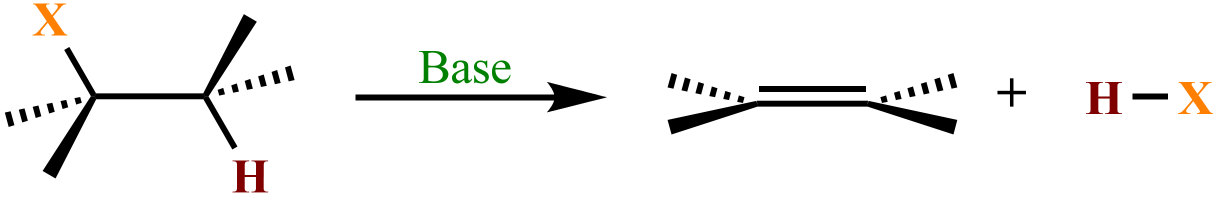
Elimination Reactions



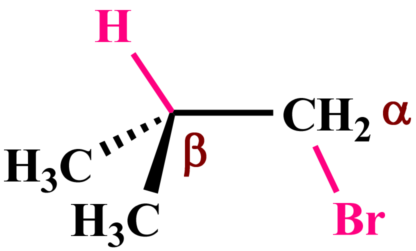
Just as there are two mechanisms of substitution (S_N2 and S_N1), there are two mechanisms of elimination (E2 and E1).

E2 mechanism — bimolecular elimination

E1 mechanism — unimolecular elimination

The E2 and E1 mechanisms differ in the timing of bond cleavage and bond formation, analogous to the S_N2 and S_N1 mechanisms.

E2 and S_N2 reactions have some features in common, as do E1 and S_N1 reactions.

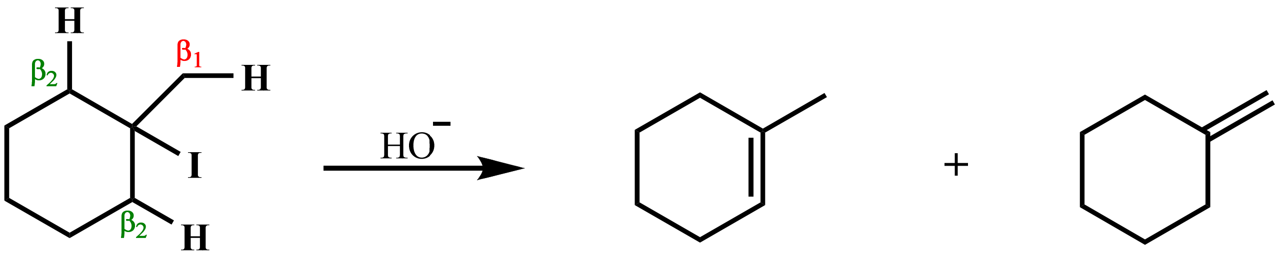


Base removes a proton from the β-carbon atom, while the halogen atom leaves from the α-carbon resulting in the formation of a π-bond. Such eliminations are also called β-elimination reactions

The Zaitsev (Saytseff) Rule

When alkyl halides have two or more different β carbons, more than one alkene product is formed.

In such cases, the major product is the more stable product—the one with the more substituted double bond. This phenomenon is called the Zaitsev rule.



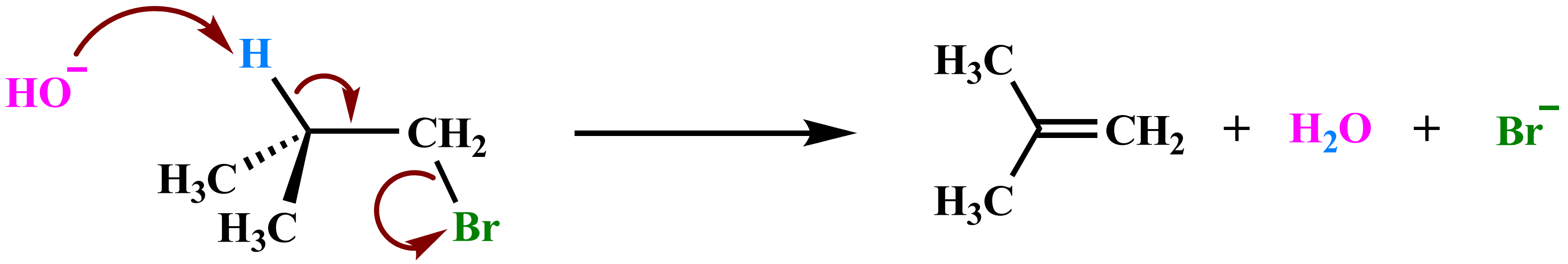
Major product
Trisubstituted alkene

Minor product
Disubstituted alkene

The Zaitsev product or the more substituted alkene product is more stable than the less substituted product. The stability of the more substituted alkene is a result of number of different contributing factors, including hyperconjugation.

Each alkyl group that can involve in hyperconjugation with the double bond stabilizes it by approximately 6 kcal/mol

The E2 Mechanism



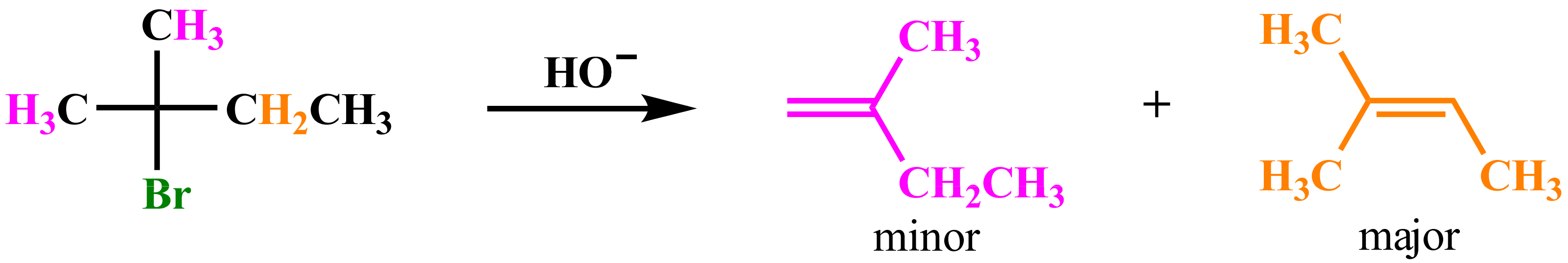
The most common mechanism for dehydrohalogenation is the E2 mechanism.

It exhibits second-order kinetics, and both the alkyl halide and the base appear in the rate equation

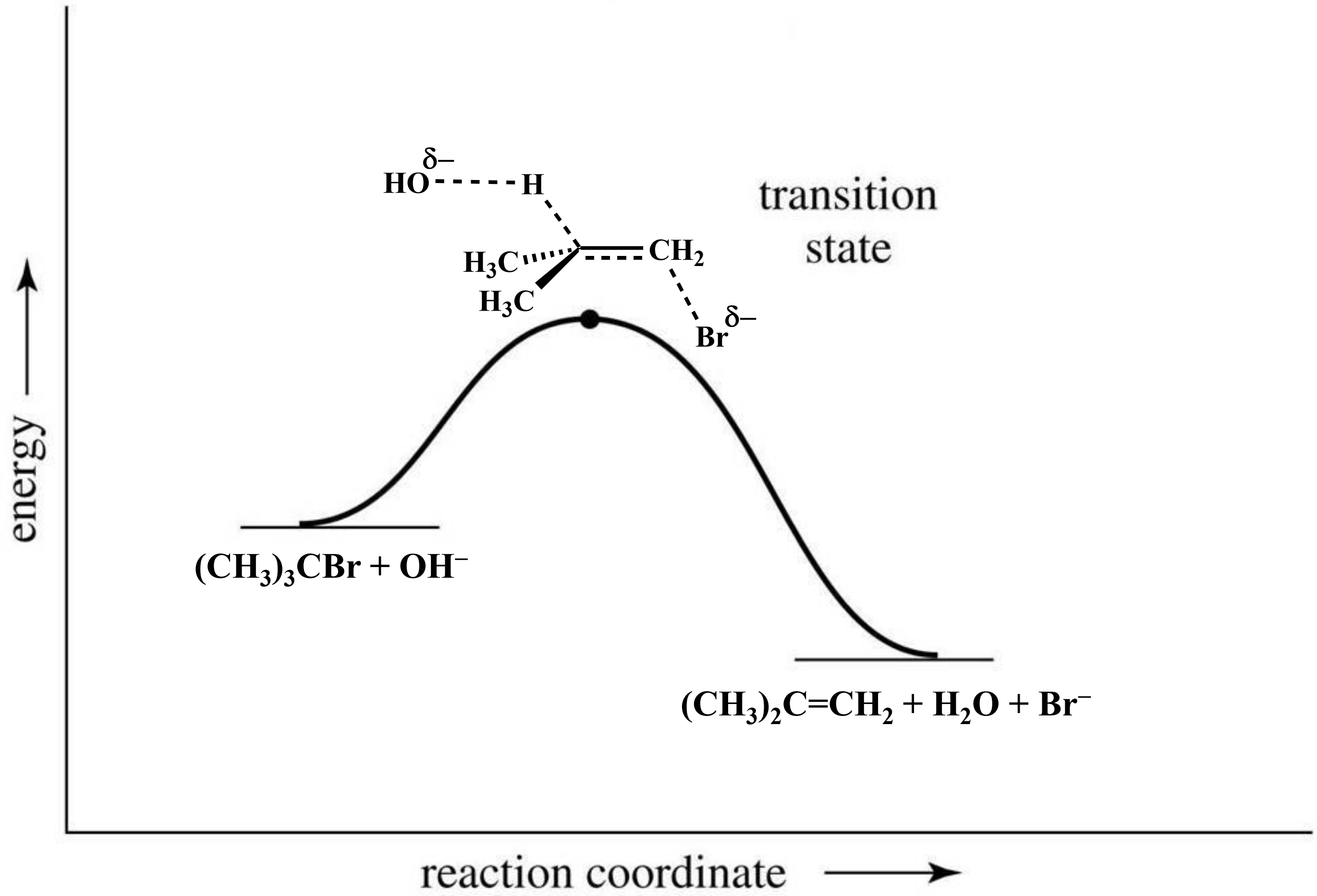
$$\mathbf{rate = k[(CH_3)_3CBr][HO^-]}$$

The reaction is concerted—all bonds are broken and formed in a single step.

E2 reactions are **regioselective** and favor the formation of Zaitsev products.



Energy Profile for an E2 Reaction



Factors Affecting the Rate of an E2 Reaction

There are close parallels between E2 and S_N2 mechanisms in how the identity of the base, the leaving group and the solvent affect the rate.

The base appears in the rate equation, so the rate of the E2 reaction increases as the strength of the base increases.

E2 reactions are generally run with strong, negatively charged bases like OH^- and OR^-.

Polar aprotic solvents increase the rate of E2 reactions

There is a partial breaking of the bond to the leaving group in the transition state. So, the better the leaving group the faster the E2 reaction.

