

Organic Chemistry, *Fourth Edition*

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Chapter 8 Alkyl Halides and Elimination Reactions

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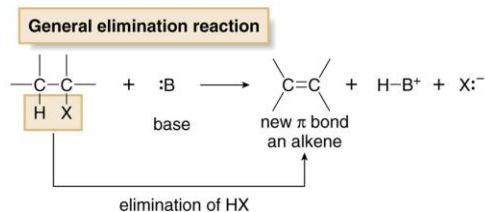
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General Features of Elimination

- Elimination reactions involve the **loss of elements** from the starting material to **form a new π bond** in the product.

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- Alkyl halides undergo elimination reactions with Brønsted-Lowry bases. The elements of HX are lost and an alkene is formed.

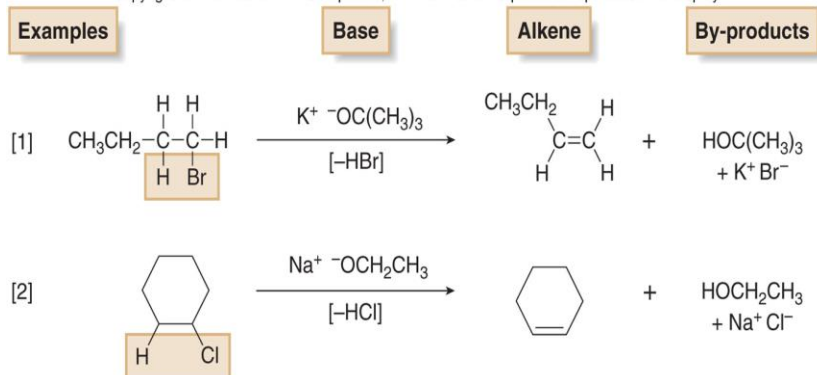


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Elimination of HX

- In both example reactions a base **removes the elements** of an acid, **HX**, from the organic starting material.

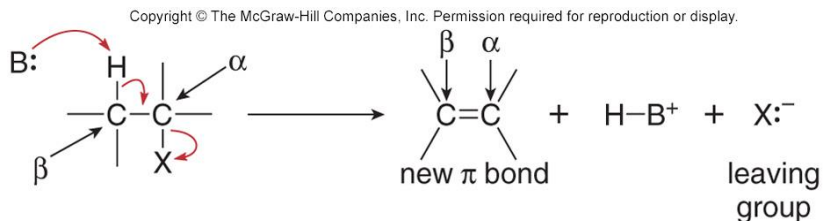
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Dehydrohalogenation

- Removal of the elements HX is called dehydrohalogenation.
- Dehydrohalogenation is an example of **β elimination**.
- The curved arrow formalism shown below illustrates how four bonds are broken or formed in the process.



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Common Bases for Dehydrohalogenation

- The most common bases used in elimination reactions are **negatively charged oxygen compounds**:
such as HO^- and its alkyl derivatives, RO^- , called alkoxides.

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Table 8.1 Common Bases Used in Dehydrohalogenation

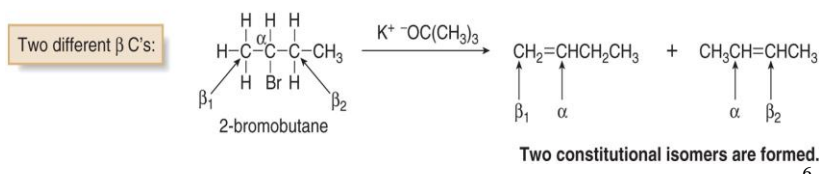
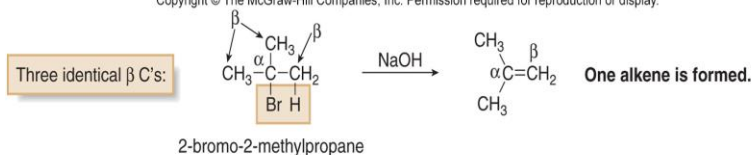
Structure	Name
$\text{Na}^+ \text{OH}^-$	sodium hydroxide
$\text{K}^+ \text{OH}^-$	potassium hydroxide
$\text{Na}^+ \text{OCH}_3^-$	sodium methoxide
$\text{Na}^+ \text{OCH}_2\text{CH}_3^-$	sodium ethoxide
$\text{K}^+ \text{OC}(\text{CH}_3)_3^-$	potassium <i>tert</i> -butoxide

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Drawing Products of Dehydrohalogenation

- Find the α carbon.
- Identify all β carbons with H atoms.
- Remove the elements of H and X from the α and β carbons and form a π bond.

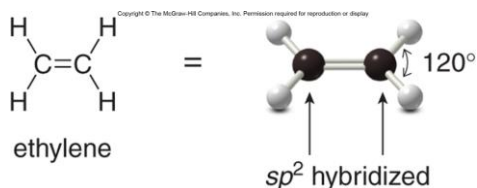
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Alkenes

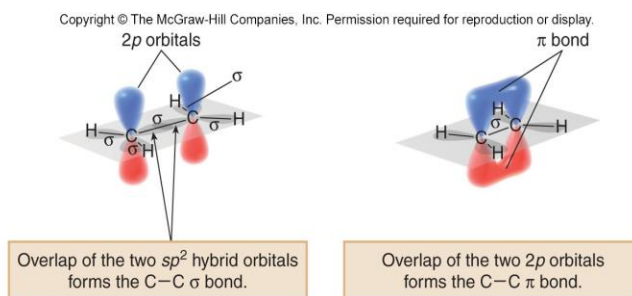
- **Alkenes** are hydrocarbons containing a carbon-carbon **double bond**.
- Each carbon of the double bond is **sp^2 hybridized**.
- The alkene carbons are **trigonal planar**.
- The **bond angles** are **120°** .



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Alkene Structure

- The double bond of an alkene consists of a σ bond and a π bond.



- The σ bond, formed by end-on overlap of the two sp^2 hybrid orbitals, lies in the plane of the molecule.
- The π bond, formed by side-by-side overlap of two 2p orbitals, lies perpendicular to the plane of the molecule. The π bond is formed during elimination.

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Classifying Alkenes

- Alkenes are classified according to the **number of carbon atoms** bonded to the carbons of the double bond.

