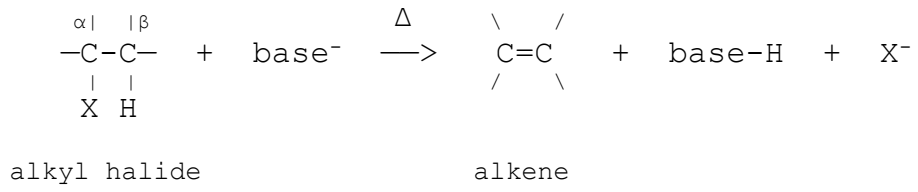
Chapter 7
Elimination Reactions of Alkyl Halides

Alkyl halides are important organic reagents because they are electrophiles in various reactions. In the preceding chapter we saw how they can react with nucleophiles in nucleophilic substitution reactions to produce a great variety of organic molecules.

We also learned in Section 6.8 that another type of reaction could compete with nucleophilic substitutions, especially with S_N1 reactions. Although we ignored this competition in Chapter 6 to better focus on our first type of organic reaction, in this chapter we assess this rival kind of reaction called an elimination reaction.

7.1 General Nature of Elimination Reactions

In substitution reactions, such as nucleophilic substitutions, an atom or group replaces another atom or group on a molecule. In **elimination reactions** two atoms or groups leave a molecule and are not replaced. Various kinds of elimination reactions exist, but this chapter explores a very important type: two atoms, a hydrogen and a halogen, depart from *adjacent* carbons of an alkyl halide.



Thus an alkyl halide yields an alkene. Because no atoms replace the eliminated atoms, a π bond forms between the adjacent carbons losing atoms. These are the α and β carbons, designated by

their proximity to the halide functional group, as in Chapter 6.

Temperature affects elimination reactions. Two reactant molecules become three product molecules, so $\Delta S°$ is positive for the reaction. Therefore, according to the equation (Section 5.2):

$$\Delta G° = \Delta H° - T\Delta S°$$

as temperature (T) increases, $\Delta G°$ decreases and becomes more favorable. Indeed, high temperatures are normally used in elimination reactions. The above balanced reaction equation does not indicate a reaction mechanism, which is our next concern.

Puzzle 7.1

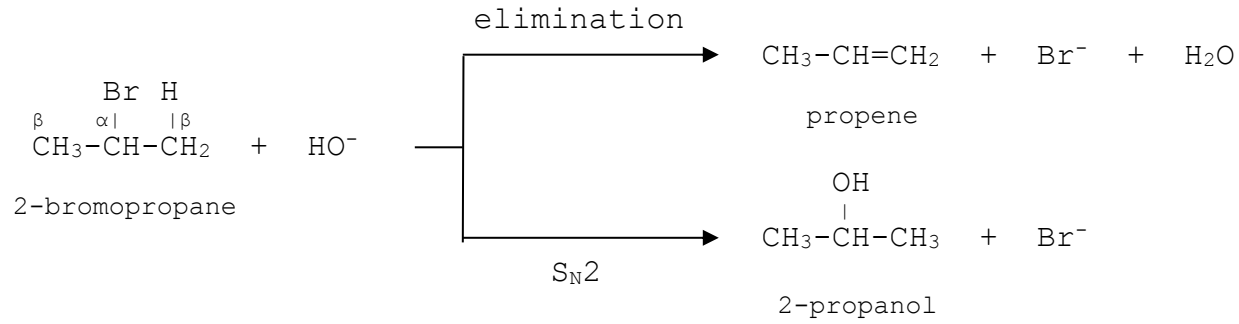
For an intermolecular S_N2 reaction of an alkyl halide, is $\Delta S°$ distinctly positive, distinctly negative, or about zero? Explain.

7.2 Kinetic Studies and Mechanisms of Elimination Reactions

Kinetic studies illuminated the mechanisms of S_N2 reactions (Section 6.3A) and S_N1 reactions (Section 6.5A). Now they will shed light on two elimination mechanisms.

7.2A Mechanism of E2 Reactions

Consider the simultaneous reactions:

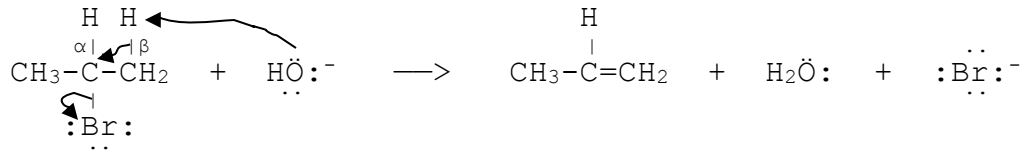


In an elimination reaction the α carbon of the alkyl halide loses a halogen and a β carbon loses a hydrogen to yield an alkene. In this alkyl halide the two β carbons are equivalent and elimination of a hydrogen from either one yields the same product. A competing S_N2 reaction produces the alcohol product. What is the mechanism of the elimination reaction?

Kinetic studies on the above elimination reaction show that its rate is first order in each of the two reactants. Its rate law follows accordingly:

$$\text{rate} = k[\text{R-Br}][\text{HO}^-]$$

Evidently, both reactants participate in (or possibly before) the rate-limiting step. Here is the simplest mechanism consistent with the kinetics:



This mechanism, confirmed by other kinds of experiments, is called **E2,** meaning a bimolecular elimination. Note that the 2 indicates the number of reactants in the rate-limiting (and only) step, not the number of steps. It is a concerted reaction, in which one mechanistic step comprises all bond making and breaking. In this regard an E2 reaction resembles an S_N2 reaction.

In this E2 mechanism the alkyl halide reacts as an *acid* electrophile by donating a β proton to a *base* nucleophile. This reaction succeeds because the donated proton leaves its electrons in a stable place: a π bond between the β and α carbons. In turn, the α carbon, which can tolerate only four bonds, must break its bond with the bromine. Fortunately, as we know from Chapter 6, the halogen is a good leaving group because it is stable after acquiring another lone pair and negative charge.

The above series of three electron arrows nicely illustrates all four rules for electron arrows (Section 5.1). Note especially how each arrow, even the second one, ends at an atom, and how each of the latter two arrows picks up where the preceding one leaves off, head to tail.

Puzzle 7.2 ———————————————————————————————————————

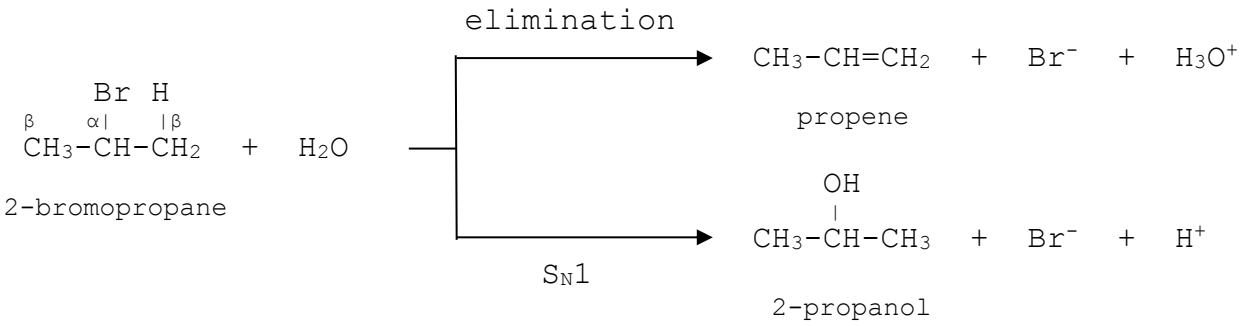
Consider the E2 reaction (ignore the concurrent S_N2 reaction):

$$CH_3O^- + CH_3CH_2CHClCH_3 \longrightarrow$$

(a) Draw the two constitutional isomers produced.
(b) Draw the mechanism (with electron arrows of course) leading to each alkene.

7.2B Mechanism of E1 Reactions

Consider the competing reactions:



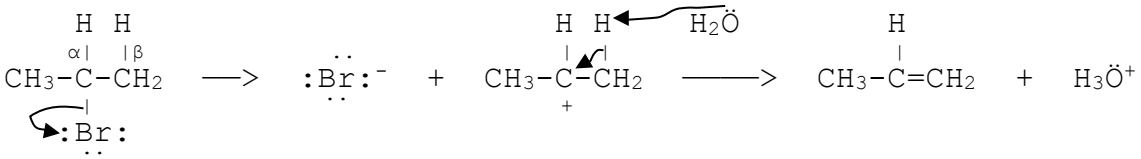
The organic reactant and organic products are identical to those during the E2 reaction of Section 7.2A. Different, however, is the inorganic reactant, water. This weak nucleophile accounts for the S_N1 product, 2-propanol, as well as a different elimination mechanism.