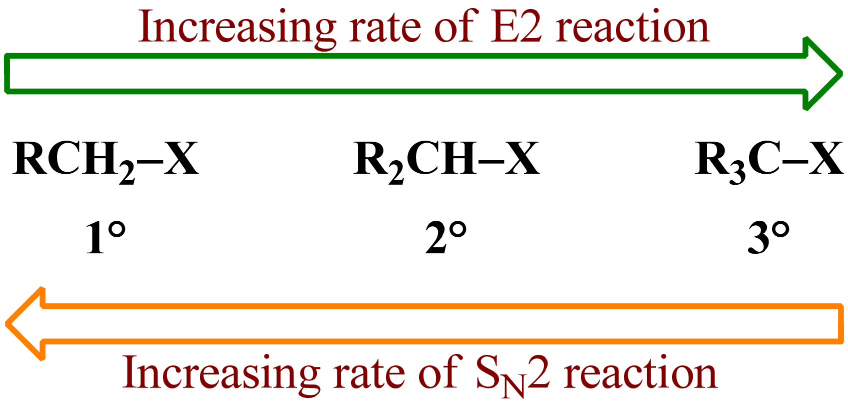
Rate of reaction follows the order,

$$R{-}I > R{-}Br > R{-}Cl > R{-}F$$

Factors Affecting the Rate of an E2 Reaction

The S_N2 and E2 mechanisms differ in how the R group affects the reaction rate.

As the number of R groups on the carbon with the leaving group increases, the rate of the E2 reaction increases.



Increasing rate of E2 reaction

$RCH_2–X$ **$R_2CH–X$** **$R_3C–X$**

1° **2°** **3°**

Increasing rate of S_N2 reaction

The increase in E2 reaction rate with increasing alkyl substitution can be rationalized in terms of transition state stability.

In the transition state, the double bond is partially formed. Thus, the transition state for a more substituted alkene is lower in energy, reducing the activation energy for the reaction and making the reaction faster.

Characteristics of an E2 Reaction

Kinetics – Second order

Mechanism – Single step

Identity of R group – More substituted halides react faster
Rate: $R_3CX > R_2CHX > RCH_2X$

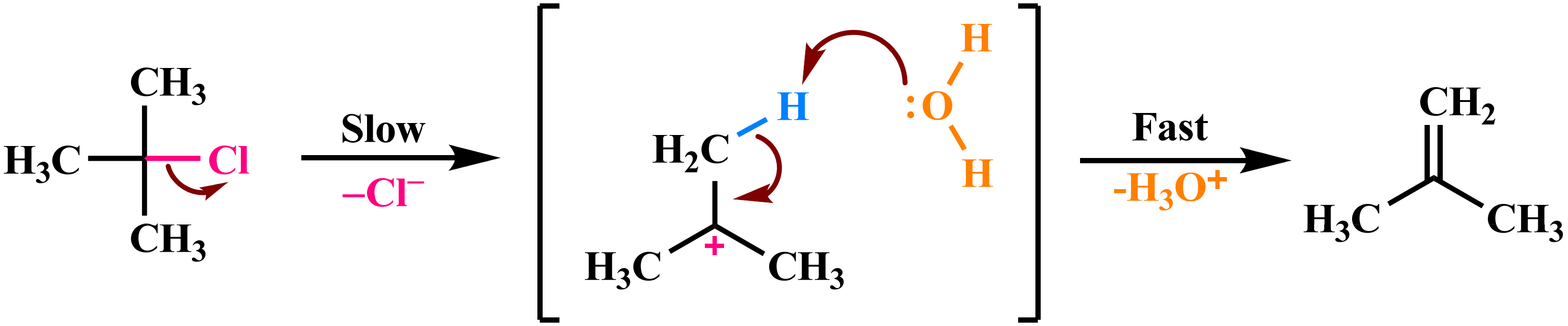
Strength of the base – Stronger bases favor the reaction

Leaving group – Better leaving group leads to faster reaction rates

Type of solvent – Favored by polar aprotic solvents

E2 reactions are stereoselective, resulting in the formation of trans-double bonds preferably.

The E1 Mechanism

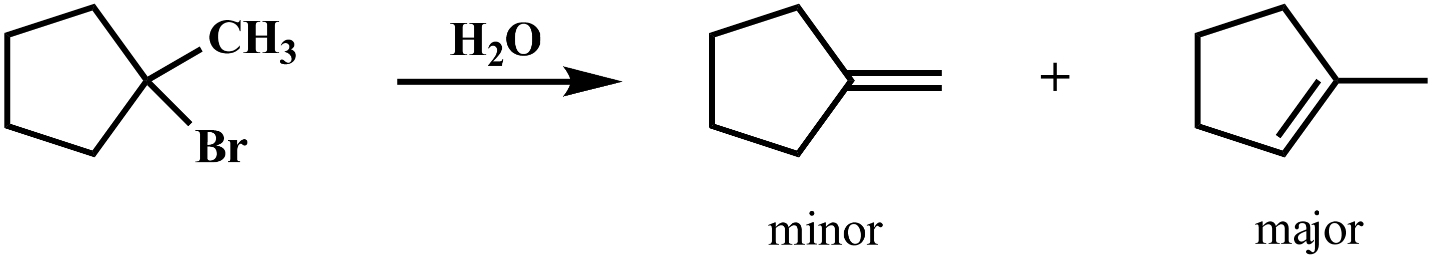


The E1 reaction proceeds via a two-step mechanism: the bond to the leaving group breaks first before the π bond is formed. The slow step is unimolecular, involving only the alkyl halide.

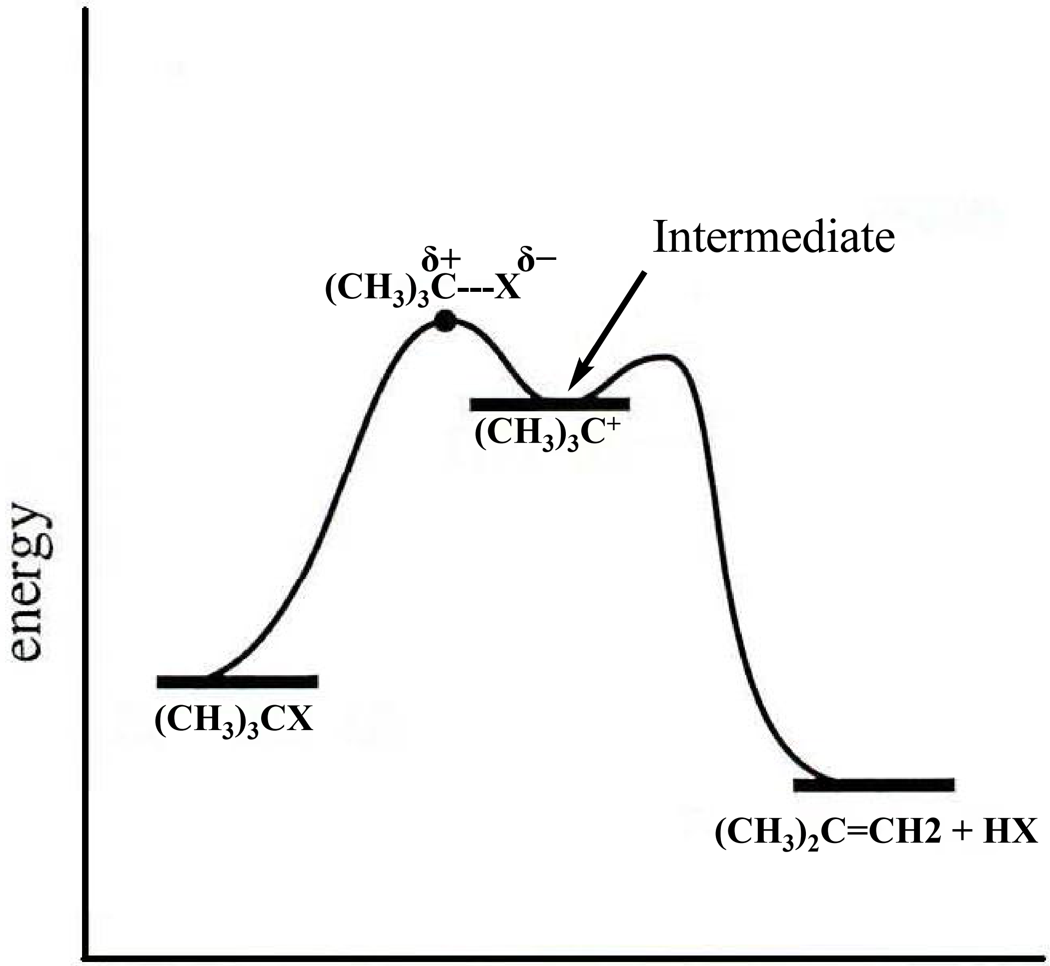
It exhibits first-order kinetics,

$$\textbf{rate} = \mathbf{k[(CH_3)_3CCl]}$$

E1 reactions also are regioselective and follow Zaitsev rule

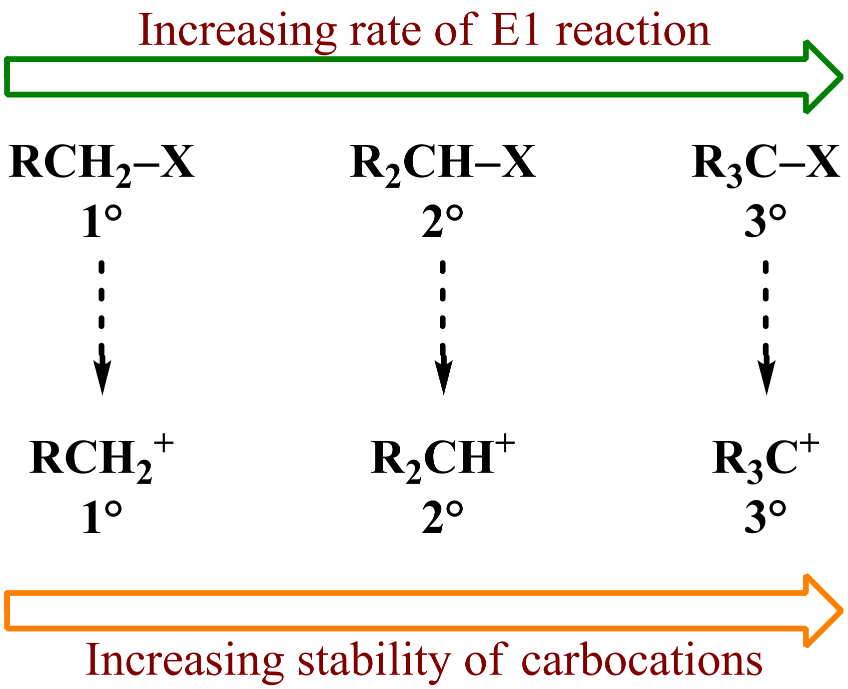


Energy Profile for an E1 Reaction



Factors Affecting the Rate of an E1 Reaction

The rate of an E1 reaction increases as the number of R groups on the carbon with the leaving group increases.



Increasing rate of E1 reaction

$RCH_2–X$
1°

$R_2CH–X$
2°

$R_3C–X$
3°

RCH_2^+
1°

R_2CH^+
2°

R_3C^+
3°

Increasing stability of carbocations

The strength of the base usually determines whether a reaction follows the E1 or E2 mechanism. Strong bases like $OH^–$ and $OR^–$ favor E2 reactions, whereas weaker bases like H_2O and ROH favor E1 reactions.