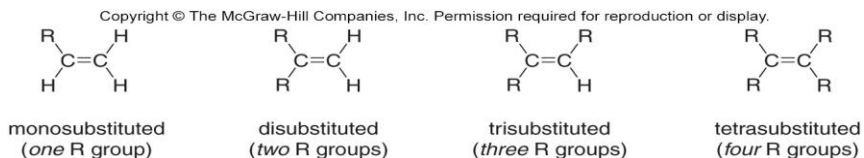
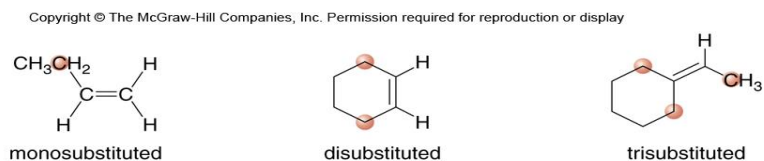


Figure 8.1



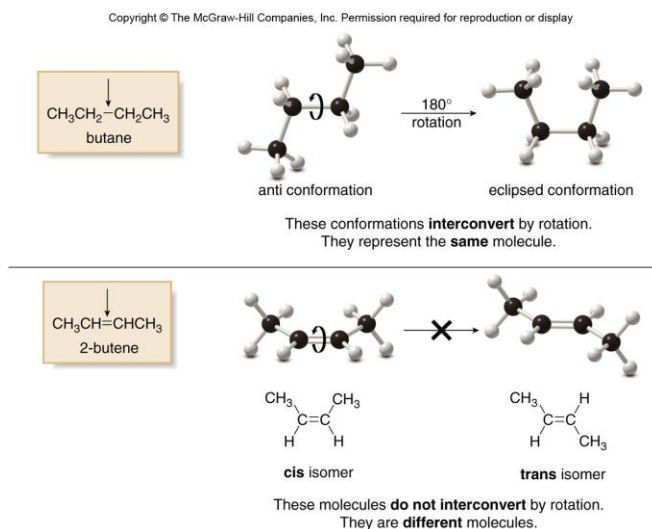
- Carbon atoms bonded to the double bond are screened in **red**.

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Restricted Rotation About Double Bonds

- Recall that even though there is free rotation around single bonds, **rotation about double bonds is restricted**.

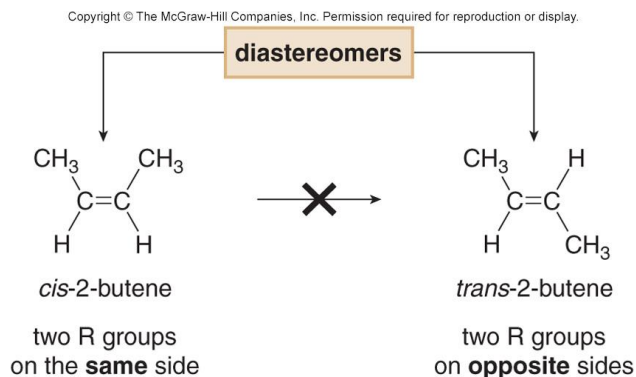
Figure 8.2



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Stereoisomers of Alkenes

- Because of restricted rotation, two stereoisomers of 2-butene are possible.
- **cis-2-Butene** and **trans-2-butene** are diastereomers (i.e., non-mirror image stereoisomers).



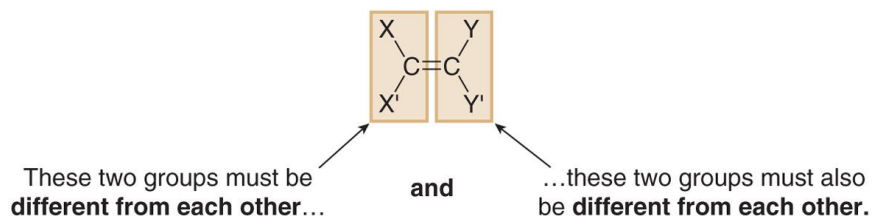
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Alkene Diastereomers

- Whenever the **two groups on each end** of a carbon-carbon double bond are different from each other, cis-trans isomers are possible.

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Stereoisomers on a C=C are possible when:

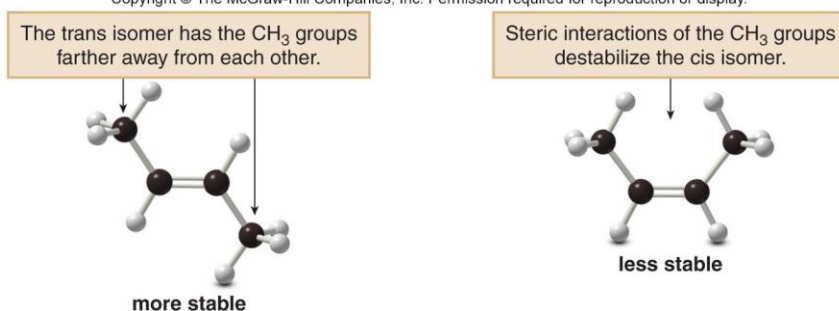


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Stability of Trans Alkenes

- In general, **trans alkenes are more stable** than cis alkenes because the groups bonded to the double bond carbons are further apart, reducing steric interactions.

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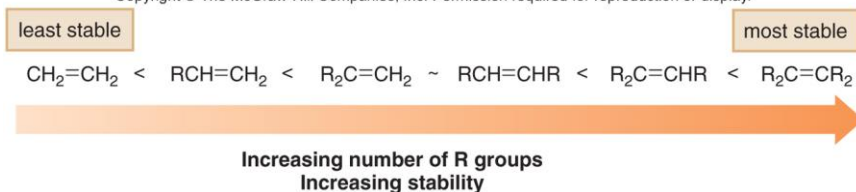


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Stability in Alkenes

- The stability of an alkene **increases as the number of R groups bonded to the double bond carbons increases**.

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Stability in Alkenes

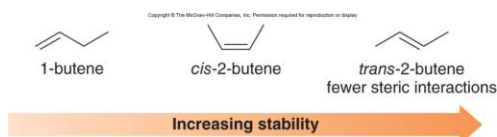
- The higher the **percent s-character**, the more readily an atom accepts electron density.
- Thus, **sp^2 carbons are more able to accept** electron density and **sp^3 carbons are more able to donate** electron density.
- Increasing the number of **electron donating groups** on a carbon atom able to accept electron density makes the alkene more stable.