Once again, kinetic studies suggest the mechanism of the above elimination reaction. This reaction is first order in alkyl bromide but zero order in water. Consistent with this information is

its rate law:

$$\text{rate} = k[\text{R-Br}]$$

The water does not react in (or before) the rate-limiting step! Such a unimolecular rate-limiting step, where only one molecule reacts, designates the elimination reaction as **E1.** Its mechanism is consistent with this and other studies:



Aside from the alkene product, this two-step reaction recalls the S_N1 mechanism. In both cases the first step is identical: the good leaving group, halide, leaves the α carbon to form a carbocation intermediate. In both cases this carbocation is the key factor in many reaction properties. In both cases the nucleophile does not react in the first step. In the E1 reaction, however, the carbocation electrophile reacts as an *acid*, donating a β proton to the *base* nucleophile. (In an S_N1 reaction the carbocation electrophile does not donate a proton to the nucleophile.) This is a reasonable step because forming a π bond fills the octet shell and neutralizes the charge of the cationic carbon.

This mechanism agrees with the unimolecular kinetics only if its first step, which excludes the base, is the slow, rate-limiting step. As explained in Section 6.5B for the identical S_N1 first step, this slowness is reasonable because a bond must break without any compensating bond formation. The kinetics of E1 reactions resemble S_N1 kinetics.

We will compare the E1 and E2 mechanisms by several criteria in the next several sections. These criteria will allow us to predict when and how E1 and E2 reactions occur.

Puzzle 7.3 ———————————————————————————————————————

Consider the E1 reaction (ignore the concurrent S_N1 reaction):

$$CH_3OH + (CH_3)_3CI \longrightarrow$$

(a) Draw the alkene product.
(b) Draw the mechanism (with electron arrows of course) for the reaction.

Puzzle 7.4 ———————————————————————————————————————

α-Pinene is a component of turpentine, found in pine trees. During its biosynthesis a carbocation yields the alkene:

Draw a mechanism for this step, using an unspecified base.

7.3 Effects of Base Strength on Elimination Reactions

In both types of elimination reactions, a base abstracts a proton from an acid.

Consequently, the strength of the acid determines the strength needed by the base. Softness does not help the base because an acid is hard (Section 4.9). In contrast, softness helps nucleophiles react with soft S_N2 electrophiles (Section 6.4C).

In E2 reactions the acid is an alkyl halide, which loses a β proton to the base. Although the most acidic proton on the alkyl halide, this β proton is weakly acidic, like protons on most carbons. Therefore, the E2 base must be strong to directly remove the proton. (A strong base has a conjugate acid with a $K_a < 10^{-7}$.)

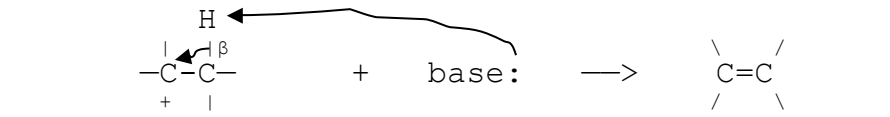
as basicity of base ↑, E2 rate ↑

Because nucleophilicity and basicity are related, but not identical, properties, a good, strong S_N2 nucleophile is often, but not always, a strong base. Table 7.1 shows four categories of bases and S_N2 nucleophiles. Among the bases in Table 7.1, only those in the column of strong bases are good for E2 reactions. The examples of *tert*-butoxide and three halide ions show that good E2 bases are not synonymous with good S_N2 nucleophiles. In fact, one can find nucleophiles with any combination of suitability and unsuitability for E2 and S_N2 reactions.

Table 7.1 Categories of Bases and S_N2 Nucleophiles

	Strong bases (good for E2)	**Weak bases** (poor for E2, good for E1)
Strong S_N2 nucleophiles (good for S_N2)	HO^-, RO^-, $-N-$, $-S^-$	Cl^-, Br^-, I^-
Weak S_N2 nucleophiles (poor for S_N2)	$(CH_3)_3CO^-$	F^-, HOH, ROH

In an E1 reaction the acid is not the alkyl halide itself, but the carbocation intermediate, which loses a β proton to the base in the second step:



very acidic carbocation
incomplete octet

uncharged
complete octet

In contrast to the β proton of an alkyl halide, the β proton of a carbocation is very acidic. It is true that this proton is bonded to a carbon, which normally does not donate a proton readily. Yet, a carbocation is exceptionally unstable and acidic. By losing a β proton, a carbocation forms a π bond, which both neutralizes its charge and completes its octet. Therefore a good E1 base can be weak. In fact, a weak base helps an E1 reaction compete against an E2 reaction, which needs a strong base. All of the bases in the last column of Table 7.1 are good, weak E1 bases.

Puzzle 7.5 ———————————————————————————————————————

Why does Table 7.1 classify *tert*-butoxide, $(CH_3)_3CO^-$, as a weak S_N2 nucleophile?

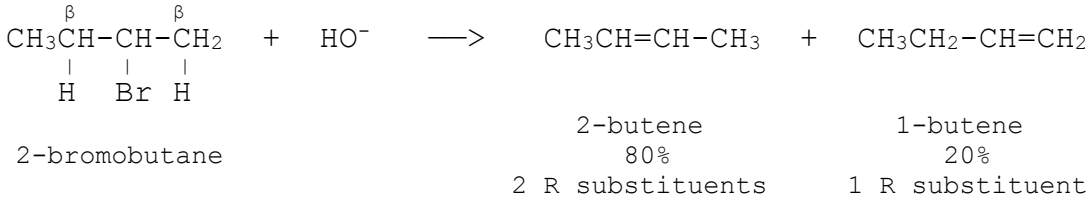
Puzzle 7.6 ———————————————————————————————————————

Classify the following as good E2 or good E1 bases:
(a) CH_3OH (b) CH_3O^- (c) CH_3NH_2 (d) $^-NH_2$

7.4 Product Constitutional Isomers of Elimination Reactions

Sometimes an elimination reaction can produce more than one alkene constitutional isomer. We know that the electrophile loses a β proton, but what if two (or three) *different* β protons could be removed?

Consider the elimination reaction:

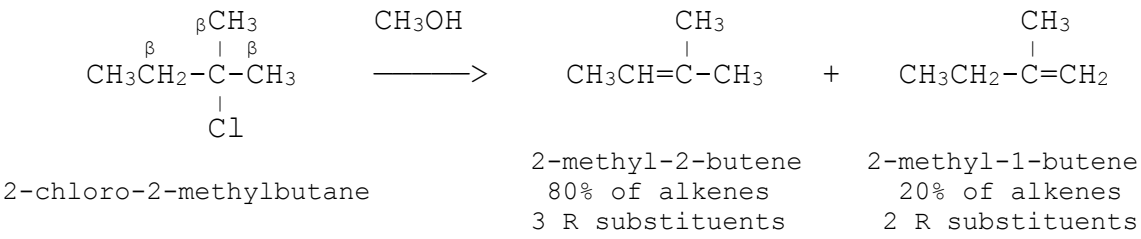


This reaction is mostly E2 because hydroxide ion is a strong base, which reacts before a carbocation forms. Note that two alkene isomers are produced. This is not surprising because the alkyl halide has two different β carbons with β hydrogens.

Why does the reaction yield more 2-butene than its isomer, 1-butene? As usual, we expect more of the product that is more stable. For reasons to be explored in Section 8.7B, an alkene isomer with more alkyl groups substituted on the carbons of its double bond is lower in energy than another isomer with fewer alkyl substituents. The first product above has two alkyl (methyl) substituents on its double bond, whereas the second product has only one alkyl (ethyl) substituent. Consequently, 2-butene is a more stable and more plentiful product than 1-butene. Yet, because their difference in energy is small, both isomers are significant products.

Actually, statistics favors the minor isomer product. Abstracting any of three β hydrogens from C(1) yields 1-butene, whereas 2-butene results from removing one of only two β hydrogens from C(3). Stability, however, is more important than statistics.