Characteristics of an E1 Reaction

Kinetics – First order

Mechanism – Two steps

Identity of R group – More substituted halides react faster
Rate: $R_3CX > R_2CHX > RCH_2X$

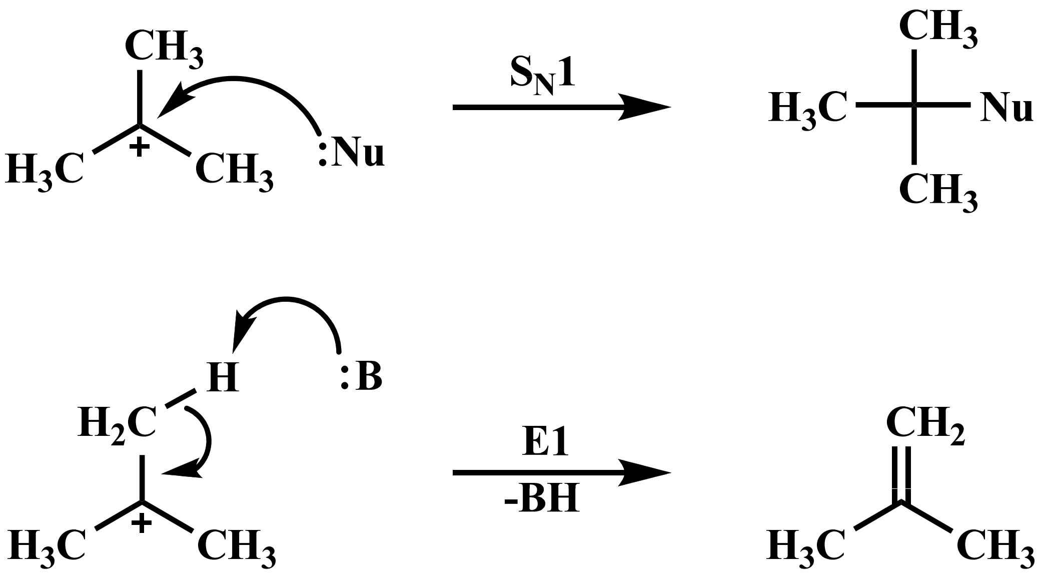
Strength of the base – Favored by weaker bases such as H_2O and ROH

Leaving group – Better leaving group leads to faster reaction rates. Just as in S_N1 reactions, the rate determining step involves the C—X bond cleavage

Type of solvent – Favored by polar protic solvents, which can stabilize the ionic intermediates

S_N1 and E1 Reactions

S_N1 and E1 reactions have exactly the same first step—formation of a carbocation. They differ in what happens to the carbocation.



Since in both the reactions, the rate determining steps are the same, they cannot be individually controlled.

Because E1 reactions often occur with a competing S_N1 reaction, E1 reactions of alkyl halides are much less useful than E2 reactions.

S_N1, S_N2, E1 or E2

3° Alkyl Halides

With strong bases: E2 elimination occurs

With weak nucleophiles or bases: A mixture of products from S_N1 and E1 reactions

1° Alkyl Halides

With strong nucleophiles: Substitution occurs by an S_N2 mechanism

With strong sterically hindered bases: Elimination occurs by an E2 mechanism

2° Alkyl Halides

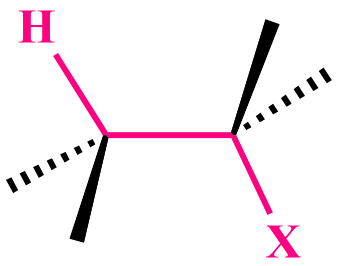
With strong bases and nucleophiles: A mixture of S_N2 and E2 reaction products are formed

With strong sterically hindered bases: Elimination occurs by an E2 mechanism

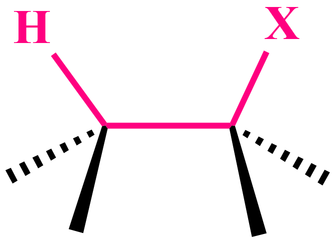
With weak nucleophiles or bases: A mixture of S_N1 and E1 products results

Stereochemistry of the E2 Reaction

The transition state of an E2 reaction consists of four atoms from the substrate (one hydrogen atom, two carbon atoms, and the leaving group, X) aligned in a plane. There are two ways for the C—H and C—X bonds to be coplanar.



anti periplanar
H and X are on the opposite side



syn periplanar
H and X are on the same side

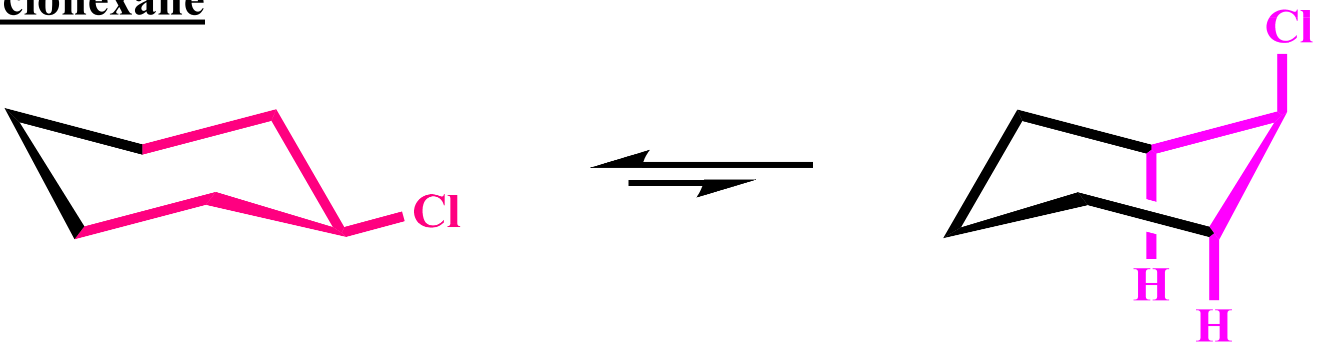
E2 elimination occurs most often in the anti periplanar geometry. This arrangement allows the molecule to react in the lower energy staggered conformation, and allows the incoming base and leaving group to be further away from each other.

The anti periplanar geometry also allows direct interaction between the bonding electrons of C—H bond and the anti-bonding orbital of the C—X bond.

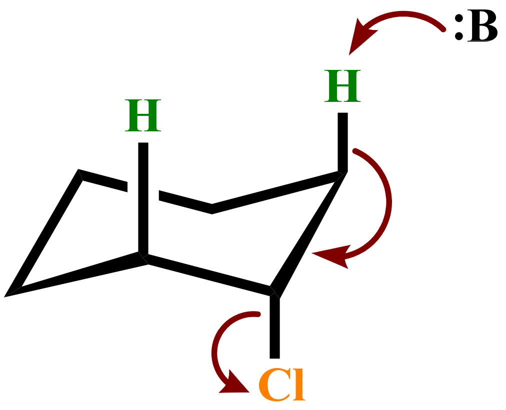
E2 Reactions in 6-Membered Rings

The stereochemical requirement of an anti periplanar geometry in an E2 reaction has important consequences for compounds containing six-membered rings.

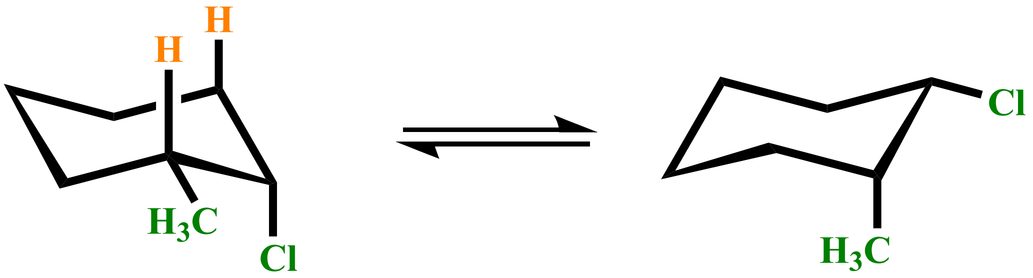
Chlorocyclohexane



For E2 elimination, the C—Cl bond must be anti periplanar to the C—H bond on a β carbon, and this occurs only when the H and Cl atoms are both in the axial position. The requirement for trans-diaxial geometry means that elimination must occur from the less stable conformer.



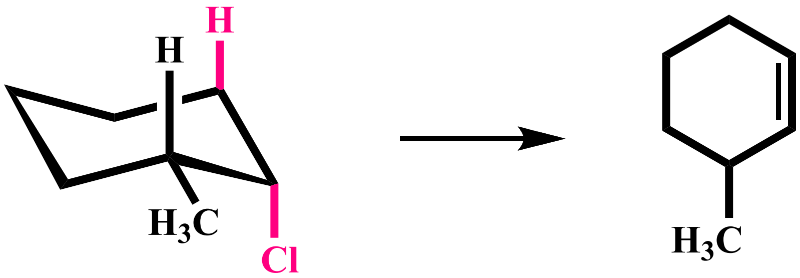
Dehydrohalogenation of *cis*-1-Chloro-2-methylcyclohexane



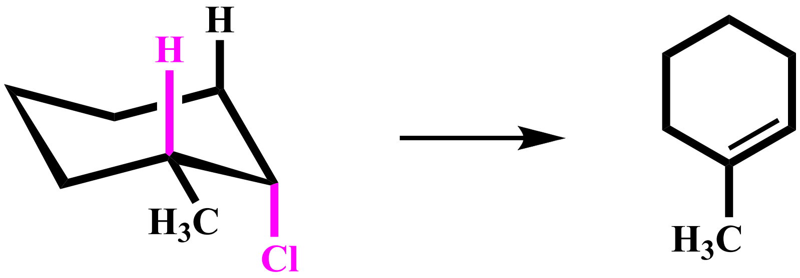
In this conformer two Hs are
anti periplanar to the Cl.

In this conformer Cl is in an
equatorial psition and has no
Hs periplanar to it.

The conformer with Cl in an axial orientation reacts to give two alkenes. The alkene that is more substituted is the major product.

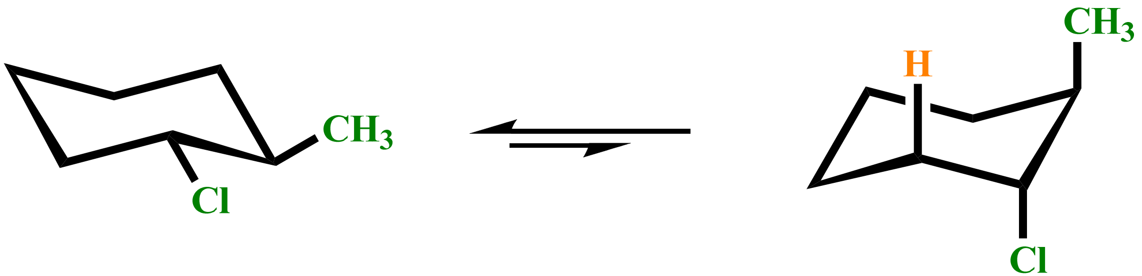


disubstituted alkene
minor product



trisubstituted alkene
major product

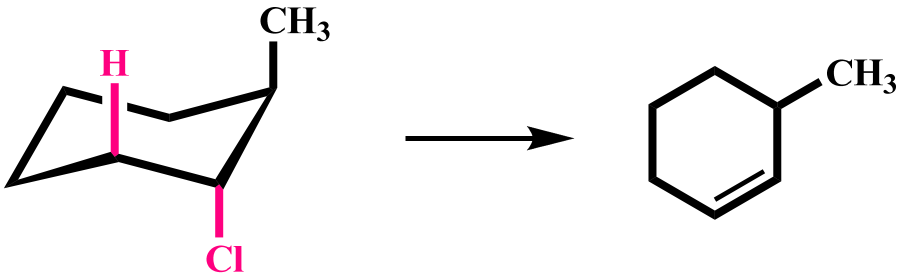
Dehydrohalogenation of *trans*-1-Chloro-2-methylcyclohexane



In this conformer Cl is in an equatorial psition and has no Hs periplanar to it.