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Stability in Alkenes

Example: Relative Stability of Butenes

- The 2-butenes (**disubstituted**) are more stable than 1-butene (**monosubstituted**).
- ***trans*-2-Butene** is more stable than ***cis*-2-butene** (less crowding).



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Elimination Mechanisms

- There are two mechanisms of elimination—**E2** and **E1**, just as there are two mechanisms of substitution, **S_N2** and **S_N1**.
- The **E2** mechanism is called **bimolecular elimination**.
- The **E1** mechanism is called **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.

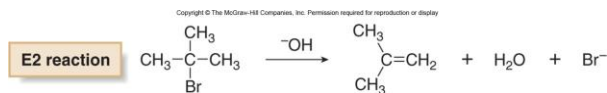
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E2 Mechanism

- 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.

$$\text{rate} = k[(\text{CH}_3)_3\text{CBr}][^-\text{OH}]$$

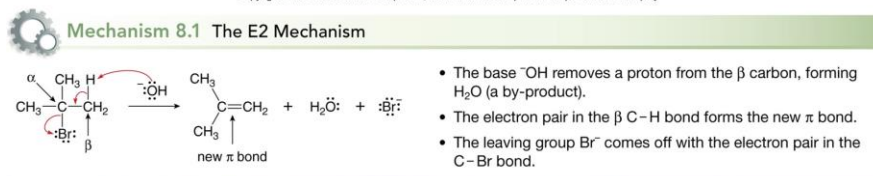
- The reaction is **concerted**—all bonds are broken and formed in a single step.



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E2 Mechanism

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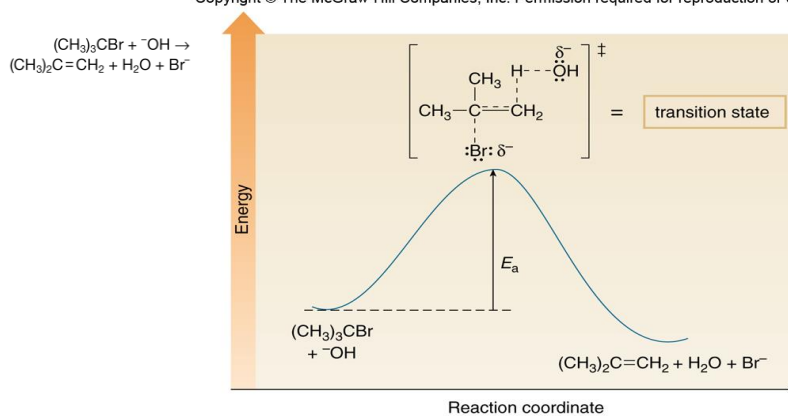
- There are close parallels between E2 and $\text{S}_{\text{N}}2$ mechanisms, the rate is affected by
 - the identity of the **base**
 - the **leaving group**
 - the **solvent**

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Energy Diagram for an E2 Reaction

Figure 8.3

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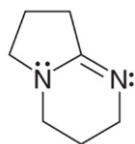
- In the transition state, the C-H and C-Br bonds are partially broken, the O-H and π bonds are partially formed, and both the base and the departing leaving group bear a partial negative charge.

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1. Bases in E2 Mechanisms

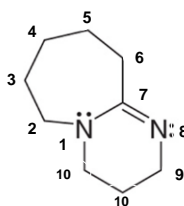
- E2 reactions are generally run with **strong**, negatively charged bases like OH^- and OR^- .
- The base appears in the rate equation, so the rate of the E2 reaction increases as the strength of the base increases.
- Two strong, sterically hindered nitrogen bases called **DBN** and **DBU** are also sometimes used.

Two useful bases for E2 reactions



DBN

1,5-Diazabicyclo(4.3.0)non-5-ene



DBU

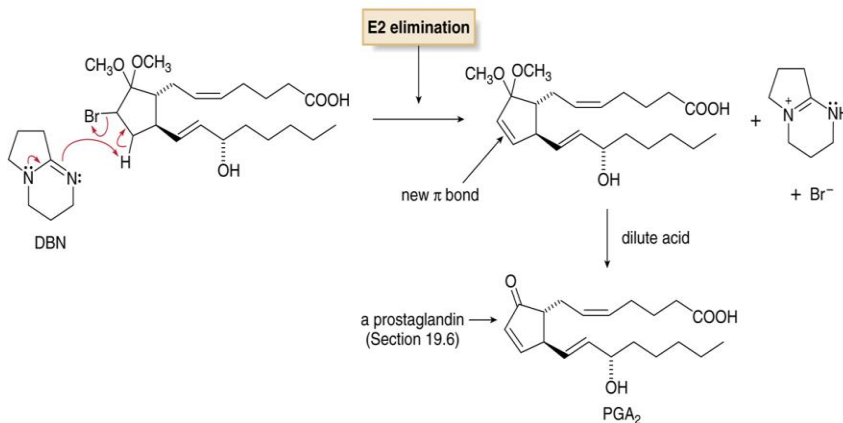
1,8-Diazabicyclo(5.4.0)undec-7-ene

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E2 Reaction with DBN

Figure 8.4

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2. Leaving Group

3. Solvent

- Because the bond to the leaving group is partially broken in the transition state, the **better the leaving group the faster the E2 reaction.**

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Order of reactivity
of RX:



Increasing leaving group ability
Increasing rate of the E2 reaction

- **Polar aprotic** solvents increase the rate of E2 reactions.

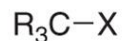
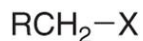
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4. Alkyl Halide Structure

- The **S_N2 and E2 mechanisms differ** in how the alkyl halide structure affects the reaction rate.
- As the number of **R groups increases** on the carbon with the leaving group, the rate of the **E2 reaction increases.**

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Increasing rate of an S_N2 reaction



1°

2°

3°

Increasing rate of an E2 reaction

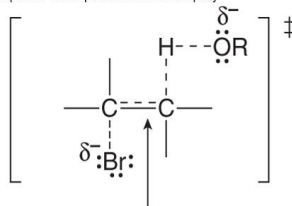
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Transition States in E2 Mechanisms

- 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.
 - This increases the **stability of the double bond** with alkyl substituents stabilizing the transition state (i.e., lowers E_a), which increases the rate of the reaction.