Now consider another elimination reaction:



This is an E1 reaction because the methanol solvent is a weak base, unsuited for an E2 reaction. Like the E2 reaction above, does this two-step mechanism yield more of the more highly

substituted alkene isomer? The major E1 product is the first isomer, which has three alkyl (methyl) substituents on its double bond. In contrast, the second, minor isomer has only two alkyl (ethyl and methyl) substituents. Evidently the more stable product is again the major product. Indeed, *most E2 and E1 reactions produce more of the alkene that is more stabilized by alkyl substituents*. Once again, statistics would predict more of the minor isomer in six-to-two ratio. Once again, however, stability is more important than statistics.

Note that the alkyl halide electrophile above actually has three β carbons. Why are only two alkene isomers produced? Two of the three β carbons lie in identical methyl groups. Any of their six β hydrogens can be lost to give the identical alkene isomer, 2-methyl-1-butene.

Puzzle 7.7 ———————————————————————————————————

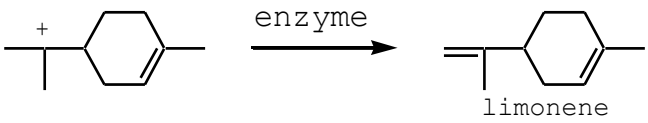
Consider the elimination reaction:

$$CH_3CH_2O^- + (CH_3CH_2)_2CICH_3 \longrightarrow$$

(a) Is this mostly an E1 or E2 reaction? Explain.
(b) Draw the alkene product(s). Disregard stereoisomers.
(c) If more than one alkene constitutional isomer is formed, which is the major product? Explain.
(d) Draw the mechanism for the reaction leading to an alkene.

Puzzle 7.8 ———————————————————————————————————

An enzyme is a huge polymer of definite shape that catalyzes biological reactions. Part of its catalytic activity involves binding substrates (i.e., reactants) to particular locations at its active (i.e., reactive) site. An enzyme controls the following step in the biosynthesis of limonene, an oil with a lemon-like odor in lemons and oranges:



(a) Without an enzyme, would limonene be the predominant constitutional isomer produced from this elimination step? Explain.
(b) By its structure how could an enzyme control the constitutional isomer produced?

7.5 Effective Electrophiles for Elimination Reactions

In Section 7.3 we examined the kinds of nucleophiles useful for elimination reactions: strong bases for E2 reactions and weak bases for E1 reactions. Now we consider the other half of the reactant story: the acid electrophiles.

7.5A Leaving Groups of Effective Electrophiles

In Chapter 6 we learned that the leaving group leaves in the rate-limiting steps of both S_N2 and S_N1 reactions. Consequently, both nucleophilic substitutions require their leaving group byproducts to be stable, weak bases, such as halide ions.

Likewise, in our elimination reactions the acid electrophile releases its leaving group in the rate-limiting step: the only step of an E2 reaction, or the first, slow step of an E1 reaction.

Accordingly these byproduct leaving groups should be stable, weak bases. Furthermore, the weaker the leaving group's basicity, the faster the elimination reaction.

as basicity of L ↓, stability of L ↑ & E2 rate ↑ & E1 rate ↑

All of the halide ions are weak bases and therefore good leaving groups. Yet, weaker basicity makes some halide ions better leaving groups than others.

$$F^- < Cl^- < Br^- < I^-$$

ability as leaving group in E2, E1, S_N2, and S_N1 reactions

We saw the same ranking for S_N2 (Section 6.4A) and S_N1 reactions (Section 6.5B). All four reaction types show the same trends in leaving groups!

Puzzle 7.9 ———————————————————————————————————

Which of the following are good leaving groups for elimination reactions?
(a) HO^- (b) $N{\equiv}C^-$ (c) H_2O (d) $CH_3CO_2^-$ (e) $^-CH_3$ (f) CH_3NH_2 (g) H^-

Puzzle 7.10 ———————————————————————————————————

More pyrophosphate groups than halides are found in organic compounds in organisms. Consider an alkyl pyrophosphate, a derivative of pyrophosphoric acid.

alkyl pyrophosphate pyrophosphoric acid

Pyrophosphoric acid has these successive K_a values: 1×10^{-1}, 3×10^{-2}, 2×10^{-6}, and 6×10^{-9}. Could the pyrophosphate ion readily leave the above alkyl pyrophosphate in an elimination reaction? Explain.

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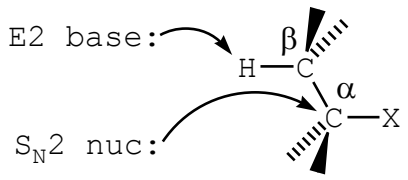
7.5B Carbon Skeletons of Effective Electrophiles

Recall that S_N2 and S_N1 reactions clearly prefer certain classes of electrophiles. Fewer alkyl groups on the α carbon of the electrophile diminish steric hindrance and favor an S_N2 reaction (Section 6.4B). In contrast, more alkyl groups on the α carbon stabilize the carbocation intermediate and favor an S_N1 reaction (Section 6.5B).

E2 reactions are not so particular. They can tolerate any class of electrophile except methyl. Of course, a methyl electrophile with only one carbon cannot yield a double bond between *two* carbons. Also, steric hindrance at the α carbon of the electrophile generally does not influence an E2 reaction, unlike an S_N2 reaction.



electrophile

different routes for E2 and S_N2 nucleophiles

Whereas an S_N2 nucleophile must penetrate to the back of the α carbon, an E2 base nucleophile can normally avoid steric hindrance by removing a β proton from the periphery of the electrophile.

Because of this tolerance, we have this listing of E2 electrophiles:

3° ≅ 2° ≅ 1°; not methyl

suitability of electrophiles for E2 reactions

Note how much this listing differs from the S_N2 ranking of electrophiles (Section 6.4B).

E1 reactions select the carbon skeletons of their electrophiles more carefully. Their first, rate-limiting step forms a carbocation, which alkyl groups stabilize by hyperconjugation (Section 6.5B). As we learned for S_N1 reactions, ordinary methyl and primary carbocations are too unstable to form. Furthermore, hyperconjugation stabilizes tertiary carbocations more than secondary carbocations. Accordingly, tertiary carbocations are easier to make than secondary carbocations. So, we rank E1 electrophiles:

3° > 2°; not 1° or methyl

suitability of electrophiles for E1 (and S_N1) reactions

Of course, S_N1 reactions, which have an identical first step, prefer their electrophiles in the same order (Section 6.5B).

Puzzle 7.11

Indicate which of the following are suitable E2 electrophiles. Explain.
(a) CH_3Br (b) CH_3CH_2I (c) $(CH_3)_2CHCl$ (d) $(CH_3)_2CHOH$ (e) $(CH_3)_3CH$
(f) $(CH_3)_3CBr$ (g) $(CH_3)_3COCH_3$ (h) $C_6H_5CH_2Cl$

Puzzle 7.12

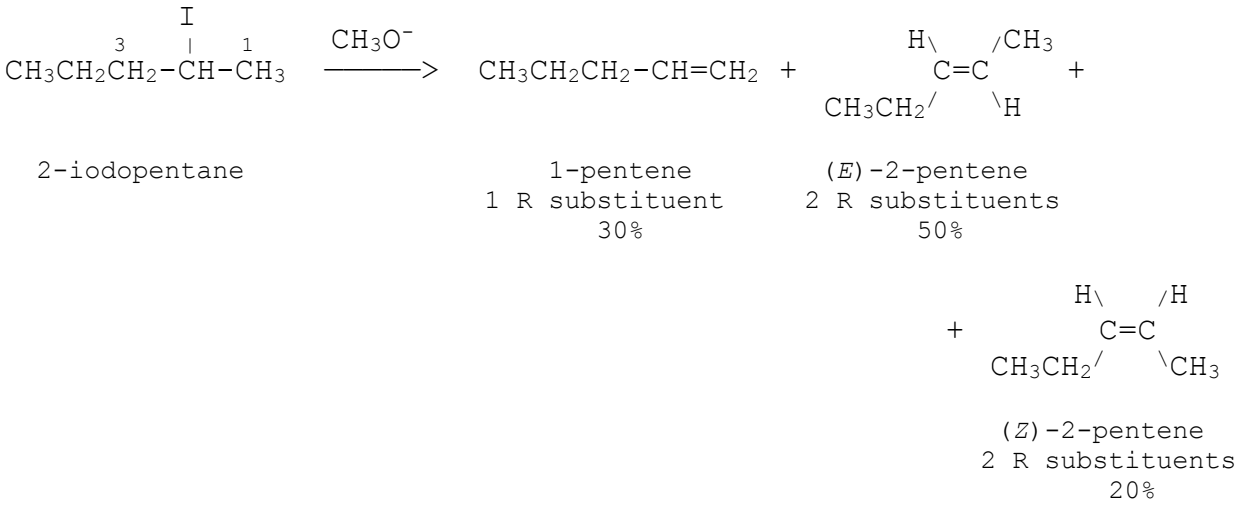
Indicate which of the compounds in Puzzle 7.11 are suitable E1 electrophiles. Explain.