In this conformer one H and one CH$_3$ are anti periplanar to the Cl.

The conformer with Cl in an axial orientation has just one β-H atom. Only one product is formed, which is not what is predicted by the Zaitsev rule.

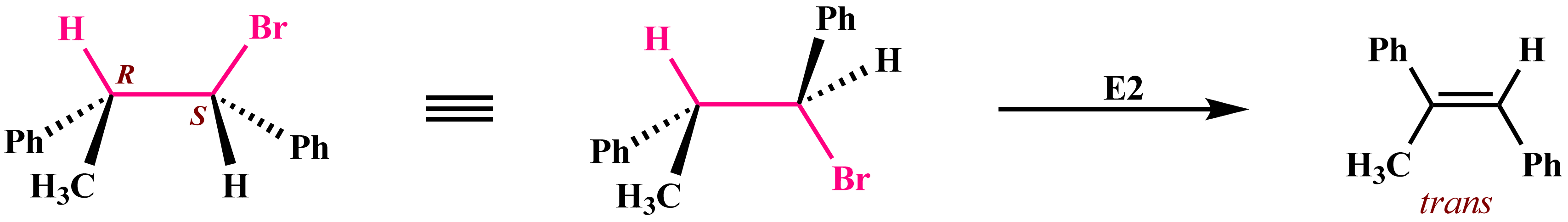


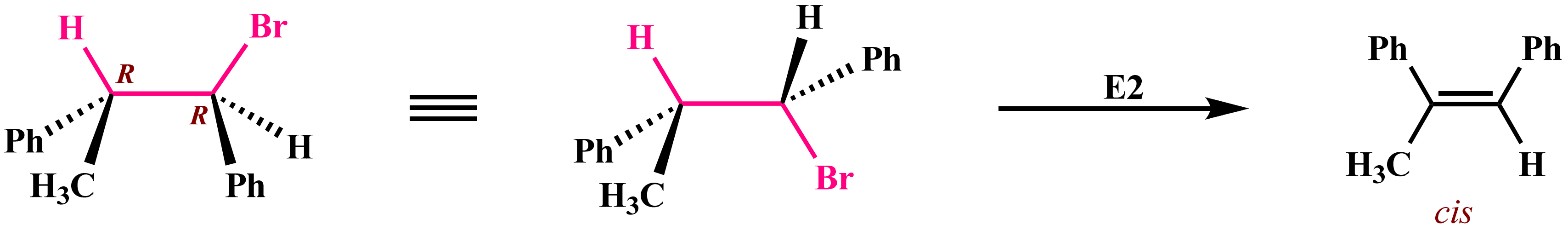
disubstituted alkene, the only product formed

In conclusion, with substituted cyclohexanes, E2 elimination should occur with a trans diaxial arrangement of the leaving group and the β-H, and as a result of this requirement, the more substituted alkene is not necessarily the major product.

Stereospecificity in E2 reactions

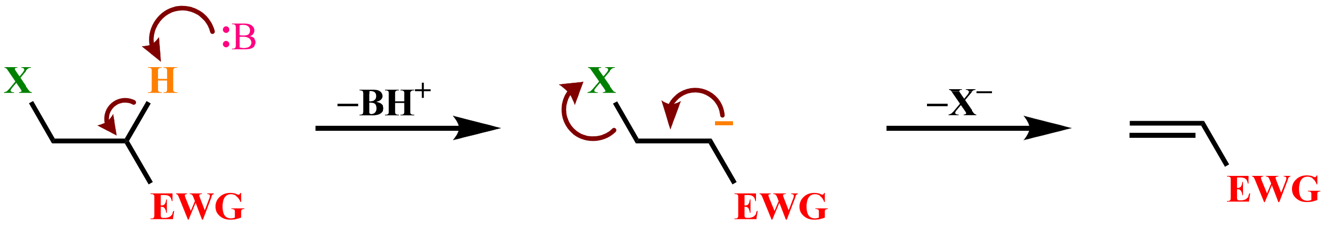
Diastereomeric starting compounds yield diastereomeric products after an E2 reaction





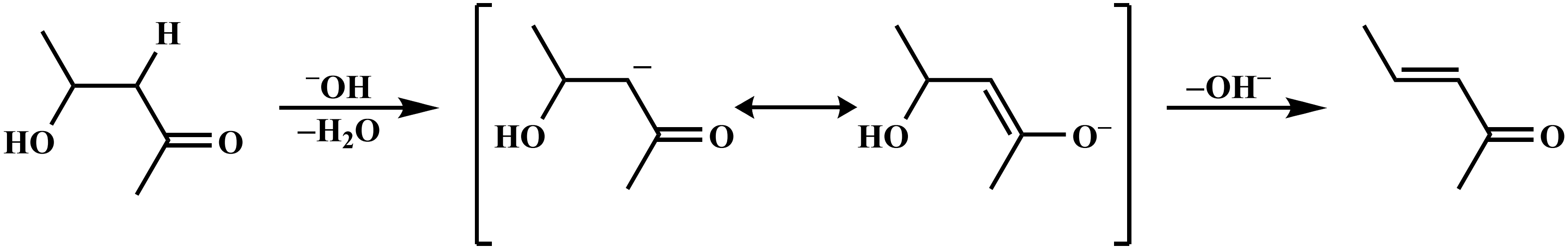
E1cB Reaction

An elimination reaction that happens when a compound bearing a poor leaving group and an acidic hydrogen is treated with a base.



E1cB stands for **Elimination Unimolecular conjugate Base**. The reaction is unimolecular from the conjugate base of the starting compound, which in turn is formed by deprotonation of the starting compound by a suitable base.

The electron withdrawing group (EWG) can be a carbonyl group (keto, aldehyde, ester), a nitro group, an electron deficient aromatic group etc. Dehydration of aldol is the most common E1cB reaction



Exercise 8-22 Classify the following solvents according to effectiveness for solvation of (i) cations and (ii) anions:

a. 2-propanone, CH_3COCH_3

b. tetrachloromethane, CCl_4

c. anhydrous hydrogen fluoride, HF

d. trichloromethane, $CHCl_3$

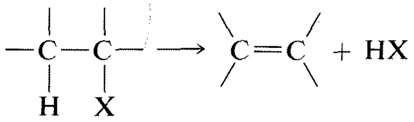
e. trimethylamine, $(CH_3)_3N$

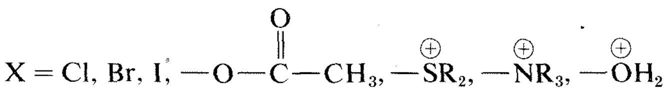
f. trimethylamine oxide, $(CH_3)_3\overset{\oplus}{N}-\overset{\ominus}{O}$

Exercise 8-23* Would you expect the S_N2 reaction of sodium cyanide with methyl bromide to be faster, slower, or about the same with $(CH_3)_2S{=}O$ or ethanol as solvent? Explain.

Elimination Reactions

Generally, an alkyl derivative, under appropriate conditions, will eliminate HX, where X is commonly a halide, ester, or -onium function, provided that there is a hydrogen located on the carbon adjacent to that bearing the X function:





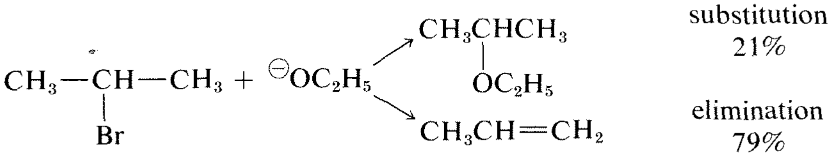
$$X = Cl, Br, I, -O-\overset{\displaystyle O}{\overset{\|}{C}}-CH_3, -\overset{\oplus}{S}R_2, -\overset{\oplus}{N}R_3, -\overset{\oplus}{O}H_2$$

An important feature of many elimination reactions is that they occur with the same combinations of reagents that cause nucleophilic substitution. In fact, elimination and substitution often are competitive reactions. Therefore it should be no surprise that substitution and elimination have closely related mechanisms.

8-8 THE E2 REACTION

8-8A Kinetics and Mechanism

The conditions used for substitution reactions by the S_N2 mechanism very often lead to elimination. The reaction of 2-bromopropane with sodium ethoxide in ethanol provides a good example:

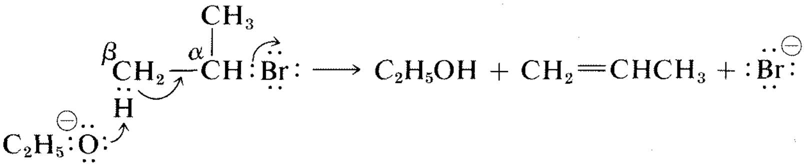


Elimination to give propene competes with substitution to give ethyl isopropyl ether. Furthermore, the rate of elimination, like the rate of substitution, is proportional to the concentrations of 2-bromopropane and ethoxide ion. Thus elimination here is a second-order reaction (it may be helpful to review Section 8-4 at this point):

$$\text{rate of substitution} = k_S[\text{RBr}][\overset{\ominus}{\text{OC}_2\text{H}_5}]$$

$$\text{rate of elimination} = k_E[\text{RBr}][\overset{\ominus}{\text{OC}_2\text{H}_5}]$$

As to the *mechanism* of this kind of elimination, the attacking base, ${}^{\ominus}\text{OC}_2\text{H}_5$, removes a proton from the β carbon more or less simultaneously with the formation of the double bond and the loss of bromide ion from the neighboring carbon:



The abbreviation for this mechanism is **E2,** E for elimination and 2 for bimolecular, there being two reactants involved in the transition state.

Exercise 8-24 An alternative mechanism for E2 elimination is the following:

$$\text{CH}_3\text{CH}_2\text{Cl} + \text{OH}^{\ominus} \underset{}{\xrightleftharpoons{\text{fast}}} {}^{\ominus}\!:\text{CH}_2\text{CH}_2\text{Cl} + \text{H}_2\text{O} \xrightarrow{\text{slow}} \text{CH}_2{=}\text{CH}_2 + \text{Cl}^{\ominus}$$

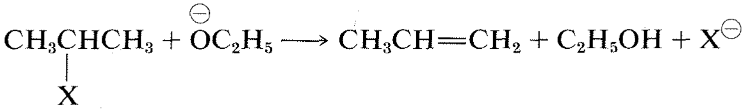
a. Would this mechanism lead to overall second-order kinetics with respect to the concentrations of $\text{OH}^{\ominus}$ and ethyl chloride? Explain.

b. This mechanism as written has been excluded for several halides by carrying out the reaction in deuterated solvents such as D_2O and C_2H_5OD. Explain how such experiments could be relevant to the reaction mechanism.

c. Does the test in Part b also rule out $CH_3CH_2Cl + \overset{\ominus}{O}H \xrightarrow{\text{slow}} :\overset{\ominus}{C}H_2CH_2Cl + H_2O \xrightarrow{\text{fast}} CH_2{=}CH_2 + Cl^{\ominus}$? Explain.