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Transition state for an E2 reaction with an alkoxide (OR^-) as base



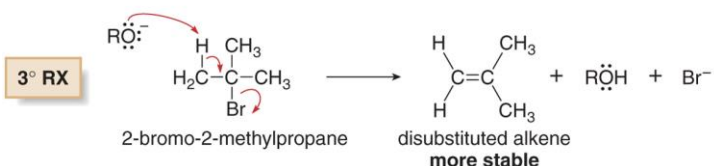
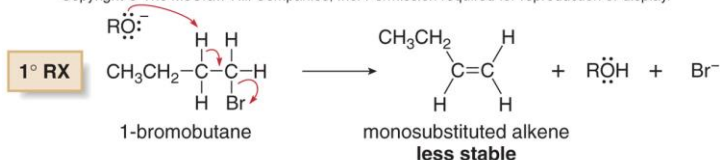
The double bond is partially formed.

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Product Stability and Rate of E2 Reactions

- Increasing the number of R groups** on the carbon with the leaving group forms more highly substituted, **more stable alkenes** in E2 reactions.
- In the reactions below, since the **disubstituted alkene is more stable**, the **3° alkyl halide reacts faster than the 1° alkyl halide**.

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E2 Mechanism Summary

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Table 8.2 Characteristics of the E2 Mechanism

Characteristic	Result
Kinetics	<ul style="list-style-type: none"> • Second order
Mechanism	<ul style="list-style-type: none"> • One step
Identity of R	<ul style="list-style-type: none"> • More substituted halides react faster. • Rate: $R_3CX > R_2CHX > RCH_2X$
Base	<ul style="list-style-type: none"> • Favored by strong bases
Leaving group	<ul style="list-style-type: none"> • Better leaving group \rightarrow faster reaction
Solvent	<ul style="list-style-type: none"> • Favored by polar aprotic solvents

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E2 Reaction in Organic Synthesis

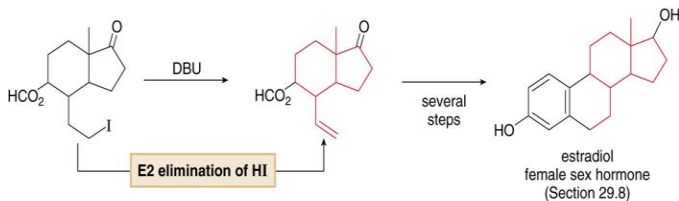
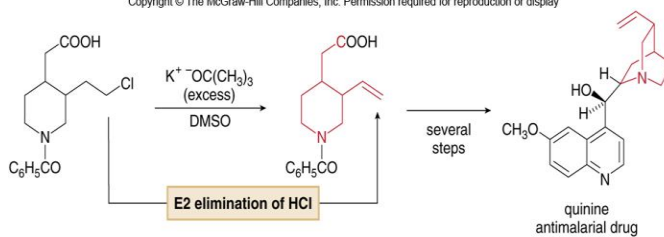
The synthesis of both quinine and estradiol involve an E2 elimination as a key step.

Figure 8.5

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Quinine, a natural product isolated from the bark of the cinchona tree native to the Andes Mountains, is a powerful antipyretic—that is, it reduces fever—and for centuries, it was the only effective treatment for malaria.

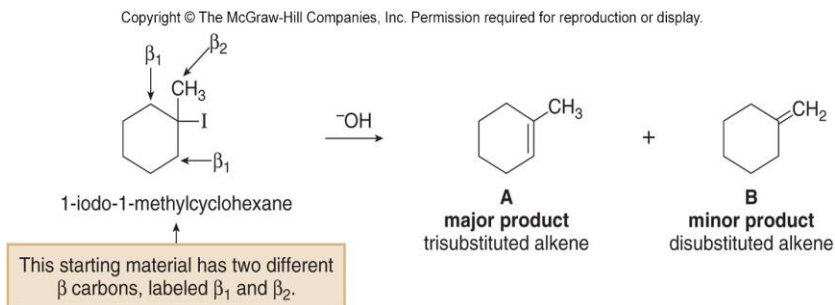


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Important in the regulation of the estrous and menstrual female reproductive cycles

The Zaitsev (Saytzeff) Rule

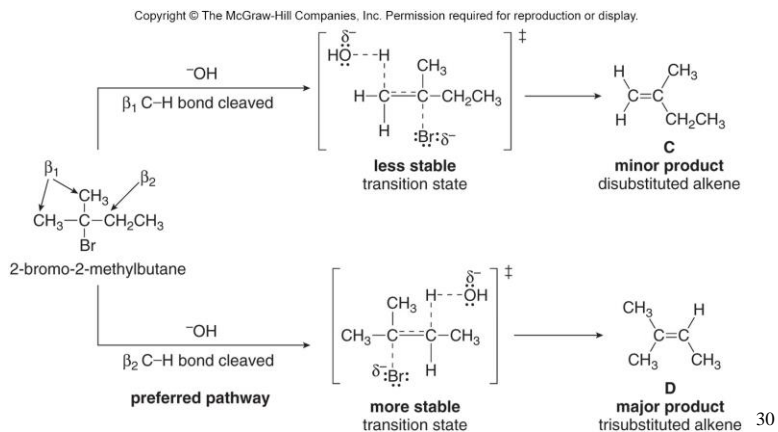
- When alkyl halides have **two or more different β carbons**, more than one alkene product can be formed.
- The Zaitsev rule predicts that the **major product** in β elimination has the **more substituted double bond**.
- This is the more stable alkene.