7.6 Stereochemistry of Elimination Reactions

In Section 7.4 we distinguished between different constitutional isomer products. Now we will make even finer, stereochemical distinctions among products.

7.6A Product Stereoisomers

Consider the elimination reaction (ignore competing nucleophilic substitutions):



The strong base, methoxide ion, makes this mostly an E2 reaction. It produces three alkenes: the first by proton abstraction from C(1), the last two by abstractions from C(3). The last two are diastereomers of each other. The first alkene is a constitutional isomer of the other two. Are the relative yields of the two constitutional isomers reasonable? The 1-pentene isomer has only 30% yield, while the 2-pentene isomer (including both stereoisomers) has 70%. This is reasonable because 2-pentene has more (two) alkyl substituents than 1-pentene with only one alkyl substituent.

Are the relative yields of the two diastereomers reasonable? In the *Z* diastereomer the ethyl and methyl groups on the same side of the double bond sterically repel each other (discussed further in Section 8.7B). The *E* diastereomer, with the two alkyl groups on opposite sides of the double bonds, avoids this steric repulsion. Accordingly, the *E* stereoisomer is more stable and so has a higher yield (50%) than the *Z* stereoisomer (20%).

Whether for molecular geometry (Section 1.6) or for conformations (Section 2.6) or here for alkenes:

as intramolecular repulsion ↑, enthalpy ↑ & stability ↓

If ethanol replaces ethoxide ion as the base in the above elimination reaction, the weaker base would pursue an E1 reaction. Although the absolute yields of the three alkenes could change, their relative yields would be similar to the above distribution. Again the more stable *E* diastereomer would form in greater yield than the *Z* diastereomer.

In general, *both E2 and E1 favor not only the more stable constitutional isomer product, but also the more stable stereoisomer product*. Thus, most E2 and E1 reactions are partially stereoselective, that is, they select a certain stereoisomer at the expense of another (Section 6.3B). Normally they are not completely stereoselective because some of both possible stereoisomers form. Yet, we will see in the next section that some E2 reactions are 100% stereoselective and some cannot make the more stable stereoisomer or even the more stable constitutional isomer.

Puzzle 7.13

Consider the elimination reaction (ignore substitutions):

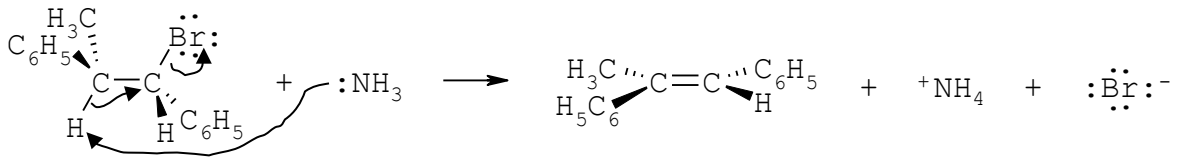
$$CH_3CHBrCH_2CH_3 + H_2O \longrightarrow$$

(a) Is this mostly an E1 or E2 reaction? Explain.
(b) Draw the constitutional isomer products. Which isomer predominates? Explain.
(c) Draw any stereoisomer products. Which stereoisomer predominates? Explain.

7.6B Steric Orientation

In the preceding section we saw that both E2 and E1 reactions tend to be partially stereoselective to produce more of the more stable *E* stereoisomer. In special situations, however, elimination reactions can be 100% stereoselective and even give solely the less stable *Z* stereoisomer. Let us investigate how steric orientation of the electrophile can affect elimination reactions.

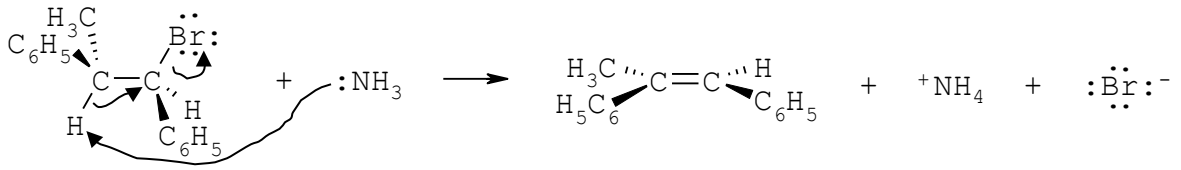
Consider an E2 elimination reaction with a special electrophile, designed to betray steric requirements in the electrophile:



(1*S*,2*R*) (*E*) only

Strongly basic ammonia (K_a of $^+NH_4 = 5 \times 10^{-10} < 10^{-7}$) assists this E2 reaction. Note the special alkyl halide with chiral atoms at the α and β carbons. Also note the uniqueness of the organic product. It is not surprising that no other constitutional isomer is produced because the electrophile has only one β carbon with a hydrogen. (The benzene ring on the α carbon has no β hydrogen.) More surprising is the lack of any *Z* stereoisomer product. Evidently this is a completely stereoselective reaction.

A very similar E2 reaction confirms this remarkable degree of stereoselectivity:



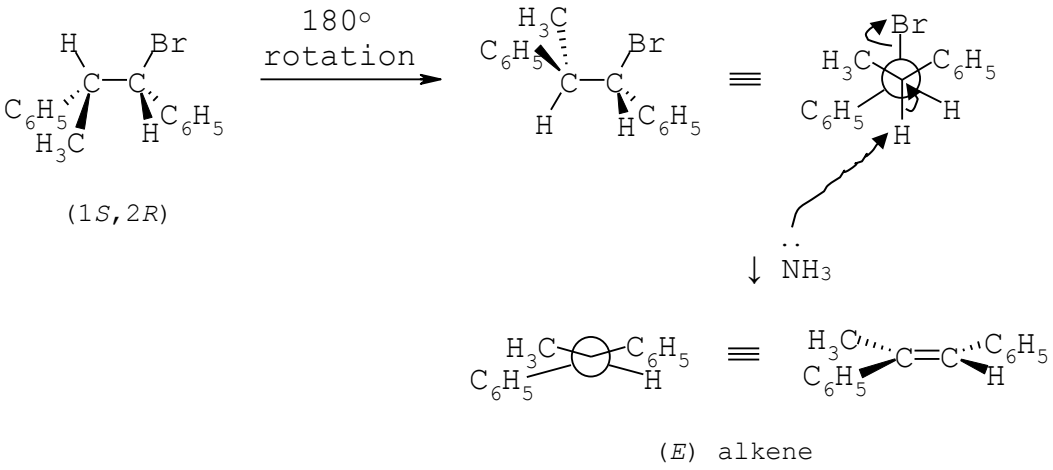
(1*R*,2*R*) less stable (*Z*) only

With its α carbon inverted, the alkyl halide reactant is a diastereomer of the previous reactant. Also 100% stereoselective, the reaction yields only one stereoisomer, the diastereomer of the previous product, although it is the less stable *Z* stereoisomer.