8-8B Structural Effects

Structural influences on E2 reactions have been studied in some detail. Like the competing S_N2 process, a good leaving group is necessary and of these, the most commonly used are the halides, Cl, Br, and I; sulfonate esters, $RS(O_2)O{-}$; and -onium ions such as ammonium, $-\overset{|\,\oplus}{\underset{|}{N}}-$, and sulfonium, $-\overset{\oplus}{\underset{|}{S}}-$:

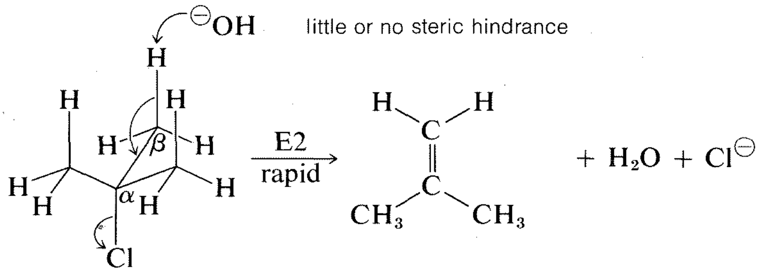


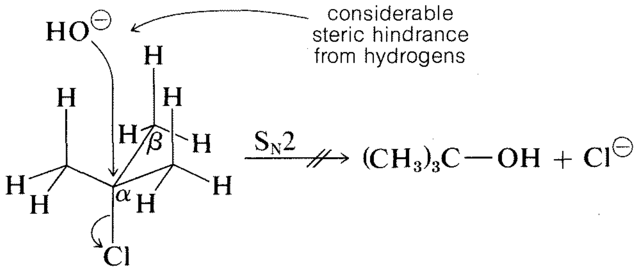
$$CH_3\underset{\displaystyle X}{\underset{|}{C}}HCH_3 + \overset{\ominus}{O}C_2H_5 \longrightarrow CH_3CH{=}CH_2 + C_2H_5OH + X^{\ominus}$$

$X = Br, I, OSO_2R, \overset{\oplus}{S}(CH_3)_2, \overset{\oplus}{N}(CH_3)_3$

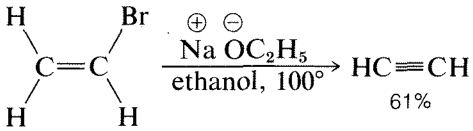
Rather strong bases generally are required to bring about the E2 reaction. The effectiveness of a series of bases generally parallels their base strengths, and the order $\overset{\ominus}{N}H_2 > \overset{\ominus}{O}C_2H_5 > \overset{\ominus}{O}H > \overset{\ominus}{O}_2CCH_3$ is observed for E2 reactions. This fact is important in planning practical syntheses, because the E2 reaction tends to predominate with strongly basic, slightly polarizable reagents such as amide ion, $\overset{\ominus}{N}H_2$, or ethoxide ion, $\overset{\ominus}{O}C_2H_5$. In contrast, S_N2 reactions tend to be favored with weakly basic nucleophiles such as iodide ion or ethanoate ion (unless dipolar aprotic solvents are used, which may markedly change the reactivity of anionic nucleophiles).

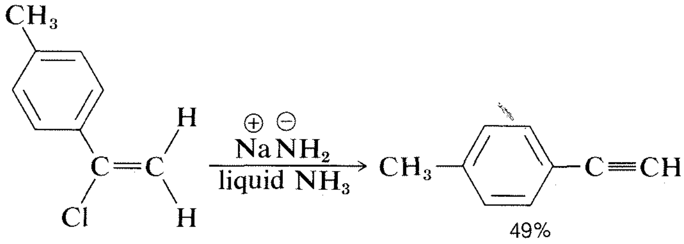
As for the alkyl group, there are two important structural effects to notice. First, at least one C–H bond adjacent (β) to the leaving group is required. Second, the ease of E2 elimination follows the order *tertiary* R > *secondary* R > *primary* R. Unlike S_N2 reactions, which are *not* observed for tertiary alkyl compounds because of steric hindrance to the approach of the nucleophile to carbon, the related E2 reaction usually occurs readily with tertiary RX compounds. The reason is that little or no steric hindrance is likely for the approach of a base to a hydrogen unless the base is exceptionally bulky:



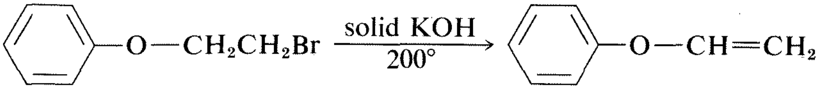


The reactivity order also appears to correlate with the C–X bond energy, inasmuch as the tertiary alkyl halides both are more reactive and have weaker carbon–halogen bonds than either primary or secondary halides (see Table 4-6). In fact, elimination of HX from haloalkenes or haloarenes with relatively strong C–X bonds, such as chloroethene or chlorobenzene, is much less facile than for haloalkanes. Nonetheless, elimination does occur under the right conditions and constitutes one of the most useful general methods for the synthesis of alkynes. For example,





The conditions and reagents used for E2 and S_N2 reactions are similar enough that it is difficult to have one occur without the other. However, E2 elimination is favored over S_N2 substitution by (a) strongly basic nucleophiles, (b) bulky nucleophiles, and (c) increasing alkyl substitution at the α carbon. It also is observed that increasing the reaction temperature generally leads to an increase in elimination at the expense of substitution. In fact, surprisingly good yields of alkene or alkyne can be obtained by adding a halogen compound directly to molten or very hot KOH with no solvent present, whereupon the product is formed rapidly and distills immediately from the hot reaction mixture:



2-bromoethoxybenzene

69%
ethenoxybenzene
(ethenyl phenyl ether)

Exercise 8-25 Write equations and mechanisms for all the products that might reasonably be expected from the reaction of 2-chlorobutane with a solution of potassium hydroxide in ethanol.

Exercise 8-26 **a.** Why is potassium *tert*-butoxide, $\overset{\oplus}{K}\overset{\ominus}{O}C(CH_3)_3$, an excellent base for promoting elimination reactions of alkyl halides, whereas ethylamine, $CH_3CH_2NH_2$, is relatively poor for the same purpose?

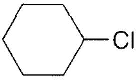
b. Potassium *tert*-butoxide is many powers of ten more effective a reagent for achieving E2 eliminations in methylsulfinylmethane (dimethyl sulfoxide) than in *tert*-butyl alcohol. Explain.

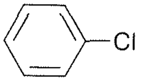
Exercise 8-27 Which one of the following groups of compounds would eliminate HCl most readily on reaction with potassium hydroxide? Draw the structure of the product and name it.

a. $(CH_3)_3CCl$ $CH_3CH_2CH_2CH_2Cl$ $CH_3CH(Cl)CH_2CH_3$

b. $(CH_3)_3CCH_2Cl$ $(CH_3)_2CHCH_2Cl$

c.

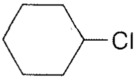


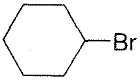


Exercise 8-28 Which one of each of the following pairs of compounds would react most rapidly with potassium hydroxide in an E2-type elimination? Draw the structure of the product and name it.

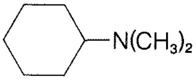
a. $(CH_3)_3COH$ $(CH_3)_3CCl$

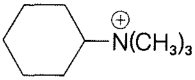
b.





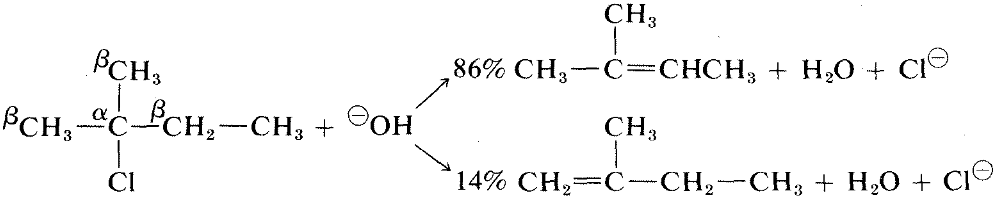
c.





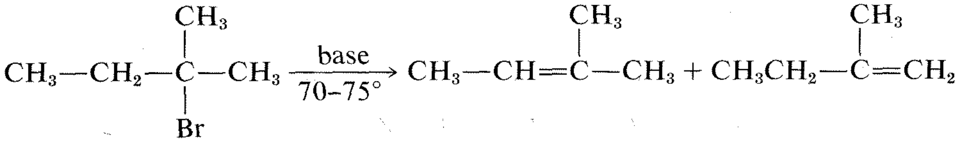
8-8C Orientation Effects in Elimination Reactions

With halides having unsymmetrical R groups, such as 2-chloro-2-methylbutane, it is possible to form two or more different alkenes, the proportion depending on the relative rates at which the different β hydrogens are removed. Most E2 eliminations of alkyl halides with common bases, such as $HO^{\ominus}$, $C_2H_5O^{\ominus}$, and $NH_2^{\ominus}$, tend to give mixtures of alkenes with a preference for the most stable alkene, which usually is the one with the *fewest* hydrogens or *most* alkyl groups attached to the carbons of the double bond. Thus

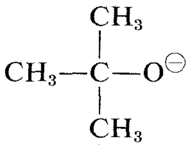


$$ {}^{\beta}CH_3\overset{\alpha}{-}\underset{\displaystyle Cl}{\overset{\displaystyle {}^{\beta}CH_3}{C}}\overset{\beta}{-}CH_2-CH_3 + {}^{\ominus}OH \begin{cases} \nearrow 86\%\ CH_3-\overset{\displaystyle CH_3}{C}=CHCH_3 + H_2O + Cl^{\ominus} \\ \searrow 14\%\ CH_2=\overset{\displaystyle CH_3}{C}-CH_2-CH_3 + H_2O + Cl^{\ominus} \end{cases} $$

However, the precise distribution of alkenes formed is found to vary enough with the nature of the leaving group, or the base used, so either product will predominate with some combination of reagents or conditions. For example, a change in the base alone can be decisive:



$$ CH_3-CH_2-\underset{\displaystyle Br}{\overset{\displaystyle CH_3}{C}}-CH_3 \xrightarrow[70\text{–}75^{\circ}]{\text{base}} CH_3-CH=\overset{\displaystyle CH_3}{C}-CH_3 + CH_3CH_2-\overset{\displaystyle CH_3}{C}=CH_2 $$

	2-methyl-2-butene	2-methyl-1-butene
Base: $C_2H_5O^{\ominus}$	70%	30%
 $CH_3-\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{C}}-O^{\ominus}$	27.5%	72.5%

8-8D Stereochemistry of E2 Reactions

The E2 reaction occurs most easily if the molecule undergoing reaction can assume a conformation, **2**, in which the leaving groups, H and X, are trans to each other and the atoms $H-C_{\beta}-C_{\alpha}-X$ lie in one plane. Elimination then proceeds from opposite sides of the incipient double bond to give an alkene of structure **3**. We shall call this mode of elimination **antarafacial** to distinguish

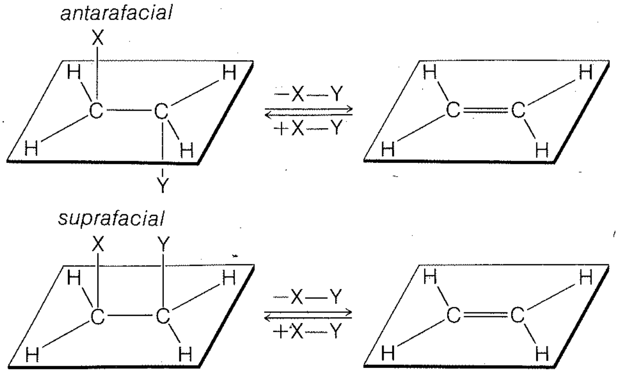
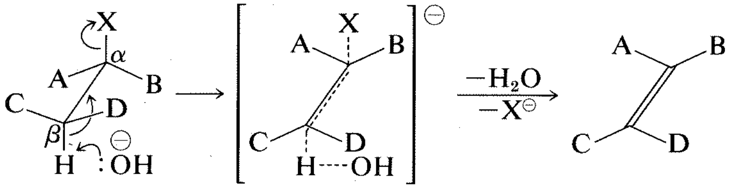