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Regioselectivity of E2 Reactions

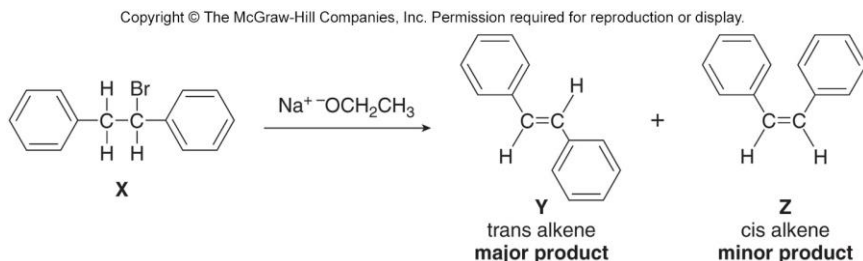
- A reaction is regioselective when it yields **predominantly or exclusively one constitutional isomer** when more than one is possible.
- Thus, the E2 reaction is regioselective.



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Stereoselectivity of E2 Reactions

- A reaction is **stereoselective** when it forms **predominantly or exclusively one stereoisomer** when two or more are possible.
- The E2 reaction is stereoselective because the more stable stereoisomer is formed preferentially.



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E1 Mechanism

- The dehydrohalogenation of (CH₃)₃CCl with H₂O to form (CH₃)₂C=CH₂ can be used to illustrate the second general mechanism of elimination, the E1 mechanism.
- An **E1 reaction** exhibits **first-order kinetics**:

$$\text{rate} = k[(\text{CH}_3)_3\text{CCl}]$$

- 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.

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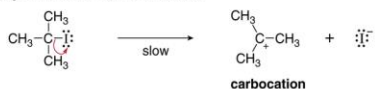
E1 Mechanism

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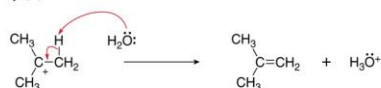
Mechanism 8.2 The E1 Mechanism

Step [1] The C-I bond is broken.



- **Heterolysis of the C-I bond** forms an intermediate **carbocation**. This is the same first step as the S_N1 mechanism. It is responsible for the first-order kinetics because it is rate-determining.

Step [2] A C-H bond is cleaved and the π bond is formed.



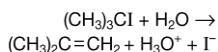
- A **base** (such as H₂O or I⁻) **removes a proton from a carbon adjacent to the carbocation** (a β carbon). The electron pair in the C-H bond is used to form the new π bond.

- In an **E2** reaction, the **leaving group** comes off **as** the β proton is removed, and the reaction occurs in one step.
- However, in an **E1**, the **leaving group** comes off **before** the β proton is removed, and the reaction occurs in two steps.

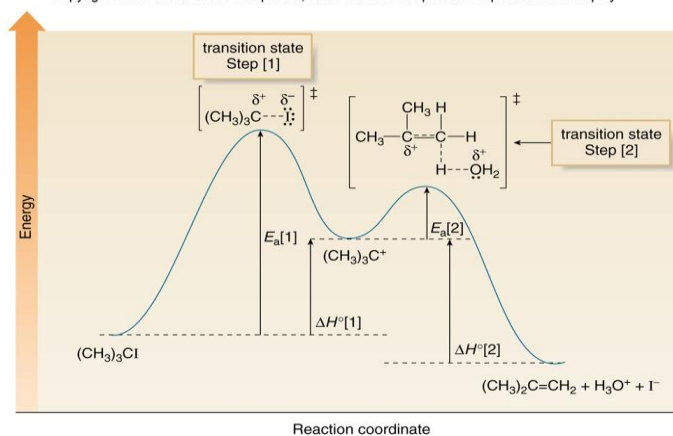
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Energy Diagram for an E1 Reaction

Figure 8.6



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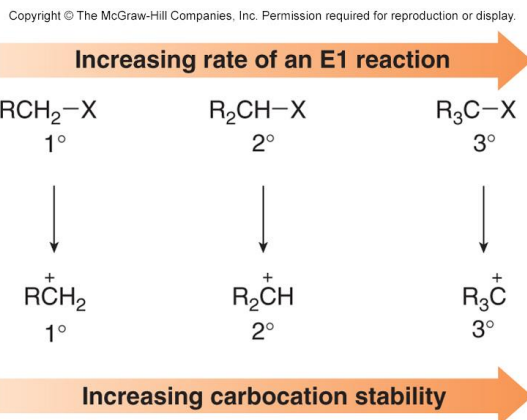


- Since the E1 mechanism has two steps, there are two energy barriers.
- Step [1] is rate-determining.

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1. Alkyl Halide Structure

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



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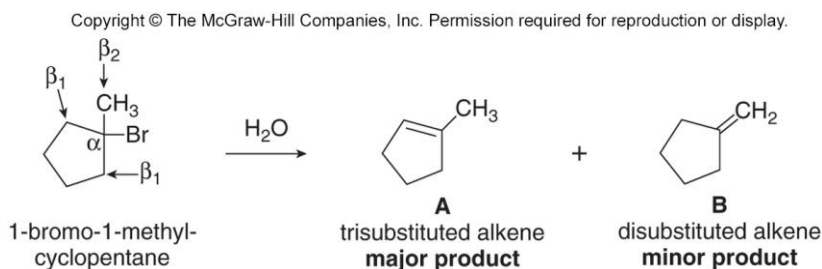
2. Base

- 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**.
 - **Weaker bases** like H_2O and ROH favor **E1 reactions**.

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Regioselectivity of E1 Reactions

- **Zaitsev's** rule applies to E1 reactions also.
- **E1 reactions** are **regioselective**, favoring formation of the more substituted, more stable alkene.



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E1 Mechanism Summary

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Table 8.3 Characteristics of the E1 Mechanism

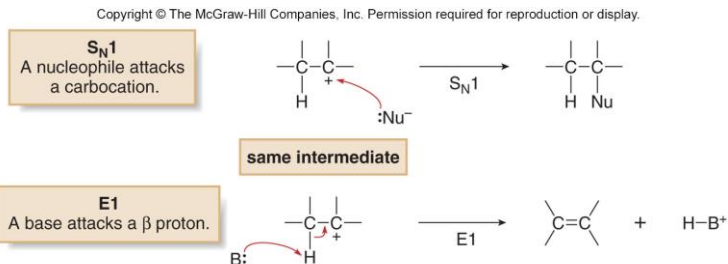
Characteristic	Result
Kinetics	• First order
Mechanism	• Two steps
Identity of R	• More substituted halides react faster. • Rate: R ₃ CX > R ₂ CHX > RCH ₂ X
Base	• Favored by weaker bases such as H ₂ O and ROH
Leaving group	• A better leaving group makes the reaction faster because the bond to the leaving group is partially broken in the rate-determining step.
Solvent	• Polar protic solvents that solvate the ionic intermediates are needed.

