assists ionization of LG Low temperature ($\text{S}_\text{N}1$) / high temperature (E2)
	
$\text{S}_\text{N}2$ and E2	E2
Secondary or primary substrate Strong unhindered base/nucleophile leads to $\text{S}_\text{N}2$ Strong hindered base/nucleophile leads to E2 Low temperature ($\text{S}_\text{N}2$) / high temperature (E2)	Tertiary or secondary substrate Concerted anti-coplanar TS Bimolecular in rate-determining step Strong hindered base High temperature