Figure 8-6 Schematic representation of antarafacial (literally "opposite-face") and suprafacial (literally "above-face") elimination or addition of a reagent X—Y to ethene

it from another possible mode of elimination that is called **suprafacial.** (See Figure 8-6).[8]



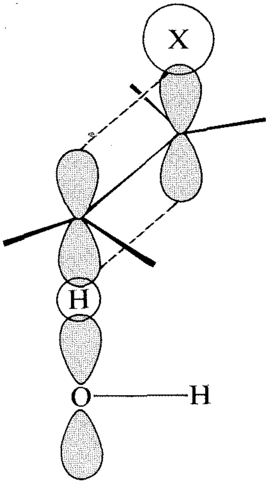
2 **3**

transition state for antarafacial (anti) elimination

---

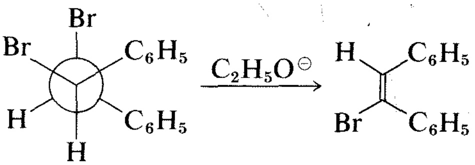
[8] Endless confusion is caused by the very prevalent use of the term "cis elimination" (or "cis addition") and "trans elimination" (or "trans addition") to denote the processes shown in Figure 8-6. At the risk of annoying those who often rightly dislike complicated names for simple processes, we have chosen to adopt the proposal of R. B. Woodward and R. Hoffmann, that elimination (or addition) which involves a *same-side* cleavage (or formation) of bonds be called **suprafacial** and the *opposite-side* cleavage (or formation) of bonds be called **antarafacial.** The alternative of using *syn* for suprafacial and *anti* for antarafacial would be simpler and easier to remember, but the terms syn and anti already are used for configurations, which is exactly what we want to avoid. The problem with the terms cis elimination (or addition) and trans elimination (or addition) is that they do not necessarily lead to products that, by other conventions, are understood to be cis and trans products, respectively. For example, to say that "trans elimination leads to cis product" is a needless confusion. It is much clearer to say that "antarafacial elimination gives the cis product"—and now there is no confusion of the mode of elimination with whatever stereochemical convention identifies the product.

The transition state for conversion of **2** to **3** is particularly reasonable because it combines some of the geometry of both the reactants and the products and therefore gives the best overlap of the reacting orbitals necessary for the formation of the π bond. This is shown more explicitly below.[9]

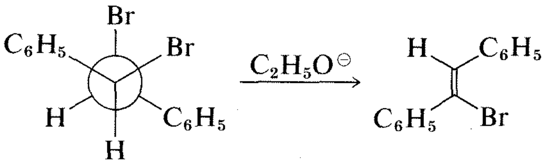


orbital model for E2 transition state

As an illustration of the stereospecificity of eliminations, the meso compound **4** gives the *cis*-alkene **5**, whereas the D,L isomers **6** give the *trans*-alkene **7** with ethoxide. Both reactions clearly proceed by antarafacial elimination:



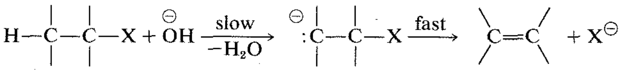
meso-1,2-dibromo-1,2-diphenylethane **4** *cis*-1-bromo-1,2-diphenylethene **5**



D,L **6** *trans* **7**

---

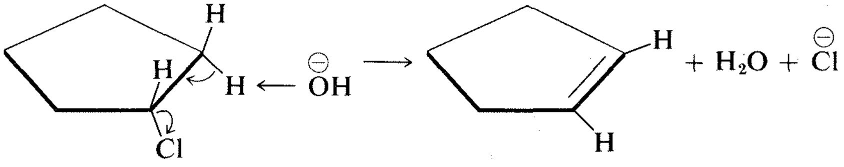
[9] Persuasive arguments have been made that many E2 reactions proceed by the sequence



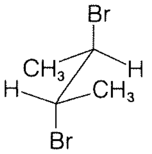
$$\mathrm{H{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X + \overset{\ominus}{O}H \xrightarrow[-H_2O]{slow} \overset{\ominus}{:}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}X \xrightarrow{fast} \gt C{=}C\lt + X^{\ominus}}$$

If this is so, antarafacial elimination still is predicted to be favored.

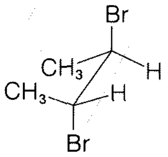
When antarafacial elimination is rendered difficult by the inability of the reacting groups to acquire the desired trans arrangement, then suprafacial elimination can occur, although less readily. An example is chlorocyclopentane, in which H and X cannot assume a trans configuration without very considerable strain but which does undergo suprafacial elimination at a reasonable rate:



Exercise 8-29 Write all the possible staggered conformations for each of the isomers of 2,3-dibromobutane, **8** and **9**:



8



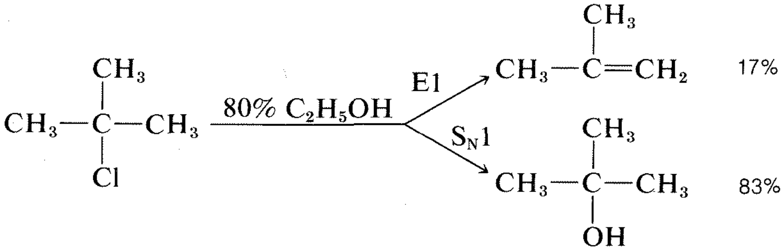
9

Show the structures of the alkenes that could be formed from each by antarafacial E2 elimination of one mole of hydrogen bromide with hydroxide ion. Which alkene should more readily eliminate further to form 2-butyne? Explain.

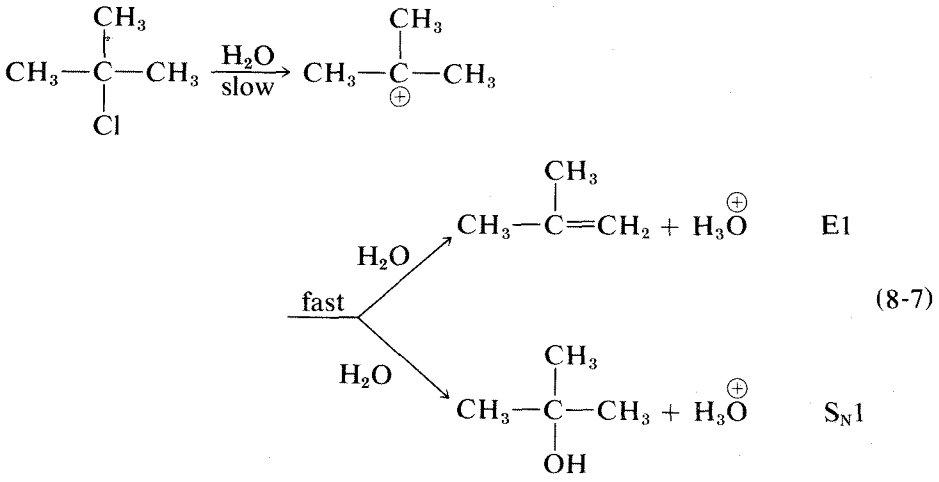
8-9 THE E1 REACTION

8-9A Scope and Mechanism

Many secondary and tertiary halides undergo E1 elimination in competition with the S_N1 reaction in neutral or acidic solutions. For example, when *tert*-butyl chloride solvolyzes in 80% aqueous ethanol at 25°, it gives 83% *tert*-butyl alcohol by substitution and 17% 2-methylpropene by elimination:



The ratio of substitution and elimination remains constant throughout the reaction, which means that each process has the same kinetic order with respect to the concentration of *tert*-butyl halide. The S_N1 and E1 reactions have a common rate-determining step, namely, slow ionization of the halide. The solvent then has the choice of attacking the intermediate carbocation at the positive carbon to effect substitution, or at a β hydrogen to effect elimination:



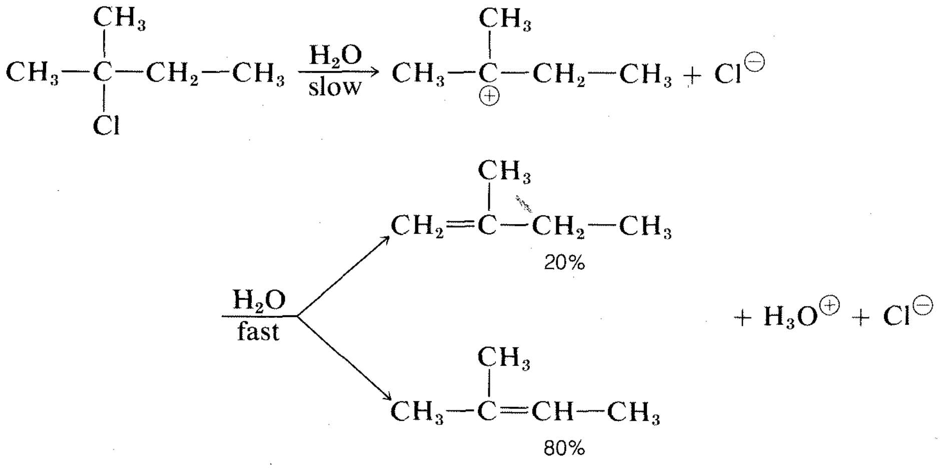
$$\mathrm{CH_3{-}\overset{CH_3}{\underset{Cl}{C}}{-}CH_3} \xrightarrow[\text{slow}]{H_2O} \mathrm{CH_3{-}\overset{CH_3}{\underset{\oplus}{C}}{-}CH_3}$$

$$\xrightarrow[\text{fast}]{H_2O} \mathrm{CH_3{-}\overset{CH_3}{C}{=}CH_2} + \mathrm{H_3\overset{\oplus}{O}} \quad \text{E1}$$

$$\xrightarrow[\text{fast}]{H_2O} \mathrm{CH_3{-}\overset{CH_3}{\underset{OH}{C}}{-}CH_3} + \mathrm{H_3\overset{\oplus}{O}} \quad S_N1 \qquad (8\text{-}7)$$

Factors influencing the E1 reactions are expected to be similar to those for the S_N1 reactions. An ionizing solvent is necessary, and for easy reaction the RX compound must have a good leaving group and form a relatively stable $R^{\oplus}$ cation. Therefore the E1 orders of reaction rates are $X = I > Br > Cl > F$ and *tertiary* R > *secondary* R > *primary* R.