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

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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.

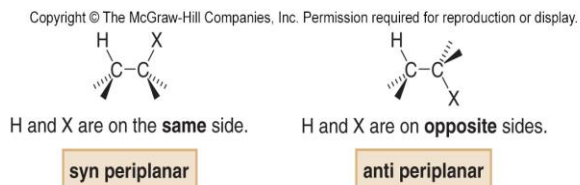


- In an S_N1 reaction, a nucleophile attacks the carbocation, forming a substitution product.
- In an E1 reaction, a base removes a proton, forming a new π bond.

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Stereochemistry of E2 Reactions

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



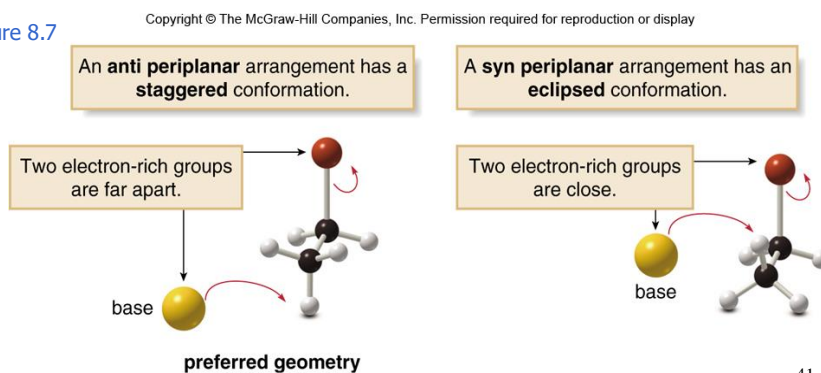
- The H and X atoms can be oriented on the same side of the molecule. This geometry is called *syn periplanar*.
- The H and X atoms can be oriented on opposite sides of the molecule. This geometry is called *anti periplanar*.

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Two Possible Geometries for E2 Reactions

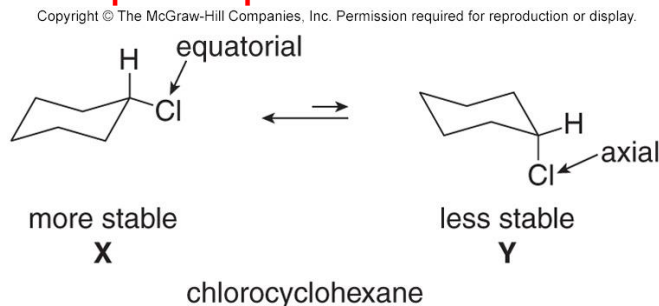
- E2 elimination occurs most often in the **anti periplanar geometry**.
- This arrangement allows the molecule to react in the **lower energy staggered conformation**, and allows the incoming base and leaving group to be further away from each other.

Figure 8.7



Anti Periplanar Geometry

- The requirement of anti periplanar geometry in an E2 reaction has **important consequences** for compounds containing six-membered rings.
 - Chlorocyclohexane exists as **two chair conformations**.
 - Conformation A is preferred since the bulkier Cl group is in the **equatorial position**.

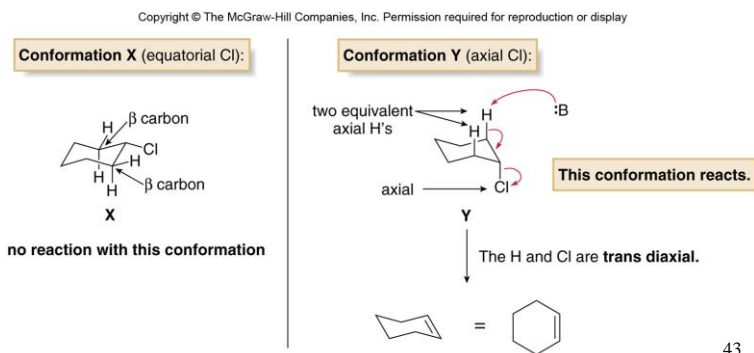


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Trans Diaxial Geometry for E2 Reactions

- 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, B**.

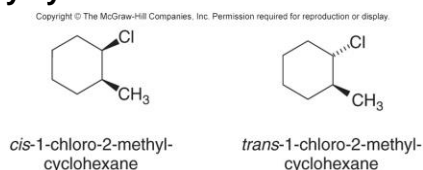
Figure 8.8



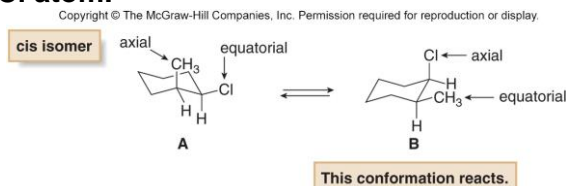
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E2 Reactions of Cis and Trans Isomers

- Consider the E2 dehydrohalogenation of *cis*- and *trans*-1-chloro-2-methylcyclohexane.



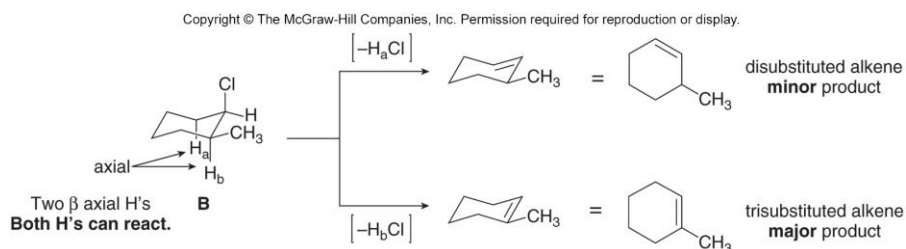
- The cis isomer:
- exists as two conformations, A and B, each of which has **one group axial and one group equatorial**.
- E2 reaction must occur from conformation B, which contains an axial Cl atom.