Thus, like S_N2 reactions, some E2 reactions can be completely stereoselective. This similarity is not surprising because both S_N2 and E2 reactions are concerted. With simultaneous bond making and breaking, a concerted reaction demands a particular orientation of reactants in

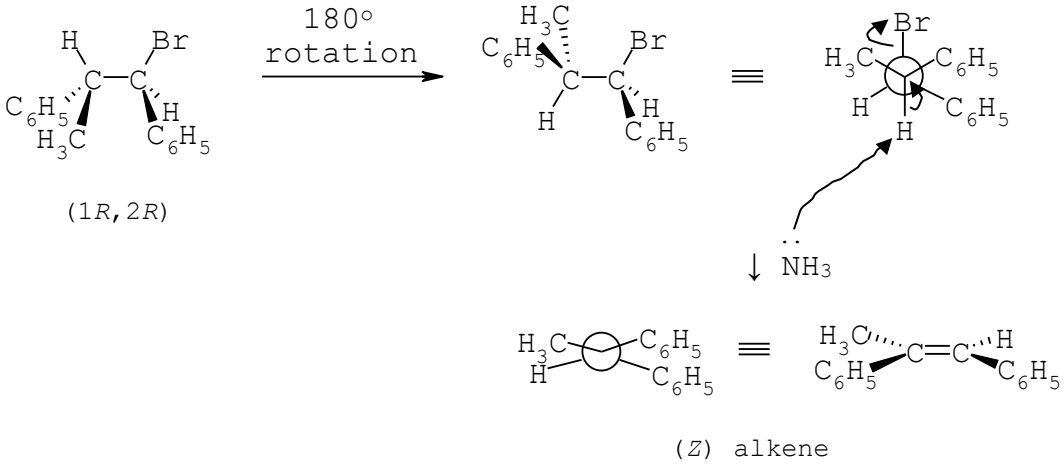
order to maximize orbital overlap of all the involved bonds so that electrons can flow readily among them. Like S_N2 reactions, E2 reactions maximize orbital overlap by the nucleophile approaching the electrophile from the back. Of course, the α and β carbons freely rotate around their mutual single bond. Yet, the E2 base normally waits to take a β proton until it and the halogen are anti (Section 2.6C).

Note that the last two reactions present their electrophiles in the desired anti conformations:



(1*S*,2*R*)

(*E*) alkene

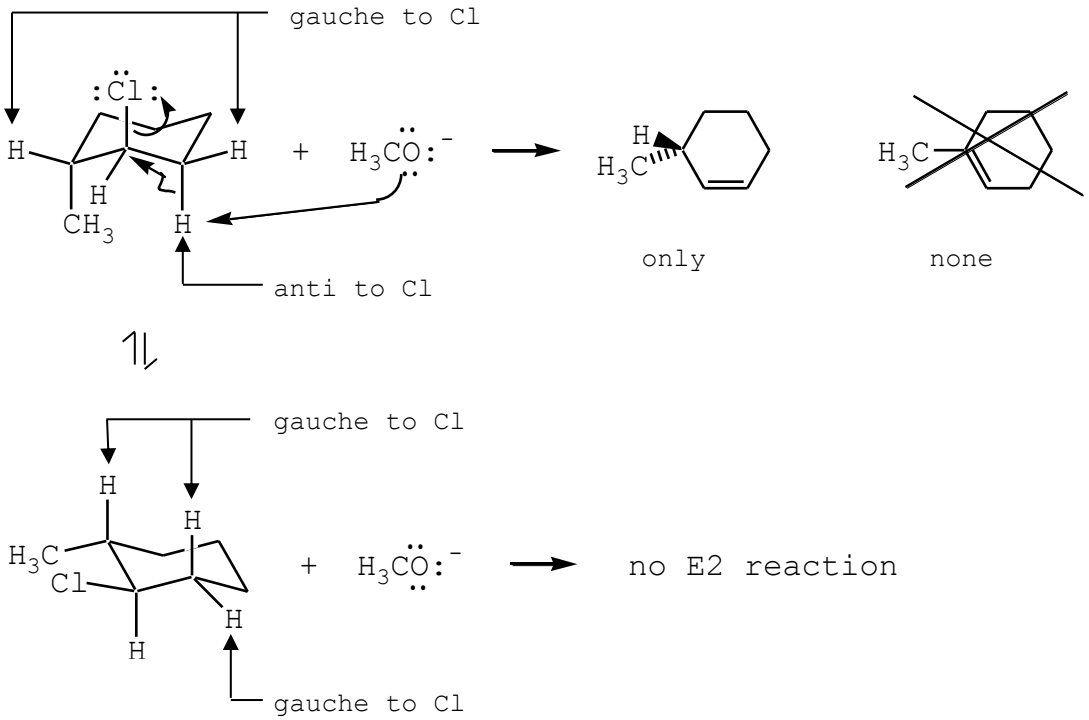


(1*R*,2*R*)

(*Z*) alkene

Each alkyl halide reacts only in its one possible anti conformation to yield only one stereoisomer. For each conformation visualize the benzene and methyl groups on the β carbon descending as the repelling σ pair of the β hydrogen folds into a non-repelling π bond. Also imagine the hydrogen and benzene ring on the α carbon ascending as the repelling σ pair of the bromine departs. Thus, one can rationalize the formation of the correct stereoisomer in each case. In general, whenever possible *E2 reactions proceed by this so-called* ***anti elimination***, with the β hydrogen and the leaving group departing from opposite sides of the electrophile.

Cyclohexyl halides, with their more restricted conformational possibilities, demonstrate a particular version of the anti E2 reaction:



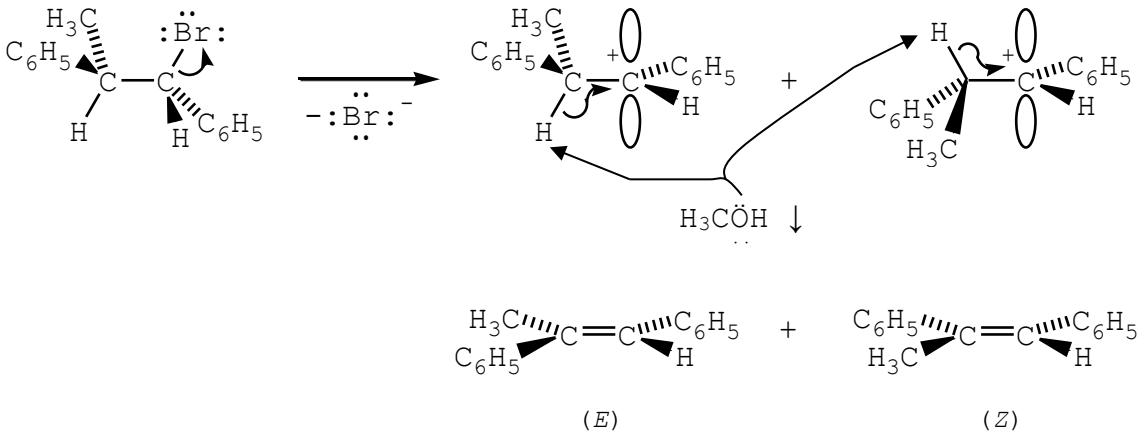
Why is only one constitutional isomer produced? In the first chair conformation of the electrophile only one β hydrogen is anti to the axial chlorine. The other two β hydrogens are gauche to the chlorine and therefore ineligible for E2 reaction.

In the electrophile's second conformation all three β hydrogens are gauche, not anti, to the equatorial chlorine. Consequently this conformation allows no E2 reaction. Indeed, no β hydrogen can ever be anti to an equatorial leaving group, as a model shows. Thus, to achieve an E2 reaction, a cyclohexyl halide must adopt a conformation that puts both the halogen and a β hydrogen axial, that is, anti to each other.

Why did we not observe this anti steric orientation in earlier E2 reactions? The earlier, simpler electrophiles had at least two hydrogens on a β carbon. Consequently, the alkyl halide could adopt at least two different anti conformations and not limit stereochemical options. The unusual electrophiles of this section were carefully chosen to be fully stereoselective. This situation is like that of S_N2 reactions in Chapter 6. We only *observe* a stereoselective inversion of configuration when the S_N2 electrophile's α carbon is a chiral atom, although back approach inverts the configuration of every S_N2 electrophile.

A few electrophiles cannot adopt an anti conformation because of geometric constraints. In that case, an E2 reaction might proceed from the second-best **syn** conformation, with the β hydrogen and leaving group on exactly the same side of the electrophile.

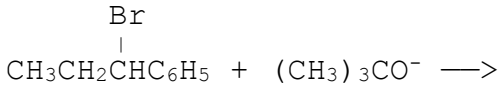
Do E1 reactions demand a particular steric orientation? Consider the E1 reaction with a weak base, methanol:



This E1 reaction yields both *E* and *Z* alkene diastereomers (although more of the more stable *E*), in contrast to the lone *E* stereoisomer from the E2 reaction of the identical alkyl bromide earlier in this section. The two stereoisomer products result from two different conformations of the carbocation intermediate. When the bond to the β hydrogen is coplanar with the empty *p* orbital of the cationic carbon, the base can take the hydrogen. Although E1 still favors the more stable *E* alkene product with less steric repulsion, E1 reactions do not require one particular conformation of their electrophiles.