With halides such as 2-chloro-2-methylbutane, which can give different alkenes depending on the direction of elimination, the E1 reaction is like the E2 reaction in tending to favor the most stable or highly substituted alkene:



$$\mathrm{CH_3{-}\overset{CH_3}{\underset{Cl}{C}}{-}CH_2{-}CH_3} \xrightarrow[\text{slow}]{H_2O} \mathrm{CH_3{-}\overset{CH_3}{\underset{\oplus}{C}}{-}CH_2{-}CH_3} + \mathrm{Cl^{\ominus}}$$

$$\xrightarrow[\text{fast}]{H_2O} \mathrm{CH_2{=}\overset{CH_3}{C}{-}CH_2{-}CH_3}\ (20\%) \;\text{ and }\; \mathrm{CH_3{-}\overset{CH_3}{C}{=}CH{-}CH_3}\ (80\%) \; + \mathrm{H_3O^{\oplus}} + \mathrm{Cl^{\ominus}}$$

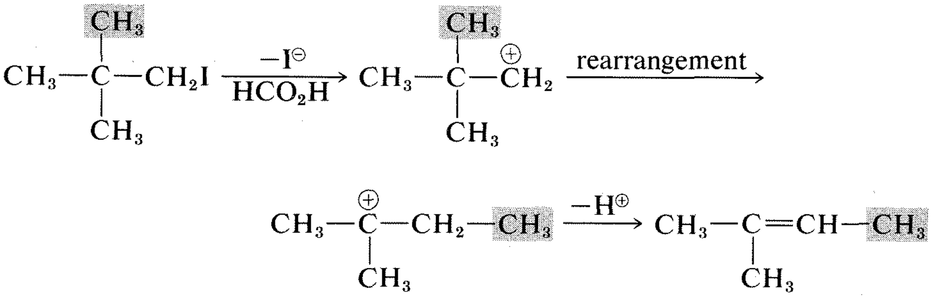
Exercise 8-30 For the reaction of Equation 8-7, would you expect the ratio of *tert*-butyl alcohol to 2-methylpropene to change significantly with changes in the nature of the leaving group [i.e., Cl, Br, I, or $\overset{\oplus}{S}(CH_3)_2$]? Give your reasoning.

Would you expect the same or different behavior as X is changed, if elimination were occurring by an *E2 mechanism* with the solvent acting as the base? Explain.

Exercise 8-31 The reaction of *tert*-butyl chloride with water is accelerated strongly by sodium hydroxide. How would the ratio of elimination to substitution products be affected thereby? Explain.

8-9B Rearrangement of Carbon Cations

Another feature of E1 reactions (and also of S_N1 reactions) is the tendency of the initially formed carbocation to rearrange, especially if a more stable carbocation is formed thereby. For example, the very slow S_N1 solvolysis of neopentyl iodide in methanoic acid leads predominantly to 2-methyl-2-butene:

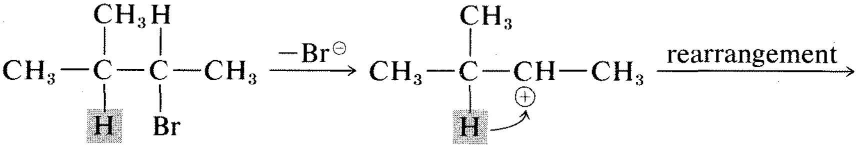


$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-CH_2I \xrightarrow[HCO_2H]{-I^\ominus} CH_3-\underset{CH_3}{\overset{CH_3}{C}}-\overset{\oplus}{C}H_2 \xrightarrow{\text{rearrangement}}$$

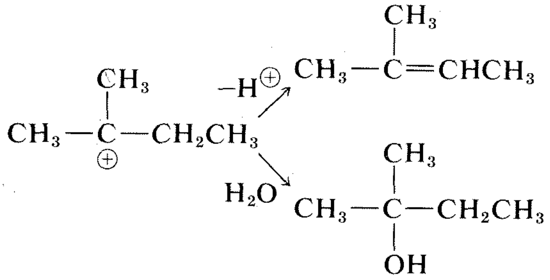
$$CH_3-\underset{CH_3}{\overset{\oplus}{C}}-CH_2-CH_3 \xrightarrow{-H^\oplus} CH_3-\underset{CH_3}{C}=CH-CH_3$$

In this reaction, ionization results in migration of a methyl group with its bonding pair of electrons from the β to the α carbon, thereby transforming an unstable primary carbocation to a relatively stable tertiary carbocation. Elimination of a proton completes the reaction.

Rearrangements involving shifts of hydrogen (as $H:^\ominus$) occur with comparable ease if a more stable carbocation can be formed thereby:



$$CH_3-\underset{H}{\overset{CH_3}{C}}-\underset{Br}{\overset{H}{C}}-CH_3 \xrightarrow{-Br^\ominus} CH_3-\underset{H}{\overset{CH_3}{C}}-\underset{\oplus}{CH}-CH_3 \xrightarrow{\text{rearrangement}}$$



Rearrangements of carbocations are among the fastest organic reactions known and must be reckoned with as a possibility whenever carbocation intermediates are involved.

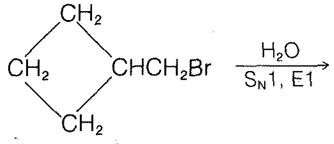
Exercise 8-32 Explain how $(CH_3)_2CDCHBrCH_3$ (where D is the hydrogen isotope of mass 2) might be used to determine whether 2-methyl-2-butene is formed directly from the bromide in an E1 reaction, or by rearrangement and elimination as shown in the preceding equations.

Exercise 8-33 Predict the products of the following reactions:

a. $CH_3CH_2CBr(CH_3)CH_2CH_3 \xrightarrow[S_N1,\ E1]{H_2O}$

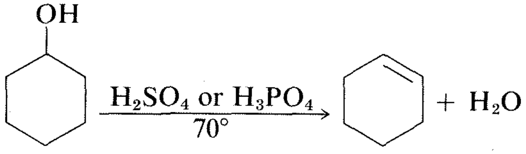
b. $(CH_3)_3CCH(CH_3)Cl \xrightarrow[S_N1,\ E1]{H_2O}$

c.



8-9C Acid-Catalyzed Elimination Reactions

Alcohols and ethers rarely undergo substitution or elimination unless strong acid is present. As we noted in Section 8-7D the acid is necessary to convert a relatively poor leaving group ($HO^\ominus$, $CH_3O^\ominus$) into a relatively good one (H_2O, CH_3OH). Thus the dehydration of alcohols to alkenes is an acid-catalyzed reaction requiring strong acids such as sulfuric or phosphoric acid:



These are synthetically useful reactions for the preparation of alkenes when the alkene is less available than the alcohol. They can occur by either the E1 or E2 mechanism depending on the alcohol, the acid catalyst, the solvent, and the temperature.

Additional Reading

J. Sicher, "The *syn* and *anti* Course in Bimolecular Olefin-Forming Eliminations," *Angew. Chem.*, Intl. Ed., **11,** 201 (1972).

F. G. Bordwell, "How Common are Base-Initiated, Concerted 1,2-Eliminations?", *Accts. of Chemical Research* **5,** 374 (1972).

A. Streitwieser, "Solvolytic Displacement Reactions at Saturated Carbon Atoms," *Chem. Rev.* **56,** 571 (1956).

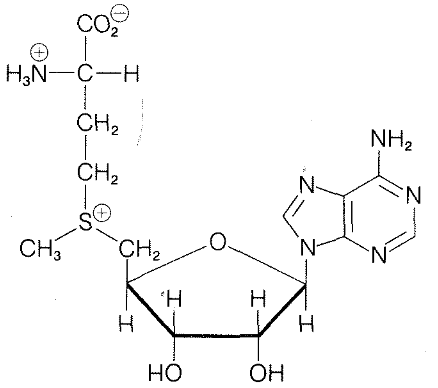
C. K. Ingold, *Structure and Mechanism in Organic Chemistry,* 2nd ed., Cornell University Press, Ithaca, N.Y., 1969.

Supplementary Exercises

8-34 Write reaction sequences, using specific and appropriate compounds, that illustrate the following conversions:

a. alcohol ⟶ ether
b. alcohol ⟶ alkene
c. alcohol ⟶ alkyl chloride
d. alcohol ⟶ nitrile (ROH ⟶ RCN)
e. alkyl chloride ⟶ sulfonium salt ⟶ alkene

8-35 *S*-Adenosylmethionine is a biologically important compound that reacts in the S_N2 manner with the *amino group* of phosphorylated 2-aminoethanol, $NH_2CH_2CH_2O$ PO_3H_2. Which carbon of *S*-adenosylmethionine would be most likely to undergo an S_N2 reaction with an RNH_2 compound? Give your reasoning and write the structures of the expected products.

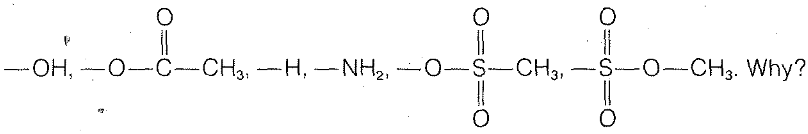

S-adenosylmethionine

8-36 Nitriles, RCN, can be prepared by S_N2 displacement of alkyl derivatives, RX, by using sodium or potassium cyanide:

$$RX + NaCN \longrightarrow RCN + NaX$$

a. Which of the following solvents would be most suitable for this reaction: water,

2-propanone, ethanol, benzene, $(CH_3)_2S{=}O$, or pentane? Give reasons for your choice.
b. Which of the six isomeric monobromoderivatives of 1-methylcyclohexene would you expect to react most rapidly with sodium cyanide? Why?
c. If you wished to make 2-phenylethanenitrile, $C_6H_5CH_2CN$, which of the following phenylmethyl compounds, RCH_2X, would you select to convert to the nitrile? $X = -F$,

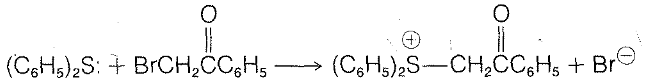


$-OH,\ -O-\overset{\overset{O}{\|}}{C}-CH_3,\ -H,\ -NH_2,\ -O-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-CH_3,\ -\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-O-CH_3$. Why?

8-37 Give a plausible explanation for each of the following observations:
a. Aqueous sodium chloride will *not* convert *tert*-butyl alcohol to *tert*-butyl chloride but concentrated hydrochloric acid will.
b. Better yields are obtained in the synthesis of isopropyl methyl ether starting with methyl iodide rather than sodium methoxide:

$$CH_3I + (CH_3)_2CHO^{\ominus}Na^{\oplus} \longrightarrow (CH_3)_2CHOCH_3 + Na^{\oplus}I^{\ominus}$$
$$(CH_3)_2CHI + CH_3O^{\ominus}Na^{\oplus} \longrightarrow (CH_3)_2CHOCH_3 + Na^{\oplus}I^{\ominus}$$

c. The following reaction proceeds only if an equivalent amount of silver fluoroborate, $Ag^{\oplus}BF_4^{\ominus}$, is added to the reaction mixture:

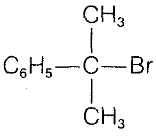


$$(C_6H_5)_2S\colon + BrCH_2\overset{\overset{O}{\|}}{C}C_6H_5 \longrightarrow (C_6H_5)_2\overset{\oplus}{S}-CH_2\overset{\overset{O}{\|}}{C}C_6H_5 + Br^{\ominus}$$

d. 1-Bromo-2-butene reacts with water to give a mixture of 2-buten-1-ol, 3-buten-2-ol, and some 1,3-butadiene.

8-38 Which compound in the following pairs would react faster under the reaction conditions? Draw the structures of the major products expected.

a. $C_6H_5CH_2CH_2Br$ or



$C_6H_5-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br$ in ethanol–water solution.

b. Same as in Part a, but with potassium iodide in acetone.
c. Same as in Part a, but with potassium hydroxide in ethanol.

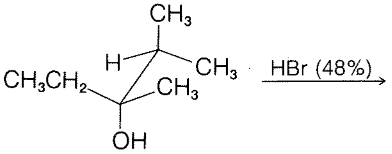
d. $CH_3CH_2\overset{\oplus}{N}(CH_3)_3\ \overset{\ominus}{B}F_4$ or $CH_3CH_2\overset{\oplus}{N}(CH_3)_3\ \overset{\ominus}{O}CH_3$ on heating in methanol solution.