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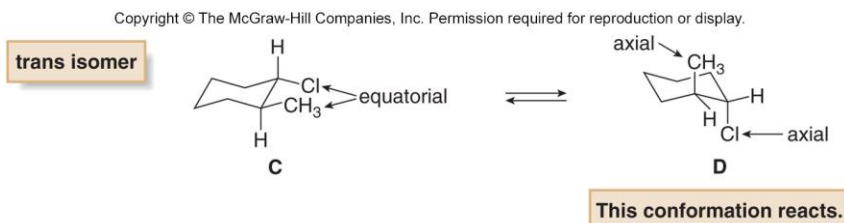
Regiochemistry of E2 Reactions on Cyclohexanes

- Because conformation B has two different axial β hydrogens, labeled H_a and H_b , E2 reaction occurs in two different directions to afford two alkenes.
- The major product contains the **more stable trisubstituted double bond**, as predicted by the Zaitsev rule.



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Axial Leaving Groups for E2 Reactions



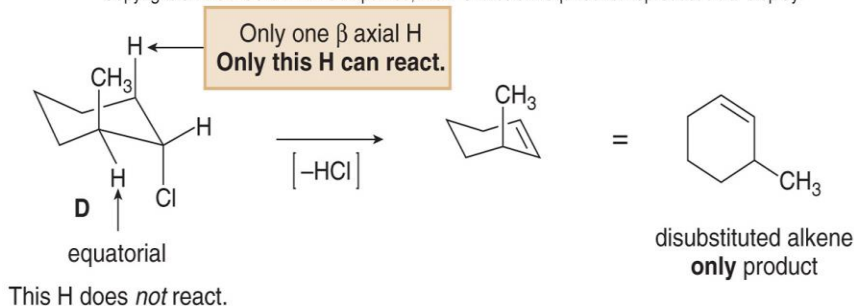
- The trans isomer (1-chloro-2-methylcyclohexane):
- exists as **two conformers**: C, having two equatorial substituents, and D, having two axial substituents.
- E2 reaction must occur from D, since it contains an axial Cl atom.

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Anti Zaitsev Products for E2 Reactions

- Because **conformer D** has only one axial β H, the E2 reaction occurs only in one direction to afford a single product.
- The most substituted, "**Zaitsev**" alkene is not the major product in this case.

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Comparison of E1 and E2 Mechanisms

- The strength of the base is the most important factor in determining the mechanism for elimination.

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Table 8.4 A Comparison of the E1 and E2 Mechanisms

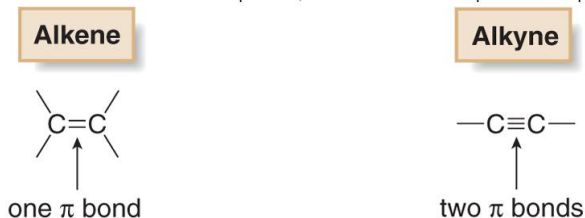
Mechanism	Comment
E2 mechanism	<ul style="list-style-type: none"> • Much more common and useful • Favored by strong, negatively charged bases, especially ^-OH and ^-OR • The reaction occurs with 1°, 2°, and 3° alkyl halides. Order of reactivity: $\text{R}_3\text{CX} > \text{R}_2\text{CHX} > \text{RCH}_2\text{X}$.
E1 mechanism	<ul style="list-style-type: none"> • Much less useful because a mixture of $\text{S}_{\text{N}}1$ and E1 products usually results • Favored by weaker, neutral bases, such as H_2O and ROH • This mechanism does not occur with 1° RX because they form highly unstable 1° carbocations.

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E2 Reactions and Alkyne Synthesis

- A single elimination reaction produces a π bond of an alkene.
- Two consecutive elimination reactions produce **two π bonds** of an alkyne.

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One elimination reaction is needed.

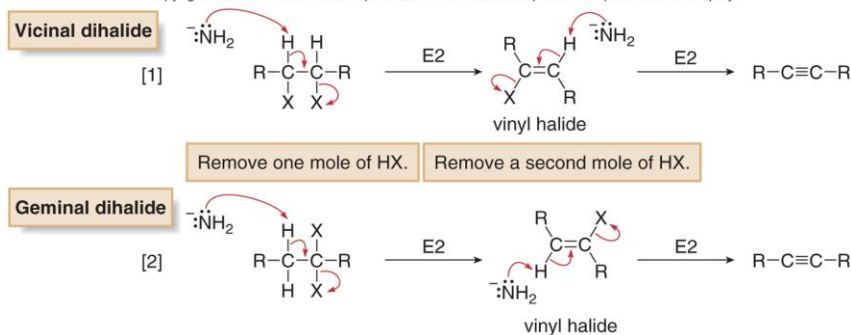
Two elimination reactions are needed.

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E2 Reactions and Alkyne Synthesis

- Two elimination reactions are needed to remove **two moles of HX** from a dihalide substrate.
- Two different starting materials can be used—a **vicinal dihalide** or a **geminal dihalide**.

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Bases for Alkyne Synthesis

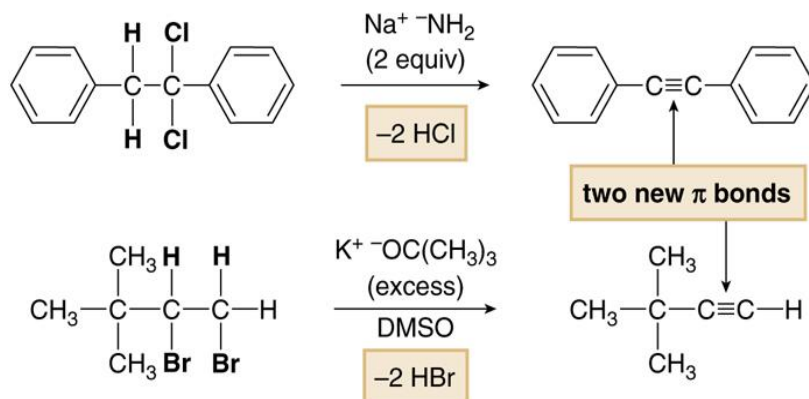
- **Stronger bases** are needed to synthesize alkynes by dehydrohalogenation than are needed to synthesize alkenes.
- The typical base used is NH_2^- (**amide**), used as NaNH_2 .
- **$\text{KOC}(\text{CH}_3)_3$** can also be used with DMSO as solvent.
- **Stronger bases** are needed to break the **stronger sp^2 hybridized C-H** bonds in the second elimination reaction.