Puzzle 7.14

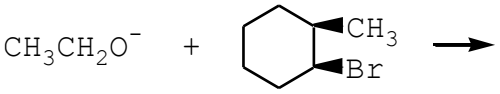
Consider the E2 reaction:



(a) Draw all the constitutional isomer products.
(b) One of the isomer products is produced in two stereoisomers. Draw the two stereoisomers.
(c) Draw the conformation of the electrophile that yields each stereoisomer of part (b).

Puzzle 7.15

Consider the elimination reaction:

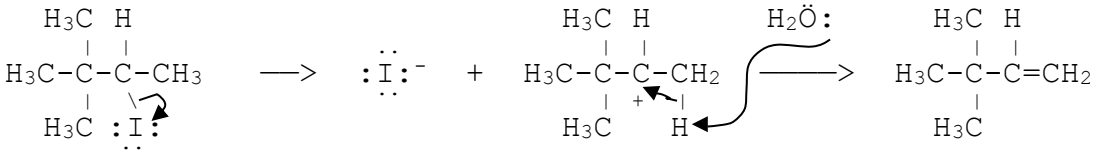


(a) Draw the alkene product(s). Explain the number of products.
(b) If more than one alkene is produced, which one predominates? Explain.

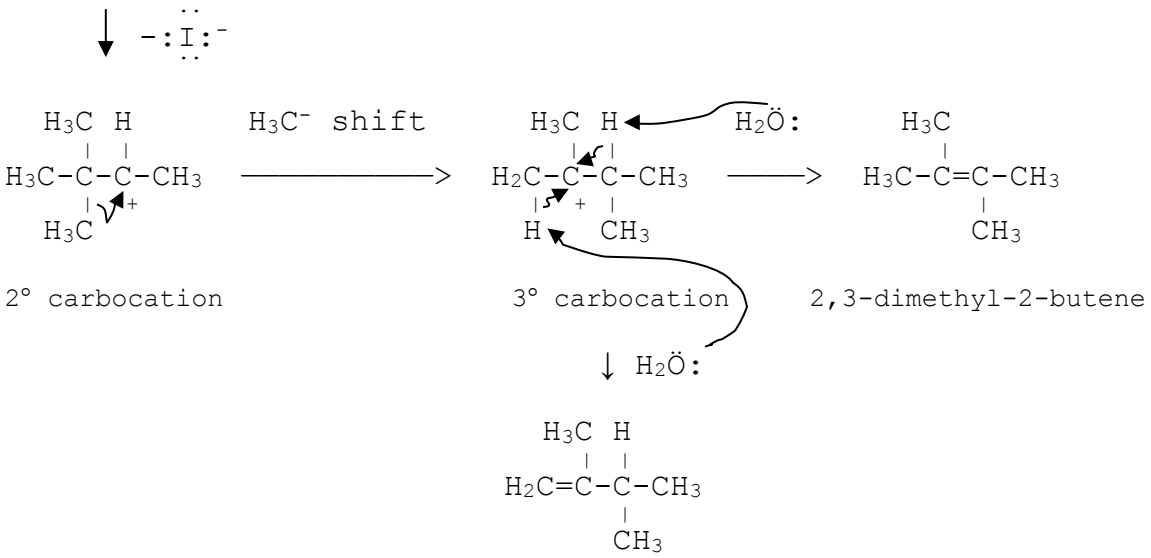
7.7 Carbocation Rearrangements in Elimination Reactions

In Section 6.5D we found that S_N1, but not S_N2, reactions sometimes occur with a carbocation rearrangement. How about elimination reactions? Because they do not generate a carbocation intermediate, E2 concerted reactions cannot undergo carbocation rearrangement. Once again E2 resemble S_N2 reactions.

In contrast, some E1 reactions give carbocations whose structure permits rearrangement. Consider the E1 reaction:



2-iodo-3,3-dimethylbutane 3,3-dimethyl-1-butene



2° carbocation 3° carbocation 2,3-dimethyl-2-butene

2,3-dimethyl-1-butene

Without a carbocation rearrangement, this reaction yields one constitutional isomer, 3,3-dimethyl-1-butene. In addition, the initial secondary carbocation can rearrange to a tertiary carbocation by a methyl shift. This second carbocation can lose either of two different β hydrogens to water to give two more unexpected isomers, 2,3-dimethyl-2-butene and 2,3-dimethyl-1-butene. The formation of rearranged isomers is another property that S_N1 and E1 reactions share.

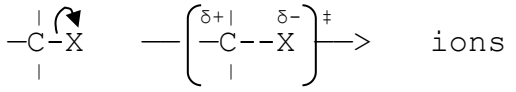
Puzzle 7.16

(a) Find an alkyl halide that can undergo an E1 carbocation rearrangement with a hydride shift.
(b) Show the reaction, including all alkene isomer products.

7.8 Preferred Solvents for Elimination Reactions

In Section 6.6 we found that S_N2 reactions with anionic nucleophiles prefer aprotic solvents, whereas S_N1 reactions favor protic solvents. Will elimination reactions follow the same pattern?

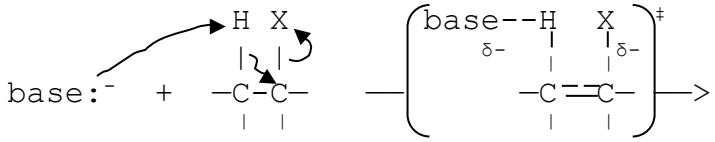
Indeed, like S_N1 reactions, E1 reactions prefer protic solvents. The reasoning is identical because the rate-limiting step is identical:



rate-limiting step of E1 reaction

A protic solvent, such as water or a small alcohol, can begin to hydrogen bond with the incipient halide anion leaving group in the transition state. Such an incipient hydrogen bond stabilizes the transition state of the rate-limiting step and lowers the activation energy of the step. Not only this step but also the whole E1 reaction is expedited. Furthermore, such protic solvents as water and alcohols are also good, weak E1 bases for the second step of the reaction.

E2 reactions normally prefer a different kind of solvent. With the exceptions of ammonia and amines, most strong bases suitable for E2 reactions are anions. As we did for S_N2 reactions in Section 6.6, let us limit this discussion to E2 reactions with anionic bases, realizing that uncharged bases may change the solvent preference. Now compare the transition state to the reactants of the only step of an E2 reaction:



rate-limiting step of E2 reaction

Although there is an incipient halide anion in the transition state, which can begin to hydrogen bond with protic solvent, the reactant base is a true anion. So a protic solvent molecule stabilizes and weakens the base by fully hydrogen bonding with it. Consequently, like most S_N2 reactions, an E2 reaction with an anionic base prefers an aprotic solvent, such as propanone or DMSO, to avoid hydrogen bonding with the base. This preference, however, is not a requirement. E2 reactions can also occur in protic solvents, but more slowly.

Puzzle 7.17 ———————————————————————————————————————

Consider the elimination reaction:

$$CH_3CHClCH_3 + Br^- \longrightarrow$$

(a) Would this make a better E1 or E2 reaction? Explain.
(b) Select a solvent that facilitates this reaction. (c) Draw the mechanism.

7.9 Comparisons of Elimination and Substitution Reactions

Let us review our knowledge of elimination reactions by summarizing and comparing this knowledge in three ways: E2 versus E1 reactions, E2 versus S_N2 reactions, and E1 versus S_N1 reactions. Keep in mind that all of this information is best understood and retained by clearly visualizing the mechanisms as reasonable interactions between nucleophiles and electrophiles.

7.9A E2 versus E1 Reactions

Table 7.2 summarizes and contrasts the essential properties of our two types of elimination reactions. Despite their differences, E2 and E1 reactions have similar preferences for electrophiles (both leaving group and carbon skeleton) and product constitutional isomers and stereoisomers. Note that many of the properties of an E1 reaction are determined by its carbocation. Finally, recall that a high temperature thermodynamically helps elimination reactions because of their positive $\Delta S°$ values (Section 7.1).