8-39 Show the products of the following reactions and indicate the stereochemistry where important.

a. *trans*-1-bromo-3-methylcyclopentane $\xrightarrow[\text{acetone}]{\text{KI}}$

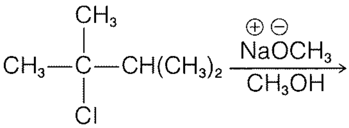
b. *trans*-1-chloro-2-methylcyclopentane $\xrightarrow[\textit{tert}\text{-butyl alcohol}]{\overset{\oplus\ominus}{\mathrm{KOC(CH_3)_3}}}$

c.



d. D-2-butanol $\xrightarrow{\text{potassium metal}}$ potassium salt $\xrightarrow{\text{L-2-chlorobutane}}$

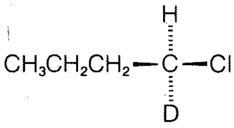
e.


$$\mathrm{CH_3{-}\underset{\underset{Cl}{|}}{\overset{\overset{CH_3}{|}}{C}}{-}CH(CH_3)_2} \xrightarrow[\mathrm{CH_3OH}]{\overset{\oplus\ \ominus}{\mathrm{NaOCH_3}}}$$

f. *meso*-1,2-dibromo-1,2-diphenylethane $\xrightarrow{\overset{\oplus\ominus}{\mathrm{KOC(CH_3)_3}}}$

8-40 The S_N1 reactions of many RX derivatives that form moderately stable carbocations are substantially retarded by adding $X^{\ominus}$ ions. However, such retardation is diminished, at given $X^{\ominus}$ concentrations, by adding another nucleophile such as $N_3^{\ominus}$. Explain.

8-41 The reaction of 1-chlorobutane with sodium hydroxide to give 1-butanol is catalyzed by sodium iodide.

a. Work out the stereochemistry to be expected for both the catalyzed and the uncatalyzed reactions if  $\mathrm{CH_3CH_2CH_2{-}\underset{D}{\overset{H}{C}}{-}Cl}$ (optically active) were used as the starting material. Show your reasoning.

b. Does retention of configuration, as the overall result of an S_N2 reaction, automatically preclude operation of the usual inversion mechanism? Explain.

8-42* Suppose a water solution was made up initially to be 0.01*M* in methyl bromide and 1.0*M* in sodium ethanoate at 50°. In water, the S_N2 rate constant for reaction of hydroxide ion with methyl bromide at 50° is 30×10^{-4} liter mole^{-1} sec^{-1}, whereas that of ethanoate ion at 50° is 1.0×10^{-4} liter mole^{-1} sec^{-1}. The ionization constant of ethanoic acid at 50° is 1.8×10^{-5}. In the following, neglect the rates of the reactions of methyl bromide with water or ethanoic acid and any further reactions of ethanoate:

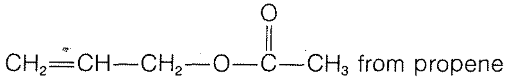
a. Calculate the hydroxide-ion concentration in the initial solution.

b. Calculate the initial rates of formation of methyl ethanoate and methanol.

c. Compute the concentrations of the organic products when the reaction is complete. Show your reasoning and justify any assumptions.

d. What kind of information would be needed to predict what products would be expected from a solution of methyl bromide and sodium hydroxide in methanol? Explain.

8-43 Indicate how you would synthesize each of the following substances from the given organic starting materials and any other necessary organic or inorganic reagents. Specify reagents and conditions. (You may have to use reactions discussed in Chapter 4.)

a. 

$\mathrm{CH_2{=}CH{-}CH_2{-}O{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}CH_3}$ from propene

b. $CH_3{-}O{-}CH_2CH_3$ from ethanol

c. $CH_3{-}O{-}C(CH_3)_3$ from *tert*-butyl alcohol

d. cyclohexene from cyclohexane

8-44 Which compound in each of the following pairs would you expect to react more readily with (A) potassium iodide in 2-propanone, (B) concentrated sodium hydroxide in ethanol, and (C) silver nitrate in aqueous ethanol? Write equations for all the reactions involved and give your reasoning with respect to the predicted orders of reactivity.

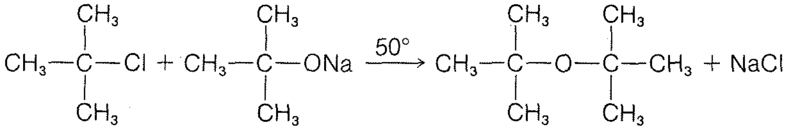
a. methyl chloride and isobutyl chloride with A, B, and C

b. methyl chloride and *tert*-butyl chloride with A, B, and C

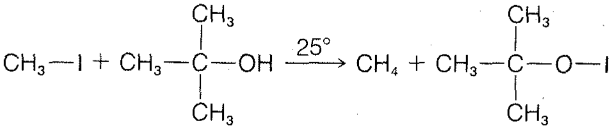
c. *tert*-butyl chloride and 1-fluoro-2-chloro-2-methylpropane with B and C

d. 1-chloro-2-butene and 4-chloro-1-butene with A, B, and C

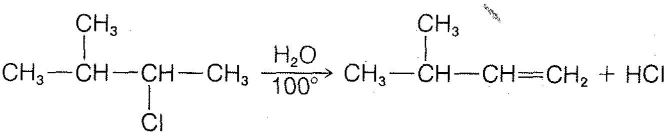
8-45 Classify each of the following reactions from the standpoint of yield, side reactions, and reaction rate as good, fair, or bad synthetic procedures for preparation of the indicated products under the given conditions. Show your reasoning and designate any important side reactions.

a. 

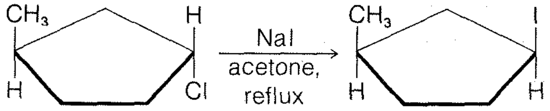
$$\mathrm{CH_3{-}\underset{CH_3}{\overset{CH_3}{C}}{-}Cl + CH_3{-}\underset{CH_3}{\overset{CH_3}{C}}{-}ONa \xrightarrow{50^\circ} CH_3{-}\underset{CH_3}{\overset{CH_3}{C}}{-}O{-}\underset{CH_3}{\overset{CH_3}{C}}{-}CH_3 + NaCl}$$

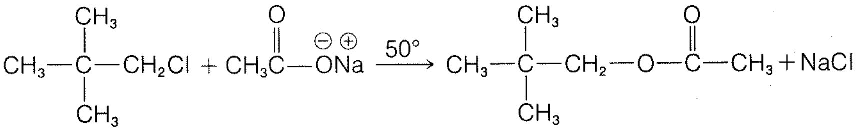
b. 

$$\mathrm{CH_3{-}I + CH_3{-}\underset{CH_3}{\overset{CH_3}{C}}{-}OH \xrightarrow{25^\circ} CH_4 + CH_3{-}\underset{CH_3}{\overset{CH_3}{C}}{-}O{-}I}$$

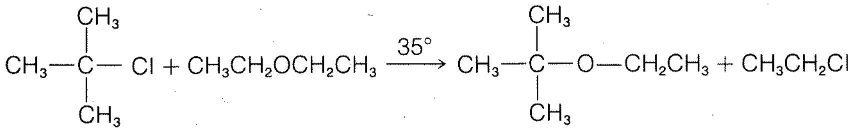
c. 

$$\mathrm{CH_3{-}\overset{CH_3}{CH}{-}\underset{Cl}{CH}{-}CH_3 \xrightarrow[100^\circ]{H_2O} CH_3{-}\overset{CH_3}{CH}{-}CH{=}CH_2 + HCl}$$

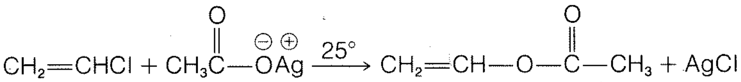
d. 

e. 

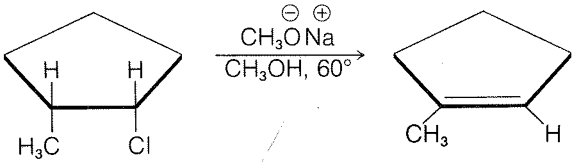
$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-CH_2Cl + CH_3\overset{O}{\overset{\|}{C}}-\overset{\ominus\,\oplus}{ONa} \xrightarrow{50^\circ} CH_3-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-O-\overset{O}{\overset{\|}{C}}-CH_3 + NaCl$$

f. 

$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-Cl + CH_3CH_2OCH_2CH_3 \xrightarrow{35^\circ} CH_3-\underset{CH_3}{\overset{CH_3}{C}}-O-CH_2CH_3 + CH_3CH_2Cl$$

g. 

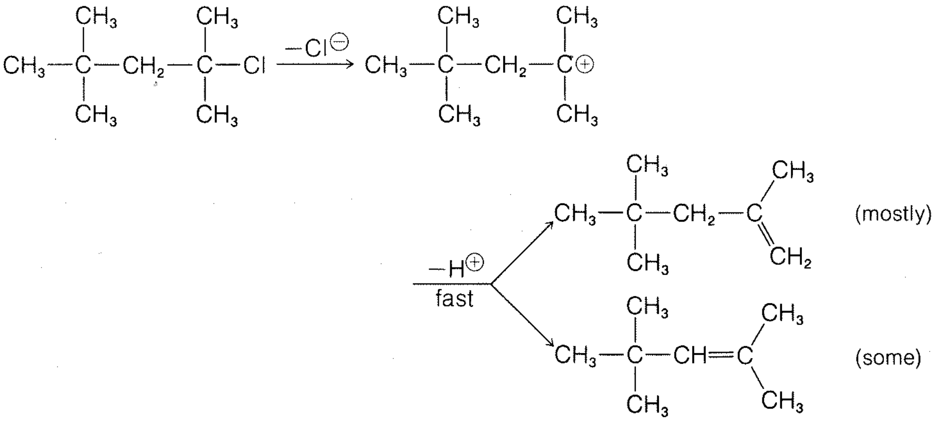
$$CH_2{=}CHCl + CH_3\overset{O}{\overset{\|}{C}}-\overset{\ominus\,\oplus}{OAg} \xrightarrow{25^\circ} CH_2{=}CH-O-\overset{O}{\overset{\|}{C}}-CH_3 + AgCl$$

h. 

8-46 Consider each of the following compounds to be in unlabeled bottles in pairs as indicated. For each pair give a chemical test (preferably a test-tube reaction) that will distinguish between the two substances. Write equations for the reactions involved.

	Bottle A	*Bottle B*
a.	$(CH_3)_3CCH_2Cl$	$CH_3CH_2CH_2CH_2Cl$
b.	$BrCH{=}CHCH_2Cl$	$ClCH{=}CHCH_2Br$
c.	$(CH_3)_3CCl$	$(CH_3)_2CHCH_2Cl$
d.	$CH_3CH{=}CHCl$	$CH_2{=}CHCH_2Cl$
e.	$(CH_3)_2C{=}CHCl$	$CH_3CH_2CH{=}CHCl$
f.	$CH_3CH_2CH{=}CHCl$	$CH_2{=}CHCH_2CH_2Cl$

8-47 Why does the following E1 reaction give more of the least substituted alkene? (Use models.)



$$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-\underset{CH_3}{\overset{CH_3}{C}}-Cl \xrightarrow{-Cl^{\ominus}} CH_3-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-\underset{CH_3}{\overset{CH_3}{C}}{\oplus}$$