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Dehydrohalogenation of Dihalides

Figure 8.9

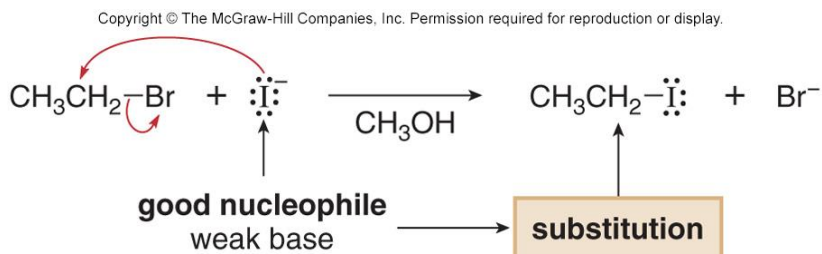
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When is the Reaction S_N1, S_N2, E1, or E2?

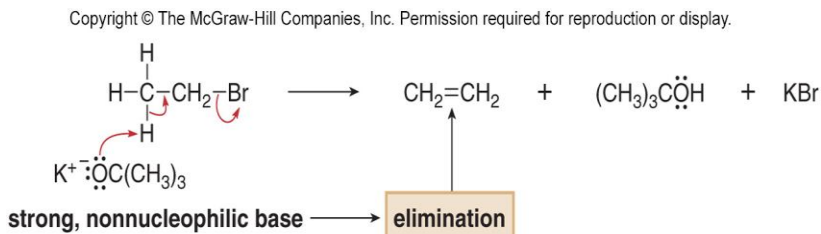
- **Good nucleophiles** that are **weak bases** favor substitution over elimination.
- These include I⁻, Br⁻, HS⁻, ⁻CN, and CH₃COO⁻.



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Bulky Bases Favor Elimination

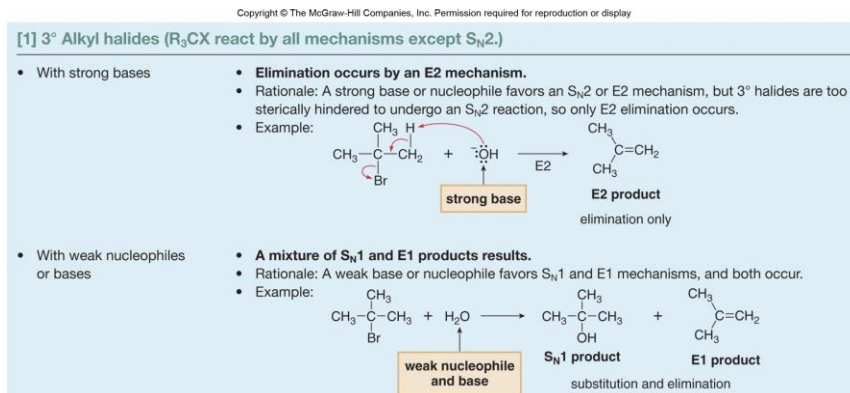
- **Bulky nonnucleophilic bases** favor elimination over substitution.
 - KOC(CH₃)₃, DBU, and DBN are too sterically hindered to attack tetravalent carbon.
- They are, however, able to remove a small proton, favoring elimination over substitution.



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Predicting Reaction Mechanisms (S_N1, S_N2, E1, or E2)

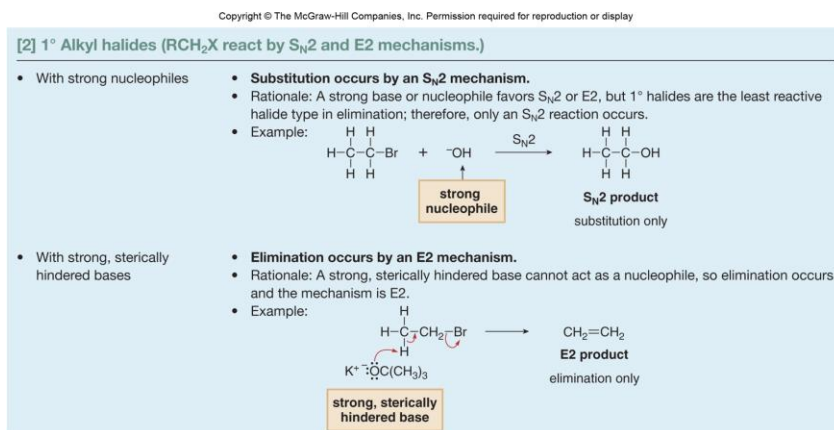
Figure 8.10



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Predicting Reaction Mechanisms (S_N1, S_N2, E1, or E2)

Figure 8.10 *continued*

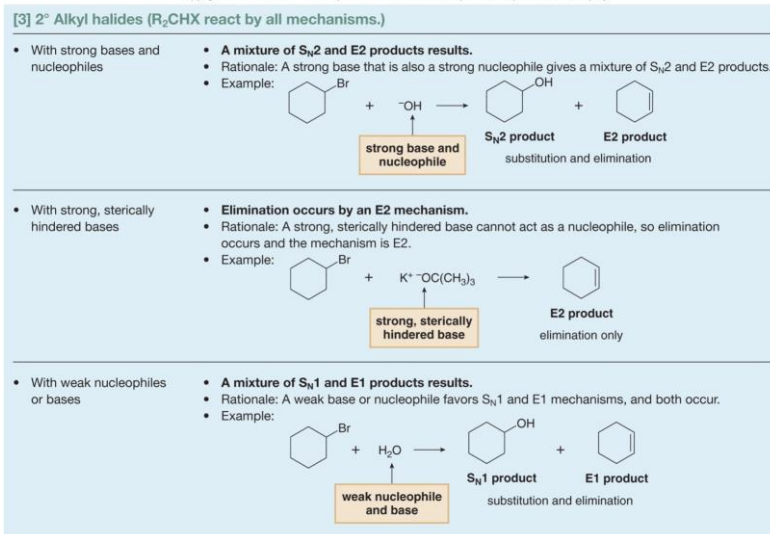


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Predicting Reaction Mechanisms (S_N1, S_N2, E1 or E2)

Figure 8.10 *continued*

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