Table 7.2 Summary of E2 and E1 Elimination Reactions

	E2	**E1**
Kinetics	1st order in both reactants (both reactants in rls)	1st order in elie only (only elie in rls)
Number of steps	1 (strong base doesn't wait)	2 or more (base awaits strong elie)
Elie's L group	Weak base needed e.g., X^- (stable byproduct)	Identical to E2
Elie's C skeleton	3° ≅ 2° ≅ 1°; not CH_3 (stabilize alkene)	3° > 2°; not 1° or CH_3 (stabilize carbocation)
Base nucleophile	Strong needed e.g., HO^-, RO^-, $-N\equiv$ (weak acid electrophile)	Weak e.g., HOH, ROH, X (strong C^+ acid)
Solvent	Aprotic favored e.g., propanone, DMSO, DMF (avoid H bonding nuc^-)	Protic favored e.g., HOH, MeOH, EtOH (start H bonding rls TS)
Regioselectivity	More substituted alkene favored (more stable)	Identical to E2
Stereochemistry	Anti elimination (stereoselective)	Unspecific (C^+ less stereoselective)
Stereoselectivity	*E* product favored if possible (more stable)	*E* product favored (more stable)
C^+ rearrangement	Never (no C^+)	Sometimes (for suitable C^+)
Temperature	High preferred (positive $\Delta S°$)	Identical to E2

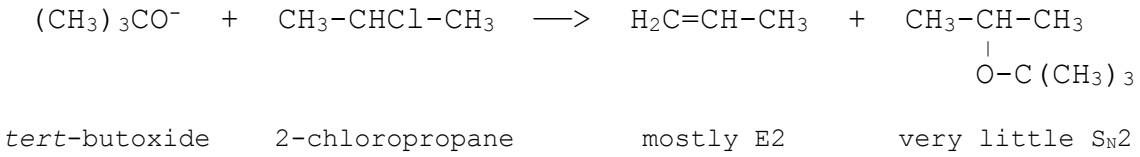
rls = rate-limiting step; nuc = nucleophile; elie = electrophile

Puzzle 7.18

To facilitate an E2 reaction at the expense of an E1 reaction, how should one adjust the following features?
(a) base concentration (b) basicity of nucleophile (c) solvent

7.9B E2 versus S_N2 Reactions

The main competition for E2 reactions is S_N2 reactions (and vice versa). Table 7.3 shows many similarities for E2 and S_N2 reactions but also a couple of important differences (besides the type of product, of course). A bulky nucleophile slows an S_N2 reaction (Section 6.4C), but a bulky base normally does not hinder an E2 reaction (Section 7.3). As a result, a very bulky base, such as *tert*-butoxide, strongly favors E2 over S_N2 reactions. For example:



Little nucleophilic substitution competes with this E2 reaction.

Table 7.3 Summary of E2 and S_N2 Reactions

	E2	**S_N2**
Kinetics	1st order in both reactants (both reactants in rls)	Identical to E2
Number of steps	1 (strong base doesn't wait)	Identical to E2 (strong nuc doesn't wait)
Elie's L group	Weak base needed e.g., X^- (stable byproduct)	Identical to E2
Elie's C skeleton	3° ≅> 2° ≅ 1°; not CH_3 (stabilize alkene)	CH_3 > 1° > 2°; not 3° (minimize steric hindrance)
Base or nuc	Strong base needed; bulky OK e.g., HO^-, RO^-, $-\ddot{N}-$ (weak acid elie)	Strong nuc needed; not too bulky e.g., HO^-, RO^-, $-\ddot{N}-$, Cl^-, Br^- (soft, weak elie)
Solvent	Aprotic favored e.g., propanone, DMSO, DMF (avoid H bonding nuc^-)	Identical to E2
Stereochemistry	Anti elimination (stereoselective)	Back approach (stereoselective)
C^+ rearrangement	Never (no C^+)	Identical to E2
Temperature	High preferred (positive & $\Delta S°$)	Moderate

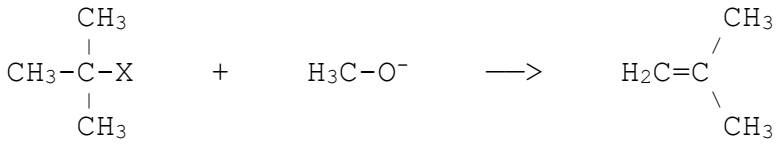
rls = rate-limiting step; nuc = nucleophile; elie = electrophile

Another feature that differentiates these competing reactions is the electrophile's carbon skeleton. Their preferences are exactly opposite. A methyl halide can undergo S_N2, but not E2, reactions:

$$H_3C\text{-}X \quad + \quad H_3C\text{-}O^- \quad \longrightarrow \quad H_3C\text{-}O\text{-}CH_3$$

methyl halide methoxide ion S_N2 only

On the other hand, a tertiary halide and a strong base react by an E2 reaction without competition from an S_N2 reaction:



tert-butyl halide methoxide ion E2 only

A final factor that assists E2 reactions at the expense of S_N2 reactions is high temperature (Section 7.1).

Just as the scarcity of competing reactions generally makes an S_N2 reaction synthetically superior to S_N1, an E2 reaction is normally used to make an alkene from an alkyl halide because it has fewer competing reactions than E1. Table 7.4 rearranges some of the material in Tables 7.2 and 7.3 to delineate the ideal conditions for making an alkene by E2 with minimal interference from E1, S_N2, and S_N1 reactions.

Table 7.4 Ideal Conditions for Making an Alkene by E2

Electrophile's C skeleton	3° > 2° > 1°; not CH_3
Base	Strong and bulky e.g., $(CH_3)_3CO^-$
Solvent	Aprotic
Temperature	High

Puzzle 7.19

To facilitate an E2 reaction at the expense of an S_N2 reaction, how should one adjust the following features?
(a) electrophile's carbon structure (b) kind of nucleophile (c) temperature

7.9C E1 versus S_N1 Reactions

S_N1 reactions provide the main competition for E1 reactions (and vice versa). Table 7.5 shows almost identical conditions for E1 and S_N1 reactions, although their products differ greatly. Thus, they generally run concurrently and often give poor yields. Just as an S_N2 reaction is a better synthetic method than an S_N1 reaction (Section 6.8), so an E2 reaction surpasses an E1 reaction in cleanly making an alkene. Although sometimes E2 reactions unavoidably contaminate S_N2 reactions, a very bulky base, such as *tert*-butoxide, always encourages E2 at the expense of S_N2 (Section 7.9B). Also, high temperatures encourage an E1 reaction more than an S_N1 reaction (Section 7.1)

Table 7.5 Summary of E1 and S_N1 Reactions

	E1	S_N1
Kinetics	1st order in electrophile (only electrophile in rls)	Identical to E1
Number of steps	2 or more (base awaits strong elie)	Identical to E1 (nuc awaits strong elie)
Elie's L group	Weak base needed e.g., X^- (stable byproduct)	Identical to E1
Elie's C skeleton	3° > 2°; not 1° or methyl (stabilize C^+)	Identical to E1
Base or nucleophile	Weak base e.g., HOH, ROH, X^- (strong C^+ acid)	Weak nuc favored e.g., HOH, ROH (strong C^+ elie)
Solvent	Protic strongly favored e.g., HOH, MeOH, EtOH (start H bonding rls TS)	Identical to E1
Stereochemistry	Unspecific (C^+ less stereoselective)	Identical to E1
C^+ rearrangement	Sometimes (for suitable C^+)	Identical to E1
Temperature	High preferred (positive $\Delta S°$)	Moderate

rls = rate-limiting step; nuc = nucleophile; elie = electrophile

Puzzle 7.20

Draw all the organic products from both the elimination and nucleophilic substitution reactions of 2-chlorobutane in methanol. Ignore stereoisomers.

Chapter Summary

1. In E2 and E1 elimination reactions, a proton and a leaving group (typically a halide ion) leave adjacent carbons of an electrophile to form an alkene.
2. An E2 reaction, a bimolecular elimination, is first order in both base and electrophile.
3. While losing a β proton to the base, an E2 electrophile forms a π bond and discharges the leaving group in a one-step mechanism.
4. An E1 reaction, a unimolecular elimination, is first order in the electrophile and zero order in

the base.
5. In the first, rate-limiting step of its multistep mechanism, an E1 electrophile dissociates into a carbocation, the key factor in an E1 reaction. In the second, fast step, the carbocation intermediate donates a β proton to the base while forming a π bond.
6. An E2 base must be strong to take a proton from a weakly acidic electrophile (typically an alkyl halide).
7. An E1 base can be weak because it takes a proton from a strongly acidic carbocation intermediate. E1 reactions generally prefer weak bases to avoid competition with E2 reactions.
8. When the electrophile has non-equivalent β protons, most E2 and E1 reactions produce more of the more stable alkene isomer with more alkyl substituents.
9. Both E2 and E1 reactions require an electrophile with a weakly basic leaving group, such as any of the halide ions.
10. Alkyl substitution at the α carbon of the electrophile promotes an E1 reaction by stabilizing the carbocation intermediate. Alkyl substitution at the electrophile's α carbon has little effect on an E2 reaction because steric hindrance is normally not an issue. Of course, a methyl electrophile cannot form an alkene by either reaction.
11. Both E2 and E1 reactions usually produce more of the more stable *E* alkene diastereomer than the *Z* diastereomer (if any).
12. By requiring anti elimination, the E2 reaction can be very stereoselective. Because of its symmetric, planar carbocation intermediate, an E1 reaction is much less stereoselective.
13. During E1, but not E2, reactions some carbocations may rearrange to yield additional alkene isomers.
14. An E1 reaction strongly prefers a protic solvent to begin hydrogen bonding the transition state of the rate-limiting step. A normal E2 reaction (with an anionic base) prefers an aprotic solvent to avoid hydrogen bonding to the base.
15. E2 and S_N2 reactions have many similar properties. Yet, they have different preferences for α alkyl substitution, nucleophilic bulk, and temperature.
16. E1 and S_N1 reactions have practically identical conditions and occur concurrently. With less competition E2 reactions are generally used to synthesize alkenes.

Additional Puzzles

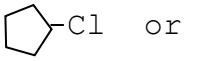
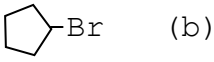
7.21 Consider making an alkene from 2-chloro-3-methylbutane while minimizing competing nucleophilic substitutions.
(a) Which reactant would you react with the alkyl halide?
(b) Which alkene constitutional isomers would be produced and which would predominate?
(c) Draw the mechanism for the reaction leading to the major isomer.

7.22 Consider the elimination reaction of 3-iodohexane with methoxide ion.
(a) Is this reaction mostly E1 or E2? Explain.
(b) Which alkene constitutional isomers would be produced and which would predominate?
(c) Specify a solvent that would facilitate this reaction.

7.23 Consider the elimination reaction of 3-bromo-2,4-dimethylpentane in ethanol.
(a) Is this reaction mostly E1 or E2? Explain.

(b) Draw the two alkene constitutional isomers produced.

7.24 For each of the following choices, decide which reacts faster with potassium hydroxide in an elimination reaction. Explain each choice. Ignore substitution reactions.

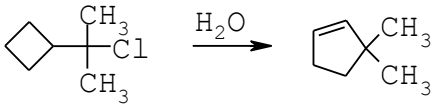
(a)  or 

(b) $(CH_3)_3CI$ or $(CH_3)_2CHI$

(c) CH_3CH_2Br or $(C_6H_5)_2CHBr$

(d) CH_3CH_2Br in water or in propanone

7.25 (a) Draw a mechanism for the reaction:

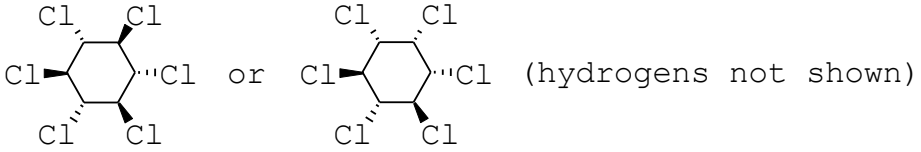


(b) What unusual kind of rearrangement occurs during this reaction, and why does it occur?

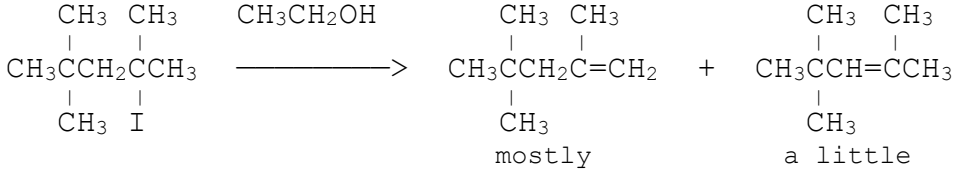
7.26 (a) Draw bromocyclohexane in a chair conformation that allows it to react in an E2 reaction with *tert*-butoxide ion (Me_3CO^-).

(b) Draw the mechanism with the organic product.

7.27 Which of the following electrophiles undergoes an elimination reaction much faster with ethoxide ion? Explain.



7.28 Explain the surprising product distribution of isomers in the reaction:

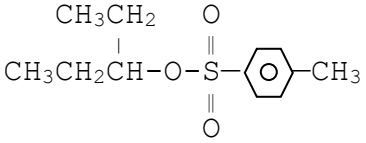


7.29 Show the reagent(s) that would best convert 2-bromo-3-methylbutane to each of the following products (not necessarily exclusively):

(a) 2-iodo-3-methylbutane (b) 3-methyl-2-butanol (c) 2-methyl-2-butene

(d) 2-methyl-1-butene

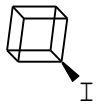
7.30 (a) After consulting Table 4.1 (Section 4.2), decide if the following compound could undergo an elimination reaction with *tert*-butoxide ion:



(b) If reaction can occur, show all alkene constitutional isomers and stereoisomers produced.

(c) Which stereoisomer predominates?

7.31 Why would the cubic molecule below, named iodocubane, not react in E1 or E2 reactions?

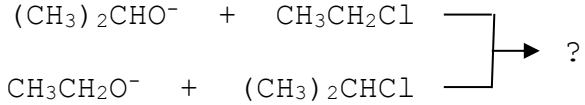


7.32 Draw the main organic product from the reaction of 1-chloropropane with each of the following reagents:
(a) HO^- at 25° (b) HO^- at 100° (c) $(CH_3)_3CO^-$ (d) Br^-

7.33 Find a *single* alkyl halide that can yield all of the following products (not necessarily exclusively), and show reagents for the conversions:
(a) 3,3-dimethyl-1-pentene (b) 2,3-dimethyl-2-pentene (c) 3,4-dimethyl-2-pentene

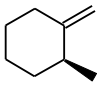
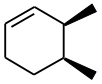
7.34 The basicity of fluoride ion varies with the nature of the solvent. What kind of solvent decreases its basicity the most?

7.35 Consider two ways to make the same nucleophilic substitution product:

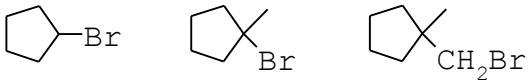


(a) Draw the organic product.
(b) Which reaction would give more of this product with less elimination? Explain.

7.36 Outline efficient syntheses that yield these major products:

(a)  (b)  (c) 

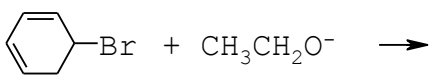
7.37 Rank the following electrophiles by reactivity for each mechanism:



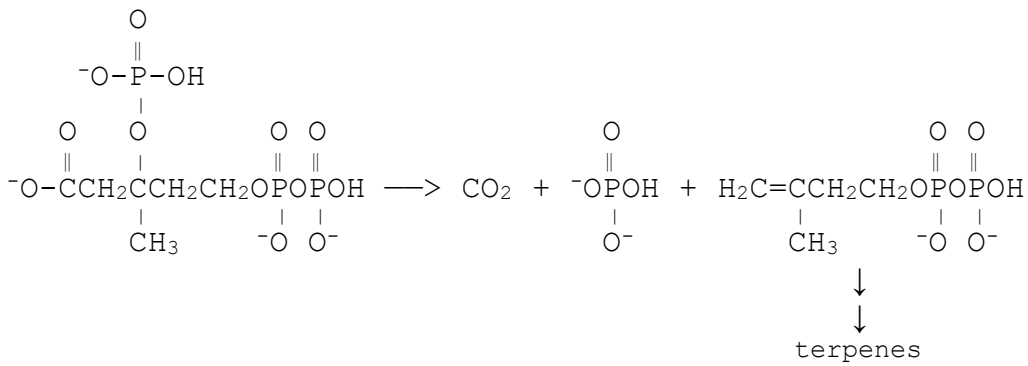
(a) S_N1 (b) S_N2 (c) E1 (d) E2

7.38 Draw the main organic products from both the elimination and nucleophilic substitution reactions of 3-iodo-2-methylpentane with the following reagents. Ignore stereoisomers.
(a) CH_3OH (b) $NaOCH_3$, propanone

7.39 Which constitutional isomer would be the predominant cyclic product from the following elimination reaction? Explain.



7.40 Another kind of elimination reaction occurs during the biosyntheses of terpenes, oils that give plants distinctive tastes and smells:



Draw a concerted mechanism for this elimination reaction.

10/06